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Impact of COVID-19 pandemics and syndemics on healthcare systems worldwide

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Impact of COVID-19 pandemics and syndemics on healthcare systems worldwide

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Editorial: Impact of COVID-19 pandemics and syndemics on healthcare systems worldwide

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COVID-19, infection, pandemics, children, pediatrics, healthcare system, diagnosis, treatment

Editorial on the Research Topic
Impact of COVID-19 pandemics and syndemics on healthcare systems worldwide

Infectious diseases have been the leading cause of death for ages. However, pandemics are cornerstones to overwhelm the countries' healthcare systems and institutional capacities, as seen in the plague in the medieval ages, Spanish flu Asian flu in 20th century, swine flu in 2009–10 and lastly, COVID-19.

The COVID-19 pandemic has altered almost every aspect of the world, including economics, social issues, health care, and politics. Many experts consider this phenomenon to be a "syndemic", as it is more than just an outbreak of a viral infectious disease.

The topic "Research Topic Impact of COVID-19 Pandemics and Syndemics on Healthcare Systems Worldwide" included sixteen articles addressing the effect of the COVID-19 pandemics on all of us. This Research Topic tried to cover issues related to the challenges of the pandemic disease on the human being and specifically pediatric healthcare, focusing on specific areas such as the prehospital system, emergency departments, ICUs, medical branches, preventive medicine, rehabilitation, sports medicine, and infection surveillance. This article collection evaluated studies on diagnosis and management of COVID-19 in children, COVID vaccination and related issues, geographical and socioeconomic inequalities of COVID-19 infection in children, and burden of COVID-19 in acute care worldwide.

The authorship of the articles represents the multcultural background taking care of the involved populations worldwide. This diversity comprises a great chance to enrich the discussion to create a fruitful guide to summarize viewpoints for most aspects of the pandemic era.

The work by Bermejo-Patón et al. "*The recovery and resilience plan on the long-term care system. Towards a deinstitutionalization?*" analyzed "Recovery and Resilience Plan (RRP)" to estimate the socioeconomic impact on Long-Term Care (LTC) in Spain, using the severe recession scenario triggered by COVID-19. They pointed out a substantial positive impact of RRP to mitigate the downturn in the Spanish economy following the pandemics.

The Turkish study "*Shedding light on the next pandemic path, from outpatient to ICU, the effect of vitamin D deficiency in the SARS-CoV-2 pandemic*" analyzed the role of

Vitamin D on unvaccinated adults and concluded that adequate levels of Vitamin D, glucose, urea, creatinine, leucocyte, aspartate transaminase, hemoglobin, C-reactive protein, troponin, platelet/thrombocyte, ferritin, D-dimer, triglycerate, glycated haemoglobin, lactate dehydrogenase are associated with decreased likelihood to be admitted to ICU.

The study from Nakata et al. on the "*Surgical productivity recovery after the COVID-19 pandemic in Japan*" analyzed a broad range of surgical procedures and reported that surgical productivity did not appear to be affected on the long term by the COVID-19 pandemic.

The work published by Hijano et al. analyzed case investigation and contact tracing as key strategies to stop transmission of COVID-19 in a single center. They concluded that prompt implementation of these strategies are feasible and have the potential to reduce viral spread in the workplace.

The findings of the study on "*Teachers as caregivers of grieving children in school in the post-COVID-19 era*" investigated teachers' needs on childhood bereavement amidst the COVID-19 pandemic may help promote policy changes that ensure teachers' needs satisfaction in the context of pediatric grief.

The population-based descriptive study "*outcome of emergency patients transported by ambulance during the COVID-19 pandemic in Osaka Prefecture, Japan*" focused on the impact of the pandemic era on patient outcome in the prehospital setting. The authors reported an alarming finding that pandemic disease reduced the rate of ambulance calls and worsened mortality of patients transported by ambulances in Osaka.

Yang et al. studied on "*Characteristics and spectrum changes of PICU cases during the COVID-19 pandemic*" using a retrospective design. The COVID-19 pandemic has exerted a certain influence on the disease spectrum of PICU admissions, indicating a need to prioritize the respiratory, neurological, and hematological oncology systems.

An economical viewpoint was brought to the scene by the study "*The impact of COVID-19 pandemic on the world's major economies: based on a multi-country and multi-sector CGE model*" and emphasized the advancement of global anti-epidemic policies targeting economic recovery.

A multinational study by the International Consortium of Primary Care Big Data Researchers (INTRePID) investigated the "*Changes in primary care visits for respiratory illness during the COVID-19 pandemic*" in primary care settings in nine countries. They highlighted the fact that COVID-19 pandemic had a major impact on primary care visits for respiratory presentations.

In a systematic review of the literature "*Impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services in low-and middle-income countries*" the authors reported disruption family planning services, antenatal and postnatal care coverage, and emergency and routine child services in the setting of the COVID-19 pandemic.

Zhao et al. performed a cost-effectiveness analysis from the perspective of Chinese healthcare system on influenza vaccination for heart failure patients: They suggested that adding the vaccine to standard regimens for Chinese patients with heart failure may represent a highly cost-effective option.

In an interesting multicenter cohort study, Zhang et al. analyzed the total joint arthroplasty (TJA) care patterns in China during the COVID-19 pandemic. They pointed out that patients undergoing TJA in China during the COVID-19 pandemic was associated with more severe preoperative conditions and decreased volume, costs, and readmission rates.

The study entitled "*Crucial and fragile: a multi-methods and multi-disciplinary study of cooperation in the aftermath of the COVID-19 pandemic*" by Rotondi et al. focused on the need for cooperation across nations, institutions, and individuals amidst pandemics. The work highlighted important aspects of cooperation during crises and paved the way for future explorations into cooperative decision-making.

Via a case study of COVID-19 in Taiyuan City, Guo et al. assessed "*the impact of vaccination and medical resource allocation on infectious disease outbreak management*". They focused on the rational allocation of vaccines and medical resources to mitigate the pandemic effects and concluded that an increased maximum capacity of medical resources, will prevent the congestion and stronger resource allocation capabilities will facilitate earlier relief within a fixed total resource pool.

Ritto et al. published a study entitled "*Data-driven, cross-disciplinary collaboration: lessons learned at the largest academic health center in Latin America during the COVID-19 pandemic*" and created a set of recommended strategies to enhance collaboration within the research institution.

In brief, we should all realize that COVID-19 is not the last pandemic. It is obvious that there will be new generations and our long years to spend with masks, sanitizers, and hand disinfectants. It is important in the long run to encourage vaccination and other preventive measures, along with determining high-risk groups to provide focused protection programs to them. This kind of approach and public health perspective will be the only recipe to protect hospitals and other health institutions from being overcrowded and overwhelmed by the disastrous situation.

Author contributions

OK: Conceptualization, Data curation, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing.

Conflict of interest

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Employee investigation and contact tracing program in a pediatric cancer hospital to mitigate the spread of COVID-19 among the workforce, patients, and caregivers

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Background: Case investigations and contact tracing are essential disease control measures used by health departments. Early in the pandemic, they were seen as a key strategy to stop COVID-19 spread. The CDC urged rapid action to scale up and train a large workforce and collaborate across public and private agencies to halt COVID-19 transmission.

Methods: We developed a program for case investigation and contact tracing that followed CDC and local health guidelines, compliant with the Occupational Safety and Health Administration (OSHA) regulations and tailored to the needs and resources of our institution. Program staff were trained and assessed for competency before joining the program.

Results: From March 2020 to May 2021, we performed 838 COVID-19 case investigations, which led to 136 contacts. Most employees reported a known SARS-CoV-2 exposure from the community ($n = 435$) or household ($n = 343$). Only seven (5.1%) employees were determined as more likely than not to have SARS-CoV-2 infection related to workplace exposure, and when so, lapses in following the masking recommendations were identified. Between June 2021–February 2022, our program adjusted to the demand of the different waves, particularly omicron, by significantly reducing the amount of data collected. No transmission from employees to patients or caregivers was observed during this period.

Conclusion: Prompt implementation of case investigation and contact tracing is possible, and it effectively reduces workplace exposures. This approach can be adapted to suit the specific needs and requirements of various healthcare settings, particularly those serving the most vulnerable patient populations.

KEYWORDS

SARS-CoV-2, COVID-19, healthcare, healthcare personnel, occupational health, contact tracing, mitigation

Introduction

Case investigation, contact tracing, isolation, and quarantine are traditional control measures used to limit the spread of infectious agents (1–5). The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) recommended scaling up and training a large workforce to collaborate across public and private agencies to isolate infectious cases and ensure contacts self-isolate to stop SARS-CoV-2 transmission (6, 7).

Contact tracing success depends on a well-trained workforce with sufficient resources to act quickly (8, 9). Contact tracing can be done in several ways. Forward-tracing protocols seek to identify and isolate individuals who may have been infected by the known case, preventing continued transmission through quarantine of contacts. In contrast, backward tracing backward contact tracing (BCT) is a method of contact tracing which aims to find primary or source cases and other cases that are linked to that source can be applied when a case does not know where the illness may have been acquired. It can aid in finding clusters and could reduce the size of superspreading events (10–12). Combining both strategies, hybrid or bidirectional contact tracing has been shown to have greater potential at mitigating spread of SARS-CoV-2 (13). The CDC outlined training, team components, and performance metrics to evaluate and enhance the process (7, 8). Real data and modelling have been used to assess the role of these metrics in curbing SARS-CoV-2 transmission in communities, healthcare facilities, nursing homes, and schools, and their effect on preventing hospitalizations and deaths as well as to monitor and contain cases as restrictions eased (14–24).

The role of asymptomatic infection in viral spread was recognized early in the pandemic, leading to multi-faceted that included testing of asymptomatic individuals. Expanding testing of close contacts enabled detection of a large burden of asymptomatic infection, and allowed for isolation of infected individuals at an early stage, interrupting viral transmission (25). Widespread low viral load of SARS-CoV-2 was shown by Vimercati et al. among asymptomatic hospital workers (26). As availability of testing increased, its use to decrease post-quarantine transmission and shortened the quarantine period was implemented (27). With these tools and knowledge, some countries aimed to mitigate SARS-CoV-2, often referred as "flattening the curve," while eithers sought to eliminate the virus, an approach known as "zero COVID-19 strategy" (28–31). The focus of the latter was on eliminating the spread of the virus through the implementation of strict public health measures, followed by a phase of containment during which economic and social activities were allowed to resume while public health measures were employed to prevent any new outbreaks from spreading widely (32). Governments that decided to utilized all means possible, from closing schools and shops, to implementing strict lockdowns or even culling animals deemed to carry the virus, in order to get the cases down to zero have fared better than countries that opted for mitigation, while it effects on the economy and civic liberties has remained a topic of discussion (28, 29). However, as more contagious variants of concern, such as delta and omicron, spread quickly, the zero COVID-19 strategy, along case investigation and contact tracing in the community became difficult for public health agencies, and many countries phased-out from these. The CDC suggested jurisdictions prioritize case investigation and contact tracing based on vulnerability, congregate settings, workplaces, and healthcare facilities, including long-term care facilities and prisons (6–8).

The impact of vaccination in preventing severe disease and mitigating overall spread of SARS-CoV-2 has been well documented (33). Higher rates of vaccination have been associated with decrease community transmission, COVID-19 associated hospitalization, and deaths (34–36). In addition, vaccination of healthcare workers was shown to be critical in mitigating nosocomial spread of SARS-CoV-2 (37, 38). Currently, a new generation of monovalent vaccines targeting an XBB.1.5, a subgroup of omicron, have been deployed and recommended (39–41). However, inequities in vaccine access and low uptake remain as key challenges in mitigating SASR-CoV-2 (42–44), which continues to continue to evolve and circulate, causing waves of infection worldwide. Most of the current variants are within the sub-omicron lineage (45). Due to high population-level immunity, there is a dissociation between number of cases and hospitalizations with older adults, those with co-morbidities, and/or who are not up to date with COVID-19 vaccinations represent most individuals needing hospitalization (46).

Here, we discuss the features and effectiveness of a COVID-19 case investigation and bidirectional contact tracing program to reduce SARS-CoV-2 transmission among healthcare workers and patients in a high-risk institution.

Methods

Setting

St. Jude Children's Research Hospital (St. Jude) in Memphis, TN specializes in caring for immunocompromised children at risk of severe COVID-19. St. Jude treats children from all 50 states and from around the world. About 8,600 patients are seen at St. Jude annually, most of whom are treated on a continuing outpatient basis. The hospital has 77 beds for patients requiring hospitalization during treatment. Most of our patients are treated as outpatients and stay in one of our housing facilities with rooms specifically designed and managed by us for families of children with cancer and other diseases. St. Jude currently has over 5,000 employees. During the pandemic, the government implemented lockdowns, school, restaurant and bar closures, and mask mandates. St. Jude created a COVID-19 mitigation program to protect patients and staff. It includes controlled access, ventilation, masking, distancing, symptom screening, asymptomatic testing, off-campus testing for symptomatic cases, vaccination, case investigation, and contact tracing (37). The COVID-19 program assessment described herein was deemed exempt research by St Jude's institutional review board with a waiver of informed consent.

COVID-19 case investigation and contact tracing team

Hospital employees were invited to volunteer part of their time ad-honorem to assist the institution by performing case investigation and contact tracing. All participants were healthcare providers (nurses, advanced practice providers, or physicians) who expressed interest and had time every week to participate. All volunteers underwent competency training for COVID-19 case investigation and contact tracing. This included understanding patient confidentiality and privacy, medical terms and principles of exposure, infection, and symptoms, as well as interpersonal, cultural sensitivity, and interviewing skills. All team members completed: (1) online training by The Association of State and Territorial Health Officials (ASTHO) and National Coalition of STD Directors (NCSD) recommended by and developed with the CDC's input (9), and (2) interactive training with processes specific to our institution and local public health authority. A total of 20 employees participated of this program (eight physicians; one advanced practice provider, and 11 nurses, five of whom were occupational health nurses).

A Case Investigation & Contact Tracing Lead coordinated schedules provided updates to institutional leadership (e.g., successful cases contacted, referred services), monitored calls, and reviewed documentation of data obtained for quality assurance. A case investigator (usually a physician or advanced practice provider) and contact tracer (usually a nurse) called employees who had a SARS-CoV-2 test positive, explained the need for isolation, and gathered information about work-related contacts who may have been exposed. The contact tracer then notified the identified contacts of their exposure, explained the need for self-quarantine, and monitored for symptoms while providing additional resources and support services. The team managed case monitoring, follow-up, and testing. While an investigator and tracer conducted majority of the initial interviews, all members were trained to do any role if needed and over the course of pandemic, the occupational health nurses served both as case investigators and contact tracers.

SARS-CoV-2 testing

Starting March 25, 2020, mandatory mid-turbinate nasal swab samples were collected from all asymptomatic on-campus personnel (irrespective of their role) every 4–7 days and tested for SARS-CoV-2 RNA. Frequency of testing was higher for those who had frequent contact with patients. Sample collection was done at a central, accessible spot-on campus. A drive-through SARS-CoV-2 testing station was created for employees with COVID-19 symptoms. All samples collected by St. Jude staff were tested by PCR at St. Jude laboratories. Testing was performed using one of three test systems: the NeuMoDx™ SARS-CoV-2 Assay (Qiagen, Hilden, Germany), the Roche Cobas6800/8800 assay (Roche Diagnostics, Risch-Rotkreuz, Switzerland), or the altona RealStar® SARS-COV-2 RT-PCR assay (altona Diagnostics, Hamburg, Germany), each of which had received emergency use authorization (EUA) by the US Food and Drug Administration (US FDA). All three methods had also undergone validation by the St. Jude Clinical COVID Laboratory and been shown to perform as expected, with comparable accuracy across all systems (37). Results were reported within 2–24 h and triggered case investigation and contact tracing. Occupational Health followed up with SARS-CoV-2 positive employees weekly until they met CDC criteria to return to work. Employees who tested positive at community labs or primary care providers were asked to report it to Occupational Health for contact tracing.

Description of the program

Employees with lab-confirmed SARS-CoV-2 were considered infectious from 2 days before symptoms (or positive SARS-CoV-2 if asymptomatic) until the end of isolation. Cases were monitored weekly until they could return to work. Employees who were within 6 feet from a case for 15 min or more cumulative within 24 h without a mask on the St. Jude campus during the infectious period were considered work-related contacts and notified immediately about potential exposure. Employees meeting the exposure definition in the community or household were classified as community and household contacts, respectively. All contacts were quarantined and monitored weekly for 14 days. Employees with a household exposure, who could not separate from the member infected with SARS-CoV-2, were monitored for longer period, as their quarantine would start when the case completed isolation. Employees on quarantine were tested 5–7 days after exposure, and/or with any new symptoms (forward tracing). All employees with SARS-CoV-2 infection were asked about known potential exposure on and off campus, as well as high-risk activities that could have led to acquiring COVID-19, to determinate the source of transmission. If exposure was unknown, investigations of cases within same working group, department, and physical location on campus were analyzed to identify a potential common source (backward tracing).

The Case Investigation & Contact Tracing Lead presented the investigation results to a panel of five physicians, four of whom were infectious diseases specialists, to decide if work-related transmission occurred. In the presence of community-based COVID-19 transmission, a workplace exposure was assumed if the case investigation suggested it was more likely than a community-based exposure. Isolation and quarantine procedures were adjusted based on the evolving CDC recommendations over the course of the pandemic (47, 48).

During the omicron wave in the US (November 2021 – February 2022), we scaled up our program without compromising employee and patient safety by: (1) recruiting more volunteers for phone triage and non-medical tasks, (2) making data collection lean by removing collection of all variables that were not critical to reporting or follow-up of the investigations, (3) using emails to report negative SARS-CoV-2 tests, (4) creating a secure live log of new SARS-CoV-2 infections, and (5) reviewing the log and extending contact tracing hours. While we make some references to observations during the omicron wave, the overall data collection during this period was reduced to what was assessed as critical to case investigation and contact tracing and is not reported in this manuscript.

Performance evaluation of the program

Based on the CDC proposed criteria to assess a case investigation and contact tracing program's performance, our program's metrics included: (1) case interviewing: time to interview from diagnosis/, time to interview from notification of positive test, time from symptom onset, time to finish investigation; (2) contact notification: contacts elicited/monitored, proportion notified, time from identification to notification; (3) contact follow-up: proportion evaluated at 7 and 14 days, proportion with symptoms evaluated within 24 h, proportion who completed self-monitoring; (4) contact tracing efficacy: percentage of new COVID-19 cases among contacts during self-monitoring.

Data capture

The Clinical Research Systems team and Occupational Health collaborated on an internal project using the web-based REDCap® application. Separate forms for case investigations, contact tracing, and follow-up were created and updated based on CDC COVID-19 guidelines. The Alerts and Notifications module in REDCap® was used to send email notifications to Occupational Health when forms were completed by contact tracers or criteria were met for case and contact follow-up. Microsoft Power BI (Microsoft, Redmond, WA) was used to create reports for tracking visits, follow-ups, contact tracing, cases, and incomplete forms. Reports were tailored to meet the local Shelby County Health Department reporting requirements. The sharing of individual identifiers was kept on a need-to-know basis and to meet the local health department reporting requirements.

Statistical analysis

Demographic and clinical data were collected and presented as frequency (%) for categorical and median (range) for continuous variables. Chi-square, Fisher's exact, Student's t-test, or Wilcoxon rank-sum tests were used for group comparisons. A 2-sided $p < 0.05$ was considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC) and R 4.2.0 (R Core Team, 2020; R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria).

Results

Cases with SARS-CoV-2 infection

From March 19, 2020, to May 31, 2021, the program identified 914 potential exposures (778 outside the hospital campus, and 136 on campus). From these contacts, 136 employees proceeded to testing positive for SARS-CoV-2 infection during the quarantine period and were then designated as COVID-19 cases. In addition, the program identified 702 employees with SARS-CoV-2 infection for a total of 838 employees COVID-19 cases (Figure 1). Demographic information was available for 670 employees (79.95%; Table 1).

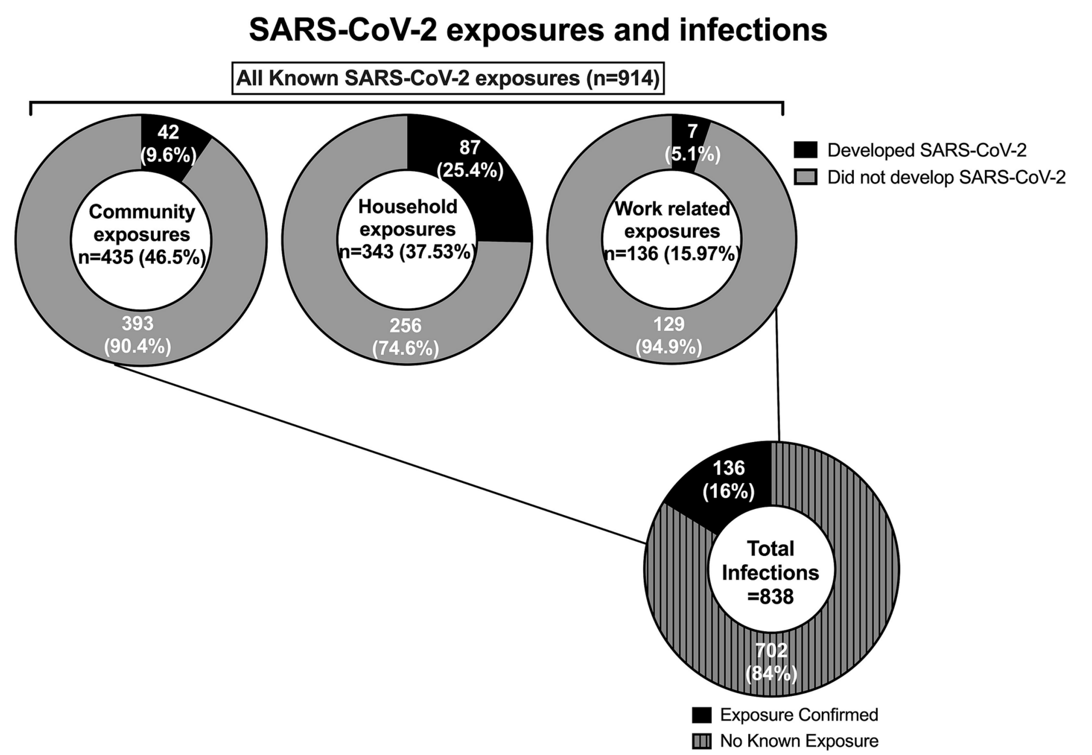

FIGURE 1
SARS-CoV-2 exposures (contacts) and infections (cases) reported to Occupational Health.

TABLE 1 Demographic information and job type of employees with SARS-CoV-2 infection.

	COVID-19 cases	
	n	%
Gender		
Female	468	69.85%
Male	202	30.15%
Age Range (years)		
18–24	28	4.18%
24–34	196	29.25%
35–44	179	26.72%
45–54	149	22.24%
55–64	107	15.97%
65+	11	1.64%
Ethnicity		
Hispanic/Latino	31	4.63%
Non-Hispanic/Latino	639	95.37%
Race		
African American	244	36.42%
Amer Indian/Alaska Native	0	0.00%
Asian	25	3.73%
Caucasian/White	360	53.73%
Native Hawaiian/Pacific Island	0	0.00%
Two or more races	10	1.49%
Other	31	4.63%
Direct Patient care		
Yes	487	72.69%
No	183	27.31%
Job category		
Advanced Practice	15	2.24%
Nursing	126	18.81%
Physician	13	1.94%
Purple	169	25.22%

The median number of monthly employee cases was 31 (8–201; Figure 2).

Of the 422 cases (50.42%) detected through the institutional asymptomatic routine testing program, 196 (56.44%) were symptomatic at diagnosis, 67 (15.88%) developed symptoms later, and 159 (37.68%) stayed asymptomatic until release from isolation. The median time between diagnosis and symptom onset was 1 (0–7) days for those with symptoms at interview and 3 (0–14) days for those who developed symptoms post-interview. A total of 378 (45.11%) cases were diagnosed because of the presence of symptoms and had no known exposure, including 212 (56.1%) employees at the St. Jude drive through testing station and 166 (43.9%) employees in other community testing centers. Thirty-eight employees (4.47%) were diagnosed following a known COVID-19 exposure [29 (76.32%) household contacts and nine in the community]. Seventeen of these were asymptomatic and never developed symptoms, 13 were pre-symptomatic, and eight were already symptomatic at the time of testing. Eight employees were reinfected during this period. The median number of days between episodes was 91 (26–300 days).

In this cohort, COVID-19 was mostly mild with low rates of hospitalization and complications. Only 25 employees (2.97%) developed pneumonia, and 22 (2.62%) had COVID-19 related hospitalization. Three cases (0.36%) required intensive care unit admission, and one (0.12%) mechanical ventilation. No deaths occurred during this period.

Before July 30, 2020, employees were required to have two SARS-CoV-2 negative tests before discontinuing their isolation. The median number of days from symptom onset to first negative test was 22 (14–41) days. On July 31, 2020, following CDC recommendations, the test-based approach was discontinued and replaced with a time-based approach, and the median number of days for isolation was reduced to 13 (13–15) days. These COVID-19 related isolation policies prompted a total of 12,392 days of recommended home-based isolation for our employees.

Contacts (employees with a known SARS-CoV-2 exposure)

914 contacts were interviewed during the study. Most (46.5%) contacts had a known COVID-19 community exposure followed by household exposure (37.53%) and work-related exposure (15.97%). We implemented universal masking 2 months after the first employee tested positive for SARS-CoV-2. This masking rule applied to everyone entering our campus irrespective of their role (employee, patient, caregiver, visitor, vendor, contractor). During this period, a shelter at home advisement for the community was established by the local public health authority, 73 out of 75 contacts were from workplace exposures, and were due to lapses in mask use and/or physical distance. As a result of routine testing, universal masking, and prompt initiation of isolation precautions when providing care to patients suspected or confirmed to have SARS-CoV-2 infections, no employee contacts resulted from exposure to patients and their caregivers. Universal masking markedly decreased the number of workplace exposures. After the initial months, most COVID-19 exposures reported by employees were from the community or home (Figure 3). Following the evolving recommendations for quarantine, the reported cohort of contacts spent a median of 14 days in quarantine following exposure to SARS-CoV-2. A total of 6,904 days were spent in home quarantine by employees with known exposure to SARS-CoV-2 who were not involved in direct patient care. In contrast, healthcare workers with direct patient care could return to work if they were asymptomatic, performed daily symptom screens, always wore masks while on campus, and underwent weekly SARS-CoV-2 testing. These employees were followed for a total of 4,439 days during the study period.

Program performance

Case interviewing

More than 98% of the case investigations were initiated within 24 h of diagnosis. The median time from diagnosis to starting the interview was 0.37 h (0–24 h). When assessing the time to interview

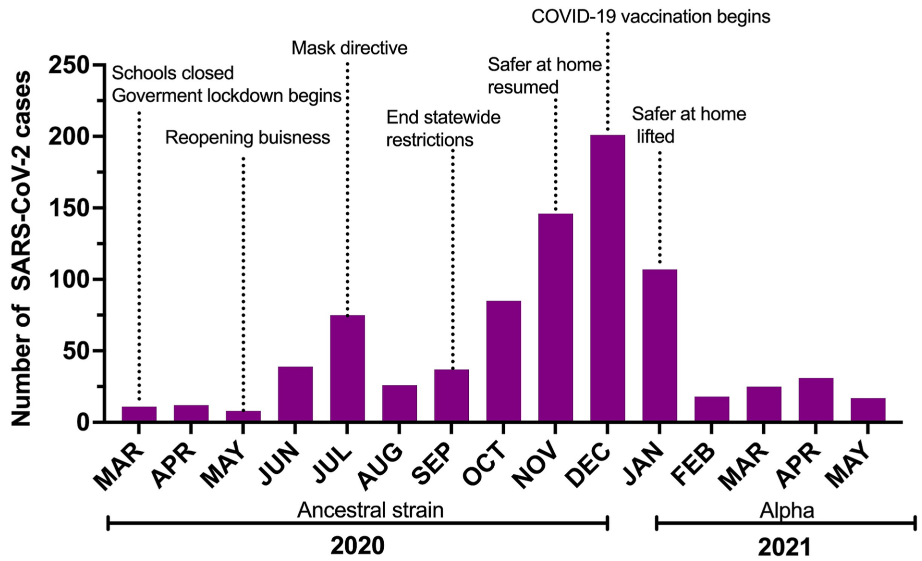

FIGURE 2
Number of SARS-CoV-2 cases reported to Occupational Health over the study period with a timeline of risk-mitigation directives and COVID-19 vaccine roll-out in Shelby County. Safer at home reflects lockdown issued by the local government.

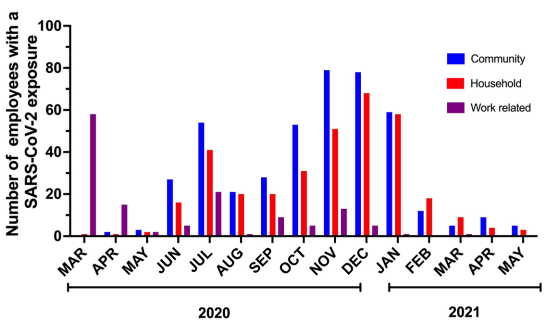

FIGURE 3
Number and type of SARS-CoV-2 exposures in employees over the study period.

from the onset of symptoms, 58.77% reported 2 days of symptoms prior to the interview, while the rest had developed symptoms within 24 h prior to or were asymptomatic at the time of the interview. Over 97% of the interviews were completed within than 24 h from notification of diagnosis (0 days; 0–1 days).

Contact notifications and follow-up

All 136 workplace contacts identified during the case investigations were notified within 24 h after identification. The median time from potential SARS-CoV-2 exposure to contact notification was 2 days (0–4 days). All 914 contacts were followed during the quarantine period, with phone interviews 7 days and 14 days after exposure required for release from quarantine. 270 contacts experienced symptoms after exposure, 136 of whom were subsequently diagnosed with SARS-CoV-2 infection. Most contacts were already symptomatic at the time of notification of the exposure; 89 others (32.96%) reported symptoms during the follow-up period. Among all symptomatic contacts, 95.2% underwent SARS-CoV-2 testing, with 136 testing positive and being then designated as cases.

Contact tracing efficacy

A total of 136 (16.22%) employees who developed SARS-CoV-2 infection had a confirmed exposure. Seven (5.1%) employees were deemed more likely to have acquired COVID-19 in the workplace than the community, compared to 42 (30.9%) and 87 (64%) of those with community or household exposure, respectively. The seven employees who acquired SARS-CoV-2 from work-related exposure resulted from six different exposure events involving 17 employees. Exposure events involved sharing a workspace or equipment, and/or eating within six feet, with none of the employees wearing masks. All these events occurred before SARS-CoV-2 vaccines became available. No transmission from employees to patients or their caregivers, and no transmission from patients to employees occurred.

Discussion

We detailed a successful COVID-19 case investigation and contact tracing program in a high-risk setting that reduced SARS-CoV-2 spread.

Daily monitoring of close contacts of cases can lead to faster diagnosis of suspected cases (49). In fact, rapid case detection (median time: 1 day) and contact tracing were shown to reduce virus spread (20). We noticed that tracking employees with known exposure and testing them quickly identified COVID-19 cases and enabled isolation, limiting exposure to others. Employees who tested positive for COVID-19 or had a known exposure were promptly contacted and instructed to leave the workplace immediately and not return until cleared by the company's occupational health department.." These notifications were made within hours, so employees who posed a risk of spreading SARS-CoV-2 spent little to no time on campus which was critical to avoid staff shortages and hospital-acquired SARS-CoV-2 (50–54). We show that a program using existing resources in healthcare settings can investigate COVID-19 cases and complete contact tracing within 24 h, mostly in a few hours. This program, combined with PCR testing for asymptomatic healthcare staff, can reduce workplace transmission to staff and patients, especially in facilities that care for immunocompromised or at-risk patients. Despite the omicron wave's rapid rise in cases, no work-related COVID-19 cases occurred, and normal operations continued due to prioritizing healthcare workers' return to work.

Case investigation and contact tracing have been essential to reduce COVID-19 transmission, especially when testing and vaccines were unavailable (55, 56). Many groups and models have reported its effectiveness, but others have found it ineffective when used alone or when the reproductive number is greater than 2.5 (21, 24, 57). Technology-based digital apps have been used to supplement or replace contact tracing in high transmission settings (58–60). We used technology to record, report, monitor, and release COVID-19-infected and exposed employees, which allowed as to adapt and sustain our program during the Omicron wave, but never implemented a digital contact tracing app. We considered this option, but security, effectiveness, ethical, and legal issues have been raised (61). Technology can meet regulatory and medical needs, and reports can monitor pandemics and inform leaders. Whether tech-based tools help or replace traditional case investigation and contact tracing is uncertain. Thus, traditional approaches such as the one described remain important.

We reflect on a few limitations of the work we describe. Traditional contact tracing, as we describe, is subject to recall bias of cases and the case investigator's history-gathering skills. Given the multiple institutional and local interventions that have been implemented during the pandemic, including universal masking and the COVID-19 vaccine mandate, it is difficult to isolate the impact of the case investigation and contact tracing program on its own. Therefore, its value must be evaluated in the context of existing literature that supports this approach. Strengths of the study include using observed data instead of predictive modelling to show the program's results in high-risk settings, evaluating the program's performance with CDC metrics, and reporting clinically meaningful outcomes. In addition, we showed that adaptability to periods of high community transmission, such as making data collection leaner, increasing the workforce, and/or using secured email for communications, is feasible to mitigate viral spread in the workplace.

With each COVID-19 wave, viral evolution, shortening of the incubation period, as well as the type of symptoms, were important challenges that led to changes in duration of isolation, quarantine, as well as recommendations about post-exposure testing (62, 63). Sumner et al. found that Omicron and Delta variants were more strongly linked to fever and cough than the original-type virus and the Alpha variant. In addition, children with an Omicron variant infection were more likely to experience lower respiratory tract symptoms and systemic manifestations (64). Similarly, Whitaker et al. noted changes in symptom patterns, with decreased reporting of loss of the sense of smell or taste for Omicron compared to previous variants, and increased reporting of cold-like and influenza-like symptoms (65). De Maria et al. reported significant differences not only in the frequency of infection among healthcare personnel, but also among the type of hospital employees who got sick, shifting from physicians early on, to nurses in subsequent waves (66). Although vaccines continue to play a significant role in mitigating SARS-CoV-2, waning immunity, along with viral evolution have prompted the need for additional doses over time, using different viral strains (34, 67). This has been particularly challenging in immunocompromised individuals who are at high-risk for severe COVID-19 and have a suboptimal response to immunizations (68, 69). Whether additional (i.e., every year) immunizations against SARS-CoV-2 with an updated vaccine formulation will become standard of care is unknown. As we continue to monitor SARS-CoV-2 dynamics, the role of case investigation and contact tracing remains to be determined.

In summary, contact tracing's success depends on strategies, contact definitions, monitoring/reporting indicators, and data collection/analysis tools (7–9). It is resource-intensive, effective in healthcare settings and we demonstrate, feasible and sustainable. We find that while universal masking on campus had a key role in reducing at work exposure events, in addition to minimizing workplace COVID-19 exposures case investigation and contact tracing provided employee re-education/monitoring, and assurance to the workforce/patients of safeguards to minimize transmission. We share the model and performance of a case investigation and contact tracing program with a small core employee health and infection control team with the ability to rapidly expand by training eligible volunteers in a pandemic setting. Such a model can be potentially adapted for different infectious disease threats and other healthcare settings.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by St Jude Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because this is research conducted through secondary use of data collected for occupational health purposes according to the 2018 Common Rule requirements. All analysis were done using aggregate data without identifiers.

Author contributions

DH: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. SD: Data curation, Formal analysis, Methodology, Writing – review & editing. JH: Conceptualization, Resources, Supervision, Writing – review & editing. LT: Data curation, Formal analysis, Methodology, Writing

– review & editing. RH: Resources, Supervision, Writing – review & editing. AG: Conceptualization, Methodology, Resources, Supervision, Writing – review & editing, Data curation, Investigation. HH: Methodology, Supervision, Writing – review & editing, Conceptualization, Data curation, Investigation, Resources.

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Conflict of interest

RH has served on advisory boards for Abbott Diagnostics and T2 Diagnostics.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Shedding light on the next pandemic path, from outpatient to ICU, the effect of vitamin D deficiency in the SARS-CoV-2 pandemic

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Background: Vitamin D insufficiency is named "the pandemic of our era" by some experts. World Health Organization warns against a "deadlier outbreak" than the COVID-19 pandemic. Critical evidence is hereby for future pandemic prevention, with special emphasis on Vitamin D.

Methods: A cross-sectional study was conducted with 172 unvaccinated adult participants, who presented to the emergency department. Blood measurements, radiological findings, and demographic features were evaluated in the four categories of "healthy adults, COVID-19 outpatients, hospitalized inpatients on the wards, and in the ICU."

Results: Results were statistically significant in association with age, gender, weight, Vitamin D, glucose, urea, creatinine, leucocyte, aspartate transaminase, hemoglobin, C-reactive protein, troponin, platelet/thrombocyte, ferritin, D-dimer, triglycerate, glycated haemoglobin, lactate dehydrogenase measurements, and chest computed tomography features (each $p < 0.050$).

Conclusion: This article presents evidence to support the importance of Vitamin D for global public health. Patients with adequate levels of Vitamin D, glucose, urea, creatinine, leucocyte, aspartate transaminase, hemoglobin, C-reactive protein, troponin, platelet/thrombocyte, ferritin, D-dimer, triglycerate, glycated haemoglobin, lactate dehydrogenase are less likely to be admitted to ICU versus being outpatients. Factors include gender, age, weight, comorbidities, and computed tomography findings. The ultimate goal is to globally minimize preventable burdens of disease and death.

KEYWORDS

public health, emergency, disease outbreak, infection, international, prevention, syndemics, future healthcare systems

Background and aims

Vitamin D insufficiency is a global health issue that afflicts more than one billion worldwide, named by some experts "the pandemic of our era" (1–3).

On World Health Organization (WHO) Director-General's May 22, 2023 speech at the World Health Assembly (WHA), a critical present-day warning was is made about a "deadlier outbreak," at a point when the number of confirmed cases had already reached nearly 767 million. Nearly seven million had lost their lives from confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the same time frame, WHO announces hundreds of new cases each week, shortly after an end to coronavirus disease 2019 (COVID-19) as a public health emergency was officially declared "with great hope" on May 4th, 2023 (4). The COVID-19 pandemic was declared a "public health emergency of international concern" on January 30th of 2020 by WHO Director-General and that it was "here to stay." The global disease outbreak threatened lives and economies, having placed enormous and growing burdens on world populations. The virus and its varients continue to pose major challenges to scientists and clinicians, destined to exploring innovative ways to mitigate severe forms of the disease (5–8). Numerous articles calculted the potential risks of overlaps of COVID-19 with other universally common pathogens, such as the seasonal-influenza (8). "Last week, COVID-19 claimed a life every three minutes and that's just the deaths we know about," said WHO Director-General in May (4). It is time to advance and chart a clear path towards future pandemic prevention.

It is time to advance and chart a clear path towards future pandemic prevention. Vitamin D emerges with benefits in the fight against SARS-CoV-2 infection, yet there is need need for further analysis. Across the board, practice-based clinical judgement supports the notion that Vitamin D reduces COVID-19 severity. Logical line of reasoning underpins the proposition. Scientists around the world are committed to improving supporting evidence (9). Recent data have suggested a protective role of Vitamin D in COVID-19-related health outcomes since Vitamin D is known to play a crucial role in immune function and inflammation (6). Studies reported that patients with moderate–severe Vitamin D deficiency (<20 ng/mL) have a higher risk for in-hospital mortality due to COVID-19 than those with higher levels of Vitamin D (10–13). A growing body of literature raises the issue of Vitamins C and D for risk assessment and therapeutic options in COVID-19 (5). Various aspects of the relationship between Vitamin D status and COVID-19-related clinical outcomes remains controversial. There are several relatively small, single-site homogeneous populations studies based on assessment of a mainstream population for reference but with certain limits of generalizability (14). Systematic reviews underline that further research is urgently needed (15).

Vitamin D_3 (cholecalciferol) is synthesized in skin by exposure to direct sunlight. Vitamin D_3 is metabolized by the liver to 25-hydroxyvitamin D (calcidiol), then converted by the kidneys to 1,25-dihydroxyvitamin D (active form, calcitriol) (16). This article refers to 25-hydroxyvitamin D as Vitamin D, hence the best way to diagnose Vitamin D deficiency.

In large numbers, Vitamin D has been found to be low in COVID-19 patients and have been related to worse outcomes in several studies (17). In one investigation, Vitamin D levels were shown to predict the outcomes in 73 patients the clinical course of both 36 severe and 37 non-severe COVID-19 patients at hospitalization, when compared with 30 control subjects. Vitamin D levels at hospital-admission strongly predicted the occurrence of worsening outcomes in COVID-19, independent of the disease severity at presentation (18). Vitamin D deficiency was associated with a higher risk of COVID-19 hospitalization in a retrospective case–control study in England, which included 80,670 participants. Odds ratios for hospital admission were 2.3–2.4 times higher for levels <50 nmol/L, but without excess mortality risk. The conclusion was reached that widespread measurements and treatment may reduce the risk (19). A total of 288 COVID-19 patients participated in another research. Patients with lower albumin ($p < 0.0005$), lower Vitamin D ($p = 0.002$), higher D-dimer ($p < 0.0005$) levels had fatal disease outcomes had. Radiographic scores were increased in patients with lower serum albumin ($p < 0.0005$) and higher D-dimer ($p < 0.0005$) levels, but showed no statistically significant differences regarding Vitamin D concentrations ($p = 0.261$). An important combined role of "low Vitamin D, low albumin, high D-dimer" was pointed out in early diagnosis of severe disease as timely indicators (7). A single-center prospective study in India with 200 COVID-19 patients found no statistically significant differences in the length of hospital stay ($p = 0.176$), need for mechanical ventilation, or mortality, between normal and Vitamin D deficiencient levels <30 ng/mL (14).

A meta-analysis from five RCTs and trial sequential analysis presented definitive evidence on the protective effect of Vitamin D supplementation on COVID-19-related intensive care unit (ICU) and mortality. Vitamin D administration resulted in a decreased risk of death and ICU admission. The pooling of the studies was claimed to reach a definite sample size. The asessment was made that the association is conclusive (6). Epigenetic changes in COVID-19 patients were discussed in an early article which aimed to explore various processes contributing to disease severity (20). Evidence remains controversial. An Mendelian randomization study reported that genetically lowered serum Vitamin D concentrations are not causally associated with COVID-19 susceptibility, severity, or hospitalized traits, but did not evaluate the role of Vitamin D supplementation (21). Supplements may offer a relatively easy option to decrease the impact of the pandemic (9, 22). Strong evidence was presented on the benefits. Vitamin D deficiency of <20 ng/mL was identified in 14.5% of the 4,599 veterans with a positive SARS-CoV-2 test. A covariate-adjusted correlation was reported for 24.1–18.7% hospitalization ($p = 0.009$) and 10.4–5.7% mortality ($p = 0.001$) in the association of Vitamin D with COVID-19. Acknowledging that the sample of veterans disproportionately male, older, and with multiple comorbidities, multivariable analyses were conducted in terms of the generalizability of the findings, to adjust for the confounding factors, and still an independent effect of lower Vitamin D levels was found to be associated with COVID-related hospitalization and mortality. The study concluded that randomized controlled trials (RCTs) are needed to evaluate the impact (23). High-quality randomized controlled trials with larger populations are necessary to explore and define the role of Vitamin D supplementation in the prevention and treatment of COVID-19 (13, 21, 23–25).

A pilot study found low serum levels of Vitamins C and D in most of the cases in a cohort of 21 critically ill COVID-19 patients in ICU. Older age and low Vitamin C level appeared co-dependent risk factors for mortality (5). An observational, single-center, pilot study of limited sample size demonstrated that Vitamin D deficiency correlated with a reduced number of natural killer cells in 29 ICU and 10 non-ICU patients with COVID-19 pneumonia, with the evaluation that the beneficial effects of Vitamin D on protective immunity in the early stages were due in part to its effects on the innate immune system (26). The results of a single-center retrospective observational study, conducted with 40 ICU-admitted confirmed COVID-19 patients, indicated that serum Vitamin D $\leq$9.9 ng/mL on admission is a predictor of in-hospital mortality (10). A total of 83 confirmed COVID-19 cases were enrolled in a retrospective, observational, single-center respiratory-ICU study in Italy. The study demonstrated that moderate–severe Vitamin D hypoVitaminosis may predict worse prognosis and increased in-hospital mortality in patients with severe COVID-19 and acute respiratory failure (13). Decreased serum levels of Vitamin D versus the healthy participants was exhibited in a study with 100 participants, consisting of 50 healthy and 50 ICU-admitted COVID-19 ($p = 0.0024$). Findings suggested a probable association of Vitamin D concentrations with immunity and the risks (27). A study, which included 175 ICU-admitted COVID-19 patients with Vitamin D deficiency <12 ng/mL, aimed to investigate the relationship between clinical course and inhospital mortality. The study group ($n = 113$) received a high dose of 300,000 IU Vitamin D_3 intramuscularly within the first 24 h of ICU admission, versus the control group ($n = 62$). Parenteral Vitamin D_3 administration did not reduce the need for intubation, length of hospital stay, and inhospital mortality (17). A cross-sectional study included 194 adults with ICU-admitted COVID-19 patients, with results that confirmed the high prevalence of Vitamin D deficiency in severe cases (60.8%) and the positive association between Vitamin D deficiency, poor prognosis, and mortality due to secondary infections (28). Even stronger evidence was presented by a systematic review and meta-analysis on 2,078 patients from nine studies on the beneficial role of Vitamin D supplementation on ICU admission ($p = 0.005$), but not on mortality ($p = 0.109$) (15).

Resilience strategies for pandemic preparedness and evidence-based public health policy will enhance human well-being accross the populations. The end of a global health emergency does not mean the global health threat is over. A high-level leaders' meeting will be held on pandemic preparedness and response at the annual WHA, set to address future pandemics. The commitment to a pandemic accord is important. The abiding threat of an "emerging deadlier pathogen" is a call for action. It is time to advance on future pandemic prevention and to chart a clear path forward towards that future (4). Mounting concern is now being voiced as the discoveries of global virology indicate that the natural order of the increasingly frequent pandemics in the coming future is inevitable (29).

In the pursuit to contribute to global health, the current cross-sectional research focuses on the role of Vitamin D levels in COVID-19 in improving clinical outcomes. The non-drug, single-center study was carried out under the coordination of Yeditepe University training hospital in Istanbul. In the metropolitan city, in a period of just over two-and-a-half months alone in 2020, ambulances responded to 35,403 SARS-CoV-2 emergency cases. The number of patients transported to-and-from state, private, and university hospitals were 29,762, 4,969, and 672 in consecutive order (30). Emergency ambulance services personnel had to design critical adaptive strategies in the complex environment of health care provision (31). The current study reports experiences from cases which originated in the emergency department of the university hospital and were either discharged for at-home follow-up or referred for hospitalization on the wards or in the ICU of the same health care institution. Demographic information of gender, age, weight, height, blood concentrations of Vitamin D, glucose, urea, creatinine, leucocyte, aspartate transaminase (AST), alanine transaminase (ALT), hemoglobin (Hgb), C-reactive protein (CRP), troponin, platelet/thrombocyte, ferritin, D-dimer, triglycerate, glycated haemoglobin (HbA1c), and lactate dehydrogenase (LDH), fibrinogen, and creatine kinase (CK), and chest CT testing were evaluated. Main emphasis was given to investigating the effect of Vitamin D levels on patient prognosis in COVID-19 patients. The study aims to shed light on the next pandemic path and to contribute to clinical competencies and public health policies for mass protection againt brutal killers of the future. The ultimate goal is to minimize the preventable impacts of morbidity and mortality on world populations.

Materials and methods

Ethics committee approval

Based on the application with file #1866, the Clinical Research Ethics Committee at Yeditepe University in Istanbul gave their approval on May 6 of 2020, with decision #1203.

The records that might reveal the identity of the volunteers were kept confidential by giving a "volunteer code" which cannot be disclosed to the public. The identity of the volunteer was assured to remain confidential even if the research results are published. By signing the written informed consent form, where viewers, polling persons, ethics committee, institution and other relevant health authorities may have direct access to your original medical records, but this information will be kept confidential, the volunteer or legal representative will have authorized such access. No payment or extra services were offered to the volunteers.

Research design

A cross-sectional research study was conducted. The aim was to investigate the effect of Vitamin D levels on patient prognosis in COVID-19 patients, shedding light on the next pandemic. The non-drug, single-center study was carried out under the coordination of Yeditepe University Faculty of Medicine Department of Emergency Medicine at the university-affiliated Kozyatagi Hospital in Istanbul. Data was collected in a period of 3 months, June 1–September 1, 2020. Blood Vitamin D, glucose, urea, creatinine, leucocyte, aspartate transaminase (AST), alanine transaminase (ALT), fibrinogen, creatine kinase (CK), hemoglobin (Hgb), C-reactive protein (CRP), troponin, platelet/thrombocyte, ferritin, D-dimer, triglycerate, glycated haemoglobin (HbA1c), lactate dehydrogenase (LDH) levels were measured. Demographic information, such as gender, age, weight, height was collected for the total number of 172 participants, adults aged $\geq$18, not vaccinated against COVID-19, who presented to the emergency department of the hospital. A "COVID-19 Patient Follow-up Form" was used in the evaluation. With voluntary participation and comprehension of informed consent, healthy adults and COVID-19 patients who met the Turkish Ministry of Health (TR MoH)'s case definition criteria were included in the study. In accordance with updated TR MoH algorithm and guidelines, confirmed cases of COVID-19 were diagnosed by positive Polymerase Chain Reaction (PCR) testing before or during ward/ICU hospitalization. The distribution of the participants was 43 healthy adults, 43 COVID-19 outpatients, 43 COVID-19 hospitalized inpatients on the wards, 43 COVID-19 hospitalized patients in the ICU. Blood measurements and demographic features were compared between the four groups. Statistically significant results of clinical importance are reported in this paper. Probable cases of COVID-19 with negative PCR results were excluded from the study. The conduct of research posed no risks for the volunteers, who were not subjected to any procedures other than blood testing used for scientific research.

Statistical analysis

The data were analyzed using the Statistical Packages of Social Sciences (SPSS) 28.0 program on the computer. Descriptive statistics were presented as mean ± standard deviation, median, minimum and maximum values for continuous variables, and as frequency and percentages for categorical variables. The conformity of the data to the normal distribution was evaluated with the Kolmogorov Smirnov test. Two independent samples *t*-test was used to compare the means of the measurements with normal distribution between the groups, and the Mann–Whitney U test was used to compare the measurement values that did not fit the normal distribution. Chi-square test or Fisher exact probability test was used to compare categorical variables. If $p < 0.05$, the difference was considered significant.

The clinical characteristics of the patients at diagnosis

TR MoH diagnostic guidelines, treatment algorithms, and updates for COVID-19 were followed in patient management. Patients were grouped under three categories, as COVID-19 outpatients, hospitalized inpatients on the wards, and in the ICU. Outpatients were followed in home isolation, without hospitalization, with treatment recommendations were < 50 years of age, without comorbidities, with normal imaging and mild pneumonia, blood lymphocyte counts ≥800/μL, serum CRP ≤ 40 mg/L, ferritin ≤500 ng/mL, D-dimer ≤ 1,000 ng/mL. Patients with findings which indicated severe course of the disease were hospitalized and monitored. These included mild-to-moderate pneumonia with respiratory rates ≥24/min, fingertip oxygen saturation (SpO2) ≤93%, mild-to-moderate pneumonia with poor prognostic criteria in the blood tests at admission, such as blood lymphocyte count <800/μL or serum CRP > 10 mg/L × upper limit of normal value or ferritin >500 ng/mL or D-dimer > 1,000 ng/mL, and severe pneumonia with changes in consciousness, respiratory distress, tachypnea or tachycardia with respiratory rates ≥30 min, SpO2 ≤ 90%, bilateral widespread >50% involvement in lung imaging, hypotension <90/60 mmHg, mean blood pressure < 65 mmHg, tachycardia >100, sepsis, septic shock, myocarditis, acute coronary syndrome, arrhythmia, acute kidney injury. Hospitalization was indicated in additional situations deemed necessary in by the consulting physician. Indications for ICU admission were respiratory rate > 30/min, signs of dyspnea and respiratory distress, oxygen saturation < 90% despite nasal oxygen support ≥5 L/min, partial pressure of oxygen in arterial blood (PaO2) <70 mmHg despite nasal oxygen support ≥5 L/min, partial pressure of oxygen in arterial blood to the fraction of inspiratory oxygen concentration (PaO2/FiO2) <300, lactate >4 mmol/L, bilateral infiltrates or multi-lobar involvement on chest radiography or tomography, hypotension with systolic blood pressure (SBP) < 90 mmHg, >40 mmHg decrease from regular SBP, mean arterial pressure < 65 mmHg, poor skin perfusion, organ dysfunction such as kidney function test, liver function test disorder, thrombocytopenia, confusion/disorientation, in the presence of immunosuppressive disease, underlying comorbidities, uncontrolled medical conditions, troponin elevation, arrhythmia. Admission to ICU critical care was indicated in additional situations deemed necessary in by the consulting physician.

Discharge criteria were the absence of fever, the need for oxygen for at least 48–72 h, and the clinician's approval. Antiviral agents targeting the virus were administered according to the TR MoH treatment guidelines for adults. The patient approach included additional clinical considerations for each individual, along with the therapeutics. Needs were assessed. Monitoring of symptoms, comorbities, and the optimal management of nutritional deficiencies were carried out, when adequate. Drug dosages, routes of administration, and the duration of treatment were outlined in the manuals for the three patient categories. As recommended, *favipiravir and/or hydroxychloroquine* were used for confirmed asymptomatic COVID-19 cases and those with uncomplicated mild-to-moderate pneumonia, who were also followed as outpatients. The same medications were used with different regimens for hospitalized probable/confirmed COVID-19 cases, including those who were uncomplicated or patients with mild-to-moderate and severe pneumonia. A large-scale study reported from Istanbul statistically significant differences in ICU admissions from 24% to 12%, and in intubations from 77% to 66%, following the addition of *favipiravir* to the national COVID-19 treatment protocol (32).

Results

Results were statistically significant in association with age ($p < 0.001$), weight ($p = 0.001$), Vitamin D ($p < 0.001$), glucose ($p < 0.001$), urea ($p < 0.001$), creatinine ($p = 0.005$), leucocyte ($p < 0.001$), aspartate transaminase (AST) ($p < 0.001$), hemoglobin (Hgb) ($p < 0.001$), C-reactive protein (CRP) ($p < 0.001$), troponin ($p < 0.001$), platelet/thrombocyte ($p = 0.015$), ferritin ($p = 0.004$), D-dimer ($p < 0.001$), triglycerate ($p = 0.019$), glycated haemoglobin (HbA1c) ($p = 0.014$), and lactate dehydrogenase (LDH) ($p < 0.001$). Vitamin D and Hgb levels were lower in ICU patients, compared to outpatients (Figure 1). All other measurements were higher in ICU patients, compared to outpatients. No statistically significant results were found to be associated with height ($p = 0.565$), levels of alanine transaminase (ALT) ($p = 0.389$), fibrinogen ($p = 0.103$), and creatine kinase (CK) ($p = 0.193$) (Table 1).

Results were statistically significant in association with gender ($p = 0.020$). There were more males than females in the ICU (29:15, 61.7:35.7%). Results were statistically significant in association with comorbidity ($p < 0.001$). There were more patients with comorbidities in the ICU than outpatients with comorbidities (39:20, 66.1:33.9%). Results were statistically significant in association with Vitamin D level ($p < 0.001$). There were more patients with severe Vitamin D deficiency in the ICU than outpatients with severe Vitamin D

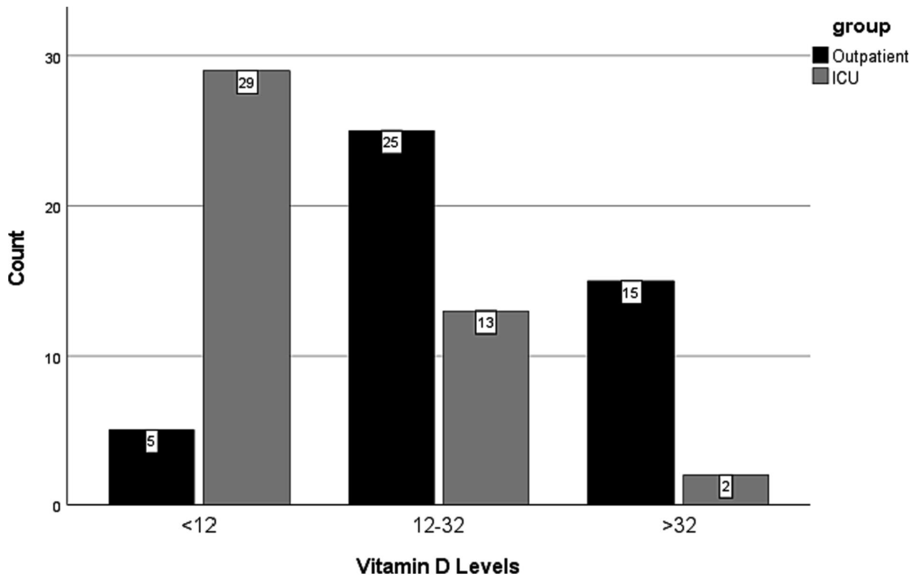

FIGURE 1
Vitamin D levels by the groups, patients in intensive care units (ICU) versus the outpatients.

deficiency (29:5, 85.3:14.7%). Results were statistically significant in association with chest CT features ($p < 0.001$). All patients with mild chest CT features were outpatients (32, 100%) (Figure 2). Nearly all patients with severe chest CT findings were in the ICU, except for one outpatient with severe chest CT findings (26:1, 96.3:3.7%) (Table 2).

Discussion

Blood measurements, radiological findings, and demographic features were compared between the four groups of the total number of 172 participants. Even numbers of healthy adults, COVID-19 outpatients, and inpatients hospitalized on the wards or the ICU were enrolled. Statistically significant results of clinical importance are reported in this paper, in terms of the critical implications for pandemic preparedness and public health.

Results were statistically significant in association with age, weight, Vitamin D, glucose, urea, creatinine, leucocyte, AST, Hgb, CRP, troponin, platelet/thrombocyte, ferritin, D-dimer, triglycerate, HbA1c, and LDH measurements ($p < 0.050$). Patients admitted to ICU were detected to have lower than normal Vitamin D and Hgb levels, compared to outpatients. All other measurements were higher in ICU patients, compared to outpatients. No statistically significant results associated with height, levels of alanine transaminase (ALT), fibrinogen, and creatine kinase ($p > 0.05$) (Table 1). Results were statistically significant in association with gender, comorbidity, Vitamin D levels, and chest CT findings ($p < 0.050$). In the outpatient setting, there were more females than males (64.3 versus 38.3%). When compared to outpatients, there were more males than females (61.7 versus 35.7%), more patients with comorbidities than those without (66.1 versus 33.9%), more patients with more severe levels of Vitamin D deficiency (85.3 versus 14.7%), and more patients with severe chest CT findings (96.3 versus 3.7%) in the ICU. Being male, having comorbidities, lower levels of Vitamin D, and severe versus mild chest CT findings might evidently be predisposing factors for admission to ICU for COVID-19 patients in the current study (Table 2).

Evidence from current research suggests particular focus on protection from Vitamin D, to reduce the risks and complications. Findings underscore the benefits of healthy Vitamin D levels. These evaluations are consistent with findings from existing literature. The study concluded that COVID-19 prognosis is poorer in patients with concurrent conditions, a recognizable inference. The presence of additional conditions was a factor associated with higher chances of being admitted to ICUs (6, 7, 10–13, 15, 17–19, 23, 28, 33). On the pressing issue of killer pandemics, researchers of the current research agree with previous studies, which indicated that further detailed analysis, stronger evidence with larger sample sizes, and valid research techniques are crucial to increase generalizability (10, 13, 15, 21, 23–25). A meaningful aspect of the study is also the fact that subjects included in the study had not been previously vaccinated for COVID-19. Since it is impossible to go back in time, there will never be a study group without vaccine-induced immunity or the same level of naturally-acquired active immunity in history again. The study interval is representative of an important period to better observe the effects of Vitamin D.

There are certain limitations to the study, which may altrenatively be develop into assets for future research. This cross-sectional study collected data to examine the associations between the blood measurements, radiological findings, demographic features in the four categories of being healthy adults, COVID-19 outpatients, hospitalized inpatients on the wards, and in the ICU. These evaluations generated valuable information, but there were certain limitations in terms of the outcome of the study. The research findings show that vitamin D deficiency may be a prognostic factor but cannot be conclusively attributed as the causative factor. This limitation arises from the cross-sectional nature of the study, in which baseline features were measured. The identified associations may or may not definitively correlate with survival outcomes. Due to the constraints in the study design, while the results reveal significant associations, a direct

TABLE 1 Comparisons of demographic factors and blood measurements by the groups, patients in intensive care units (ICU) versus the outpatients.

	Group	Mean	*n*	Std. deviation	Median	Minimum	Maximum	*p* value
Age	ICU	66.6818	44	13.65994	65.5000	24.00	102.00	<0.001[a]*
	Outpatient	45.3778	45	13.16726	47.0000	22.00	77.00	
	Total	55.9101	89	17.10571	57.0000	22.00	102.00	
Weight	ICU	78.7500	44	7.85368	78.5000	63.00	96.00	0.001[a]*
	Outpatient	70.5556	45	14.54391	70.0000	50.00	108.00	
	Total	74.6067	89	12.36437	76.0000	50.00	108.00	
Height	ICU	169.5455	44	6.90956	169.0000	158.00	182.00	0.565[a]
	Outpatient	168.6222	45	8.09121	165.0000	158.00	188.00	
	Total	169.0787	89	7.50186	167.0000	158.00	188.00	
Vitamin D	ICU	11.5911	44	11.11248	8.2300	0.76	63.00	<0.001[b]*
	Outpatient	31.0987	45	17.66086	26.4800	5.33	91.93	
	Total	21.4545	89	17.67762	18.9200	0.76	91.93	
Glucose	ICU	175.3636	44	67.78698	156.0000	98.00	366.00	<0.001[b]*
	Outpatient	111.1852	27	20.18575	107.0000	87.00	166.00	
	Total	150.9577	71	62.91728	126.0000	87.00	366.00	
Urea	ICU	77.7955	44	47.57837	60.0000	15.00	213.00	<0.001[b]*
	Outpatient	11.5714	42	3.36512	11.5000	7.00	23.00	
	Total	45.4535	86	47.53244	22.0000	7.00	213.00	
Creatinine	ICU	1.4332	44	1.74797	0.9000	0.39	10.00	0.005[b]*
	Outpatient	0.7336	42	0.16894	0.7200	0.40	1.12	
	Total	1.0915	86	1.29737	0.7500	0.39	10.00	
Leucocyte	ICU	12251.5909	44	6709.85355	9900.0000	2100.00	33500.00	<0.001[b]*
	Outpatient	5947.7273	44	2144.92247	5850.0000	2300.00	11000.00	
	Total	9099.6591	88	5880.05873	7550.0000	2100.00	33500.00	
Aspartate transaminase (AST)	ICU	67.8864	44	91.58075	46.5000	10.00	616.00	<0.001[b]*
	Outpatient	35.4286	42	37.28738	23.0000	13.00	195.00	
	Total	52.0349	86	71.97098	34.5000	10.00	616.00	
Alanine transaminase (ALT)	ICU	43.3636	44	46.63370	27.5000	6.00	283.00	0.389[b]
	Outpatient	36.8095	42	35.06665	23.0000	8.00	174.00	
	Total	40.1628	86	41.28121	25.0000	6.00	283.00	
Fibrinogen	ICU	426.0682	44	180.03584	376.0000	173.00	971.00	0.103[b]
	Outpatient	507.3750	8	144.71838	466.5000	378.00	819.00	
	Total	438.5769	52	176.29680	405.5000	173.00	971.00	
Creatine kinase (CK)	ICU	469.6364	44	1095.43915	105.0000	0.00	5316.00	0.193[b]
	Outpatient	87.5000	4	91.59512	60.0000	11.00	219.00	
	Total	437.7917	48	1053.46484	99.5000	0.00	5316.00	
Hemoglobin (Hgb)	ICU	11.8977	44	2.39423	12.1500	6.90	18.40	<0.001[a]*
	Outpatient	13.4795	44	1.55662	13.6500	8.70	16.70	
	Total	12.6886	88	2.15952	12.9000	6.90	18.40	
C-reactive protein (CRP)	ICU	175.3682	44	125.54618	159.5000	6.70	513.00	<0.001[a]*
	Outpatient	18.3953	43	24.87602	8.0000	1.00	95.00	
	Total	97.7839	87	120.05856	34.0000	1.00	513.00	

(Continued)

TABLE 1 (Continued)

	Group	Mean	*n*	Std. deviation	Median	Minimum	Maximum	*p* value
Troponin	ICU	237.4136	44	616.96710	27.0000	0.40	2761.00	<0.001[b]*
	Outpatient	0.0105	6	0.00122	0.0100	0.01	0.01	
	Total	208.9253	50	583.19079	24.5000	0.01	2761.00	
Platelet/ thrombocyte	ICU	291739.3864	44	144229.62025	282500.0000	229.00	877000.00	0.015[a]*
	Outpatient	231090.9091	44	72574.52246	226000.0000	65000.00	393000.00	
	Total	261415.1477	88	117536.92265	251000.0000	229.00	877000.00	
Ferritin	ICU	506.8818	44	422.85096	388.5000	13.00	1500.00	0.004[b]*
	Outpatient	490.0000	39	1530.15393	131.0000	13.00	9680.00	
	Total	498.9494	83	1085.75318	316.0000	13.00	9680.00	
D-dimer	ICU	1.6441	44	1.42420	1.3000	0.10	7.10	<0.001[b]*
	Outpatient	0.5019	32	0.42675	0.3700	0.04	2.08	
	Total	1.1632	76	1.24918	0.6000	0.04	7.10	
Triglycerate	ICU	186.2857	42	85.08655	181.5000	58.00	388.00	0.019[a]*
	Outpatient	128.2667	15	63.49631	111.0000	55.00	313.00	
	Total	171.0175	57	83.50353	153.0000	55.00	388.00	
Glycated haemoglobin (HbA1c)	ICU	6.6523	44	1.32533	6.3000	4.90	11.70	0.014[b]*
	Outpatient	5.7200	10	0.70522	5.5500	5.00	7.30	
	Total	6.4796	54	1.28186	6.2000	4.90	11.70	
Lactate dehydrogenase (LDH)	ICU	501.3182	44	212.23142	478.0000	129.00	1059.00	<0.001[a]*
	Outpatient	205.8387	31	106.73678	168.0000	124.00	640.00	
	Total	379.1867	75	228.58080	303.0000	124.00	1059.00	

*$p < 0.050$ statistically significant.
Reference ranges for blood tests: Vitamin D (<12 ng/dL deficient, 12–32 ng/dL insufficient, >32–150 adequate, 150 high, possible toxicity), glucose (<100 mg/dL), urea (<50 mg/dL), creatinine (0.5–0.9 mg/dL for women, 0.7–1.2 mg/dL for men), leucocyte (5,000–10,000/mm), AST (<35 units/L for women, <48 units/L for men), ALT (<35 units/L for women, <46 units/L for men), Fibrinogen (190–430 mg/dL), CK (26–192 U/L for women, 39–308 U/L for men), Hgb (11.7–16 g/dL for women, 13.1–17.2 g/dL for men), CRP (<5 mg/L), troponin (<0.16 ng/mL), thrombocyte (150,000–450,000 platelets/mcL), ferritin (10–350 ng/mL for women, 30–400 ng/mL for men), D-dimer (<0.42 mg/L), triglycerate (37–148 mg/dL), HbA1c (<4.5%), LDH (135–215 units/L for women, 135–225 units/L for men).
[a]Two independent samples *t*-test.
[b]Mann-Whitney U test.

cause-and-effect relationship cannot be inferred between Vitamin D deficiency and ICU admission. This descriptive cross-sectional study characterized the prevalence of and the disease outcomes in the COVID-19 population under investigation. This prevalence study examined the data on COVID-19 and Vitamin D status at one particular time point. Results of the cross-sectional study helps generate the hypothesis that may shedding light on the next pandemic path and illuminate that a similar longitudinal study is worth the investment, lending to the creation of stronger cohort studies or randomized control trials. Causality should be further investigated. The results obtained in the study prove that large nutritional studies should be planned to show the clear benefits of vitamin D status for COVID-19 prognosis.

At the time the research was run, delimitations were set to reflect a broader picture in the management of COVID-19 patients. Specific decisions were made at the intiation of the study, at a time when vaccinations were not yet available and little was known worldwide about the disease. Since this study did not aim to investigate vitamin D metabolism or bone development, the carrier protein albumin levels were not taken into account. Preliminary results are promising. Research outcomes were quickly implemented into clinical practice because COVID-19 was a pressing issue with high levels of mortality, and there was a darth of definitive evidence on how to approach the patients. The world is at the next stage now, with accumulated knowledge from various sources. Thus, we are presently ready to take a more refined approach to obtain categorical evidence.

Study findings suggest that further assessments of nutritional deficiencies are worthwhile. The scope should be expanded to help measure nutritional value. Further research methodology should describe additional components, beyond the value of Vitamin D. Assessments should include the measurement of serum albumin. Several tests serve to evaluate nutritional status, including biochemical data, medical findings, procedures, nutrition-focused physical examination, analysis of the size, functional capacity, and history of the patient. Serum visceral proteins, such as albumin and prealbumin of shorter half-life, are used as markers of the nutritional status and prognosis predictors, especially in the presence of multiple-organ disease involvement. Easily measurable biomarkers of malnutrition, such as prealbumin, may be of interest, along with thorough physical examination, as predictors of the prognosis for surgical outcomes and of mortality in severe illnesses. Other markers of the nutritional status such as urinary creatinine or 3-methylhistidine as indicators of muscle protein breakdown have not found widespread use. Vitamin D deficiency is common and has detrimental effects on musculoskeletal

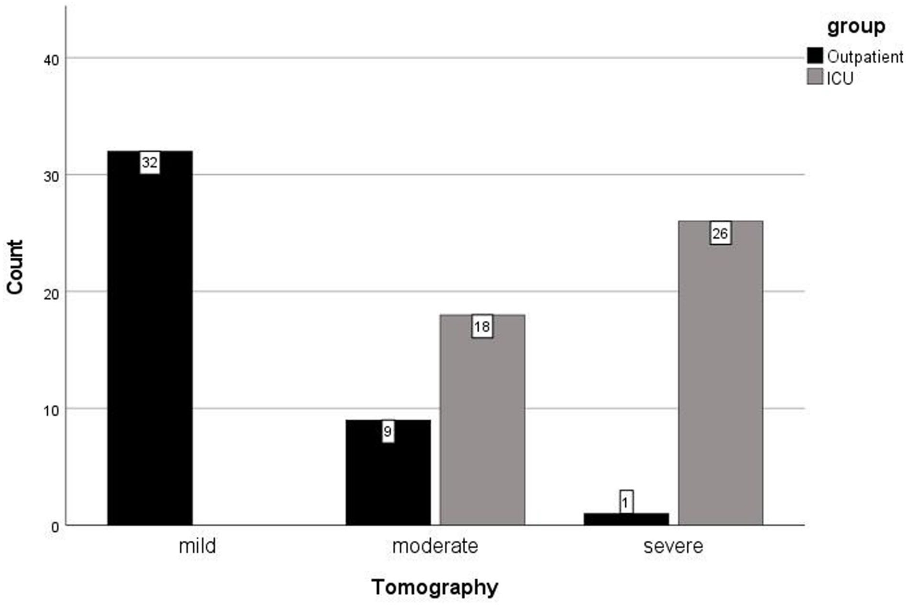

FIGURE 2
Computer tomography chest imaging manifestations by the groups, patients in intensive care units (ICU) versus the outpatients.

health, cardiovascular disease, autoimmunity and cancer. Studies have suggested a possible interaction between vitamin D and IGF-1. The usefulness of serum insulin-like growth factor-1 concentration as a specific marker for detecting malnutrition is clinically controversial (34, 35). In future hospital-based cross-sectional studies, it is suggested to highlight the role of vitamin D by adding more relevant biomarkers or variables that can relate to the mechanism of action. Advanced investigations and reevaluations are critical, to know the true impact, as this information is also pertinent to group comorbidities.

The idea of vitamin D's role in immune response is well-established. The protective effect of Vitamin D in preventing disease exacerbations, intensive care hospitalization, and mortality is widely recognized. In our study, it was observed that people with low vitamin D levels suffered from SARS Cov 2 more severely than those with high vitamin D levels. Current research presents novel evidence from Istanbul, on the prognostic and therapeutic role of Vitamin D in COVID-19. This study supports previous evidence from different locations. Considering the impact of geography on vitamin D status, the significance of the study is implied in its location. Studies need to be intensified in this region of the world, which offers rich dynamics regarding vitamin D deficiencies. Vitamin D deficiency remains an important problem in Turkey, despite the abundance of sunlight in the country (36, 37). In a study of prevalence over 60% of Turkish adults were found to be Vitamin D deficient (38). A meta-analysis, with a sample size of 111,582 from 40 studies, estimated the prevalence of Vitamin D deficiency to be 63% for the overall population (37). Lack of nutrition knowledge and poor dietary habits, excessive amount of time spent indoors, conservative dressing style covering a significant part of the skin may be some of the most commun causes. Scholarly views have been also expressed that this may be related to an enzyme defect or lack of intestinal absorption in the Turkish population (39). There are studies from two other cities, namely Izmir and Canakkale, in Turkey which investigated whether vitamin D levels are associated with the need for mechanical ventilation, ICU admission and length of stay, hospitalization, and COVID-19 related in-hospital mortality in critically ill COVID-19 patients (40, 41). It is thus important, to emphasize the importance of regional studies.

This article fulfills an important task in emphasizing that Vitamin D may potentially be an invaluable mitigation tool and prevent the next pandemic from turning into a global public health crisis (42).

Conclusion

Is your blood cholecalciferol ready for the next pandemic? The effect of Vitamin D deficiency in the SARS-CoV-2 pandemic sheds light on the next pandemic path, perhaps for the future of humankind. Results of the current study show that measurable variables of health are meaningful prognostic predictors of COVID-19 severity. Even though conclusive evidence is not presented as proof of causality, vitamin D deficiency emerges as a prominent prognostic factor, in the cross-sectional research. Further investigation is suggested, based on the results of which indicate that patients with higher Vitamin D and Hgb blood measurements are seemingly less likely to be admitted to ICU and more likely to be treated as outpatients. Gender, age, comorbidities, chest CT findings, weight, glucose, urea, creatinine, leukocyte, AST, CRP, troponin, platelet/thrombocyte, ferritin, D-dimer, triglyceride, HbA1c, and LDH are all factors which impact disease severity and outcomes in predicted patterns.

This article highlights the importance of Vitamin D for global public health, by presenting evidence from Istanbul, a metropolis of two continents. Eminent factors affecting COVID-19 prognosis are reported in an effort to improve the outcomes of future outbreaks, with hard-earned lessons from recent universal experiences. There will inevitably be new pandemic agents, some more lethal than SARS-CoV-2, but we can reduce the risks.

The current topic remains an urgent matter of critical importance. The ultimate goal is to globally minimize preventable burdens of disease and death.

TABLE 2 Gender, comorbidity, Vitamin D levels, and computer tomography (CT) chest imaging comparisons by the groups, patients in intensive care units (ICU) versus the outpatients.

			Group		Total	*p* value
			ICU	Outpatient		
Gender comparisons by the groups						
Gender	Female	Count	15_a	27_b	42	0.020*
		% within gender	35.7%	64.3%	100.0%	
	Male	Count	29_a	18_b	47	
		% within gender	61.7%	38.3%	100.0%	
Total		Count	44	45	89	
		% within gender	49.4%	50.6%	100.0%	
Comorbidity comparisons by the groups						
Comorbidity	No	Count	5_a	25_b	30	<0.001*
		% within comorbidity	16.7%	83.3%	100.0%	
	Yes	Count	39_a	20_b	59	
		% within comorbidity	66.1%	33.9%	100.0%	
Total		Count	44	45	89	
		% within comorbidity	49.4%	50.6%	100.0%	
Vitamin D level comparisons by the groups						
Vitamin D	Severe deficiency	Count	29_a	5_b	34	<0.001*
		% within Vitamin D level	85.3%	14.7%	100.0%	
	Moderate deficiency	Count	13_a	25_b	38	
		% within Vitamin D level	34.2%	65.8%	100.0%	
	Normal	Count	2_a	15_b	17	
		% within Vitamin D level	11.8%	88.2%	100.0%	
Total		Count	44	45	89	
		% within Vitamin D level	49.4%	50.6%	100.0%	
CT chest imaging comparisons of by the groups						
CT	mild	Count	0_a	32_b	32	<0.001*
		% within CT	0.0%	100.0%	100.0%	
	moderate	Count	18_a	9_a	27	
		% within CT	66.7%	33.3%	100.0%	
	severe	Count	26_a	1_b	27	
		% within CT	96.3%	3.7%	100.0%	
Total		Count	44	42	86	
		% within CT	51.2%	48.8%	100.0%	

Chi-square test. *$p < 0.050$ statistically significant. Each subscript letter denotes a subset of group categories whose column proportions do not differ significantly from each other at the 0.05 level. Fisher's Exact test. *$p < 0.050$ statistically significant. Each subscript letter denotes a subset of grup categories whose column proportions do not differ significantly from each other at the 0.05 level.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by based on the application with file #1866, the Clinical Research Ethics Committee at

Yeditepe University in Istanbul gave their approval on May 6 of 2020, with decision #1203. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

FC: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing. VT: Conceptualization, Investigation, Writing – original draft, Writing – review & editing, Methodology, Supervision. EK: Formal analysis, Methodology, Writing – review & editing. DC: Investigation, Validation, Writing – review & editing. SS: Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The recovery and resilience plan on the long-term care system. Towards a deinstitutionalization?

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Introduction: After the crisis caused by Covid-19, among other socioeconomic problems, the fragility of the organizations that make up the Spanish Long-Term Care System was revealed. These events prompted the Recovery and Resilience Plan (RRP). The aim of this study is to estimate the socioeconomic impact on Long-Term Care (LTC) of the investment delivered by the RRP. In addition, to fulfil our main aim, a secondary and necessary aim was to calculate the most current social accounting matrix (SAM) of the Spanish economy.

Methods: We analyse the components of the demand linked to the RRP investment allocated to LTC, and subsequently, based on Input–Output methodology, we calculate a social accounting matrix (SAM) of the Spanish economy to estimate the overall economic return.

Results: The results obtained using the SAM model proposed herein evidence the multiplier effect of the RRP invested in LTC. Every euro allocated to the RRP generates 4 euros in income for Households, Firms and the External Sector, 3.4 euros in industrial output, and returns 0.6 euros in taxes and social contributions to the Government. This also entails creating 26,410 direct and indirect jobs as well as 10,059 induced ones.

Discussion: Given the severe recession scenario triggered by the consequences of COVID-19, the results of this study highlight the significant multiplier effect that RRP investment may generate to alleviate the downturn in the Spanish economy and, more specifically, in the Spanish LTC System.

KEYWORDS
long-term care, recovery and resilience plan, social accounting matrix, Input–Output methodology, economic return, deinstitutionalization

1 Introduction

According to data provided by the World Health Organization (1), Covid-19 has caused more than 4 million deaths, with approximately 186 million people having been infected. Since the pandemic began, social distancing has been the fundamental strategy to stop the spread of the virus. This measure was the main cause of the lockdown in March and April 2020, which, together with the fear of contagion and the uncertainty of households and institutions, had a significant impact on economic activity and employment. In addition, this recession has occurred in a context of general low economic growth [secular stagnation according to Summers (2)], high levels of indebtedness, extreme inequality in the distribution of income, population aging in advanced economies (3) and serious hysteresis problems (4).

The impact on the Spanish economy has been especially significant. According to IMF (5), the main reason is the importance of the tourism sector, in addition to the scarcity of large companies and the large number of temporary employment contracts. Figure 1 clearly shows the decline in economic activity in Spain during 2020 and part of 2021 compared to 2019, taking as a reference the sales data collected by the Spanish Tax Agency (6). These data reflect that the immediate consequence of the lockdown announced in March 2020 was an intense drop in sales, which decreased by more than 30% and which, in some activities, reached 100% over a long period. As can be seen in Figure 1, after the minimum reached in April 2020, a strong recovery process began in the first weeks, which stagnated in August, and then resurged in December when activity appeared to approach the initial level.

This economic context has made it necessary to implement a reform plan, not only to support the post-crisis recovery, but also to counteract the impact of this crisis on economic activity. In this respect, the instruments made available by the European Community to its Member States will play a decisive role. Among them, the Recovery and Resilience Facility is the main policy measure employed to mitigate the economic and social impact of the coronavirus pandemic and make European economies and societies more sustainable and resilient. As stated in European Commission (7), the Facility is a temporary recovery instrument that allows the Commission to raise funds to help each Member State implement reforms and investments through its national Recovery and Resilience Plan (RRP). To benefit from the support of the Facility, Member States must submit their RRP to the European Commission, setting out the reforms and investments to be implemented by end-2026. The Member States can then receive financing up to a previously agreed allocation.

This study focuses on evaluating the effect that the Recovery and Resilience Plan (RRP) may have on the demand and production associated with care under the Spanish Long-Term Care System (LTCS) (8). According to information published by the Government of Spain, the objective of the RRP is to accelerate economic and social recovery after the COVID-19 crisis and to increase growth capacity in the medium and long term. The RRP is organized in four cross-cutting pillars (ecological transition, digital transformation, territorial and social cohesion, and gender equality) that are aligned with the six basic pillars of the EU Recovery and Resilience Facility (7). As further explained in the Annex 1 of the Supplementary material those four pillars of Spain's RPP are structured around 10 policy areas that define the bulk of investments in 30 components ranging from the urban agenda, the fight against depopulation and the development of agriculture, to the modernization and reinforcement of the tax and pension system. Other areas include the improvement of infrastructures and ecosystems, education, and the modernization of science and business.

Within the eighth policy area, the RRP seeks to promote well-being by improving care, in addition to reinforcing the three traditional pillars of the Welfare State (education, health and social services). To do this, it addresses the issues of financing and managing organizations and the social capital that the system brings together, efficiently articulating the powers of the different public administrations and public-private cooperation for the implementation of personal care, reinforcing mechanisms and equipment for long-term care, incorporating new technologies to improve home care and promoting universal accessibility.

The first specific challenge to be addressed is to promote change in the long-term care model, introducing reforms that simplify procedures and reduce waiting lists, reinforce the quality of professional services and conditions and increase the coverage of benefits. The key question is to promote services that reinforce more person-centred care and promote deinstitutionalization. The

FIGURE 1
Trend of economic activity in Spain (2019–2021). Source: Agencia Tributaria (6).

reinforcement of care contributes to the objectives of the demographic challenge in the areas affected by depopulation and is aligned with the actions related to older adults, active aging and care for dependency, which constitute one of the action lines of the National Strategy against the Demographic Challenge (9).

Additionally, the care sector has a high capacity for job creation, mainly as a result of the rise in life expectancy in Spain. These jobs are also non-polluting, non-relocatable and essential for enhancing the well-being of the population. There remains considerable scope for improvement in the demand for long-term care in Spain. The country invests only 0.75% of GDP in this care, which is half the OECD average. Investing in care will reduce the structural barriers that limit women's access to the labour market, helping increase the female employment rate, generating important tax returns in the future and expanding the base of Social Security contributors.

Against this backdrop, the aim of this paper is to estimate the socioeconomic impact of improvements in organizational structure, social capital and well-being, financed by the investment derived from the RRP. Thus, we first set out to analyse the demand that will be generated in the Spanish economy with the application of the funds destined to improve long-term care. In a second step, we study its impact on production and, subsequently, on the generation of employment and income in Spain, breaking this down, to a large extent, by economic sectors.

To this end, we calculate the social accounting matrix (SAM) multipliers of the Spanish economy in 2021 to subsequently obtain the effect of the demand shock generated by RRP investment allocated to the LTCS.

This article is organized in four sections. Following this introduction, the second section describes the general characteristics of the RRP in Spain and the measures it includes in relation to dependent care. The third section focuses on the methodology employed and the data sources used, while the fourth section presents the preliminary results obtained, and draws conclusions.

2 Materials and methods

This analysis uses a SAM model based on Input–Output methodology to calculate the impact of the measures included in the RRP on the Spanish economy at a sectoral level. Initially, the Input–Output Tables (IOTs, hereinafter) developed by Leontief (10) were mainly focused on analyzing the effects produced in industrial activity by exogenous changes in final demand and by the exchange of goods and services between different economic sectors. The annex to this document contains a more detailed specification of the characteristics of the Leontief model. Briefly, the equilibrium solution in the model allows us to determine the increase or decrease in production at the sectoral level in response to changes in final demand. In our case, this refers to the investment derived from the RRP.

However, the results obtained with the basic Leontief model omit the effects caused by the interrelationship between production, production factors, income distribution and final demand. The SAMs represent an extension of the tables used in the Input–Output model with which the previous limitations are overcome. A SAM is a square matrix whose elements represent the transactions carried out in an economy over a specific period (11). The economic models based on the SAM allow for more efficient modelling of the relationships between added value and final demand to complete the circular flow of income.

SAMs based on Input–Output methodology are of great importance as a tool to estimate various socioeconomic spillover effects in a country's economy and they have been widely used in research evaluating the impact of different demand shocks in a national economic system (12–20), and also at regional level for the case of Spain (21–24).

As indicated in Cardenete et al. (21), SAMs integrate data from the National Accounts into the basic Input–Output model, thus completing the interdependence of the productive sectors and final demand with the exchanges that take place between productive factors and final demand. At a general level, a SAM contains production accounts, income distribution accounts in which factors of production occur, income use accounts in which operations between institutional sectors appear, capital transactions, and accounts which include exchanges with the External Sector.

Table 1 shows the basic structure of a generic SAM, which reflects the circular flow of income for an economic system. Such a structure is applied in this analysis for the Spanish economy in 2021. The rows represent the income received from the elements of each column and the columns reflect the income distributed between the elements of each row. Therefore, each component of the SAM indicates the bilateral flow between the accounts that come together in that element, such that a cell *ij* of the SAM would correspond to the income of the sector of row *i* that comes from the sector of column *j*. Given that the SAM contains all the transactions carried out by the agents of the economy, the accounting identity by which the expenditure carried out by the economic agents must be equal to the income obtained must be fulfilled and, consequently, the sum of each column of the SAM must be equal to the sum of each row.

To better harmonize the SAM data with the final demand components obtained from the 2021 National Accounts records, the table used in the 2015 Input–Output models was projected to 2021, following the Euro method described in Eurostat (25). The fundamentals of this method involves an iterative procedure that, in this case, allowed us to make the estimates for 2021 using the projection from 2015 to 2021 of the value added at the sectorial level and of the various categories included in the final demand block, both contained in the National Accounting records prepared by the INE.

Equation 1 shows the equilibrium solution of our SAM model, which captures the effect of an exogenous demand shock $\mathbf{df}^{\mathbf{PRR}}$ on the economy in terms of total output $\mathbf{x}^{\mathbf{PRR}}$ by using the SAM multipliers matrix $\mathbf{M}$, which is further explained in the Annex 2 of the Supplementary material.

$$\mathbf{x}^{\mathbf{PRR}} = \mathbf{M}\cdot\mathbf{df}^{\mathbf{PRR}} \quad (1)$$

$\mathbf{df}^{\mathbf{PRR}}$ is a column vector of size 29 × 1 containing the investment allocation for the specific economic sectors according to the RRP targets for LTC. Applying multipliers matrix $\mathbf{M}$ of size 29 × 29 to $\mathbf{df}^{\mathbf{PRR}}$ allows us to obtain the column vector of size 29 × 1 of total output $\mathbf{x}^{\mathbf{PRR}}$, not only as regards the initial investment requirements, but also including the spillover effects on the industrial and institutional sectors of the economy. Once $\mathbf{x}^{\mathbf{PRR}}$ is known, employment $\mathbf{l}^{\mathbf{PRR}}$ depending on this level of output can be obtained as follows:

TABLE 1 Basic structure of the social accounting matrix.

	Sectors	Wages	Social contributions	Capital	Other net taxes on production	Indirect taxes on products	Direct taxation	Induced consumption of households	Government consumption	Endogenous investment	Imports	Exports	Exogenous consumption of households	Exogenous investment
Sectors	Interindustry consumption (64 × 64)							Consumption	Consumption	Investment		Exports	Consumption	Investment
Wages	Wages													
Social contributions	Social Contributions							Social Contributions				Social Contributions	Social Contributions	
Capital	GOS + RM													
Other net taxes on production	Taxes													
Indirect taxes on products	Taxes							Taxes	Taxes	Taxes			Taxes	Taxes
Direct taxation								Taxes	Taxes			Taxes	Taxes	
Induced consumption of households		Wages	Social contributions	ENE + RM				Consumption						
Government consumption			Social contributions		Taxes	Taxes	Taxes	Transfers				Transfers		
Endogenous investment				Fixed Capital consumption				Savings	Savings			Savings	Savings	
Imports	Imports	Wages	Social contributions		Taxes	Taxes	Taxes	Imports						
Exports														
Exogenous consumption of households									Transfers					
Exogenous investment				Inv				Savings	Savings			Savings	Savings	

Source: Own elaboration.

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$$\mathbf{l}^{\mathbf{PRR}} = \hat{\mathbf{l}}_{\mathrm{d}} \cdot \mathbf{x}^{\mathbf{PRR}} \quad (2)$$

where $\hat{\mathbf{l}}_{\mathrm{d}}$ is a diagonal matrix where $\mathbf{l}_{\mathrm{d}} = \frac{\mathbf{l}_j}{\mathbf{X}_j}$ is the vector of direct coefficients of employment $\mathbf{l}$ by industry.

This SAM model also allows us to split the total effect on output, employment and value added into what Stone (26) and Pyatt and Round (27) defined as **N1**, **N2** and **N3** multipliers, by partitioning the matrix in an additive fashion as follows:

$$\mathbf{M} = \mathbf{N_1} + \mathbf{N_2} + \mathbf{N_3} \quad (3)$$

where **N1** is the matrix of direct multipliers (or "own" multipliers), which includes only the traditional Leontief multipliers reflecting the monetary worth of sectoral output generated directly and indirectly to support the exogenous demand vector $\mathbf{df}^{\mathbf{PRR}}$. **N2** is the matrix of indirect multipliers (or "open loop" multipliers), which records how the different components of exogenous demand vector $\mathbf{df}^{\mathbf{PRR}}$ are transmitted to households, firms and the Government. Finally, **N3** is defined as the matrix of "closed loop" multipliers, capturing the feedback effects from households, firms and the Government and interindustry transactions. This additive decomposition, which is illustrated in Figure 2 and further explained in the Annex 2 of the Supplementary material, provides what Steenge et al. (29) called a "walk through the economic system". This is fundamental to evaluate the share of output, income and employment depending directly on the demand shock caused by RRP investment and the induced and feedback effects resulting from the spillover impacts on the economic system.

3 Results

For the sake of clarity, the results obtained in this study are presented in three different sections. Firstly, the SAM results estimated for the Spanish economy in 2021 are presented; the multipliers resulting from the allocation of RRP investment are shown in the second section, and finally the results from the monetary flows are presented in the third section.

3.1 Social accounting matrix

This section presents the main characteristics of the SAM of the Spanish economy estimated for 2021. First, the different categories used to classify the industrial sectors, factors of production and institutional agents included in the SAM are described. In the case of productive sectors, the analysis was carried out considering the 64 categories that appear in the Statistical Classification of Economic Activities (NACE Rev.2). This classification is standardized and is

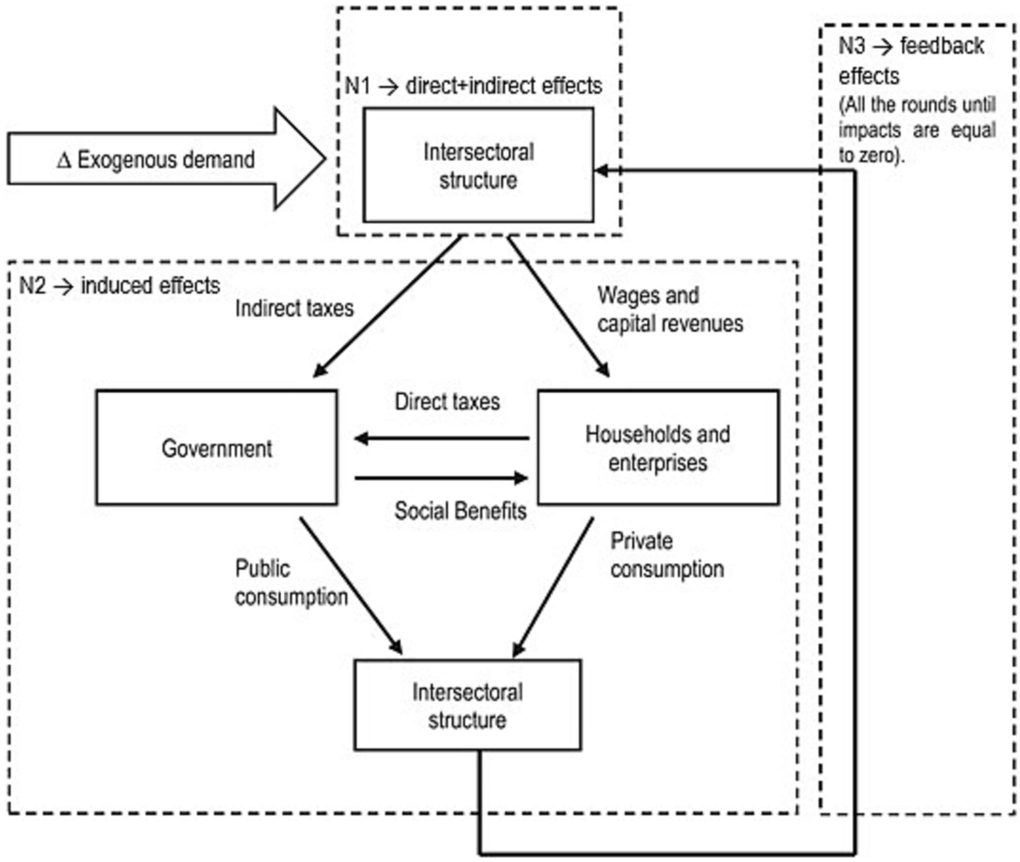


FIGURE 2
Decomposition of SAM multipliers. Source: Own elaboration based on (28).

compatible with the structure of the tables used in the Input–Output models for the Spanish economy prepared by the Spanish Institute of Statistics [INE, in its Spanish acronym; (30)]. For a better understanding of the results, the final sectorization scheme that will be applied in our SAM model follows the classification of 15 sectors considered by the INE, where the category of "Health Services and Social Services Activities" is divided into two independent activities, "Health care services" and "Social care services in residential establishments; social services without accommodation," resulting in the classification of 16 sectors that appears in Table 2.

The results in the submatrix of intersectoral intermediate flows in the SAM of dimension (16 × 16) are obtained by the Eurostat interactive method described in the methodology section. Having defined the block of accounts for flows between productive activities, the accounts related to the two productive factors considered (Labour and Capital), the Investment/Savings account and the accounts that represent the institutional sectors in the model are described below (Households, Public Sector, Financial and non-financial Institutions, External Sector). This information is contained in the SAM's submatrix (13 × 16) of primary factors and in the submatrix (16 × 13) of final uses. The first 4 rows of the primary factor submatrix make up a fundamental block (4 × 16) that contains the added value components corresponding to the remuneration paid from the different productive sectors for the use of labour and capital factors (salaries, gross surplus exploitation and mixed income, social contributions and other net taxes on production). Reading this block by columns allows us to observe the distribution of remunerations to the different economic sectors for the use of productive factors, thus reflecting the process of primary distribution of income.

TABLE 2 Industry classification.

S01	Agriculture, forestry and fishing
S02	Energy supply, water supply and waste management activities
S03	Food, beverages, tobacco and textiles
S04	Manufacture
S05	Construction
S06	Wholesale and retail trade
S07	Transport
S08	Accommodation and food service activities
S09	Information and communication
S10	Financial and insurance activities
S11	Real estate activities
S12	Professional, scientific and technical activities; administrative and support service activities
S13	Public administration, defence and education
S14	Health services
S15	Social work activities
S16	Arts, entertainment and recreation; other service activities; activities of household and extra-territorial organizations and bodies

Source: Own elaboration based on the Input–Output framework for the Spanish economy (30).

The rest of the elements in the submatrices of primary factors and final uses report on the flows of operations between the institutional agents of the model. Household activity is mainly reflected in the Consumption account, but also in monetary flows with the Public Administration and the External Sector in the form of transfers and taxes. In turn, the Public Sector is represented by its own current spending, social contributions paid by employers, social contributions received, net indirect taxes on production, taxes on products and imports and direct taxes (Personal Income Tax). Finally, the external sector is mainly represented by imports and exports, together with transfers from institutional sectors exchanged with the rest of the world.

For the purpose of this study, consumption operations are disaggregated into two accounts to distinguish between autonomous household consumption, which does not depend on the remuneration of production factors, and endogenous consumption, which is associated with the wages received by households for their participation in production. Applying a similar criterion, investment was broken down into an account that reflects endogenous gross capital formation linked to the increase in productive capacity and an exogenous account associated with autonomous investment. Similarly, the external sector was broken down into the endogenous part, corresponding to imports that depend on the income generated in production, and the exogenous part, which corresponds to exports that depend on the income generated in the rest of the world. The purpose of this distinction is to identify the endogenous part of consumption, gross capital formation and imports that will enter into the endogenization process linked to the calculation of the multipliers of the SAM model, as opposed to the exogenous component of demand, which is formed by the consumption of households covered with income that does not come from the production process, residential investment by households, plus investment in modernization of companies, and exports.

3.2 Impact of RRP investment in the Spanish long-term care system

This section presents the main results obtained from the SAM model described above. First, the sectoral disaggregation of the RRP investment focused on the LTCS is presented. Following the report of the 22nd component addressing Spain's RRP, the amount of investment proposed to enhance the LTC system is 2,083.9 million euros. These investment funds are mainly intended for the following purposes: evaluations and analyses; dissemination and awareness-raising campaigns; the construction and refurbishment of residential institutions; remodelling and equipping innovative day-care centres; technology for long-term care. As can be seen in the first column of Table 3, the full amount of 2,083 million euros can be split into certain components of a column vector that entails the exogenous demand shock to be estimated using our SAM model. The distribution by industry was implemented according to the information published in the 22nd component report, where the total amount to be invested is split into different components as follows: 1,282.8 million euros to the economic sector of "Construction" for construction and refurbishment of residential institutions, and for the acquisition of equipment; 275.4 million euros to the economic sector of "Information and communication" for investment in

TABLE 3 PRR investment allocation and total output generated.

	PRR investment	Total output
S01	0.0	45.6
S02	0.0	228.7
S03	0.0	158.6
S04	0.0	615.6
S05	1,282.8	1,651.1
S06	0.0	391.5
S07	0.0	168.8
S08	0.0	163.0
S09	275.4	452.9
S10	0.0	141.5
S11	0.0	251.4
S12	12.2	357.4
S13	0.0	314.3
S14	34.3	215.3
S15	89.4	137.9
S16	0.0	115.9
Remuneration of labour	0.0	1,475.2
Remuneration of capital	0.0	969.7
Net taxes on production	0.0	12.1
Tax on products	146.8	318.8
Social contributions	0.0	402.8
Income transfers	0.0	1,213.3
Direct taxes	0.0	218.3
Induced consumption of households	0.0	2,297.3
Endogenous Investment	0.0	44.9
Payouts to external sector	242.9	979.4
Public sector	0.0	1,274.0
Total PRR investment in LTC	**2,083.9**	**14,615.2**

Fiscal return
1,098.7

Results in million euros. S01: Agriculture, forestry and fishing; S02: Energy supply, water supply and waste management activities; S03: Food, beverages, tobacco and textiles; S04: Manufacture; S05: Construction; S06: Wholesale and retail trade; S07: Transport; S08: Accommodation and food service activities; S09: Information and communication; S010: Financial and insurance activities; S011: Real estate activities; S012: Professional, scientific and technical activities; administrative and support service activities; S013: Public administration, defence and education; S014: Health services; S015: Social work activities; S016: Arts, entertainment and recreation; other service activities; activities of household and extra-territorial organizations and bodies.
Source: Own elaboration.

technology for long-term care; 12.2 million euros to the economic sector of "Professional, scientific and technical activities; administrative and support service activities" to perform evaluations, analyses and dissemination and awareness-raising campaigns; 123.7 million euros to each of the economic sectors "Health services" (34.3 million euros) and "Social work activities" (89.4 million euros) for the remodelling of innovative day-care centres. The remaining amount of investment is included in the indirect taxes linked to these purchases (146.8 million euros) and in imports (242.9 million euros).

The second column of Table 3 shows the results of the total output generated by the above-mentioned demand shock. This level of output is not only determined by the sectoral impact on production derived from the allocation of RRP investment previously described, which is considered the direct impact. To estimate the total gain in production, it is also necessary to take into account that the initial demand shocks caused by RRP investment are transmitted to the production system, where interindustry backward linkages generate a multiplicative effect on output, which is considered the indirect impact. Moreover, besides industrial inputs, economic sectors also demand additional labour,

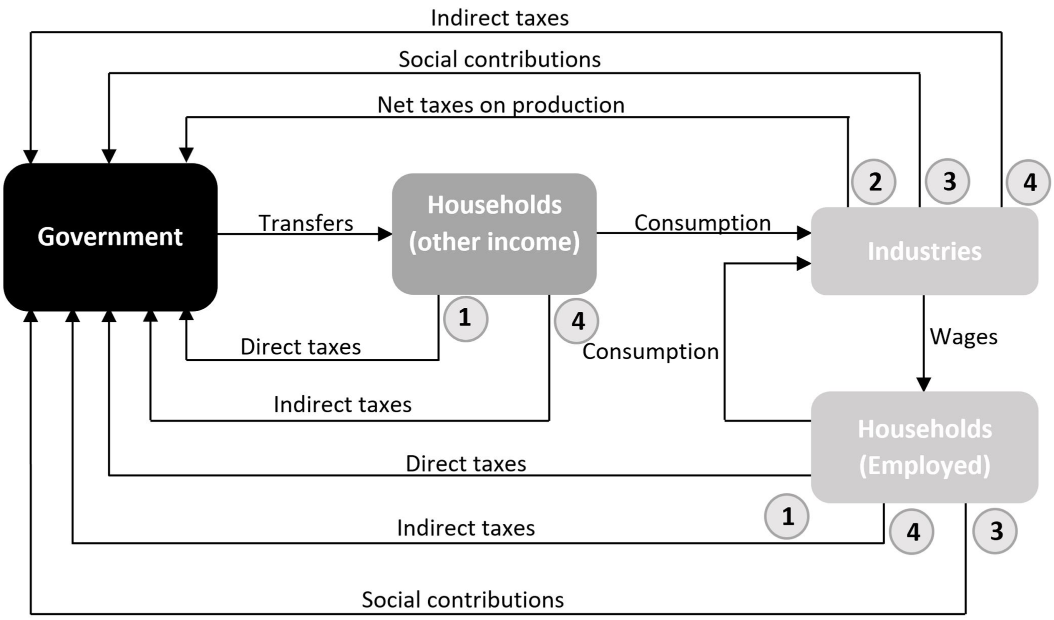


FIGURE 3
Fiscal return on PRR investment. Source: Own elaboration.

increasing the total wage amount in the economy that will subsequently be spent by households, generating a complementary round of demand shocks, which is considered the induced effect.

Consequently, the output results in Table 3 include the total effect derived from the initial demand shock caused by RRP investment (direct, indirect and induced effects). At the aggregate level, this means that 2,083.9 million euros of increased demand creates 5,409.5 million euros of total output not only in the investee sectors, but also within the rest of the economic system. Consequently, the monetary RRP investment effect accounts for an overall multiplier effect on production of 2.6 from the initial investment (2,083.9 million euros). The sectors "Construction" (30.52%) and "Manufacture" (11.38%) benefit most, followed by "Information and communication" (8.37%), "Wholesale and retail trade" (7.24%), "Professional, scientific and technical activities; administrative and support service activities" (6.61%), and "Public administration, defence and education" (5.81%).

Apart from these effects on production, the SAM model can contribute to evaluating the systemic impacts to understand and quantify the income generation from the RRP investment. As can also be seen in the second column of Table 3, the initial demand shock generates 1,475.2 million euros in wages and 969.7 million euros in gross operating surplus and mixed income to households and firms, while 402.8 million euros in social contributions and 12.1 million euros in other net taxes on production revert to the Government. This means that the total value added generated from the initial shock in demand accounts for 2,457 million euros, which leads to an overall multiplier effect on income of 1.2 from the initial investment (2,083.9 million euros). Furthermore, the total effect caused by RRP investment returns another 318.8 million euros to the Government in the form of indirect taxes on products and 218.3 million euros in direct taxes. It requires 44.9 million euros in additional investment and imports worth 979.4 million euros, and it allows households to increase income by 2,297.3 million euros, as well as transfers by the Government for 1,274 million euros.

Thus, a large share of the income generated by RRP investment generates revenues for the Government via fiscal returns. Figure 3 shows the four possible channels through which the Government receives these revenues after the initial demand shock. The first would be the direct income taxes paid by households receiving transfers from Government and by households of workers involved in the production to meet RRP investment (218.3 million euros). The second channel involves the net taxes on production, derived from the increase in the level of output sustained by RRP investment (12.1 million euros). This increase in production includes all the direct, indirect and induced impacts previously defined. The third channel comprises the social contributions that employers and employees pay according to the total wages received by the workers depending on the RRP investment (252.4 million euros). Lastly, the fourth channel accounts for the indirect tax on goods and services purchased to meet the RRP investment (402.8 million euros). As Table 3 shows, the total fiscal return accounts for 1098.7 million euros, which is 52.7% of the initial amount invested.

The previous output results serve as the basis for calculating the number of jobs sustained by RRP investment according to Equation 2. Table 4 shows the employment by industry required to obtain the production generated by the initial demand shock. The first column contains total employment, while the remaining columns display the decomposition of the multiplier effect according to the three types considered in the study (direct plus indirect, induced and feedback). The results at the aggregate level reveal that 33.2% of the employment generated corresponds to direct jobs and 24.9% to indirect jobs, while induced jobs account for 22.1% and the remaining 19.8% is due to the feedback effect. Given that RRP investment is massively allocated to "Construction," 27.9% of the employment generated is linked to this industry (12,688 jobs), followed by "Public administration, defence and education" (5,083.9) and "Professional, scientific and technical activities;

TABLE 4 Employment sustained by PRR investment.

	Total effect	N1		N2	N3
		Direct effect	Indirect effect	Induced effect	Feedback effect
S01	504.6	0.0	87.7	134.3	282.6
S02	401.9	0.0	200.1	100.5	101.2
S03	505.2	0.0	132.7	121.7	250.8
S04	1,950.9	0.0	1,497.1	216.6	237.2
S05	12,688.0	9,857.8	2,356.3	234.4	239.5
S06	4,260.4	0.0	1,534.4	981.7	1,744.4
S07	1,169.9	0.0	528.4	283.1	358.3
S08	2,171.8	0.0	376.5	544.4	1,250.9
S09	3,812.6	2,750.0	793.7	138.1	130.9
S10	635.4	0.0	242.8	143.0	249.6
S11	459.8	0.0	236.4	84.3	139.1
S12	4,742.1	340.9	2,654.5	834.5	912.2
S13	5,083.9	0.0	259.3	3,632.9	1,191.7
S14	2,107.6	335.9	122.4	1,151.4	497.8
S15	2,768.8	1,795.0	60.9	605.4	307.4
S16	2,229.9	0.0	247.8	852.3	1,129.7
Total	**45,492.6**	**15,079.7**	**11,330.7**	**10,058.7**	**9.023,5**

Total effect = N1 Direct effect + N1 Indirect effect + N2 Induced effect + N3 Feedback effect. Employment in number of equivalent jobs. S01: Agriculture, forestry and fishing; S02: Energy supply, water supply and waste management activities; S03: Food, beverages, tobacco and textiles; S04: Manufacture; S05: Construction; S06: Wholesale and retail trade; S07: Transport; S08: Accommodation and food service activities; S09: Information and communication; S010: Financial and insurance activities; S011: Real estate activities; S012: Professional, scientific and technical activities; administrative and support service activities; S013: Public administration, defence and education; S014: Health services; S015: Social work activities; S016: Arts, entertainment and recreation; other service activities; activities of household and extra-territorial organizations and bodies.
Source: Own elaboration.

administrative and support service activities" (4,742.1). The result in "Construction" is mainly based on the direct and indirect effect, which explains 96.3% of the employment generated in this industry (12,214.1 over 12,688 jobs) and accounts for 65.4% of the direct employment and 20.8% of the indirect employment sustained by RRP investment in all industries. Regarding induced employment, "Public administration, defence and education" is ranked first (3,632.9 jobs), followed by "Health services" (1,151.4) and "Wholesale and retail trade" (981.7).

3.3 Final results from monetary flows

As described in Eq. 3 in the Annex 2 of the Supplementary material, the bottom right-hand element of the endogenous block of the SAM is the H matrix, which contains the monetary flows describing the secondary distribution of income from the Government to Households, Firms and the External Sector (on the receiving benefit side) and vice versa (on the contributing side, through the payment of direct income taxes, social contributions, taxes on products and net taxes on production).

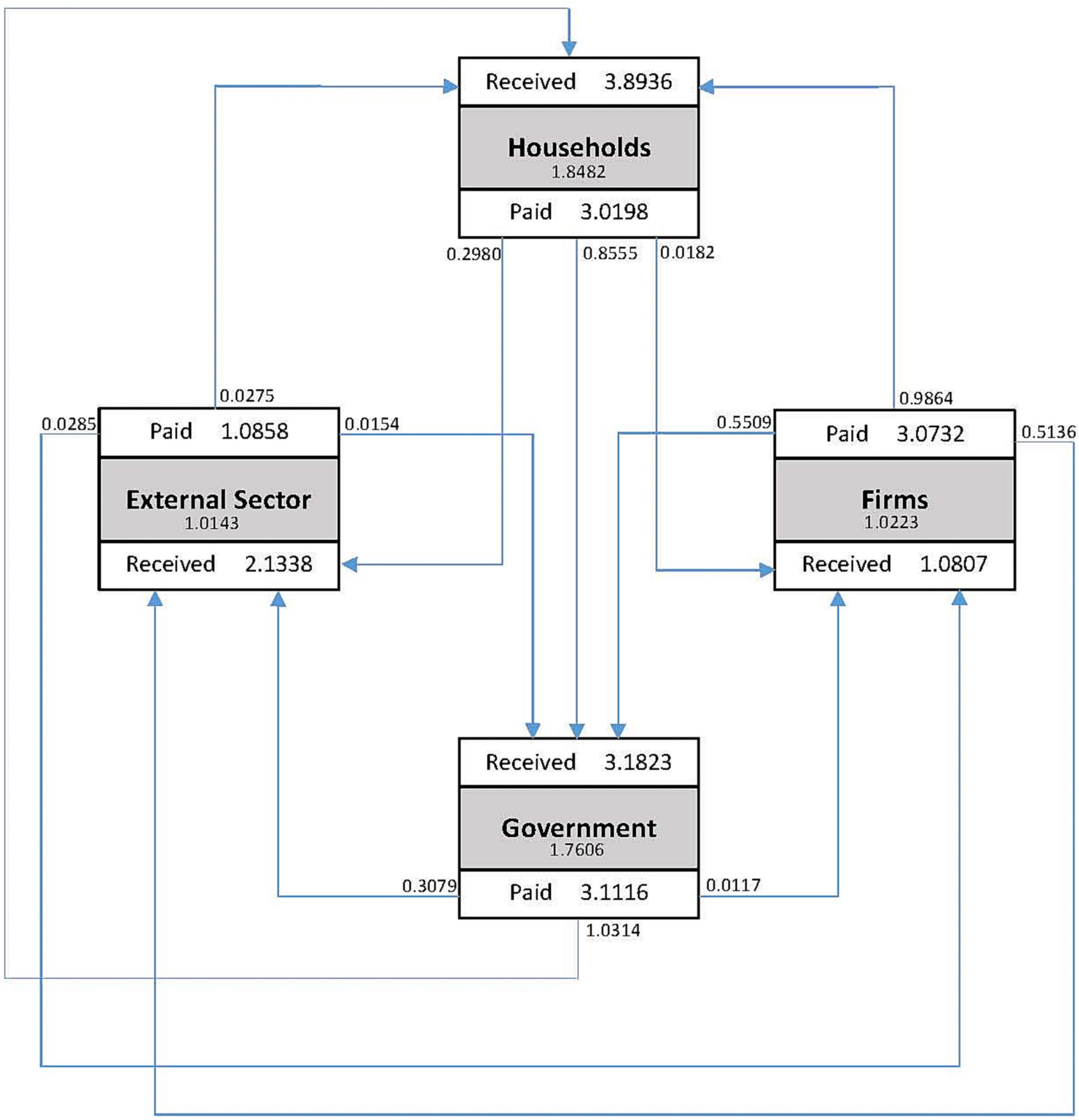
The H matrix shows the systemic results of giving one unit of income to a particular institutional agent and its effects on the other institutional agents (Households, Firms, the Government and the External Sector in our analysis). The H matrix provides a summary of the results after a walk through the system, i.e., condensing the circular flow of income explained above. Reading the H matrix by columns reveals the multiplier effect of one unit of income on other institutional agents. By rows, it shows how much money is received by an institutional agent when increasing one unit of income in other institutional agents.

Figure 4 gives an overview of the H matrix resulting from the demand shock caused by RRP investment. The Totals row reflects the multiplier effect for each euro received by every institutional agent. The flows below the H matrix show how the multiplier effect is generated for each institutional agent and subsequently paid to the other ones. Thus, the Government is the institutional agent generating the largest return with 3.1116 euros per euro received, which is further split into 0.3079 to the External Sector, 0.0117 to Firms, 1.0314 to Households and 1.7606 to the Government itself. The External Sector is the lowest income generator (1.0858 euros per euro received). The diagram also shows that Households are the institutional agent that benefits the most, earning 3.8936 euros per euro received by the other agents. Besides the above-mentioned 1.0314 euros received from the Government, Households receive 0.9864 euros from Firms and 0.0275 euros from the External Sector. In net terms, therefore, Households and the External Sector receive more than they pay (0.9719 euros and 1.0552 respectively), while the Government (−0.5237 euros) and particularly Firms (−1.9854 euros) show a negative balance.

4 Discussion

The emergence of the COVID pandemic at the beginning of 2020 was undoubtedly a turning point for the health and social fields, as well as for the other sectors of society. The economic accounts of countries deserve special attention. Public deficits increased by 11, 9.7, 9.5, 9.2,

H Matrix	Households	Firms	External Sector	Government	
Households	1.8482	0.9864	0.0275	1.0314	**3.8936**
Firms	0.0182	1.0223	0.0285	0.0117	**1.0807**
External Sector	0.2980	0.5136	1.0143	0.3079	**2.1338**
Government	0.8555	0.5509	0.0154	1.7606	**3.1823**
	3.0198	**3.0732**	**1.0858**	**3.1116**	



Source: Own elaboration

FIGURE 4
H Matrix and additive decomposition of multiplier effects. Source: Own elaboration.

7.2, 5.7 and 4.2% for Spain, Greece, Italy, France, the EMU, Portugal and Germany, respectively, with the corresponding increase in public debt to levels of 120, 205.6, 155.8, 115.7, 100, 133.6 and 69.8%, respectively (31). In response to this impact, the 30 lines of action corresponding to the RRP described in the introduction will be supported by the inflow of 140 billion euros in transfers and credits for the period 2021–2026 (12–14% GDP), which will enable a sustained increase in the Spanish GDP of 2.6 percentage points on average each year until 2031.

This is an ambitious plan for the Spanish economy that, if the design is properly executed, would produce a radical structural change in the functioning of the economy within the four main areas considered (ecological transition, digital transformation, territorial and social cohesion and gender equality) and their 10 levers. Success would allow Spain not only to rise in the ranking of developed economies, in terms of modernization, growth and development, but also to act as a leader in economic transformation, creating an itinerary that other world economies could replicate, addressing similar areas of action and applying comparable procedures. However, the evidence to date shows that funds are being received and distributed much more slowly than expected. This shortfall is exacerbated by the present commodity crisis, rising inflation and the increased cost of borrowing. Together, these factors make it very difficult to quantify the impact of the amount budgeted in the RRP.

The lines of action in the RRP referring to the Spanish LTCS focus on the transition towards a de-institutionalized model, featuring person-centred care and the development of community services and home care. Success in these areas would help overcome the limitations caused by the pandemic, and also correct inefficiencies in the LTCS that have accumulated since its inception, enabling managers to better address future challenges. Moreover, this approach takes social interests into account, as many individuals responsible for dependent persons are calling for a new model of care in which the latter can live most of the time at home, receiving the services they need and enjoying a higher quality of life and well-being (8).

The deinstitutionalization motivated by the fragility of the residential care system for older adults with the emergence of COVID-19, together with the premise that families should be able to remain at home for as much of their lives as possible, make it necessary to reorient the Spanish LTCS. Arguably, a feasible solution in the short term, and one that is plausible and viable in the long term, is the vigorous development of the home help service, together with a greater adaptation of homes to the needs of dependent persons. These changes should be effected placing the interests and preferences of dependents at the heart of the system. In the macroeconomic scenario, this would create a greater number of jobs (direct, indirect and induced) generate more added value and distribute income, lending more weight to social contributions, salaries and wages than to capital remuneration. However, we are currently unaware of the extent of these impacts, which depends on whether the service that generates them is residential care or home help. Accordingly, research is needed to estimate the impact inherent to each type of benefit and to assess the effect produced on the quality of life of dependent individuals (and by extension, that of their families). This focus is necessary so that policymakers can be offered accurate, appropriate information with which to determine the type of service that should be preferred.

In view of the above, this study establishes the bases to estimate the socioeconomic impact that the application of the RRP on the Spanish LTCS can produce in the Spanish economy. In the proposed procedure, we first describe the components of the demand linked to the investment initiatives included in the 22nd component addressing Spain's RRP and then estimate the total production necessary to satisfy this demand and calculate the jobs and income thereby generated, using our novel construction of the SAM for the Spanish economy.

The first outcomes presented focus on the features of the SAM, to evaluate the investment effects of the RRP. As previously stated, SAMs reflect the interdependence of the productive sectors and final demand with the exchanges that take place to distribute the level of income generated in the production process. This makes SAMs extremely useful for evaluating the economic impact of demand shocks, not only related to investment like the RRP plan presented here but also to spending on consumption by private and public institutions.

Having built the SAM, one of the first significant outcomes achieved, we then used it to model the RRP investment delivered in the Spanish LTCS. This modelling shows that an initial investment of 2,083.9 million euros creates 5,409.5 million euros of industrial output and generates 2,457 million euros in income for households, firms, government and the external sector, including a fiscal return of 1,098.7 million euros from taxes and social contributions. Additionally, the analysis shows that households benefit most from the RRP, receiving almost 4 euros from each euro generated, while the Government is the institutional agent obtaining the largest return (3.1 euros in one euro received under the Plan).

In addition, this level of production creates around 45.5 thousand jobs (33.2% of which are direct, 24.9% indirect, 22.1% induced and 19.8% derived from the feedback effect). From another standpoint, 2.18 jobs are created for every €100,000 invested. These results are certainly valuable as they prove that the type of investment provided by the RRP not only generates substantial benefits in terms of increasing tax revenues but also it supports employment, some of which is directly linked to the LTCS sector.

The Spanish LTCS was originally expected to have a very positive macroeconomic impact, creating 262,735 new jobs and 190,000 induced jobs, and potentially leading to the incorporation of 115,000 informal caregivers into the formal market. The expected annual fiscal return was around two billion euros, obtained as higher tax revenues and social contributions and a lower rate of unemployment (32). This forecast was subsequently re-examined. Thus, Herce et al. (33) calculated that fewer jobs would be created (in the range 160,000–175,000 jobs, depending on the methodology applied) Another study predicted a figure of 154,523 jobs, with an annual average of 137,000 jobs during the period 2007–2011, and a fiscal return of 27% via taxes and payroll contributions (34). A further study focused on the structural reform of the Spanish LTCS in 2012, concluding that it produced an additional 151,353 jobs in Spain (direct, indirect and induced) in 2012 (35).

However, to the best of our knowledge, only one study has evaluated the impact in Spain of the RRP, in terms of new jobs created. This study found that the provision of this extraordinary financing to the Spanish LTCS would generate 440,319 jobs (direct and indirect, plus induced effects) (28). This figure contrasts sharply with the 45,493 jobs estimated in the present study. The main reason for this discrepancy is that the cited study assumed public financing of 13,961 million euros, rather than the 2,083.9 million euros assigned officially in the RRP. Therefore, the present study is the first to estimate the macroeconomic impact of the RRP alone on employment.

The original design of the catalogue of benefits expected for the Spanish LTCS defines two large groups: service benefits and economic benefits (37). While the service ones have a significant preferential character, the economic ones have a residual and secondary character in preference of order of assignment. Previous studies have shown that the provision of services contributes to the creation of a greater number of jobs, production and added value than economic benefits. Thus, two out of every three jobs are generated by services while the remaining third are generated by economic benefits. If only service benefits were provided, in 2012, some 150,000 more jobs would have been created to meet the same needs of dependent people, replacing the economic benefits existing at that time (38). On the other hand, for every million euros invested in economic benefits, 16.88 jobs would be created (53.02% direct, 24.53% indirect and 22.45% induced), while every million euros invested in service benefits would generate 41.91 jobs of which 68.41% are direct, 9.16% indirect and 22.43% induced (35). In addition, given that obtaining these figures entails the use of Input–Output models, spillover effects on the different sectors of the economy can be observed. In another study, we showed the importance of the social work activities sector, given its weight within the dependency model, and its low return (39).

The main limitations of the present study are mostly related to the underlying assumptions of the Input–Output methodology. SAM models assume a fixed average technology for each economic sector, and so the input coefficients cannot change. In addition, the SAM model yields a constant return to scale and no supply constraints are considered, a question that is inadequately addressed in basic Input–Output models. Furthermore, the Spanish Input–Output table for 2021 has not yet been published, and so it was necessary to project the most recent Input–Output table available for Spain (2015), using National Accounting records. However, this approach might produce inaccuracies related to interindustry consumption.

5 Conclusion

The policy actions included in the RRP for the Spanish LTCS are intended to address the weaknesses in the system, both those pre-existing the pandemic and also, most especially, those that emerged during the crisis, specifically, the fragility of the residential care service (40). The emergence of COVID-19 in Spain led to the death of 26,500 dependent persons living in residential care, between March 2020 and May 2021, with an excess mortality of 43.5%, in addition to affecting mental health and quality of life, both for residents and family members (41).

The results of this study highlight the significant multiplier effect that RRP investment may produce to alleviate the downturn in the Spanish economy. To accomplish this, a SAM model was built for 2021, using data from basic IOTs and National Accounting data. SAM models are extremely efficient for describing how demand shocks generate and distribute production and income to both industrial and institutional sectors of the economy. Among other advantages of SAM models, they make it possible to estimate the impact on employment according to the level of production estimated and explain how institutional sectors benefit from income generation (by using the H Matrix embedded in the SAM).

The present study is of great methodological importance, providing a solid basis for evaluating different impacts on the economy (for example, we model the impact of increased or reduced expenditure on items such as pensions, education or other social priorities), by constructing a social accounting matrix (the most recent of its type). Finally, this new tool is used to evaluate the impact of the RRP, showing it to have very positive consequences for society. Nevertheless, further research is needed to provide a basis for upcoming analysis in enabling a comparison on how RRP investment has been allocated to healthcare (particularly to LTCS) and whether the potential return has met the initial expectations. The outcomes of this future research would not be only exceptionally interesting for Spain but also for the rest of European Member States.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found at: https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176806&menu=resultados&idp=1254735976608#!tabs-1254736195147.

Author contributions

FB-P, RP-R, MEA-S and PM-M: conceptualization, writing—review and editing, visualization, and supervision. FB-P: methodology and writing—original draft preparation. RP-R and PM-M: formal analysis, project administration, and funding acquisition. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1130132/full#supplementary-material

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Outcome of emergency patients transported by ambulance during the COVID-19 pandemic in Osaka Prefecture, Japan: a population-based descriptive study

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Background: The novel corona virus (COVID-19) pandemic occurred worldwide. Although an excessive burden was placed on emergency medical institutions treating urgent and severe patients, its impact on patient outcome remains unknown. This study aimed to assess the impact of the COVID-19 pandemic in 2021 on the emergency medical services (EMS) system and patient outcomes in Osaka Prefecture, Japan.

Methods: This was a retrospective descriptive study with a study period from January 1, 2019 to December 31, 2021. We included patients who were transported by ambulance and had cleaned data that was recorded in the ORION system. The study endpoints were the number of patients transported by ambulance and the number of deaths among these patients in each month. To assess the impact of the COVID-19 pandemic on the EMS system, the incidence rate ratio (IRR) and 95% confidence interval (CI) were calculated using 2019 as the reference year. Mortalities were evaluated based on deaths in the emergency department and deaths at 21 days after hospitalization.

Results: The numbers of patients transported by ambulance were 500,194 in 2019, 443,321 in 2020 (IRR: 0.88, 95% CI: 0.87–0.88), and 448,054 in 2021 (IRR: 0.90, 95% CI: 0.89–0.90). In 2019, the number of patients transported by ambulance and who died in the emergency departments was 4,980, compared to 5,485 in 2020 (IRR: 1.10, 95% CI; 1.06–1.44) and 5,925 in 2021 (IRR: 1.19, 95% CI: 1.15–1.24). In 2019, the number of patients who died within 21 days after hospitalization was 11,931, compared to 11,913 in 2020 (IRR; 1.00, 95% CI; 0.98–1.03) and 13,376 in 2021 (IRR; 1.12, 95% CI; 1.09–1.15).

Conclusion: The COVID-19 pandemic decreased the number of ambulance requests and worsened mortality of patients transported by ambulance in Osaka Prefecture during 2021.

KEYWORDS

COVID-19, pandemic, emergency medicine, EMS system, public health, epidemiology

Introduction

Novel coronavirus (COVID-19), confirmed in Wuhan, China in December 2019, spread not only in China but throughout the world (1–7). In Japan, the number of COVID-19 patients exceeded 1.7 million as of December 31, 2021 (8). COVID-19 is characterized by symptoms common to ordinary upper respiratory tract infections, such as fever, cough, general malaise, and some patients are even asymptomatic (2, 5, 7, 9). However, the severely ill patients, which account for about 20% of the patients with COVID-19, require intensive care, mainly mechanical ventilation and extracorporeal membrane oxygenation.

As the number of COVID-19 patients increased, especially in the United States and European countries, the number of healthcare workers infected with COVID-19 also increased, and the healthcare system, including emergency medical services (EMS) and intensive care, experienced a critical situation. The healthcare system in Japan is operated from public healthcare insurance, and the EMS system, through which an ambulance can be called, is a public service (10). Since the outbreak of COVID-19, patients with fever have visited specific medical institutions that can treat COVID-19 and have been diagnosed and treated for COVID-19. However, on weekends including holidays and at night when these medical institutions are not open, patients with sudden fever call for an ambulance and are transported to those emergency medical institutions that provide COVID-19 care. Many of these medical institutions include critical care centers that treat severe trauma and out-of-hospital cardiac arrest (OHCA). As a result, an excessive burden was placed on these emergency medical institutions that treat urgent and severe patients, but the impact of this situation on patient outcomes remains unknown.

Osaka Prefecture is the largest metropolitan area in western Japan, with a population of 8.8 million people and approximately a half million calls for ambulances each year (11). Since the first patient with COVID-19 occurred in Osaka Prefecture on January 23, 2020, the cumulative number of COVID-19 patients in Osaka Prefecture as of December 31, 2021 was 203,790 (12). We previously showed the impact of the spread of COVID-19 in 2020 on the EMS system and patient outcomes of those transported by ambulance (13, 14). However, in Japan, there was a marked increase in the number of COVID-19 patients in 2021 compared to 2020, which may have had a further impact. Therefore, the purpose pf this study was to assess the impact of the COVID-19 pandemic in 2021 on the EMS system and patient outcomes using population-based emergency patient registry in Osaka, Japan.

Materials and methods

Study design and settings

This was a retrospective descriptive study with a study period from January 1, 2019 to December 31, 2021. We included patients in this study who were transported by ambulance and who had cleaned data that was recorded in the ORION system. Therefore, we excluded patients who were not registered in the ORION system or had missing data.

In 2020, 8,837,685 people lived in the 1905 km^2 area of Osaka Prefecture. Of that population, 4,235,956 people (47.9%) were male and 2,441,984 people (25.4%) were older adults, aged 65 years old or more (10). Because the ORION data is anonymized without specific personal data, such as patient name, date of birth, and address, the requirement of obtaining patients' informed consent was waived. This study was approved by the Ethics Committee of Osaka University Graduate School of Medicine, Suita, Japan (approval number: 15003). This manuscript was written based on the STROBE statement to assess the reporting of cohort and cross-sectional studies (15).

EMS system and hospitals in Osaka Prefecture and Japan

The EMS system is basically the same as that used in other areas of Japan. In Osaka Prefecture, EMS systems such as ambulance dispatch systems are operated by each local government, and ambulances are dispatched by calling 1-1-9. In 2021, the EMS system was operated by 26 fire departments (298 ambulances) and 26 fire control stations. In 2018, there were 517 medical institutions (105,994 beds) in Osaka Prefecture (16), of which 288 are emergency medical hospitals including 16 critical care centers that are designated to accept patients with life-threatening emergency diseases such as severe trauma and sepsis. Since the introduction of the ORION system, EMS personnel at the scene select the appropriate hospital for emergency patients rather than a dispatcher.

The ORION system

Information on the system configuration of ORION was previously described in detail (17, 18). The EMS personnel at the scene operate the ORION smartphone app for each emergency patient. All of the data input into the cellphone app, such as vital signs and the time of the call to the hospital for acceptance, are also recorded. The cellphone app data are accumulated in the ORION cloud server, and in cooperation with the dispatched EMS personnel, data managers at each fire department directly input or upload the ambulance record of each emergency patient so that it can be connected with the app data. Furthermore, the operators of each hospital also directly input or upload the patient's data, such as diagnoses and outcomes, after hospital acceptance. The results of the aggregated data in the ORION system are fed back to every fire department and emergency hospital. The Department of Public Health of Osaka Prefecture can also analyze the effects of health policy on the emergency medical system using these collected data. The ORION system has been in place in all fire departments and emergency hospitals in Osaka Prefecture since January 2016.

Data collection and quality control

The ORION system checks for errors in the inputted in-hospital data, and the staff of each emergency hospital can correct them if necessary. Through these tasks, cellphone app data, ambulance records, and the in-hospital data such as diagnosis and prognosis can be comprehensively registered for each patient transported by an ambulance. The registered data is cleaned by the Working Group to analyze the emergency medical care system in Osaka Prefecture (17). Among the collected and cleaned data, we excluded inconsistent data that did not contain all of the cellphone app data, ambulance records, and in-hospital data such as diagnosis and prognosis. In addition, we also excluded patients whose sex as registered by the fire department did not match that registered by the hospital or whose sex was missing. We also excluded patients whose age input by the fire department and that by the hospital differed by 3 years or more. When this difference was present, we defined the age input by the hospital as the patient's true age.

Endpoints

The primary endpoints of this study were the number of patients transported by ambulance and the number of deaths among these patients for each month. These endpoints were calculated using the ORION dataset. In addition, the principal diagnoses of the patients who died were classified according to the ICD-10.

Statistical analysis

Firstly, we revealed patient characteristics as descriptive study. Categorical variables were described by real numbers and percentages, while continuous variables were described by medians and interquartile range (IQR). Age groups were categorized as children (0–14 years), adults (15–64 years), and older adults (65 years and older). The reasons for the ambulance call were divided into "fire accident," "natural disaster," "water accident," "traffic accident involving car, ship, or aircraft," "injury, poisoning, and disease due to industrial accident," "disease and injury due to sports," "other injury," "trauma due to assault," "acute disease," "interhospital transport" and "other."

Secondary, to assess the impact of the COVID-19 pandemic on the EMS system, the incidence rate ratio (IRR) and 95% confidence interval (CI) were calculated using 2019 as the reference year. Next, the number of the dead among these patients by reason for the ambulance call for each month of the above years was calculated, and the IRR and 95% CI were calculated in the same way. The IRR was calculated based on the population of Osaka Prefecture determined by the census in 2020 (11). Mortalities were evaluated based on deaths in the emergency department and deaths at 21 days after hospitalization.

In addition, IRRs and 95% CIs were calculated for subgroup analysis limited to patients who called for an ambulance because of "acute disease." The age groups were classified as children (0–19 years), adults (20–64 years), and older adults (65 years and older). As in the main analysis, the number of the dead among these patients was calculated on a monthly basis, and the IRR and 95% CI were calculated in the same way. Finally, the odds ratios (ORs) and 95% CIs were calculated to evaluate the percentage of mortality by reason for ambulance call. Statistical analyses were implemented using STATA version 16.0MP (STAT Corp., College Station, TX, United States).

Results

In this study, we included 1,381,581 data-cleaned patients who registered in the ORION system. Of these patients, 500,206 patients were in 2019, 443,321 patients were in 2020, and 448,054 patients were in 2021 (Figure 1). Figure 2 shows the incidence of COVID-19 patients in Osaka and the incidence of patients transported by ambulance during study periods.

Table 1 shows the patient characteristics in this study. The median of age was 71 years [interquartile range (IQR): 46–82], and 705,972 patients (50.7%) were male. The most common reason for ambulance call was "acute disease" in 946, 778 patients (68.0%), followed by "other injury" (220,149, 15.8%) and "traffic accident" (98,583, 7.1%). The outcome of these patients at the emergency departments were hospitalization in 594,090 (42.7%), discharge home in 760,145 (54.6%), interhospital transfer in 20,840 (1.5%), and death in 16,390 (1.2%). Among the hospitalized patients, the outcomes at 21 days after hospitalization were 167,883 (28.4%) for continuation of hospitalization, 342,102(57.8%) for discharge home, 44,643 (7.5%) for interhospital transfer, and 37,270 (6.3%) for death.

Table 2 shows the number of patients transported by ambulance in 2019, 2020, and 2021 by reason for ambulance call and IRRs and 95% CIs. The numbers of patients transported by ambulance were 500,194 in 2019, 443,321 in 2020 (IRR: 0.88, 95% CI: 0.87–0.88), and 448,054 in 2021 (IRR: 0.90, 95% CI: 0.89–0.90). The most common reason for an ambulance call in 2020, 2021, and 2019 was "acute disease," with the following numbers: 340,655 in 2019, 300,502 in 2020, and 305,611 in 2021. The lowest IRR during the study period for reason for ambulance call was for "disease and injury due to sport" in both 2020 (IRR: 0.57, 95% CI: 0.53–0.60) and 2021 (IRR: 0.69, 95% CI: 0.65–0.73). In terms of the IRR for number of patients transported by ambulance by month, April had the lowest IRR in 2020 (IRR: 0.78, 95% CI: 0.76–0.79), and January had the lowest IRR in 2021 (IRR: 0.78, 95% CI: 0.77–0.79).

Table 3 shows the number of patients transported by ambulance, IRRs and 95% CIs by age group for each year. For children, the number of patients transported by ambulance decreased throughout the year in 2020 and 2021, with the lowest IRR in January 2021 (IRR: 0.42, 95% CI: 0.40–0.45). For adults, the IRRs were lowest in April 2020 (IRR: 0.76, 95% CI: 0.74–0.78) and January 2021 (IRR: 0.76, 95% CI: 0.74–0.78). Among older adults, the IRR was lowest in April 2020 (IRR: 0.84, 95% CI: 0.82–0.85), whereas the numbers of patients transported by ambulance in March 2021 (IRR: 0.99, 95% CI: 0.97–1.01), October 2021 (IRR: 1.00, 95% CI: 0.98–1.01), and December 2021 (IRR: 1.01, 95% CI: 0.99–1.03) were similar to those in 2019 before the COVID-19 pandemic.

Table 4 shows the number of patients who were transported by ambulance and died in the emergency departments for each year. In 2019, the number was 4,980, compared to 5,485 in 2020 (IRR: 1.10,

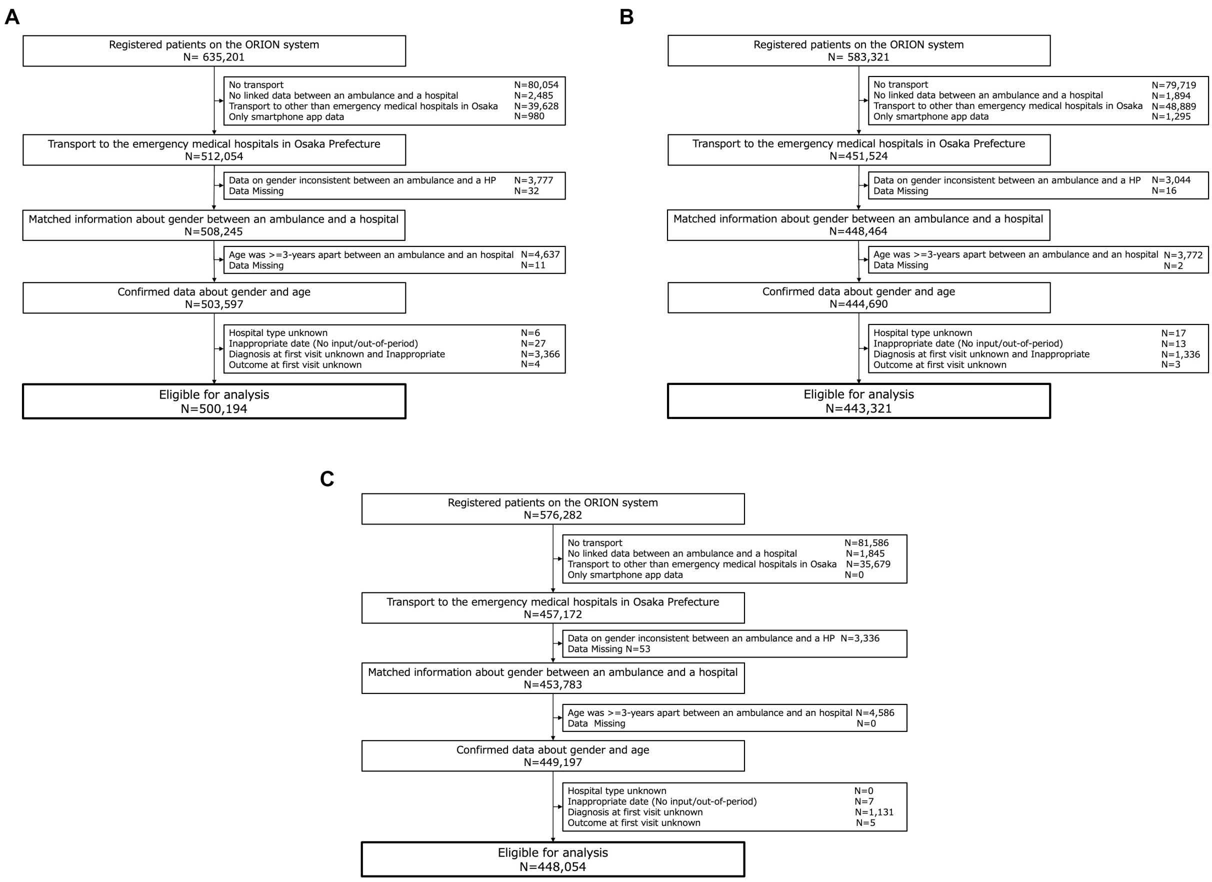

FIGURE 1
Patient flow in this study.

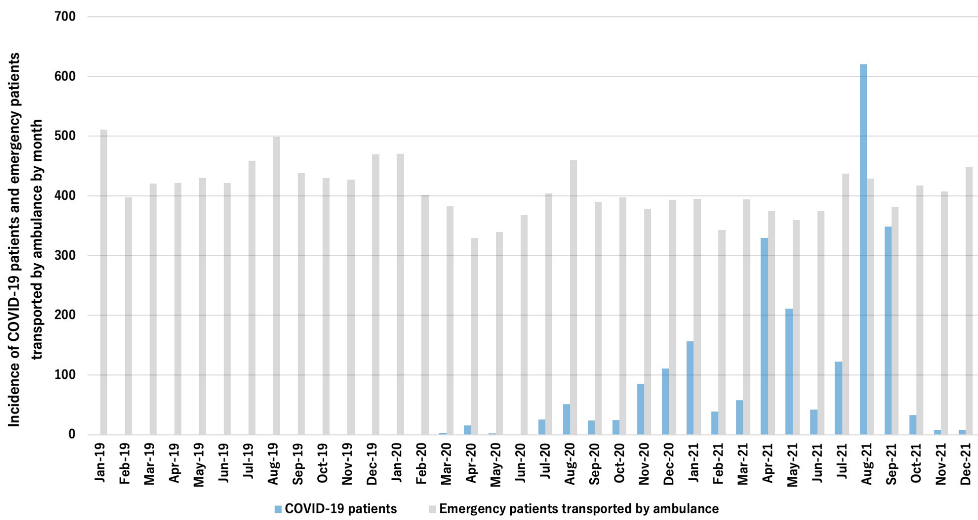

FIGURE 2
Incidence of emrgency patients transported by ambulance and COVID-19 patients per 100,000 residents.

95% CI: 1.06–1.44) and 5,925 in 2021 (IRR: 1.19, 95% CI: 1.15–1.24). In 2020, August had the highest IRR (IRR: 1.34, 95% CI: 1.16–1.54) and in 2021, May had the highest IRR (IRR: 1.46, 95% CI: 1.27–1.67).

Table 5 shows the number of patients who died within 21 days after hospitalization and the IRR for each year. In 2019, the number was 11,931, compared to 11,963 in 2020 (IRR: 1.00, 95% CI:

TABLE 1 Clinical characteristics of patients in this study.

Characteristic	Total (*n* = 1,391,581)		2019 (*n* = 500,206)		2020 (*n* = 443,321)		2021 (*n* = 448,054)	
Age, years, median (IQR)	71	(46–82)	70	(43–81)	71	(47–82)	72	(47–83)
Age group, n (%)								
0–19 years old	94,208	(6.8)	39,592	(7.9)	25,819	(5.8)	28,797	(6.4)
20–64 years old	4,79,463	(34.5)	1,74,002	(34.8)	1,51,924	(34.3)	1,53,537	(34.3)
Over 65 years old	8,17,910	(58.8)	2,86,612	(57.3)	2,65,578	(59.9)	2,65,720	(59.3)
Male, *n* (%)	7,05,972	(50.7)	2,52,828	(50.5)	2,25,222	(50.8)	2,27,922	(50.9)
Reason for ambulance call, n (%)								
Fire accident	1,095	(0.1)	412	(0.1)	353	(0.1)	330	(0.1)
Natural disaster	47	(0.0)	10	(0.0)	13	(0.0)	24	(0.0)
Water accident	149	(0.0)	52	(0.0)	43	(0.0)	54	(0.0)
Traffic accidents involving car, ship, and aircraft	98,583	(7.1)	36,199	(7.2)	31,134	(7.0)	31,250	(7.1)
Injury, poisoning, and disease due to industrial accident	12,677	(0.9)	4,798	(1.0)	3,933	(0.9)	3,946	(0.9)
Disease and injury due to sport	6,374	(0.5)	2,825	(0.6)	1,604	(0.4)	1,945	(0.5)
Other injury	2,20,149	(15.8)	77,819	(15.6)	71,762	(16.2)	70,568	(15.8)
Trauma due to assault	7,408	(0.5)	2,796	(0.6)	2,474	(0.6)	2,138	(0.5)
Self-induced injury	9,030	(0.6)	2,954	(0.6)	3,067	(0.7)	3,009	(0.6)
Acute disease	9,46,778	(68.0)	3,40,665	(68.1)	3,00,502	(67.8)	3,05,611	(68.0)
Interhospital transfer	88,935	(6.4)	31,497	(6.3)	28,334	(6.4)	29,104	(6.4)
Others	356	(0.0)	179	(0.0)	102	(0.0)	75	(0.0)
Place, n (%)								
Home	8,33,230	(59.9)	2,93,704	(58.7)	2,67,834	(60.4)	2,71,742	(60.6)
Public space	3,26,861	(23.5)	1,20,642	(24.1)	1,01,342	(22.9)	1,04,877	(23.4)
Workplace	31,956	(2.3)	11,603	(2.3)	10,166	(2.3)	10,187	(2.3)
Road	1,84,581	(13.3)	68,710	(13.7)	59,339	(13.4)	56,532	(12.6)
Other	14,903	(1.1)	5,547	(1.1)	4,640	(1.0)	4,716	(1.1)
Outcome at emergency department, n (%)								
Hospitalization	5,94,090	(42.7)	2,03,894	(40.8)	1,93,060	(43.5)	1,97,136	(44.0)
Discharge to home	7,60,145	(54.6)	2,84,183	(56.8)	2,38,026	(53.7)	2,37,936	(53.1)
Interhospital transfer	20,840	(1.5)	7,105	(1.4)	6,721	(1.5)	7,014	(1.6)
Death	16,390	(1.2)	4,980	(1.0)	5,485	(1.2)	5,925	(1.3)
Other	116	(0.0)	44	(0.0)	29	(0.0)	43	(0.0)
Outcomes at 21 days after hospitalization, n (%)								
Continuation of hospitalization	1,67,883	(28.4)	56,489	(27.9)	55,256	(28.7)	56,138	(28.5)
Discharge to home	3,42,102	(57.8)	1,21,131	(59.8)	1,10,606	(57.5)	1,10,365	(56.0)
Interhospital transfer	44,643	(7.5)	12,885	(6.4)	14,675	(7.6)	17,083	(8.7)
Death	37,270	(6.3)	11,931	(5.9)	11,963	(6.2)	13,376	(6.8)

IQR; interquartile range.

0.98–1.03) and 13,376 in 2021 (IRR: 1.12, 95% CI: 1.09–1.15). In the analysis by month, the number of dead patients did not increase or decrease in 2020, whereas in 2021, the number increased in March (IRR: 1.12, 95% CI: 1.03–1.22), April (IRR: 1.37, 95% CI: 1.26–1.49), May (IRR: 1.29, 95% CI: 1.18–1.41), August (IRR: 1.21, 95% CI: 1.11–1.33), and October (IRR: 1.12, 95% CI: 1.02–1.22). There were no

TABLE 2 Number of emergency patients registered in the Osaka emergency information research intelligent operation network system.

Reason for ambulance call	January	February	March	April	May	June	July	August	September	October	November	December	Total
Fire accident													
2019	58	37	40	34	33	21	38	26	35	29	25	36	412
2020	52	37	28	22	29	18	24	31	12	26	26	48	353
2021	34	28	31	33	23	19	24	22	17	23	35	41	330
IRR: 2019 vs. 2020 (95% CI)	0.90 (0.60–1.33)	1.00 (0.62–1.62)	0.70 (0.42–1.16)	0.65 (0.36–1.14)	0.88 (0.51–1.49)	0.86 (0.43–1.69)	0.63 (0.36–1.08)	1.19 (0.69–2.09)	0.34 (0.16–0.68)	0.90 (0.51–1.58)	1.04 (0.58–1.88)	1.33 (0.85–2.11)	0.86 (0.74–0.99)
IRR: 2019 vs. 2021 (95% CI)	0.59 (0.37–0.91)	0.76 (0.45–1.27)	0.78 (0.47–1.27)	0.97 (0.58–1.62)	0.70 (0.39–1.22)	0.90 (0.46–1.77)	0.63 (0.36–1.08)	0.85 (0.46–1.55)	0.49 (0.26–0.89)	0.79 (0.44–1.42)	1.40 (0.81–2.44)	1.14 (0.71–1.83)	0.80 (0.69–0.93)
Natural disaster													
2019	0	0	0	0	0	3	2	1	0	4	0	0	10
2020	8	0	0	0	0	1	2	0	0	2	0	0	13
2021	0	0	0	0	0	0	0	22	0	0	0	2	24
IRR: 2019 vs. 2020 (95% CI)	NA	NA	NA	NA	NA	0.33 (0.01–4.15)	1.00 (0.07–13.80)	NA	NA	0.50 (0.05–3.49)	NA	NA	1.30 (0.53–3.31)
IRR: 2019 vs. 2021 (95% CI)	NA	NA	NA	NA	NA	NA	NA	22.00 (3.56–907.95)	NA	NA	NA	NA	2.40 (1.11–5.62)
Water accident													
2019	5	3	6	2	2	2	7	9	9	3	1	3	52
2020	3	4	2	6	3	5	4	2	4	5	2	3	43
2021	3	3	5	2	2	5	9	7	2	6	5	5	54
IRR: 2019 vs. 2020 (95% CI)	0.60 (0.09–3.08)	1.33 (0.23–9.10)	0.33 (0.03–1.86)	3.00 (0.54–30.39)	1.50 (0.17–17.96)	2.50 (0.41–26.25)	0.57 (0.12–2.25)	0.22 (0.02–1.07)	0.44 (0.10–1.59)	1.67 (0.32–10.73)	2.00 (0.10–117.99)	1.00 (0.13–7.47)	0.83 (0.54–1.26)
IRR: 2019 vs. 2021 (95% CI)	0.60 (0.09–3.08)	1.00 (0.13–7.47)	0.83 (0.20–3.28)	1.00 (0.07–13.80)	1.00 (0.07–13.80)	2.50 (0.41–26.25)	1.29 (0.43–4.06)	0.78 (0.25–2.35)	0.22 (0.02–1.07)	2.00 (0.43–12.36)	5.00 (0.56–236.49)	1.67 (0.32–10.73)	1.04 (0.70–1.55)
Traffic accident involving car, ship, or aircraft													
2019	2,620	2,510	2,997	3,248	3,024	2,878	3,198	3,068	3,067	3,207	3,223	3,159	36,199
2020	2,635	2,578	2,679	1,891	2,127	2,658	2,843	2,695	2,678	2,820	2,712	2,818	31,134

(Continued)

10.3389/fpubh.2023.1322236

TABLE 2 (Continued)

Reason for ambulance call	January	February	March	April	May	June	July	August	September	October	November	December	Total
2021	2,379	2,303	2,590	2,442	2,219	2,625	2,814	2,505	2,432	2,952	2,812	3,177	31,250
IRR: 2019 vs. 2020 (95% CI)	1.01 (0.95–1.06)	1.03 (0.97–1.09)	0.89 (0.85–0.94)	0.58 (0.55–0.62)	0.70 (0.67–0.74)	0.92 (0.88–0.97)	0.89 (0.84–0.94)	0.88 (0.83–0.93)	0.87 (0.83–0.92)	0.88 (0.84–0.93)	0.84 (0.80–0.89)	0.89 (0.85–0.94)	0.86 (0.85–0.87)
IRR: 2019 vs. 2021 (95% CI)	0.91 (0.86–0.96)	0.92 (0.87–0.97)	0.86 (0.82–0.91)	0.75 (0.71–0.79)	0.73 (0.69–0.78)	0.91 (0.86–0.96)	0.88 (0.84–0.93)	0.82 (0.77–0.86)	0.79 (0.75–0.84)	0.92 (0.88–0.97)	0.87 (0.83–0.92)	1.01 (0.96–1.06)	0.86 (0.85–0.88)
Injury, poisoning, and disease due to industrial accident													
2019	348	321	370	365	374	385	497	542	455	406	370	365	4,798
2020	279	317	274	282	253	349	344	504	342	368	316	305	3,933
2021	281	257	334	278	259	348	394	354	314	376	384	367	3,946
IRR: 2019 vs. 2020 (95% CI)	0.80 (0.68–0.94)	0.99 (0.84–1.16)	0.74 (0.63–0.87)	0.77 (0.66–0.90)	0.68 (0.57–0.80)	0.91 (0.78–1.05)	0.69 (0.60–0.80)	0.93 (0.82–1.05)	0.75 (0.65–0.87)	0.91 (0.78–1.05)	0.85 (0.73–1.00)	0.84 (0.72–0.98)	0.82 (0.79–0.86)
IRR: 2019 vs. 2021 (95% CI)	0.81 (0.69–0.95)	0.80 (0.68–0.95)	0.90 (0.78–1.05)	0.76 (0.65–0.89)	0.69 (0.59–0.81)	0.90 (0.78–1.05)	0.79 (0.69–0.91)	0.65 (0.57–0.75)	0.69 (0.60–0.80)	0.93 (0.80–1.07)	1.04 (0.90–1.20)	1.01 (0.87–1.17)	0.82 (0.79–0.86)
Disease and injury due to sport													
2019	135	166	232	232	252	281	289	295	309	227	213	194	2,825
2020	141	144	51	23	17	76	146	282	225	192	194	113	1,604
2021	71	109	154	137	89	157	276	199	140	222	210	181	1,945
IRR: 2019 vs. 2020 (95% CI)	1.04 (0.82–1.33)	0.87 (0.69–1.09)	0.22 (0.16–0.30)	0.10 (0.06–0.15)	0.07 (0.04–0.11)	0.27 (0.21–0.35)	0.51 (0.41–0.62)	0.96 (0.81–1.13)	0.73 (0.61–0.87)	0.85 (0.69–1.03)	0.91 (0.75–1.11)	0.58 (0.46–0.74)	0.57 (0.53–0.60)
IRR: 2019 vs. 2021 (95% CI)	0.53 (0.39–0.71)	0.66 (0.51–0.84)	0.66 (0.54–0.82)	0.59 (0.47–0.73)	0.35 (0.27–0.45)	0.56 (0.46–0.68)	0.96 (0.81–1.13)	0.67 (0.56–0.81)	0.45 (0.37–0.55)	0.98 (0.81–1.18)	0.99 (0.81–1.20)	0.93 (0.76–1.15)	0.69 (0.65–0.73)
Other injury													
2019	7,116	5,753	6,317	6,400	6,157	5,891	6,312	6,518	6,253	6,800	6,785	7,516	77,818
2020	6,936	6,151	5,925	5,021	5,237	5,536	6,037	5,837	5,752	6,645	6,133	6,552	71,762
2021	6,299	5,344	6,116	5,368	5,035	5,066	5,834	5,437	5,129	6,548	6,740	7,652	70,568

(Continued)

TABLE 2 (Continued)

Reason for ambulance call	January	February	March	April	May	June	July	August	September	October	November	December	Total
IRR: 2019 vs. 2020 (95% CI)	0.97 (0.94–1.01)	1.07 (1.03–1.11)	0.94 (0.91–0.97)	0.78 (0.76–0.81)	0.85 (0.82–0.88)	0.94 (0.91–0.98)	0.96 (0.92–0.99)	0.90 (0.86–0.93)	0.92 (0.89–0.95)	0.98 (0.94–1.01)	0.90 (0.87–0.94)	0.87 (0.84–0.90)	0.92 (0.91–0.93)
IRR: 2019 vs. 2021 (95% CI)	0.89 (0.86–0.92)	0.93 (0.89–0.96)	0.97 (0.93–1.00)	0.84 (0.81–0.87)	0.82 (0.79–0.85)	0.86 (0.83–0.89)	0.92 (0.89–0.96)	0.83 (0.80–0.86)	0.82 (0.79–0.85)	0.96 (0.91–1.00)	0.99 (0.96–1.03)	1.02 (0.99–1.05)	0.91 (0.90–0.92)
Trauma due to assault													
2019	268	207	232	232	224	228	226	256	225	217	229	252	2,796
2020	250	225	229	171	197	210	218	185	197	202	185	205	2,474
2021	157	157	193	133	169	165	200	166	147	241	195	215	2,138
IRR: 2019 vs. 2020 (95% CI)	0.93 (0.78–1.11)	1.09 (0.90–1.32)	0.99 (0.82–1.19)	0.74 (0.60–0.90)	0.88 (0.72–1.07)	0.92 (0.76–1.12)	0.96 (0.80–1.17)	0.72 (0.59–0.88)	0.88 (0.72–1.06)	0.93 (0.76–1.13)	0.81 (0.66–0.98)	0.81 (0.67–0.98)	0.88 (0.84–0.93)
IRR: 2019 vs. 2021 (95% CI)	0.59 (0.48–0.72)	0.76 (0.61–0.94)	0.83 (0.68–1.01)	0.57 (0.46–0.71)	0.75 (0.61–0.93)	0.72 (0.59–0.89)	0.88 (0.73–1.08)	0.65 (0.53–0.79)	0.65 (0.53–0.81)	1.11 (0.92–1.34)	0.85 (0.70–1.04)	0.85 (0.71–1.03)	0.76 (0.72–0.81)
Self-induced injury													
2019	197	195	245	216	254	291	286	270	254	258	240	247	2,953
2020	265	217	250	184	253	270	315	267	316	297	204	229	3,067
2021	254	259	268	228	224	246	254	248	265	249	239	275	3,009
IRR: 2019 vs. 2020 (95% CI)	1.35 (1.11–1.63)	1.11 (0.91–1.36)	1.02 (0.85–1.22)	0.85 (0.70–1.04)	1.00 (0.83–1.19)	0.93 (0.78–1.10)	1.10 (0.94–1.30)	0.99 (0.83–1.18)	1.24 (1.05–1.47)	1.15 (0.97–1.37)	0.85 (0.70–1.03)	0.93 (0.77–1.11)	1.04 (0.99–1.09)
IRR: 2019 vs. 2021 (95% CI)	1.28 (1.06–1.55)	1.33 (1.10–1.61)	1.09 (0.92–1.31)	1.06 (0.87–1.28)	0.88 (0.73–1.06)	0.85 (0.71–1.01)	0.89 (0.75–1.06)	0.92 (0.77–1.10)	1.04 (0.88–1.24)	0.97 (0.81–1.15)	1.00 (0.83–1.20)	1.11 (0.93–1.33)	1.02 (0.97–1.07)
Acute disease													
2019	34,239	25,757	26,544	26,370	27,524	27,131	29,555	32,882	27,935	26,681	26,538	29,499	3,40,655
2020	30,857	25,663	24,224	21,363	21,760	23,247	25,619	30,656	24,781	24,418	23,563	24,351	3,00,502
2021	25,283	21,683	25,002	24,280	23,620	24,286	28,665	28,821	25,163	26,088	25,236	27,484	3,05,611

(Continued)

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TABLE 2 (Continued)

Reason for ambulance call	January	February	March	April	May	June	July	August	September	October	November	December	Total
IRR: 2019 vs. 2020 (95% CI)	0.90 (0.89–0.92)	1.00 (0.98–1.01)	0.91 (0.90–0.93)	0.81 (0.80–0.82)	0.79 (0.78–0.80)	0.86 (0.84–0.87)	0.87 (0.85–0.88)	0.93 (0.92–0.95)	0.89 (0.87–0.90)	0.92 (0.90–0.93)	0.89 (0.87–0.90)	0.83 (0.81–0.84)	0.88 (0.88–0.89)
IRR: 2019 vs. 2021 (95% CI)	0.74 (0.73–0.75)	0.84 (0.83–0.86)	0.94 (0.93–0.96)	0.92 (0.90–0.94)	0.86 (0.84–0.87)	0.90 (0.88–0.91)	0.97 (0.95–0.99)	0.88 (0.86–0.89)	0.90 (0.89–0.92)	0.98 (0.96–0.99)	0.95 (0.93–0.97)	0.93 (0.92–0.95)	0.90 (0.89–0.90)
Interhospital transport													
2019	2,897	2,445	2,626	2,732	2,553	2,492	2,662	2,560	2,493	2,581	2,601	2,855	31,497
2020	2,895	2,451	2,367	1,924	1,959	1,996	2,395	2,424	2,282	2,493	2,533	2,615	28,334
2021	2,608	2,180	2,450	2,390	2,323	2,293	2,393	2,542	2,381	2,369	2,460	2,715	29,104
IRR: 2019 vs. 2020 (95% CI)	1.00 (0.95–1.05)	1.00 (0.95–1.06)	0.90 (0.85–0.95)	0.70 (0.66–0.75)	0.77 (0.72–0.81)	0.80 (0.75–0.85)	0.90 (0.85–0.95)	0.95 (0.90–1.00)	0.92 (0.86–0.97)	0.97 (0.91–1.02)	0.97 (0.92–1.03)	0.92 (0.87–0.97)	0.90 (0.89–0.91)
IRR: 2019 vs. 2021 (95% CI)	0.90 (0.85–0.95)	0.89 (0.84–0.94)	0.93 (0.88–0.99)	0.87 (0.83–0.92)	0.91 (0.86–0.96)	0.92 (0.87–0.97)	0.90 (0.85–0.95)	0.99 (0.94–1.05)	0.96 (0.90–1.01)	0.92 (0.87–0.97)	0.95 (0.89–1.00)	0.95 (0.90–1.00)	0.92 (0.91–0.94)
Other													
2019	14	9	13	11	13	12	11	7	11	7	11	60	179
2020	9	6	9	11	9	5	8	15	4	11	5	10	102
2021	6	2	5	10	5	12	9	4	8	5	5	4	75
IRR: 2019 vs. 2020 (95% CI)	0.64 (0.25–1.59)	0.67 (0.20–2.10)	0.69 (0.26–1.75)	1.00 (0.39–2.54)	0.69 (0.26–1.75)	0.42 (0.11–1.27)	0.73 (0.25–1.99)	2.14 (0.82–6.21)	0.36 (0.08–1.23)	1.57 (0.56–4.78)	0.45 (0.12–1.42)	0.17 (0.08–0.33)	0.57 (0.44–0.73)
IRR: 2019 vs. 2021 (95% CI)	0.43 (0.13–1.19)	0.22 (0.02–1.07)	0.38 (0.11–1.15)	0.91 (0.35–2.36)	0.38 (0.11–1.15)	1.00 (0.41–2.43)	0.82 (0.30–2.17)	0.57 (0.12–2.25)	0.73 (0.25–1.99)	0.71 (0.18–2.61)	0.45 (0.12–1.42)	0.07 (0.02–0.18)	0.42 (0.32–0.55)
Total													
2019	47,897	37,403	39,622	39,842	40,410	39,615	43,083	46,434	41,046	40,420	40,236	44,186	5,00,194
2020	44,330	37,793	36,038	30,898	31,844	34,371	37,955	42,898	36,593	37,479	35,873	37,249	4,43,321
2021	37,375	32,325	37,148	35,301	33,968	35,222	40,872	40,327	35,998	39,079	38,321	42,118	4,48,054

(Continued)

TABLE 2 (Continued)

Reason for ambulance call	January	February	March	April	May	June	July	August	September	October	November	December	Total
IRR: 2019 vs. 2020 (95% CI)	0.93 (0.91–0.94)	1.01 (1.00–1.03)	0.91 (0.90–0.92)	0.78 (0.76–0.79)	0.79 (0.78–0.80)	0.87 (0.86–0.88)	0.88 (0.87–0.89)	0.92 (0.91–0.94)	0.89 (0.88–0.90)	0.93 (0.91–0.94)	0.89 (0.88–0.90)	0.84 (0.83–0.85)	0.89 (0.88–0.89)
IRR: 2019 vs. 2021 (95% CI)	0.78 (0.77–0.79)	0.86 (0.85–0.88)	0.94 (0.92–0.95)	0.89 (0.87–0.90)	0.84 (0.83–0.85)	0.89 (0.88–0.90)	0.95 (0.94–0.96)	0.87 (0.86–0.88)	0.88 (0.86–0.89)	0.97 (0.95–0.98)	0.95 (0.94–0.97)	0.95 (0.94–0.97)	0.90 (0.89–0.90)

IRR, incidence rate ratio; CI, confidence interval; NA, not assessed. IRR is for 2020 versus 2019.

TABLE 3 Number of emergency patients registered in the ORION system by age group.

Age group	January	February	March	April	May	June	July	August	September	October	November	December	Total
Total													
2019	47,897	37,403	39,622	39,842	40,410	39,615	43,083	46,434	41,046	40,420	40,236	44,186	5,00,194
2020	44,330	37,793	36,038	30,898	31,844	34,371	37,955	42,898	36,593	37,479	35,873	37,249	4,43,321
2021	37,375	32,325	37,148	35,301	33,968	35,222	40,872	40,327	35,998	39,079	38,321	42,118	4,48,054
IRR:2019 vs. 2020 (95% CI)	0.93 (0.91–0.94)	1.01 (1.00–1.03)	0.91 (0.90–0.92)	0.78 (0.76–0.79)	0.79 (0.78–0.80)	0.87 (0.86–0.88)	0.88 (0.87–0.89)	0.92 (0.91–0.94)	0.89 (0.88–0.90)	0.93 (0.91–0.94)	0.89 (0.88–0.90)	0.84 (0.83–0.85)	0.89 (0.88–0.89)
IRR:2019 vs. 2021 (95% CI)	0.78 (0.77–0.79)	0.86 (0.85–0.88)	0.94 (0.92–0.95)	0.89 (0.87–0.90)	0.84 (0.83–0.85)	0.89 (0.88–0.90)	0.95 (0.94–0.96)	0.87 (0.86–0.88)	0.88 (0.86–0.89)	0.97 (0.95–0.98)	0.95 (0.94–0.97)	0.95 (0.94–0.97)	0.90 (0.89–0.90)
Children (age: 0–14 years)													
2019	4,151	2,784	3,001	3,368	3,481	3,724	3,618	3,254	3,102	2,893	2,766	3,450	39,592
2020	3,328	2,480	2,090	1,748	1,682	1,851	2,173	2,192	2,009	2,213	2,116	1,937	25,819
2021	1,748	1,697	2,262	2,588	2,605	3,036	2,904	2,307	2,026	2,629	2,482	2,513	28,797
IRR:2019 vs. 2020 (95% CI)	0.82 (0.79–0.86)	0.89 (0.85–0.94)	0.70 (0.67–0.74)	0.51 (0.49–0.54)	0.50 (0.48–0.53)	0.56 (0.53–0.58)	0.66 (0.63–0.69)	0.73 (0.70–0.76)	0.69 (0.66–0.72)	0.79 (0.76–0.83)	0.80 (0.76–0.84)	0.60 (0.57–0.63)	0.68 (0.67–0.69)

(Continued)

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TABLE 3 (Continued)

Age group	January	February	March	April	May	June	July	August	September	October	November	December	Total
IRR:2019 vs. 2021 (95% CI)	0.42 (0.40–0.45)	0.61 (0.57–0.65)	0.75 (0.71–0.80)	0.77 (0.73–0.81)	0.75 (0.71–0.79)	0.82 (0.78–0.86)	0.80 (0.76–0.84)	0.71 (0.67–0.75)	0.65 (0.62–0.69)	0.91 (0.86–0.96)	0.90 (0.85–0.95)	0.73 (0.69–0.77)	0.73 (0.72–0.74)
Adults (age: 15–64 years)													
2019	14,886	12,338	13,760	13,820	14,200	14,235	15,904	17,296	14,929	14,354	13,411	14,869	1,74,002
2020	14,312	12,370	12,323	10,553	11,145	12,458	14,256	15,734	12,888	12,759	11,719	11,407	1,51,924
2021	11,321	10,300	12,244	11,875	11,687	12,137	15,070	15,973	13,428	13,375	12,635	13,492	1,53,537
IRR:2019 vs. 2020 (95% CI)	0.96 (0.94–0.98)	1.00 (0.98–1.03)	0.90 (0.87–0.92)	0.76 (0.74–0.78)	0.78 (0.77–0.80)	0.88 (0.85–0.90)	0.90 (0.88–0.92)	0.91 (0.89–0.93)	0.86 (0.84–0.88)	0.89 (0.87–0.91)	0.87 (0.85–0.90)	0.77 (0.75–0.79)	0.87 (0.87–0.88)
IRR:2019 vs. 2021 (95% CI)	0.76 (0.74–0.78)	0.83 (0.81–0.86)	0.89 (0.87–0.91)	0.86 (0.84–0.88)	0.82 (0.80–0.84)	0.85 (0.83–0.87)	0.95 (0.93–0.97)	0.92 (0.90–0.94)	0.90 (0.88–0.92)	0.93 (0.91–0.95)	0.94 (0.92–0.97)	0.91 (0.89–0.93)	0.88 (0.88–0.89)
Older adults (age: ≥65 years)													
2019	28,864	22,281	22,861	22,654	22,729	21,656	23,561	25,884	23,015	23,173	24,059	25,867	2,86,604
2020	26,690	22,943	21,625	18,597	19,017	20,062	21,526	24,972	21,696	22,507	22,038	23,905	2,65,578
2021	24,306	20,328	22,642	20,838	19,676	20,049	22,898	22,047	20,544	23,075	23,204	26,113	2,65,720
IRR:2019 vs. 2020 (95% CI)	0.92 (0.91–0.94)	1.03 (1.01–1.05)	0.95 (0.93–0.96)	0.82 (0.81–0.84)	0.84 (0.82–0.85)	0.93 (0.91–0.94)	0.91 (0.90–0.93)	0.96 (0.95–0.98)	0.94 (0.93–0.96)	0.97 (0.95–0.99)	0.92 (0.90–0.93)	0.92 (0.91–0.94)	0.93 (0.92–0.93)
IRR:2019 vs. 2021 (95% CI)	0.84 (0.83–0.86)	0.91 (0.90–0.93)	0.99 (0.97–1.01)	0.92 (0.90–0.94)	0.87 (0.85–0.88)	0.93 (0.91–0.94)	0.97 (0.95–0.99)	0.85 (0.84–0.87)	0.89 (0.88–0.91)	1.00 (0.98–1.01)	0.96 (0.95–0.98)	1.01 (0.99–1.03)	0.93 (0.92–0.93)

IRR, incidence rate ratio; CI, confidence interval. IRR is for 2020 versus 2019.

TABLE 4 Number of deaths in the emergency department after hospital arrival registered in the ORION system.

	January	February	March	April	May	June	July	August	September	October	November	December	Total
2019	664	497	436	399	366	334	320	339	357	350	413	505	4,980
2020	531	519	467	423	412	332	367	453	401	414	507	659	5,485
2021	687	539	484	505	533	364	395	443	389	436	500	650	5,925
IRR (95% CI); 2019 vs. 2020	0.80 (0.71–0.90)	1.04 (0.92–1.18)	1.07 (0.94–1.22)	1.06 (0.92–1.22)	1.13 (0.98–1.30)	0.99 (0.85–1.16)	1.15 (0.98–1.34)	1.34 (1.16–1.54)	1.12 (0.97–1.30)	1.18 (1.02–1.37)	1.23 (1.08–1.40)	1.30 (1.16–1.47)	1.10 (1.06–1.14)
IRR (95% CI); 2019 vs. 2021	1.03 (0.93–1.15)	1.08 (0.96–1.23)	1.11 (0.97–1.27)	1.27 (1.11–1.45)	1.46 (1.27–1.67)	1.09 (0.94–12.7)	1.23 (1.06–1.43)	1.31 (1.13–1.51)	1.09 (0.94–1.26)	1.25 (1.08–1.44)	1.21 (1.06–1.38)	1.29 (1.14–1.45)	1.19 (1.15–1.24)

IRR, incidence rate ratio; CI, confidence interval.

TABLE 5 Number of deaths among hospitalized patients in the emergency department after hospital arrival registered in the ORION system.

	January	February	March	April	May	June	July	August	September	October	November	December	Total
2019	1,325	1,018	1,006	961	927	808	901	847	890	984	1,096	1,168	11,931
2020	1,251	1,070	1,058	912	898	839	870	915	872	979	1,062	1,237	11,963
2021	1,432	1,011	1,129	1,314	1,195	897	961	1,027	951	1,099	1,101	1,259	13,376
IRR (95% CI); 2019 vs. 2020	0.94 (0.87–1.02)	1.05 (0.96–1.15)	1.05 (0.96–1.15)	0.95 (0.87–1.04)	0.97 (0.88–1.06)	1.04 (0.94–1.15)	0.97 (0.88–1.06)	1.08 (0.98–1.19)	0.98 (0.89–1.08)	0.99 (0.91–1.09)	0.97 (0.89–1.06)	1.06 (0.98–1.15)	1.00 (0.98–1.03)
IRR (95% CI); 2019 vs. 2021	1.08 (1.00–1.17)	0.99 (0.91–1.08)	1.12 (1.03–1.22)	1.37 (1.26–1.49)	1.29 (1.18–1.41)	1.11 (1.01–1.22)	1.07 (0.97–1.17)	1.21 (1.11–1.33)	1.07 (0.97–1.17)	1.12 (1.02–1.22)	1.00 (0.92–1.09)	1.08 (0.99–1.17)	1.12 (1.09–1.15)

IRR, incidence rate ratio; CI, confidence interval.

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reasons for ambulance calls that showed a statically significant impact between 2019 and 2020, and no statistically significant differences were identified between 2019 and 2020.

Table 6 shows the number of deaths in the emergency department by reason for ambulance call. Mortality increased statistically for "acute disease," from 1.2% (4,166/340,665) in 2019 to 1.5% (4,615/300,502, OR: 1.26, 95% CI: 1.21–1.31) in 2020 and 1.7% (5,049/305,611, OR: 1.36, 95% CI: 1.30–1.41) in 2021. As well, mortality increased statistically for "fire accident," from 3.9% (16/412) in 2019 to 8.2% (27/330, OR 2.21, 95% CI: 1.12–4.46) in 2021.

Table 7 shows the number of deaths within 21 days after hospitalization by reason for ambulance call. Mortality increased statistically for "acute disease" and "interhospital transport." In patients with ambulance calls for "acute disease," the morality rates were 6.9% (9,827/142,147) in 2019, 7.3% (9,856/135,151, OR: 1.06, 95% CI: 1.03–1.09) in 2020, and 7.9% (11,067/139,757, OR: 1.16, 95% CI: 1.13–1.19). In patients with ambulance calls for "interhospital transport," the morality rates were 4.7% (1,215/25,884) in 2019, 5.4% (1,300/24,102, OR: 1.16, 95% CI: 1.07–1.26) in 2020, and 5.8% (1,398/23,938, OR: 1.21, 95% CI: 1.11–1.31).

Discussion

This study revealed the outcomes of patients transported by ambulance in Osaka Prefecture from 2019 to 2021. The number of patients transported by ambulance decreased in 2020 and also in 2021 compared to 2019. However, the number of deaths among patients transported by ambulance in 2020 was the same as that in 2019, whereas not only deaths in the emergency department but also deaths among patients transported by ambulances after hospitalization increased in 2021. This population-based descriptive study of the impact of the COVID-19 pandemic will be useful for planning health care systems and policies.

The number of patients transported by ambulance in 2021 was about the same as that in 2020 and was decreased compared to that in the pre-pandemic period. In particular, the number of the patients transported due to traffic accidents and industrial accidents decreased, whereas that of the patients transported due to sports increased slightly. This trend was also observed in other countries (19–26). A study in northwestern Italy reported a decrease in emergency room visits due to the COVID-19 pandemic but an increase in emergency room visits by ambulance (25). A study by Bosson et al. assessing the relationship between hospital admission due to COVID-19 and EMS transports for time-sensitive emergencies in Los Angeles revealed that the number of patients transported by ambulance for traffic accidents decreased during the COVID-19 pandemic, whereas the number of patients transported by ambulance for stroke, ST-segment elevation myocardial infarction, and OHCA increased (24). Thus, the number of these patients may have decreased during the COVID-19 pandemic due to the restriction of socioeconomic activities caused by the lockdown (24). Furthermore, the number of patients transported by ambulance for acute diseases also decreased in 2021 compared to the pre-COVID-19 pandemic period. The impact of the COVID-19

TABLE 6 Proportion of deaths in the emergency department registered in the ORION system during the study period.

Reason for ambulance call	Mortality rate % (*n*/*N*)						2020 vs. 2019		2021 vs. 2019	
	2019		2020		2021		OR	(95% CI)	OR	(95% CI)
Fire accident	3.9	(16/412)	4.0	(14/353)	8.2	(27/330)	1.02	(0.45–2.27)	2.21	(1.12–4.46)
Natural disaster	0	(0/10)	0	(0/13)	4.2	(1/24)	NA	—	NA	—
Water accident	38.5	(20/52)	30.2	(13/43)	25.9	(14/54)	0.69	(0.27–1.77)	0.56	(0.22–1.38)
Traffic accident involving car, ship, or aircraft	0.2	(57/36,199)	0.2	(66/31,134)	0.2	(68/31,250)	1.35	(0.93–1.95)	1.38	(0.96–2.00)
Injury, poisoning, and disease due to industrial accident	0.5	(22/4,798)	0.6	(23/3,933)	0.3	(12/3,946)	1.28	(0.68–2.41)	0.66	(0.30–1.40)
Disease and injury due to sport	0	(0/2,825)	0	(0/1,604)	0.1	(2/1,945)	NA	—	NA	—
Other injury	0.4	(340/77,819)	0.5	(345/71,762)	0.5	(373/70,568)	1.10	(0.94–1.28)	1.21	(1.04–1.41)
Trauma due to assault	0.3	(7/2,796)	0.1	(3/2,474)	0.2	(4/2,138)	0.48	(0.08–2.12)	0.75	(0.16–2.94)
Self-induced injury	9.3	(274/2,954)	10.5	(323/3,067)	9.9	(297/3,009)	1.15	(0.97–1.37)	1.07	(0.90–1.28)
Acute disease	1.2	(4,166/340,665)	1.5	(4,615/300,502)	1.7	(5,049/305,611)	1.26	(1.21–1.31)	1.36	(1.30–1.41)
Interhospital transport	0.2	(65/31,497)	0.3	(74/28,334)	0.2	(72/29,104)	1.27	(0.89–1.80)	1.20	(0.85–1.70)
Other	7.3	(13/179)	8.8	(9/102)	8.0	(6/75)	1.24	(0.45–3.26)	1.11	(0.33–3.29)
Total	1.0	(4,980/500,206)	1.2	(5,485/443,321)	1.3	(5,925/448,054)	1.25	(1.20–1.30)	1.33	(1.28–1.38)

OR, odds ratio; CI, confidence interval; NA, not assessed.

TABLE 7 Number of deaths among hospitalized patients registered in the ORION system during the study period.

Reason for ambulance call	Mortality rate % (*n*/*N*)						2020 vs. 2019		2021 vs. 2019	
	2019		2020		2021		OR	(95% CI)	OR	(95% CI)
Fire accident	11.6	(19/164)	6.3	(9/143)	9.7	(13/134)	0.51	(0.20–1.24)	0.82	(0.36–1.83)
Natural disaster	0	(0/3)	0	(0/3)	0	(0/5)	NA	—	NA	—
Water accident	27.8	(5/18)	11.8	(2/17)	32.0	(8/25)	0.35	(0.03–2.65)	1.22	(0.27–5.93)
Traffic accident involving car, ship, or aircraft	2.0	(122/6,221)	1.6	(94/5,705)	2.1	(118/5,500)	0.84	(0.63–1.11)	1.10	(0.84–1.43)
Injury, poisoning, and disease due to industrial accident	1.2	(19/1,536)	1.3	(16/1,270)	1.7	(21/1,239)	1.02	(0.49–2.10)	1.38	(0.70–2.72)
Disease and injury due to sport	0.3	(1/389)	0	(0/233)	0.7	(2/297)	NA	—	2.63	(0.14–155.57)
Other injury	2.4	(583/24,339)	2.2	(533/24,149)	2.5	(597/23,477)	0.92	(0.82–1.04)	1.06	(0.95–1.20)
Trauma due to assault	1.7	(5/289)	1.5	(4/262)	0.5	(1/183)	0.88	(0.17–4.14)	0.31	(0.01–2.83)
Self-induced injury	9.4	(127/1,345)	10.2	(144/1,406)	10.9	(148/1,360)	1.09	(0.84–1.42)	1.17	(0.91–1.52)
Acute disease	6.9	(9,827/142,147)	7.3	(9,856/135,151)	7.9	(11,067/139,757)	1.06	(1.03–1.09)	1.16	(1.13–1.19)
Interhospital transport	4.7	(1,215/25,884)	5.4	(1,300/24,102)	5.8	(1,398/23,938)	1.16	(1.07–1.26)	1.21	(1.11–1.31)
Other	7.9	(8/101)	8.5	(5/59)	6.4	(3/47)	1.08	(0.26–3.95)	0.79	(0.13–3.51)
Total	5.9	(11,931/202,436)	6.2	(11,963/192,500)	6.8	(13,376/196,962)	1.06	(1.03–1.09)	1.16	(1.13–1.19)

OR, odds ratio; CI, confidence interval; NA, not assessed.

pandemic on changes in patient behavior has been reported in various ways (27, 28). In France, the COVID-19 pandemic reduced initiation of treatment with cardiovascular and antidiabetic drugs (27). In Japan, the COVID-19 pandemic reduced outpatient visits for epilepsy, Parkinson's disease, and Alzheimer's disease slightly but significantly in April 2020 (28). This study also found that the COVID-19 pandemic changed patient behavior, such as calling for an ambulance, and that it had not returned to pre-COVID-19 pandemic levels in 2021. The COVID-19 vaccination coverage in Japan was 80% in 2021, and the effect of preventive measures against COVID-19, such as vaccine dissemination, remains clear. We will continue to evaluate changes in patient behavior, such as for ambulance calls, as vaccination coverage increases.

The mortality of patients transported by ambulance in 2020 compared to 2019 did not change, but mortality in 2021 increased. Several studies have reported that patient outcomes were affected by the COVID-19 pandemic (29–31). Surek et al. (29) found that hospitalizations for acute cholecystitis and uncomplicated appendicitis were markedly reduced during the COVID-19 pandemic, whereas hospitalizations for complicated appendicitis and acute mechanical intestinal obstruction increased, as did the mortality from emergency surgery. A study of OHCA in South Korea found that the time from arrival at the scene to the start of resuscitation activities and transport time were prolonged by the need to secure isolation wards and by the increased requirement for personal protective equipment in the prehospital situation (31). In Japan, bystander cardio-pulmonary resuscitation for OHCA patients decreased during the COVID-19 pandemic (30). Thus, factors such as delays in patient access to medical care, decreased treatment performance due to the wearing of infection protection equipment by healthcare workers, and lower rates of prehospital first aid may have affected patient outcomes. These factors were brought about by the need to prevent COVID-19 infection, and widespread use of vaccine may ameliorate these factors. Therefore, we intend to evaluate these effects in the future.

There are several limitations in this study. First, we analyzed IRR on a population basis and did not adjust for various confounding factors. Second, the ORION registry registered patient data from all fire departments and medical institutions only in Osaka Prefecture, so the prognosis of patients transported to medical institutions outside of Osaka Prefecture was not known. Third, we utilized data from a particular region in Japan, which may not be widely applicable elsewhere due to variations in COVID-19 infection rates and insurance systems across different nations. Finally, as this is an observational study, there may be unknown confounding factors.

In conclusion, the COVID-19 pandemic decreased the number of ambulance requests and increased the mortality of patients transported by ambulance in Osaka Prefecture during 2021. The EMS system may have been affected by an increase in special demands, such as the pandemic of infectious diseases.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: data cannot be shared publicly because of the Protection Ordinance for Personal Information in Osaka Prefecture. Requests to access these datasets should be directed to YK, orion13@hp-emerg.med.osaka-u.ac.jp.

Author contributions

YK: Conceptualization, Writing – original draft, Data curation, Investigation, Methodology, Project administration, Resources, Visualization, Writing – review & editing. KT: Conceptualization, Data curation, Formal analysis, Methodology, Resources, Software, Visualization, Writing – review & editing. HD: Conceptualization, Methodology, Resources, Writing – review & editing. JM: Conceptualization, Data curation, Methodology, Resources, Writing – review & editing. SN: Conceptualization, Data curation, Resources, Writing – review & editing. JT: Conceptualization, Data curation, Methodology, Resources, Writing – review & editing. TH: Conceptualization, Data curation, Resources, Writing – review & editing. TK: Conceptualization, Data curation, Formal analysis, Methodology, Resources, Software, Validation, Writing – original draft, Writing – review & editing. JO: Conceptualization, Funding acquisition, Methodology, Resources, Supervision, Writing – review & editing. TM: Conceptualization, Data curation, Resources, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Surgical productivity recovery after the COVID-19 pandemic in Japan

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Introduction: Previous studies demonstrated that the surgical productivity regressed in 2020. This study therefore explored whether the COVID-19 pandemic had any significant lasting effect of reducing the surgical productivity in Japan. This is a retrospective observational study which is an extension of the previous ones.

Methods: The authors analyzed 18,805 surgical procedures performed during the study period from April 1 through September 30 in 2016–22. A non-radial and non-oriented Malmquist model under the variable returns-to-scale assumptions was employed. The decision-making unit (DMU) was defined as a surgical specialty department. Inputs were defined as (1) the number of assistants, and (2) the surgical duration. The output was defined as the surgical fee. The study period was divided into 42 one-month periods. The authors added all the inputs and outputs for each DMU during these study periods, and computed its Malmquist index, efficiency change and technical change. The outcome measures were its annual productivity, efficiency, and technical changes between the same months in each year.

Results: There was no statistically significant difference in annual productivity, efficiency, and technical changes between pre-pandemic and post-pandemic periods.

Discussion: No evidence was found to suggest that the COVID-19 pandemic has any significant lasting effect of reducing the surgical productivity.

KEYWORDS
COVID-19, productivity change, Malmquist index, surgery, efficiency change, technical change, Japan

Introduction

It has been more than 3 years since the novel coronavirus disease (COVID-19) pandemic was first identified in Wuhan, China in 2019 (1, 2). In response to the COVID-19 pandemic, healthcare resources were intensively allocated to COVID-19 countermeasures, which consequently reduced the resources available for other healthcare areas, such as surgery (3). For example, a university hospital reduced the number of elective surgeries in April-May, 2020, in order to alleviate the manpower shortage in the emergency rooms for febrile patients suspected of COVID-19 infection (4). These COVID-19 countermeasures, combined with extreme restrictions on routine health services, might have led to a collapse of the entire healthcare system (5). As a result of these healthcare resources allocation shifts, the productivity progress of surgery that was unrelated to COVID-19 countermeasures suffered a negative impact from the COVID-19 pandemic in 2020 (5). Although the Japanese government declared four states of emergency in Tokyo to control the COVID-19 pandemic in 2020–2021, these states of emergency did not regress the surgical productivity (3).

Besides the states of emergency, a large number of public and hospital policies have subsequently been designed and implemented since to fight against the COVID-19 pandemic and to prevent the collapse of the healthcare system in Japan. The total effects of these policies were not yet fully investigated. In addition, it is totally unknown whether the negative impact in 2020 has any lasting influence on surgical productivity. In the present study, we investigated the lasting effects of the COVID-19 pandemic on surgical productivity changes.

We used the Malmquist model to assess surgical productivity changes in our previous studies (3, 5). Since 2000, methods of objective measurement of efficiency and productivity have made rapid advances in the fields of economics, business administration and engineering (6, 7). Data envelopment analysis (DEA) is a standard method for efficiency measurement, while the Malmquist index (MI) model is a longitudinal form of DEA. The MI model assesses productivity changes over multiple time periods, which can be decomposed into efficiency changes (ECs) and technical changes (TCs), to determine the root causes of productivity changes (8).

This study was performed to determine the surgical productivity changes in the pre- and post-pandemic periods using the MI model; it was also performed to evaluate the long-term effects of the COVID-19 pandemic on efficiency and technical changes. We hypothesized that the COVID-19 pandemic had a significant lasting effect of reducing the surgical total factor productivity.

Materials and methods

The Institutional Review Board of Teikyo University approved a series of our studies on surgical efficiency and productivity. The need for consent was waived by the Institutional Review Board because of the retrospective observational study design. We intentionally used similar methods of data collection, analysis framework and statistical analysis because the present study is an extension of our previous ones that investigated the relationship between the COVID-19 pandemic and surgical productivity changes (3, 5).

Data

Teikyo University Hospital is in metropolitan Tokyo, Japan, and serves ~1,000,000 individuals. It has 1,152 beds and an annual surgical volume of ~9,000 cases in 13 surgical specialties. This hospital is located in a prefecture where the state of emergency was initially declared by the Japanese government, and the hospital was acutely impacted by the COVID-19 pandemic (9). We collected data from all the surgical procedures performed in the main operating rooms of Teikyo University Hospital from April 1 through September 30 in 2020–22. We also collected those data from April 1 through September 30 in 2016–19 for use as pre-pandemic control data. Data were extracted from the Teikyo University Hospital electronic medical record system. Because of our budget and time constraints, we collected data only for 6 months (April–September) each year (3). Although there was a partial overlap of the data in 2020 and 2021 with our previous studies (3, 5), it was essential to include these data in the present study for evaluating the lasting effects of the COVID-19 pandemic on surgical productivity changes. Especially, 2022 was the year when the COVID-19 pandemic calmed down and the situation was returning to normalcy. Therefore, we partially used the same sample with our previous studies (3, 5).

The following exclusion criteria were used in this study. First, surgical procedures performed under local anesthesia by surgeons were excluded because the resource utilization for these procedures is substantially different and does not permit a clinically meaningful comparison with major surgical procedures. Oral, ophthalmic, and dermatological surgical procedures were excluded because most of these surgeries are minor procedures that can be performed under local anesthesia without anesthesiologists' involvement. In addition, procedures performed under general anesthesia in these specialties do not represent the regular activity of surgeons. Second, procedures in which the patients died within 1 month after surgery were excluded to maintain a constant quality outcome. Although patient death within 1 month after surgery does not accurately represent surgical outcome quality, it was the only available outcome measure that was common among the various surgeries analyzed in this study (8). Third, surgical procedures that were not reimbursed under the surgical payment system in 2016–22 were excluded. Finally, the surgical cases with incomplete records were excluded (3).

Malmquist index (MI)

MI represents the dynamic productivity change of a decision-making unit (DMU) between two time periods; it is an example of comparative statics analysis (6, 7). MI is based on data envelopment analysis (DEA), which evaluates the relative efficiency of DMUs against a static efficient frontier during a single period. MI can be used to compare DEA results between two time periods, and divide the productivity change into two components: efficiency change (EC) and technical change (TC) (6). MI is defined as the product of EC and TC, where EC represents the degree of change in DMU's efficiency, while TC represents the change in efficient frontiers between the two time periods. The productivity change of a DMU between Periods 1 and 2 is mathematically represented as follows (6).

$$\mathrm{EC} = \frac{\text{Efficiency of the DMU in Period 2 relative to the Period 2 frontier}}{\text{Efficiency of the DMU in Period 1 relative to the Period 1 frontier}}$$

$$\mathrm{TC} = \left(\frac{\text{Efficiency of the DMU in Period 1 relative to the Period 1 frontier}}{\text{Efficiency of the DMU in Period 1 relative to the Period 2 frontier}} \times \frac{\text{Efficiency of the DMU in Period 2 relative to the Period 1 frontier}}{\text{Efficiency of the DMU in Period 2 relative to the Period 2 frontier}}\right)^{\frac{1}{2}}$$

$$\mathrm{MI} = \mathrm{EC} \times \mathrm{TC}$$

Analysis framework

We used a non-radial and non-oriented Malmquist model under variable return-to-scale assumptions (6, 10). A DMU was defined as a surgical specialty department. The inputs were the number of medical doctors who assisted the surgery (assistants), as well as the duration of the surgery from skin incision to closure (surgical duration). The output was the surgical fee. Each surgical procedure was assigned a code corresponding to the surgical fee. It is classified as K000- K915 in the Japanese surgical fee schedule and is called "K codes." Each surgical procedure is assigned to one of the K codes which correspond with surgical fees. The fee is identical regardless of who (an experienced surgeon or a surgical trainee) performs surgery if they have medical licensure, how many assistants they use, or how long it takes to complete surgery (11–14). Other fees for blood transfusion, medications, special insurance medical materials and anesthesia were excluded. The monetary values of surgical fees were originally expressed in the Japanese yen, and were converted to U.S. dollars at $1 = 140 yen to facilitate understanding by international readers.

Comparison

The study period was divided into six 1-month periods in each year, which adds up to 42 one-month periods in our seven-year study. The sums of all inputs and outputs were used to compute MI, EC, and TC for each DMU during the 42 one-month study periods. We calculated the annual changes in productivity, efficiency, and technique between the same months in each year; these calculations were performed using DEA-Solver-Professional Software Version 15.1 (Saitech, Inc., Tokyo, Japan) (6, 10). We defined in this study the annual changes in 2016–17, 2017–18, and 2018–19 as "pre-pandemic," while the annual changes in 2019–20, 2020–21, and 2021–22 as "post-pandemic." We focused on the total effects of the pandemic on the surgical productivity because the short-term effects had already been reported in our previous papers (3, 5). Therefore, we aggregated the post-pandemic data and compared them to the pre-pandemic ones.

All surgical departments in the sample were assigned MI, EC, and TC values; their natural logarithms were calculated to allow interpretation as percent changes (10, 15, 16). Natural logarithm of MI values greater than, equal to, and less than 0 indicated increased, unchanged, and decreased productivity from Period 1 to 2, respectively. Similarly, natural logarithms of EC and TC > 0 indicated efficiency and technical improvements, respectively. The natural logarithm of MI equals the sum of natural logarithms of TC and EC (10, 16).

The following 10 surgical specialty departments were included in our analysis; cardiovascular surgery, emergency surgery, general surgery, neurosurgery, obstetrics & gynecology, orthopedics, otolaryngology, plastic surgery, thoracic surgery, and urology. The natural logarithms of MI, EC, and TC were obtained for each surgical specialty department according to corresponding 1-month periods during the study period; their means and standard errors were calculated (16).

Statistical analysis

Excel Statistics Software (Social Survey Research Information Co., Ltd., Tokyo, Japan) was used for statistical analysis. The natural logarithms of MIs, ECs, and TCs for surgical specialties were compared between pre-pandemic and post-pandemic periods, and those of each period against 0 using *t*-tests. *P*-values < 0.05 were considered statistically significant (16, 17).

Results

We analyzed 18,805 surgical procedures performed from April 1 through September 30 in 2016–22. The characteristics of surgery are shown in Tables 1, 2. The total surgical volume per year has decreased by 11% in the post-pandemic period compared to the pre-pandemic period.

The natural logarithms of MIs (percent productivity changes) were shown in Table 3. The productivity change of all surgical procedures was not significantly different from zero, which means that there was no productivity change either during pre-pandemic or during post-pandemic period. There was no statistically significant difference in overall productivity change between pre-pandemic and post-pandemic periods. The subgroup analysis demonstrated that obstetrics & gynecology and thoracic surgery had significantly different productivity changes between pre-pandemic and post-pandemic periods ($p = 0.0015$ and $p = 0.0057$, respectively).

The natural logarithms of ECs (percent efficiency changes) were shown in Table 4. The efficiency change of all surgical procedures was not significantly different from zero, which means that there was no efficiency change either during pre-pandemic or during post-pandemic period. There was no statistically significant difference in overall efficiency change between pre-pandemic and post-pandemic periods. The subgroup analysis demonstrated that there were no surgical specialties that had different efficiency changes between pre-pandemic and post-pandemic periods.

The natural logarithms of TCs (percent technical changes) were shown in Table 5. The technique of all surgical procedures regressed significantly during the pre-pandemic period ($p = 0.0005$). It regressed by 7.4% on average during the pre-pandemic period. However, there was no statistically significant difference in overall technical change between pre-pandemic and post-pandemic periods. The subgroup analysis demonstrated that there were no surgical specialties that had different technical changes between pre-pandemic and post-pandemic periods.

Discussion

On the contrary to our hypothesis presented in Introduction, no evidence was found to suggest that the COVID-19 pandemic has any significant lasting effect of reducing the surgical productivity. There was no statistically significant difference in productivity change between pre-pandemic and post-pandemic periods. In other words, the surgical productivity has fully recovered to the pre-pandemic level by 2022 despite a short-term productivity regress in 2020 (5). In addition, our subgroup analysis demonstrated

TABLE 1 Characteristics of surgery 2016–2019 (pre-pandemic period).

Specialty	Cases/year	Assistants/case	Surgical duration/case (min)	Fee/case (US dollars)
Cardiovascular surgery	245 (28)	2.86	214	6,177
Emergency surgery	342 (77)	1.75	129	2,148
General surgery	526 (24)	2.16	191	2,896
Neurosurgery	159 (22)	1.77	190	5,868
Obstetrics and gynecology	351 (36)	2.01	103	2,022
Orthopedics	508 (26)	2.41	118	2,164
Otolaryngology	185 (4)	1.49	116	1,592
Plastic surgery	137 (1)	1.54	108	1,412
Thoracic surgery	114 (2)	1.94	142	4,283
Urology	253 (5)	1.73	119	2,148
All surgical procedures	2,821 (177)	2.06	144	2,848

The numbers in the parenthesis in cases/year are the average number of surgical procedures per year that were performed outside the regular hospital hours, including late nights and holidays.
Assistants/case, surgical duration/case, and fee/case are expressed in means.
The monetary values of surgical fees were converted to U.S. dollars at \$1 = 140 yen.

TABLE 2 Characteristics of surgery 2020–2022 (post-pandemic period).

Specialty	Cases/year	Assistants/case	Surgical duration/case (min)	Fee/case (US dollars)
Cardiovascular surgery	256 (20)	3.43	162	5,214
Emergency surgery	344 (50)	2.37	118	2,196
General surgery	485 (13)	2.48	192	3,008
Neurosurgery	102 (11)	2.12	192	6,264
Obstetrics and gynecology	312 (28)	2.08	119	2,105
Orthopedics	430 (25)	2.73	138	2,593
Otolaryngology	130 (2)	1.42	123	1,737
Plastic surgery	104 (0)	2.29	145	1,896
Thoracic surgery	96 (0)	2.83	176	4,243
Urology	249 (6)	2.12	121	2,920
All surgical procedures	2,508 (159)	2.45	147	2,920

The numbers in the parenthesis in cases/year are the average number of surgical procedures per year that were performed outside the regular hospital hours, including late nights and holidays.
Assistants/case, surgical duration/case and fee/case are expressed in means.
The monetary values of surgical fees were converted to U.S. dollars at \$1 = 140 yen.

that there were no surgical specialties, except obstetrics & gynecology and thoracic surgery, that had different productivity, efficiency or technical changes between pre-pandemic and post-pandemic periods.

Although the findings above may appear similar to our previous results (3), their scientific contribution is totally different. In the previous study (3), we compared ten-day time periods which included or excluded the states of emergency in short study period. In contrast, we compared the same month in the consecutive years in pre- and post-pandemic periods over seven years in the present study. Our previous study focused only on the effects of states of emergency (3), while the comparison in the present study included all the relevant public and hospital policies that were designed and implemented in addition to the states of emergency. This study has revealed the total effects of all public and hospital policies on annual surgical productivity, efficiency and technical changes between pre-pandemic and post-pandemic periods, which were unknown from the previous study (3). This is the first study in Japan to elucidate the lasting effects of the COVID-19 pandemic on annual surgical productivity changes by using 7-year actual surgical data.

The reason for the findings above is impossible to identify from the present study because many public and hospital policies have changed during the pandemic. The first state of emergency started in April and ended in May 2020 in Tokyo. In response to this state of emergency, Teikyo University Hospital limited the number of elective surgeries on April 6, but removed all the limitation on May 25, 2020. It has not restricted the number of elective surgeries since. Although this change may have reduced the surgical productivity in the short term (5), it had no effects on surgical productivity for our study period of 2016–22.

TABLE 3 Percent productivity changes.

Specialty	Pre-pandemic	Post-pandemic
Cardiovascular surgery	+1.8 ± 9.2	−0.5 ± 5.1
Emergency surgery	+5.6 ± 4.8	−3.1 ± 6.6
General surgery	+2.2 ± 10.5	+2.5 ± 9.1
Neurosurgery	−1.8 ± 5.5	−0.2 ± 9.1
Obstetrics and gynecology**	+4.4 ± 2.2	−6.3 ± 2.1*
Orthopedics	−2.1 ± 8.2	+1.6 ± 7.8
Otolaryngology	+6.0 ± 4.7	+13.4 ± 18.9
Plastic surgery	−6.0 ± 20.1	−19.5 ± 16.8
Thoracic surgery**	−27.5 ± 8.0*	+8.2 ± 9.1
Urology	+6.4 ± 7.0	−9.5 ± 5.4
All surgical procedures	−1.1 ± 2.9	−1.3 ± 3.2

The values are expressed as mean ± SE.
*Indicates that the value is significantly different from 0 ($p < 0.05$).
**Indicates that there was a statistically significant difference between "pre-pandemic" and "post-pandemic" ($p < 0.05$).

TABLE 4 Percent efficiency changes.

Specialty	Pre-pandemic	Post-pandemic
Cardiovascular surgery	+1.4 ± 8.4	+5.0 ± 4.3
Emergency surgery	+8.8 ± 5.7	+1.5 ± 9.0
General surgery	−6.8 ± 13.1	+4.9 ± 12.6
Neurosurgery	+3.6 ± 5.6	+5.0 ± 8.1
Obstetrics and gynecology	+8.2 ± 4.2	−5.2 ± 7.2
Orthopedics	−0.2 ± 12.3	+7.1 ± 8.9
Otolaryngology	+23.2 ± 8.8*	+10.7 ± 17.3
Plastic surgery	+26.1 ± 18.5	−25.7 ± 21.3
Thoracic surgery	−19.3 ± 8.0*	+3.9 ± 12.0
Urology	+17.3 ± 10.2	−9.5 ± 9.3
All surgical procedures	+6.2 ± 3.3	−0.2 ± 3.8

The values are expressed as mean ± SE.
*Indicates that the value is significantly different from 0 ($p < 0.05$). There was no statistically significant difference between "pre-pandemic" and "post-pandemic."

There were some surgical specialties that showed significant changes in productivity, efficiency, and technique during the study periods. For example, obstetrics & gynecology significantly reduced productivity during the post-pandemic period ($p = 0.0092$), while thoracic surgery reduced productivity during the pre-pandemic period ($p = 0.0031$). It is also difficult to specify any causes for these changes from the present study. However, our hospital appointed new chief surgeons in these two surgical departments during our study period, which might have affected their productivity changes. In addition, the number of obstetrics & gynecology and thoracic surgery cases decreased after the pandemic by 10–15%. No other surgical specialties had significantly different productivity, efficiency or technical changes between pre-pandemic and post-pandemic periods.

TABLE 5 Percent technical changes.

Specialty	Pre-pandemic	Post-pandemic
Cardiovascular surgery	+0.1 ± 3.7	−5.4 ± 3.0
Emergency surgery	−3.9 ± 3.7	−4.6 ± 6.3
General surgery	+7.0 ± 10.6	−2.4 ± 9.4
Neurosurgery	−4.6 ± 3.7	−5.3 ± 2.7
Obstetrics and gynecology	−3.9 ± 4.1	−1.1 ± 7.5
Orthopedics	−8.0 ± 9.7	−5.5 ± 5.1
Otolaryngology	−16.3 ± 8.1	+2.7 ± 20.4
Plastic surgery	−25.4 ± 9.2*	+6.3 ± 18.1
Thoracic surgery	−8.3 ± 4.0	+4.3 ± 10.6
Urology	−10.6 ± 6.1	0.0 ± 7.9
All surgical procedures	−7.4 ± 2.1*	−1.1 ± 3.0

The values are expressed as mean ± SE.
*Indicates that the value is significantly different from 0 ($p < 0.05$). There was no statistically significant difference between "pre-pandemic" and "post-pandemic."

It is well-known that large Japanese hospitals with more than 400 beds actively perform after-hours surgeries and other procedures during the pandemic (18). However, judging from the data shown Tables 1, 2 on the average number of surgical procedures that were performed outside the regular hospital hours, no differences in the ratio of after-hour surgeries before and after the pandemic were noted. Teikyo University Hospital had already been performing a significant number of after-hour surgeries (6.3%) before the pandemic, and did not more actively perform them (6.4%) in the post-pandemic period.

Since the present study is an extension of our previous ones (3, 5), it has similar methodological limitations. First, we could not exclude the effects of the revisions in the nation-wide fee schedules from our analysis in productivity changes. There were three revisions on April 1 in 2018, 2020, and 2022 during our study period (12–14). However, our previous study demonstrated that the effects of revisions were insignificant in productivity change (16). We can assume that these revisions had a minimal impact on our conclusions without seriously biasing our analysis. Second, our results in the present study may be false negative. We analyzed 18,805 surgical procedures over 7 years, which is expected to be a sufficiently large sample. The power analysis demonstrated that the possibility of type II errors in our sample was 0.0072 when we fail to reject the null hypothesis that the post-pandemic percent productivity change of all the surgical procedures equals zero (19). Therefore, the possibility of type II errors is small enough although we cannot completely exclude the possibility of false negative results. Third, generalization may be impossible because this study was conducted in a single large teaching hospital in Tokyo. Specifically, the generalizability of our findings is limited because of our focus on a single country and a specific healthcare context. However, Tokyo was one of the most impacted areas by the COVID-19 pandemic in Japan (9). If our hospital in Tokyo fully recovered its surgical productivity from the COVID-19 pandemic, other hospitals in Japan should also have recovered. In addition, there is an advantage to studying surgical productivity in a single hospital. Since one of the significant resource inputs is ancillary services such as operating room nursing practices, all these factors are held constant in a single hospital. By analyzing surgical departments in the same hospital, they all face the same systemic advantages and disadvantages of those services (20). Fourth, the study's focus on Japan is narrow in scope. It would greatly enhance the relevance of our findings if comparisons were made with other hospitals within Japan or with hospitals in other countries. However, the data were unavailable for us.

Conclusion

In conclusion, no evidence was found to suggest that the COVID-19 pandemic has any significant lasting effect of reducing the surgical productivity in Japan. The overall productivity, efficiency, and technique did not significantly differ between pre- and post-pandemic periods. Kumagai showed that after the second state of emergency declaration, the decline in the number of physician visits caused by the spread reduced by almost half, and that the staying-at-home effect did not persist (21). These findings suggest that the surgical productivity has recovered to the pre-pandemic level by 2022 despite a short-term productivity regress in 2020. Our findings would be one of the valuable lessons learned from our experience of the COVID-19 pandemic. Based on our findings for healthcare policy and surgical practice, we can better deal with the pandemic if the similar one hits us again in the future. A comparative analysis with other hospitals or countries could provide a more comprehensive understanding of the pandemic's impact on surgical productivity.

Transparency statement

There was a partial overlap of the data with our previous studies. It was essential to include these data in the present study for evaluating the long-term effects of the COVID-19 pandemic on surgical productivity changes.

Author's note

This study was presented in part on June 5, 2023 at Euroanesthesia 2023 Meeting of European Society of Anaesthesiology and Intensive Care held in Glasgow, UK.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Teikyo University Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

YN: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. YW: Data curation, Formal analysis, Software, Writing – review & editing. AO: Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Data-driven, cross-disciplinary collaboration: lessons learned at the largest academic health center in Latin America during the COVID-19 pandemic

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Introduction: The COVID-19 pandemic has prompted global research efforts to reduce infection impact, highlighting the potential of cross-disciplinary collaboration to enhance research quality and efficiency.

Methods: At the FMUSP-HC academic health system, we implemented innovative flow management routines for collecting, organizing and analyzing demographic data, COVID-related data and biological materials from over 4,500 patients with confirmed SARS-CoV-2 infection hospitalized from 2020 to 2022. This strategy was mainly planned in three areas: organizing a database with data from the hospitalizations; setting-up a multidisciplinary taskforce to conduct follow-up assessments after discharge; and organizing a biobank. Additionally, a COVID-19 curated collection was created within the institutional digital library of academic papers to map the research output.

Results: Over the course of the experience, the possible benefits and challenges of this type of research support approach were identified and discussed, leading to a set of recommended strategies to enhance collaboration within the research institution. Demographic and clinical data from COVID-19 hospitalizations were compiled in a database including adults and a minority of children and adolescents with laboratory confirmed COVID-19, covering 2020–2022, with approximately 350 fields per patient. To date, this database has been used in 16 published studies. Additionally, we assessed 700 adults 6 to 11 months after hospitalization through comprehensive, multidisciplinary in-person evaluations; this database, comprising around 2000 fields per subject, was used in 15 publications. Furthermore, thousands of blood samples collected during the acute phase and follow-up assessments remain stored for future investigations. To date, more than 3,700 aliquots have been used in ongoing research investigating various aspects of COVID-19. Lastly, the mapping of the overall research output revealed that between 2020 and 2022 our academic system produced 1,394 scientific articles on COVID-19.

Discussion: Research is a crucial component of an effective epidemic response, and the preparation process should include a well-defined plan for organizing and sharing resources. The initiatives described in the present paper were successful in our aim to foster large-scale research in our institution. Although a single model may not be appropriate for all contexts, cross-disciplinary collaboration and open data sharing should make health research systems more efficient to generate the best evidence.

KEYWORDS

COVID-19, cross-disciplinarity, research collaboration, research management, research data, data science, data management, health data analysis

Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 infection, has triggered an urgent global research effort to mitigate its impact. At the time, it was essential to devise effective strategies to reduce the rate, severity, and economic aftermath of SARS-CoV-2 infection (1–3). This scenario persists, owing to the recognition that many patients present a post-acute COVID-19 syndrome (PACS), which can appear as an intricate combination of persisting and novel symptoms (2). In recent years, collaboration among healthcare researchers with diverse expertise and access to large-scale patient data has emerged as a critical approach to enhancing research quality and efficiency (4–11). Cross-disciplinary collaboration involves a joint and equal contribution from a broad range of health research experts, crossing disciplinary boundaries to work collaboratively (12–16). This emerging view of science can and should also be employed for PACS, following the efforts during the acute phase of the pandemic.

In response to the COVID-19 outbreak in Brazil (one of the most affected countries), the *Hospital das Clínicas & Faculdade de Medicina da Universidade de São Paulo* (HC-FMUSP), the largest academic health system in Latin America, established a crisis committee in January 2020. Over the following 2 years, the HC-FMUSP complex admitted over 9,000 patients with suspected SARS-CoV-2 infection, mostly moderate and severe cases. To cope with surge in demand for COVID-19 care during the first wave of the pandemic (from March through August 2020), the crisis committee converted the Central Institute, one of the eight HC-FMUSP institutes, into a specialized COVID-19 inpatient facility, with a total of 900 beds (including 300 intensive care beds) (17, 18).

At the onset of the pandemic, several research groups initiated clinical studies on COVID-19 and explored various preventive strategies for the disease (19). In May 2020, HC-FMUSP installed an emergency institutional taskforce, aimed to support research infrastructure and logistics for those studies, which had until then been conducted with a low degree of connection and collaboration among teams. A set of institutional cross-disciplinary research initiatives to study and provide solutions for COVID-19 was thus implemented by this taskforce, with the purpose of fostering scientific collaborations among groups affiliated with HC-FMUSP. This enterprise was designed to reach far beyond co-authorship and, instead, involved joint institutional efforts across disciplines with a focus on cooperation, equity, and transparency (20–23). This paper aims to describe, in detail, the successful implementation of such initiatives (including flow management routines to capture, organize, share and analyze large amounts of data), and outline the challenges and barriers identified over the course of this unprecedented experience in the country.

Materials and methods

Context

This paper examines the benefits and challenges of an institutional research management initiative implemented to facilitate large-scale, cross-disciplinary scientific collaborations during the COVID-19 pandemic. In response to the urgent need for knowledge about the disease and the resource constraints faced during the pandemic, all the actions described below were designed and implemented simultaneously, rendering this a particularly challenging and complex endeavor.

Overall strategy and governance

Research managing strategies were planned in three main areas: organization of a large database consisting of clinical data from hospitalized COVID-19 patients; setting-up of a multidisciplinary taskforce to conduct follow-up assessments of these patients; and organization of a biobank of blood samples collected both during inpatient stay and follow-up assessments.

A COVID-19 Steering Committee was established, comprising institutional leaders with expertise in scientific management and representatives from the COVID-19 crisis committee. This committee shared several key responsibilities, including mapping, monitoring, and supporting research groups utilizing data from the institutional databases. The committee also proposed strategies to encourage collaborative publications and approved applications from HC-FMUSP researchers seeking access to the databases. To ensure fair decision-making, the vice-chair of FMUSP has served as an adjunct member of the Steering Committee, responsible for reviewing and adjudicating appeals from dissatisfied applicants regarding committee decisions.

To ensure effective management of the COVID-19 data organization initiatives, specific teams were created for each of the three institutional fronts. Additionally, a small team was responsible for the overall day-to-day management of these fronts. This group, led by a university full professor who was also a member of the Steering Committee, facilitated communication and collaboration, acting as a catalyst for the exchange of relevant information and intelligence related to COVID-19 research within the institution (Figure 1). With support from the FMUSP Library, this direct management team prepared an institutional data management plan for the various initiatives, which was validated by the COVID-19 Steering Committee and approved by the HC-FMUSP board of directors. This document outlined the criteria for granting access to institutional data and biological material, as well as periods of retention prior to open data sharing.

Regarding the initial financing for the research initiatives outlined in this report, the HC-FMUSP superintendence rapidly provided seed funds generated from a crowdfunding campaign launched during the pandemic[1] (see details of funding allocation in Supplementary materials).

Implementation of actions and collaborative data collection

Institutional database of hospitalizations due to COVID-19

The dedicated inpatient facility for COVID-19 patients was operational at the Central Institute of HC-FMUSP until September 2020, coinciding with the abatement of the first wave of COVID-19 cases in São Paulo. From then onwards, inpatient admissions due to acute COVID-19 during the subsequent waves of the pandemic continued to take at HC-FMUSP, being allocated to different units of the hospital complex.

In May 2020, HC-FMUSP initiated the development of the institutional database focused on hospitalization data. This database included information from consecutive patients admitted for at least 24 h as inpatients due to suspected SARS-CoV-2 infection. The HC-FMUSP Information Technology (IT) Center extracted data from structured fields within electronic health records (EHR) and populated the database. These records followed a specific case report form designed for COVID-19 within the HC-FMUSP EHR system, facilitating the collection of pertinent information during hospital admissions. The basic set of variables was defined by a panel of experts in clinical emergencies, intensive care and infectious diseases, combined with the case report form proposed by the World Health Organization to globally standardize COVID-19 records (24). Data

1 #HCCOMVIDA initiative; https://www.viralcure.org/hc.

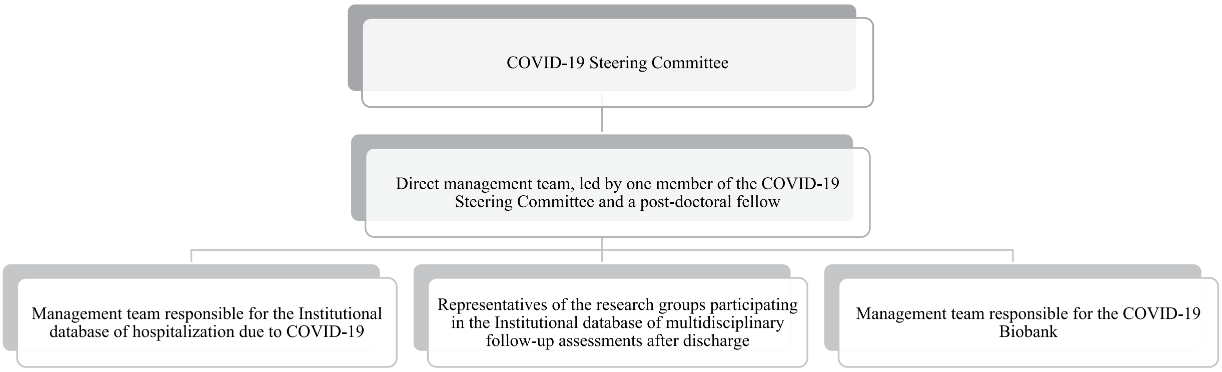

FIGURE 1
Flow-chart of HC-FMUSP research-managing structure to foster large-scale cross-disciplinary collaborative research studies on COVID-19.

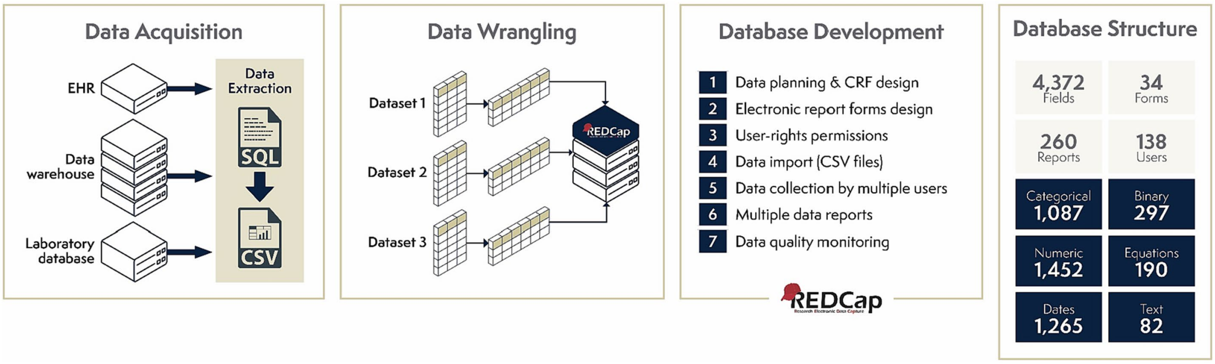

FIGURE 2
Data curation processes involved in the development of HC-FMUSP COVID-19 institutional databases. EHR, electronic health record; SQL, Structured Query Language; CSV, Comma-separated values; CRF, case report form.

regarding vital signs, laboratory and radiology tests, and drug prescriptions were also extracted by the IT Center, assisted by physicians to determine where the most accurate clinical information was available within the EHR. A team of data science specialists was hired to organize all data into a set of variables usable for research, further data mine EHR, and organize all the processes involved in the construction of the institutional databases (including, cleaning, structuring, and reconciliation; Figure 2). The database was stored on a Research Electronic Data Capture (REDCap) system (25) hosted at HC-FMUSP servers.

This database was further expanded with two additional sources: 1. contributions from research groups who agreed to share the data that they had already been collecting for their own studies with inpatients; and 2. information manually extracted from unstructured fields of the EHR by a taskforce of young researchers supervised by experienced scientists, in order to fill missing data for selected variables.

Gradually, this hospitalization database was integrated with information from two other institutional initiatives which are described below (i.e., the multidisciplinary follow-up assessment of COVID-19 patients after in-hospital discharge, and the COVID-19 biobank).

Direct access to data from the hospitalization database was provided solely by the direct management team, after swift authorization of the COVID-19 Steering Committee using objective and previously advertised criteria. This ensured objectivity and transparency in the process of granting access to the data.

Multidisciplinary follow-up assessments after discharge

The multidisciplinary follow-up assessment program of COVID-19 patients was carried out from October 2020 to April 2021, as detailed elsewhere (26). All surviving adult (≥18 years) patients that had been admitted to HC-FMUSP between March and August 2020 due to COVID-19 were consecutively invited for a follow-up visit that should occur around 6 months after their hospitalization. Comorbid conditions prior to COVID-19 were identified using the hospitalization database described in the previous sub-section, and patients with a previous diagnosis of dementia or end-stage cancer were excluded. Additional exclusion criteria were pregnant or postpartum patients, subjects living in nursing homes or long-term care facilities, and insufficient physical mobility to leave home.

The plans for this follow-up initiative were extensively advertised throughout HC-FMUSP, and all interested research groups were invited to participate. To ensure cooperation and minimize inconvenience for the patients, groups were required to collect data in an integrated and coordinated manner.

To optimize participants' time during the in-person visit, participants of the follow-up cohort were initially evaluated remotely. All interviews and protocols that could be administered remotely were answered during this telehealth consultation, taking advantage of the infrastructure and training of health care professionals that were implemented for innovative tele-ICU practices during the pandemic at HC-FMUSP (27–29). Most in-person assessments were streamlined on a single day, approximately 1 week after the remote evaluation, optimizing the use of institutional resources, maximizing multidisciplinary interchange of experiences, and fostering a comprehensive outlook on the health needs of the subjects who underwent those follow-up assessments. Participants with a history of ICU admission and diagnosed with lung damage during hospitalization, according to predefined criteria (30, 31), were invited for a second visit to undergo specific tests (plethysmography, cardiac stress test and chest computed tomography). To facilitate interactions between research groups and to avoid the physical circulation of subjects and their relatives, all in-person evaluations (except radiological exams) were conducted at one single hospital sector. Two separate facilities were used: a temporary outpatient center for patients without a history of ICU admission during in-hospital stay and the clinical research center at the *Instituto do Coração* at HC-FMUSP for patients who had been admitted to an ICU during acute COVID-19 (26).

The multidisciplinary follow-up assessment also included the evaluation of hospitalized pediatric COVID-19 patients (<18 years), specifically focusing on multisystem inflammatory syndrome in children (MIS-C) (32). To facilitate this assessment, a dedicated outpatient clinic was established at HC-FMUSP's Children's Institute, where patients were scheduled for visits every 6 months. The prospective studies conducted on children and adolescents that had COVID-19 encompassed various areas, such as linear and pubertal development, dietary habits, mental health, innate immunity errors, autoimmune conditions, metabolomics, gut microbiota, genetic determinants, bone mineral density, and home-based exercise training (33).

Collected data were stored on the REDCap system hosted at HC-FMUSP, fully integrated with the hospitalization database. Access to those data was provided solely but with swift authorization by the direct management team. The variables that could be accessed by each participating team and the principles for the collaborative sharing of information were agreed between those groups. Information on periods of retention for the broader sharing of those data was included in the institutional data management plan.

COVID-19 biobank

Our institution's COVID-related activities included a pioneering effort to collect and store large amounts of biological material from hospitalized COVID-19 patients for both short-term and future scientific studies. This initiative utilized an existing biobank at the Tropical Medicine Institute of HC-FMUSP, which had prior approval from the Brazilian Council of Ethics in Research to incorporate residual biological material from diagnostic samples collected during routine clinical procedures at HC-FMUSP, with explicit patient consent. A dedicated COVID-19 branch of the biobank was established at the Central Laboratory of HC-FMUSP, allowing for the systematic processing and storage of leftover blood samples collected from hospitalized COVID-19 patients starting in June 2020.

Creation of a COVID-19 curated collection within the institutional digital library of academic papers at the FMUSP-HC system

Using DSpace software and in line with the institution's strategic needs, the FMUSP-HC Library developed a COVID-19 curated collection within the Intellectual Production Observatory of the FMUSP-HC academic system – OPI.[2] OPI is an institutional digital library of academic papers created in 2014 to facilitate the mapping, monitoring and analyzing of quantitative metrics related to the research output of FMUSP-HC groups.

Ethical approval, consent and data security aspects

The implementation of all actions described in this paper strictly followed ethical and data security principles, adhering to standards of consent, privacy, confidentiality, and data protection. All research protocols included in the initiatives described herein received ethical approval. The multidisciplinary follow-up cohort integrates the results of several research projects led by health specialist teams within HC-FMUSP. All projects were approved by HC-FMUSP's institutional review board (CAPPesq – *Comissão de Ética para Análise de Projetos de Pesquisa*) (approval numbers 4.270.242, 4.502.334, 4.524.031, 4.302.745 and 4.391.560). Participants provided signed informed consent.

In 2020, voluntary medical students made efforts to obtain informed consent for the COVID-19 biobank from hospitalized individuals and their relatives during their inpatient stay. These efforts were continued through subsequent telephone and face-to-face contacts during the follow-up program.

To ensure data security and confidentiality, the REDCap system hosted at HC-FMUSP complies with U.S. Health Insurance Portability and Accountability Act (HIPAA) and the Brazilian General Personal Data Protection Act (in Portuguese, LGPD). Researchers accessing data and samples are required to sign agreements acknowledging the ethical and legal responsibilities and ensuring strict confidentiality of participants' data.

Results

Institutional databases

Institutional database of hospitalizations due to COVID-19

Data from COVID-19 hospitalizations were consistently extracted and compiled in the research database from all disease waves, through June 2022. By that date, the institutional research database contained hospitalization data from more than 4,500 adults with laboratory-confirmed diagnosis of COVID-19, including cases from March 2020 to June 2022 (see Table 1; Supplementary Table S1), with approximately 350 fields from each patient (see Supplementary Table S2). The pediatric database including hospitalization data from more than 150 children and adolescents admitted to HC-FMUSP due to COVID-19 was organized by research groups based at the specialized HC-FMUSP's Children's Institute.

2 https://observatorio.fm.usp.br/handle/OPI/42970

TABLE 1 Baseline and hospitalization characteristics of adult patients (≥ 18 years) with confirmed SARS-Cov-2 infection hospitalized from 2020 to 2022 available in our database.

Hospitalization database	
Laboratory-confirmed COVID-19 cases[a]	N = 4,686
Age – mean (±standard deviation)	58.5 (±16.2)
Sex – *N* (%)	
Female	2,140 (45.7%)
Male	2,546 (54.3%)
Charlson comorbidity score – mean (±standard deviation)	3.3 (±2.1)
WHO clinical progression scale[b] – frequency in different categories	
3–4	671 (14.3%)
5	1,605 (34.2%)
6	181 (3.9%)
7–8-9	2,229 (47.6%)
Events during hospitalization	
Hospital stay, duration in days – mean (±standard deviation)	16.2 (±15.9)
Admission to intensive care unit (ICU) – *N* (%)	3,227 (68.9%)
Intubation – *N* (%)	2,230 (47.6%)
Renal replacement therapy – *N* (%)	956 (20.4%)
In-hospital death – *N* (%)	1,501 (32.0%)

[a]Either: (1) positive reverse-transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 on swab from nasopharyngeal and/or oropharyngeal samples (collected at admission and repeated after 48 h if negative); or (2) positive testing by chemiluminescent immunoassays to detect serum antibodies, performed for highly suspect cases with at least two negative RT-PCR samples or for whom an RT-PCR test was not available up to day 10 of symptom onset. Patients with nosocomial COVID-19 infections were excluded. [b]WHO scale categories: 3–4, no continuous supplemental oxygen needed; 5, continuous supplemental oxygen only; 6, continuous positive airway pressure ventilation, bi-level positive airway pressure or high flow nasal oxygen; 7–8-9, invasive mechanical ventilation and/or extra-corporeal membrane oxygenation (ECMO). WHO Working Group on the Clinical Characterization and Management of COVID-19 infection (2020).

The collaborative efforts of several teams at HC-FMUSP were crucial to maximize the quality of the data compiled in the hospitalization database above. The teams from the HC-FMUSP Infectious Diseases section and the HC-FMUSP Central Laboratory were responsible for developing and overseeing the application of the criteria for laboratory-based diagnosis of COVID-19 (34, 35). The Pulmonology and Radiology teams worked to validate and apply the criteria for radiological diagnosis of COVID-19 mainly based on lung computed tomography (CT) findings. The Infectious Diseases team, together with the Pulmonology and Radiology groups, devised the clinical criteria for highly suspect cases of COVID-19 (36). Using the defined criteria, the specialized Epidemiological Surveillance team at HC-FMUSP validated the inclusion of cases in the institutional research database while excluding patients with nosocomial COVID-19 infections.

Finally, the expertise of two HC-FMUSP groups involved in environmental research allowed the generation of neighborhood variables based on each patient's zip code of residence. These variables included factors such as air pollution levels and exposure to green areas, which were incorporated into the research database to help explore potential environmental risk factors associated with post-COVID-19 syndrome (37).

Upon completion of the database and case validation, the possibility of accessing the institutional database above was widely advertised in successive calls open to HC-FMUSP-based research groups. Thus far, the database has been used in 17 published studies, attracting several research groups (36, 38–53) (see Supplementary Table S3). The hospitalization database is currently being used for a few additional analyses, and it will continue to be accessible for new studies proposed in the near future. This unique database also provides the means for assessing long-term outcome of patients, as it provides a profusion of baseline data on the different clinical parameters, allowing the continuous horizontal follow-up of patients.

Multidisciplinary follow-up assessments of COVID-19 patients after hospital discharge

More than 20 HC-FMUSP-based research groups from different disciplines agreed to join the multidisciplinary follow-up assessment program, bringing human and operational resources to make the collection of comprehensive data from hundreds of patients feasible over a few months without the need for large external financial resources.

From October 2020 to April 2021, over 700 adults (mean age 54.8 ± 14.1 years, 53% male) were reassessed between 6 and 11 months after hospitalization due to COVID-19, using the structured multidisciplinary protocol (26) (see flowchart in Figure 3). The resulting database, comprising approximately 2000 fields for each subject (see Supplementary Table S2), has thus far been used in 15 publications (30, 31, 33, 37, 54–64) (see Supplementary Table S4), and it is continuously accessible for new studies.

This collaborative experience paved the way for an ambitious multidisciplinary grant proposal submitted to the state-run São Paulo Research Foundation (FAPESP), to fund two additional waves of follow-up assessments of the same cohort (after three and after 4 years of hospital admission), combining research proposals from the different groups involved thus far. This proposal, worth approximately 1.8 million dollars, was awarded by FAPESP at the beginning of 2023 acknowledging the potential impact of the proposed research on advancing the understanding, prevention, and treatment of COVID-19.

COVID-19 biobank

By October 2020, blood serum and plasma samples had been collected, processed, and stored at -80° C from over 2,000 patients hospitalized due to COVID-19 at HC-FMUSP. Additional vials of serum were stored for more than 700 patients who agreed to attend the follow-up visit. In total, the biobank contains over 45,000 blood vials (each of containing approximately 0.5 mL). To date, over 3,700 aliquots have been dispensed for 10 different ongoing research initiatives investigating pathophysiological aspects of COVID-19, relating distinct acute symptoms and sequelae of the disease to a wide range of biomarkers of inflammation, neurodegeneration, intestinal permeability, peptidomics and metabolomics, among others (see Supplementary Table S5).

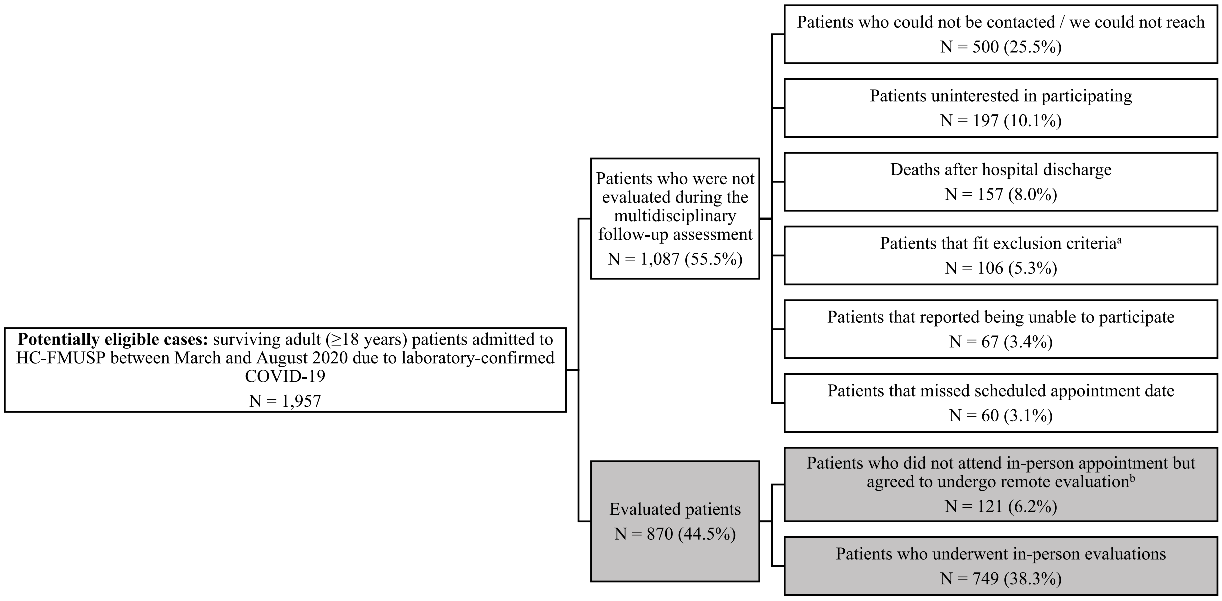

FIGURE 3
Flowchart of the multidisciplinary follow-up assessment program cohort. [a]Exclusion criteria: previous diagnosis of dementia or end-stage cancer, pregnant or postpartum patients, patients living in nursing homes or long-term care facilities or insufficient physical mobility to leave home. [b]Participants who consented with remote assessments but declined the invitation to attend in-person appointments due to health concerns. Despite the implementation of measures to mitigate exposure risk during follow-up evaluations, there was still a level of heightened health apprehension, since the multidisciplinary follow-up assessments occurred between October 2020 and January 2021, when the pandemic was still at its peak in São Paulo.

There was considerable variability in how these biomarker studies were conceived, including one top-down initiative led by the COVID-19 Steering Committee related to the assessment of a large panel of inflammatory markers, whereby all research groups with expertise and interest in the field at HC-FMUSP were contacted and encouraged to work collaboratively, planning and conducting analyses on hundreds of samples and sharing costs of consumables.

Up until now, two collaborative papers from the above studies have been published (65, 66).

COVID-19 curated collection within the institutional digital library of academic papers

By the end of 2022, the FMUSP-HC System's researchers had authored 1,394 papers on COVID-19 published in high-impact journals, encompassing original articles, case reports, technical notes, reviews, commentaries and editorials. From these 1,394 papers, at least 90 comprised original studies containing patient data. A total of 48% of the articles housed in the institutional digital library of academic papers are accessible through open access. FMUSP-HC has actively encouraged researchers to submit their work for publication in open access journals, reflecting a strategic alignment with the broader movement toward open science.

Implementation challenges

The COVID-19 Steering Committee and the research management team faced several implementation challenges during the course of their work at HC-FMUSP. These challenges, their possible causes and the ways by which they were dealt with are discussed in the sub-items below and summarized in Table 2.

Dissemination of information and questions regarding leadership

Large academic health system complexes like HC-FMUSP often face communication challenges, hindering the dissemination of information about institutional initiatives (22, 67). During the pandemic, our research management teams encountered difficulties in reaching all potentially interested research groups. Additionally, the shift toward a more collaborative research approach was met with hesitation by the HC-FMUSP scientific community, leading to concerns about conflicts over leadership and data ownership.

To address these challenges, we appointed experienced and respected HC-FMUSP researchers to lead different components of the institutional initiatives. We maintained frequent communication with these leaders to make strategic decisions and ensure consistent implementation of actions with transparency and cooperation. Several channels of communication were used to increase overall institutional awareness about the principles of inclusion, transparency, and cooperation of the initiatives, through small-group discussions, sharing of presentations, and sending of memos and progress reports. This process was time-consuming but rewarding, since approximately 23% of the total number of research groups of HC-FMUSP (50 out of 220) eventually agreed to participate in the collaborative initiatives. Over time, open communication appeared to reduce the number of conflicts regarding leadership, data ownership, and data sharing that had initially arisen.

Despite our efforts to improve communication and promote collaboration among research groups at HC-FMUSP, some expressed

TABLE 2 Challenges identified during the implementation of institutional research initiatives at HC-FMUSP in the COVID-19 pandemic.

Challenges	Barriers	Actions taken
How to disseminate information about the initiatives within the HC-FMUSP system	Fragmented institutional communication	Frequent and detailed internal communication about the initiatives (one-on-one discussions with research leaders, presentations to groups and internal collegiate, repeated electronic memos to mailing lists, progress reports to participating research groups) Building of an open website (https://sites.google.com/view/covid-19-hcfmusp)
How to overcome conflicts regarding leadership, ownership of information and data sharing	Habits of research groups to work either individually or with a few trusted partners	Identification of (and frequent communication with) a few experienced and respected HC-FMUSP researchers willing to manage key components of the institutional collaborative research initiatives Transparent alignment with those leaders to guide the uniform implementation of actions fostering maximal inclusion of (and cooperation between) potentially interested research groups Stressing of the principles of inclusion, transparency and cooperativeness in all communications with research groups Access to data from the REDCap databases provided solely by the direct management team, after swift authorization of the COVID-19 Steering Committee using objective and previously advertised criteria
How to award fair credit and co-authorship opportunities in publications	Frustration of professionals that might not have opportunities to exercise their research interests due to overload of clinical and management work during the pandemic Risk of honorary authorship	Use of a corporate coauthor including members selected according to objective criteria (i.e., professionals who helped significantly in the construction of the hospital databases). Setting of rules whereby individuals from the corporate coauthor were invited to contribute intellectually to (and approve the final version of) original papers that used data from significant numbers (>800) of patients For other key professionals from the crisis committee who had no familiarity with or interests in research on clinical aspects of COVID-19, use of a second corporate name cited in the Acknowledgements sections of manuscripts. Some of those individuals were also invited to contribute intellectually to specific papers evaluating non-clinical aspects of COVID-19 Avoidance of inclusion of coauthors that did not meet the criteria of the International Committee of Medical Journal Editors. Professors whose leadership was restricted to research administration of the initiatives were listed as authors only in specific cases when they did take part in the planning of investigations and analyses, interpretation of results and writing-up of manuscripts
How to facilitate the hands-on use of institutional databases by researchers	Lack of familiarity of the research groups with the databases' structure	Strengthening of the role of the direct research managing team shown in Figure 1 in the overseeing of the research teams that worked on analyses using the databases. The management team helped researchers to select data fields relevant to their study goals and to understand how those elements were coded in the databases, as well as working to prevent unnecessary duplication of analyses by different groups, errors in the interpretation of numbers and variables, and discrepancies when similar data was reported across separate papers
How to balance the choice of instruments for the multidisciplinary follow-up assessments of patients	Multiplicity of interests of different research groups Risk of duplication/overlap of information collected using different scales Risk that questions proposed by some research groups would not be valued as equally meritorious by other teams	Validation by the COVID-19 Steering Committee of the direct management team as the mediator in the negotiations between research groups, in order to ensure that the assessment battery would be as thorough as possible without overburdening research participants Democratic mediation of decisions, in order to facilitate the inclusion of the largest possible number of research groups with diverse interests
How to deal with ethical issues regarding use of data from hospitalized patients with COVID-19	Risk of privacy breaches, re-identification and misuse of data extracted from medical records Difficulties to obtain informed consent from hospitalized patients or their family members for storing blood samples in the biobank	Recruitment of a team of medical students to seek informed consent during in-hospital stay from patients and family members for storing leftover blood from diagnostic tests Use of the follow-up visit conducted months after hospitalization to retrospectively obtain permission for use of leftover blood from diagnostic tests stored during hospitalization Request for the Brazilian National Research Ethics Committee to grant permission for the scientific use of de-identified healthcare data and biological materials from patients deceased due to COVID-19, considering the invaluable importance of medical research during the extraordinary pandemic circumstances
How to minimize delays in the dispensing and use of blood samples from the biobank	Lack of previous experience of the management teams Overload of the management teams with work on the other fronts of data organization Difficulties of potentially interested research groups to allocate funds to cover costs of processing/analyzing samples	Top-down orientation for individual research groups to work collaborative in the sharing of costs whenever possible Submission of a multidisciplinary grant proposal to FAPESP in order to raise further funds for large-scale analyses of samples Expansion of opportunities for experienced groups outside the HC-FMUSP system to get access to blood samples for collaborative studies

FAPESP, Fundação de Amparo à Pesquisa do Estado de São Paulo (São Paulo Research Foundation); HC-FMUSP, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo; REDCap, Research Electronic Data Capture.

dissatisfaction with their level of inclusion and access to information. To address this, we launched a website for the institutional initiatives.[3] While this initiative was implemented relatively late in the process (September 2022), we hope that it will serve as a valuable resource for all interested parties, providing updates on progress, relevant publications, and opportunities for involvement in ongoing research activities.

Questions about credit and authorship

A second challenge we faced was how to give credit to the healthcare professionals and management teams of HC-FMUSP whose contributions were essential in creating the institutional databases discussed in this paper. A corporate coauthor, the *HC-FMUSP COVID-19 Study Group*, was created to acknowledge their contributions, and grant them opportunities to have some degree of intellectual involvement in research activities. This group, consisting of 31 professionals, was selected based on objective criteria. We set a rule whereby those individuals would be invited to contribute intellectually to (and approve the final version of) all the original scientific publications that would be based on data collected from significant amounts (>800) of patients from the institutional databases. The goal was to acknowledge individuals that did not take part in the conception and writing of the first draft of articles, but who helped significantly in the construction of the databases. The use of such corporate coauthor gave the opportunity for its members to contribute intellectually to the interpretation of the results and finalization of several manuscripts.

The contributions of other key professionals from the crisis committee who had no familiarity or interests in research on clinical aspects of COVID-19 was acknowledge by the creation of a second corporate name (*HC-FMUSP COVID-19 task force*), quoted in the Acknowledgements sections of manuscripts, listing individuals and the key contributions within the group involved in overall infrastructure and logistics during the pandemic. Some of those individuals were also invited to contribute intellectually to (and therefore were included as individual authors in) a few specific manuscripts evaluating non-clinical aspects of COVID-19, e.g., costs of care (44).

An associated challenge that emerged concerned the risk of professors involved in the management of the initiatives being offered honorary co-authorship in any papers that utilized the institutional databases, simply based on their administrative leadership. This situation was deemed unacceptable as per the guidelines recommended by the International Committee of Medical Journal Editors (68), and also went against the principle of true cooperativeness that our institution aimed to bring to the initiatives. Therefore, the professors whose leadership was restricted to research administration of the initiatives were neither included as members of the corporate coauthor cited above (*HC-FMUSP COVID-19 Study Group*) nor individually named in the list of authors of papers (except in situations in which those leaders did play an intellectual role in the planning of investigations and analyses, interpretation of results and writing-up of manuscripts).

3 https://sites.google.com/view/covid-19-hcfmusp

Lack of familiarity with and/or difficulties understanding the databases' structure

A third challenge faced by our group was that some research groups presented a degree of unfamiliarity with and/or difficulties to understand the databases' structure, the clinical case definitions based on key variables for symptom-based, laboratory and radiological diagnoses (34, 35), and the structured flow for inclusion and exclusion of cases (36). To address this, the research managing team (Figure 1) played a constant role in overseeing and assisting research teams. Through repeated interactions, the managing team developed domain-expertise, gaining a deep understanding of the database structure and variables, and ultimately helping researchers in the selection of relevant data fields and comprehension of how the data was coded within the database. This domain-expertise facilitated the application of data to healthcare problems and research questions (10, 69), preventing duplication of analyses, interpretation errors, and discrepancies in reported data across papers.

Choice of instruments and examinations to be included in the multidisciplinary follow-up assessment battery

A fourth challenge involved negotiations among research groups with different interests to determine the scope of the multidisciplinary follow-up assessments. The goal was to ensure a comprehensive assessment while avoiding to burden the participants. Compromises were made to prevent overlap and reach consensus on assessment instruments. The leadership (Figure 1) mediated these negotiations, aiming to democratize access to the program for diverse research groups, and most research groups demonstrated flexibility and a willingness to compromise.

Participants' consent

A most relevant challenge faced over the course of the institutional initiatives described herein regarded patient consent. Our overall approach was carefully planned to avoid privacy breaches, re-identification, and misuse of data extracted from medical files. The Good Clinical Practice (GCP) guidelines (70) were followed to guarantee ethical and scientific quality standards in the conduction of the studies.

Obtaining patient or family members consent for the COVID-19 biobank data was a complex and time-consuming process due to the conditions of hospital strain and strict isolation needs. The follow-up visits conducted months after hospitalization were highly valuable to retrospectively obtain permission for use of leftover blood from diagnostic tests stored during hospitalization. The use of blood samples from surviving patients for which we had not obtained consent was strictly forbidden. For deceased patients, the prospect of posthumously using their biological samples for research was discussed with the next-of-kin whenever possible, in order to obtain consent. Nonetheless, during the unusual and hectic circumstances of the COVID-19 pandemic, identifying and successfully contacting deceased patients' relatives was often not realistic. Considering the invaluable importance of medical research during the pandemic, and to prevent further loss of human life, the Brazilian National Research Ethics Committee granted permission for de-identified healthcare data and biological materials from patients deceased due to COVID-19 to be used by research groups in their ethically approved research projects, even without patient consent.

Difficulties in the dispensing of blood samples from the biobank

A final challenge was the imbalance between the large amount of stored blood samples and the slow rate of dispensing of such biological material for use in research studies. The research management teams were unprepared for this initiative (given its novelty) and burdened with work at the two other fronts of data organization, causing delays in advertising the biobank and providing samples to approved studies. This frustrated research groups at HC-FMUSP eager to utilize the material promptly. Some interested groups also faced financial constraints for sample processing and analysis. However, the recently approved grant by FAPESP has secured funds for biomarker investigations, benefiting from the stored samples. Furthermore, we have expanded collaboration opportunities with external research groups (both from Brazil and abroad), offering access to samples and clinical data for joint investigations. Research collaboration agreements are currently under preparation, whereby we will share both blood samples and clinical data for additional investigations in collaboration with those groups. These measures will help to increase the pace of sample dispensing and facilitate research using the valuable resources of the biobank.

Recommended strategies to enhance collaboration within research institutions

Based on the lessons learned from the actions described in this paper, combined with previous literature (10, 16, 22, 69, 71–73), we present in Table 3 a set of recommendations for strategies aimed at enhancing collaboration within research institutions. The rationale behind these recommendations is to foster collaborations, complementing rather than replacing traditional research. All of the strategies summarized in Table 3 were fully or partially implemented in our institutional approach.

Discussion

Based on the relatively large size of the databases that the HC-FMUSP teams were able to compile, the institutional initiatives described in the present paper may be judged as successful in their aim to foster productive, large-scale research. These initiatives captured demographic and clinical data from thousands of COVID-19 cases treated in a densely urbanized region from a low-and-middle-income country (LMIC), organized in interconnected REDCap databases, available for investigations by over 30 research groups so far. Additionally, follow-up data from hundreds of COVID-19 patients, assessed 6 to 11 months after hospitalization through comprehensive in-person evaluations, have been used by more than 20 research groups. Finally, thousands of blood samples collected during the acute phase and follow-up assessments remain stored for future investigations. Most papers published within this initiative were interdisciplinary, with an unprecedented level of interaction between internal groups that had not previously worked together. To our knowledge, this was the first large-sized collaborative experience of such kind inside an academic hospital complex in Brazil.

Innovative strategies, different from traditional clinical research methods, are necessary to drive advances into the healthcare field and further improve public health (5). Implementing collaborative research management models offers several advantages, including pooling diverse knowledge, enhancing research productivity, cross-disciplinary fertilization, and improved access to expertise, equipment, and funds (7). The extraordinary context of the COVID-19 pandemic confirmed the notion that complex human health problems demand innovative and collaborative solutions combining knowledge from different scientific disciplines (2, 3, 7). Additionally, the pandemic has emphasized the decisive role of data sharing and open access to scientific publications in expediting scientific advancement with efficiency. During the global health crisis, journals and publishers responded by unlocking access to their content and by promoting a marked decrease in the time required for article publication. Furthermore, there has been a surge in the release of preprints, albeit without formal peer review. While these initiatives have accelerated the pace of scientific communication, they have concurrently evidenced the essential need for rigor in the scientific community. While not a fit-for-all solution, large-scale cross-disciplinary research management models, like the one described in this paper, can foster collaboration, reduce inefficiency, and produce high-quality, large-scale research results (20).

While over thirty studies on COVID-19 have been published in peer-reviewed journals using institutional databases (30, 31, 33, 36–66), contributing significant data to the existing literature, there was a considerable delay in their production, with most being accepted for publication in late 2021, or later. The delay in publishing findings from institutional databases can be attributed to various factors such as research groups being involved in completing their own studies and others being overwhelmed with healthcare and teaching activities during the pandemic. However, the major cause of the publication delay was the time required for organizing this process in our institution. Additionally, the high submission rate of COVID-19-related manuscripts from different parts of the world to highly-ranked peer-reviewed journals possibly led to an increased level of competitiveness, resulting in a higher threshold for acceptance of papers by those journals. Nonetheless, we are optimistic about the future of the program as we consolidate the data, establish the biobank, and receive grant support, which will ensure a more robust and sustainable program.

Regarding the multidisciplinary follow-up initiative, the COVID-19 Steering Committee encouraged participating groups to publish interim findings [e.g., (58)]. However, most teams opted to wait until data collection was completed in April 2021. By that time, several observational studies on long COVID had already been published by research groups from China, Europe, and the United States [e.g., (74–77)], and that led to some of our manuscripts being rejected by high-profile journals on the grounds of lack of novelty.

For the blood samples from the COVID-19 biobank, there were difficulties and delays in dispensing aliquots, which may explain why only two studies have been published to date using this biological material. Nevertheless, our collection of biological material is still regarded as highly precious, as it was obtained from a large sample of unvaccinated COVID-19 patients for whom we have also comprehensive data both about the acute disease and follow-up assessments. This explains the current interest raised by external research groups both from Brazil and abroad in using such databases in further collaborative research studies with HC-FMUSP teams.

TABLE 3 Strategies recommended for enhancing collaboration within research institutions, based on lessons learned and previous literature.

Recommendations		Discussion
1	Start by creating a clearly defined governance board	The defined governance board will be responsible for: 1. establishing policies and guidelines for data collection, documentation, storage, retention, and sharing, ensuring that the data is appropriately managed throughout the entire research lifecycle; 2. establishing policies to ensure compliance with ethical guidelines and with relevant data security regulations (safeguarding data against unauthorized access, breaches, and data loss); 3. establishing clearly defined protocols and mediating the sharing of resources, such as equipment, data, facilities, or funding, to support collaborative research; 4. mapping, monitoring, and supporting the efforts of research groups to produce research papers; 5. in the domain of health research, this board could take on the responsibility of identifying common/standardized measures for health conditions that would benefit a majority of, or all, the institution's researchers; and any measures necessary for specific studies of higher interest at any given time. That could lead to the proposition of strategies to foster cross-disciplinary studies of institutional, national or global interest. The leadership positions could be assigned through institutional allocation or determined by votes from the research community.
2	Build infrastructure and resources	Institutions should allocate adequate funding to support research, investing in robust research organizational infrastructure, encompassing both the physical structures and systems as well as the underlying support personnel necessary for institutionally managed research collaborations.
3	Establish diverse multidisciplinary research teams	Complex research challenges require expertise from various disciplines. By creating diverse multidisciplinary research teams, institutions can leverage different perspectives and knowledge to address various research questions.
4	Establish clearly defined roles and responsibilities	Clearly define roles, responsibilities, and expectations for each collaborator involved in the research collaboration. Establishing a framework for decision-making, task allocation, and accountability helps prevent misunderstandings and ensures that everyone knows their contribution and commitment to the collaboration.
5	Create a team of professional data analytics and data science experts	To effectively handle large datasets and/or datasets that involve the integration of secondary data (such as data extracted from electronic health records), it is important to create a dedicated team of professional data analytics and data science experts to ensure that data is accurate, consistent, and reliable. The team should develop robust processes to prevent data errors, duplicates, and inconsistencies, resulting in improved data quality and integrity. Additionally, they should streamline data integration, standardization, and harmonization across various systems and departments. The team's responsibilities also encompass managing data throughout its lifecycle, including identifying and mitigating security risks, ensuring data protection and compliance, and providing necessary technical assistance and support.
6	Establish a proficient hands-on research managing team	A hands-on research managing team, possessing a comprehensive understanding of the data and of the institutional research goals, will assist researchers in selecting relevant data fields and facilitate the application of data to their research questions, thereby avoiding redundant analyses, interpretation errors, and inconsistencies in reported data across various papers
7	Establish effective communication	Establish open lines of communication to facilitate information-sharing, exchange of ideas, and updates on progress. Clear and frequent communication helps build trust, resolve conflicts, and keep all collaborators engaged and informed. Innovative methods could be used; e.g. technology tools such as collaboration platforms or websites to present results and updates; or chatbots with 24/7 availability to provide quick and accurate responses to common queries, saving time for employees and reducing the burden on human resources by assisting with frequently asked questions, policy inquiries, or providing access to relevant documents and resources (complementing human communication rather than replacing it). It is also vital to establish feedback mechanisms by creating channels for employees to provide feedback, suggestions, and concerns. This can be through surveys, suggestion boxes, or regular feedback sessions.
8	Build trust and respect among collaborators, focusing on cooperation, equity, and transparency	Foster an environment of trust, respect, and integrity among collaborators. Encourage open and honest discussions, acknowledge diverse perspectives, and value each collaborator's contributions. Trust is essential for sharing resources, data, and research findings.
9	Ensure mutual benefit for all parts involved, emphasizing meaningful outcomes	Ensure that all parties involved in the research collaboration can derive benefits from the partnership. Identify how each collaborator's expertise, resources, or access to data can contribute to the collaborative effort, creating an advantageous situation for all. In the context of healthcare research, collaborative research must also always be carried out within a voluntary participation scenario governed by values of reciprocity with and non-exploitation of the patients and service of the public good.
10	Prioritize the timely sharing and dissemination of research findings	Request that collaborators swiftly publish their work in reputable scientific journals to make it accessible to the broader scientific community. Additionally, institutions can organize meetings, conferences, symposiums, and workshops to facilitate the exchange of knowledge and promote dialog among researchers.
11	Strengthen national and international research collaborations	Data from a single research center are less relevant than data collected from multiple centers; therefore, it is crucial to incorporate institutional data into a broader research network.

Moreover, a new wave of biomarker investigations by HC-FMUSP groups is expected to take place thanks to the funds that have been recently secured through the large grant approved by FAPESP.

Efforts to foster large-scale data-driven research require multidisciplinary collaboration, crossing the boundaries of healthcare, with additional teams required with skills spanning statistics, computational systems and data science (6, 78, 79). Implementation of EHR brings healthcare closer to data science, computational biology, and artificial intelligence (10). In our initiatives, we applied artificial intelligence and contemporary computational methods to analyze hospitalization data through collaborations with computer science groups (30, 48, 50). Caution is advised regarding such secondary uses of healthcare data from EHR due to potential misinterpretation and concerns about data quality, especially missing or inaccurate data (72). Nevertheless, routine healthcare data, i.e., data generated from routine, standard care of patients, may be a particularly valuable source to inform treatment decisions, because it better represents the real-world uncontrolled conditions faced in clinical practice.

Albeit large, our COVID-19 hospitalization databases were substantially more modest in size compared to initiatives conducted in other settings using EHR. While we collected data from thousands of patients during hospital stays and hundreds of follow-up assessments, studies in other countries have included hundreds of thousands or millions of subjects [e.g., (80–86)]. However, our institutional approach combining different sources of data and involving several teams working in collaboration improved the quantity and quality of the health data obtained from each subject. This led to the construction of comprehensive institutional databases from a representative cohort of subjects from a large LMIC city, with information on complex patients with multi-morbidity and polypharmacy, and who were treated in a real-world setting. These databases include detailed information for subjects from racial-ethnic minorities, socioeconomically disadvantaged, and other underprivileged or discriminated-against populations, who continue to experience a disproportionate share of many acute or chronic diseases and adverse health outcomes (9, 87, 88). Despite all the limitations and challenges, the implemented collaborative research actions resulted in one of the largest severe COVID-19 cohorts with in-person follow-up multidisciplinary evaluations to date.

As it appears to be the norm in most universities (16, 22, 67), the different research groups at HC-FMUSP distinguish themselves by their varied areas of interest, assumptions, priorities, methods, and research practices. These structural and cultural differences between disciplines may constitute significant barriers to collaborative research, and that was a difficulty faced during the implementation of our institutional collaborative COVID-19 research approach. It is not uncommon for talented, high-performing research leaders to find collaboration unnatural, after years working to set themselves apart and propel their academic careers (89). Up until now, there is limited research that explicitly examines how to encourage collaboration in settings similar to the HC-FMUSP system (16, 22, 73). Additional studies are necessary to increase understanding on how to further help researchers to overcome barriers and lean toward more collaborative science. Institutional initiatives such as the one described herein should be evaluated using qualitative survey methods, in order to investigate the perceptions of members of the research community about the proposed management approach and the challenges faced during its implementation.

Conclusion

Several experts have predicted that we are moving toward an era of research where openly shared data will become the norm (5, 10, 23, 90, 91). The results obtained from shared knowledge and discovery diminish the importance of securing intellectual property of healthcare data (without forgoing patient's privacy) (90, 91). Consequently, independent research might become less sustainable than collaborative research. Thus, researchers are beginning to prepare for a future when science will be led by those who have the resources and skills to exploit knowledge assets fastest, rather than by those who own it (23). In this context, scientific collaboration provides a highly effective means to produce knowledge by allowing the sharing of skills, expertise and resources (5, 15).

Research is a crucial component of an effective epidemic response, and the preparation process should include a well-defined plan for organizing and sharing data. This aspect is just as important as all other elements of the response. Although a single model may not be appropriate for all contexts, cross-disciplinary collaboration should make health research systems more efficient to generate the best evidence (5). The top-down collaborative model implemented at HC-FMUSP during the COVID-19 pandemic has the aspiration to motivate a broader use of such kind of institutional approach to enable further scientific developments, helping to transform health care and improve human health. Our current COVID-19 databases may serve as prototypes for the development of additional databases addressing other areas of clinical interest. Such large-scale databases are likely to grow more rapidly, be more complete and be more useful if the three following conditions are met: universal use of automatically-extracted electronic health records; a greater acceptance of cross-disciplinary collaboration; and the cultivation of a culture of more open data sharing.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found at: Data available in our institutional databases mentioned in this paper can be accessed for COVID-related research with (1) a study protocol approved by a research ethics committee and (2) a Data Use Request. Data access instructions can be found at: https://sites.google.com/view/covid-19-hcfmusp.

Ethics statement

The studies involving humans were approved by CAPPesq – Comissão de Ética para Análise de Projetos de Pesquisa. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

AR: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. AA: Investigation, Writing – review & editing. CC: Investigation, Project administration, Writing – review &

editing. HS: Investigation, Writing – review & editing. PF: Funding acquisition, Project administration, Resources, Writing – review & editing. VS: Funding acquisition, Project administration, Resources, Writing – review & editing. MG: Investigation, Project administration, Writing – review & editing. LK: Investigation, Project administration, Writing – review & editing. EK: Writing – review & editing. AP: Investigation, Writing – review & editing. VC: Data curation, Formal analysis, Investigation, Writing – review & editing. KS: Data curation, Formal analysis, Investigation, Writing – review & editing. EA: Data curation, Methodology, Writing – review & editing. AS: Investigation, Writing – review & editing. ES: Investigation, Writing – review & editing. UR: Investigation, Writing – review & editing. RF: Investigation, Writing – review & editing. AM-M: Investigation, Writing – review & editing. AL: Investigation, Writing – review & editing. MSa: Investigation, Writing – review & editing. JF: Investigation, Writing – review & editing. CS: Investigation, Writing – review & editing. TM: Investigation, Writing – review & editing. NG: Investigation, Writing – review & editing. LL: Investigation, Writing – review & editing. MB: Investigation, Writing – review & editing. LB: Investigation, Writing – review & editing. AD: Investigation, Writing – review & editing. MSe: Investigation, Writing – review & editing. JM: Investigation, Writing – review & editing. OF: Investigation, Writing – review & editing. VR: Investigation, Writing – review & editing. MM-C: Investigation, Writing – review & editing. SC: Investigation, Writing – review & editing. GC: Investigation, Writing – review & editing. EB: Investigation, Writing – review & editing. RC: Investigation, Writing – review & editing. TB: Investigation, Writing – review & editing. GB: Conceptualization, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1369129/full#supplementary-material

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The impact of COVID-19 pandemic on the world's major economies: based on a multi-country and multi-sector CGE model

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Objective: To quantitatively assess the impact of COVID-19 pandemic on public health, as well as its economic and social consequences in major economies, which is an international public health concern. The objective is to provide a scientific basis for policy interventions.

Subject and methods: This study utilizes a multi-country, multi-sector CGE-COVID-19 model to analyze the repercussions of the pandemic in 2022. The research focuses on quantifying the effects of COVID-19 on the macroeconomy and various industry sectors within six economies: the United States, China, the EU, the United Kingdom, Japan, and South Korea.

Results: The COVID-19 pandemic shock had the most significant impact on China and the EU, followed by notable effects observed in the United States and the United Kingdom. In contrast, South Korea and Japan experienced relatively minimal effects. The reduction in output caused by the pandemic has affected major economies in multiple sectors, including real industries such as forestry and fisheries, and the services such as hotels and restaurants.

Conclusion: The overall negative macroeconomic impact of the epidemic on major economies has been significant. Strategic interventions encompassing initiatives like augmenting capital supply, diminishing corporate taxes and fees, offering individual subsidies, and nurturing international cooperation held the potential to mitigate the detrimental economic consequences and enhance the global-economic amid the pan-demic. Consequently, this study contributes to the advancement of global anti-epidemic policies targeting economic recovery. Moreover, using the CGE-COVID-19 model has enriched the exploration of general equilibrium models in PHEIC events.

KEYWORDS

COVID-19 pandemic, public health, economic impact, CGE model, multi-country analysis, policy interventions

1 Introduction

During the Spring Festival in 2020, COVID-19 pandemic broke out, and the number of confirmed cases in 1 month quickly surpassed that of SARS in 2003. The World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern (PHEIC) due to its speed, infectivity and difficulty in prevention and control. However, the epidemic has since spread rapidly worldwide, and the strain has continued to mutate. Countries worldwide have continued to explore ways to prevent the spread of the epidemic, with some countries adopting measures such as "home quarantine" and "restrictions on entry and exit" (1, 2). Most countries implemented or extended various preventive measures as the epidemic raged. COVID-19 pandemic caused significant damage to people's health (3, 4) and dealt a massive blow to the world economy (5, 6).

In 2022, the advent of the more transmissible Delta and Omicron COVID-19 variants precipitated a surge in global infection rates, intensifying the struggle to control the pandemic. This health crisis, compounded by the Russia-Ukraine conflict, has triggered escalating food and energy inflation. Consequently, the international trade context and economic stability are declining, particularly as the pandemic persists in the Asia-Pacific, Europe, and North America, burdening supply chains and decelerating economic growth. Despite efforts to reinstate the international economic order, it confronts both internal and external tribulations: domestic markets languish, consumer spending is tepid, and import growth remains stunted; simultaneously, diminishing external demand is resulting in substantial order losses for export businesses, potentially amplifying systemic economic risks.

By 2023, a semblance of normalcy began to return, heralding the onset of an economic resurgence post-COVID-19. However, the future of the international economy continues to be fraught with uncertainty, with ongoing disruptions to industrial supply chains stymieing economic recovery. Presently, the JN.1 COVID-19 variant has been detected in 12 nations. Its proliferation has led health authorities in the UK and the US to brace for a possible pandemic resurgence. On December 19, 2023, the World Health Organization issued a preliminary risk assessment, classifying JN.1 as a "Variant of Concern."

The COVID-19 pandemic has profoundly affected economic structures, social employment, supply chains, and financial systems, with a recovery trajectory that is highly unpredictable. In response, nations worldwide have enacted a battery of monetary and fiscal policies, including quantitative easing, to bolster consumption and mitigate the pandemic's detrimental impact. Consequently, evaluating the effects of these policies has become a pressing concern for policymakers and scholars alike. This paper introduces an innovative model designed to assess policy effectiveness and to inform the refinement of economic recovery strategies.

2 Review of the literature

Research on the economic impact of PHEIC, particularly epidemic diseases, has focused on healthcare costs, focusing on both direct expenses (such as public health resourcing and treatment costs) and indirect costs (such as production impacts due to labor losses due to work stoppages) associated with the disease (7, 8). Sands et al. argue that the assessment of the economic risk of an epidemic should take complete account of the evaluation of the risk of the disease to the economic system (9). Brahmbhatt and Dutta equally argue that even if the chances of illness and death from some infectious diseases such as SARS are slight, the uncoordinated, panicked prevention and control measures taken to avoid infection could cause significant economic damage (10).

In response to the impact of epidemics (such as SARS, H1N1, and so on) on the economic system, several scholars have quantified the economic impact of epidemics on various countries and regions of the world. Ridel et al. found that social factors such as the growth of international trade and the transfer of large amounts of labor across borders contributed to the spread of epidemics and infections (11). Dixon et al. evaluated the impact of the H1N1 pandemic on the US economy with a CGE (Computable General Equilibrium) model (12). They found that the impact of the influenza peak on demand (such as reduced international travel and leisure activities) for US tourism was noticeably more significant than the impact of supply (such as reduced productivity). Keogh-Brown et al. estimate the hazards of different levels of "pandemic" disease by constructing a UK-France-Belgium-Netherlands multi-country multisectoral CGE model, which finds that school closures and preventive absenteeism double the potential economic costs impact in these countries, and that prudent prevention and control plans can help mitigate high policy costs (13). Lee and McKibbin used the G-Cubed model to assess the economic impact of SARS on nine Asia-Pacific countries and regions, including China. They concluded that the economic impact of SARS on countries such as China was mainly in terms of the consumption behavior of households and businesses (14). Orish has found that epidemics such as Cholera and Ebola can worsen poverty in Africa, particularly in sub-Saharan African countries, and have a direct negative impact on the economies of infected countries, thereby reducing economic growth and productivity in these countries (15).

However, some scholars have also focused on individuals' or governments' behavioral decisions and choices during epidemics. "SARS-type" effects suggest that outbreaks of infectious diseases have high human and economic costs in terms of illness and death and that even when the chances of eventual disease or the death toll are small, they cause severe economic disruption so that active government policies will have positive expected effects. For example, Brahmbhatt and Dutta conduct a game-theoretic analysis of the economic damage caused by SARS in East Asia in 2003 and the plague in India in 1994 respectively, and show that proactive government action can largely avoid unnecessary economic damage caused by the epidemic (10). Ridel et al. found that the growth of international trade, large cross-border movements of people, and incomplete public health systems all contribute to the spread of infections and epidemics so that countries would prioritize disease surveillance and develop a strategy based on early warning and rapid response mechanisms (11). As for prevention and control research, Meltzer et al. and Prager et al. conducted separate studies on the threat of a potential pandemic influenza outbreak to US industrial operations and the overall economy (8, 16). They both found that proactive prevention and control measures such as increased personnel engagement and government action could save business and personal treatment expense and effectively mitigate net losses in GDP. Jackson et al. also found that the health care and overhead savings from more cost-effective prevention strategies far exceeded the costs of pandemic preparedness and management (17).

COVID-19 pandemic went from being the most extensive "Black Swan event"[1] to the most prominent "Grey Rhino event",[2] and its domino effect is increasingly being studied by economists. Fernando and McKibbin estimate economic losses in 24 industrial countries over seven scenarios. The worst-case scenario sees a sharp fall in consumption and investment, leading to a sharp fall in stock prices and a sharp fall in bond profits (18). Hofman's analysis concludes that COVID-19 pandemic impedes labor mobility, thereby reducing productivity, disrupting supply chains, inhibiting exports, leading to increased uncertainty, and directly causing a further decline in trade and manufacturing growth, severely affecting the world economy (19). Appleby argues that while fiscal subsidies and loose monetary policies implemented by many governments, especially those of large countries, will increase the fiscal burden on countries and bring about global inflation, attempts by some countries to initiate new trade frictions on the pretext of epidemic prevention and control will increase the cost of international trade (20). Li et al. conclude that containing the spread of the disease should be prioritized over restoring economic activity by conducting a longitudinal survey of people's expectations of epidemic control and maintaining positive economic growth (21). In addition, several scholars have explored the macroeconomic or industrial economies of different countries and regions separately, arguing that the epidemic had a significant deterrent effect on economic growth and caused powerful shocks to capital markets, labor markets, and people's living standards and that the right policy mix could reasonably reduce losses in all areas (22–36).

Reviewing the available literature, it is evident that the following areas need for improvement in the economic impact of epidemics: Upon reviewing the existing literature, it becomes apparent that there are certain deficiencies in understanding the economic impact of epidemics. Firstly, previous international research has predominantly focused on the localized economic consequences of specific epidemics such as H1N1, H5N1, and SARS, neglecting a comprehensive analysis of the macroeconomic and industrial impact on a global scale. Consequently, the broader implications of "pandemic" epidemics on the global economy remain understudied. Secondly, while scholars have offered qualitative insights and recommendations on the effects of COVID-19 pandemic on macroeconomics or specific industries within specific regions, there is a lack of quantitative analyses that encompass a comprehensive evaluation of the global economic system. Furthermore, existing studies often exhibit limitations by narrowly setting parameters for specific aspects, such as demand or trade, within general equilibrium models, which compromises the validity of the evaluation results.

To address these deficiencies, this study introduces three significant innovations. Firstly, a multi-country, multi-sector CGE-COVID-19 model is constructed to comprehensively assess the macroeconomic and industrial impacts of the New Coronary Pneumonia epidemic on the six major economies: the US, China, the UK, the EU, Japan, and South Korea (Figure 1). This approach enables a thorough understanding of the epidemic's effects across different sectors and countries. Secondly, the study evaluates the effectiveness of policies implemented by these countries and regions in response to the epidemic. By considering the diverse impacts of COVID-19 pandemic on various economic aspects (such as supply and demand, trade, etc.) and the range of countermeasures employed (such as capital supply, subsidies, etc.), the model parameters are accurately set to provide valuable insights for global economies in formulating policy measures to mitigate the impact of epidemics. Lastly, the utilization of the CGE-COVID-19 model expands the exploration of general equilibrium modeling within the context of Public Health Emergency of International Concern (PHEIC) events, offering a novel and comprehensive approach to studying the economic consequences associated with such events.

After review, we found that most of the studies on COVID-19 epidemic are statistical analyses or review studies, and there is a lack of empirical analysis of relevant models, not to mention nonlinear analysis of various economic indicators. The COVID-19 epidemic has directly caused a slump in international trade and a rise in unemployment, and indirectly affected global Industry sector restructuring, leading to a global recession. Therefore, this paper strives to fill the gaps in the literature by providing a comprehensive analysis of the economic impact of COVID-19 epidemic on a global scale, evaluating policy responses, and utilizing an innovative modeling approach. By addressing these deficiencies, this research aims to contribute to the advancement of knowledge in the field of epidemic economics and assist policymakers in developing effective strategies for economic recovery.

3 Theoretical basis

3.1 General equilibrium theory and CGE model

Johansen established the CGE model, based on the general equilibrium theory, to evaluate the impact of tax policy changes on the economy (37). After 60 years of refinement and development, the CGE model has been widely used by academics and research institutions evaluating the impact of domestic and international factors on the economy of one or more countries.

The CGE model rests on the premise that an economy's commodities and production factors, when subjected to external shocks under open market conditions, can precipitate adjustments in a nation's import and export dynamics through the mechanism of international trade. These adjustments potentially trigger a domino effect of economic activities within the domestic economy and induce variations in the prices as well as the supply and demand of goods and production factors internationally. The model posits that these shifts continue until global market transactions reach a new equilibrium where supply aligns with demand, engendering impacts on production, income, consumption, social welfare, and the broader spectrum of investment and trade activities—both domestically and across other economies. A typical global CGE model is depicted in Figure 2. The GTAP (Global Trade Analysis Project) model, which is now widely used by academics, is a multi-country (38), multi-sector

1 "Black Swan event" describes an unexpected, rare, and impactful occurrence that defies conventional predictions and is difficult to anticipate.

2 "Grey Rhino event" is a likely and visible risk that is often overlooked or underestimated, leading to significant impact.

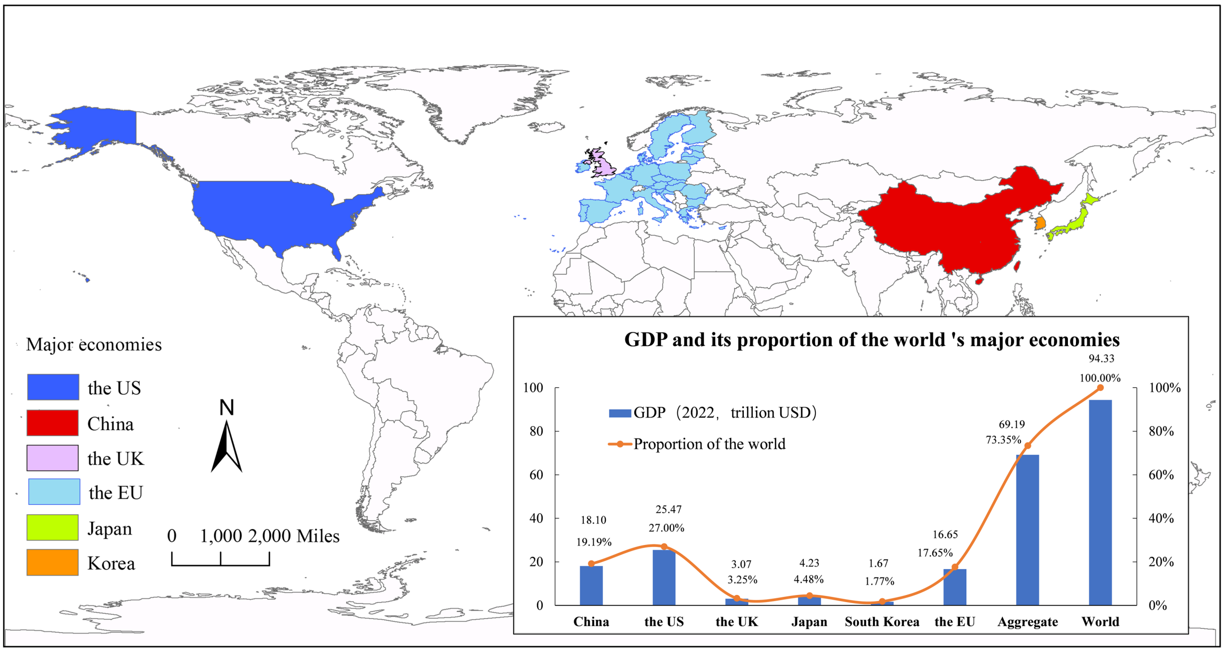

FIGURE 1
Distribution of the world's major economies and their economic conditions in the study. The US, China, the UK, the EU, Japan and South Korea are the countries and regions severely affected by the current COVID-19 pandemic outbreak. The combined GDP of these six economies accounts for 70% of the global economy, and substantial economic and trade links exist among these countries.

global CGE model designed by Prof. Thomas W. Hertel of Purdue in the USA, based on neo-classical economic theory (39).

The GTAP model can analyze the impact of political and economic factors on the macro economy (GDP, population income and consumption, social welfare level, capital return, trade balance, etc.) and industries (output and product prices, etc.) of one or more countries from a global perspective. Therefore, a CGE model can be constructed to assess the impact of the New Coronary Pneumonia outbreak on the economies of the US, China, the UK, the EU, Japan, and South Korea, and to explore the effects of the policies of the above economies in response to the outbreak.

3.2 The theoretical logic of the impact of COVID-19 on economic shocks

The underlying theoretical rationale and the mechanism of internal variable transmission for this paper are outlined in Figure 2A. Our primary theoretical foundation revolves around the mutual influences among various indicators. The dynamic mechanism is predicated on two aspects: the economic impact exerted by the COVID-19 pandemic on different economies, and the diverse policy measures these economies have deployed to counteract the pandemic's adverse effects.

Drawing from a literature review, we understand the pandemic's impact in terms of direct and indirect effects. Ultimately, these effects resonate across macro, micro, and meso-economic levels.

From a microdata perspective, the factors at play include epidemiological characteristics and individual behavioral responses. Epidemiologically, factors such as confirmed cases, recoveries, deaths, and quarantine are responsible for direct effects. Indirect effects emerge from shutdowns, caregiving, absenteeism due to quarantine, and lifestyle changes, all of which disrupt economic activities. These aspects, at the meso level, lead to hindered element flows, supply chain fractures, and increased risk premiums, inflicting indelible damage on macroeconomic influence. This, in turn, affects the three pillars of economic growth: investment, consumption, and exports, corresponding to the supply side, demand side, and trade aspect scenarios set out in our study.

At the macro level, the CGE-COVID-19 model sits at the core of our impact transmission mechanism. As depicted in Figure 2B, this model is a quintessential global CGE framework. It envelops the six major world economies and the variations in their economic indicators.

3.3 Macroeconomic closure

The GTAP10 database, which is anchored to the year 2014, has been updated to facilitate an accurate analysis of the COVID-19 pandemic's impact on the economies of the US, China, the UK, the EU, Japan, and South Korea. For the purposes of the CGE-COVID-19 model, the database now includes 2022 data on population, GDP, capital stock, and trade for each of the aforementioned regions. This update utilizes the dynamic recursive approach as outlined by Walmsley et al. (40), which integrates technology variables with GDP variables within the macroeconomic closure of the baseline scenario. Consequently, the model database incorporates exogenously specified economic indicators (GDP), capital stock, demographic data, and labor force composition (divided into skilled and unskilled labor) for each country or region, as well as other macroeconomic data, projected recursively to the year 2022 as illustrated in Figure 3.

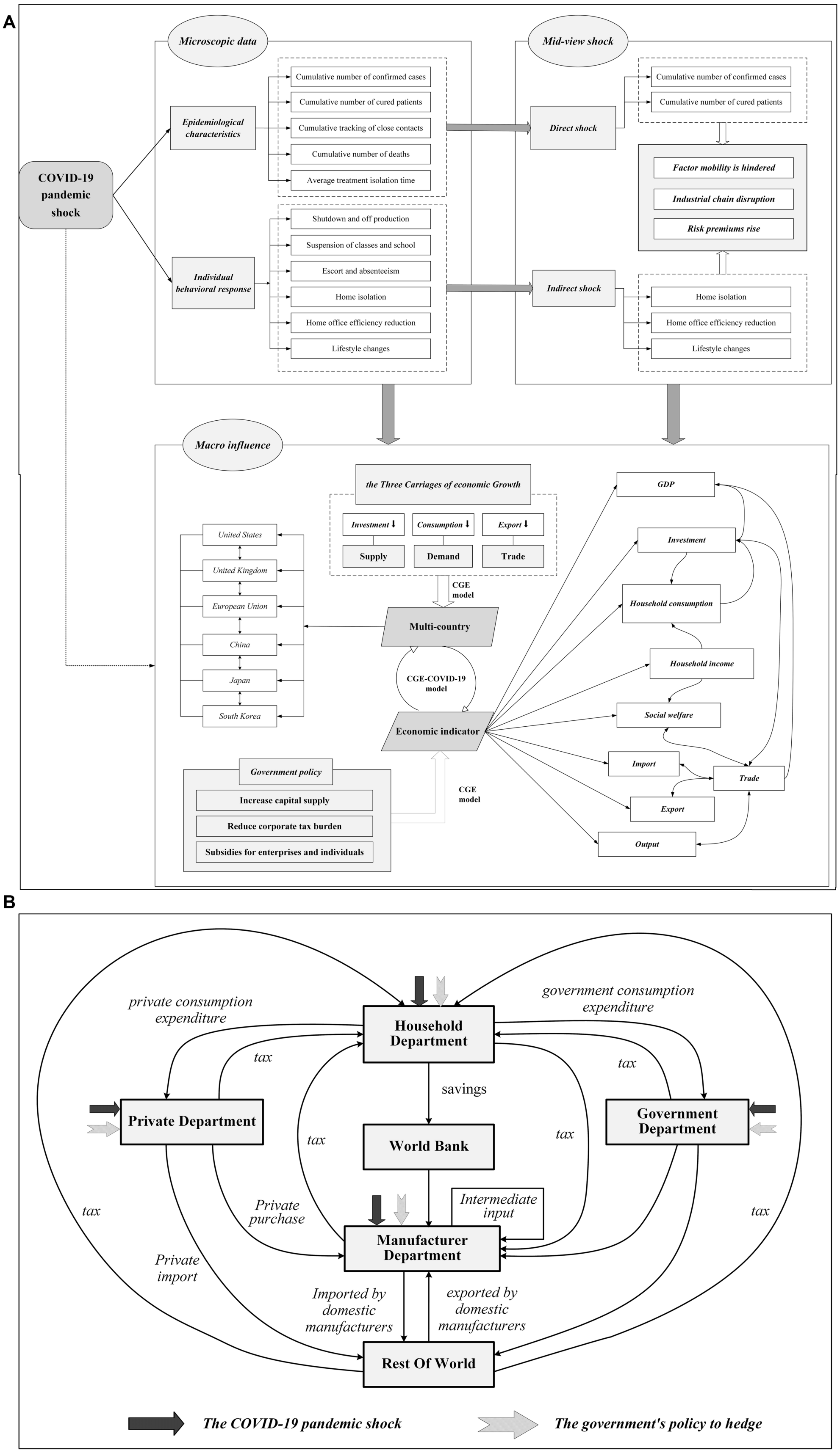

FIGURE 2
A global CGE model with COVID-19 shocks and government policies. **(A)** Analyzing COVID-19 Economic Impact Micro, Meso, Macro Perspectives, **(B)** CGE-COVID-19 Model.

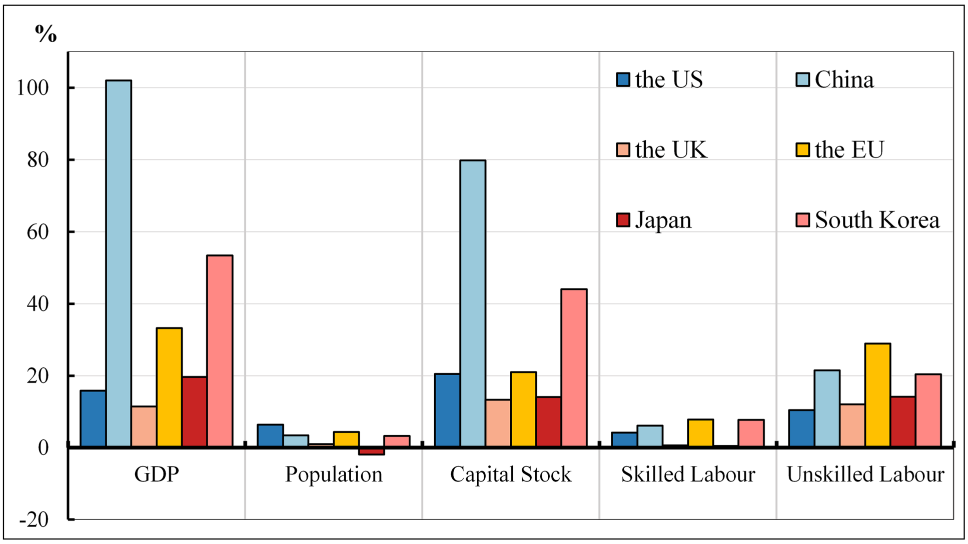

FIGURE 3
Growth rates of macro variables (2014–2022; %). Source: GDP and population data from IMF, capital and labor force data from CEPII global forecasts.

To align with the model's short-term closure requirements, the original 65 industry sectors contained within the database have been consolidated into 24 aggregated sectors. To streamline the presentation of this paper, these sectors are denoted in Table 1 as S1 through S24, and this numerical labeling is consistently used in lieu of sector names in all subsequent figures.

3.4 Scenario setting

3.4.1 Supply (production), demand (consumption), and the trade environment

Given the epidemic's impact on the economy, the supply side of labor supply was greatly affected by the closure measures. In the short term, businesses ceased production and stopped working, and the movement of the labor force was reduced, all of which had an enormous impact on the labor supply; additionally, as the response policy tended to restrict the movement of people, it also had a significant impact on consumption and trade.

(1) The US. As the epidemic repeatedly occurs, a conservative estimate of the average time that the epidemic shuts down production in US businesses is 1 month. The US unemployment rate in March 2022 is 3.611%.[3] Accordingly, assuming that the number of days of labor supply in the US is halved to 15 days for the year, combined with the reduction in labor supply due to unemployment, the labor supply level is set to fall by 6%.[4]

(2) China. Localized outbreaks of epidemics in China have led to the suspension of work, production and schooling in many places, and the inability of the labor force to arrive for average production has caused significant economic losses to society. This paper assumes that the number of days that various frontline labor forces in China cannot typically work due to work stoppages is 10 days, based on the data of the National Bureau of Statistics of China, and adopted the processing methods of Dixon et al. and Zheng et al. (12, 41), the labor supply level is set to fall by 5% in China.

(3) The UK and the EU. The actual day of labor supply in the UK are assumed to be reduced by 12 days; the closure measures in the EU countries are essentially 15 days, and due to the better developed manufacturing sector in European countries, this results in an assumed loss of 10 days of actual labor supply in the EU. Likewise, the combined unemployment caused by the epidemic results in a 6% reduction in labor supply in the UK and EU countries.[5]

(4) Japan and South Korea. These countries are two indispensable links in the global production chain. The break in the global production chain and the contraction in consumption have forced some companies in Japan and South Korea to cut production due to their heavy reliance on external demand. Thus, it is conservatively assumed that the epidemic caused an actual loss of 1 week in labor supply days in both countries, resulting in a 3% drop in their supply of labor.[6]

3 https://data.worldbank.org.cn/indicator/SL.UEM.TOTL.ZS?view=chart

4 Manufacturing is the main sector affected (manufacturing and real estate account for 17% of US GDP and the cultural and entertainment industries account for 40%), while other industries such as power generation, telecommunications, communications, education and the internet are still able to work and work online.

5 In view of the situations of the UK and the EU are similar to the US, for the purpose of calculation, the labor supply level is also set to fall by 6%.

6 The average working hours in East Asian countries are relatively long, 45h per week in Japan and 46.5h per week in South Korea, both of which are similar to China's level. For the purpose of calculation, the one-day labor supply levels in China, Japan, and South Korea have been equated in this study.

TABLE 1 Sector numbers and names.

Sectors	Sectors breakdown details	Sectors	Sectors breakdown details
S1	Cereals and crops	S14	Essential drugs
S2	Fruit and vegetable products	S15	Petrochemical, rubber and plastic products
S3	Oil and sugar crops	S16	Hotel catering industry
S4	Plant fiber	S17	Construction industry
S5	Animal husbandry	S18	Real estate leasing and property
S6	Forestry and fisheries	S19	Traffic communication
S7	Mineral deposits and energy products	S20	Public utility service
S8	Tobacco, alcohol and non-staple food	S21	Retail, wholesale and business activities
S9	Fur and textile clothing	S22	Financial and insurance services
S10	Wood and paper products	S23	Education and health
S11	Transportation and mechanical equipment	S24	Entertainment and leisure
S12	Metals and metal products	OA	Overall level
S13	Electronic equipment		

(5) International Demand and Trade Facilitation. The US is the world's largest consumer market, and weak demand will directly drag on exports from major trading partners such as China, Canada, Mexico, Japan and Germany. China's consumption dominates the structure of the economy.[7] Taking into account of innovative growth due to the epidemic (digital economy), compensatory growth, or government initiatives to exceed expectations with reforms to promote growth, China's consumption level is set to fall by 5%[8] for the year and the level of trade facilitation with other countries by 3%.[9] Economies such as the EU, where the service sector is the main export, suffer heavy losses in the sector, even causing a global service sector crisis. Based on WIOD (2016) data, the average level of cross-border services as a percentage of all industries in the US, UK, EU, Japan and South Korea, which were most seriously affected, was 24.10%, and international tourism expenditure as a percentage of total imports was 19.98%. Based on the number of days considered in the previous section, and considering incentive policies, this paper sets the level of international demand to fall by 5%.[10] Since the onset of the new epidemic, global consumption levels and trade facilitation levels have been severely affected.[11] Therefore, the average labor supply and consumption levels in other economies are assumed to decrease by 1%, the level of trade facilitation between countries and regions of the world to fall by 3%, and the international market equilibrium to deteriorate by 0.3%.

In summary, scenario 1 in Table 2 is formed.

3.4.2 Response in China

For a brief presentation, the relevant parameters of the model's countermeasures are obtained from the policy and measures of each country. Taking China as an example, since 15 May 2022, the Chinese central bank decided to lower the foreign exchange deposit reserve ratio of financial institutions by 1 percentage point, stabilizing the impact of the epidemic on the RMB exchange rate as a result of absorbing the 2020 experience.

(1) China increased the capital supply set. The Central Bank will increase the support of prudent monetary policy to the real economy. Thereby setting China to increase capital supply by 8%.[12]
(2) China reduces the level of taxation. A shift from the current pattern of tax cuts, mainly for VAT, to a reduction in social

7 In the eurozone, tourism, catering, aviation and manufacturing are some of the industries that European countries rely on to survive are even more seriously affected, the UK's annual car production will decline due to the epidemic, European tourism is damaged, tourism workers face great risk of unemployment; Japan and South Korea's economy relies heavily on exports, the supply chain production in both countries is seriously hampered.

8 Calculated based on the relevant data of the National Bureau of Statistics of China.

9 According to the OECD's "Trade Facilitation Index," China's overall ranking is only 51st in 2022, which is 44th in 2019.

10 Based on WIOD (2016) data, the average level of cross-border services as a percentage of all industries in the US, UK, EU, Japan and South Korea, which were most seriously affected, was 24.10%, and international tourism expenditure as a percentage of total imports was 19.98%. Based on the number of days considered in the previous section, and considering incentive policies, the level of international demand was set to fall by 5%.

11 A few important facts: global container freight rates continue to climb, with the market price of containers on some routes once soaring to more than 10 times; global port congestion, with dozens of cargo ships still lined up in large ports such as Los Angeles and Long Beach, California, waiting for weeks to unload; and a report by consultancy firm Deloitte showing that more than 80% of industries face supply chain disruptions and 75% of companies are considering withdrawing their factories overseas and setting them up closer to home.

12 In 2022, the People's Bank of China will increase the support of prudent monetary policy for the real economy, and increase re-loans of 100 billion yuan to support coal development and use and enhance energy storage; The Chinese government has introduced a series of policies to promote investment, such as nearly 6 trillion yuan of new infrastructure "investment projects.

TABLE 2 Impact of COVID-19 pandemic on selected countries and response scenarios in 2022.

Scenario setting	Scenario	Scenario descriptions
COVID-19 pandemic shock	Scenario 1	Labor supply levels fell by 6% in the US, 6% in the UK, and 6% in the EU. China's labor supply levels fell by 5%, Japan's and South Korea's labor supply declined by 3% each, and global consumption levels in major economies declined by 5%. Other economies' average labor supply and consumption levels fell by 2%. The level of trade facilitation between countries and regions fell by 3%, and the balance of international markets deteriorated by 0.3%.
Government Policy response	Scenario 2	China has increased the volume of capital supply by 8%, reduced the corporate tax burden by 12, and 4% subsidy for enterprises and individuals, respectively.
	Scenario 3	The US has increased the volume of capital supply by 10% and the UK by 3%. The EU countries increased capital supply by 5% and introduced a 4% subsidy for businesses and individuals, Japan increased capital supply by 1%, and South Korea introduced a 4% subsidy for household consumption. The rest of the world's economies increased the capital supply by 2%.
	Scenario 4	In response to the impact of the epidemic (scenario 1), China (scenario 2) and economies around the world (scenario 3) take a variety of effective measures.

security and corporate income tax rates, setting China to reduce its corporate tax burden by 12%.[13]

(3) China increases subsidies to businesses and individuals. In 2022, China is assumed to implement a 4% subsidy for both enterprises and individuals.[14]

To summarize, China responds to the epidemic's impact (scenario 1) by increasing the volume of capital supply by 8%, reducing the corporate tax burden by 12%, and implementing a 4% subsidy for companies and individuals respectively, resulting in scenario 2 in Table 2.

3.4.3 Responses in other regions

Abroad, the epidemic also pushed countries to introduce economic underwriting policies.

(1) Assume that quantitative easing monetary policy in the US raises the capital supply by 10%.[15]
(2) The UK is assumed to increase the capital supply by 3% in 2022.[16]
(3) Assume that the EU countries increase the capital supply by 5% and implement a 4% subsidy for businesses and individuals.[17]
(4) Japan is assumed to increase the capital supply by 1%.[18]
(5) Set South Korea to subsidize household consumption by 4%.[19]
(6) Set the rest of the world economies to increase the capital supply by 2%.

In summary, this leads to scenario 3 in Table 2.

3.4.4 Global response

The scenario setting demands a comprehensive understanding of the interplay between economic indicators, serving as both a critical exposition of the model's parameters and a logical framework for the study. The COVID-19 pandemic has precipitated a contraction of labor supply within nations. This contraction has a dual impact: firstly, it directly diminishes household incomes through increased unemployment and underemployment, thereby curtailing consumer purchasing power. Secondly, elevated unemployment levels lead to a reduction in enterprise production capacity, lowering total societal output and, consequently, Gross Domestic Product (GDP). Moreover, the pandemic's effects extend beyond national borders, attenuating domestic production and potentially leading to a decline in the volume and diversity of exported goods, which in turn results in diminished export revenues. Concurrently, a slump in domestic demand may lessen the importation of goods; however, the continued need for essential commodities that cannot be produced locally necessitates sustained importation, potentially leading to a fall in export prices relative to import prices and, ultimately, a deterioration in the terms of trade.

In the face of economic downside uncertainty, economies worldwide should take collaborative measures to address downside risks and seek policy changes to reduce uncertainty. In response to the

13 According to the policy of the State Taxation Administration of China, the part of the annual taxable income of small and low-profit enterprises not exceeding 1 million yuan shall be included in the taxable income at a reduced rate of 12.5%, and the enterprise income tax shall be paid at a tax rate of 20%. For enterprises in need of key state support, the enterprise income tax shall be levied at a reduced rate of 15%.

14 On March 18, 2020, the Department of Consumption of the Ministry of Commerce of China encouraged qualified regions and enterprises to launch various types of consumption coupons and shopping coupons for specific groups, specific commodities and specific fields; In 2021, from the central to local relevant departments, enrich the effective supply of consumption and stimulate consumer demand, and issue different consumption vouchers.

15 In early 2021, the President of the US signed the $1.85 trillion American Assistance Program Act. By mid-March 2021, the total fiscal stimulus plate of the two administrations in the US has reached $5.65 trillion, which is 26.4% of 2019 GDP.

16 On October 27, 2021, UK Chancellor of the Exchequer Rishi Sunak announced the Autumn 2021 Budget Report, which plans to raise an additional 150 billion pounds (about $183.96 billion) in fiscal funding over the next three years.

17 In April 2021, the European Commission unveiled a debt package called "Next Generation EU," which aims to raise a total of 800 billion euros over the next 5years to promote regional economic rejuvenation.

18 On April 26, 2022, the Japanese Cabinet launched an economic rescue plan with a total fiscal expenditure of 6.2 trillion yen, including a total scale of 13.2 trillion yen including private funds.

19 On May 12, 2022, South Korea drafted an additional budget of 59.4 trillion won to help the small businesses cope with the pandemic.

impact of the epidemic (Scenario 1), both China (Scenario 2) and the world's economies (Scenario 2) take a variety of practical measures, resulting in Scenario 4 in Table 2.

4 Results and discussion

4.1 Macroeconomic impact

4.1.1 Assessment of the impact of COVID-19 pandemic on the world's major economies

(1) GDP. COVID-19 pandemic caused a 3.60% decline in China's GDP. This finding is in line with forecasts by duan et al. (41), which estimates that the epidemic may lower China's economic growth by 3.5%. COVID-19 pandemic also caused GDP declines in the US, the UK, the EU, Japan and South Korea. Its impact on the macro economy is global (42), and asymmetric across economies (43). In general, the negative impact of the epidemic on the GDP growth of the EU was the largest, followed by the impact on China. In addition, the impact on South Korea, the UK and the US was also significant, and the impact on Japan was the least.

(2) Social welfare level. COVID-19 pandemic hurt social welfare levels in all economies, but there were large differences in the magnitude of the changes. The EU experienced the largest decline in social welfare levels at USD564,245 million, followed by the US and China, reaching USD459.240 billion and 404.907 billion USD, respectively. The UK, Japan and South Korea all experienced lower declines in social welfare at less than USD100 billion.

(3) Household income and consumption. Consumption is generally considered to be influenced by income and expectations. Expectations of disposable income during the epidemic are the most important driver of expected consumption growth (44). COVID-19 pandemic had a dampening effect on the growth of both household income and consumer spending in all major economies. Specifically, the epidemic may cause the most significant decline in residential income in the EU and China, with a decline of 3.84 and 3.60%, respectively. In contrast, the decline in the US, the UK and South Korea was around 2.50%, and Japan had the most negligible impact. The epidemic had an immense impact on consumer spending in China, with a decline of 7.38%. It may also reduce consumer spending in the EU, the US, South Korea and the UK by 4.77, 3.15, 3.12 and 3.11% respectively, while it had the least negative impact on consumer spending in Japan, with a decline of 1.32%.

(4) Net return on capital. The epidemic increases capital market volatility (45) and divergence of capital returns across sectors (46). The COVID-19 pandemic caused a significant reduction in the return on capital in all countries, especially by 7.10% in China, 6.57% in the US, 6.04% in the EU, 4.88% in the UK and 4.50% in South Korea, respectively, while Japan had the slightest change in net return on capital. Such a situation is detrimental to global investment and may lead to disinvestment and short-term capital flight from these countries.

(5) Terms of trade. COVID-19 pandemic improved the terms of trade by 0.22% in China, 0.47% in Japan and 0.09% in South Korea. However, it had a worsening effect on other countries. The EU's trade terms deteriorated the most, with a decline of 0.20%, while that of the UK and the US worsened by about 0.09%.

(6) Import and export. Hayakawa and Mukunoki found significantly negative effects of COVID-19 pandemic on both export and import (47). The share of import and export trade decreased in all six economies during the outbreak of COVID-19 pandemic, which was likely to reduce China's exports by 3.16% and imports by 6.58%. The possible reason was that the epidemic adversely affected investment and consumption demand in China, and reduced investment and consumption demand. Among the export impaction of other economies under the epidemic, the exports in Japan fell the most, with a decline of 5.13%. In contrast, the UK, South Korea, the EU and the US exports also fell by 3.39, 3.16, 2.58 and 2.30%, respectively. Regarding imports, the US, the UK, the EU, Japan and South Korea experienced negative impacts, with an enormous negative impact on the US, which fell by 6.13%. In addition, Japan's import decline was the smallest, with a decline of 1.96%, and the import decline of the other four economies ranged from 2.56 to 3.58%.

(7) Trade balance. Under the outbreak of COVID-19 pandemic, it would likely reduce the US deficit by USD 114.633 billion, and increase the EU's trade surplus by USD 57.352 billion, China's by USD 57.132 billion, and the UK's by USD 5.733 billion. However, it will likely reduce Japan's trade surplus by USD 28.955 billion and South Korea's by USD 5.638 billion.

(8) Discussion.

Firstly, the analysis of macroeconomic indicators is in Figure 4 shows that the Novel Coronavirus outbreak has harmed all economies. Combining the changes in GDP, social welfare levels, household income and consumption expenditure, and net capital gains, China and the EU suffered the most significantly from the epidemic shock, with all macroeconomic indicators falling at the top of the list; the US and the UK were affected to a lesser extent than China and the EU; and South Korea and Japan were affected the least. The decline in GDP, as noted in the study, is not isolated but intricately linked to a substantial reduction in social welfare levels. This correlation underscores the direct implications of the economic downturn caused by the pandemic on the overall well-being of the population. Furthermore, the dampening effect on household income and consumer spending, particularly pronounced in the EU and China, aligns seamlessly with observed declines in GDP, highlighting a direct relationship between household financial health and a country's economic performance during a crisis.

Secondly, the significant reduction in the net return on capital across countries signifies increased capital market volatility, reflecting the reported divergence of capital returns across sectors during the pandemic. This dynamic underscores the challenges faced by investors and raises concerns about potential disinvestment and capital flight. Additionally, the varied impact on terms of trade emphasizes the interconnectedness of economies globally, with some countries experiencing improvements while others face deteriorations. This underscores the importance of a nuanced understanding of international trade dynamics during crises.

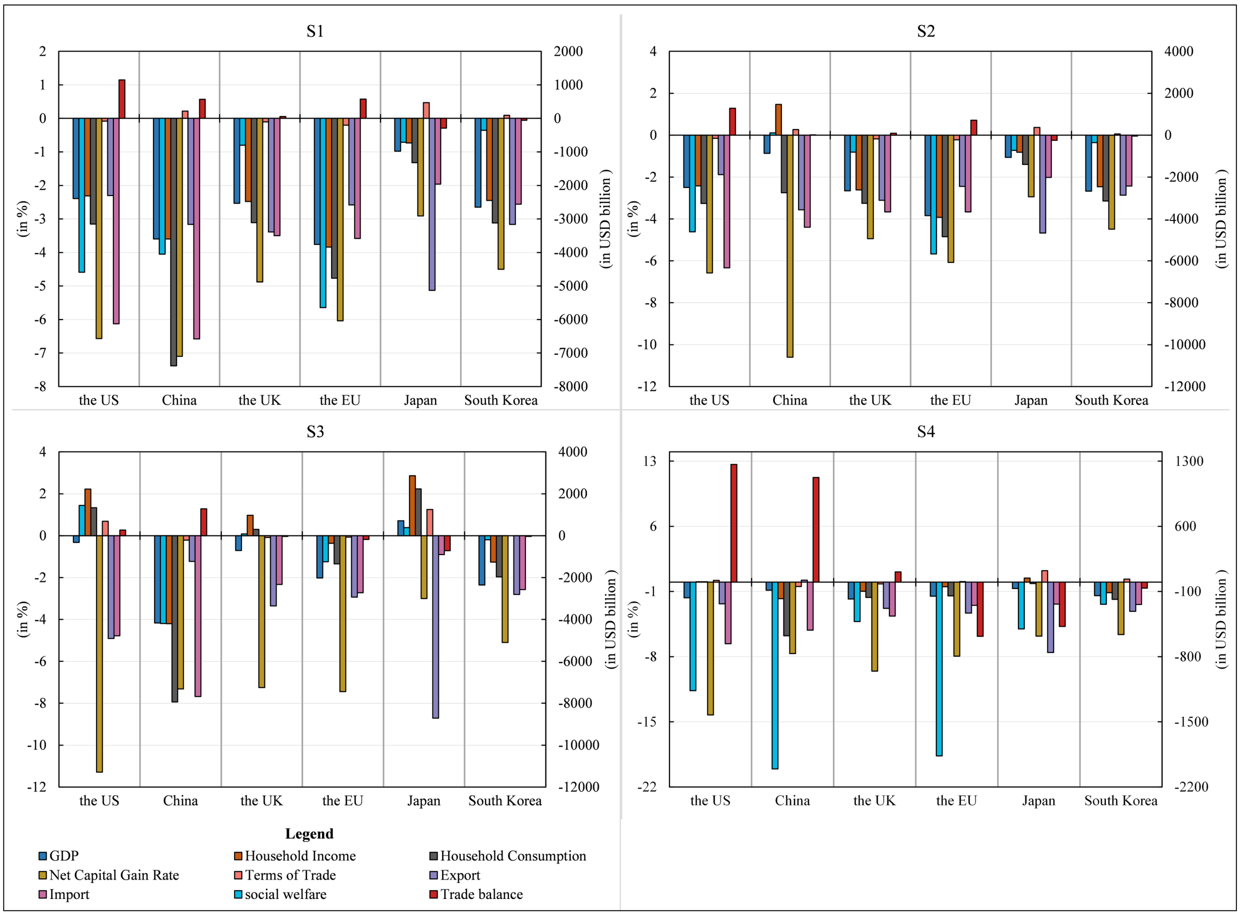

FIGURE 4
Macroeconomic impact of COVID-19 pandemic on major economies in 2022 GDP, household income, consumer spending, net capital gain rate, terms of trade, export and import (all in %), and the level of social welfare and trade balance (both in USD billion). Source: compiled from CGE-COVID-19 pandemic model results.

Thirdly, the negative effects of the pandemic on both export and import, coupled with changes in trade balances, further highlight the interconnected nature of global trade. The disruptions in supply chains and reduced demand contribute to a synchronized decline in both exports and imports across economies. Importantly, the study's findings reveal global economic disparities, with the EU and China being more severely affected than the US and the UK. These varying degrees of resilience and vulnerability underscore the need for tailored economic policies and recovery strategies.

Finally, a holistic interpretation of the interconnected dynamics among these economic indicators significantly enhances the study's credibility and applicability. It provides a more nuanced understanding of the intricate relationships shaping the global economic landscape in the aftermath of the COVID-19 pandemic, offering valuable insights for policymakers, economists, and stakeholders navigating the complexities of post-crisis recovery.

4.1.2 Economic effects of China's countermeasures

Different responses produce different effects (48–52). The government's strong guarantee policies stimulate economic recovery (53). Appropriate policy responses are necessary (54–58).

(1) China's unilateral response to the epidemic would result in a 0.87% drop in China's GDP. It would raise China's social welfare levels by USD 10,381 million, as well as a potential 1.47% increase in China's income and a 2.75% drop in China's consumer expenditure. China's unilateral response to the epidemic presents a nuanced trade-off between economic growth and the effectiveness of countermeasures, resulting in a 0.87% decrease in GDP and 10,381 million emphasizes the impact on the well-being of the population. Concurrently, the positive correlation between government guarantee policies and an increase in social welfare levels by USD. The potential 1.47% increase in China's income suggests complex linkages between government responses and the financial prosperity of residents. Simultaneously, the 2.75% drop in consumer expenditure reflects the intricate interplay between stimulus measures and individual spending behavior, requiring a nuanced examination.

(2) This scenario could also reduce China's net return on capital by 10.60% and improve the terms of trade by 0.27%. This was mainly because China's export fell by 3.56% and its import fell by 4.39%, significantly improving compared with the import share in Scenario 1. The 10.60% reduction in China's net return

on capital signals challenges in maintaining profitability amid the crisis, highlighting the delicate balance between recovery measures and a conducive environment for private investment. The 0.27% improvement in China's terms of trade, coupled with changes in export and import percentages, underscores the intricate relationship between countermeasures and global trade dynamics.

(3) China's response had a positive effect on China's investment and consumption demand, which led to an increase in imports. While China experiences positive outcomes, including improved social welfare, income, and trade balance, the impact on other economies is less optimistic. Decreases in the US deficit and increases in the EU and UK trade surpluses underscore the complex global economic interdependencies, emphasizing the far-reaching consequences of economic measures undertaken by one country.

(4) In addition, an increase in China's trade surplus of USD 1,425 million significantly reduced China's trade surplus compared to Scenario 1 (no measures), contributing to a reduction in trade frictions. For other economies, the scenario could reduce the US deficit by USD 128,450 million and increase the EU and UK trade surpluses by USD 70,854 million and USD 9,056 million, respectively. China's countermeasures led to an improvement in China's terms of trade, social welfare levels, and residents' income, while also resulting in a reduction in its surplus. However, the impact on other economies was less positive and may have even led to a decline in GDP, social welfare levels, residents' income, consumption, and net capital gains in the US, UK, EU, Japan, and South Korea. Specifically, the US deficit decreased, while the trade surpluses of the UK and EU increased and those of Japan and South Korea decreased.

4.1.3 Economic effects of countermeasures taken by other economies in the world

(1) GDP. Measures taken by other economies in the world to deal with the epidemic may increase Japan's GDP by 0.71% while reducing China's GDP by 4.17%, which would significantly negatively impact China's GDP growth. South Korea and the EU had a greater negative impact, with GDP falling by 2.35 and 2.02%, while the UK and the US had a smaller GDP decline.

(2) Social welfare level. It may lead to an improvement in the level of social welfare in the US, Japan and the UK, with the US having the best effect, increasing by USD 144.598 billion, Japan by USD 38.530 billion, and the UK by USD 7.936 billion, respectively. However, China, the EU and South Korea experienced a deterioration in the social welfare levels, with China experiencing the largest decline of USD 419.346 billion, followed by the EU with a decline of USD 124.330 billion and South Korea with the smallest decline of USD 19.79 billion.

(3) Household income and consumption. The household income of Chinese would decrease by 4.20%, and the consumption and expenditure of Chinese residents would also decrease significantly by 7.94%. It may also have a promoting effect on the income of residents in the US, the UK and Japan, in which the income of residents in Japan increased by 2.86%, the income of residents in the US and the UK increased by 2.22 and 0.97% respectively, while the income of residents in South Korea and the EU declines to various degrees. In addition, this scenario may increase consumer spending in Japan, the US and the UK by 2.23, 1.33 and 0.30%, respectively, while it falls in South Korea and the EU by 1.97 and 1.35%, respectively.

(4) Net return on capital. Scenario 3 may reduce the net return on short-term capital by 7.32% in China, 11.29% in the US, and 7.44% in the EU, respectively. In other economies, the net return on short-term capital may fall, with the UK falling by 7.25 percent, South Korea by 5.10 percent, and Japan by 3.0 percent.

(5) Terms of trade, Import and export. The terms of trade improved by 1.25 and 0.69% for Japan and the US, remained unchanged for South Korea and worsened for China, the UK and the EU. China's exports fell 1.23%, while imports fell 7.68%. In other major economies except for China, Japan's exports fell by 8.71%, while those of the US, the UK, the EU and South Korea fell by 4.91, 3.35, 2.93 and 2.81%, respectively. In addition, the imports of the US, the UK, the EU, Japan and South Korea also have a negative impact, with the US having the most significant decline of 4.78% and Japan having the smallest decline of 0.90%.

(6) Trade balance. China's trade surplus increased by USD 128,658 million, a significant increase compared to Scenarios 1 and 2, which worsened China's international trade environment. In addition, the US trade deficit would decrease by USD 26.942 billion, while the trade surpluses of Japan, the EU, the UK and South Korea would decrease.

(7) Discussion.

Compared to Scenario 1, the policy responses to the epidemic in major economies such as the US, UK, Europe, Japan, and South Korea had contrasting effects in Scenario 2. These responses had a positive impact on indicators like GDP, terms of trade, social welfare levels, residents' income, and trade balance in the aforementioned six economies. However, the impact on China was more negative, resulting in a significant decline in China's GDP and a notable increase in its trade surplus. The economic effects of countermeasures reveal a web of intricate relationships between various indicators.

Firstly, the impact on GDP demonstrates a nuanced connection with Social Welfare Level. An increase in GDP in certain economies, such as Japan, is correlated with an improvement in social welfare, indicating a positive relationship between overall economic output and societal well-being. The connection between GDP and Household Income and Consumption is also evident. The rise in GDP, particularly in the US, Japan, and the UK, corresponds with an increase in household income and consumer spending. This underscores the interdependence between macroeconomic indicators and individual financial well-being.

Secondly, net return on capital reveals a complex dynamic between short-term capital returns and GDP. The decline in net returns in China, the US, and the EU suggests that economic policies impacting short-term capital flows have repercussions on the profitability of investments, indicating an intricate link between capital mobility and financial returns.

Thirdly, terms of trade, import and export, and trade balance are intricately connected. The improvement in the terms of trade for Japan and the US is associated with reduced trade deficits and negative impacts on imports. This demonstrates how changes in the balance of trade can influence the terms under which countries engage in international commerce.

Finally, trade balance and household income and consumption are intertwined. The increase in China's trade surplus corresponds with a potential decrease in trade surpluses for other nations. This shift in trade dynamics can have implications for the income and consumption patterns of households, showcasing the delicate balance between international trade and domestic economic conditions.

4.1.4 Macroeconomic effects of countermeasures adopted by all major world economies

(1) GDP. Measures taken by all of the world's major economies in response to the outbreak could reduce GDP by 1.44–1.81% in the UK, the US, the EU and South Korea, resulting in a 0.86% decline in GDP in China and a 0.68% decline in Japan. Compared to Scenario 1 (COVID-19 pandemic impacts), Scenario 4 boosts GDP growth in all these economies.

(2) Social welfare level. It would likely reduce the level of social welfare in China by USD 2006.04 billion, and also more significantly in the EU and the US, by USD 186.638 billion and USD 116.561 billion respectively, with smaller decreases in Japan, the UK and South Korea, and a minor decrease in South Korea.

(3) Household income and consumption. More representatively, regarding residents' income, the US and Japan saw a slight increase of 0.05 and 0.44%, respectively; regarding residents' consumption expenditure, the US saw a slight increase of 0.05%.

(4) Net return on capital. The net rate of return on capital declines in all economies, with the US experiencing the largest decline in the net rate of return on short-term capital at 14.25%, the UK, the EU and China experiencing declines in the net rate of return on short-term capital of 9.55, 7.95 and 7.66% respectively, and Japan and South Korea experiencing the most negligible reductions, but also at 5.80 and 5.63%, respectively.

(5) Terms of trade. Scenario 4 is likely to worsen the terms of trade for both China and the EU, with both decreasing by 0.47 and 0.18% respectively; however, the conditions of trade improve for Japan, South Korea, the US and the EU, with 1.23, 0.32, 0.20 and 0.06% improvements, respectively.

(6) Import and export. Scenario 4 resulted in an increase of 0.21% in China's exports and a decrease of 5.15% in imports;. In contrast, other economies' share of exports and imports still declined. In terms of exports, Japan dropped the most, with a decrease of 7.56%, and exports of the US, the EU, South Korea and the UK were down more significantly, by 2.32–3.31%; in terms of imports, the US dropped the most, by 6.60%, and Japan, the EU, South Korea and the UK saw a significant fall in imports, with a drop of around 2.50%.

(7) Trade balance. The trade surplus in China and the UK would increase by USD 112.501 billion and USD 10.960 billion, respectively. Furthermore, the trade surpluses of the EU, Japan and South Korea decreased by USD58.171 billion, USD47.607 billion and USD6.445 billion, respectively.

(8) Discussion.

The reduction in GDP across major economies, ranging from 1.44 to 1.81%, directly influences the social welfare level. This decrease in GDP translates into diminished resources for social programs, leading to a substantial drop in social welfare, notably in China, the EU, and the US. Simultaneously, changes in GDP have direct ramifications on household income and consumption patterns. Slight increases in residents' income and consumption in the US and Japan highlight the interdependence between overall economic stability and individual financial well-being. The decline in GDP also contributes to a global reduction in the net return on capital, showcasing the intricate relationship between economic health and capital market performance.

In addition, the decrease in social welfare levels has implications for household income and consumption. Reduced social welfare potentially leads to decreased disposable income, influencing residents' spending behavior and reshaping consumption patterns. This intricate linkage emphasizes the broader societal impact of macroeconomic policies. The decline in the net return on capital globally is closely tied to changes in the terms of trade. Economic conditions affecting capital returns also impact the terms on which countries engage in international trade. This, in turn, influences import and export dynamics, with China experiencing increased exports and decreased imports. Other economies witness declines in both exports and imports, showcasing the interconnectedness of international trade networks.

It is important that the shifts in import and export patterns further impact the trade balance. China's increased exports and decreased imports contribute to a larger trade surplus, while the US and other economies face changes in their respective trade balances. Understanding these dynamic connections is crucial for policymakers and analysts, as changes in one economic indicator can have cascading effects throughout an economy. The complex network of interactions underscores the need for a holistic approach in economic analysis and decision-making.

In conclusion, compared to Scenario 1, 2 and 3, Scenario 4 (policies in which major economies jointly respond to the epidemic) boosts GDP, social welfare levels, household income and consumption expenditure in these countries from an overall perspective. However, it is worth noting that the decline in net capital gains in all countries is greater than in Scenario 1 (when no measures are taken). Therefore, economies should consider adopting a synergistic policy approach to counter the negative macroeconomic impact of the New Coronavirus outbreak.

4.2 Industry sector economic impact

4.2.1 Assessment of the impact of COVID-19 pandemic on the world's industry economies

It is important to recognize the impact of COVID-19 pandemic on the structure of the economy (59). The lockdown policy has spillover effects (60, 61), especially in the food industry, the real estate activities, the constructions and the general services (62). The CGE-COVID-19 model was applied to calculate the impact of the pandemic on the output level of each sector in the world's major economies in Figure 5.

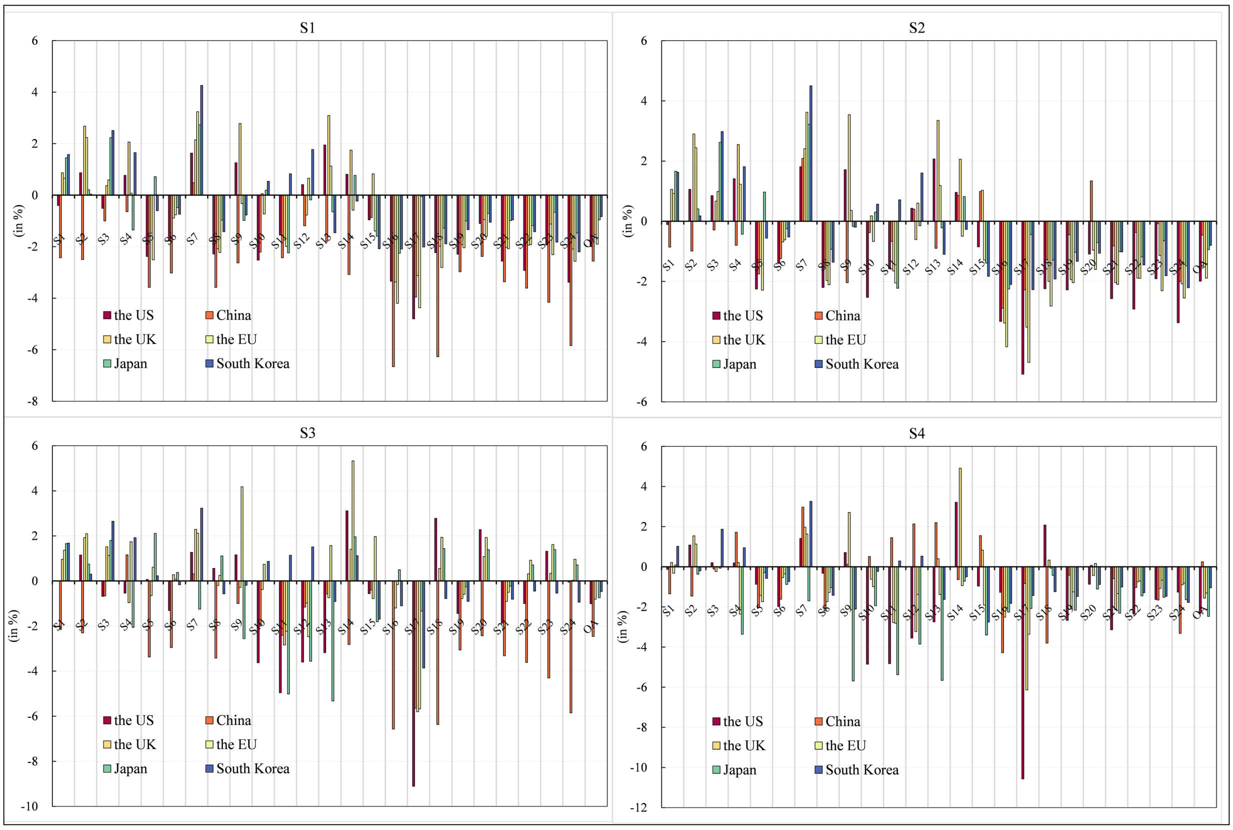

FIGURE 5
Impact of COVID-19 pandemic shock on sectors in 2022 (%). Source: compiled from CGE-COVID-19 model results.

(1) The US and China. The total output level of the US decreased by 2% during the outbreak of COVID-19 pandemic. From the perspective of various sectors, only seven showed positive output growth, while the output level of the remaining 17 sectors all showed varying degrees of decline. Among them, the output level of the construction industry fell the most, by 4.8%. The production level of service sectors such as recreation and leisure, hotel and catering, financial and insurance services, retail, wholesale and commercial activities also declined significantly, ranging from 2.56 to 3.38%. The total output of China decreased by 2.56%. From the perspective of sectors, only the output of mineral deposits and energy products increased slightly by 0.48%, while the output of the other 23 Industry sector sectors declined significantly. This is largely in line with Kekeç et al., who found that the Turkish mining industry was affected to some extent by COVID-19 pandemic, but recovered quickly (63). Service sectors such as real estate leasing and property, recreation and leisure, education and health, construction, and financial and insurance services were hit hard, with output levels likely to fall by 3.61 to 6.27%. The reason is that these sectors belong to the tertiary industry, which is most affected by the decline in consumer demand and employment demand.

(2) the EK and the EU. The total output level of the UK fell by 1.53%, with the output level of the hotel and catering industry falling the most by 3.37%. In addition, the output level of construction, entertainment and leisure, retail, wholesale and commercial activities, real estate leasing and property, financial and insurance services, transportation and communication, and other service sectors also declined significantly, with a decrease of 1.92 to 3.12%. The total output of the EU decreased by 1.9%. COVID-19 pandemic caused the output of 17 sectors in the EU to decline to various degrees, among which the output of construction, hotel and catering industry, real estate leasing and property, entertainment and leisure, education and health, retail, wholesale and business activities, transportation and communication and other services declined significantly. Its decline was in the range of 2.04 to 4.37%.

(3) Japan and South Korea. The total output level in Japan decreased by 0.96%, with a significant decline in the output of services such as hotels and catering, entertainment and leisure, real estate leasing and property, financial and insurance services, transportation and communication, retail, wholesale and commercial activities. Among them, the output of hotels and catering decreased by 2.25%. The decline in the output of real economic sectors such as transportation and machinery equipment, petrochemical, rubber and plastic products, and plant fibers was also relatively evident. The total output of South Korea decreased by 0.83%. Regarding sector changes, the service industry was the most affected. The top five industries with output impact were recreation and leisure, the hotel and catering industry, the construction industry, real estate leasing and property, and education and health.

The epidemic has an average negative impact on the total output of major economies, especially China, followed by the US, the UK and the European Union. In contrast, Japan and South Korea have a more negligible impact. In terms of the changes in various sectors, the epidemic has reduced the output of forestry, fishery, tobacco, alcohol, non-staple food and other real sectors in major economies, as well as hotel and catering industries, construction industry, real estate leasing and property, transportation and communications, public utility services, retail and wholesale and business activities, financial and insurance services, education, health, culture, entertainment and leisure. In terms of the service sector, which has a sizeable general impact, the epidemic has the greatest negative impact on China, followed by the US, and the most negligible impact on Japan. Specifically, the hotel and catering industry experienced the most significant decline in China, the UK and Japan, while real estate leasing and property output declined the most in China.

4.2.2 Economic effects of China's countermeasures

(1) The US. In addition, the total output of the US decreased by 1.99%. In terms of the output change of various sectors in the US, the output of electronic equipment, mineral and energy products, fur and textile and clothing, plant fiber, fruit and vegetable products, basic pharmaceuticals, oil and sugar crops, metals and metal products increased, among which the output of electronic equipment increased by an enormous amount of 2.07%. However, the decline in construction, recreation and leisure, hotels and restaurants, financial and insurance services, retail, wholesale and business activities, transportation and communication, and other service sectors was still significant.
(2) China. Under China's unilateral measures to deal with the epidemic, the level of China's total output decreased by 0.46%, among which mineral resources and energy products, petrochemical rubber and plastics, basic medicines, metals and metal products, and utility services increased slightly. Among them, the output of mineral resources and energy products increased by 2.09%, but output in the remaining 19 sectors still fell.
(3) The UK and the EU. The total output of the EU decreased by 1.89%. In contrast, the output of the entire economic sectors, such as mineral and energy products, fruit and vegetable products, plant fibers, electronic equipment, oil and sugar crops, cereals and crops, metal and metal products, fur and textile and clothing increased. Among them, the output of mineral and energy products increased by the most (3.62%). However, the other 16 sectors' output declined to various degrees. The total output of the UK decreased by 1.52%. Except for the physical sectors such as fur and textile and clothing, electronic equipment, fruit and vegetable products, plant fibers, mineral and energy products, basic medicines, grains and crops, petrochemical, rubber and plastic products, oil and sugar crops, wood products and paper products, the output of the remaining 14 sectors all declined to various degrees. The output of the service sectors such as construction, hotel and catering, entertainment and leisure, retail, wholesale and business activities, real estate leasing and property fell significantly.
(4) Japan and South Korea. Japan's total output level fell 0.94%, with the output growth in seven sectors: mineral deposits and energy products, oil and sugar crops, cereals and crops, animal husbandry, essential medicines, fruit and vegetable products, wood products and paper products. It also led to a decrease of 0.80% in South Korea's total output level. Regarding the changes in the output levels of various production sectors, the output of the entire economic sectors, such as mineral resources and energy products, oil and sugar crops, plant fibers, cereals and crops, and metals and metal products increased slightly. Among them, the output of mineral resources and energy products increased by 4.50%. The output of the other 16 sectors declined, among which, the output of the service sectors such as construction, entertainment and leisure, hotel and catering, real estate leasing and property declined significantly, with a decline in the range of 1.02 to 2.27%.

The various measures taken by China in response to the outbreak were able to significantly mitigate the impact of the Newcastle pneumonia outbreak on China's total output level. However, the impact on the other five economies' total output levels was insignificant.

4.2.3 Economic effects of countermeasures taken by other economies in the world

As seen in Figure 5, the response measures taken by economies other than China had little impact on China's Industry sector sector's output level. However, they were able to significantly mitigate the impact of the epidemic shock in the US, UK, EU, Japan and South Korea.

(1) The US. Responses from economies other than China could result in a potential 1.01% decline in total US output. By sector, output levels are likely to rise in essential medicines, mineral and energy products, furs and textile clothing, fruit and vegetable products, tobacco and alcohol by-products, livestock, real estate rental and property, utility services, and education and health, with cereal and crop output unchanged, but output in 14 other sectors is likely to fall.
(2) China. China's total output declined by 2.46%, with the output of plant fiber, minerals and energy products rising by 1.16 and 0.31%, respectively. At the same time, the remaining 22 sectors show a decline in output, with the service sectors of hotels and restaurants, real estate rental and property, recreation and leisure, construction, education and health, and financial and insurance services showing a more pronounced decline in output levels. However, comparing Scenario 2, it can be seen that adopting policies to deal with the epidemic in the US, Japan, the UK, the EU and South Korea had a minor impact on China's output.
(3) The UK and the EU. The EU total output level fell by 0.81%, with notable rises in output in the real economy sectors of minerals and energy products, fruit and vegetable products, oil and sugar crops, essential medicines, cereals and crops, forestry and fishing, with the most impressive growth of 2.29% in the output of minerals and energy products. In contrast, output in the other 13 sectors rose by varying degrees. The level of total

UK output rose by 0.02%. Looking at the sectors, except construction, transport and communications, retail, wholesale and business activities, hotels and restaurants, metals and metal products, and transport and machinery equipment, which registered declines, construction saw the largest decrease of 5.67%, while metals and metal products and transport and machinery equipment also saw more pronounced declines; the rest of the sectors saw an increased output, with basic pharmaceuticals production topping the list with a 5.33% increase.

(4) Japan and South Korea. Japan's total output level fell by 0.74%. From a sectoral perspective, except for livestock, basic pharmaceuticals, oil and sugar crops, cereals and crops and other physical sector output rose by 1.66–2.11%, real estate rental and property, utility services, education and health and other services sector output level rose by about 1.40%; however, electronic equipment, transport and machinery equipment, metal and metal products, plant fibers and other physical sector output level fell by a still more prominent, in the range of 2.06 to 5.32%. Total output in South Korea fell by 0.47%. The output levels of the real sectors of petrochemicals and rubber and plastic products, electronic equipment, tobacco and alcoholic beverages, furs and textiles and clothing, forestry and fisheries, and all services declined. In contrast, the output of the real sectors of minerals and energy products, oil and sugar crops, and cereals and crops showed an enormous increase of 1.68–3.23%.

4.2.4 Macroeconomic effects of countermeasures adopted by all major world economies

(1) The US. Total output in the US fell 2.31% as other major economies took measures to deal with the impact of the pandemic. The output of basic drugs, mineral and energy products, fruit and vegetable products, fur and textile and clothing, oil and sugar crops, plant fibers, real estate leasing and property management sectors increased, among which the output of basic drugs increased the most by 3.21%. The other 17 sectors' output fell to varying degrees, with construction recording the largest decline of 10.57%. Compared with Scenario 1, the total output level of the US decreased further under Scenario 4, which may be related to the fact that the economic growth of the US mainly relies on net exports and inventories, and some economic stimulus measures are long-term mechanisms that can backfire in the short term.

(2) China. In this scenario, China's total output level increases by 0.25%. In terms of the various departments, the output of mineral and energy products, electronic equipment, metal and metal products, plant fibers, petrochemical, rubber and plastic products, transportation and machinery and equipment, wood products and paper products, fur and textile and clothing, public utility services increased, especially the output of mineral and energy products increased by 2.97%. This indicated that if the world's major economies took anti-epidemic measures, they could effectively mitigate the adverse impact of COVID-19 pandemic on China's output. Under Scenario 4, China's output levels improve across all sectors, resulting in a 0.25% increase in total domestic output. The change in output across sectors shows an increase in the output level in minerals and energy products, electronic equipment, and metals and metal products, with the output of minerals and energy products, in particular, increasing by 2.97%. However, the scenario works less well for the other five developed economies, which may be related to the relatively low value-added of Chinese products and the greater scope for development.

(3) The UK and the EU. The total output level of the EU may decrease by 1.31%. In addition to mineral and energy products, fruit and vegetable products, public utility services and other sectors, which increased slightly by 1.63, 1.13 and 0.16%, the output of the other 21 sectors decreased to varying degrees, among which the output of the construction industry decreased the most, by 3.36%. This scenario can mitigate the epidemic's negative impact by reducing the EU output. Meanwhile, the aggregate output level of the UK fell by 1.56%. The output of basic medicines, fur and textile and clothing, mineral and energy products, fruit and vegetable products, petrochemical, rubber and plastic products, electronic equipment, grains and crops, plant fibers, real estate leasing and property increased, with the output of basic medicines rising by 4.91%. Under Scenario 4, a slight decrease in the level of UK aggregate output compared to Scenario 1. Compared with Scenario 1, the level of the UK aggregate output was likely to decline slightly under Scenario 4.

(4) Japan and South Korea. The output level of Japan decreased by 2.47%, in which the output level of all sectors declined except for the weak growth of 0.09% in grain and crops. Among them, the output level of real economic sectors such as fur and textile and clothing, electronic equipment, transportation and mechanical equipment, metal and metal products, petrochemical, rubber and plastic products, and plant fibers declined considerably, with the decline ranging from 3.36 to 5.69%. Under Scenario 4, the total domestic output of South Korea slightly decreased by 1.05%. In terms of the changes in the output level of each sector, the output of the actual economic sectors such as mineral resources and energy products, oil and sugar crops, cereals and crops, plant fibers, metals and metal products, transportation and machinery and equipment increased, among which the output of mineral resources and energy products increased the most, reaching 3.26%. The output of the other 18 sectors declined to various degrees, with petrochemical, rubber and plastic products and fur and textile and clothing falling the most, by 2.75 and 2.11%, respectively. This may be since Japan was greatly affected by the upstream and downstream of the Industry sector chain, and the high degree of foreign trade dependence between the two countries.

4.3 Sensitive analysis

Considering the results of the above analysis, we conducted two robustness tests. The first sensitivity analysis examined

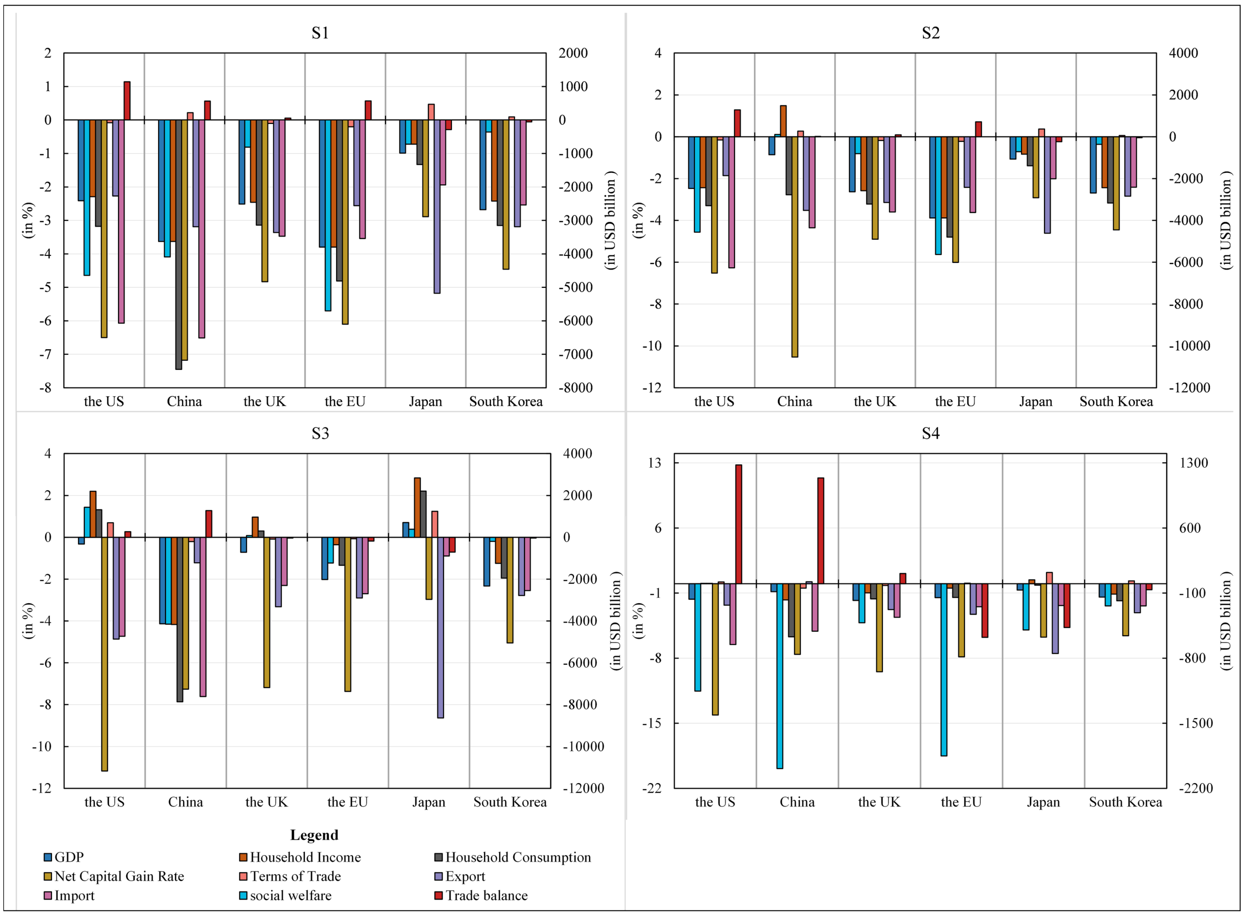

FIGURE 6
Robustness Test 1—Macroeconomic impact. Source: compiled from CGE-COVID-19 model results.

changes in the Armington elasticity of domestic and imported product sources (PSBD) Product Source (PS) and Brand Distribution (BD), Variations in the Elasticity of Product Source (PS) and Brand Distribution (BD) for both Domestic and Imported Products. A higher PSBD means greater substitutability between domestic and imported product sources, and vice versa. To assess the impact of this parameter, PSBD values for product sources were increased by 50%, respectively. As shown in Figures 6, 7, the results of sensitivity analysis show that the numerical difference from the original study is kept within the negligible range of 1%, thus confirming the robustness of the initial conclusion.

The second sensitivity analysis examines the effect of changes in the elasticity of Armington on the distribution of product sources in import regions. This parameter is closely related to the trade diversion effect. A higher PSBD suggests that, for the six economies studied in this paper, it is easier to make up for product import shortfalls by importing products from other countries. PSBD values were increased by 50% for each product type. Similar to the first sensitivity analysis, the results show that the numerical difference from the original study results is within the negligible range of 1%, thus reaffirming the robustness of the preliminary conclusions (see Figures 8, 9).

5 Conclusion

Based on the CGE-COVID-19 model, this study provides a thorough analysis of the impact of the 2022 new coronavirus pneumonia epidemic on the supply and demand sides of the world's major economies: China, the US, the UK, the European Union, Japan, and South Korea. This is an expansion of current studies that focus primarily on the impact of the epidemic on individual countries (26, 28). Furthermore, considering the economic consequences of the epidemic, potential countermeasures that may be adopted by China and other countries in response to the crisis are simulated and analyzed. After a comprehensive analysis of the results, the following conclusions can be drawn.

First, the COVID-19 pandemic harmed GDP growth, terms of trade, social welfare level, household income and consumption expenditure, the net return on capital, and import and export of all economies. The COVID-19 pandemic leads to a reduction in the supply of labor in a country. On the one hand, underemployment directly reduce household income and reduce consumers' purchasing power. On the other hand, the rise of unemployment directly leads to the decline in the production capacity of enter-prises, the reduction of domestic production, the reduction of the quantity and type of

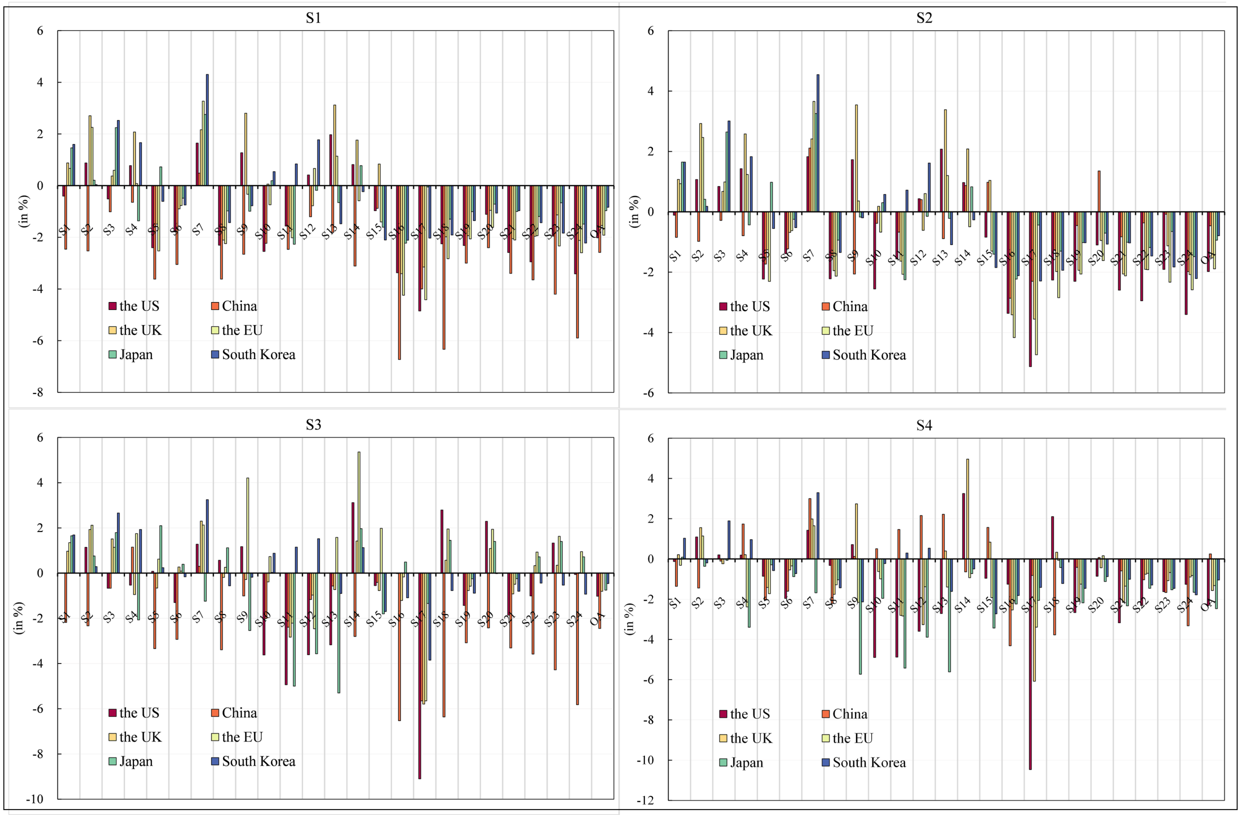

FIGURE 7
Robustness Test 1—Industry sector economic impact. Source: compiled from CGE-COVID-19 model results.

export commodities, resulting in a decline in export income. However, if some key commodities cannot be produced domestically, it may be necessary to continue to import, which is prone to the decline of export prices relative to import prices, thus leading to the deterioration of the terms of trade. This is consistent with the majority of scholars finding a significant negative impact of the pandemic on the global economy (41, 50). Based on the changes in GDP, social welfare level, household income and consumption expenditure, and net return on capital, China and the EU suffered the most apparent losses caused by the epidemic's impact, with all macroeconomic indicators falling at the forefront. The US and the UK have been hit less than China and the EU. In addition, South Korea and Japan were the least affected. Therefore, the overall negative impact of COVID-19 pandemic on the macro economy of major economies was significant and needed to be paid great attention to (42).

Second, since labor is one of the basic elements of production, the reduction in labor supply directly leads to the decline in the productive capacity of many industries and enterprises. Therefore, in the short term, total social output may be affected. COVID-19 pandemic hurt the aggregate output of major economies on average, especially China, followed by the US, the UK and the EU, while it had a negligible impact on Japan and South Korea. However, the impact on different industries is heterogeneous (62). In terms of sectoral changes in output levels in major economies, the similarities were that the pandemic crisis reduced the output of services, and manufacturing sectors (forestry, fishery, real sectors such as tobacco, alcohol and non-staple food, hotels, catering, construction, estate leasing, property, transportation and communication, public utility services, retail and wholesale, commercial activities, financial and insurance services, education and health, entertainment and leisure) (32, 36).

Third, government intervention helps the economy recover (53, 54). China's policies yielded a positive influence on various aspects, including the terms of trade, the level of social welfare, households income and the trade balance, thus leading to a reduction in the surplus. The proactive measures adopted by China in response to the pandemic crisis played a pivotal role in effectively mitigating its detrimental effects on the GDP (30, 31). These policies include fiscal policy, monetary policy, labor market policy, foreign trade policy, industrial upgrading and structural adjustment. Only when these measures are coordinated and synergistic can they effectively promote economic recovery (64).

This paper thus puts forward the following policy recommendations for countries to alleviate the epidemic: firstly, increase macroeconomic policy support by adopting an active fiscal policy on the one hand and fully applying monetary policy on the other; secondly, appropriately increase enterprise subsidies to address the demand for funds for enterprises to resume work and production; thirdly, provide subsidies to individuals and households to boost

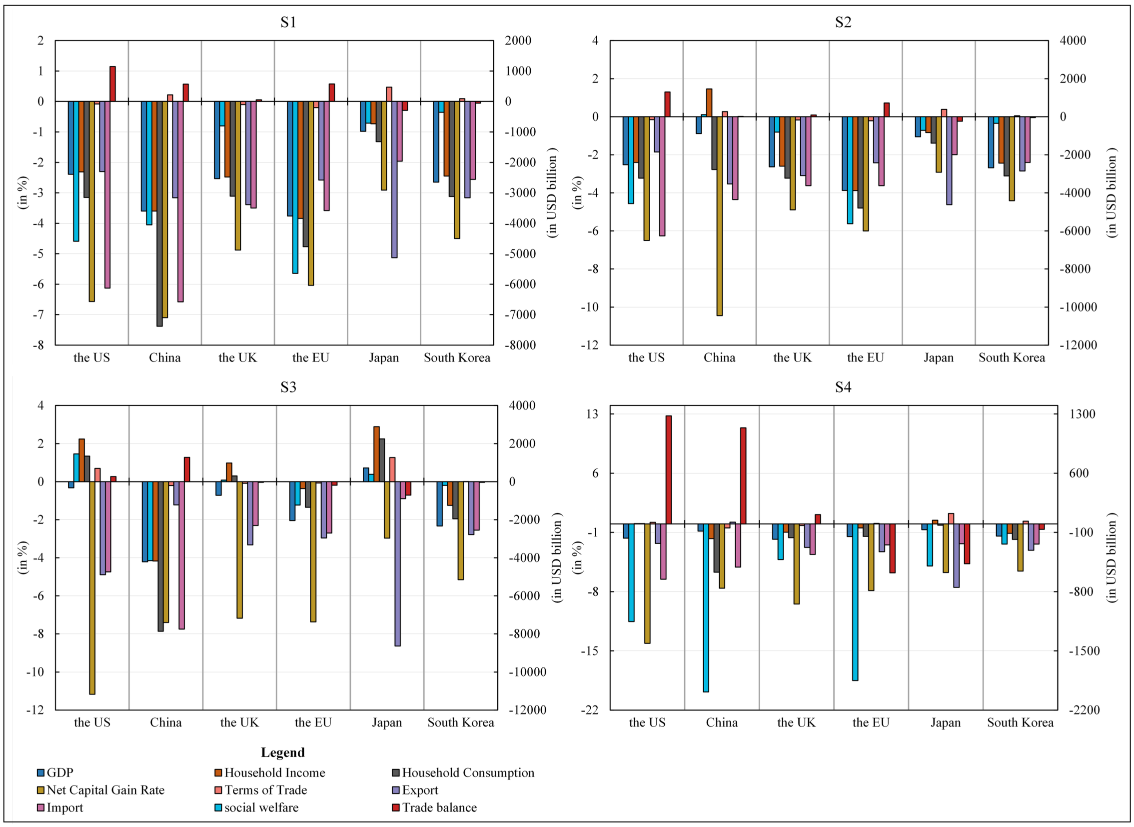

FIGURE 8
Robustness Test 2—Macroeconomic impact. Source: compiled from CGE-COVID-19 model results.

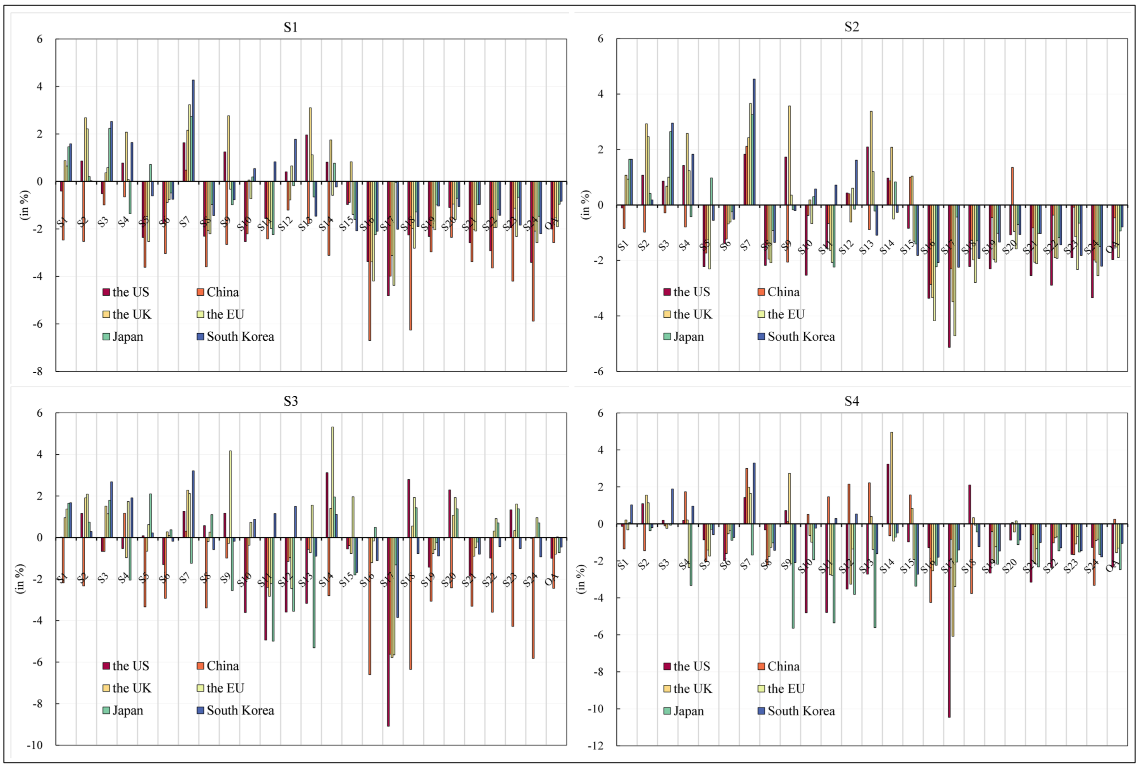

FIGURE 9
Robustness Test 2—Industry sector economic impact. Source: compiled from CGE-COVID-19 model results.

domestic demand and consumption (65, 66); fourthly, employment is a matter of national importance and livelihood, and the employment pressure should be kept vigilant. In response to the challenges posed by the COVID-19 pandemic, there is a pressing need to expedite the cultivation and advancement of emerging industries and dynamic energy sources (67, 68). Moreover, urgent attention should be given to the development of crucial infrastructure in sectors such as new energy and healthcare. Additionally, it is imperative to ensure the stability of the existing employment structure and ratios while making concerted efforts to bolster enterprises in their capacity to absorb labor. The last but not the least, establishing a global response mechanism to jointly address the next pandemic.

What needs to be stressed is that the COVID-19 epidemic has had a huge impact on the economy and society in the past 3 years, and will have a profound impact on future economic development. At this stage, it is particularly important for our research to provide data support for governments to adopt practical, scientific and accurate responses to the epidemic. However, there is an unavoidable problem that the epidemic situation changes rapidly, and there may be deviations between the data analysis results and the actual situation due to technical obstacles and difficulties in obtaining data, which should be further explored in future studies.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

MS: Conceptualization, Methodology, Software, Supervision, Writing – original draft. SY: Data curation, Formal analysis, Investigation, Writing – review & editing. TC: Funding acquisition, Resources, Visualization, Writing – review & editing. JZ: Investigation, Project administration, Formal analysis, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1338677/full#supplementary-material

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Impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services in low-and middle-income countries: a systematic review of the literature

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Background: The COVID-19 pandemic has had a multifaceted impact on maternal and child services and adversely influenced pregnancy outcomes. This systematic review aims to determine the impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services in low- and middle-income countries.

Methods: The review was reported following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A primary search of electronic databases was performed using a combination of search terms related to the following areas of interest: "impact' AND 'COVID-19' AND 'maternal and child health services' AND 'low- and middle-income countries. A narrative synthesis approach was used to analyse and integrate the results.

Results: Overall, 45 unique studies conducted across 28 low- and middle-income countries met the inclusion criteria for the review. The findings suggest the number of family planning visits, antenatal and postnatal care visits, consultations for sick children, paediatric emergency visits and child immunisation levels decreased compared to the pre-pandemic levels in the majority of included studies. An analytical framework including four main categories was developed based on the concepts that emerged from included studies: the anxiety of not knowing (1), overwhelmed healthcare systems (2), challenges perceived by healthcare professionals (3) and difficulties perceived by service users (4).

Conclusion: The COVID-19 pandemic disrupted family planning services, antenatal and postnatal care coverage, and emergency and routine child services. Generalised conclusions are tentative due to the heterogeneity and inconsistent quality of the included studies. Future research is recommended to define the pandemic's impact on women and children worldwide and prepare healthcare systems for future resurgences of COVID-19 and potential challenges beyond.

Systematic review registration: PROSPERO (CRD42021285178).

KEYWORDS

COVID-19, maternal and child healthcare services, low- and middle-income countries, women, paediatric

Introduction

The coronavirus disease (COVID-19) pandemic has had a profound impact on the world, causing not only considerable disruptions to daily life but it has tragically resulted in a significant number of deaths worldwide. According to the World Health Organization (WHO), as of June 5, 2023, there have been more than 767 million confirmed cases of COVID-19, including more than 6.9 million deaths globally (1). Countries around the world have responded to the COVID-19 outbreaks with a range of measures aimed at controlling the spread of the virus and protecting their populations (2). The specific actions taken included imposing lockdowns, movement restrictions, mass testing, contact tracing, mask mandates and hygiene practises (3). Countries have collaborated with each other in sharing data, research and resources and implemented travel restrictions, border closures and mandatory quarantine measures (3).

The COVID-19 restrictions have had a multifaceted impact on healthcare access and delivery. Firstly, routine healthcare services, including non-urgent medical procedures, routine screenings and preventive care, were disrupted due to the re-organisation of the healthcare system to meet the needs of patients diagnosed with COVID-19 (4–6). Secondly, access to healthcare facilities was limited as a result of restrictions on movement and transportation challenges (7, 8). It was also noted that patients tend to avoid seeking healthcare due to fear of contracting COVID-19 in healthcare settings (9). Thirdly, COVID-19 has disproportionately affected healthcare delivery for vulnerable populations and exacerbated existing health disparities (10–12). A WHO survey has recently disclosed that disruptions to healthcare services were predictably greater in low- and middle-income countries (LMICs) than in high-income countries (HICs) (13). Finally, the existing studies have described that outbreaks and responses to them may cause unintentional indirect health ramifications. For instance, the overall use of healthcare services, deliveries in health facilities and malaria admissions decreased by 18% (14), 80% (15) and 40% (15), respectively, during the West African Ebola virus outbreak. It was also estimated that mortality rates from the Ebola virus were comparable to deaths from non-Ebola conditions (16–18). There are concerns that these trends are repeated during the COVID-19 pandemic.

The scale of the COVID-19 pandemic has significantly affected maternal and child services and adversely influenced pregnancy outcomes. A recent systematic review and meta-analysis suggested that maternal mortality, stillbirth, ruptured ectopic pregnancy, and maternal depression increased during the pandemic (19). Other studies report a rise in iatrogenic preterm birth and caesarean delivery amongst infected mothers (20, 21). Furthermore, a number of reports express concerns that the indirect impact of the pandemic might be similar to the direct influence of the virus, specifically in low-income settings (20, 22). A modelling study involving 118 LMICs estimated that the reductions in coverage by maternal and child services might lead to more than a million additional child deaths (23). Another study estimated that a COVID-19-focused approach may have led to 30% additional maternal and child deaths across four different LMICs (24). However, the current understanding of the COVID-19 effects on maternal and child healthcare services is mainly based on pooled estimates of data gathered globally or across HICs, and the number of studies drawing together results from multiple LMICs remains limited (9, 25). Therefore, this systematic review aims to determine the impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services in LMICs.

Abbreviations: COVID-19, Coronavirus Disease; SARS-COV-2, Severe Acute Respiratory Syndrome Coronavirus 2; WHO, World Health Organization.

Methods

The protocol for this review was registered on PROSPERO (CRD42021285178) in advance. This study was reported following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (26).

Search strategy

The following five electronic databases were searched: Scopus, Pubmed, Embase, Web of Science, and The Cochrane Central Register of Controlled Trials on October 15, 2021 and updated on June 29, 2023. Search terms combined three overlapping areas with keywords such as 'impact' AND 'COVID-19' AND 'maternal and child health services' AND 'LMICs' (see Supplementary Files 1, 2). Publication bias was reduced by searching conference records and unpublished literature using Google Scholar, OpenGrey, EThOS, the British Library Catalogue and Copac theses. In addition, backward and forward citation tracking was adopted to include studies and review records.

Selection criteria

Studies were eligible if they evaluated the impact of the COVID-19 outbreak on access to and delivery of maternal and child healthcare services in LMICs as defined by World Bank criteria (27). Studies were excluded if they met one of the following conditions: (1) non-research-based articles, such as conference abstracts, commentaries, opinion pieces, book chapters and editorials; (2) are not written using the Latin alphabet, Russian or Kazakh; (3) abstract is not available; (4) or full text is not available.

Identification and data extraction

Titles and abstracts of identified records were exported to EndNote X8 and screened by AK to exclude irrelevant studies and duplicates. A random sub-sample of 20% of titles and abstracts were screened by a second reviewer (MAO) to ensure the accuracy of selection. Full text articles were inspected again (AK, MAO, MJN and ASS) for relevance according to the inclusion criteria.

Data from included studies were extracted into a spreadsheet by MJN and a random sub-sample of 40% was reviewed by AK and MAO. Discrepancies were addressed by involving a fourth reviewer (ASS). The level of agreement between AK and MAO was 75%, and between AK and ASS was 80%.

Quality assessment

The methodological quality of the included records was assessed depending on their design. The 14-item Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (28) was applied in accordance with nine criteria, as five criteria were not applicable. The 12-item Quality Assessment Tool was utilised for Pre-Post (Before-After) Studies With No Control Group (29), the 9-item Quality Assessment Tool was used for Case Series Studies (28), the 7-item Quality Assessment Tool was applied for Mixed-Methods Studies (30) and the 10-item Critical Appraisal Skills Programme (CASP) checklist was adopted for qualitative studies (31) (see Supplementary File 3). AK completed a full quality assessment. MAO ensured the accuracy at this stage by independently assessing 20% of records.

Data synthesis

A narrative synthesis approach developed by Popay and colleagues (32) was applied to explain and integrate the results.

Firstly, the preliminary synthesis of quantitative data was conducted in order to describe patterns across the included studies grouped by four indicators: impact on maternity service use, impact on maternity service provision, impact on postnatal care and impact on utilisation of child health services. Textual descriptions of studies and tabulation were used as specific tools. A formal meta-analysis was not performed due to considerable heterogeneity in settings and outcome measures.

Secondly, the experiences of service users and healthcare professionals regarding access to and delivery of maternal and child healthcare services during the pandemic were analysed using the Framework Method following the guidelines developed by Gale and colleagues (33). This method includes seven distinct stages: transcription, familiarisation with the data, coding, developing a working analytical framework, applying the analytical framework, charting the data into framework matrix, and interpreting the data. As the review collated data from published studies, the initial stage of transcription was not applicable. The familiarisation stage included reading and rereading the studies included in the review. Further, data from the results sections of included studies were coded and preliminary concepts were defined inductively. Similar concepts were grouped into categories and sub-categories independently by the first author (AK) and were discussed with the other researchers (MAO and ASS) to ensure the range and depth of the coding. The defined categories and sub-categories were then organised into the working analytical framework, which was applied to the results sections of the included studies by systematically coding in a line-by-line manner. Once appropriate codes and categories were assigned, data was charted into the framework matrix by listing illustrative quotations by category and sub-category from each study.

Results

The original search yielded 2,492 articles through database searching, 11 through other sources and 1,132 through search update. Overall, 945 articles were removed as duplicates and 2,485 articles were excluded for not meeting the inclusion criteria. The full texts of the remaining 205 papers were examined, 45 of which were included to the review. The detailed selection process is presented in the PRISMA flow diagram below (Figure 1).

Overview of included studies

Studies were published between 2020 and 2023 solely in English. Overall, 14 studies reported data from four low-income countries (34–47), 21 studies were focused on 13 lower-middle income countries (48–68), seven studies were conducted in five upper-middle income countries (69–75) and three were multi-centred (76–78). Out of 45 included studies, 11 studies were cross-sectional (41, 45, 48, 51, 55–57, 65, 69, 70, 76), 14 were pre-post studies (34, 38, 49, 50, 52, 53, 56, 62, 64, 72–75, 77), nine were time-series (35, 37, 39, 43, 58, 59, 67, 71, 78), five were mixed methods (36, 42, 47, 61, 63) and six were qualitative (40, 44, 46, 54, 60, 68). The included studies' characteristics are summarised in Table 1.

The results of the current review will be presented in two parts. Firstly, the impact on access to and delivery of maternal and child healthcare services will be presented in accordance with four groups of indicators. In the second part, the experiences of service users and healthcare professionals regarding the pandemic's impact on access to and delivery of maternal and child healthcare services will be introduced.

Impact on maternity service use and provision

Family planning services

In nine studies (34, 38, 41, 47, 49, 58, 67, 76, 77), the analysis showed interruptions in family planning services (76), a decrease in attendance of family planning visits (77), in the overall number of such visits (34, 41, 47, 49, 58, 67) and family planning acceptance rate (38) compared to the pre-COVID-19 levels. Although some authors observed a reduction in the number of new contraceptive acceptors (45) and difficulties accessing contraceptives (73), Tilahun and colleagues reported an increased contraceptive acceptance rate in Ethiopia (42). Three studies declared impaired abortion care during the pandemic in Ethiopia and India (38, 45, 66).

Antenatal and postnatal care coverage

Twenty-seven studies reported on antenatal care coverage during the pandemic using various metrics (34, 36–38, 42, 43, 47, 49–51, 56, 58, 59, 61–63, 65, 67, 70–78). Albeit no changes were made to the standard antenatal care protocol in the majority of settings, increased interruptions in antenatal care (76) and a decrease in antenatal care coverage (42), antenatal recruitment rate and prenatal visit completion rate (59), antenatal care registrations (62), number/proportion of antenatal care visits (34, 36–38, 47, 49, 56, 58, 61, 65, 67, 71, 72, 74, 75) and attendance (50, 51, 70, 77, 78) was noticed in most cases as compared to the pre-pandemic period. However, Pillay and colleagues (73) observed no difference in the number of first antenatal care visits in South Africa and Lydon and colleagues (43) detected an increased number of first antenatal visits and no difference in the number of fourth antenatal visits in Mozambique. No difficulties in accessing

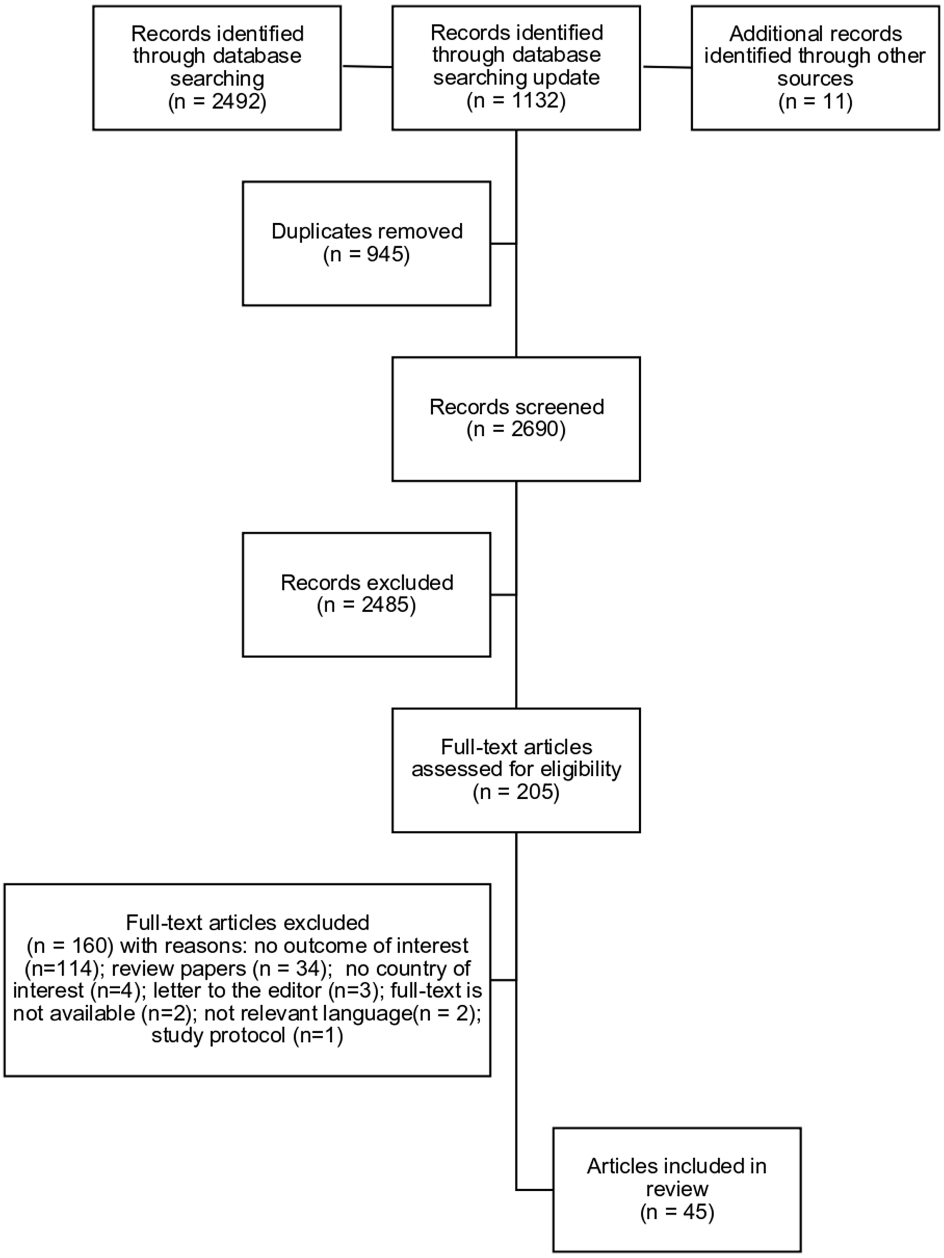

FIGURE 1
PRISMA flow chart.

antenatal care were declared in one study originated from India (63). Due to the restrictions imposed during the COVID-19 pandemic, authors noticed a declining trend in the number of first routine laboratory tests (58), first and second trimester sonography (58, 66) and pregnant women receiving the second dose of tetanus toxoid vaccine during pregnancy (49). Furthermore, as per Burt and colleagues (37), the number of attendances for prevention of mother-to-child transmission of HIV dropped than stabilised in Uganda. A surge in the number of high-risk pregnancies was described in one study (56).

Although three studies highlighted reduced postnatal care (45, 67, 78), it was not universal as postnatal care coverage surged in Ethiopia (42).

Virtual care protocols

Despite the active promotion of virtual services during the pandemic, only one study from Cameroon reported an increase in the use of telemedicine services (57). According to Goyal and colleagues, just 3.6% of pregnant women living in India exploited teleconsultations amongst more than a thousand respondents (66).

Impact on institutional delivery

Included studies showed mixed results concerning institutional deliveries that comprise normal vaginal deliveries and caesarean sections. Even though eight studies highlighted a reduction in the number/proportion of institutional deliveries (36, 49–51, 56, 61, 62, 67, 71), six reports (38, 43, 63, 73–75) observed growth and two studies (34,

TABLE 1 Characteristics of included studies.

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
1	Abdela et al., 2020 (34)	Ethiopia (low-income)	To assess the effect of prevention measures on essential healthcare services at Dessie Referral Hospital	Pre-post	Patients attending different essential healthcare services	Census	Not reported	Number of mothers delivering at the hospital	No difference
								Family planning visits	Decreased
								Antenatal care visits	Decreased
								Neonatal admissions	Decreased
								Childhood emergency visits	Decreased
2	Abdul-Mumin et al., 2021 (48)	Ghana (lower middle-income)	To describe the impact of the COVID-19 pandemic on new born care by comparing morbidity and mortality between the COVID-19 era and the preceding year in the Neonatal Intensive Care Unit (NICU) at Tamale Teaching Hospital, Ghana	Cross-sectional	Neonates admitted to the Neonatal Intensive Care Unit (NICU)	Census	2,901	Admissions of inborn neonates	Decreased
								Neonates born at home	Decreased
								Proportion of referrals to the NICU from other facilities	Increased
								Admissions due to neonatal infections	Decreased
								Admissions due to prematurity and complications, and neonatal jaundice	Increased
3	Abebe et al., 2021 (35)	Ethiopia (low-income)	To assess the impact of COVID-19 on the trends of nonCOVID follow-up visits and admissions at Tikur Anbessa Specialised Hospital (TASH), Addis Ababa, Ethiopia	Time-series	Patients at TASH	Census	12,314 (follow-up visits) and 5,693 (hospital admissions) – (General data)	Paediatric emergency admissions	Decreased
								Admissions from the general paediatric follow-up clinics	Decreased
4	Ahmed et al., 2021 (77)	multi-centred Bangladesh (lower middle-income) Nigeria (lower middle-income) South Africa (upper middle-income)	To assess the disruption in utilisation of maternal, neonatal and child health care as a result of the COVID-19 pandemic in three LMICs	Pre-post	Users of the maternal, neonatal and child health services	Census	Not reported	Attendance of antenatal care	Decreased
								Attendance of family planning clinics	Decreased
								Child immunisation	Decreased
								Facility vaginal delivery rates	Decreased in Bangladesh Mixed in Nigeria and South Arica
								Caesarean section delivery rates	Decreased in Bangladesh Mixed in Nigeria and South Arica
5	Akuaake et al., 2020 (69)	South Africa (upper middle-income)	To describe and compare the effect of the level 5 national COVID-19 lock-down measures on the workload and case mix of paediatric patients presenting to a district-level emergency centre in Cape Town, South Africa	Cross-sectional	Patients less than 13 years of age that presented to the emergency centre of Mitchells Plain Hospital	Convenience	9,982	Children emergency centre visits	Decreased
								Presentations of respiratory diseases, infectious diseases and injuries	Decreased

(Continued)

TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
6	Assefa et al., 2021 (76)	multi-centred Burkina Faso (low-income) Ethiopia (low-income) Nigeria (lower middle-income)	To characterise the impacts of the COVID-19 pandemic on the interruptions on health services from the perspectives of both HCPs and community members in three sub-Saharan African countries, Burkina Faso, Ethiopia, and Nigeria	Cross-sectional	Healthcare providers and community members	Not reported	900 healthcare providers and 1797 community members	Interruptions in antenatal care	Increased
								Interruptions in folate supplementation	Increased
								Interruptions in family planning	Increased
								Interruptions in maternal and child services	Increased
7	Baloch et al., 2021 (49)	Pakistan (lower middle-income)	To assess the utilisation of reproductive, maternal, neonatal, and child health services at the primary healthcare level during the first wave of the COVID-19 outbreak in Sindh, Pakistan	Pre-post	Users of the reproductive, maternal, neonatal, and child health services	Convenience	Not reported	First antenatal visits	Decreased
								Number of pregnant women receiving the second dose of tetanus toxoid vaccine during pregnancy	Decreased
								Number of normal vaginal deliveries	Decreased
								Family planning visits	Decreased
								Number of children receiving their scheduled vaccination	Decreased
8	Singh et al., 2021 (50)	India (lower middle-income)	To quantify the potential impact of the COVID-19 pandemic on maternal and child health services in the state of Uttar Pradesh, India	Pre-post	Users of the maternal and child public health facilities of District Sant Kabir Nagar in Uttar Pradesh, India.	Not reported	Not reported	Number of institutional deliveries	Decreased
								Attendance of antenatal care services	Decreased
								Immunisation services	Decreased
9	Shapira et al., 2021 (78)	multi-centred Cameroon (lower middle-income) Democratic Republic of Congo (low-income) Liberia (low-income) Malawi (low-income) Mali (low-income) Nigeria (lower middle-income) Sierra Leone (low-income) Somalia (low-income)	To quantify the disruption of maternal and child health services during the COVID-19 pandemic using nation- ally comprehensive administrative data in eight sub-Saharan African nations	Time-series	Users of the maternal and child health services	Census	9,499,075	Number of outpatient department consultations	Decreased
								Number of child vaccinations	Decreased
								Number of institutional deliveries	Decreased (in 5 countries)
								Attendance of antenatal care services	Decreased
								Postnatal care visits	Decreased

(Continued)

TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
	Shakespeare et al., 2021 (51)	Zimbabwe (lower middle-income)	To compare maternal and perinatal outcomes before and after lockdown was implemented	Cross-sectional	Users of the government tertiary level maternity unit in Bulawayo, Zimbabwe	Not reported	Not reported	Workload	No difference
								Number of deliveries	Decreased (not significant)
								Number of Caesarean section deliveries	Decreased (not significant)
								Attendance of antenatal care services	Decreased
								Maternal mortality	No difference
								Stillbirth rate	Decreased (not significant)
								Number of early neonatal deaths	Increased (not significant)
11	Rahul et al., 2020 (51)	India (lower middle-income)	To analyse the impact of this pandemic on the management of paediatric surgical cases at four tertiary care centres in Northern India.	Pre-post	Paediatric patients who underwent surgery	Census	100	Total emergency cases	Decreased
								Number of patients who left against medical advice	Increased
12	Qureshi et al., 2021 (53)	India (lower middle-income)	To evaluate the extent by which the lockdown, imposed by the government, has impacted the activity of admissions to the tertiary maternity hospital in Srinagar	Pre-post	Patients admitted to the tertiary maternity hospital in Srinagar	Census	Not reported	Total number of emergency admissions	Decreased (significant)
								Number of patients admitted with intrauterine device	Increased (significant)
								Number of patients with eclampsia	Increased (significant)
								Number of patients admitted with ectopic abruptions, obstructed labour and postpartum haemorrhage	No difference
13	Muhaidat et al., 2020 (70)	Jordan (upper middle-income)	To identify how the lockdown circumstances in Jordan have affected antenatal care provision to pregnant women across the country	Cross-sectional	Women residing in Jordan who are currently pregnant	Not reported	944	Attendance of antenatal care	Decreased (significant)
14	Pires et al., 2021 (36)	Mozambique (low-income)	To assess the impact of Covid-19 pandemic Government restrictions on access to maternal and child healthcare services	Mixed-methods	Users of maternal and child health care unit for survey and 19 females participants for interviews (mothers, pregnant women, traditional birth attendants and nurses)	Not reported	Qualitative component: 19 (10 users and 9 nurses)	Number of home deliveries	Increased (not significant)
								Number of pregnant women attending their first antenatal visit	Increased (not significant)
								Number of women completing four antenatal visits	Increased (not significant)
								Number of well-baby visits	Increased (not significant)
								Number of elective Caesarean sections	Decreased (not significant)
								Number of hospital deliveries	Decreased (significant)

(Continued)

TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
15	Onchonga et al., 2021 (54)	Kenya (lower middle-income)	To understand the health-seeking behaviour of women who were pregnant during the onset of the COVID-19 pandemic in Kenya	Qualitative	Women who had attended at least one antenatal care clinic in a county referral hospital in Kenya	Purposive	26	Attendance of antenatal care	Decreased
								Delays in reaching the health facility	Increased
								Delays related to the experience of pregnant women at healthcare facilities	Increased
16	Ogundele et al., 2020 (55)	Nigeria (lower middle-income)	To assess early effects of the COVID-19 pandemic on paediatric surgical practise in Nigeria	Cross-sectional	Paediatric surgeons (consultants and senior registrars) currently practising in Nigeria	Not reported	74	Number of elective surgeries	Decreased
								Number of emergency surgeries	Decreased
17	Doubova et al., 2021 (71)	Mexico (upper middle-income)	To estimate the overall effect of the pandemic on essential health service use and outcomes in Mexico, describe observed and predicted trends in services over 24 months, and to estimate the number of visits lost through December 2020	Time-series	Users of the Mexican Institute of Social Security	Not reported		Number of antenatal care visits	Decreased
								Number of facility deliveries	Decreased
								Caesarean section rate	No difference
								Number of consultations for sick children	Decreased
								Number of childhood vaccinations	Decreased
18	Burt et al., 2021 (37)	Uganda (low-income)	To quantify the indirect impact of COVID-19 on maternal, neonatal and childhood outcomes at KNRH in Kampala	Time-series	Users of the Kawempe National Referral Hospital	Not reported	14,401 antenatal care attendances, 33,499 deliveries, 111,658 attendances for childhood services and 57,174 sexual and reproductive health service attendances	Number of antenatal care visits	Decreased
								Number of attendances for prevention of mother-to-child transmission of HIV	Decreased
								Number of women treated for high blood pressure, eclampsia and pre-eclampsia, adverse pregnancy outcomes (stillbirths, low-birth-weight and premature infant births)	Increased
								Rate of neonatal unit admissions	Increased
								Rate of neonatal deaths	Increased
								Maternal mortality	No difference
								Immunisation clinic attendance	Decreased
19	Caniglia et al., 2021 (72)	Botswana (upper middle-income)	To evaluate the association between the COVID-19 lockdown and the risk of adverse birth outcomes in Botswana	Pre-post	Women who delivered a singleton baby after at least 24 weeks' gestation in 2017–2020 between January 1 and July 20	Census	68,448	Number of births	No difference
								Number of antenatal visits	No difference
								Risk of any adverse birth outcome	Decreased
								Risk of any severe birth outcomes	Decreased

(Continued)

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TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
20	Desta et al., 2021 (38)	Ethiopia (low-income)	To assess the impacts of COVID-19 on essential health services delivery in Tigray, Northern Ethiopia	Pre-post	Users of essential health services in Tigray	Purposive	Not reported	Family planning acceptance rate	Decreased
								Number of antenatal care visits	Decreased
								Number of women who received comprehensive abortion care	Decreased
								Number of children under 2 years of age who have received second dose of measles	Decreased
								Number of institutional deliveries	Increased
								Number of caesarean section deliveries	Increased
								Number of still births	Increased
								Number of children who received all vaccine doses before 1st birthday	Increased
								Number of under 5 children screened and had moderate and severe malnutrition	Increased
21	Hategeka et al., 2021 (39)	Democratic Republic of the Congo (low-income)	To evaluate the impact of the pandemic on the use of essential health services during the first wave of the pandemic in Kinshasa	Time-series	Users of health facilities across Kinshasa	Not reported	3,467,713	The use of maternal health services	No difference
								Child immunisation	No difference
22	Pillay et al., 2021 (73)	South Africa (upper middle-income)	To assess the impact of COVID-19 and restrictions imposed to limit viral transmission on routine health services in South Africa	Pre-post	Users of health services in South Africa	Not reported	Not reported	Access to contraceptives	Decreased
								Number of first antenatal care visits	No difference
								Number of deliveries in public health facilities	Increased
								Maternal mortality	Increased
								Neonatal deaths	Increased
								Child immunisation	Decreased
23	Hailemariam et al., 2021 (40)	Ethiopia (low-income)	To explore COVID-19 related factors influencing antenatal care service uptake in rural Ethiopia	Qualitative	Pregnant women residing in rural districts of Bench-Sheko Zone, and healthcare providers working in the local health care facilities	Purposive	44 pregnant women and 9 healthcare providers	Health facility barriers	Increased
								Quality of care	Decreased
								Difficulties in accessing maternal health care	Increased
								Anxiety	Increased
								Fear of getting COVID-19	Increased

(Continued)

TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
24	Goyal et al., 2021 (56)	India (lower middle-income)	To assess the indirect effect of the COVID-19 pandemic on the health of pregnant women and foetal-maternal outcomes	Pre-post	Users of the e Department of Obstetrics and Gynaecology at All India Institute of Medical Sciences	Not reported	Not reported	Number of admissions	Decreased
								Number of institutional deliveries	Decreased
								Number of high risk pregnancies	Increased
								Number of antenatal care visits	Decreased
25	Enyama et al., 2020 (57)	Cameroon (lower middle-income)	To describe the impact of the COVID-19 pandemic on the clinical activity of paediatricians	Cross-sectional	Paediatricians practising in Cameroon	Not reported	101	Number of paediatric outpatient consultations	Decreased
								Use of telehealth	Increased
26	Enbiale et al., 2021 (41)	Ethiopia (low-income)	To study the effect of preventive COVID-19 measures on essential healthcare services in selected primary and tertiary care settings of Amhara region, Ethiopia	Cross-sectional	Users of healthcare facilities at Amhara region	Not reported	Not reported	Number of family planning visits	Decreased (not significant)
								Number of institutional deliveries	Increased
								Child immunisation	No difference
								Number of institutional deliveries	Decreased
27	Yadollahi et al., 2022 (58)	Iran (lower middle-income)	To assess the impact of the COVID-19 pandemic on maternal healthcare indices and care providers' performance	Time-series	Users of the Shiraz University of Medical Sciences, Shiraz, Southern Iran		63,000 pregnant women	Number of preconception healthcare visits	Decreased
								Number of first routine laboratory tests	Decreased
								Number of prenatal care visits	Decreased
								Number of first and second trimester sonography	Decreased
28	Tilahun et al., 2022 (42)	Ethiopia (low-income)	To examine the effects of the pandemic (COVID-19) on maternal and child health service utilization	Mixed-methods	Qualitative component: decision-makers, health workers, patients and delegates from non-governmental organisations	Qualitative component: purposive Quantitative component: not reported	Qualitative component: 74	Accessibility and quality of routine health services	Decreased
								Utilisation of maternal and child health services	Decreased
								Number of challenges on the commitment of health worker	Increased
								Resources supply	Decreased
								Contraceptive acceptance rate	Increased(not significant)
								Antenatal care coverage	Decreased (not significant)
								Number of skilled deliveries	No difference
								Postnatal care coverage	Increased (significant)
								Child immunisation	Increased (not significant)

(Continued)

TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
29	Tikouk et al., 2023 (59)	Morocco (lower middle-income)	To evaluate the impact of the COVID-19 pandemic on antenatal indicators in the region of Guelmim Oued Noun, Morocco	Time-series	Users of public health services at the region of Guelmim Oued Noun, Morocco	Not reported	Not reported	Antenatal recruitment rate	Decreased
								Recruitment rate of pregnant women visits in the 1st quarter of pregnancy	Decreased
								Prenatal visit completion rate	Decreased
								Average number of visits per pregnancy	Decreased
30	Thahir et al., 2023 (60)	Indonesia (lower middle-income)	To explore the experiences of Indonesian mothers and midwives from a rural regency regarding maternal and child health services delivery during the pandemic	Qualitative	Mothers and midwifes in four sub-districts in Banggai, Indonesia	Random	21 mothers and 6 midwives	Health service change	Service relocation, reduces services, health service changes specific to COVID-19, support within the health service for mothers affected by the pandemic
								Perceived barriers to service delivery	Mothers' perceived barriers for accessing service, midwives' perceived barriers for providing service
								Family impact	Financial impact, emotional impact
31	Sinha et al., 2022 (61)	India (lower middle-income)	To estimate utilisation of maternal, perinatal healthcare services after the lockdown was implemented in response to the COVID-19 pandemic compared to the period before.	Mixed-methods	Women who delivered before and after lockdown	Not reported	Quantitative component: 199 Qualitative component: 25	Number of antenatal care visits	Decreased
								Proportion of institutional deliveries	Decreased
								Faces issues	Fear of contracting COVID-19, poor quality of services, lack of transportation, financial constraints, poor mental conditions (feeling down, depressed or hopeless)
32	Sharma et al., 2023 (62)	India (lower middle-income)	To document the impact of COVID-19 on essential maternal and child health services in India based on the national Health Management Information System	Pre-post	Users of maternal and child health services	Census	Not reported	Antenatal care registrations	Decreased
								Number of pregnant women provided with emergency obstetric care	Decreased
								Number of institutional deliveries	Decreased
								Number of home deliveries	Increased
								Child immunisation	Increased

(Continued)

TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
33	Requena-Mullor et al., 2022 (74)	Dominican Republic (upper middle-income)	To analyse the differences in perinatal outcomes and birth characteristics in two groups of pregnant women, and whether these differences are due to changes in pregnancy monitoring because of the COVID-19 situation	Pre-post	Women who gave birth before and during the pandemic	Census	Overall: 1109 Before pandemic: 496 During pandemic: 613	Number of antenatal visits	Decreased
								Number of instrumental and caesarean deliveries	Increased
								Skin-to-skin contact after birth	Decreased
								Introduction of early breastfeeding	Decreased
34	Padhye et al., 2022 (63)	India (lower middle-income)	To present users' and providers' perspectives about the effect of the pandemic on maternal health services in select districts of Assam	Mixed-methods	Service users and providers	Quantitative component: random Qualitative component: purposive	Quantitative component: 114 pregnant and recently delivered mothers Qualitative component: 38 healthcare providers and 18 Village Health Sanitation and Nutrition Committee members and	Access to antenatal care	Not changed
								Transportation issues	Increased
								Expenses for healthcare services	Increased
								Opportunities to participate in health planning at the local level	Decreased
								Proportion of caesarean section deliveries	Increased
								Number of still-births	Increased
35	Millimouno et al., 2023 (64)	Guinea (lower middle-income)	To analyse the effect of COVID-19 on routine maternal and neonatal health services in Guinea	Pre-post	Users of maternal and neonatal health services in three referral hospitals - Hôpital National Ignace Deen (HNID), Hôpital Regional de Mamou (HRM) in Mamou and Institut de Nutrition et de Santé de l'Enfant (INSE)	Exhaustive	Not reported	Mean monthly number of deliveries	Decreased in HNID Increased in HRM
								Obstetric complications	Increased in HNID Decreased in HRM
								Mean monthly number of maternal deaths	Increased in HNID and HRM
								Mean monthly number of neonatal admissions	Decreased in INSE
								Mean monthly number of neonatal deaths	Decreased in INSE

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TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
36	Mhajabin et al., 2022 (65)	Bangladesh (lower middle-income)	To present the effect of the early phase of COVID-19 on the coverage of essential maternal and newborn health services in a rural subdistrict of Bangladesh	Cross-sectional	Group 1: women who were on the third trimester of pregnancy during April–June 2020 Group 2: women who were on the third trimester of pregnancy during August–October 2019 Group 3: women who gave birth during April–June 2020 Group 4: women who gave birth in August–October 2019	Random	Group 1: 111 Group 2: 115 Group 3: 163 Group 4: 166	Number of women received at least one antenatal care service from a medically trained provider	Decreased (not significant)
								Number of visits by a medically trained provider	Increased (not significant)
								Birth, antenatal care, postnatal care and essential newborn care coverage	No difference
37	Lydon et el., 2022 (36)	Mozambique (low-income)	To measure the effects of the COVID-19 on maternal and perinatal health services and outcomes in Mozambique	Time-series	Users of public health facilities providing antenatal or maternity services in Nampula Province	Census	Not reported	Number of first antenatal care visits	Increased
								Fourth antenatal care visits completed	No difference
								Number of facility deliveries	Increased
								Adverse birth outcomes	No difference
38	Kabagenyi et al., 2022 (43)	Uganda (low-income)	To understand the extent to which COVID-19 interrupted access and utilisation of FP information and services during the lockdown in Uganda	Qualitative	Policy makers, implementers, researchers and family planning service providers	Purposive	21	Disrupted service delivery	No outreaches conducted, limited availability of family planning commodities, low family planning access and utilisation and inadequate human recourses or health workers
								Mobility hindrances	Difficulty in finding transport means, high cost of transport and restricted movement
								Responsive reproductive health services	Referral services offered to family planning clients and distribution of family planning commodities
								Financial related disruptions	Loss of employment and unemployment

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TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
39	Goyal et al., 2022 (66)	India (lower middle-income)	To assess the difficulties faced by the pregnant women in seeking appropriate antenatal care due to the restrictions imposed during the COVID-19 pandemic	Cross-sectional	Pregnant women enlisted in the study area just before the enforcement of the lockdown	Multistage (convenience, purposive and census)	1,374	Perceived difficulties	Due to the restrictions in getting adequate nutrition (76.5%), accessing transportation facilities (35.4%), consultations from doctors (22.4%), getting an ultrasonography scan (48.7%). Overall, 21.9% of women could not access safe abortion services. Only 3.6% of respondents ever took any teleconsultation services offered by the government. Most of them felt unsatisfied compared with routine visits (77.5%).
40	Gebreegziabher et al., 2022 (45)	Ethiopia (low-income)	To assess trends in selected maternal and child health services performance in the context of COVID-19 pandemic	Cross-sectional	Users of maternal and child health services in Addis Ababa City	Not reported	Not reported	Number of postnatal care visits	Decreased
								Number of new contraceptives accepters	Decreased
								Safe abortion care	Decreased
								Number of under-5 years old children treated for pneumonia	Decreased
41	Emmanuel et al., 2022 (67)	Pakistan (lower middle-income)	To appraise the effects of containment and lockdown policies on reproductive, maternal, newborn and child health service utilisation in Pakistan	Time-series	Users of all public reproductive, maternal, newborn and child health services	Census	Not reported	Family planning visits	Decreased
								Number of antenatal care visits	Decreased
								Number of institutional deliveries	Decreased
								Number of caesarean sections	Decreased
								Number of postnatal care visits	Decreased
								Child immunisation	Decreased

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TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
42	Bliznashka et al., 2022 (46)	Mozambique (low-income)	To understand caregiver utilisation and provider delivery of child health services since the start of the pandemic	Qualitative	Caregivers with a child less than 2.5 years, facility-based providers, community health workers and district health services staff	Purposive	61	COVID-19 knowledge	Limited knowledge
								COVID-19 knowledge influences on health-seeking behaviour	Misconceptions, fear of COVID-19, structural changes, reduced income and rising cases of malnutrition
								Perceived barriers and challenges faced by facility-based providers	Lack of caregiver compliance with risk mitigation measures, caregiver fear of COVID-19 risk mitigation measures, lack of caregiver knowledge about COVID-19 and lack of supplies and protective equipment
								COVID-19 influences on families and communities	Increased food insecurity, increased prices, reduced livelihoods and reduced interactions with others
43	Bekele et al., 2022 (47)	Ethiopia (low-income)	To assess maternal, newborn and child health service utilisation during the first 6 months of the COVID-19 pandemic compared with prior to the pandemic	Mixed-methods	Quantitative component: users of the maternal, newborn and child health services Qualitative component: doctors, nurses, midwives and clinical officers	Not reported	Quantitative component: not reported Qualitative component: 31	Number of new family visits	Decreased (significant)
								Sick under 5 child visits	Decreased (significant)
								Number of antenatal and postnatal care visits	Decreased (not significant)
								Child immunisation	No difference
								Perceived barriers	Fear of disease transmission, economic hardship and transport service disruptions and restrictions
								Enablers of service utilisation	Communities' decreased fear of COVID-19 and awareness-raising activities

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TABLE 1 (Continued)

N	Authors, year	Country (income group)	Aim	Study design	Study population	Sampling	Sample size	Outcome(s) reported	Findings
44	Basnet et al., 2022 (68)	Nepal (lower middle-income)	to explore the experiences of maternity service providers during the pandemic, examining their perspectives from the point of individuals, families, society, institutions and government	Qualitative	Front-line health care providers	Purposive	10	Fear of COVID-19 at work	Causes of fear (transmission and uncertain outcomes), manifestations of fear (anxiety, irritability, loss of sleep, excessive handwashing and weight loss) and coping with fear.
								Challenges at work	Managing visiting crowding in hospital, staffing issues at work, issues with protective equipment at work and trainings and guidelines
								Changes at workplace and services	Changes in work infrastructures, changes in procedure and new protocols
								Factors influencing motivations to work	Enablers (professional responsibility to society) and impediments (no support and motivation from family and colleagues)
								Stigma due to COVID-19	Family/neighbours and institutions
								Impact on services	Decreased service utilisation and perceived poor quality of care
45	Thsehla et al., 2023 (75)	South Africa (upper middle-income)	To investigate the indirect effects of COVID-19 on maternal and child health in different geographical regions and relative wealth quintiles	Pre-post	Users of public maternal and child health services	Not reported	4,956	Child immunisation	Decreased
								Incidence and mortality due to child pneumonia, diarrhoea and severe acute malnutrition	Decreased
								First antenatal visits	Increased (not significant)
								Caesarean section delivery rates	Increased (not significant)
								Maternal mortality	Increased (not significant)

42) did not find any changes with respect to this indicator. The results varied depending on the setting in three multi-centred studies (64, 77, 78), making it difficult to provide a generalised conclusion. Home delivery rate rose based on the results of two studies originated from Mozambique and India (36, 62) and reduced in Ghana (48).

Birth outcomes

The impact of the COVID-19 pandemic on birth outcomes was reported in eight studies. Maternal mortality rates increased (64, 73, 75) and remained unaffected (37, 51) in three cases and two cases, respectively. A growth in stillbirth levels was observed in two studies (38, 63), and a decline was reported in one instance (51). Diverse results were obtained concerning the risk of adverse birth outcomes and obstetric complications (43, 64, 72).

Impact on child service use and provision

Despite the fact that the rate of neonatal admissions increased in Uganda (37), its overall number declined in Ethiopia, Ghana and Guinea (34, 48, 64) as compared to the pre-pandemic period. Furthermore, a decrease in the number of consultations for sick children and emergency visits was observed in four different countries – Cameroon (57), Mexico (71), Ethiopia (34, 35) and South Africa (69). In the context of the COVID-19 pandemic, the level of early neonatal deaths increased in Uganda, Zimbabwe, Guinea and South Africa (37, 51, 64, 73). The majority of studies reported a fall in child immunisation levels (37, 38, 49, 71, 73, 75, 77–79). However, three studies highlighted that the number of children receiving scheduled vaccination increased in Ethiopia (38, 42) and India (62) and no changes with respect to this indicator were found in two studies from Ethiopia and Mozambique (39, 41).

Experiences of service users and healthcare professionals

Identified concepts relevant to service users' and healthcare professionals' experiences regarding the impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services were grouped into four main framework categories: the anxiety of not knowing (1), overwhelmed healthcare systems (2), challenges perceived by healthcare professionals (3) and difficulties perceived by service users (4). The respective sub-categories within each of these categories are reported in the section below. Illustrative quotations within each category are presented in Table 2.

The anxiety of not knowing

The anxiety of not knowing about COVID-19, particularly in the early stages of the pandemic, was a common and understandable response to the rapidly evolving situation. According to the participants, limited knowledge about the disease, misconceptions and stigma, and fear of contagion contributed to this anxiety.

Limited knowledge

Considering that COVID-19 was a completely new disease and there was little information available, participants demonstrated only basic and rather limited knowledge about its causes, symptoms, transmission and potential consequences (36, 46, 47). It was noted that COVID-19 is "a very dangerous disease" (46), which "can be transmitted through air/breathing, shaking hands, kissing, contact with others" (47). The essential measures, such as wearing a mask (36, 47), washing hands (36) and social distancing (36) were mentioned as helping to protect yourself and others from the disease.

Misconceptions and stigma

COVID-19 has not only been a health crisis but also a social and psychological challenge, leading to the rapid spread of misinformation (40, 42, 46, 47, 54, 61, 68). Misconceptions ranged from false information about its origin to conspiracy theories about its existence. In particular, participants believed that the virus "attacks animals" (46) and implied that it "may not be real" (47). Furthermore, it was reported that people diagnosed with COVID-19 or who had recovered from the virus were being victimised (54) and experienced discrimination as people tend to "badmouth" (54), "refrain from meeting them" (40) and "not go near them" (61). However, participants also highlighted that public awareness campaigns focusing on disseminating accurate information helped to address misconceptions and reduce stigma across different communities (42).

Fear of contagion

COVID-19 demonstrated rapid community transmission, resulting in widespread outbreaks across countries and continents. The exponential growth in cases has instilled fear of contagion in many individuals and communities (36, 40, 42, 44, 46, 47, 54, 60, 61, 68). Participants shared that healthcare facilities were considered as potential sources of COVID-19 transmission (36, 40, 42, 44, 47, 60); therefore, they tend to postpone or avoid general healthcare visits and antenatal care due to the "fear of acquiring the disease" (47). Participants also highlighted having anxious thoughts about the requirement to wash hands frequently (68) and the fear of testing positive for COVID-19 (40). Nevertheless, some participants underlined that "fear has slowly decreased" (68) when lockdowns were lifted (47).

Overwhelmed healthcare services

During the COVID-19 pandemic, healthcare services in LMICs faced overwhelming issues due to the rapid and widespread transmission of the virus. A number of contributing factors were discussed, including insufficient staffing levels, disrupted flows of commodities, decreased quality of care, limited access due to transportation issues and patient flow fluctuations.

Insufficient staffing levels

Healthcare staff during the pandemic have been reassigned to the COVID-19 units (40, 44), leaving maternity and child services with fewer resources. Furthermore, participants highlighted that the pandemic had exacerbated the pre-existing "chronic shortage" (68) of healthcare staff, which resulted in longer waiting times (36, 54, 61). The increased risk of exposure to the virus amongst healthcare staff has also led to a significant reduction of available workforce, and there were cases where no healthcare workers were able to attend patients (54, 60).

TABLE 2 Illustrative quotations.

Categories and sub-categories (relevant studies)	Illustrative quotations
1 The anxiety of not knowing	
1.1 Limited knowledge (36, 46, 47)	"Media expresses it well; we know well it is also an infected person who can transmit it …" (47) "It can be transmitted through air/ breathing, shaking hands, kissing, contact with others and when face masks are not applied properly" (47) "…a very dangerous disease that can spread from person to person." (46) "…a worldwide disease, which is very lethal, and communicable." (46) "…respiratory disease that attacks the lungs, it causes coughs, muscle pains and diarrhoea." (46) "…disease that came from China that attacks animals." (46) "…it's a flu, in which the person has a cough, headache, neck pain, feels cold and has fever." (36) "…we have to wash our hands with water and soap or ashes." (36) "… we have to use masks, whenever we go out!" (36) "…if the person travels to a country contaminated by Covid-19 he has to be quarantined for 14 days." (36) "…everyone needs to use masks and maintain social distancing of 1.5 m." (36)
1.2 Misconceptions and stigma (40, 42, 46, 47, 54, 61, 68)	"…disease that came from China that attacks animals." (46) "…as my contemporaries started testing positive for COVID (…) the uncertainty around COVID further instilled more fear in me. (…) Later when I got posted in an isolation ward and saw many patients getting discharged. This allayed my fear to some extent…" (68) "I do not believe it exists, especially in our area. It might be real / exist in other areas/countries. They just suspect and take everyone into an isolation/quarantine center, but they are healthy and free of any signs and symptoms… "(47) "…I have never seen anyone with such a real problem in our area. We have heard about it on radio and TV, so I found it difficult to believe and I do not believe it is real" (47) "There are huge gaps, misconceptions, and challenges in practical preventive practices. They even perceived that the disease may not be real. Clients recovered from COVID-19 without any sign and symptom disseminated the information to the community and based on that the community misconceived that the virus might not be real from the beginning." (47) "Everywhere you move, there is corona testing; you do not have an option for not to be tested and it is mandatory for everyone. The problem is that they test you in an open field where everybody can watch you. If, unfortunately, I become positive, I will be taken to hospital publicly, without keeping my secret." (40) "I have witnessed that women who visit a health facility for any reason were considered to bring the virus into the community; thus, people refrain from meeting them." (40) "Those who go to the hospital are victimized." (54) "If they see me going to the hospital, they will badmouth about me." (54) "The infected person lives a lonely life during isolation. I do not want to be a victim." (54) "Recently, the neighboring lane was sealed. It has been only a week that the lane had opened. The entire family staying in front of us was COVID positive. We got so scared that neither did we go down nor let our children go down. We told the rest of the neighbors also to not go near them." (61) "Gradually the community start adapts to the pandemic and their fear for the disease reduces time to time. Moreover, the community gets health information about coronavirus through health extension workers and through different media channels…" (42) "The health extension workers, health officers, and health facility workers were giving health education, using montarbo on every cluster of health centres." (42)

(Continued)

TABLE 2 (Continued)

Categories and sub-categories (relevant studies)	Illustrative quotations
1.3 Fear of contagion (36, 40, 42, 44, 46, 47, 54, 60, 61, 68)	"…I started washing hands frequently. (…) I had repetitive thoughts of washing my hands even during sleep…" (68) "You can have this risk [risk of contagion] at transport and at health facilities during service provision and from other clients/patients. That is the first fear." (47) "Health professionals subjected to additional COVID-19 related tasks, patient flow decreased due to emerging concerns and fears of contracting the disease." (47) "I have postponed my follow up at that time for fear of acquiring the disease from health professionals/health centres. The same is true for other clients in our area and some mothers have received their visit in private clinics as we perceived almost all staff were infected." (47) "The community has been frightened of contracting the disease at the beginning." (47) "At the beginning of Covid-19 occurrence, the community panicked and feared acquiring the disease." (47) "At the beginning of coronavirus some people did not want to receive the services for fear of contracting the disease. So, client flow at that time has decreased." (47) "The flux of patients is reduced; it may be because they fear coming to the hospital thinking that they might be contaminated here in the Nampula Central Hospital" (36) "I do not want to know my test results, because I cannot with stand the stress of being positive for corona virus. I have heard a story of many individuals who had attempted suicide." (40) "I do not think that health facility environment is neat at this time. I doubt that they might not frequently clean surfaces, walls, chairs, and materials needed for treatment. If I go to health facility, I may contact with those unclean materials and get infected with the virus." (40) "Health facilities give service for all clients coming from different areas; this results in overcrowding and makes it easier for corona transmission. Thus, rather than going to health facility, I prefer seeking advice from health extension worker." (40) "Pregnant women who did not visit antenatal care could deliver safely without any problem, but if she gets infected with corona, she will be seriously ill and may not even survive. So, I would advise pregnant women not to visit health facility in this dangerous time." (40) "How would one compare the benefit that the baby gets from antenatal care service utilization with the risk of getting corona by visiting health facility? In my opinion, the virus is much more serious than the problem that may occur to the baby from not using antenatal care service." (40) "You see because we fear that hospital, they told us that there is a COVID-19 suspect. I went to the clinic and they injected me. … I am now worried." (44) "I feared getting infected. I rather stay at home than get infected with the new virus." (54) "I have heard a lot about the virus and I will not want to be a statistic." (54) "…and I avoid going to the health centre, unless it is really urgent, because of this new infection." (36) "We never went out as my daughter is very young. We never took her out because of so many cases of Corona infections." (61) "When I was about to give birth, I felt so worried to go to the hospital. I was afraid that I might get COVID because we can get COVID in the hospital." (60) "I'm just worried about my baby and family. I am still giving the services for the mothers, but I cut the duration. I mean I do not accept any patients after hours." (60) "Generally the impact of COVID-19 in all health services especially in immunization service; parents were absent from the service area due to fear…" (42) "Right now, the entire community members have no fear or concern about acquiring the disease (…) we are not concerned about client decrement related to COVID-19. Specially after the 5 months state of emergency was lifted things are returned to pre-COVID time." (47) "I feared going near the [patient's] bed initially, but now my fear has slowly decreased after being posted to COVID hospital." (68) "The caregivers reduced their consultations at the health facilities because of the fear of the unknown." (46)
2 Overwhelmed healthcare services	

(Continued)

TABLE 2 (Continued)

Categories and sub-categories (relevant studies)	Illustrative quotations
2.1 Insufficient staffing levels (36, 40, 44, 54, 60, 61, 63, 68)	"Although non-COVID wards have lesser patient flow, it is impossible to pool staff because our hospital has always had a chronic shortage of staff. In situations where pooling may be possible, the staff are reluctant to take up duties as they lack skills required for maternity services." (68) "During this corona virus period, health care providers are facing huge challenges as staffs are assigned in different corona virus related tasks such as: isolation room, provision of health education, screening centres and etc. In this case, it is difficult for a single health care provider to provide antenatal care service alone and it would even be much more difficult on market days where most pregnant women often chose to visit antenatal care." (40) "Of course, we see that in some places the there is a lot of prioritization on COVID-19 services. So we see that already especially when you go to the grass roots where we have very few health workers at the facility." (44) "The fact that health workers who need to do [provide family planning services]; are the same health workers who are engaged in other tasks at the health facility. But also, as organizations, we had to shift. You cannot keep focusing on only family planning when people in the community are getting COVID-19." (44) "There are not enough healthcare workers. It's frustrating to wait for so long." (54) "Last time I went but there was no healthcare worker to attend to patients." (54) "Unavailability of healthcare providers." (63) "The number of health professionals has decreased, and they leave early, so the waiting time has increased a bit." (36) "… in the wards there is only one nurse per shift, and because of the pandemic if one gets sick, we will be forced to work every day to cover her!" (36) "First of all, there was only one person who was managing the hospital billing counter section. The queues were long, and one hospital staff was trying to manage the queue." (61) "The midwife said that the vaccination officer would come, but he never came. So, I need to take him to Puskesmas." (60)
2.2 Disrupted flows of commodities (pharmaceuticals and essential goods) (40, 42, 44, 60)	"Since the corona virus pandemic, we are facing a serious shortage of essential drugs and supplies like: alcohol, iron, face mask, and other personal protective equipment." (40) "I do not think the health care facilities in this pandemic period have the necessary materials for providing antenatal care service....the Medias, the government, and everybody is saying corona, corona, corona..." (40) "In the last few months of my pregnancy, I did not get the Angel [multi-micronutrient supplement] anymore. The Posyandu was cancelled at that time. I came to the Puskesmas, but the midwife said there was no more stock." (60) "It is difficult now to ask the pharmacy warehouse for a new supply. I have heard that the supply is very limited, and most of the supplements will expire soon." (60) "In recent times there are shortages and interruptions of BCG [Bacille Calmette-Guérin] vaccines. We provide BCG vaccine for two weeks by sharing vaccine from other health facilities in the town but we have no BCG vaccine today onward…" (42) "Corona cannot be a reason for the difficulty to get inputs. Of course, there was a person who was transporting vaccination inputs from the woreda. After corona, he has not been willing to resume his usual task which is transporting the inputs." (42) "I do not think there was too much impact on availability of commodities because we had cargo planes coming in; they were not stopped. National Medical Stores was open and I am not sure if really the delivery of National Medical Stores was affected by COVID-19. Also, I am not sure there was a great impact on our commodities but it was access to the commodities that was affected." (44)

(Continued)

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TABLE 2 (Continued)

Categories and sub-categories (relevant studies)	Illustrative quotations
2.3 Decreased quality of care (40, 42, 46, 60, 61, 63, 68)	"This days everyone is talking about CORONA virus, and I do not think that healthcare providers have a time to treat pregnant women as usual. Thus, what is the point of visiting a health facility for antenatal care if you do not have enough time to be treated and advised?" (40) "Before COVID, we cared for our patients more closely with frequent conversations and patting on the back or holding hands to make them feel cared for was common. This was appreciated by the patient as well. Now due to the distancing rules, I feel we are providing inadequate mental health support to the patients in terms of them feeling adequately cared for." (68) "Before the pandemic patients were keen to let them stay longer in hospital as they perceived better postnatal care at the hospital, but now they wish to get discharged as soon as they deliver which is also risky as the patient may not receive adequate postnatal care." (68) "Before, the consultations were frequent or monthly, currently, consultations such as family planning, post-natal and pre-natal are done every 3 months." (46) "Higher proportion of C-section deliveries especially in private health facilities." (63) "Increased number of still-births." (63) "Two women were asked to lie down on a 2.5 feet narrow delivery table in labour room. I was one of them. I was very scared of falling. Moreover, the toilet in the labour room was very dirty. The floor was blood-stained and the toilet had a foul stinking smell of urine." (61) "I went there [the auxiliary Puskesmas] twice in the afternoon, but the Puskesmas was always closed. The registration counter was closed. It's not like what I thought. It seems they closed [the service] earlier because of this Corona. Next visit, I tried to go to another Puskesmas, but the service was only until midday." (60) "Because during this Corona the immunisation and [weight] measurement service was not there [Posyandu] anymore. […], I had to take my child to the Puskesmas for immunisation. But I did not go there, so I do not know his weight. The place is far away." (60) "…it was difficult to give services on maternal and child health because there were direction and advice given not come at health institutions, due to this the performance now achieved is low. But on the immunization service had no negative impact on performance…" (42) "The accessibility and quality of the MCH [maternal and child health] service were highly cracked by the COVID-19 pandemic, i.e., poor quality with low accessibility of the usual health services…" (42) "The quality and coverage were affected by the pandemic. The service given was not adequate as the previous [services are given before COVID-19], the health workers were not actively involved in the routine health care services except emergency services, the community also not utilizing the health facility for MCH [maternal and child health] services…" (42) "All components (…) were very low during this year as compared to the last year with the same month. Home delivery was high during the pandemic as compared to before the pandemic (…). There is a facility that completely closes services like FP [family planning], ANC [antenatal care], and PNC [postnatal care]; except emergency. The services were totally/completely closed in the city area. Generally, there is low service utilization, accessibility and coverage; and a high number of home delivery due to the pandemic effect…" (42) "The Skilled delivery performance already low achievement before the COVID-19 occurrence, after COVID-19 the maternal health services follow-up activities were decreased too…" (42) "There is an impact on immunization, clients were worried about COVID–19 due to this they did not come to health institutions and missed different services." (42) "Unavailability of ultrasound check-up." (63) "Unavailability of laboratory services." (63)

(Continued)

TABLE 2 (Continued)

Categories and sub-categories (relevant studies)	Illustrative quotations
2.4 Transportation-related issues (40, 44, 47, 54, 61, 63, 68)	"…we have observed increased fresh and macerated stillbirth…this may be due to lack of transportation for timely arrival to the hospital, late admission of women at 41 to 42 weeks of pregnancy, and decreased antenatal visits. We could have saved more babies had they arrived earlier in their pregnancy." (68) "Initially…mothers were staying at hospital unnecessarily due to absence of transportation/ambulance/." (47) "Travel restrictions are also another reason for low client flow which is more pronounced amongst mothers from far kebeles." (47) "Now, transportation cost is doubled. For this reason, I am forced to pay for two seats. Besides, it's mandatory to wear a face mask unless they do not allow you to use the service. It is difficult for me to afford all those things where my income is decreased by the pandemic already." (40) Even now with the restrictions on movements, that affected their [family planning users'] continuity of the product. So, for those people who were in lockdown, getting their new shot for Depo or oral contraception pills was difficult. This affected them in terms of continuity of access and utilisation of family planning methods." (44) "There were clients coming to us [for family planning services], during the lockdown. They were accessing FP [family planning] services but not very much especially during the month of April and May–during that [total] lockdown." (44) "Regarding access and utilization, we had challenges with health workers accessing facilities because the transport fares had been hiked. When transport fairs are hiked, that means we have challenges with them getting to work until of recent that the situation has certainly improved. However, in the beginning they worked with skeleton staff for the first three months of the pandemic." (44) "Public transport is overcrowded, it is risky using it during this time." (54) "Unavailability of transport to reach the health facilities." (63) "I did not get an auto on time. Bus service was not operational. Due to this, I faced great difficulties during my pregnancy and at the time of delivery." (61) "My delivery happened at home; the baby had come out. I could not make it to the hospital as I could not arrange for a mode of transport on time." (61)
3 Challenges perceived by healthcare professionals	
3.1 Emotional toll (40, 42, 68)	"Whenever I talked with my neighbour, they advised me to take annual leave to stay home and take care of my child. However, being a government health worker, I was not allowed to take any type of leave during this period. This was so stressful for me to cope with." (68) "One day I was in close contact with a patient, (…) providing cold sponging to a pregnant lady with a high fever. The ward was so busy that I could not find time to adequately wash my hands. Soon after that day, I tested positive for COVID." (68) "…either having a separate operating room dedicated for COVID positive patients or operating on COVID positive patients at the separate COVID hospital would help reduce the exposure COVID amongst the staff." (68) "I had undue pressure from my family to quit my job due to fear of COVID. My line manager provided a lot of support for my mental health and welfare. This gave me confidence to convince my family and continue my job." (68) "My neighbours spread a rumour that I was COVID positive when I was home for 2 days. I felt stigmatized being labelled as COVID positive and people stared at me with suspicion and also ran away from me on the street. COVID has been used as a reason to stigmatise health workers. However many weeks later when one of them got infected with COVID and they needed my help. They started treating me nicely." (68) "The discrimination towards health workers is so strong that they consider all health workers as a vehicle for COVID transmission in the community. Even my sister-in-law stopped talking to me. My children were not allowed to play in the public playground which is just in front of my house. This was hard for me to take on as my relatives were discriminating me, let alone the community people." (68) "After working the whole day in the work place, at night I go home; imagine the risk I could bring to my family. Why would I take such a risk? Where the government is not even willing to pay a risk allowance, let alone arrange accommodation for staff. I have a family to support; I no longer have interest to work in this environment." (40) "Generally speaking, the health workers feels fear of the pandemic, lacks PPE [personal protective equipment] and low commitment to serve before COVID were the major things which make their commitment under questions…" (42)

(Continued)

TABLE 2 (Continued)

Categories and sub-categories (relevant studies)	Illustrative quotations
3.2 Shortage of personal protective equipment (40, 42, 68)	"As most people lost jobs, many hospital staff were the only bread earners of their family. In addition, as the Hospital did not provide adequate masks, we had to spend our own money to purchase the masks at extortionist prices to protect ourselves. Even if the hospital provided salary on time would be great motivation to me and my staff." (68) "Our demand for PPE took long to go up the bureaucratic channel. When it did reach the right section of the hospital they were not clear about the procurement system in emergencies like the pandemic due to a lack of clarity of the administrative and financial regulations. Local philanthropic agencies finally donated some PPE to us." (68) "If we take, for example, shortage of personal protective equipment, without them, the risk of transmitting the corona virus will be increased. To decrease the risk of transmission, we usually compromise the routine antenatal care service. For instance, we may not perform physical examination or draw blood, even if necessary." (40) "The commitment of health workers was highly challenged and they are obligated to stop their routine activity due to frustration and lack of personal protective equipment. As any other community they have fear and frustration; lack of personal protective equipment's…makes them fear…" (42)
3.3 Lack of service users' compliance (36, 68)	"Managing extra people visiting the hospital was a real challenge for us. The number of security personnel was increased. This too did not work as the visitors verbally abused the security personnel and threatened to physically assault the personnel if they attempted to stop the visitors from entering the hospital. Furthermore, they spat all over the place when they were stopped. We try to do our best to minimize the number of visitors and motivate the visitors to comply with the hygiene measures. However, the compliance was poor as it seemed the visitors did not take COVID seriously so we could do nothing." (68) "… patients and visitors do not wear masks and the cabin (private) rooms are always crowded with a lot of people visiting the patients. This is unsafe for everyone." (68) "…the health professionals refuse to treat patients with no masks and that did not wash their hands!." (36)
4 Difficulties perceived by service users	
4.1 Reduced/lost income and food insecurity (44, 46, 54, 60, 61)	"Before the coronavirus I used to be able to bring something for my daughter to eat. Now that the doors have closed during this time of coronavirus, my livelihood is very complicated. What I manage today is not 70% of what I used to get before the pandemic. This disease brought me some losses, life is so difficult in order to raise the children. For my daughter's food am sacrificing at the moment." (46) "In terms of nutrition the situation changed, the pandemic affected the whole economy of our community, markets were closed, very little was produced in the small farms, because people had movement restrictions... a lot of effort was done last year aiming at reducing [malnutrition] cases, but suddenly everything stopped. The children were the first to be affected by this situation." (46) "…things have been difficult lately. For example, yesterday at home we slept without dinner because we had nothing to eat." (46) "…there are days we sleep hungry, we have a house we used to rent but there are no clients now, there are days we go hungry." (46) "Many of the caregivers lost their jobs and maybe businesses closed, because the market fairs were closed and that resulted in low income for many families and it became difficult for them to buy food to feed their children." (46) "There is no money, only a few went to the fields to cultivate hence there is no produce, in the markets there are not a lot of things and the products prices have gone up." (46) "She [daughter] does eat, but the prices of products have hiked a lot because of coronavirus [...]. Before yesterday, I went to buy Danone for my daughter and I saw that the price had change from 25 Meticais to 30 meticais and I was not able to buy. When I asked, they told me that coronavirus has blocked all the money." (46) "Nowadays, when I go to the fields, at 04:00, I do not come back at 09:00 but at 06:00. This coronavirus has reduced our production, because we do not spend a lot of time like we used to before. Money today has disappeared and if we do not produce and sell, we will not have money to buy clothes for her." (46) "There is lack of money nowadays and lack of food. The prices of food products have gone up and the men are complaining a lot that they are not able to buy things for children like before. There are no jobs." (46) "Many having lost jobs during the lockdown, they are going to increase on poverty level. As a result, many young girls are going to get married to poor families and definitely poverty will also increase." (44) "I shut my business during the corona time, now I do not have money at all." (54) "My husband lost his job and we were depending on him. Now we have nothing." (54) "For our child there are lots of expenses, which are difficult to bear after both my husband's and mother's jobs were lost. My breast milk is also not adequate because I am not able to have enough food." (61) "Now, we are struggling because there is no income at all. […] I once went there [Puskesmas] when I was pregnant. Maybe about 1–2 km on walking. In there, I checked my pregnancy and paid around Rp25,000. So, I only came once because it was better to buy food than to pay for the Puskesmas. […] I was not strong enough to walk for 2 km away." (60) "I could not take my son to the Puskesmas every month because I was afraid of paying something while I had no money. My husband does not have it [job], right? I only went there [Puskesmas] to bring my son for immunisation." (60)

(Continued)

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TABLE 2 (Continued)

Categories and sub-categories (relevant studies)	Illustrative quotations
4.2 Increased put-of-pocket expenditure (54, 63, 68)	"The results for PCR test in our hospital takes up to 7 days. This creates an additional burden for patients who are admitted on a separate bed just to rule out COVID infection as the bed charges are ~10 USD/day. A patient recently came out negative for COVID who spent 7 days at the hospital was unable to pay the hospital charges of ~45 USD. As all expenses are out-of pocket, this is just so unfair to poor patients who have little means to afford it. Lack of adequate communication by staff and unclear administrative/finance regulations on the provision of free beds has led to this mishap." (68) "Paying for services is very expensive. I could not afford it." (54) "Services are not always cheap. You have to buy medicines all the time." (54) "Higher expenses for the health services." (63)
4.3 Healthcare providers' unprofessional behaviour (40, 42, 54, 61, 68)	"As my neighbor told me, healthcare providers often use the same glove for different clients, and they do not use alcohol regularly; I think all they do care about is only for themselves. Some of them even move here and there but they do not change their gloves before toughing you." (40) "I would not advice pregnant women to visit a health facility during this corona virus period. What I heard from those who visit a health facility is completely discouraging; health care providers often disgrace you and even insult you. Though, I do not blame them for doing so since they are taking a high risk; just think about working in the corona virus period? Hum... they have a family too." (40) "Sometimes the harassment is too much to bear." (54) "Healthcare workers are abusive and rude to the patients sometimes." (54) "My previous experience was not pleasing. I will not be comfortable with the same healthcare provider." (54) "I missed my last ultrasound during my pregnancy. Nurses used to avoid coming close. Doctors were not physically examining/touching. They used to observe from a distance, it was a very strange feeling. Nurses did not even talk properly." (61) "It is difficult to explain in words what I have gone through during my pregnancy. I would not recommend others to go to that public hospital for delivery. Behaviour of hospital staff was unprofessional; I was not allowed to see the doctor. They told me to come in after two days." (61) "The health workers were not giving the health services by keeping the professional ethics. The commitment to serve the community by keeping all the professional ethics was very low and compromised…" (42) "…The on-call physicians are reluctant to attend calls immediately and in most cases, they come only when called many times. This was not the case before COVID. Back then we had very prompt visits." (68)

Disrupted flow of commodities

Restrictions on travel, border closures, and lockdown measures during the COVID-19 pandemic disrupted the global chain of pharmaceuticals and essential goods (40, 42, 44, 60). Participants emphasised that they faced "a serious shortage of essential drugs and supplies" (40) and a limited supply of vaccines (42). Nevertheless, one participant noted incoming cargo planes continued to operate during the COVID-19 pandemic, maintaining the flow of essential commodities (44).

Decreased quality of care

Concerns regarding the quality of care were expressed by both service users and healthcare professionals (40, 42, 46, 60, 61, 63, 68). Service users experienced delays or cancellations of services (46), faced challenges in accessing healthcare facilities (42) and expressed concerns about infection control measures (61). Healthcare providers, in turn, highlighted that COVID-19 restrictions resulted in reduced personalised attention and care as "frequent conversations and patting on the back or holding hands" (68) were not possible. The availability of crucial services, such as ultrasound check-ups and laboratory services was limited (63). The preference of service users (mothers) to be discharged earlier after giving birth was also observed by healthcare providers, which undermined the quality of postnatal care (68). Moreover, healthcare professionals noted that the number of stillbirths and caesarian sections increased, whereas the proportion of skilled deliveries decreased in comparison to the pre-pandemic levels (42). According to participants, service users tend to miss their immunisation appointments due to safety concerns (42).

Transportation-related issues

A number of transportation-related issues impacting access to healthcare facilities became a significant challenge for many people across LMICs (40, 44, 47, 54, 61, 63, 68). Participants emphasised that public transportation systems reduced or suspended their operating services during the pandemic, which resulted in "late admission of women at 41 to 42 weeks of pregnancy" (68), absence of transportation options for patients from remote areas (47, 63) and cases where "delivery happened at home" (61). Notably, service users also "were staying at hospital unnecessarily" (47) due to the limitations of transportation services. Although seeking medical care was amongst the essential activities allowed during lockdowns, restrictions on movement worsened access to healthcare facilities (44). Furthermore, participants shared that "transport fares had been hiked" (44), leading to financial constraints and making it difficult for them to afford transportation (40, 44).

Challenges perceived by healthcare professionals

Healthcare professionals experienced numerous challenges during the COVID-19 pandemic as they played a critical role in caring for patients and managing healthcare systems during a global health crisis. Some of the key challenges highlighted by participants included emotional toll, shortage of personal protective equipment and lack of service users' compliance.

Emotional toll

Healthcare professionals had to cope with significant emotional stress and mental health challenges due to witnessing the suffering of patients (68) and fear for their own health and that of their families (40, 68). Participants also reported experiencing harassment and discrimination from members of the public who perceived them as "a vehicle for COVID transmission in the community" (68). Such hostile attitude towards healthcare professionals endangered their job motivation and commitment (42, 68).

Shortage of personal protective equipment

During the pandemic, there were widespread shortages of personal protective equipment (40, 42, 68), leading healthcare professionals to resort to buying it by themselves "at extortionist prices "(68) or relying on donations from philanthropic agencies (68). Inadequate access to protective equipment increased fear and risks of infection (42), which forced healthcare professionals to "compromise the routine antenatal care service" (40) by not performing physical or laboratory examinations.

Lack of service users' compliance

Healthcare professionals encountered issues with service users' compliance in following recommended health guidelines (36, 68). In particular, some individuals demonstrated aggressive behaviour by threatening "to physically assault the personnel if they attempted to stop the visitors from entering the hospital" (68) or were reluctant to wear masks or practise social distancing (36, 68).

Difficulties perceived by service users

Participants of the study shared difficulties that affected their healthcare experiences and overall well-being. Reduced/lost income and food insecurity, increased out-of-pocket expenditure and healthcare professionals' unprofessional behaviour were reported as major ones.

Reduced/lost income and food insecurity

The economic impact of the COVID-19 pandemic on LMICs has been significant and exacerbated existing vulnerabilities. Many businesses had to shut down or reduce operations, resulting in widespread job losses and furloughs. Participants noticed that "many of the caregivers lost their jobs" (46) and they are struggling "because there is no income at all" (60). Loss of livelihoods, food price inflation, and disruptions to agricultural activities made it challenging to meet basic food needs (44, 46, 54, 60, 61). Participants admitted that "it was better to buy food than to pay" (60) for healthcare services.

Increased Out-of-pocket expenditure

Participants highlighted that increased out-of-pocket expenditure for healthcare services during the pandemic had considerable implications for individuals and families with limited financial resources (54, 63, 68). High healthcare costs resulted in avoided medical care and heightened health risks (54, 68).

Healthcare providers' unprofessional behaviour

Service users admitted to facing numerous cases of healthcare providers' unprofessional behaviour. Unprofessional behaviour involved a lack of empathy and compassion for patients and their families during such challenging times (42). Patients described their experience as "completely discouraging" (40) and "not pleasing" (54) because healthcare professionals were "abusive and rude" (54). Inappropriate adherence to infection control measures, such as using "the same glove for different clients" (40) and reluctance to physically examine patients (61) and attend calls (68) was also mentioned as examples of unprofessional behaviour.

Discussion

Main findings

Based on the findings from 45 unique studies conducted across 28 LMICs, the current review suggests that the COVID-19 pandemic disrupted access to and delivery of maternal and child services. In particular, the number of family planning visits, antenatal and postnatal care visits, consultations for sick children, paediatric emergency visits and child immunisation levels decreased as compared to the pre-pandemic levels in the majority of included studies. In contrast, a rise was observed in the number of neonatal admissions and early neonatal deaths. Inconclusive results were acquired concerning the number of institutional deliveries, adverse birth outcomes and obstetric complications.

The analytical framework that comprised four main categories of the anxiety of not knowing (1), overwhelmed healthcare systems (2), challenges perceived by healthcare professionals (3) and difficulties perceived by service users (4) was developed based on the concepts that emerged from included studies. Participants shared that limited knowledge about COVID-19, along with misconceptions and fear of contagion, led to people avoiding seeking healthcare. Unsurprisingly, participants also highlighted that maternity and child healthcare services were disrupted by significant challenges presented during the pandemic, including insufficient staffing levels, disrupted flow of commodities, decreased quality of care and transportation-related issues. On a personal level, healthcare professionals have reported experiencing a profound emotional toll, shortage of personal protective equipment and lack of service users' compliance in the context of high workload due to the constant demand for healthcare services. Service users, in turn, have reported that issues, such as reduced/lost income and food insecurity, increased out-of-pocket expenditure and healthcare professionals' unprofessional behaviour affected their ability to receive timely care. Identified main categories and respective sub-categories relevant to service users' and healthcare professionals' experiences regarding the impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services were closely linked and largely overlapped. For example, healthcare professionals and service users shared the anxiety of not knowing about the novel coronavirus, which may have led to decreased quality of provided care and a lack of patient compliance. Overwhelmed healthcare services, in turn, have contributed to an enormous emotional toll amongst healthcare professionals and may have been a reason for their unprofessional behaviour noted by service users.

Strengths and limitations

To our knowledge, this is the first systematic review aiming to determine the impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services in LMICs. A further strength is that the review used a comprehensive approach, searching through studies from all LMICs, which allowed to include data from different countries and cultural backgrounds. However, this approach presented several limitations. Firstly, due to the heterogeneity of included studies, the variety of reported outcomes and their limited quality, it was not possible to conduct a meta-analysis; therefore, the final interpretation of quantitative data was made based on descriptive-analytical procedures. Such considerable heterogeneity also suggests that the findings of the current review should be interpreted with caution. Secondly, although it was possible to extract general concepts relevant to service users' and healthcare professionals' experiences regarding the impact of the COVID-19 pandemic on access to and delivery of maternal and child healthcare services, there is not enough evidence to assess whether these apply to all LMICs. There might be regional or clinical characteristics that have not been identified in this review. Finally, the comparability of findings across the included studies may be limited due to wide variability in periods (first wave, lockdown, second wave, etc.) when studies were conducted, local public health messaging to which people were exposed, national-specific circumstances and cultural differences. Also, the majority of studies were focused on African countries, which made it challenging to generalise any conclusions about LMICs.

Comparison with literature from high-income countries

Similar to the findings of the current review, disruptions in the antenatal and postnatal care coverage were observed by numerous studies from HICs. In particular, a decrease in the number of antenatal visits (80–87), prenatal genetic diagnostic procedures (88) and performed obstetric ultrasound scans (89, 90) was reported alongside reduced postnatal care (91) in the United States, United Kingdom, Italy, Belgium and Saudi Arabia. These informal comparisons might suggest that healthcare professionals and patients from both HICs and LMICs perceived similar challenges during the COVID-19 pandemic. However, no change in antenatal care attendance (92, 93) and an increased number of the first-trimester prenatal screenings (94) were determined in the United States and Italy, respectively, highlighting inconsistencies in the obtained results due to wide variability of possible influencing factors. Although the results from LMICs were inconclusive regarding obstetric complications, the data from the United States and Israel suggests a decline in the number of obstetric emergency department visits (95, 96) and obstetric hospitalisations (97). This underlines the need for detailed analyses and the consideration of specific contexts in order to provide firm conclusions.

According to the report by the World Health Organization, disruption in the delivery of maternal and child health services was caused by two main reasons: "changes in demand and patient behaviour" and "changes in health-care supply" (98). This corroborates the findings of the current review that patients' healthcare-seeking behaviour considerably changed due to the fear of contagion and misconceptions about COVID-19. Several studies from HICs support this statement by reporting that patients tend to cancel or ignore their appointments due to the risk of COVID-19 exposure and expressed a preference for shorter hospital stays after giving birth (80, 99–103). Reduced income and food insecurity during the pandemic have also played a significant role in influencing healthcare-seeking behaviour in LMICs. It seems predictable that individuals may prioritise meeting basic needs over seeking healthcare in situations of severe economic hardship, particularly in resource-scarce settings. Such changed maternity care-seeking behaviour determined in the current review might need to be perceived as potentially contributing to poorer birth outcomes. Even though the findings of the review were mixed, it appears reasonable to assume that not attending antenatal care visits, for example, might be associated with poorer pregnancy outcomes.

The alterations in the healthcare-seeking behaviour happened in the context of overwhelmed healthcare systems, leading to challenges to the quality of delivered care. It is important to note that increased use of telemedicine has only rarely been mentioned in studies of LMICs (47) albeit it was extensively discussed across studies conducted in HICs (93, 104–106). This indicates that whilst antenatal and postnatal care has transformed into a hybrid mode in HICs, minimising the pandemics' impact on maternity and child care, antenatal and postnatal care services in LMICs faced often unavoidable ramifications. The COVID-19 pandemic has once again demonstrated inequalities between societies and regions as the majority of technological benefits were available to financially secure patients from HICs.

Implications for research and practice

In order to generate clear directives for improvements, future research should aim at creating a set of indicators, allowing for direct cross-country comparisons and enabling to evaluate the scale of maternal and child healthcare disruptions during the pandemic. Moreover, future research studies may need to perform a comprehensive analysis of actions undertaken throughout the COVID-19 pandemic, which can be used to develop a healthcare delivery plan for emergency situations. This may help to build resilient healthcare systems in low-resource settings.

By considering the findings of the present review, future healthcare policies might need to prioritise helping LMICs adopt telemedicine into their healthcare systems. This would require a comprehensive approach that involves collaboration between governments, healthcare providers, technology developers and communities as a range of major challenges, such as limited access to reliable internet connectivity, lack of technical resources, electricity outrages, absence of clear regulations governing telemedicine, data privacy concerns, digital illiteracy and cultural resistance to change should be addressed. Supporting healthcare professionals after the COVID-19 pandemic to address the physical, mental and emotional toll they have experienced is also crucial to ensure a sustainable and resilient healthcare workforce. Providing regular counselling sessions, implementing flexible scheduling options, offering opportunities for continuing education and developing resilience-building programmes might help healthcare professionals recover from the impact of the pandemic. Finally, establishing collaboration and sharing experiences amongst countries seems essential to prepare maternal and child health services for future pandemics and improve global health outcomes. Facilitating collaborative research projects, offering cross-border training and knowledge exchange, empowering communities to implement community-led interventions and promoting culturally sensitive approaches may assist in enhancing pandemic preparedness.

Conclusion

The current review has identified that COVID-19 has presented an unparalleled challenge to maternal and child health services in LMICs by disrupting family planning services, antenatal and postnatal care coverage, and emergency and routine child services. However, generalised conclusions are tentative due to the heterogeneity and inconsistent quality of the included studies. Investigating the pandemic's impact is crucial to mitigate its negative consequences on women and children worldwide and prepare healthcare systems for future resurgences of COVID-19 and potential challenges beyond.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

AK: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. M-AO: Data curation, Investigation, Methodology, Writing – review & editing. MN: Data curation, Formal analysis, Writing – review & editing. AS-S: Conceptualization, Formal analysis, Funding acquisition, Methodology, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1346268/full#supplementary-material

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Characteristics and spectrum changes of PICU cases during the COVID-19 pandemic: a retrospective analysis

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Objective: This study aims to compare the changes in the disease spectrum of children admitted to the Pediatric Intensive Care Units (PICU) during the COVID-19 pandemic with the three years prior to the pandemic, exploring the impact of the COVID-19 pandemic on the disease spectrum of PICU patients.
Methods: A retrospective analysis was conducted on critically ill children admitted to the PICU of Hunan Children's Hospital from January 2020 to December 2022, and the results were compared with cases from the same period between January 2017 and December 2019. The cases were divided into pre-pandemic period (January 2017–December 2019) with 8,218 cases, and pandemic period (January 2020–December 2022) with 5,619 cases. General characteristics, age, and gender were compared between the two groups.
Results: Compared to the pre-pandemic period, there was a 31.62% decrease in the number of admitted children during the pandemic period, and a 52.78% reduction in the proportion of respiratory system diseases. The overall mortality rate decreased by 87.81%. There were differences in age and gender distribution between the two periods. The length of hospital stay during the pandemic showed no statistical significance, whereas hospitalization costs exhibited statistical significance.
Conclusion: The COVID-19 pandemic has exerted a certain influence on the disease spectrum of PICU admissions. Implementing relevant measures during the pandemic can help reduce the occurrence of respiratory system diseases in children. Considering the changes in the disease spectrum of critically ill PICU children, future clinical prevention and treatment in PICUs should continue to prioritize the respiratory, neurological, and hematological oncology systems.

KEYWORDS
COVID-19 pandemic, PICU, disease spectrum, children, spectrum changes

1 Introduction

The novel coronavirus (coronavirus disease 2019, COVID-19) is characterized by high pathogenicity, high transmissibility, and a high rate of asymptomatic carriers. China has implemented various strategic measures such as advocating mask-wearing, increasing hand hygiene practices, and limiting population movement (online education, home isolation) which have affected the number of hospitalizations and disease patterns among both inpatients and emergency patients (1). Recent studies indicate that patient visits to hospitals decreased significantly after the outbreak of COVID-19, leading to corresponding changes in disease patterns (2–4). Orlei Ribeiro de Araujo et al. (5) found that the coronavirus disease 2019 pandemic strongly affected Brazilian PICUs, reducing admissions, length of stay, and the epidemiological profile. The measures to oppose the coronavirus disease 2019 pandemic may have prevented thousands of PICU hospitalizations across the country. It is widely acknowledged that the reduction in hospital visits could be attributed to the decreased incidence of infectious diseases due to measures aimed at controlling the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (6–10). However, no research has yet explored the impact of the COVID-19 pandemic on the number of cases and disease patterns in the Pediatric Intensive Care Units (PICU) in Hunan Province in China. This study aims to investigate the number of admissions and disease patterns in the PICU of Hunan Children's Hospital during the COVID-19 pandemic period, compare them with pre-pandemic data, analyze relevant changes in disease patterns, and provide guiding insights for pediatric disease prevention and treatment in the field of critical care medicine.

2 Data and methods

2.1 Study subjects

The study subjects included all inpatients admitted to the PICU of Hunan Children's Hospital between January 1, 2017, and December 31, 2022. The PICU of Hunan Children's Hospital is established on January 5, 1988. It is the National Clinical Key Specialty of People's Republic of China. It currently has 91 medical staff, 20 are doctors, 71 are nurses, 2 of the medical staff have got doctor's degree, and 18 of the medical staff have got Master's degree. And it serves the children from all over Hunan province. Patient information, including gender, age, and disease diagnosis, was collected. In cases with multiple diagnoses, the first diagnosis was used for classification and statistics.

2.2 Study methods

Neglecting the initial impact of the pandemic on inpatients, the period from January 1, 2017, to December 31, 2019, was designated as the pre-pandemic group, while the period from January 1, 2020, to December 31, 2022, was designated as the pandemic group. The changing patterns of disease in the two groups were compared. Following commonly used age divisions for children, hospitalized children were categorized into five stages: infancy (29 days to less than 1 year old), toddlerhood (1 to less than 3 years old), preschool age (3 to less than 6 years old), school age (6 to less than 12 years old), and adolescence (12 to less than 18 years old). And ICD-10 was used to collect the diagnosis in the standardized classification system.

2.3 Study definitions

We defined improved status as the patient's physical condition has not fully recovered, but has been significantly improved and is gradually developing towards the recovery line of disease. We defined cure status as the patients have been completely cured. We defined uncovered status as the patients have not been completely cured.

2.4 Statistical methods

Statistical analyses were performed using the SPSS statistical software program, version 25.0 (IBM Corporation, Armonk, NY, USA). Categorical data were presented as proportions or percentages (%), and comparisons between groups were analyzed using the χ^2 test with a significance level of $\alpha = 0.05$, considering $P < 0.05$ as statistically significant differences. Continuous variables were expressed as median and interquartile range, as normality tested by using normal probability cumulative distribution chart method, was not met. Comparison between groups was thus performed using Mann-Whitney U-test.

3 Results

3.1 Basic characteristics of patients

A total of 8,218 cases were included in the pre-COVID-19 group, and 5,619 cases were included in the post-COVID-19 group. The number of patients in the post-COVID-19 group decreased by 30.12% compared to the pre-COVID-19 group. Among them, 8,621 cases were male children, and 5,216 cases were female, with a male-to-female ratio of 1.65. The gender distribution difference between the two groups was not statistically significant ($P > 0.05$) (Table 1).

3.2 Age distribution of patients

In the post-pandemic period, the proportion of infant patients was 36.32%, significantly lower than the pre-pandemic period (56.33%) ($P < 0.01$). However, the proportions of preschool, school-age, and adolescent patients increased in the post-pandemic group. Specific age distribution values are shown in Table 2.

3.3 Disease composition by systems before and after the pandemic

We classified the disease spectrum into respiratory, digestive, nervous, urinary, hematological-oncological, immune, endocrine, critical illness, infectious, genetic-metabolic, cardiovascular, accidental injury, and other systems. The composition of diseases for each system is depicted in Figure 1.

TABLE 1 Gender distribution of patients in the Pre-COVID-19 and post-COVID-19 groups.

Group	Male	Female	Total
Pre-COVID-19 group	5,151 (62.68%)	3,067 (37.32%)	8,218
Post-COVID-19 group	3,470 (61.75%)	2,149 (38.25%)	5,619

TABLE 2 Distribution of patients in the Pre- and post-COVID-19 groups.

Group	Infant	Toddler	Preschool	School	Adolescent
Pre-COVID 19 group	3,909 (47.57%)	2,033 (24.74%)	1,108 (13.48%)	970 (11.80%)	198 (2.41%)
Post-COVID 19 group	2,050 (36.48%)	1,256 (22.35%)	971 (17.28%)	978 (17.41%)	364 (6.48%)

The results reveal that in the pre-COVID-19 group, the top six diseases in the disease spectrum were: (1) Respiratory system diseases (severe pneumonia, acute laryngitis, acute respiratory distress syndrome, etc.), 3,597 cases; (2) Neurological system diseases (epilepsy, viral encephalitis, purulent meningitis, etc.), 1,305 cases; (3) Hematological-oncological system diseases (leukemia, immune thrombocytopenia, hemophagocytic syndrome, etc.), 727 cases; (4) Digestive system diseases (acute gastroenteritis, acute liver failure, etc.), 644 cases; (5) Accidental injuries (poisoning, drowning, car accidents, etc.), 497 cases; (6) Critical illnesses (sepsis, septic shock, organ failure due to various causes, etc.), 470 cases.

In the post-COVID-19 group, the top six diseases in the disease spectrum were: (1) Respiratory system diseases, 1,683 cases; (2) Neurological system diseases, 1,052 cases; (3) Hematological-oncological system diseases, 693 cases; (4) Digestive system diseases, 538 cases; (5) Accidental injuries, 438 cases; (6) Critical illnesses, 326 cases.

3.4 Analysis of hospitalization Status before and after the pandemic

An analysis was performed on the improved rate, cure rate, mortality rate, uncovered rate, average length of hospital stay, and evaluated hospitalization costs for the case data in both groups see Figure 2. In the pre-COVID-19 group, the improved rate is 80.06%, the cure rate is 8.15%, the uncovered rate is 10.72% and the mortality rate is 1.07%. In the post-COVID-19 group, the improved rate is 70.48%, the cure rate is 10.68%, the uncovered rate is 9.58% and the mortality rate is 0.27%. The mortality rate in the PICU during the pandemic control period decreased significantly ($P < 0.01$). The median total length of hospital stay in the pre-COVID-19 group was 12 [8, 20] days, with an average hospitalization cost of 23,775.79 [14,357.42, 43,162.87] yuan. And we calculated the hospitalization costs by using the hospital system, and it is stable in Hunan Province. In the post-COVID-19 group, the median length of hospital stay was 13 [8, 23] days, with an median hospitalization cost of 23,114.49 [13,339.08, 49,074.27] yuan. While there was no statistically significant difference in hospitalization costs, there was a statistically significant difference in hospitalization days, ($P < 0.05$).

4 Discussion

4.1 Age characteristics

The majority of PICU admissions were concentrated among infants and toddlers, accounting for 72.31% and 58.83% of PICU admissions in the pre- and post-COVID-19 periods, respectively.

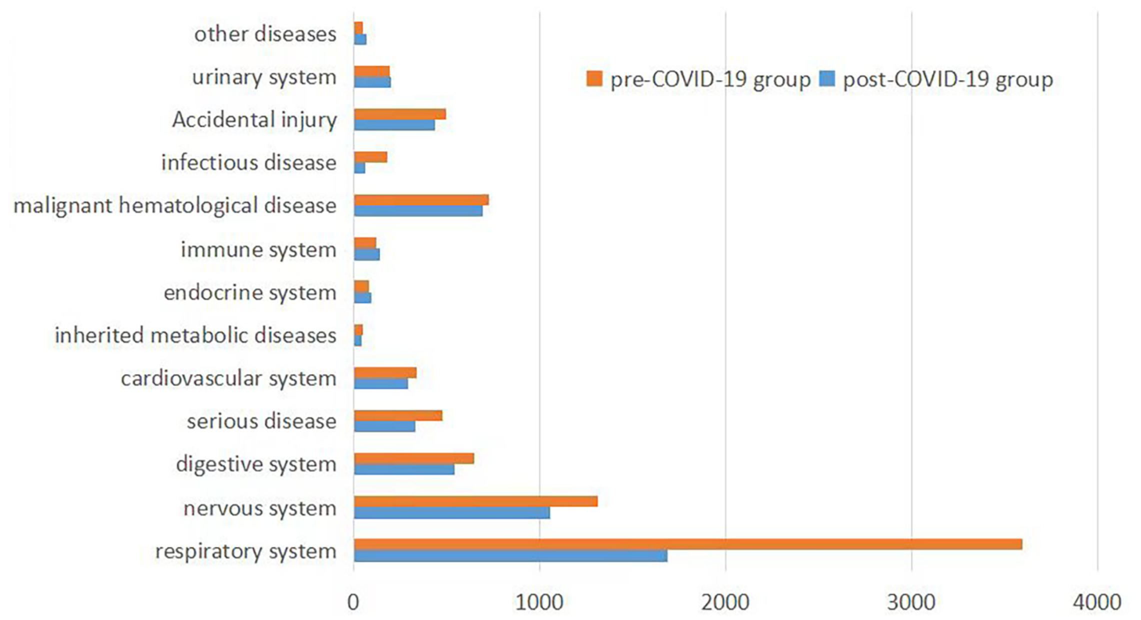

FIGURE 1
Disease composition of patients in the Pre- and post-COVID-19 groups.

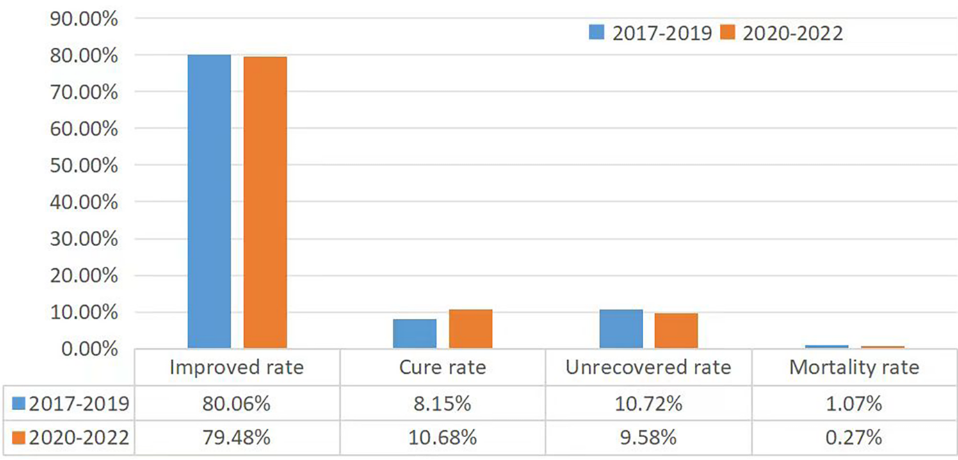

FIGURE 2
Analysis of disease outcomes in the Pre- and post-COVID-19 groups.

During the pandemic, the proportion of infants and toddlers decreased, while the proportion of children from preschool to adolescence increased. This decrease in infants and toddlers may be attributed to reduced exposure to the external environment during the pandemic and increased emphasis on personal hygiene and protection due to the pandemic's impact on parents. The increase in the proportion of children from preschool to adolescence might be influenced by negative psychological factors related to the pandemic (11), highlighting the importance of focusing on children's mental health during such periods (12).

4.2 Impact analysis of COVID-19 on PICU admissions at Hunan Children's Hospital

The results of this study indicate that while the pandemic did not change the rankings of the top eight disease categories, it significantly influenced the composition of diseases in categories nine to twelve. The COVID-19 pandemic had a certain impact on the disease spectrum of PICU admissions, primarily leading to a significant reduction in the proportion of respiratory system diseases and infectious diseases. The inclusion of three years of data before and after the pandemic, totaling 13,918 cases, reduces the potential error arising from small sample size and strengthens the persuasiveness of this study.

This study revealed a decrease of 53.04% and 66.12% in respiratory system diseases and infectious diseases, respectively. This suggests that the pandemic, while controlling the spread of the novel coronavirus, also curbed the occurrence of respiratory and infectious diseases. Possible reasons include: (1) Government measures to control movement of individuals, adoption of online learning by schools, reduced child outings and gatherings, along with pandemic prevention education such as mask-wearing, increased social distancing, and hand hygiene, led to a decrease in opportunities for cross-infection (13, 14); (2) As the only Grade 3 Children's Specialized Hospital in Hunan Province, our hospital's pre-pandemic inpatients largely comprised patients from other areas. During the pandemic, due to complex treatment procedures and factors like lockdowns, many children with mild symptoms were either observed and treated at home or sought nearby medical care. Simultaneously, the maturation of internet hospitals has led many parents to opt for online consultations, reducing the back-and-forth trips to the hospital and the risk of cross-infection for both patients and their families; (3) Starting from August 2021, Hunan Province progressively initiated the administration of COVID-19 vaccines for students of all ages, in accordance with the province's joint prevention and control mechanism. The COVID-19 vaccine is considered a safe and effective tool to prevent severe infection, hospitalization, and death (15–18). Additionally, the vaccination rate for influenza vaccines has increased significantly compared to pre-pandemic levels, leading to a notable decrease in the incidence of influenza and pneumonia (19).

4.3 Impact analysis of COVID-19 on diagnosis and treatment in Hunan Children's Hospital's PICU

Jeng-Hung Wu et al. (20) found that during the COVID-19 epidemic with strict public restrictions, critically ill patients admitted to the PICU decreased but had increased disease severity, prolonged length of stay in the PICU, and higher mortality, reflecting the impact of quarantine and limited medical access. In this study, in the post-COVID-19 period, there was an increase in the average hospitalization cost and an extension of the average length of hospital stay for patients admitted to the PICU of Hunan Children's Hospital. This increase and extension can be attributed to several factors. Most notably, during the pandemic, children with milder conditions often chose home or outpatient treatment instead of seeking inpatient care. Therefore, those who did come to the hospital and required hospitalization tended to have more urgent and critical conditions, often accompanied by complications and comorbidities, making their cases relatively complex. The rise in costs and prolonged hospitalization could also be related to changes in the spectrum of pathogens during the pandemic period.

4.4 Study limitation

This is a single center study, and more valuable findings will be found in a nationwide multicenter large sample study. And this is a retrospective study, we don't conduct long-term follow-up on the PICU patients.

5 Conclusion

Analyzing the cases admitted to the PICU during the pandemic period provides insight into the changing trends of pediatric disease spectrum. This understanding serves as a scientific basis for improving pediatric medical care and enhancing the quality of critical care for children. During non-pandemic periods, the focus of children's prevention and treatment remains on respiratory system diseases, neurological system diseases, and hematological-oncological diseases.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Hunan Hospital Ethics Committee. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

YY: Conceptualization, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. YH: Data curation, Investigation, Methodology, Writing – original draft. JH: Investigation, Project administration, Writing – review & editing. HY: Data curation, Writing – review & editing. XZ: Supervision, Writing – review & editing. ZX: Conceptualization, Supervision, Writing – review & editing. XL: Conceptualization, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Crucial and fragile: a multi-methods and multi-disciplinary study of cooperation in the aftermath of the COVID-19 pandemic

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In addressing global pandemics, robust cooperation across nations, institutions, and individuals is paramount. However, navigating the complexities of individual versus collective interests, diverse group objectives, and varying societal norms and cultures makes fostering such cooperation challenging. This research delves deep into the dynamics of interpersonal cooperation during the COVID-19 pandemic in Canton Ticino, Switzerland, using an integrative approach that combines qualitative and experimental methodologies. Through a series of retrospective interviews and a lab-in-the-field experiment, we gained insights into the cooperation patterns of healthcare and manufacturing workers. Within healthcare, professionals grappled with escalating emergencies and deteriorating work conditions, resisting the "new normalcy" ushered in by the pandemic. Meanwhile, manufacturing workers adapted to the altered landscape, leveraging smart working strategies to carve out a fresh professional paradigm amidst novel challenges and opportunities. Across these contrasting narratives, the centrality of individual, institutional, and interpersonal factors in galvanizing cooperation was evident. Key drivers like established relational dynamics, mutual dependencies, and proactive leadership were particularly salient. Our experimental findings further reinforced some of these qualitative insights, underscoring the pivotal role of recognition and the detrimental effects of uncertainty on cooperative behaviors. While contextual and sample-related constraints exist, this study illuminates vital facets of cooperation during crises and lays the groundwork for future explorations into cooperative decision-making.

KEYWORDS

interpersonal cooperation, COVID-19 pandemic, crisis management, collaborative decision-making, mixed methods

1 Introduction

Amid the profound challenges of global crises, cooperation crystallizes as the bedrock of human adaptability and collective resilience. To effectively counter these crises, cooperationis paramount, requiring the concerted efforts of nations (1, 2), institutions, corporations (3), and individuals (4). Although the vast benefits of cooperative endeavors during emergencies are evident, the personal sacrifices and the allure of prioritizing self-interest pose significant barriers (5).

Cooperation's multifaceted nature means it's influenced by numerous factors: the perennial tug-of-war between immediate self-interest and broader collective well-being (6); the challenge of harmonizing various group interests during emergencies (7); societal influences, including an innate preference to aid in-group members over out-group members (8); and overarching norms and cultural tenets (3, 9, 10).

The recent COVID-19 pandemic underscored the fragility and importance of cooperation among individuals (Bavel et al., 2020), revealing complex dynamics. In this light, our study delves deep into interpersonal cooperation within Canton Ticino, Switzerland. Employing a multi-method approach, our research synthesizes insights from a retrospective qualitative study with findings from a lab-in-the-field experiment conducted between April 2021 and November 2022, targeting healthcare and manufacturing workers.

Our qualitative research unearths varied dynamics of cooperation across healthcare and manufacturing sectors. Healthcare professionals grappled with myriad challenges, from surging workloads to fears of contagion. Their actions were predominantly reactive, aiming to mitigate the immediate repercussions of the pandemic. Conversely, the manufacturing sector showed adaptability, steering toward long-term operational adjustments and capitalizing on the unforeseen opportunities presented by smart working. Common threads like the pivotal role of recognition, especially in high-stress scenarios, were observed across both sectors. This insight framed our lab-in-the-field experiment, which quantitatively validated the impact of recognition on cooperative behaviors. The results spotlighted the ebbing of cooperation under persistent stress without a clear endpoint in sight.

Our research offers an intricate examination of cooperation during the COVID-19 pandemic in Canton Ticino, Switzerland. Through this meld of qualitative and quantitative methodologies, we derive a nuanced understanding of cooperation's multifaceted nature. These findings have far-reaching implications, highlighting the need for astute strategies to nurture cooperation during crises.

For ease of navigation, this paper unfolds as follows: Section 1 reviews the literature on interpersonal cooperation. Section 2 establishes the context of our study in Canton Ticino. Section 3 outlines our methodological design, while Section 4 presents our findings. Finally, Section 5 provides a synthesis of our insights, reflecting on the broader implications and suggesting directions for future research and policymaking.

2 Literature review

2.1 Fostering interpersonal cooperation in the COVID-19 pandemic: challenges and opportunities for global public goods

Samuelson's definition of public goods identifies two characteristics: non-rivalry in consumption and non-excludability (11). Non-rivalry means a public good's use does not reduce its availability to others, while non-excludability indicates nobody can be excluded from its benefits, irrespective of their contribution. Global health, transcending borders, embodies a global public good (12), reflecting the interconnectedness of nations in addressing health challenges (1).

The COVID-19 pandemic underscores the significance of global public goods. It reveals strong incentives for free-riding when individual contributions appear insignificant. Inadequate cooperation can compromise public good provision, evident in the vaccine nationalism seen in the vaccine distribution (13). Marginalized populations face repercussions due to this disparity (14).

Our paper investigates interpersonal cooperation during crises, examining diverse individuals confronting a shared challenge. Cooperation's essence lies in its dynamics, with humans oscillating between cooperation and defection. Cooperators bear costs for the group's well-being [(5): 1560], while defectors pursue personal gain without considering collective interests. Despite its inherent costs, cooperation is pervasive, extending to interactions among unrelated individuals (4, 15), signifying its critical role in societies.

2.2 Factors affecting interpersonal cooperation

Various factors, including social norms, cultural influences, reciprocity, reputational concerns, and evolutionary mechanisms, influence the emergence and maintenance of cooperative behaviors among individuals. Additionally, the characteristics, rules, and dynamics of the group (or organization) to which individuals belong play a crucial role in fostering cooperation.

2.2.1 Group-related factors

Group-related factors include elements like group membership, cohesion, and uniformity (16). Recognizing a common goal, feeling equal, satisfaction within the group, acknowledging interdependence, and shared identity all heighten interpersonal cooperation (17). The group's organizational structure influences cooperation. Effective communication, clarity in roles, available tools and resources, and recognized leadership all impact cooperative behavior (18, 19). Leaders foster trust and a "we are all in this together" belief (20), facilitating coordination against external threats (16). Furthermore, seeing others as cooperative boosts one's propensity to cooperate (21).

2.2.2 Individual-level factors

Individual-level factors also influence cooperative behavior during unexpected and unknown events. Among these factors, trust in institutions, governments, and scientists plays a significant role (22). Trust in science is particularly crucial during epidemics, as it helps prevent small-scale outbreaks from escalating into large-scale emergencies. Trust in science, experts, and institutions determines citizens' compliance with public health policies, restrictions, and guidelines (23). However, building and maintaining trust can be challenging in times of uncertainty and risk (24). The perception and handling of risk also play a crucial role in cooperation during crises. How individuals represent and interpret risk impacts their motivation to take action. When risk is viewed as a stimulating challenge, individuals are more motivated to act. Conversely, perceiving risk as a threat to be avoided diminishes individual motivation (25).

In interpersonal cooperation, particularly in the workplace, professional identity emerges as a critical aspect. Professional identity encompasses professional ethics, including ethical knowledge, beliefs, skills, and implicit and explicit norms related to one's profession (26). Professional identity may conflict with institutional, family, or personal expectations, leading to conflicts at the intra-, interpersonal, and intergroup levels. Effectively managing these conflicts becomes essential for cooperation, as unresolved conflicts can lead to group dissolution while reinforcing interpersonal cohesion and cooperation dynamics.

2.2.3 External factors

External levers can also be employed to enhance cooperation. Extensive research indicates that several mechanisms can effectively promote cooperative behavior. These include punishments (27), rewards (28), observability (29), and moral suasion (30).

Punishments can serve as a powerful tool to deter defection and promote cooperation. By imposing penalties or sanctions on individuals who engage in non-cooperative behavior, the costs of defection are heightened, thus incentivizing individuals to choose cooperative actions. This helps maintain social order and discourage free-riding tendencies (27). Conversely, rewards can act as positive reinforcements for cooperative behavior. When individuals are offered incentives or benefits for engaging in cooperative actions, they are more likely to contribute to the common good willingly. The prospect of receiving rewards can motivate individuals to prioritize collective interests over personal gains, fostering a culture of cooperation (28).

Observability, or the degree to which individual actions are visible or known to others, can significantly impact cooperative behavior. When people know their actions are being observed and evaluated by others, they tend to exhibit higher levels of cooperation. Social scrutiny creates pressure to conform to cooperative norms as individuals strive to maintain a positive reputation and avoid reputational costs associated with non-cooperative behavior (29).

Moral suasion involves appeals to individuals' moral values and sense of ethical responsibility to encourage cooperative behavior. By emphasizing the moral dimensions of cooperation and highlighting its importance for the well-being of the group or society, individuals are more likely to engage in cooperative actions driven by their intrinsic motivation to do what is morally right (30).

2.3 Enhancing understanding of cooperation during crises: a mixed-methods study in real-world settings

Our paper builds upon the existing literature on cooperation during global crises, and it introduces several innovative elements that enhance our understanding of this phenomenon. Firstly, we adopt a mixed methods approach by combining a retrospective qualitative study with a lab-in-the-field experiment. This comprehensive approach allows us to capture the nuances of cooperation experiences during the COVID-19 pandemic and complement them with behavioral observations in a Public Goods Game, a well-established experimental tool in the social sciences for studying cooperation.

Secondly, we go beyond the conventional behavioral economics approach, which often relies on laboratory experiments with a sample of students. Instead, we investigate cooperation in real-world settings, specifically focusing on the healthcare and manufacturing sectors within Canton Ticino, Switzerland. By studying cooperation in the field, we are able to observe and analyze behaviors in the actual context where cooperation takes place, providing valuable insights that may not be fully captured in controlled laboratory environments.

Thirdly, our study examines both individual-level and contextual factors and explores their interplay in shaping cooperation. We recognize that cooperation is influenced not only by individual characteristics and motivations but also by the broader social and organizational contexts in which it occurs. By considering both individual and contextual factors, we offer a more comprehensive understanding of the complex dynamics that underlie cooperation during a crisis.

3 The context

Canton Ticino, in southern Switzerland, predominantly speaks Italian. With a diverse population and economy, it's influenced by both Swiss and Italian traditions. Like many regions, it faced challenges during the COVID-19 pandemic, especially being close to Lombardy, a major pandemic hotspot in Europe. To control the virus's spread, Canton Ticino enforced lockdowns and other measures.

During the pandemic, the healthcare sector had to restructure extensively. Hospitals like "Ospedale La Carità" and "Clinica Luganese" became dedicated COVID-19 centers. This transformation caused significant adjustments for healthcare workers, with many redeployed to new roles. On March 13, 2020, due to the escalating situation, the Swiss government even suspended the maximum workday length regulations for hospital staff.

Amidst these challenges, healthcare workers, especially those in COVID wards, faced immense pressure and moral dilemmas, as cited by (31). Cross-border health workers, making up 14% of the healthcare workforce in Ticino, dealt with the contrasting COVID-19 management strategies between Ticino and Northern Italy, fostering confusion. When Northern Italy became a pandemic epicenter on February 21, 2020, Italian authorities enforced stricter measures (32). In contrast, Ticino adopted a milder approach, emphasizing individual responsibility.

Consequently, these contrasting measures created uncertainty, especially for cross-border healthcare professionals regularly moving between the two regions. This emphasized the need for cooperation among healthcare workers.

The manufacturing sector too encountered challenges. Many companies in Ticino halted or reduced production due to supply chain disruptions, resulting in significant revenue losses. Reorganization required workers to adjust, underlining the importance of cooperation, which, despite uncertainties, showed resilience as the pandemic evolved. This study focuses on understanding this resilience amidst challenges faced by workers in health and manufacturing sectors.

4 Data and methods

The paper presents two consecutive studies on interpersonal cooperation during the Covid-19 pandemic. The first study employed a qualitative approach, referencing existing literature to grasp cooperation dynamics in this unique context. Through online interviews, researchers examined interpersonal cooperation's intricacies, challenges, and influencing factors during the pandemic.

Using insights from the qualitative study, the next phase implemented a lab-in-the-field experiment. This aimed to further probe hypotheses regarding interpersonal cooperation under stress. By manipulating variables and observing behavior, researchers gleaned insights complementing the qualitative data.

Integrating qualitative and experimental methods facilitated a holistic understanding of cooperation during the pandemic. The qualitative study provided deep insights into real-life experiences, while the experimental phase enabled hypothesis testing. Together, they sought to enrich the understanding of cooperation in crisis contexts.

The Cantonal Ethical Committee reviewed both protocols. The qualitative study did not require ethical approval under Swiss human research law, but still followed the Declaration of Helsinki with participants giving oral consent. However, the experimental study received approval from the Ethical Committee before data collection (no. 2021-01914CE 3952).

4.1 Data

4.1.1 Qualitative study

We conducted a qualitative study using Braun and Clarke's methodology (33) for its depth. Through online interviews, we focused on healthcare workers from the Canton Hospital Organization (Ente Ospedaliero Cantonale, EOC) from April to December 2021. This timeframe captures Switzerland's first three COVID-19 waves and the start of the vaccine roll-out in January 2021.

Using intensity and maximum variation sampling (34), we captured diverse cooperation experiences. With an EOC-affiliated physician, we identified key departments: intensive care, emergency, and internal medicine. Our sample aimed for diversity, factoring in gender, residence status, and deployment during the pandemic, duties, role, leadership, and age.

We invited potential participants; 45 showed interest, but 29 were finalized due to accessibility issues.

Simultaneously, we explored the manufacturing sector between April and May 2021 to compare findings with healthcare. Partnering with four local industries (fashion, furniture, electronics), we used a similar recruitment approach, resulting in a varied sample of 20 managers and employees from Ticino.

Overall, our diverse sample comprised 49 participants, detailed in Table 1.

The entire research team discussed the results of the qualitative study in the healthcare and manufacturing sectors to identify operational hypotheses regarding the drivers and barriers of interpersonal cooperation that could be effectively tested in the experimental study. The hypotheses were pre-registered.

4.1.2 Lab-in-the-field experiment

The results of the qualitative study were tested in a second experimental study. In this case, we investigated the propensity for cooperation among healthcare and manufacturing workers using a public good game (PGG). The PGG is a standard game in experimental social sciences (35). In the basic game, participants are given a small initial sum of money and must decide how much to contribute to a "common pool." The resources transferred to the common pool are multiplied by a constant and then divided among the game participants. Each participant keeps for themselves the resources they did not contribute to the common pool. From a purely theoretical standpoint, according to Nash equilibrium, no participant should contribute anything to the common pool because any rational agent would maximize their own profit by keeping all the money for themselves, regardless of what others do. However, experimental literature shows that Nash equilibrium is rarely achieved. Typically (36), those who contribute more to the common pool are referred to as "cooperators," while those who contribute less are called "defectors."

TABLE 1 Sample of the qualitative study.

Healthcare workers ($n = 29$)
14 women, 15 men
8 cross-borders, 21 residents
19 working in COVID hospitals, 10 in non-COVID hospitals
10 working in emergency department, 14 in intensive care, 5 in internal medicine
8 physicians, 21 nurses
7 (out of 21) nurses and 8 (out of 8) physicians with professional responsibility
24–65 y.o., mean age 49 y.o.
Manufacturer workers ($n = 20$)
8 women, 12 men
12 crossborders, 8 residents
11 working in smartworking, 9 in presence
28–63 y.o., mean age 45[MOU2]

The Public Good Game (PGG) was conducted using a between-subjects experimental design, incorporating four main treatment manipulations. In the baseline condition, participants engaged in the classic PGG for 10 rounds. In the recognition treatment, the top contributor was visually acknowledged with the display of two applauding hands on the screen. In the stress treatment, participants were required to make their decisions within a specific time limit indicated by a timer on the screen. In the extra-rounds treatment, participants unexpectedly received information that they had to play an additional 10 rounds. Additionally, three cross-treatments were introduced, where two treatments were combined. These cross-treatments resulted in the following three additional conditions: extra-rounds/stress, extra-rounds/recognition, and stress/recognition.

Consistent with common practices in experimental economics games, participants were remunerated based on their choices. On average, participants received approximately 22 Swiss francs per person, which were delivered through Amazon vouchers of equivalent value. The experiments lasted on average 45 min including the wearing of the sensors used to track their heart rate and electrocardiogram. After completing the experimental game, participants were administered a brief questionnaire. The questionnaire collected demographic information, employment details and included inquiries about psychological traits such as trust level and the Italian version of the Big Five Personality Traits, as proposed by Chiorri et al. (37). Additionally, the questionnaire encompassed two questions related to caution when interacting with people, a self-assessment of risk preferences, and people's willingness to help others.

Furthermore, we employed the Global Preferences Survey (38) to measure pure generosity and positive reciprocity. Additionally, we incorporated a set of questions on cooperation, which had been validated by Lu et al. (39).

It should be noted that the original plan for the experiment was to be conducted online without any strategic interaction. However, due to the favorable epidemiological situation and the development of a dedicated computer platform for conducting on-the-move behavioral economics experiments, the decision was made to conduct the experiments in person with strategic interaction. This change in approach came with a trade-off: due to time and sample constraints, we were unable to include in the experiment an in-group/out-group manipulation which were originally included in the pre-registration.

Between May and November 2022, a series of experiments were conducted using a newly developed computer platform. The platform consists of multiple components, with one of its key features being the management of historical data from wearable sensors. It also includes functionalities for anonymized operator management and efficient handling of the experiment results. Moreover, the platform incorporates functional modules that offer additional features, such as the behavioral economics games, specifically the Public Good Game utilized in this study, and artificial intelligence modules that provide valuable insights beyond manual analysis capabilities. Through the utilization of this platform, participants' heart rate and electrocardiogram were continuously monitored throughout the experimental sessions. The final working sample comprised 31 participants, resulting in a total of 767 observations.

4.2 Methods

4.2.1 Qualitative study

Participants partook in semi-structured online interviews, recorded and subsequently transcribed verbatim. Ensuring confidentiality, all identifying details were removed. Adopting Braun and Clarke's (33) thematic analysis approach, these transcripts were meticulously analyzed. To adhere to COVID-19 safety protocols, interviews were conducted online, incorporating strategies to enrich data quality as recommended by Caiata Zufferey and Aceti (40).

Each interview, informed by a semi-structured guide featuring open-ended prompts (e.g., "Reflect upon workplace conflicts during the pandemic: can you elucidate their origins and your response?"), was a dialog. Beyond the guiding questions, participants were free to explore and emphasize any topic they deemed relevant. Interviews varied in length, ranging from 40 to 80 min.

For a systematic thematic analysis, we embraced Braun and Clarke's (33) iterative stages, commencing with an intimate understanding of the data, which involved revisiting the transcripts multiple times. This was followed by coding, theme identification, theme review, understanding inter-theme relationships, and finally, synthesizing findings for the report. A single researcher, who was also the interviewer, embarked on an inductive coding process, marking both manifest and latent content. Throughout the analysis, the research team convened regularly, deliberating on code assignments and interpretations. Any differences in perspectives were debated and resolved collaboratively, ensuring a multi-faceted understanding of the data.

4.2.2 Lab-in-the-field experiment

In our analysis of data derived from lab-in-the-field experiments, we implemented a structured three-step statistical approach to elucidate the dynamics of interpersonal cooperation and the impact of various treatments.

4.2.2.1 Step 1: initial comparative analysis

Initially, we employed a combination of non-parametric and parametric statistical tests to rigorously evaluate the data. Specifically, we utilized *T*-tests (a parametric test) and Mann–Whitney tests (a non-parametric test) for this purpose.

4.2.2.2 Step 2: identifying predictors of cooperation

Subsequently, we harnessed the power of machine learning through the implementation of a Random Forest algorithm, utilizing data from questionnaires and wearable sensors. This advanced analytical method was selected for its proficiency in handling high-dimensional data and its ability to identify the most relevant predictors from a potentially large pool of characteristics. The algorithm analyzed a wide array of variables, including demographic information, psychological traits (such as trust and the Big Five Personality Traits), risk preferences, and measures of generosity and reciprocity, among others. The objective was to pinpoint specific attributes of participants that significantly influenced their propensity toward interpersonal cooperation.

4.2.2.3 Step 3: exploring the influence of individual characteristics

In the final stage of our analysis, we applied a linear regression model to delve deeper into the relationship between individual contributions in the Public Good Game (PGG) and a set of explanatory variables. This encompassed treatment variables, the most salient predictors identified by the Random Forest, and additional control variables (e.g., gender, age, healthcare worker status). Linear regression was chosen for its effectiveness in quantifying the strength and direction of associations between the dependent variable (PGG contribution) and independent variables.

For the execution of these analyses, we utilized Python for the Random Forest algorithm, owing to its robust machine learning libraries, and STATA for conducting the non-parametric tests, parametric tests, and Ordinary Least Squares (OLS) regression.

5 Results

In this section, we delineate our research findings, commencing with insights from the qualitative study and transitioning to the outcomes of the lab-in-the-field experiment. The qualitative results shed light on the multifaceted challenges, determinants of cooperation, and anticipated outcomes. Participant quotations, rendered in English, are showcased in Appendix Table 1A for richer context. For confidentiality, these quotes are anonymized. Using the qualitative insights as a bedrock, we subsequently delve into the lab-in-the-field experiment's results, offering empirical validations and deeper

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perspectives on the dynamics of interpersonal cooperation amidst the pandemic.

5.1 Qualitative study

From the data analysis, a clear distinction arises between the experience of cooperation in the healthcare sector and that in manufacturing. In the healthcare sector, the objective of the workers was to face the emergency, while also resisting the "new normality" imposed by the pandemic. Healthcare workers confronted a specific set of challenges for an extended duration, with interpersonal cooperation playing a crucial role in their work environment. They were tasked with *delivering extraordinary effort*, where extraordinary encompassed both exceptional in terms of quality and quantity of work, and deviation from the established norms. Participants described managing the fear of contagion, coping with worsening working conditions, grappling with a decline in the quality of care, dealing with uncertainty in planning, navigating the confusion of professional roles, adapting to non-standardized decision-making processes, facing emotional burden, and experiencing limitations in their personal lives (#1–8). Certain challenges were particularly severe for cross-border healthcare workers, who found themselves compelled to undertake lengthy journeys between their residences and workplaces or to remain in temporary lodgings in Switzerland (#9–10).

Overcoming these challenges depended on several *individual, institutional, and interpersonal conditions*. Characteristics related to the worker's personality or professional identity – such as optimism, resilience, trust in their colleagues and in the institution, adaptability, and work ethics – played a crucial role in enabling healthcare providers to cope with the extraordinary workload (#11–15). The leadership provided by direct superiors and the availability of spaces and time for effective communication were instrumental in facilitating effective cooperation, as well as institutional support and timely and consistent information (#16–18). Beyond these individual and institutional conditions, however, the strength of the group was the true driving force behind the extraordinary effort exerted by healthcare providers (#19). Several elements contributed to this cohesion and cooperation within the team: the presence of an external enemy, the virus, created a sense of shared purpose and unity; the high stakes involved, namely the care of others, further reinforced the commitment to collective action; the hospital, as a defined and bounded space and time, provided a significant divide between individuals inside and outside its confines, and reinforced the sense of belonging among those within; the urgent time frame imposed by the waves of the pandemic heightened the need for collaborative efforts; the shared condition of ignorance, with all team members grappling with the uncertainties of the virus, fostered a sense of togetherness and mutual support (#20–25). These factors contributed to the development of a strong collective identity where mutual recognition played an important role: the healthcare workers acknowledged their shared experiences and goals, therefore they perceived themselves as strongly connected to each other and as being part of a functional and interconnected group. This group was characterized by the attenuation of formal differences, the intensification of functional specificities, the transcendence of traditional roles, and the promotion of interprofessional attitudes. In such a context, cooperation could flourish (#26).

However, as time progressed, another main challenge surfaced, related to the *legitimacy* of the extraordinary effort performed by healthcare providers. Participants described how the enthusiasm experienced during the first wave gradually diminished. This decline was not solely due to physical exhaustion but also resulted from a perceived decrease in their sense of purpose and appreciation for their work. The "extraordinary effort," which once they considered necessary, became unacceptable to them due to the erosion of the principles that had previously justified it. These principles included the exceptional nature of the event due to its unpredictability and transience, the recognition from hierarchies of the extraordinary nature of their work, and the shared commitment of all stakeholders (healthcare providers, patients, and society) in the fight against the common enemy. The participants expressed feelings of being disrespected and unrecognized as the pandemic advanced through its waves: with the pandemic no longer catching them by surprise, their expectation for improved hospital organization heightened; additionally, they bitterly perceived their exceptional efforts as taken for granted; finally, they believed that a significant number of individuals, including both patients and colleagues, were neglecting their responsibilities, rejecting containment measures or vaccination (#27–31). This situation undermined their commitment with patients, hierarchical structures, and colleagues. Consequently, many participants responded by withdrawing and resorting to bureaucratic actions, which reflected a retreat from active cooperation and a diminished sense of purpose (#32).

The experience of cooperation of the workers in the manufacturing sector was significantly different. Right from the outset, their stated goal was to recreate a "new normality" within the ongoing pandemic. Their primary challenge revolved around *adapting to smart working*, which entailed modifying the work environment and communication tools while maintaining the same corporate objectives (#33). In this context, smart working has entailed ambivalence, encompassing both opportunities and challenges. On the one hand, it fostered greater organization and focus, optimizing time management and offering increased flexibility, especially for cross-border workers, who could avoid long travels to reach their workplace (#34–37). On the other hand, it posed several obstacles, including the need for leaders to exercise control, the scarcity of interpersonal communication, the absence of informal interactions, the integration of professional and personal life boundaries, and – of course – the necessity to acquire technological skills (#38–43).

Also in this case, effectively managing these challenges relied primarily on *individual, institutional and interpersonal factors*. Of particular importance were the workers' adherence to the company's goals, their aptitude for learning – especially regarding the adoption of new communication tools – and their ability to organize themselves in the absence of a structured environment (#44–45). The inputs provided by the direct supervisor or by the company in general also proved to be important in successfully addressing the challenges of the new working conditions. Leaders were expected to demonstrate supportive and visible guidance, actively engaging with their teams and offering personalized direction and oversight even when working remotely. Regular scheduled online meetings were crucial regarding to this. Expressing concern for employees and their well-being through active listening and tangible gestures, such as providing ergonomic chairs delivered to their homes, helped foster a sense of care and support. Furthermore, organizational consistency ensured that measures and guidelines were clear and coherent across all company levels. This gave employees a sense of stability and trust in decision-making (#46–49). Finally, the quality of pre-existing relational assets, encompassing the significance of the group's history, a sense of belonging, and the nature of informal relationships that had developed before the pandemic, contributed to a foundation of resilience and mutual reliance. The lack of this relational capital could negatively impact on cooperation. On the contrary, the intensity of interdependence within the team influenced the willingness of individuals to cooperate actively: the stronger the perceived interdependence, the more likely people were to engage in cooperative efforts (#50–51).

Unlike healthcare professionals, workers in the manufacturing sector did not express particular suffering due to the prolonged nature of the pandemic. Their objective was to adapt to the new work conditions by addressing challenges and capitalizing on opportunities. Consequently, they embraced a long-term perspective and utilized the duration of the experience as a chance for better learning how to effectively acclimate to it. Ultimately, they did not question the *legitimacy* of their effort and were even hoping that some of the new working conditions could continue also in the future (#52).

To consolidate our findings from both the healthcare and manufacturing worker samples, we identify [MOU1] key factors operating at various levels that enhanced cooperation. Despite the distinct experiences of cooperation in the two professional settings, our qualitative study highlights the presence of individual enabling elements, institutional conditions, and interpersonal driving factors. Each of these played a critical role in promoting and sustaining the extraordinary cooperation among workers during the COVID-19 pandemic. Individual enabling elements encompassed aspects of personality (such as optimism, trust, and resilience), skills (adaptability, learning ability, and organizational competences), as well as professional identity and ethics. Institutional conditions included consistency in information and organization, the availability of effective communication spaces for teams, and supportive and actively present leadership. Interpersonal driving factors involved the intensity and cohesion of the group, the awareness of its interdependence, and a sense of mutual support during the pandemic. Among these various factors, the significance of internal and external *recognition* [MOU2] emerges as a central theme. In both samples, feeling part of a group of people with shared experiences and goals (internal recognition) considerably reinforced willingness and cooperative attitudes. Likewise, receiving signs of respect and acknowledgement for work accomplished amidst the extraordinary circumstances of the pandemic (external recognition) yielded similar outcomes.

On the contrary, the absence of these two forms or recognition diminished cooperative engagement. The *lack of transience* in the new working conditions also arises as pivotal, albeit in different ways. For healthcare workers subjected to extraordinary stress levels, the duration had a negative impact on cooperation. Conversely, for workers in the manufacturing sector who glimpsed new opportunities, the enduring nature of their situation acted as an incentive for adaptation. The *level of stress*, therefore, also emerges as an influential element capable of modulating the impact of recognition and duration.

5.2 Lab-in-the-field experiment

Building upon the valuable insights from the qualitative analysis, our research takes a significant step forward by investigating whether the mesosocial and the microsocial factors identified in the qualitative phase are relevant in shaping cooperation within the Public Good Game (PGG).

First, we focus on macrosocial conditions. Our objective in this phase is to recreate the circumstances faced by workers during the COVID-19 pandemic in a controlled environment, including the recognition (a lack thereof) of their extraordinary work, the presence (or absence) of time constraints causing stress, and the transient (or non transient) nature of the event. These conditions were implemented as treatment manipulations in our experimental settings, as outlined in Section 3. The results of this exercise are depicted in Table 2 and Figure 1.

To examine the impact of these treatments on cooperation, we compared the average contributions across all players and the 10 repetitions between the baseline and the main treatment manipulations, which include stress, recognition, and extrarounds. Our analysis reveals significant differences in cooperation levels among these treatments.

Offering recognition to the players results in a marginal increase in cooperation compared to the baseline (*t*-test p-value = 0.065, Two-sample Wilcoxon rank-sum (Mann–Whitney) test p-value = 0.100). Conversely, the unexpected requirement to play additional rounds significantly hampers cooperation (*t*-test $p < 0.001$, Two-sample Wilcoxon rank-sum (Mann–Whitney) test $p < 0.001$). However, no statistically significant difference in cooperation is found between the baseline and the treatment under stress (*t*-test p-value = 0.478, Two-sample Wilcoxon rank-sum (Mann–Whitney) test p-value = 0.380), suggesting that the presence of a stressful event *per se* does not increase cooperation.

Further analysis examines the effect of recognition with and without stress. Cooperation is significantly higher in the presence of stress when players receive recognition (*t*-test $p < 0.001$, Two-sample Wilcoxon rank-sum (Mann–Whitney) test $p < 0.001$), suggesting that offering recognition can sustain cooperation during stressful events. Moreover, the difference in cooperation levels between cooperation under stress with and without recognition (Recognition/Stress – Stress) and cooperation levels with and without recognition (Recognition-Baseline) is greater than 0 (32.42), indicating that offering recognition is particularly efficient during stressful situations when players may need an extra boost to sustain cooperation.

TABLE 2 Contributions in the PGG by treatment manipulation and across 10 rounds.

	Average contribution
Baseline	57.0079
Recognition	63.8495
Stress	53.7358
Extrarounds	37.82
Extrarounds/Stress	68.125
Extrarounds/Recognition	58.0583
Recognition/Stress	93

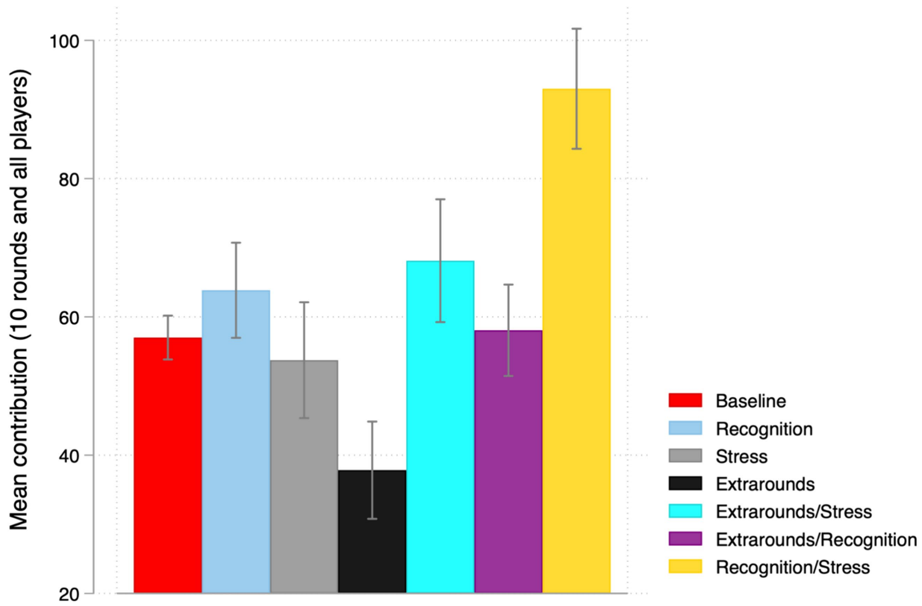

FIGURE 1
Contributions in the PGG by treatment manipulation and across 10 rounds.

Cooperation is also higher in the extraround treatment when there is stress (t-test $p<0.001$, Two-sample Wilcoxon rank-sum (Mann–Whitney) test $p<0.001$). However, the difference between cooperation levels in the presence of stress with and without extrarounds (Extrarounds/stress – Stress) and cooperation levels with and without extrarounds is not significantly different from 0 (4.7), suggesting that the presence of stress alone cannot help in sustaining cooperation when the transient nature of the event disappears. In contrast, the difference between extrarounds under stress and recognition under stress is highly statistically significant (t-test $p<0.001$, Two-sample Wilcoxon rank-sum (Mann–Whitney) test $p<0.001$), once again highlighting the importance of properly rewarding cooperation, especially during stressful events, for its sustainability.

Next, we aim to identify the top variables that influence cooperative behavior across different treatments in the game. The findings are visually presented in Figure 2, representing the results of the Random Forest model described in the methods section. More specifically, Figure 2 is not merely a representation of data; it is a visual synthesis that provides a comprehensive overview of the key variables that emerged as significant influencers of cooperative behavior, as determined by the Random Forest model.

The initial findings depicted in Figure 2 reveal that factors such as group dynamics, social interactions, and personal attributes have a more substantial impact on cooperative behavior than objective situational factors like physiological stress indicators measured through wearable sensors. This emphasizes the significance of personal and social elements over physiological responses in understanding and fostering cooperation. When we closely examine the 10 most important variables selected, a clear picture emerges regarding the specific characteristics and attitudes that strongly influence cooperation within the PGG. These variables encompass a range of factors, including the willingness to take risks, possessing a cooperative personality, actively listening to others' opinions, considering and integrating diverse viewpoints within a group, and enjoying cooperation with team members. Other important variables are: finding happiness in collective work, the importance of having a dependable partner, displaying a reserved and quiet demeanor, and cultivating a collaborative mindset toward achieving common success. These findings underscore the significance of personal attributes, effective communication skills, and a positive attitude toward teamwork as key drivers of cooperative behavior. Importantly, these results align closely with the insights from the previous qualitative analysis, further bolstering our findings' validity and reliability.

As depicted in Figure 2, there is a noticeable distinction in the importance of the first two variables compared to the others. This visual observation led us to prioritize these two variables and utilize them as controls in the Ordinary Least Squares (OLS) model.

Table 3 presents the results of the Ordinary Least Squares (OLS) model, as described in the Methods section above. The first three columns focus on the treatments without stress, while the last three columns analyze the treatments with stress. Columns 1 and 4 display the associations between treatments and cooperation while controlling solely for the number of rounds. Columns 2 and 5 introduce additional variables such as age, gender, and being a healthcare worker. Finally, columns 3 and 6 include the two variables selected through the Random Forest Algorithm, namely risk aversion and a self-assessed measure of cooperation.

The results indicate several significant findings. Firstly, when considering the impact of treatments, offering recognition emerges as a crucial factor in sustaining cooperation under stress. The coefficient for recognition is consistently positive and statistically significant in columns 4–6. Additionally, the absence of transience in the event significantly reduces cooperation when no other control variables are considered. However, when adding controls it becomes insignificant.

Regarding the control variables, men exhibit lower levels of cooperation compared to women in the absence of stress, and this difference is statistically significant. However, in the presence of stress,

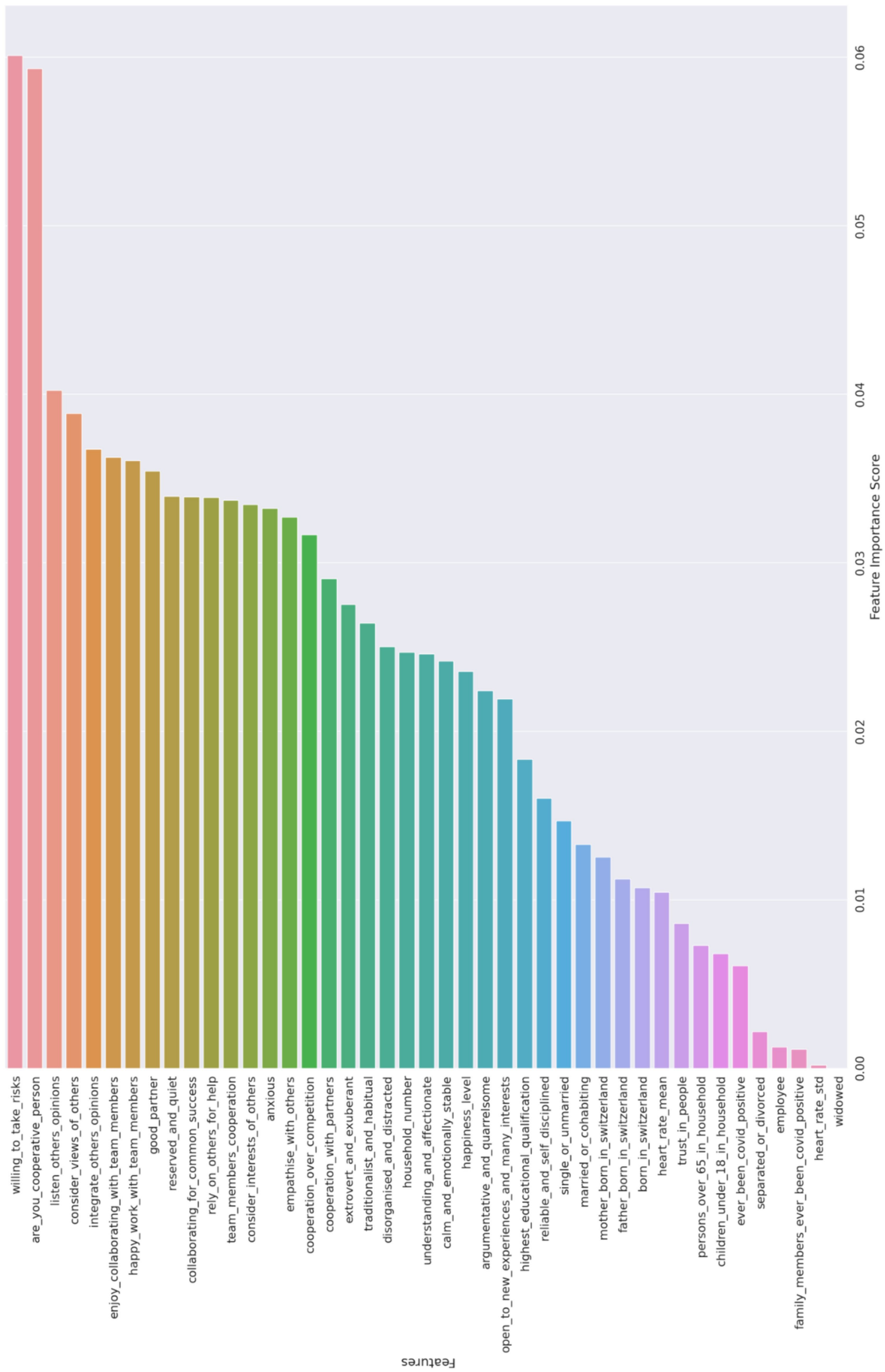

FIGURE 2
Variables in order of importance for the Random Forest model.

no significant gender difference is observed. Furthermore, in the presence of stress, risk aversion is found to have a negative relationship with cooperation, indicating that more risk-averse individuals tend to contribute less. Conversely, being a cooperative person, as measured by the self-assessed measure of cooperation, is positively associated with cooperation in the presence of stress. Overall, there is no

TABLE 3 OLS contribution at the individual level.

	No stress			Stress		
	(1)	(2)	(3)	(4)	(5)	(6)
	Contribution					
Recognition	6.003 (3.772)	−0.611 (3.670)	−1.600 (3.684)	39.20*** (6.598)	45.17*** (7.625)	23.57** (7.315)
Extrarounds	−21.39** (6.654)	−8.913 (6.420)	−8.008 (6.430)	11.78 (10.96)	−4.151 (10.83)	−14.37 (9.475)
Rounds	0.133 (0.448)	0.177 (0.416)	0.177 (0.415)	0.255 (0.892)	0.217 (0.759)	0.459 (0.652)
25–34		31.11*** (7.441)	34.70*** (7.572)			
35–44		40.61*** (7.560)	44.26*** (7.691)		−38.63*** (6.556)	−26.43*** (6.068)
45–54		19.23** (7.417)	22.26** (7.649)		−43.44 (25.73)	−5.922 (23.31)
Male		−15.19*** (2.724)	−15.95*** (2.736)		9.060 (25.37)	25.61 (22.78)
Health-care worker		−4.255 (3.213)	−3.795 (3.282)		8.875 (7.404)	61.88*** (10.23)
Risk scale			0.151 (0.0875)			−1.097*** (0.201)
Cooperative person			0.0471 (0.143)			2.399*** (0.367)
Constant	57.14*** (2.964)	36.06*** (7.786)	18.83 (13.90)	52.40*** (6.132)	79.35*** (9.130)	−98.04** (31.22)
Observations	634	634	634	123	123	123

Standard errors in parentheses. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

substantial difference in terms of contribution between healthcare and manufacturing workers as being a healthcare worker shows a positive and statistically significant relationship with contribution only in column 6 of Table 3.

6 Discussion and conclusions

This paper delves into the dynamics of interpersonal cooperation in Canton Ticino, Switzerland, during the COVID-19 pandemic. A qualitative study uncovers varied cooperation experiences in the healthcare and manufacturing sectors, elucidating sector-specific challenges and coping strategies. Moreover, our findings underscore the crucial roles of individual, institutional, and interpersonal factors. The lab-in-the-field experiment reinforces the vital role of internal and external recognition, emphasizing that prolonged stress conditions can erode cooperation. The synthesis of qualitative and quantitative methodologies allows a comprehensive exploration of cooperation, particularly within the framework of the Public Good Game (PGG).

From a methodological standpoint, our research offers a pioneering approach in examining cooperation during crises. The qualitative dimension provided a deep dive into the lived experiences during the pandemic, while the behavioral economics experiments offered empirical evidence on cooperation's underlying mechanisms. The merger of these methodologies illuminated complex patterns, providing a multifaceted research design suitable for other disciplines.

Yet, potential limitations exist. Our study, while offering valuable insights into the dynamics of interpersonal cooperation during the COVID-19 pandemic in Canton Ticino, Switzerland, navigates through inherent methodological and contextual constraints that merit acknowledgment. First and foremost, our reliance on voluntary email responses for participant recruitment may have introduced a selection bias, potentially limiting the representativeness of our sample. This is further complicated by the attrition of healthcare professionals during the recruitment phase, where out of 45 initially interested individuals, 16 were unreachable, raising concerns about the possible impact on the study's findings due to non-random sample attrition. Moreover, the geographical specificity of our study, focused solely on Canton Ticino, coupled with the concentration on only the healthcare and manufacturing sectors, could restrict the generalizability of our results. While this focus allows for a deep exploration of these sectors during an unprecedented global crisis, it may not capture the full spectrum of cooperation dynamics present in other sectors or regions, which could respond differently to similar stressors. The experimental component of our research, conducted in a lab-in-the-field setting, while innovative, encounters limitations in sample size. The number of participants in these experiments was relatively small, necessitating caution in the extrapolation of results. This constraint underscores the challenge of achieving generalizable findings from experimental data, a common hurdle in behavioral economics research that requires careful consideration in interpreting and applying our results. Furthermore, while the integration of qualitative and quantitative methods enriches our understanding of cooperation, this methodological amalgamation introduces complexities in data synthesis and interpretation. Balancing the depth of qualitative insights with the empirical rigor of quantitative analysis poses challenges, particularly in ensuring that the nuanced, context-specific findings from the qualitative study are adequately reflected in the broader quantitative analysis.

Lastly, the timing of the study, amid the COVID-19 pandemic, presents both an opportunity and a limitation. While it offers a unique lens through which to view cooperation under crisis conditions, it also means that the findings are influenced by the extraordinary circumstances of the pandemic. This context-specific factor may affect the durability of our conclusions and their applicability to other crisis or non-crisis conditions, necessitating further research to explore the persistence of observed behaviors beyond the pandemic context.

However, the insights from this research have critical implications for crisis management. They highlight the pivotal role of recognition in maintaining cooperation during stressful times. The significance of both a strong collective identity and institutional acknowledgment underscores the need for effective collaboration during crises. Looking ahead, future studies should address these constraints, broadening their scope to provide a more holistic perspective on cooperation dynamics in diverse scenarios. This will aid in crafting strategies to foster collective action during global challenges.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Comitato etico cantonale c/o Ufficio di sanità Via Orico 5 6501 Bellinzona. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

VR: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. MB: Conceptualization, Software, Validation, Writing – review & editing. GL: Conceptualization, Software, Writing – review & editing. ML: Formal analysis, Writing – review & editing. LU: Conceptualization, Resources, Supervision, Validation, Writing – review & editing. SD'O: Formal analysis, Software, Validation, Writing – review & editing. MR: Formal analysis, Visualization, Writing – review & editing. LB: Conceptualization, Validation, Writing – review & editing. MC: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1368056/full#supplementary-material

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Factors associated with difficulty in hospital acceptance during the COVID-19 pandemic period in Osaka Prefecture, Japan: a population-based study

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Background: In many countries, emergency medical systems were responsible for initial treatment of patients with COVID-19. Generally, acceptance by medical institutions may not be sufficient, and it may take much time to determine the medical institution to which to transport the patient. This problem is termed "difficulty in hospital acceptance (DIH)," and it is used as a key performance indicator in the assessment of the EMS in Japan. The purpose of this study was to reveal the factors associated with the DIH during the COVID-19 pandemic using dataset in the ORION (Osaka emergency information Research Intelligent Operation Network system).

Methods: This was a retrospective descriptive study with a 3-year study period from January 1, 2019 to December 31, 2021. We included patients who were recorded in the ORION system during the study period. The primary endpoint was defined as DIH. Multivariable logistic regression model was used to assess factors associated with DIH during the COVID-19 pandemic and calculated their adjusted odds ratio (AOR) and associated 95% confidence interval (CI).

Results: 1,078,850 patients included in this study. Of them, 41,140 patients (3.8%) experienced DIH and 1,037,710 patients (96.2%) did not experience DIH. The median age was 71 years (IQR: 45–82), and 543,760 patients (50.4%) were male. In this study, SpO_2, body temperature, and epidemic period of COVID-19 were associated with difficulty in hospital acceptance. The highest AOR of SpO2 was 80% or less (AOR: 1.636, [95% CI: 1.532–1.748]), followed by 81–85% (AOR: 1.584, [95% CI: 1.459–1.721]). The highest AOR of body temperature was 38.0–38.9°C (AOR: 1.969 [95% CI: 1.897–2.043]), followed by 39°C or higher (AOR: 1.912 [95% CI: 1.829–1.998]). The highest AOR of epidemic period of COVID-19 was the 4th wave (AOR: 2.134, [95% CI: 2.065–2.205]), followed by the 3rd wave (AOR: 1.842, [95% CI: 1.785–1.901]).

Conclusion: In this study, we revealed factors associated with the DIH during the COVID-19 pandemic. As various factors are involved in the spread of an unknown infectious disease, it is necessary not only to plan in advance but also to take appropriate measures according to the situation in order to smoothly accept emergency patients.

KEYWORDS
emergency medical service, COVID-19, pandemic, prognosis, public health, epidemiology

Introduction

Novel coronavirus (COVID-19) was first identified in Wuhan, China, in December 2019, and has since spread worldwide, including to Japan (1–7). COVID-19 is an infectious virus that causes severe respiratory failure. The patient with COVID-19 requires respiratory assistance and extracorporeal membrane oxygenation (ECMO), and emergency medical systems were responsible for initial treatment of patients with COVID-19 in many countries. Initially, because the infection route of COVID-19 was unknown, many medical workers such as physicians and nurses were required to take strict infection precautions, and these strict infection precautions affected the treatment of non-COVID-19 patients. However, as the pathogenesis of COVID-19 was revealed and the development of vaccines and vaccination against COVID-19 progressed, infection precautions against COVID-19 were phased out worldwide. In Japan, the Infectious Disease Control Law was revised in May 2023, with the infection precautions against COVID-19 lifted, and the usual medical care system has been recovered (8).

In Japan, the Emergency Medical System (EMS) is a public service, and patients can call for an ambulance free of charge. After the patient calls, the patient is evaluated by EMS personnel at the scene, and the appropriate medical institution is selected to which to transport the patient based on that evaluation. The EMS personnel at the scene negotiate with doctors and nurses in the emergency medical institutions for permission to transport the patient. However, depending on the patient's condition and the time of day when the patient called for an ambulance, acceptance rates differ by institutions, and acceptance by the nearest medical institution cannot be assumed; there may be delays in determining the institution to which to transport the patient. This problem is termed "difficulty in hospital acceptance (DIH)," and it is used as a key performance indicator in the assessment of the EMS in Japan. We have previously identified factors related to DIH (9). However, it remains unclear whether the epidemic period of COVID-19 infection or patient status affected the DIH during the COVID-19 pandemic period. Review of this pandemic and determining the impact of the COVID-19 pandemic on the EMS are critical when considering policies against infectious disease pandemics in the future.

Osaka Prefecture, the largest metropolitan area in western Japan, has a population of 8.8 million people and generates approximately a half million calls for ambulances each year (10). Since the first patient with COVID-19 was identified in Osaka Prefecture on January 23, 2020, the cumulative number of COVID-19 patients in Osaka Prefecture as of December 31, 2021 was 203,790 (11). In Osaka Prefecture, emergency patients transported by ambulance have been registered in the ORION system since 2015 (12, 13). The purpose of this study was to reveal the factors associated with the DIH during the COVID-19 pandemic using ORION data.

Materials and methods

Study design and settings

This was a retrospective descriptive study with a 3-year study period from January 1, 2019 to December 31, 2021. We included patients who were recorded in the ORION system during the study period. Therefore, exclusion criteria for this study were cases with missing data and inter-hospital transfer cases.

In 2020, 8,837,685 people lived in the 1905 km^2 area of Osaka Prefecture. Of that population, 4,235,956 people (47.9%) were male and 2,441,984 people (25.4%) were considered older adult, aged 65 years old or more (10). Because the ORION data is anonymized without specific personal data, such as patient name, date of birth, and address, the requirement of obtaining patients' informed consent was waived. This study was approved by the Ethics Committee of Osaka University Graduate School of Medicine, Suita, Japan (approval number: 15003). This manuscript was written based on the STROBE statement to assess the reporting of cohort and cross-sectional studies (14).

Ems system and hospitals in Osaka Prefecture

The EMS system is basically the same as that used in other areas of Japan. In Osaka Prefecture, EMS systems such as ambulance dispatch systems are operated by each local government, and ambulances are dispatched by calling 1–1–9. In 2021, the EMS system was operated by 26 fire departments (298 ambulances) and 26 fire control stations. In 2018, there were 517 medical institutions (105,994 beds) in Osaka Prefecture (15), of which 288 are emergency medical hospitals including 16 critical care centers that are designated to accept patients with life-threatening emergency diseases such as severe trauma and sepsis. Since the introduction of the ORION system, EMS personnel at the scene select the appropriate hospital for emergency patients rather than a dispatcher.

The ORION system

Information on the system configuration of ORION was previously described in detail (12, 13). The EMS personnel at the scene operate the ORION smartphone app for each emergency patient. All of the data input into this cellphone app, such as vital signs and the time of the call to the hospital for acceptance, are also recorded. The cellphone app data are accumulated in the ORION cloud server, and in cooperation with the dispatched EMS personnel, data managers at each fire department directly input or upload the ambulance record of each emergency patient so that it can be connected with the app data. Furthermore, the operators of each hospital also directly input

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or upload the patient's data, such as diagnoses and outcomes, after hospital acceptance. The results of the aggregated data in the ORION system are fed back to every fire department and emergency hospital. The Department of Public Health of Osaka Prefecture can also analyze the effects of health policy on the emergency medical system using these collected data. The ORION system has been in place in all fire departments and emergency hospitals in Osaka Prefecture since January 2016.

The COVID-19 pandemic in Osaka Prefecture

We have previously revealed the characteristics and outcome of patients with COVID-19 in Osaka Prefecture (16). In Japan, based on the Infectious Diseases Control Law, patients diagnosed as having COVID-19 using a polymerase chain reaction (PCR) test or antigen test at medical institutions were reported to the public health department and the number of patients was counted and published until May 2023 (8). In Osaka Prefecture, as in other countries, the number of patients with COVID-19 increased as the genetic form of COVID-19 changed (11). The public health department took the lead in arranging medical institutions for patients diagnosed as having COVID-19 who required inpatient care. As the number of COVID-19 patients increased and it became difficult to provide inpatient care, doctors and nurses were assigned to loading facilities such as hotels, and these facilities were used as temporary medical facilities to accommodate COVID-19 patients. In Osaka Prefecture, the epidemic period of COVID-19 infection was defined as the first wave (1/29/2020–6/13/2020), second wave (6/14/2020–10/9/2020), third wave (10/10/2020–2/28/2021), fourth wave (3/1/2021–6/20/2021), fifth wave (6/21/2021–12/16/2021), and sixth wave (12/17/2021–6/24/2022) based on the number of patients newly infected with COVID-19 (Figure 1) (17). Because we used an annual data set in this study, we only included 2 weeks for the six wave (12/17/2021–12/31/2021).

Data collection and quality control

The ORION system checks for errors in the inputted in-hospital data, and the staff of each emergency hospital can correct them if necessary. Through these tasks, cellphone app data, ambulance records, and the in-hospital data such as diagnosis and prognosis can be comprehensively registered for each patient transported by an ambulance. The registered data is cleaned by the Working Group to analyze the emergency medical care system in Osaka Prefecture (12). Among the collected and cleaned data, we excluded inconsistent data that did not contain all of the cellphone app data, ambulance records, and in-hospital data such as diagnosis and prognosis. In addition, we also excluded patients whose sex as registered by the fire department did not match that registered by the hospital or whose sex was missing. We also excluded patients whose age input by the fire department and that by the hospital differed by 3 years or more. When this difference was present, we defined the age input by the hospital as the patient's true age.

Endpoints

The primary endpoint was defined as DIH. In this study, DIH was defined as a case in which the patient stayed at the scene for more than 30 min and required more than 4 attempts to determine which

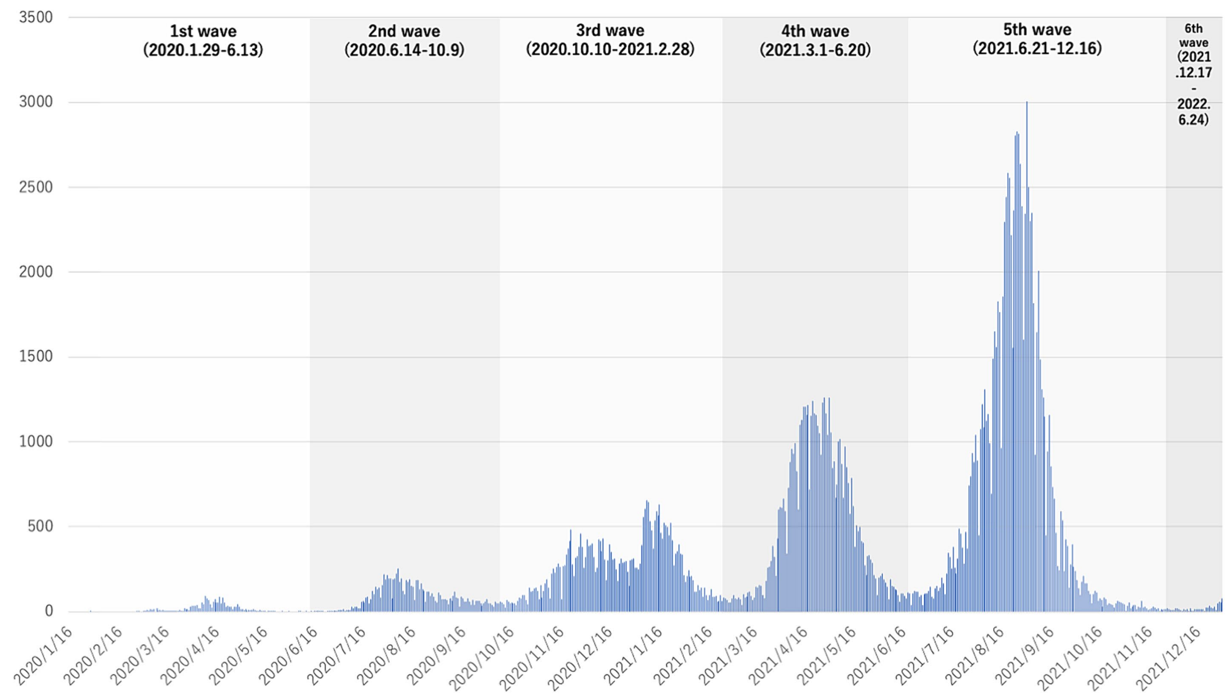

FIGURE 1
The number of patients with COVID-19 per week during the study period.

medical institution to transport to based on the definition by the Fire and Disaster Management Agency (18). The secondary endpoint was mortality of patients with DIH for each COVID-19 epidemic period. Mortality was calculated as the percentage of patients who died within 21 days of ambulance transport among the patients hospitalized after ambulance transport.

Statistical analysis

In this study, we used a multivariable logistic regression model to assess factors associated with DIH during the COVID-19 pandemic and calculated their adjusted odds ratio (AOR) and associated 95% confidence interval (CI). A multivariable logistic regression model was conducted using forced entry methods. Based on a previous study (9), potential covariates were age group, gender, saturation of oxygen (SpO_2), disturbance of consciousness, body temperature (BT), time of day, day of the week, place of occurrence, reason for ambulance call, and the epidemic period of COVID-19. Because we hypothesized that the suggested COVID-19 infection would affect hospital acceptance, we entered body temperature and SpO_2 into the regression model as explanatory variables. Age groups were classified into children (0–14 years), adults (15–64 years) and older adult (over 65 years). SpO_2 was classified in 5% increments, and those below 80% were integrated. BT was classified in 1°C increments, and those above 39°C and below 34°C were merged. Disturbance of consciousness was classified by Glasgow Coma Scale (GCS) and classified as coma (GCS: 3–8) and non-coma (GCS: 9–15). Time periods were classified as daytime (8:00–17:59) and nighttime (0,00–7:59, 18:00–23:59). Reason for ambulance call was classified into "Fire accident," "Natural disaster," "Water accident," "Traffic accident involving car, ship, or aircraft," "Injury, poisoning, and disease due to industrial accident,"" Disease and injury due to sports,"" Other injury,"" Trauma due to assault," "Self-induced injury," and "Acute disease." The COVID-19 epidemic period was classified based on the definition by Osaka Prefecture. In addition, as a subgroup analysis, ORs and 95% CIs for potential covariates were calculated using the multivariate logistic regression model separately for each COVID-19 epidemic period. Data are presented as medians and interquartile ranges (IQR) for continuous variables and as percentages for categorical variables. Statistically significant differences were defined as those with $p < 0.05$, and SPSS Statistics ver. 27.0 J (IBM) was used as the statistical software.

Results

Figure 2 shows the patient flow in this study. During the study period, 1,391,581 patients were registered in the ORION system. Patients with missing data (BT: $n = 172{,}102$, GCS: $n = 58{,}075$, SpO_2: $n = 10{,}411$) and inter-hospital transfer cases ($n = 72{,}143$) were excluded, resulting in 1,078,850 patients being included in this study. Of them, 41,140 patients (3.8%) experienced DIH and 1,037,710 patients (96.2%) did not experience DIH.

Table 1 shows the characteristics of the study patients. The median age was 71 years (IQR: 45–82), 68,765 (6.4%) were children, 625,431 (58.0%) were adults, 384,654 (35.7%) were older adults, 543,760 (50.4%) were male, and 535,090 (49.6%) were female. The SpO_2 was 86–90% in 28,627 patients (2.7%), 81–85% in 10,021 patients (0.9%), and below 80% in 16,134 patients (1.5%), and 25,742 patients (2.4%) were in a coma. Among the patients with fever, the BT was 37.0–37.9°C in 195,335 patients (18.1%), 38.0–38.9°C in 63,574 patients (5.9%), and ≥ 39.0°C in 49,817 patients (4.6%). The most common calling location was home (696,057, 64.5%), followed by a public space (191,160, 17.7%). The most common reason for the ambulance call was "acute disease" (786,416, 72.9%), followed by "other injury" (180,226, 16.7%). Regarding the epidemic of COVID-19, the number of patients in the pre-pandemic period was 425,768 (39.5%), with 121,247 (11.2%) in the 1st wave, 117,787 (10.9%) in the 2nd wave,

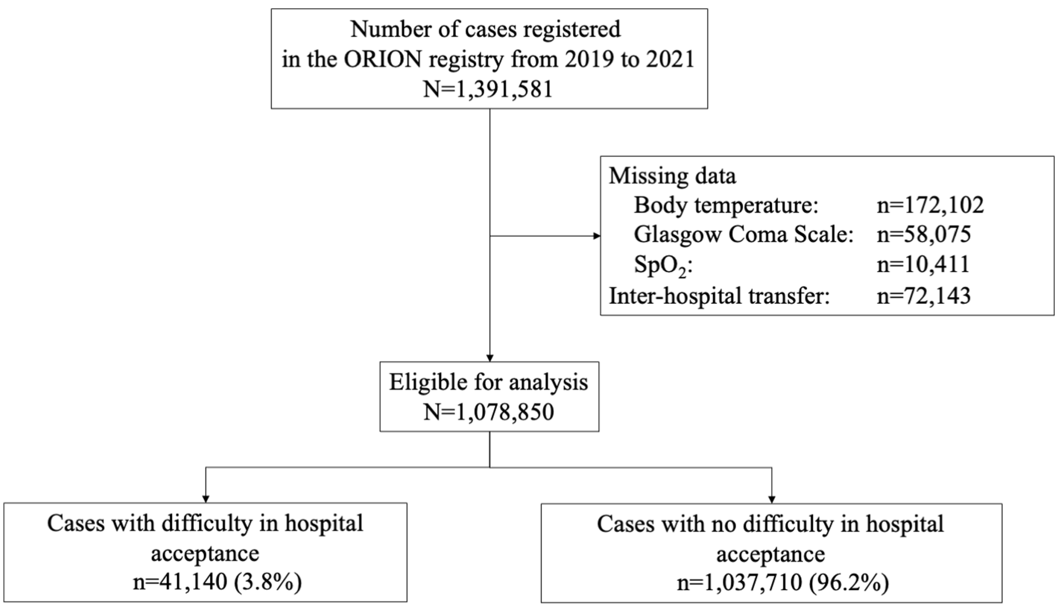

FIGURE 2
The patient flow in this study.

TABLE 1 Patient characteristics.

	Total		Difficulty in hospital acceptance		No difficulty in hospital acceptance	
	(*n* = 1,078,850)		(*n* = 41,140)		(*n* = 1,037,710)	
Age, years, median (IQR)	71	(45–82)	69	(45–82)	71	(45–82)
Age groups, *n* (%)						
Children (0–14 years old)	68,765	(6.4)	956	(2.3)	67,809	(6.5)
Adult (≥18 years, <65 years)	6,25,431	(58.0)	22,825	(55.5)	6,02,606	(58.1)
Older adult (≥65 years)	3,84,654	(35.7)	17,359	(42.2)	3,67,295	(35.4)
Sex, *n* (%)						
Male	5,43,760	(50.4)	21,879	(53.2)	5,21,881	(50.3)
Female	5,35,090	(49.6)	19,261	(46.8)	5,15,829	(49.7)
Saturation of oxygen (SpO_2)						
96–100%	8,89,012	(82.4)	31,740	(77.2)	8,57,272	(82.6)
91–95%	1,35,056	(12.5)	6,003	(14.6)	1,29,053	(12.4)
86–90%	28,627	(2.7)	1,704	(4.1)	26,923	(2.6)
81–85%	10,021	(0.9)	643	(1.6)	9,378	(0.9)
≤80%	16,134	(1.5)	1,050	(2.6)	15,084	(1.5)
Loss of consciousness						
Coma (GCS: 3–8)	25,742	(2.4)	1,557	(3.8)	24,185	(2.3)
Not coma (GCS: 9–15)	10,53,108	(97.6)	39,583	(96.2)	10,13,525	(97.7)
Body temperature						
<34°C	2,157	(0.2)	88	(0.2)	2,069	(0.2)
34.0–34.9°C	2,748	(0.3)	87	(0.2)	2,661	(0.3)
35.0–35.9°C	1,11,346	(10.3)	3,365	(8.2)	1,07,981	(10.4)
36.0–36.9°C	6,53,873	(60.6)	22,007	(53.5)	6,31,866	(60.9)
37.0–37.9°C	1,95,335	(18.1)	9,254	(22.5)	1,86,081	(17.9)
38.0–38.9°C	63,574	(5.9)	3,778	(9.2)	59,796	(5.8)
≥39.0°C	49,817	(4.6)	2,561	(6.2)	47,256	(4.6)
Time of day						
Daytime (9:00–17:59)	5,24,581	(48.6)	13,853	(33.7)	5,10,728	(49.2)
Nighttime (0:00–8:59, 18:00–23:59)	5,54,269	(51.4)	27,287	(66.3)	5,26,982	(50.8)
Day of the week						
Weekday	7,69,644	(71.3)	27,578	(67.0)	7,42,066	(71.5)
Weekends	3,09,206	(28.7)	13,562	(33.0)	2,95,644	(28.5)
Location, *n* (%)						
Home	6,96,057	(64.5)	25,560	(62.1)	6,70,497	(64.6)
Public space	1,91,160	(17.7)	8,586	(20.9)	1,82,574	(17.6)
Workspace	26,907	(2.5)	587	(1.4)	26,320	(2.5)
Road	1,52,826	(14.2)	5,900	(14.3)	1,46,926	(14.2)
Other	11,900	(1.1)	507	(1.2)	11,393	(1.1)
Reason for ambulance call, *n* (%)						
Fire accident	843	(0.1)	70	(0.2)	773	(0.1)
Natural disaster	34	(0.0)	2	(0.0)	32	(0.0)
Water accident	57	(0.0)	1	(0.0)	56	(0.0)
Traffic accident involving car, ship, or aircraft	82,901	(7.7)	2,410	(5.9)	80,491	(7.8)

(Continued)

TABLE 1 (Continued)

	Total		Difficulty in hospital acceptance		No difficulty in hospital acceptance	
	(*n* = 1,078,850)		(*n* = 41,140)		(*n* = 1,037,710)	
Injury, poisoning, and disease due to industrial accident	10,641	(1.0)	294	(0.7)	10,347	(1.0)
Disease and injury due to sports	5,342	(0.5)	140	(0.3)	5,202	(0.5)
Other injury	1,80,226	(16.7)	7,267	(17.7)	1,72,959	(16.7)
Trauma due to assault	6,058	(0.6)	690	(1.7)	5,368	(0.5)
Self-induced injury	6,059	(0.6)	1,110	(2.7)	4,949	(0.5)
Acute disease	7,86,416	(72.9)	29,146	(70.8)	7,57,270	(73.0)
Other	273	(0.0)	10	(0.0)	263	(0.0)
COVID-19 pandemic periods, *n* (%)						
Pre-pandemic period (2019/01/01–2020/01/28)	4,25,768	(39.5)	12,062	(29.3)	4,13,706	(39.9)
1st wave (2020/01/29–2020/06/13)	1,21,247	(11.2)	4,646	(11.3)	1,16,601	(11.2)
2st wave (2020/06/14–2020/10/09)	1,17,787	(10.9)	4,123	(10.0)	1,13,664	(11.0)
3st wave (2020/10/10–2021/02/28)	1,27,181	(11.8)	6,340	(15.4)	1,20,841	(11.6)
4st wave (2021/03/01–2021/06/20)	97,417	(9.0)	5,652	(13.7)	91,765	(8.8)
5st wave (2021/06/21–2021/12/16)	1,74,174	(16.1)	7,731	(18.8)	1,66,443	(16.0)
6st wave (2021/12/17–2021/12/31)	15,276	(1.4)	586	(1.4)	14,690	(1.4)

GCS, Glasgow Coma Scale; IQR, interquartile range.

127,181 (11.8%) in the 3rd wave, 97,417 (9.0%) in the 4th wave, 174,174 (16.1%) in the 5th wave, and 15,276 (1.4%) in the 6th wave.

Table 2 shows the factors associated with DIH during the COVID-19 pandemic. In this study, the factors associated with DIH were as follows: older adults (AOR: 1.226, [95% CI: 1.199–1.254]), coma (AOR: 1.333, [95% CI: 1.263–1.408]), nighttime (AOR: 1.975, [95% CI: 1.933–2.018]), weekends (AOR: 1.223, [95% CI: 1.198–1.250]), public space (AOR: 1.323, [95% CI: 1.289–1.358]), and road (AOR: 1.376, [95% CI: 1.326–1.429]). The SpO_2 values associated with DIH were 91–95% (AOR: 1.147, [95% CI: 1.114–1.182]), 86–90% (AOR: 1.476, [95% CI: 1.400–1.555]), 81–85% (AOR: 1.584, [95% CI: 1.459–1.721]), and 80% or less (AOR: 1.636, [95% CI: 1.532–1.748]). For BT, they were 37.0–37.9°C (AOR: 1.506 [95% CI: 1.468–1.545]), 38.0–38.9°C (AOR: 1.969 [95% CI: 1.897–2.043]), and 39°C or higher (AOR: 1.912 [95% CI: 1.829–1.998]). The most relevant epidemic period of COVID-19 was the 4th wave (AOR: 2.134, [95% CI: 2.065–2.205]), followed by the 3rd wave (AOR: 1.842, [95% CI: 1.785–1.901]).

Table 3 shows the factors associated with DIH in the pre-pandemic period, the 1st wave, when COVID-19 was first prevalent, and the 4th wave, when cases with DIH occurred most frequently. The AOR for $SpO_2 < 80\%$ was 1.333 (95% CI: 1.157–1.536), whereas the AORs were 1.649 (95% CI: 1.365–1.991) in the 1st wave and 2.221 (AOR: 1.919–2.570) in the 4th wave. The AOR of 39°C or higher was 1.104 (95% CI: 1.002–1.216), whereas the AORs were 3.092 (95% CI: 2.732–3.499) in the 1st wave and 2.360 (AOR: 2.109–2.642) in the 4th wave.

Figure 1 shows the mortality among the cases with DIH during each epidemic period. The highest mortality occurred in the 4th wave (3.9%, 219/5652), followed by the 3rd wave (3.5%, 224/6340).

Discussion

In this study, we revealed that factors related to COVID-19, such as BT and SpO_2, and the COVID-19 epidemic period were associated with DIH during the COVID-19 pandemic period in Osaka Prefecture, Japan. Furthermore, we found differences in the influence of each variable during the epidemic periods of COVID-19. This study, which analyzed a population-based emergency patient registry to assess the impact of emerging infectious disease on the EMS system, may help to examine the impact of the spread of new emerging infectious diseases on the healthcare system in future.

The epidemic period was associated with DIH, and the 4th wave was most associated with DIH in this study. Considering that the number of COVID-19 patients peaked in the 5th wave in Osaka Prefecture (11), it was likely that social confusion in the early phase of the pandemic and the large number of COVID-19 patients were not the only factors associated with the DIH. Park et al. reported a prolonged prehospital time for all patients, excluding those with out-of-hospital cardiac arrest, during the COVID-19 pandemic in 2020 (19). In a study of patients with ischemic stroke, Velasco et al. reported prolonged time from ambulance dispatch to hospital arrival during the pandemic period (20). Furthermore, a systemic review of prehospital care for patients with suspected stroke or transient ischemic attack (TIA) revealed that transport delay for patients with suspected stroke or TIA increased during the COVID-19 pandemic (21). In contrast, a systemic review of severe trauma during the restriction policy period in the first wave of the COVID-19 pandemic reported that the number of severe trauma patients decreased during this wave of the COVID-19 pandemic, but severity and mortality

TABLE 2 Factors associated with difficulty in hospital acceptance during the COVID-19 pandemic in 2020–2021.

	Difficulty in hospital acceptance % (*n*/*N*)		Adjusted OR (95% CI)		*p* value	
Age groups, *n* (%)						
Children (0–14 years old)	1.4	(956/68,765)	0.315	(0.295–0.337)	<	0.001
Adult (≥18 years, <65 years)	3.6	(22,825/625,431)	Reference			
Older adult (≥65 years)	4.5	(17,359/384,654)	1.226	(1.199–1.254)	<	0.001
Sex, *n* (%)						
Male	4.0	(21,879/543,760)	Reference			
Female	3.6	(19,261/535,090)	0.888	(0.870–0.906)	<	0.001
Saturation of oxygen (SpO_2)						
96–100%	3.6	(31,740/889,012)	Reference			
91–95%	4.4	(6,003/135,056)	1.147	(1.114–1.182)	<	0.001
86–90%	6.0	(1,704/28,627)	1.476	(1.400–1.555)	<	0.001
81–85%	6.4	(643/10,021)	1.584	(1.459–1.721)	<	0.001
≤80%	6.5	(1,050/16,134)	1.636	(1.532–1.748)	<	0.001
Loss of consciousness						
Coma (GCS: 3–8)	6.0	(1,557/25,742)	1.333	(1.263–1.408)	<	0.001
Not coma (GCS: 9–15)	3.8	(39,583/1,053,108)	Reference			
Body temperature						
<34°C	4.1	(88/2,157)	0.989	(0.796–1.230)		0.924
34.0–34.9°C	3.2	(87/2,748)	0.889	(0.716–1.103)		0.284
35.0–35.9°C	3.0	(3,365/111,346)	0.894	(0.862–0.928)	<	0.001
36.0–36.9°C	3.4	(2,2007/653,873)	Reference			
37.0–37.9°C	4.7	(9,254/195,335)	1.506	(1.468–1.545)	<	0.001
38.0–38.9°C	5.9	(3,778/63,574)	1.969	(1.897–2.043)	<	0.001
≥39.0°C	5.1	(2,561/49,817)	1.912	(1.829–1.998)	<	0.001
Time of day						
Daytime (9:00–17:59)	2.6	(13,853/524,581)	Reference			
Nighttime (0:00–8:59, 18:00–23:59)	4.9	(27,287/554,269)	1.975	(1.933–2.018)	<	0.001
Day of the week						
Weekday	4.4	(13,562/309,206)	Reference			
Weekends	3.6	(27,578/769,644)	1.223	(1.198–1.250)	<	0.001
Location, *n* (%)						
Home	3.7	(25,560/696057)	Reference			
Public space	4.5	(8,586/191160)	1.323	(1.289–1.358)	<	0.001
Workspace	2.2	(587/26907)	0.694	(0.633–0.760)	<	0.001
Road	3.9	(5,900/152826)	1.376	(1.326–1.429)	<	0.001
Other	4.3	(507/11900)	1.407	(1.282–1.543)	<	0.001
Reason for ambulance call, *n* (%)						
Fire accident	8.3	(70/773)	2.521	(1.967–3.232)	<	0.001
Natural disaster	5.9	(2/32)	2.279	(0.543–9.558)		0.260
Water accident	1.8	(1/56)	0.409	(0.056–2.972)		0.377
Traffic accident involving car, ship, or aircraft	2.9	(2,410/82,901)	0.702	(0.665–0.741)	<	0.001

(Continued)

TABLE 2 (Continued)

	Difficulty in hospital acceptance		Adjusted OR (95% CI)		p value	
	% (n/N)					
Injury, poisoning, and disease due to industrial accident	2.8	(294/10,641)	1.114	(0.980–1.267)		0.098
Disease and injury due to sports	2.6	(140/5,342)	0.859	(0.724–1.020)		0.083
Other injury	4.0	(7,267/180,226)	1.294	(1.258–1.331)	<	0.001
Trauma due to assault	11.4	(690/6,058)	2.666	(2.454–2.897)	<	0.001
Self-induced injury	18.3	(1,110/6.059)	5.566	(5.195–5.963)	<	0.001
Acute disease	3.7	(29,146/786,416)	Reference			
Other	3.7	(10/273)	1.006	(0.532–1.902)		0.985
COVID-19 pandemic periods, *n* (%)						
Pre-pandemic period (2019/01/01–2020/01/28)	2.8	(12,062/425,768)	Reference			
1st wave (2020/01/29–2020/06/13)	3.8	(4,646/121,247)	1.375	(1.328–1.423)	<	0.001
2st wave (2020/06/14–2020/10/09)	3.5	(4,123/117,787)	1.208	(1.165–1.252)	<	0.001
3st wave (2020/10/10–2021/02/28)	5.0	(6,340/127,181)	1.842	(1.785–1.901)	<	0.001
4st wave (2021/03/01–2021/06/20)	5.8	(5,652/97,417)	2.134	(2.065–2.205)	<	0.001
5st wave (2021/06/21–2021/12/16)	4.4	(7,731/174,174)	1.577	(1.532–1.624)	<	0.001
6st wave (2021/12/17–2021/12/31)	3.8	(586/15,276)	1.411	(1.296–1.536)	<	0.001

GCS, Glasgow Coma Scale; OR, odds ratio; CI, confidence interval.

remained the same (22). Another study analyzing a multicenter trauma registry in Japan reported that time related to prehospital care increased during the pandemic in 2020, but in-hospital mortality did not change (23). As more patient occupy treatment space at medical facilities, emergency patients will have to be transported by ambulance to distant medical facilities because the facilities will not be able to accept excess patients. The COVID-19 pandemic may have limited the number of medical facilities accepting emergency patients because of the need for precautions against infection among healthcare workers. Based on these results and reports of previous studies, the number of patients with severe pneumonia and respiratory failure requiring ventilation and ECMO exploded in the 4th wave of this study, even among relatively young patients, due to a genetic alteration in the COVID-19 virus. As a result, emergency and critical care centers with intensive care units (ICUs) were permanently full and could not accept new emergency patients. In fact, according to the ECMO net open data source, the number of patients on ECMO in Osaka Prefecture increased in the 4th wave (24). After the 5th wave, when the infectivity of the COVID-19 virus increased but the rate of severe COVID-19 patients decreased, the rate of DIH decreased. It may thus be necessary to plan in advance or modify the medical system as appropriate to accommodate and discharge severe patients in order to smoothly accept emergency patients in the event of an unknown infectious disease pandemic in the future.

Secondarily, the analysis by epidemic period showed that the OR for fever was higher in the 1st wave than in the 4th wave. In the early stage of the COVID-19 pandemic, the route of infection and symptoms were unknown, and even nonspecific symptoms such as fever required suspicion of COVID-19 infection. In addition, because the route of infection and infectivity were unknown, healthcare workers were required to take very strict infection control measures. However, lockdowns were conducted in many countries around the world, and the distribution of infection prevention equipment was also halted. As a result, many medical facilities were unable to accommodate patients due to a shortage of infection prevention equipment and insufficient infection control measures. Indeed, there was a lack of infection prevention equipment during the COVID-19 pandemic in Japan (25). The risk of the spread of unknown infectious diseases will continue to exist, and it will be necessary for medical institutions and governments to stockpile sufficient infection prevention equipment against pandemic risk.

For SpO_2, the OR was higher in the 4th wave than in the 1st wave. This may be due to the fact that the number of patients with severe respiratory failure requiring ventilators or ECMO increased as a result of the increased risk of severe illness caused by virus mutation, and ICUs for ventilating patients were permanently full. Indeed, in a registry study of several trauma patients in the Netherlands, the peak of COVID-19 patients had a negative impact on trauma care in that fewer severe trauma patients were admitted to the ICUs and worse outcomes were experienced, especially for patients with mild-to-moderate head trauma (26). Unlike with infection control equipment, ICUs cannot be stockpiled for future outbreaks. It would also not be economically feasible to maintain a constant reserve of ICUs in case of a pandemic. Therefore, during an infectious disease pandemic, it is necessary to convert ordinary ICUs into beds for severely infected patients. However, if the number of severely ill patients exceeds the capacity of ICUs, triage by doctors may be necessary to accommodate the patients in the ICUs or it may be necessary to have a system in which many physicians coordinate and decide where to transport patients. In the future, it will be necessary to establish a triage algorithm that included ethical considerations regarding the appropriateness of ICU admission. In addition, self-injured patients were associated with

TABLE 3 Factors associated with difficulty in hospital acceptance during the COVID-19 pandemic in 2020–2021 by pandemic period.

	Pre-pandemic (2019.1.1–2020.1.28)				1st wave (2020.1.29–2020.6.13)				4th wave (2021.3.1–2021.6.20)			
	Difficulty in hospital acceptance, % (*n*/*N*)		Adjusted OR (95% CI)		Difficulty in hospital acceptance, % (*n*/*N*)		Adjusted OR (95% CI)		Difficulty in hospital acceptance, % (*n*/*N*)		Adjusted OR (95% CI)	
Age groups, *n* (%)												
Children (0–14 years old)	1.2	(368/31,512)	0.409	(0.367–0.456)	1.4	(92/6,683)	0.285	(0.230–0.352)	1.6	(104/6,687)	0.204	(0.167–0.249)
Adult (≥18 years, <65 years)	2.6	(6,236/242,800)	Reference		3.6	(2,577/71,463)	Reference		5.9	(3,365/56,573)	Reference	
Older adult (≥65 years)	3.6	(5,458/151,456)	1.282	(1.231–1.335)	4.6	(1,977/43,101)	1.346	(1.259–1.439)	6.4	(2,183/34,157)	1.163	(1.094–1.236)
Sex, *n* (%)												
Male	3.0	(6,413/214,018)	Reference		4.0	(2,484/61,581)	Reference		5.9	(2,931/49,343)	Reference	
Female	2.7	(5,649/211,750)	0.880	(0.848–0.913)	3.6	(2,162/59,666)	0.902	(0.849–0.959)	5.7	(2,739/48,074)	0.965	(0.913–1.020)
Saturation of oxygen (SpO_2)												
96–100%	2.8	(9,876/353,431)	Reference		3.5	(3,570/100,975)	Reference		5.1	(3,968/78,322)	Reference	
91–95%	2.9	(1,472/51,607)	1.071	(1.011–1.134)	4.7	(652/13,925)	1.151	(1.051–1.259)	7.6	(970/12,762)	1.293	(1.197–1.397)
86–90%	3.3	(366/10,986)	1.305	(1.170–1.457)	6.7	(216/3,231)	1.569	(1.351–1.822)	10.6	(343/3,236)	1.690	(1.495–1.911)
81–85%	3.6	(135/3,777)	1.377	(1.155–1.642)	6.8	(79/1,166)	1.574	(1.241–1.997)	10.9	(133/1,223)	1.760	(1.458–2.125)
≤80%	3.6	(213/5,967)	1.333	(1.157–1.536)	6.6	(129/1,950)	1.649	(1.365–1.991)	12.7	(238/1,874)	2.221	(1.919–2.570)
Loss of consciousness												
Coma (GCS: 3–8)	4.2	(424/10,118)	1.353	(1.220–1.499)	5.5	(169/3,085)	1.127	(0.956–1.329)	5.7	(5,439/95,028)	1.234	(1.062–1.434)
Not coma (GCS: 9–15)	2.8	(11,638/415,650)	Reference		3.8	(4,477/118,162)	Reference		8.9	(213/2,389)	Reference	
Body temperature												
<34°C	3.6	(25/704)	1.144	(0.762–1.717)	2.6	(6/227)	0.778	(0.343–1.767)	4.5	(11/220)	0.782	(0.421–1.453)
34.0–34.9°C	1.9	(20/1,077)	0.644	(0.412–1.005)	4.0	(15/371)	1.327	(0.788–2.235)	4.2	(10/223)	0.816	(0.429–1.551)
35.0–35.9°C	2.7	(1,292/47,007)	0.962	(0.905–1.021)	2.5	(348/13,925)	0.821	(0.732–0.921)	4.7	(388/9,286)	0.856	(0.768–0.955)
36.0–36.9°C	2.9	(7,365/256,953)	Reference		3.0	(2,285/75,493)	Reference		5.0	(2,767/58,562)	Reference	
37.0–37.9°C	2.9	(2,127/73,626)	1.101	(1.047–1.157)	5.7	(1,138/20,130)	2.015	(1.871–2.170)	7.7	(1,382/17,848)	1.711	(1.597–1.832)
38.0–38.9°C	3.0	(743/25,139)	1.252	(1.157–1.355)	7.9	(505/6,376)	2.947	(2.653–3.272)	10.1	(654/6,462)	2.196	(1.998–2.413)
≥39.0°C	2.3	(490/21,262)	1.104	(1.002–1.216)	7.4	(349/4,725)	3.092	(2.732–3.499)	9.1	(440/4,816)	2.360	(2.109–2.642)
Time of day												
Daytime (9:00–17:59)	1.7	(3,497/202,737)	Reference		2.7	(1,576/58,051)	Reference		4.3	(2,105/48,566)	Reference	
Nighttime (0:00–8:59, 18:00–23:59)	3.8	(8,565/223,031)	2.276	(2.184–2.371)	4.9	(3,070/63,196)	1.859	(1.743–1.981)	7.3	(3,547/48,851)	1.833	(1.730–1.942)

(Continued)

TABLE 3 (Continued)

	Pre-pandemic (2019.1.1–2020.1.28)				1st wave (2020.1.29–2020.6.13)				4th wave (2021.3.1–2021.6.20)			
	Difficulty in hospital acceptance, % (*n*/*N*)		Adjusted OR (95% CI)		Difficulty in hospital acceptance, % (*n*/*N*)		Adjusted OR (95% CI)		Difficulty in hospital acceptance, % (*n*/*N*)		Adjusted OR (95% CI)	
Day of the week												
Weekdays	2.6	(7,961/301,238)	Reference		3.6	(3,118/87,145)	Reference		5.5	(3,859/69,839)	Reference	
Weekends	3.3	(4,101/124,530)	1.230	(1.184–1.279)	4.5	(1,528/34,102)	1.236	(1.160–1.317)	6.5	(1,793/27,578)	1.182	(1.115–1.254)
Location, *n* (%)												
Home	2.6	(7,081/270,444)	Reference		3.7	(2,982/80,236)	Reference		5.7	(3,651/63,934)	Reference	
Public space	3.3	(2,627/79,270)	1.365	(1.302–1.431)	4.8	(964/19,883)	1.327	(1.227–1.434)	7.3	(1,225/16,815)	1.304	(1.215–1.400)
Workspace	1.5	(159/10,393)	0.661	(0.556–0.786)	2.1	(61/2,895)	0.609	(0.457–0.810)	3.0	(73/2,443)	0.666	(0.514–0.862)
Road	3.3	(2,032/60,930)	1.399	(1.312–1.493)	3.5	(583/16,894)	1.288	(1.147–1.446)	4.8	(633/13,073)	1.326	(1.185–1.482)
Other	3.4	(163/4,731)	1.383	(1.176–1.626)	4.2	(56/1,339)	1.563	(1.183–2.064)	6.1	(70/1,152)	1.554	(1.207–2.001)
Reason for ambulance call, *n* (%)												
Fire accident	7.7	(27/350)	3.045	(2.048–4.528)	5.2	(5/96)	1.546	(0.623–3.836)	10.4	(8/77)	2.040	(0.968–4.298)
Natural disaster	7.7	(1/13)	3.669	(0.471–28.591)	–	–	–		–	–	–	
Water accident	0	(0/19)	–		0	(0/7)	–		0	(0/4)	–	
Traffic accident involving car, ship, or aircraft	2.5	(827/32,476)	0.795	(0.726–0.872)	2.4	(222/9,078)	0.642	(0.561–0.763)	3.4	(255/7,404)	0.579	(0.491–0.682)
Injury, poisoning, and disease due to industrial accident	2.0	(85/4,223)	1.099	(0.869–1.389)	3.3	(38/1,137)	1.422	(0.989–2.045)	3.4	(30/892)	0.957	(0.643–1.426)
Disease and injury due to sports	2.0	(5/253)	0.889	(0.670–1.179)	3.4	(8/232)	1.062	(0.519–2.176)	4.5	(17/376)	1.022	(0.620–1.684)
Other injury	3.6	(2,533/69,811)	1.559	(1.485–1.637)	3.7	(774/20,882)	1.249	(1.146–1.361)	5.2	(822/15,868)	1.085	(1.000–1.179)
Trauma due to assault	10.4	(258/2,489)	3.044	(2.660–3.484)	11.9	(91/767)	2.773	(2.201–3.492)	10.6	(50/473)	1.598	(1.181–2.161)
Self-induced injury	14.8	(322/2,169)	5.763	(5.089–6.527)	16.5	(115/698)	5.001	(4.049–6.175)	22.8	(129/567)	4.891	(3.981–6.010)
Acute disease	2.6	(7,953/311,541)	Reference		3.8	(3,393/88,324)	Reference		6.0	(4,339/71,732)	Reference	
Other	3.4	(5/147)	1.253	(0.511–3.072)	0	(0/26)	–		8.3	(2/22)	1.394	(0.322–6.041)

GCS, Glasgow Coma Scale; OR, odds ratio; CI, confidence interval.

DIH in this study. This may be related to socioeconomic and cultural factors. To reveal the effect of socioeconomic and cultural factors, we plan further studies in the future.

There are several limitations in this study. First, the ORION system could collect data on emergency patients transported to emergency hospitals and emergency critical care centers within Osaka Prefecture but not on emergency patients transported to medical institutions other than these emergency medical institutions in Osaka Prefecture or to medical institutions outside Osaka Prefecture because the ORION system is operated by Osaka Prefecture and cannot be expanded to areas outside of Osaka Prefecture. In addition, no data were collected on the prognosis of patients who were not transported and who were transferred to other medical institutions. Furthermore, we could not collect detailed medical history data, such as medications and pregnancy. In this analysis, socioeconomic status, such as patient income and educational background, could not be evaluated because no data exist. Finally, this study was an observational study and unknown confounding factors could not be evaluated.

Conclusion

In this study, we identified factors associated with the DIH during the COVID-19 pandemic. As various factors are involved in the spread of an unknown infectious disease, it is necessary not only to plan in advance but also to take appropriate measures according to the situation in order to smoothly accept emergency patients.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: The data that support the findings of this study are available from Osaka Prefectural government, but the availability of these data is restricted. Data cannot be shared publicly because of the Protection Ordinance for Personal Information in Osaka Prefecture. Requests to access these datasets should be directed to YK, orion13@hp-emerg.med.osaka-u.ac.jp.

Ethics statement

The studies involving humans were approved by the Ethics Committee of Osaka University Graduate School of Medicine. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because the ORION data is anonymized without specific personal data, such as patient name, date of birth, and address, the requirement of obtaining patients' informed consent was waived.

Author contributions

YK: Conceptualization, Investigation, Methodology, Project administration, Writing – original draft. KT: Conceptualization, Formal analysis, Methodology, Resources, Software, Visualization, Writing – review & editing. SN: Conceptualization, Data curation, Resources, Writing – review & editing. JT: Conceptualization, Data curation, Resources, Writing – review & editing. TH: Conceptualization, Data curation, Resources, Writing – review & editing. HD: Conceptualization, Data curation, Resources, Writing – review & editing. TK: Conceptualization, Data curation, Methodology, Resources, Software, Validation, Writing – original draft, Writing – review & editing. JO: Data curation, Funding acquisition, Resources, Supervision, Writing – review & editing. TM: Conceptualization, Data curation, Resources, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Teachers as caregivers of grieving children in school in the post-COVID-19 era: using the self-determination theory to conceptualize teachers' needs when supporting grieving children's mental health

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Background: It has been estimated in recent studies that more than 1.5 million children worldwide lost a caregiver due to the COVID-19 pandemic. Childhood bereavement is associated with heightened risks of impaired academic and social performance, mental health issues, substance use disorders, and higher mortality rates. Yet children may receive insufficient support post-loss. Although the role of school psychologists in supporting grieving students has been examined, little is known about the role of teachers in this context. Specifically, knowledge about teachers' needs when supporting bereaved children is lacking.
Objective: The study's aim was to explore teachers' needs, drawing upon a well-established framework—self-determination theory (SDT)—which focuses on three human needs considered essential for optimal functioning: autonomy, competence, and relatedness.
Methods: Employing a qualitative approach, 36 teachers were interviewed about their needs when supporting grieving students. Interviews were transcribed and then analyzed using thematic content analysis.
Results: Analysis revealed three SDT-related needs: knowledge (theory- and practice-related), acknowledgment, and support (emotional and practical).
Conclusions: The findings enhance our theoretical understanding of childhood bereavement and may promote policy changes that ensure teachers' needs satisfaction. Its significance lies in the basic premise that supporting teachers' needs in the context of pediatric grief may eventually lead to their optimal ability to enact best practices for supporting grieving students' well-being.

KEYWORDS
self-determination theory, childhood grief, teachers as caregivers, post-COVID-19, qualitative case study research

Introduction

Mental health and coping with grief are at the forefront of concerns in the post-COVID-19 era (1–3). Grieving children are particularly vulnerable, as losing a loved one may profoundly impact child development (4). Childhood bereavement is associated with heightened risks of impaired academic and social performance, mental health issues, substance use disorders, and even high mortality rates (5, 6). Yet children are at risk of receiving little to no support post-loss (7). Although the role of psychologists and school counselors in supporting grieving children has been examined (8), research into the role of teachers lags far behind. Particularly, little is known about teachers' needs when dealing with bereaved children. This pilot study examined how teachers' needs were manifested in the context of grieving children by drawing upon a well-established framework—self-determination theory [SDT; (9)]—which focuses on the fulfillment of human needs for optimal functioning. The study's importance lies in the basic premise that understanding teachers' needs can lead to intervention programs that promote teachers' optimal functioning.

Childhood bereavement and the school context

According to childhood bereavement estimation models in the US, by the age of 18, one in fourteen children (7.2%) will experience the death of a parent or sibling (10). More than 1.5 million children worldwide were estimated to have lost a caregiver during COVID-19 pandemic (11). Relatedly, 70% of American teachers reported having a grieving student in their classroom (12). Yet, the issue of teachers' coping with childhood bereavement has received little academic attention, nor is this issue evident in teacher education formal curricula.

Childhood bereavement studies have mainly focused on teachers' role perceptions or attitudes toward grieving children (13, 14), or toward death education in general (15–18), whereas the issue of teachers' needs has yet to be addressed. Furthermore, although grieving children's needs from schools have been explored (19), teachers' needs have not been investigated, a surprising lack given that gratifying grieving children's needs is assumed to be conditioned upon recognizing and gratifying their caregivers' needs first (20). Although teachers are not expected to provide therapy for their students, they can provide support regarding academic and social issues arising from bereavement, as well as monitor children's mental health. In fact, social support (21–23), acknowledgment (24), and school-based support was argued to facilitate grieving students' adjustment both in the US (25) and Europe (14). Hence, this study aims to fill this knowledge gap by exploring teachers' needs using SDT lens.

SDT and teachers' needs

Self-determination theory [SDT; (9)] highlights the importance of supporting one's basic psychological needs to ensure optimal functioning. These needs—autonomy, competence, and relatedness—have been found to facilitate high-quality engagement and well-being (26, 27). The need for *autonomy* refers to the experience of authenticity, full willingness, and volition when carrying out an activity; autonomy frustration, by contrast, involves feeling controlled by externally enforced or self-imposed pressures (9). Scholars in the field of teacher education have argued that teacher autonomy may be supported by enabling their choices, encouraging their self-initiation, providing them with a rationale for their work, and acknowledging their perspectives and feelings (27). The need for *competence* refers to one's need to feel effective and capable of realizing objectives (9). Competence frustration involves feelings of doubts about one's efficacy. Therefore, teachers' competence may be supported by a mentor or school principal who communicates a message of trust in the teacher's ability to cope with challenges and provides a clearly structured work plan and assistance in coping with failures when requested (27). The need for *relatedness* comprises an individual's desire to maintain secure and satisfying relationships with others (9). Relatedness satisfaction involves the experience of intimacy and genuine connection with others, whereas relatedness frustration involves the experience of relational exclusion and loneliness. It was argued that teachers' relatedness may be supported by a mentor or other school figures (e.g., counselors) when these individuals show interpersonal involvement, devote resources and time, and express a willingness to help and a belief in the teacher (27).

Self-determination theory has been previously applied to explore teachers' needs and the ways these affect their students' learning (28). Kaplan (27) highlighted the necessity of establishing a needs-supportive school environment for teachers during challenging periods. The focus of this study was thus on understanding the aspects that support or hinder the satisfaction of these needs in the context of teachers' coping with grieving children. In line with the SDT premise, it was assumed that supporting teachers' needs in the context of pediatric grief would eventually lead to their ability to enact best practices for supporting students' optimal functioning.

Research question

What are teachers' needs in the context of supporting grieving children, and how are these needs manifested in relation to SDT (autonomy, competence, and relatedness)?

Method

Study design

Exploring a phenomenon such as teachers' subjective needs calls for a qualitative methodology, which captures the multifaceted nature of human experience from the individual's standpoint (29). This method is particularly suitable for the study of grief-related issues.

Participants

The study involved 36 teachers who had a grieving student in their classroom. Teachers' ages ranged from 23 to 64 (8 were young adults—23–30; 9 were 31–40; 8 were 41–50; and 11 were above fifty years old), and their teaching seniority ranged from 1 to 35 years (14 were new teachers with 1–10 years of teaching experience; 6 had 6–20 years of experience; and 16 had above twenty years of teaching experience). Circumstances of the loss were varied: 16 involved anticipated deaths (e.g., cancer), and 20 involved sudden deaths (heart attack/accident/homicide/suicide), as presented in Table 1.

Ethics and procedure

The study was approved by the Institutional Ethics Committee of the Academic College (No. 2021_153) [name removed for peer-review]. Written informed consent was obtained from all participants. Participants were told they could withdraw at will. Participants were recruited via snowball sampling (30), an acceptable method in qualitative research. Additionally, messages were posted on social media platforms. Forty teachers expressed an interest in participating, out of whom four eventually declined, deciding that they had no time to be interviewed. After interviewing 36 participants we determined that the saturation criteria had been met (31). Each interview lasted 45–90 min. Interviews were recorded and transcribed. Participant anonymity was ensured by concealing personal information and using pseudonyms in the scientific reports.

TABLE 1 Demographics of study participants.

Background variables			Frequency ($N = 36$)
Techers' demographics	Gender	Male	7
		Female	29
	Age	23–30	8
		31–40	9
		41–50	8
		>50	11
	Years of teaching experience	1–10	14
		11–20	6
		>20	16
Bereaved students' demographics	Age	8–11	13
		12–14	9
		15–18	14
	Education level	Elementary school	13
		Middle school	9
		High school	14
	Circumstances of death	Accident	7
		Anticipated medical reason (e.g., cancer)	16
		Sudden medical situation (e.g., heart attack)	7
		Suicide	5
		Homicide	1
	Years since death	1–3	18
		4–7	12
		8–10	4
		>10	2
	Student's relationship with the deceased	Parent	22
		Sibling	10
		Grandparent	2
		Close friend	2

Data collection

In-depth interviews were held by the author and two third-year psychology students who belong to the research lab headed by the author. Interviewers received targeted training by the author, who has extensive experience with qualitative methodology. A two-stage interview procedure, previously used in a qualitative inquiry of loss (32, 33), was used. In the first stage, a general open-ended question was presented. Specifically, participants were asked to reflect about their experiences with grieving students by addressing the following statement/question: "I would like to understand teachers" experiences when dealing with grieving children in their classroom. Can you please share your experience and relate to your needs (as a teacher)? You may begin with whatever feels comfortable to you". This invitation allowed participants to freely elaborate about whatever they felt was significant in their experience, enabling the interviewer to examine interviewees' spontaneous responses and ask for further elaboration. In the second stage several predefined questions were presented to evoke further elaboration. At the end of each interview, the interviewer confirmed that the interviewee felt well, emotionally.

Data analysis

Interviews were analyzed using Braun and Clarke's (34) six-phase thematic analysis process.

Specifically, both deductive and inductive analyses were conducted, in a two-step procedure as follows. In the first round, deductive analysis was performed using SDT as an interpretive lens to capture participants' perceived needs. Specifically, the aim was to identify phrases and discourse segments that characterized the participants' accounts of their needs, with a focus on autonomy, competence, and relatedness, while remaining open to possible additional themes that could arise as potential needs. In the second round, an inductive thematic analysis was employed. During this analytic process, data segments that were identified in the previous round as reflecting teachers' needs were analyzed, as we searched for salient themes emerging from the texts. Next, the data were read to identify meaningful units, followed by open coding. During this process, we carefully read and reread the data, to further identify and consolidate relevant themes which would later be conceptualized (35). This careful analysis was conducted to ensure that no important themes were overlooked. It should be emphasized that three independent coders (the author and two research assistants) independently analyzed the initial data, followed by recurrent brainstorming. Cases of disagreement were discussed and settled through conceptual clarification and consensus.

Trustworthiness

Qualitative inquiry does not traditionally claim to produce "absolute truths" but rather to achieve "trustworthiness" (36).

Hence, "investigator triangulation" was performed by the three researchers during coding, analysis, and interpretation of the data. Moreover, "prolonged engagement" was achieved by holding lengthy interviews with the participants, during which trust could be built, and rich and thick data could be produced. Member checking was also conducted, and participants' responses were included in the findings. Finally, the author and interviewers consistently examined their own preconceptions, emotions, and values (i.e., representing the principle of reflexivity) and the ways in which their interpretations or the interviewers' encounters with the participants may have been affected.

Findings

The qualitative analysis revealed three overarching themes that represent teachers' main needs: the need for knowledge (theoretical alongside practical), the need for acknowledgment, and the need for support. The following excerpts demonstrate these needs. All names used are pseudonyms.

The need for knowledge

All participants mentioned their need for knowledge: both theoretical (e.g., how children cope and understand grief) and practical (e.g., how to initiate a fruitful conversation). They also mentioned that there was no clear policy of how to respond, suggesting that this lack of clarity was a barrier preventing the knowledge and guidance they needed in such situations:

> There is no tool kit or clear policy on how to deal with such situations. I didn't receive any prior training or guidance about such incidents. So, I felt quite helpless… I didn't feel like I was capable of managing this situation without knowing anything about it… I wasn't sure how to act and I had many dilemmas… Why don't we receive such training as teachers? It's part of life. This is the kind of thing that clearly will happen at some point to one of our students (Rebecca, supporting a student who lost a mother to a heart attack).

As seen, Rebecca felt she needed training, and that this lack of training damaged her ability to feel competent in managing the situation. Josef further elaborated about the types of knowledge he felt he needed:

> I needed some training that would include, first of all, knowledge—let's say, about how children typically cope with grief psychologically, how they understand it, what the grief stages or processes are, what I should expect, etc. But I also need to know practically—how to approach him [the grieving student], how to respond in different situations, and so on (Josef, supporting a student who lost a father to suicide).

Josef mentions the need for theoretical alongside practical training. However, when such professional training was not available, some teachers chose to rely on their own experience as a source of knowledge, as conveyed by Noa:

> I did not receive any training, but, you know, I personally experienced a loss as a child. So, I felt I knew how to manage it and generally what to expect (Noa, supporting a student who lost a sibling to cancer).

Personal experience with loss not only helped the teachers feel knowledgeable, and thus capable of managing these situations (in theory), but also helped them connect to the grieving child:

> I lost my brother as a child, so I felt I was able to connect to her [the grieving child], and I have my own way of looking at it… But this doesn't mean teachers shouldn't be trained for it. I happen to have had my own experience. But what does a teacher who didn't experience loss do?! (Bracha, supporting a student who lost a sibling in a car accident).

In some cases, teachers benefited from the experience of people in their own personal surroundings who had experienced loss:

> You may find it funny, but what helped me the most was the fact that my husband is an orphan. I found myself consulting with him about how to act (Dina, supporting a student who lost a father to a disease).

Another aspect mentioned by teachers was the need for formal policies and guidelines regarding the management of such cases. In the face of no clear policy, some teachers received a message they had the freedom to autonomously manage these situations. But unlike the common assumption that freedom to act is considered desirable, in this particular situation—when teachers had no prior personal experience with loss—the lack of policy and formal guidelines made them feel lost and incompetent:

> I was told I had the freedom to manage it the way I believed best, but I actually felt the opposite: I wanted guidance and some instruction. I had many dilemmas. Before the funeral, at the *shiva*, throughout the first year. Everything evoked a dilemma. And I was not sure how to manage it and whether I was actually doing it successfully. I felt insecure and exhausted (Dina).

It seems that too much freedom may actually impede teachers' sense of competence as well as their ability to autonomously mange students' grief situations; whereas formal policy would in fact promote teachers' coping.

The need for acknowledgment

Teachers mentioned their need to receive acknowledgment of their own emotional turmoil:

> It was really difficult. I knew the mother [the deceased] closely and I really was shocked. No one asked me how **I** was doing. I'm expected to function. A teacher should first have a place

> for herself to process these things. We are human (Lea, supporting a student who lost a mother to an accident).

As appears from Lea, teachers themselves may be grieving. In addition, sometimes teachers' own personal fears can be awakened—an aspect that is overlooked:

> It was tough for me. I started having nightmares. Thoughts about my own kids: what would have happened to them if I died. My heart was broken (Tamar, supporting a student who lost a mother to an illness).

As seen, teachers felt they needed to be asked about their own emotions, but this was not acknowledged by school-related personnel, as they are expected to be the ones who function well, regardless. In addition, teachers described their own self-disenfranchisement:

> I remember being in such agony when I found out about the death and yet I quickly pushed that aside and started functioning, making sure my student received support… But what about what I needed?! (Inbar, supporting a student who lost a sibling to an illness).

> I gave myself ten minutes to cry and then I had to pull myself together and function… but I didn't really give myself the time I needed to process my own grief… I was so alone with it (Vered, supporting a student who lost a close friend).

It appears that acknowledgment is a necessary first step for teachers. Such acknowledgment is also essential for teachers' ability to enact autonomous behaviors when providing support for their students.

The need for support

Teachers mentioned their need to receive support from school mental health professionals, such as school counselors or school psychologists, in order to feel "enveloped" and able to personally manage their students' grief situations:

> …School was not OK. I should have received support from the school counselor. After all, I was the one supporting the student! But there's no help for teachers in the system. Eventually, I decided to quit (Tamar).

> I think that teachers should first receive support prior to supporting their students. I was so attuned to my students and how to support them… **I'm not sure for how long one can support a student without being supported themselves** (Debora, supporting a student who lost a sibling to homicide).

Teachers perceived their role as child-supporters; however, they needed support themselves in order to feel competent to continuously support their students. Not receiving such support was perceived as impeding the support they gave their students:

> I felt quite alone there in the situation. **I could have done better had I had some support myself**… I needed some practical advice. But also, I needed some emotional support… I came and said I needed support, but I got the impression that the school psychologist was overloaded with work… We have a teacher meeting on a weekly basis, and usually it's such a waste of time. Instead, they could provide better support to teachers about such situations (Judith, supporting a student who lost a close friend).

Teachers also mentioned that this support should be provided continuously:

> I ended up turning to the school counselor, and she did help me. She gave me some advice and instruction. But, you know, it's needed all the time. It doesn't end after the first week. But as a teacher you are sort of left alone with it after the first week (Avital, supporting a student who lost a parent to suicide).

Discussion

The main objective of the current study was to gain an understanding of a previously overlooked phenomenon—teachers' needs in the context of pediatric grief—using the SDT lens. Specifically, it aimed to understand what components enable or impede teachers' sense of autonomy, competence, and relatedness. The study highlighted three main themes representing teachers' needs: knowledge (theory and practice), acknowledgment, and support. Each of these needs was related to two SDT needs. Conceptualizing teachers' needs sheds light on how to optimally attend to teachers' needs, which may ultimately relate to better outcomes for grieving children. The innovative aspect of this study thus involved its pioneer emphasis on teachers' needs rather than those of school counselors and psychologists, as well as on the use of SDT as a framework to explore teachers' needs rather than students' needs. Figure 1 presents the intersection between teachers' needs and the SDT needs related to them.

Supporting teachers' *competence* in the context of pediatric grief

As explained, the need for *competence* refers to one's need to feel effective and capable of realizing objectives (9). The study's findings highlight that teachers' sense of competence when supporting grieving children could be achieved by providing them with both *knowledge* and *support*. Knowledge, as perceived by the teachers, consisted of three aspects: theoretical knowledge, practical knowledge, and formal policy. This finding aligns with prior research in the field of teacher education (not in the context of loss), that argued that teachers' competence may be supported by a clearly structured work plan and assistance when requested (27). In this vein, the current study further highlights the necessity for support, knowledge, and clear policy to promote

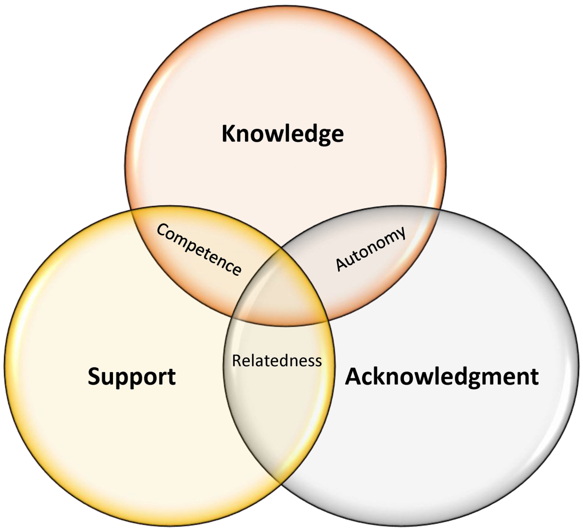

FIGURE 1
The intersection between teachers' needs and SDT needs.

teachers' sense of competence in the context of pediatric grief. Additionally, it echoes previous studies in the field of pediatric grief, advocating for the need to formulate clear school policies (19) and to provide formal teacher training to enable best practices (14).

Supporting teachers' *autonomy* in the context of pediatric grief

As mentioned, the need for *autonomy* refers to the experience of authenticity when acting (9). The study's findings highlighted that teachers' sense of autonomy when supporting grieving children may be achieved by providing both *knowledge* and *acknowledgment*. Similarly, in prior research in the field of teacher education (not in the context of loss), it has been suggested that teacher autonomy may be supported by acknowledging their perspectives and feelings and enabling their choices (27). Yet, interestingly, whereas under ordinary circumstances autonomy frustration involves feeling controlled by externally enforced pressures (9), the current study highlights that in the context of pediatric grief, teachers actually seem to crave externally-imposed guidelines (in terms of policy that informs knowledge). In their absence, they seem to feel unable to authentically navigate the mission of supporting their grieving students. This finding is unique and stands in contrast to traditional thinking/perceptions.

Supporting teachers' *relatedness* in the context of pediatric grief

The need for *relatedness* comprises an individual's desire to maintain satisfying relationships with others (9). In the field of teacher education, teachers' relatedness may be supported by a school figure (e.g., principal, counselor) who show interpersonal involvement, devote resources, and express a willingness to help (27). Indeed, the study highlights that teachers' sense of relatedness when supporting grieving children could be achieved by providing them with both *support* and *acknowledgment*. Both aspects are expected to be provided by school figures such as school mental health professionals. In their absence, the teachers experienced a frustration of their need for relatedness, which prevented them from being able to provide optimal support for their students.

In summary, providing teachers with knowledge, in terms of both theory and practice; acknowledging their struggles; and supporting them throughout the process are all essential for the satisfaction of teachers' needs for competence, autonomy, and relatedness. The fulfillment of such needs will ultimately facilitate their ability to best support their grieving students. These three components should be attended to when designing policy, teachers' training and resources allocation in the context of pediatric grief.

Limitations and implications

The study's contribution lies in its theoretical insights on the insufficiently explored issue of teachers' needs when dealing with grieving children. Yet it has several limitations. First, knowledge about teachers' coping over time should be gained from longitudinal studies. Second, the transferability of findings may be limited due to the small sample size ($N = 36$) and given that the sample consisted mostly of women. However, we believe that a sample that consists mostly women is adequate considering the overall gender imbalance in the field of teacher education (37). Additionally, in bereavement research, smaller samples are generally deemed sufficient. Future studies should focus on analysis divided into age groups—elementary, middle, and high school. Future studies should attempt to classify and analyze the data in accordance with these abovementioned distinguishing characteristics. That is, since such an approach would allow deeper interpretations drawn from the data. Furthermore, prior experience of personal loss and/or years of teaching experience may have an impact on the three needs identified in the study and, as such, should be investigated. Finally, future research should be conducted among teachers of various cultures and minority groups (38, 39), as participants' backgrounds have been found to be an essential factor affecting their adjustment to stressful situations (40, 41).

In conclusion, this study provides theoretical insights into teachers' needs when supporting grieving children. This topic has received surprisingly little research attention despite grief's potential to profoundly affect school-aged children's mental health. The study has important implications for the theory of childhood bereavement within the context of school-based support; enables a better understanding of the components underlying teachers' sense of autonomy, competence, and relatedness when supporting grieving children; may improve the design of practical training for teachers; and promotes policy changes that would enable best teacher practices. Finally, the COVID-19 pandemic has highlighted the urgency of exploring the role of teachers in supporting grieving students and the ways in which teachers' needs can be supported (42) to most effectively facilitate the support of children.

Data availability statement

The datasets presented in this article are not readily available because as this is a qualitative research data can not be deposited in order to keep participates' privacy. It will be available upon demand, with a justified reason, to ensure maximum protection of participants' anonymity. Requests to access the datasets should be directed to RF, rivipsy@gmail.com.

Ethics statement

The studies involving humans were approved by the study was approved by the Institutional Ethics Committee of Achva Academic College (Approval No. 2021_153). Written informed consent was obtained from all participants. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

RF-L: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Changes in primary care visits for respiratory illness during the COVID-19 pandemic: a multinational study by the International Consortium of Primary Care Big Data Researchers (INTRePID)

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Objectives: The majority of patients with respiratory illness are seen in primary care settings. Given COVID-19 is predominantly a respiratory illness, the INTernational ConsoRtium of Primary Care BIg Data Researchers (INTRePID), assessed the pandemic impact on primary care visits for respiratory illnesses.

Design: Definitions for respiratory illness types were agreed on collectively. Monthly visit counts with diagnosis were shared centrally for analysis.

Setting: Primary care settings in Argentina, Australia, Canada, China, Norway, Peru, Singapore, Sweden and the United States.

Participants: Over 38 million patients seen in primary care settings in INTRePID countries before and during the pandemic, from January 1st, 2018, to December 31st, 2021.

Main outcome measures: Relative change in the monthly mean number of visits before and after the onset of the pandemic for acute infectious respiratory disease visits including influenza, upper and lower respiratory tract infections and chronic respiratory disease visits including asthma, chronic obstructive pulmonary disease, respiratory allergies, and other respiratory diseases.

Results: INTRePID countries reported a marked decrease in the average monthly visits for respiratory illness. Changes in visits varied from −10.9% [95% confidence interval (CI): −33.1 to +11.3%] in Norway to −79.9% (95% CI: −86.4% to −73.4%) in China for acute infectious respiratory disease visits and – 2.1% (95% CI: −12.1 to +7.8%) in Peru to −59.9% (95% CI: −68.6% to −51.3%) in China for chronic respiratory illness visits. While seasonal variation in allergic respiratory illness continued during the pandemic, there was essentially no spike in influenza illness during the first 2 years of the pandemic.

Conclusion: The COVID-19 pandemic had a major impact on primary care visits for respiratory presentations. Primary care continued to provide services for respiratory illness, although there was a decrease in infectious illness during the COVID pandemic. Understanding the role of primary care may provide valuable information for COVID-19 recovery efforts and planning for future global emergencies.

KEYWORDS

COVID-19, acute respiratory illness, chronic respiratory illness, primary care, asthma, COPD, reason for visit, international comparison

1 Introduction

In the 3 years since the World Health Organization (WHO) declared COVID-19 a global pandemic, there have been over 659 million cases with over 6.5 million deaths worldwide (1, 2). The COVID-19 pandemic has presented unprecedented challenges to primary health care globally. Governments have implemented policies to prioritize using healthcare resources to treat COVID-19 patients and prevent the spread of the disease, such as quarantines, virtual work/school, wearing a mask, and social distancing. Although changes occurred rapidly in response to the COVID-19 pandemic (3), we have not yet determined the implications of these changes for other respiratory diseases. Numerous papers describe the potential and real impact of COVID-19 on primary care (4, 5). Huston et al. described the role of primary care in triaging and treating patients with COVID-19 in six well-resourced countries, including Australia, New Zealand, Canada, the Netherlands, the United Kingdom, and the United States (6). They discussed the negative impact of COVID-19 on access to primary care, the stress of decreased patient encounters on financial viability, and the capacity of primary care to respond to such a widespread pandemic. Research has identified socioeconomic disadvantage as an independent risk factor for death following a COVID-19 infection in individuals with type 2 diabetes (7) and those with other long-term conditions (8). There was wide variation in COVID-19 mortality rate between countries (9).

Upper respiratory illness is one of the most common diagnoses seen in primary care, accounting for 5–20% of ambulatory visits (10–13). Each year, in the United States alone, 20 million people with respiratory illnesses account for 64 million visits to primary care (14). Primary care serves over 90% of patients with lower respiratory illness or pneumonia. Since COVID-19 is predominantly a respiratory illness, primary care practices have been on the front lines of care for COVID-19 patients. Their role includes diagnosis, triage to the appropriate level of care, supportive care, treatments, and immunizations since they became available. While primary care has continued to provide in-person and virtual visits throughout the pandemic, the impact of COVID-19 on primary care visits for respiratory illness is unknown.

The INTernational ConsoRtium of Primary Care BIg Data Researchers (INTRePID) began as a collaboration between primary care researchers across the globe in response to the COVID-19 pandemic (15). INTRePID participants provide de-identified aggregated electronic data from electronic health records and billing claims data. Data are harmonized and analyzed centrally at the University of Toronto Department of Family and Community Medicine.

While respiratory infection is among the most common diagnoses in primary care, there is limited evidence of the impact of COVID-19 on respiratory illness care in primary care (12). The purpose of this paper is to describe the international experience of primary care practices related to respiratory illness before and during the COVID-19 pandemic.

2 Materials and methods

2.1 Study design

This study employed a retrospective observational design to investigate the impact of the COVID-19 pandemic on primary care visits for respiratory illnesses across 9 countries. The study period spanned from January 1, 2018, to December 31, 2021.

2.2 Data sources

Data for this study were gathered from diverse sources, including electronic medical records and billing claims. Specifically, information was sourced from visits to primary care physicians in Australia, Canada, China, Norway, Singapore, Sweden, and the United States. Moreover, data were obtained from primary care clinics in Argentina and Peru, encompassing visits to various healthcare providers within a primary care setting.

The dataset covers the period from January 1, 2018, to December 31, 2021, with the exception of Peru, where visit data was available only from January 2019. Although the onset of the pandemic varied across countries, for the purpose of this study, we defined the pre-pandemic period as January 2018 to March 2020, and the pandemic period as April 2020 to December 2021 in all countries except for China, where the pandemic was declared by the end of January 2020.

The representativeness of the data regarding primary care physician visits varied by country (Supplementary Table S1). Further detailed information about the INTRePID datasets can be found elsewhere, as described in prior publications (16, 17).

2.3 Primary outcome

The primary outcome was monthly visits for respiratory conditions across different countries, taking into account both virtual and in-person visits and categorizing them based on the type of respiratory condition, regardless of age, gender or other demographic factors. Virtual visits included video-calls and telephone consultations between patients and primary care physicians. Consultations associated with diagnostic codes for respiratory conditions were identified in each country and divided into eight groups: asthma, emphysema/chronic obstructive pulmonary disease (COPD), respiratory allergies, other respiratory diseases, lower respiratory tract infection (LRTI), upper respiratory tract infection (URTI), influenza and COVID-19. Because of variations in reporting, we use the general term influenza to include all reported influenza-like illnesses. COVID-19 includes both suspected and confirmed cases as some coding systems do not differentiate between the two. These groups were also combined to form two major categories, chronic respiratory diseases (asthma, COPD, respiratory allergies, other respiratory diseases) and infectious respiratory diseases (LRTI, URTI, influenza, COVID-19). Singapore data specific to COVID-19 were unavailable in the first year of the pandemic because they were recorded in a different system. See Supplementary Tables S2–S10 for a full description of diagnostic codes and description of the billing coding systems used for categorization in each of the countries.

2.4 Statistical analysis

We conducted an analysis to compare pre-pandemic and pandemic time periods to determine the impact of COVID-19 on primary care for each country. We calculated the difference between the average volume of respiratory monthly visits before and after the onset of the COVID-19 pandemic in each country, along with 95% confidence intervals (CI) and associated *p*-values using Welch's t-test, with a significance level of 0.05. This statistical approach was chosen to account for potential variations in sample sizes and variances between the two time periods. Additionally, we computed the percent change in average monthly visits from pre-pandemic to pandemic, along with 95% CI, for all countries and conditions.

Accounting for the variation within the different studied groups, we calculated the standardized difference in means using Cohen's d test with Hedges correction. This adjustment accounts for biases in small sample sizes. Cohen's d is defined as the difference in means divided by an estimate of the pooled standard deviation and incorporates a correction factor based on the size of the samples being compared (18, 19).

Furthermore, we visually presented the proportion of respiratory visits as a percentage of total visits by respiratory condition and by modality (in-person vs. virtual). These visit rates were calculated using total monthly visits (of any reason) as denominators except in Sweden and Peru. For these countries, we used total coded visits as the denominator, as uncoded visits were more likely to be with other health-care providers and potentially occurred concomitantly with a visit to a primary care physician. We generated a plot illustrating the trends in respiratory visits throughout the studied timeframe, alongside a trendline representing the incidence of new COVID-19 cases per 100,000 population. The data points for this plot were extracted from https://ourworldindata.org/coronavirus (20).

We supplemented our data analysis by conducting a survey among INTRePID collaborators, who served as points of contact in each country and were actively engaged in their local, regional, and national COVID response efforts. The survey aimed to describe the accessibility of care for patients with COVID-19 during the first and second years of the pandemic. Based on the framework developed by Huston et al. (6), which delineates the roles of various healthcare sectors in COVID-19 assessment, our survey employed a 5-point Likert scale offering respondents a range of options to indicate the frequency of occurrence for specific scenarios or activities related to COVID-19 care accessibility. Respondents could select from the following response options: "always," "common," "sometimes," "occasionally," and "never.." Refer to Supplementary Table S11 for a comprehensive description of the questionnaire employed.

2.5 Patient and public involvement

Patients and the public were not involved in the study design phase due to its highly technical nature; however, members of the public in INTRePID countries read the manuscript to ensure acceptable methods and interpretation. Specifically, the Patient and Clinician Engagement (PaCE) group, a well-established international patient advisory committee within the North American Primary Care Research Group (NAPCRG) (21), confirmed that our study was of public interest and offered important feedback on our results and discussion.

3 Results

For all INTRePID countries, when comparing the pandemic period with the pre-pandemic period, there was a decrease in infectious disease visits that was greater than the decrease observed for chronic respiratory illness visits (Figures 1, 2; Table 1). Decreases

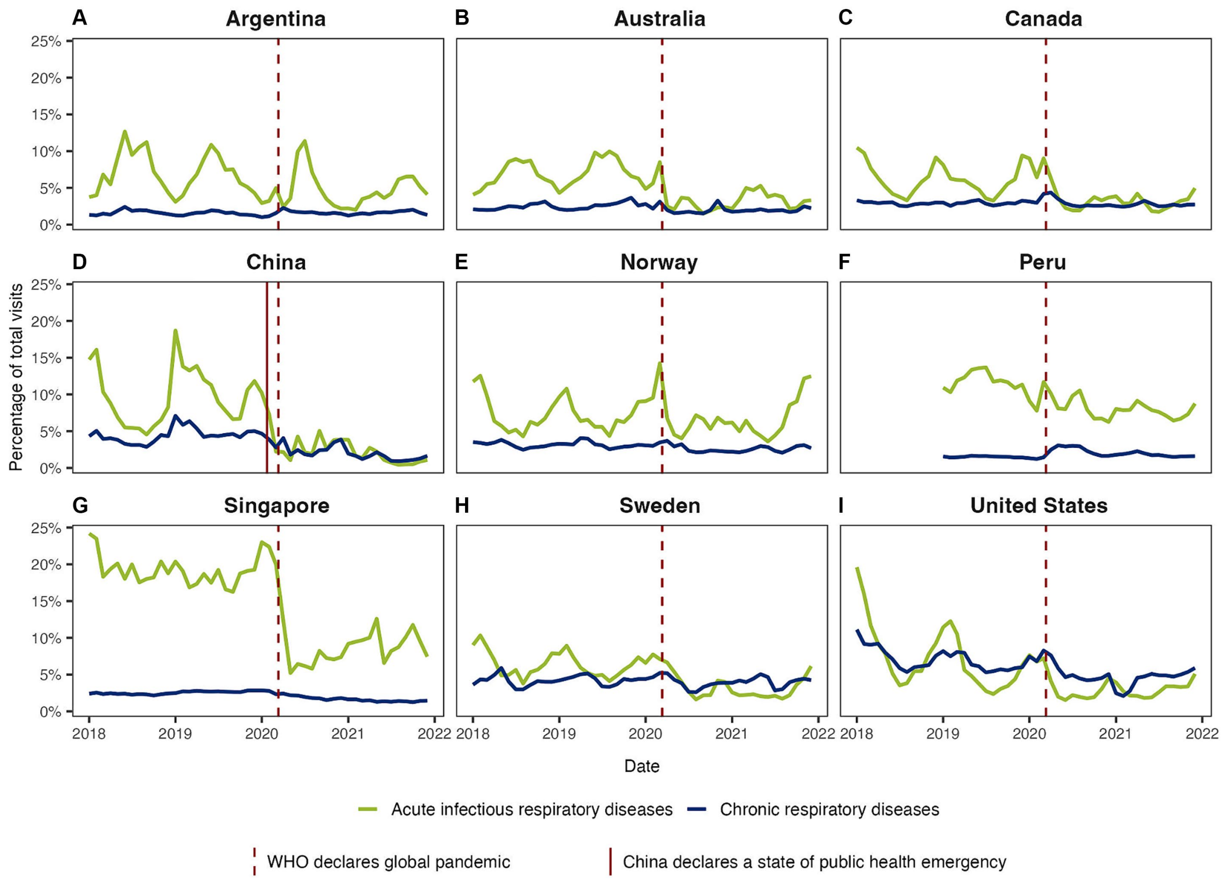

FIGURE 1
Overall visit rates for infectious and chronic respiratory illness during the pre-pandemic and pandemic periods in **(A)** Argentina, **(B)** Australia, **(C)** Canada, **(D)** China, **(E)** Norway, **(F)** Peru, **(G)** Singapore, **(H)** Sweden, and **(I)** United States. Trendlines show the monthly rates of respiratory visits over time. The rates were calculated by dividing the number of respiratory visits by the total visits to primary care services within each month and are expressed as percentages (%).

in the average number of monthly visits for acute infections ranged from −10.9% in Norway to −79.9% in China and were statistically significant in all countries (p=<0.05) except Norway. In Argentina and Norway, the reduction in acute respiratory infections was less pronounced because COVID-19 consultations contributed to almost half of these visits (Figure 3; Supplementary Figure S1). Decreases in chronic respiratory illness visits ranged from −2.1% to −59.9% and showed a statistically significant drop in China, Norway, Singapore, and the United States (Table 1; Figure 2). There was a drop in mean visit rates in all countries for most acute infectious respiratory conditions, with Singapore and the USA showing substantial declines in all sub-categories (Table 2; Supplementary Figure S2). Statistically significant changes in the average number of visits between the pandemic and pre-pandemic periods coincided with high standardized mean differences (exceeding 0.8 standard deviation units) (Tables 1, 2). It was interesting to note that in countries such as Canada, Norway, Peru, Sweden and in the US the patterns of respiratory condition visits in our primary care setting grossly mimicked the national COVID-19 waves (Figure 3).

Most of the INTRePID countries reported less seasonal variation for infectious respiratory disease during the pandemic compared to the pre-pandemic period. Supplementary Figures S3–S10 show monthly rates of respiratory visits by category in each country. These data demonstrated no influenza spike during the first 2 years of the pandemic (Supplementary Figure S3). Similar to influenza, visits for other URTI declined across INTRePID countries (Supplementary Figure S4). As expected, with a decline in influenza, LRTIs, including pneumonia, decreased dramatically during the pandemic (Supplementary Figure S5).

Primary care visits for COVID-19 varied between the INTRePID countries with different fluctuations over time. Australia, China, Singapore, and Peru had few COVID-19 visits in primary care (0–1.3% of total visits). Conversely, Argentina and Norway reported large numbers of primary care COVID-19 visits accounting for 5.9–10.4% of visits. Canada, Sweden, and the United States had a moderate rate of COVID-19 visits accounting for 1.6–2.6% of all visits (Figure 3; Supplementary Figures S1, S6).

Seasonal variation for respiratory allergies continued throughout the pandemic (Supplementary Figure S7). COPD visits were fairly constant during the pandemic with slight variation. Norway, Canada, and the United States reported a modest decline in COPD visits, while the other countries were essentially unchanged

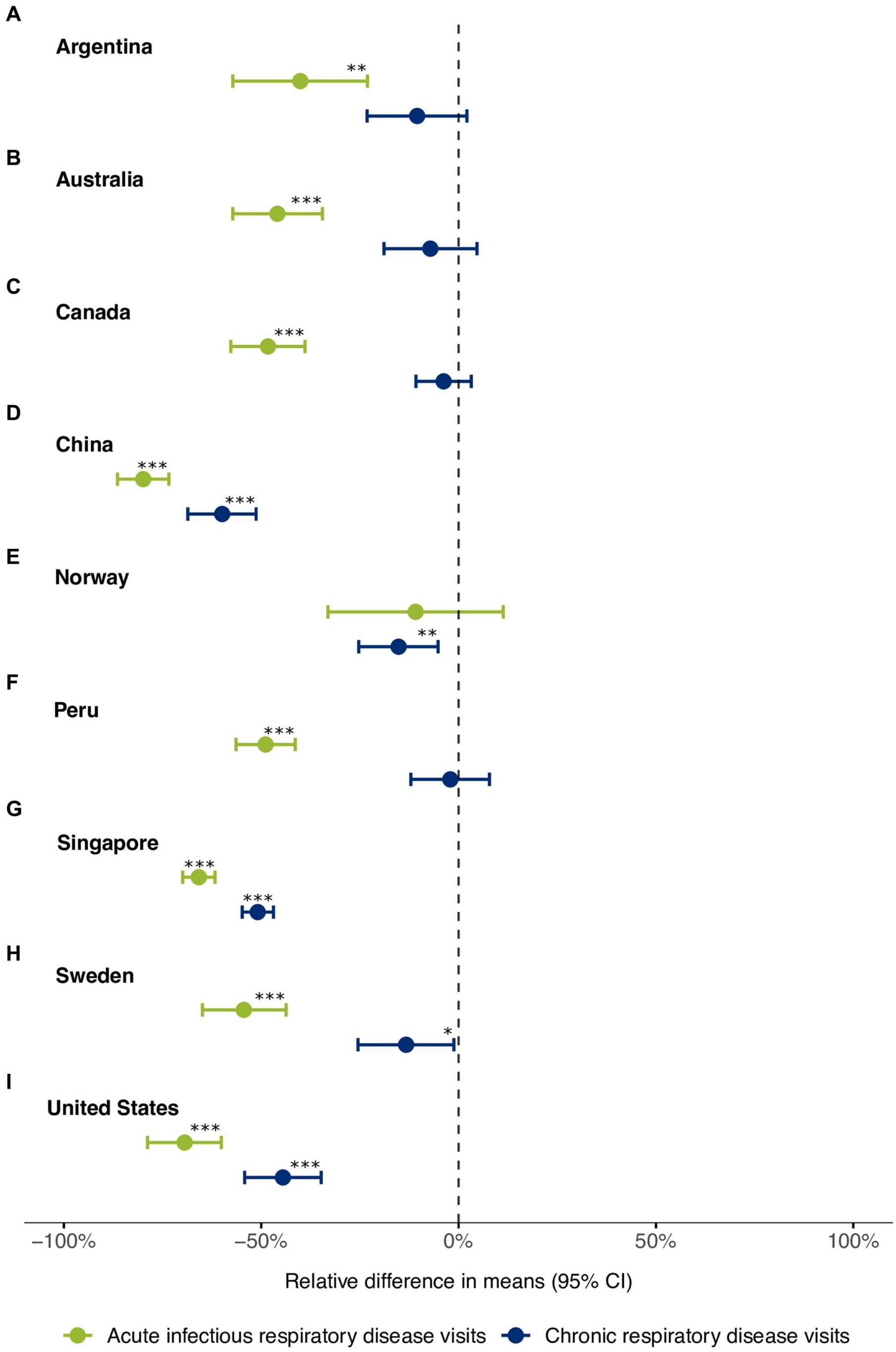

FIGURE 2
Relative difference in mean monthly visits for acute and chronic respiratory conditions between the pre-pandemic and the pandemic periods in **(A)** Argentina, **(B)** Australia, **(C)** Canada, **(D)** China, **(E)** Norway, **(F)** Peru, **(G)** Singapore, **(H)** Sweden, and **(I)** United States. Differences in mean monthly visits, 95% confidence intervals, and *p*-values were calculated using Welch's t-test. The dots represent the relative difference in means between the two periods and are expressed as percentages (%). The error bars denote the 95% confidence intervals. Significance levels are indicated as follows: $*p < 0.05$; $**p < 0.01$; $***p < 0.001$.

(Supplementary Figure S8). Asthma visit rates showed little change during the pandemic (Supplementary Figure S9).

Virtual visits for respiratory conditions in Canada were more common than in-person visits. In Norway, virtual visit rates were comparable to in-person visit rates, while in other countries, virtual visit rates were either negligible or lower than in-person visits during the pandemic (Figure 4).

The survey conducted among INTRePID representatives from participating countries revealed that assessment centers were the most frequent sites for COVID-19 diagnosis in both the first and second

TABLE 1 Change in average monthly acute and chronic respiratory visits in the pre-pandemic and pandemic periods.

Country	Pre-pandemic Mean (SD)	Pandemic Mean (SD)	Change in monthly mean visits between pandemic and pre-pandemic periods: Absolute mean change (95% CI)[1]	*P*-value[1]	Relative mean change % (95% CI)	Standardized mean difference (95% CI)[2]
Argentina						
Acute infectious respiratory disease visits	6,770 (3,238)	4,054 (2,094)	-2,717 (−4,274, −1,160)	**0.001**	−40.1 (−57.2, −23.1)	**−0.95 (−1.56, −0.34)**
Chronic respiratory disease visits	1,549 (436)	1,386 (303)	−163 (−378, 52)	0.13	−10.5 (−23.2, 2.1)	−0.4 (−1.00, 0.16)
Australia						
Acute infectious respiratory disease visits	8,866 (2,936)	4,800 (1,891)	−4,066 (−5,476, −2,656)	**<0.001**	−45.9 (−57.2, −34.5)	**−1.58 (−2.24, −0.92)**
Chronic respiratory disease visits	3,184 (802)	2,956 (587)	−227 (−631, 176)	0.5	−7.16 (−18.9, 4.67)	−0.31 (−0.89, 0.27)
Canada						
Acute infectious respiratory disease visits	4,459 (1,516)	2,306 (693)	−2,153 (−2,818, −1,488)	**<0.001**	−48.3 (−57.7, −38.9)	**−1.72 (−2.40, −1.05)**
Chronic respiratory disease disease visits	2,107 (285)	2,026 (246)	−81 -235, (74)	0.3	−3.8 (−10.8, 3.2)	0.29 (−0.87, 0.28)
China						
Acute infectious respiratory disease visits	672 (272)	135 (93)	−537 (−655, −419)	**<0.001**	−79.9 (−86.4, −73.4)	**−2.55 (−3.32, −1.78)**
Chronic respiratory disease visits	307 (71)	123 (59)	−184 (−222, −146)	**<0.001**	−59.9 (−68.6, −51.3)	**−2.75 (−3.54, −1.95)**
Norway						
Acute infectious respiratory disease visits	93,239 (35,920)	83,094 (39,330)	−10,145 (−32,400, 12,110)	0.4	−10.9 (−33.1, 11.3)	−0.26 (−0.84, 0.31)
Chronic respiratory disease visits	38,431 (6,492)	32,572 (7,591)	−5,858 (−10,054, −1,663)	**0.007**	−15.2 (−25.3, −5.2)	**−0.82 (−1.42–0.22)**
Peru						
Acute infectious respiratory disease visits	497,476 (82,097)	254,339 (71,894)	−243,136 (−297,181, −189,092)	**<0.001**	−48.9 (−56.4, −41.4)	**−3.11 (−4.11–2.12)**
Chronic respiratory disease visits	64,405 (7,975)	63,022 (11,738)	−1,383 (−8,062, 5,296)	0.7	−2.1 (−12.1, 7.8)	−0.13 (−0.80, 0.54)
Singapore						
Acute infectious respiratory disease visits	19,815 (2,473)	6,776 (1,732)	−13,039 (−14,263, −11,816)	**<0.001**	−65.8 (−69.9, −61.7)	**−5.88 (−7.12, −4.56)**
Chronic respiratory disease visits	2,612 (284)	1,283 (209)	−1,329 (−1,472, −1,185)	**<0.001**	−50.9 (−54.8, −46.9)	**−5.14 (−6.33, −3.95)**
Sweden						
Acute infectious respiratory disease visits	2,069 (584)	944 (451)	−1,125 (−1,426, −824)	**<0.001**	−54.4 (−64.9, −43.7)	**−2.09 (−2.80, −1.37)**
Chronic respiratory disease visits	1,365 (315)	1,183 (305)	−182 (−364, −0.69)	**0.049**	−13.3 (−25.5, −1.2)	−0.58 (−1.16, 0.01)
United States						
Acute infectious respiratory disease visits	1,375 (880)	420 (183)	−954 (−1,310, −599)	**<0.001**	−69.4 (−78.8, −60.1)	**−1.40 (−2.04, −0.75)**
Chronic respiratory disease visits	1,321 (350)	733 (246)	−588 (−761, −414)	**<0.001**	−44.5 (−54.2, −34.8)	**−1.86 (−2.56, −1.18)**

[1]Welch Two Sample t-test. [2]Hedges'g effect size statistics. The magnitude is assessed using the thresholds provided by Cohen (22): <(+/−)0.2 "negligible," <(+/−)0.5 "small," <(+/−)0.8 "medium," (+/−) > 0.8 "large". Bolded values denote statistical significance at the 95% confidence level or a standardized mean difference of large magnitude.

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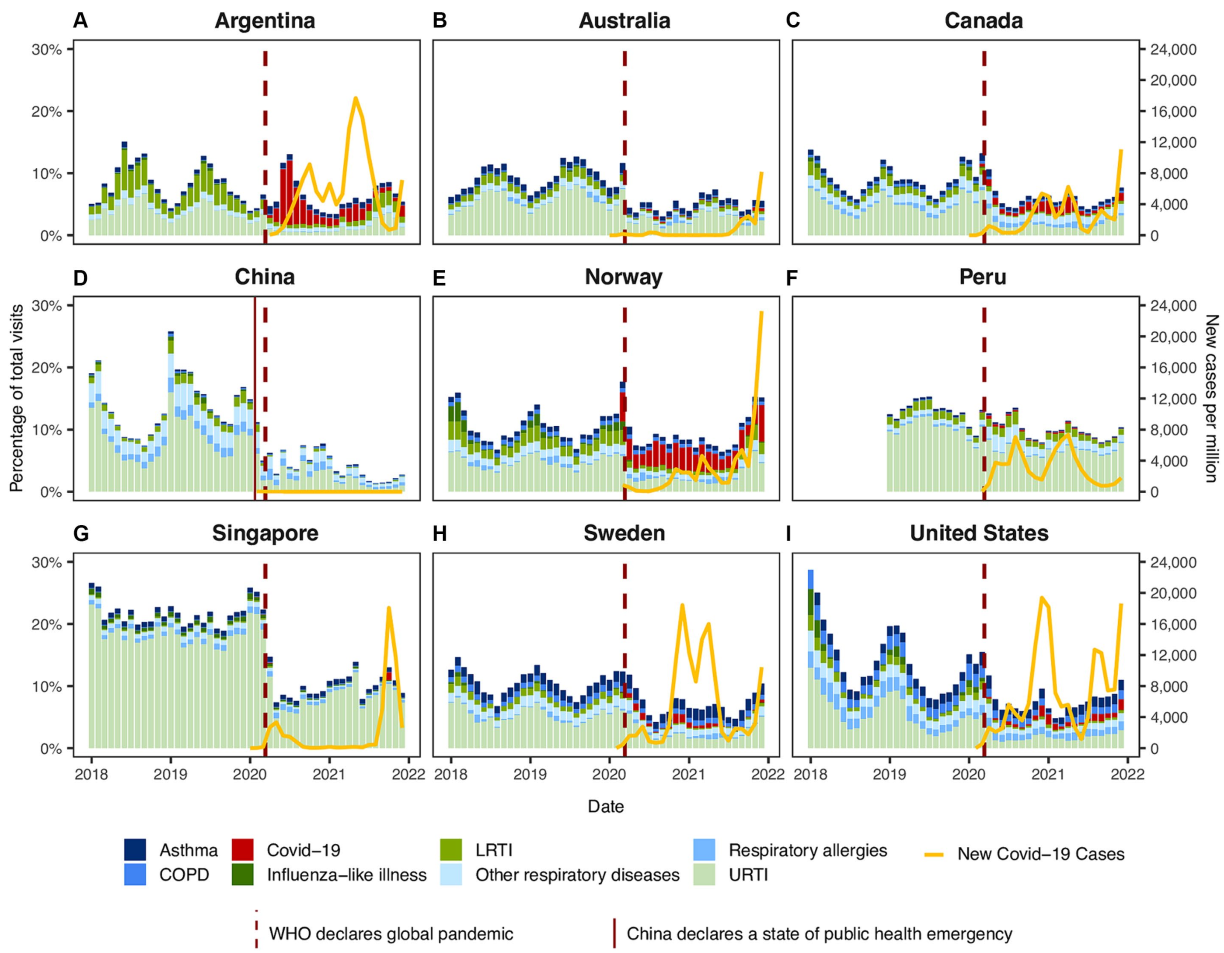

FIGURE 3
Respiratory visit rates by respiratory conditions in **(A)** Argentina, **(B)** Australia, **(C)** Canada, **(D)** China, **(E)** Norway, **(F)** Peru, **(G)** Singapore, **(H)** Sweden, and **(I)** United States. Stack column charts display monthly rates for different categories of respiratory visits. The rates were calculated by dividing the number of respiratory visits by the total visits to primary care services within each month and are expressed as percentages (%). The yellow line represents number of new COVID-19 cases per million. Source: https://ourworldindata.org/coronavirus (20).

years of the pandemic (Table 3). Many countries mentioned emergency departments as sites for COVID-19 diagnosis, although their prevalence slightly decreased during the second year of the pandemic. Primary care settings occasionally served as sites for COVID-19 assessment, with a slight increase noted during 2021. In contrast, virtual visits were prevalent throughout the first two years of the pandemic. Table 3 summarizes the survey responses.

4 Discussion

4.1 Impact of COVID-19 pandemic on primary care visits for respiratory illnesses

Our study found a notable decline in the rate and average monthly volume of primary care visits for respiratory concerns following the onset of the COVID-19 pandemic. Acute respiratory infection visits experienced a more pronounced decrease compared to non-infectious chronic respiratory illness visits. This trend suggests that COVID-19 mitigation measures likely impacted infections such as influenza and URTIs, while chronic respiratory illnesses such as COPD and asthma were less amenable to these efforts. Predictably, COVID-19 had a lesser effect on seasonal respiratory illnesses such as allergies. Our findings align with existing research demonstrating a decrease in respiratory virus activity during the COVID-19 pandemic. This decline has been linked to reductions in cases of acute respiratory illnesses and influenza-like illnesses. Furthermore, studies have shown a positive impact on chronic respiratory diseases, with fewer hospital admissions for asthma and COPD exacerbations during the pandemic's early stages, which coincides with the implementation of national lockdowns and non-pharmaceutical interventions (23).

The changes observed in non-infectious respiratory illnesses might stem from reduced access to in-person primary care or insufficient reporting of virtual visits not accounted for in the available data. Before COVID-19, only a few primary care practices conducted virtual visits, and there may have been delays in recording, coding, and reporting virtual visits during the early phase of the pandemic.

4.2 Regional variations in respiratory illness visits

While non-COVID-19 acute infection visits generally decreased, this change varied across countries participating in INTRePID. For

TABLE 2 Change in average monthly respiratory visits by category in the pre-pandemic and pandemic periods.

	Pre-pandemic	Pandemic	Change in monthly mean visits between pandemic and pre-pandemic periods			
Country	Mean (SD)	Mean (SD)	Absolute mean change (95% CI)[1]	*P*-value[1]	Relative mean change % (95% CI)	Standardized mean difference (95% CI)[2]
Argentina						
URTI	3,830 (1,601)	1,090 (984)	−2,740 (−3,496, −1,983)	**<0.001**	−71.5 (−83.4, −59.7)	**−1.97 (−2.67, −1.27)**
LRTI	2,757 (1,560)	858 (661)	−1,898 (−2,573, −1,224)	**<0.001**	−68.9 (−81.1, −56.7)	**−1.49 (−2.14, −0.84)**
Influenza-like illness	184 (150)	15 (17)	−169 (−228, −109)	**<0.001**	−91.8 (−96.5, −87.2)	**−1.46 (−2.10, −0.81)**
Asthma	549 (183)	646 (165)	98 (−3.9, 199)	0.059	17.7 (−1.9, 37.3)	0.55 (−0.04, 1.13)
COPD	106 (24)	92 (17)	−14 (−26, −2.4)	**0.019**	−13.2 (−23.3, −3.1)	−0.67 (−1.26, −0.07)
Respiratory allergies	55 (22)	53 (18)	−1.9 (−14, 10)	0.7	−3.6 (−23.8, 16.6)	−0.09 (−0.66, 0.48)
Other respiratory diseases	839 (245)	595 (205)	−245 (−375, −114)	**<0.001**	−29.1 (−42.1, −16)	**−1.05 (−1.67, −0.44)**
Australia						
URTI	7,257 (2,379)	3,846 (1,619)	−3,411 (−4,575, −2,246)	**<0.001**	−47.0 (−58.6, −35.4)	**−1.61 (−2.27, −0.95)**
LRTI	1,490 (501)	608 (311)	−882 (−1,120, −645)	**<0.001**	−59.2 (−69.5, −48.9)	**−2.02 (−2.73, −1.32)**
Influenza-like illness	119 (112)	42 (64)	−76 (−128, −25)	**0.005**	−64.7 (−90.9, −38.5)	**−0.80 (−1.40, −0.20)**
Asthma	1,387 (297)	1,340 (211)	−47 (−195, 101)	0.5	−3.4 (−13.6, 6.8)	−0.17 (−0.75, 0.40)
COPD	295 (55)	293 (37)	−1.6 (−28, 25)	>0.9	−0.7 (−9.5, 8.1)	−0.03 (−0.61, 0.54)
Respiratory allergies	349 (369)	479 (480)	130 (−126, 387)	0.3	37.2 (−43.1, 117.6)	0.30 (−0.27, 0.88)
Other respiratory diseases	1,153 (325)	844 (247)	−309 (−475, −143)	**<0.001**	−26.8 (−38.8, −14.8)	**−1.03 (−1.64, −0.42)**
Canada						
URTI	3,481 (1,082)	1,282 (500)	−2199 (−2,674, −1,723)	**<0.001**	−63.2 (−70.7, −55.7)	**−2.46 (−3.22, −1.70)**
LRTI	824 (309)	194 (79)	−629 (−755, −503)	**<0.001**	−76.5 (−81.7, −71.2)	**−2.60 (−3.38, −1.82)**
Influenza-like illness	142 (149)	30 (29)	−114 (−174, −53)	**<0.001**	−78.9 (−91, −66.8)	**−0.98 (−1.59, −0.37)**
Asthma	504 (93)	437 (73)	−67 (−115, −19)	**0.007**	−13.3 (−21.9, −4.7)	−0.78 (−1.37, −0.18)
COPD	277 (40)	205 (32)	−72 (−93, −51)	**<0.001**	−26 (−32.4, −19.6)	**−1.93 (−2.62, −1.24)**
Respiratory allergies	364 (126)	457 (149)	93 (11, 175)	**0.028**	25.5 (1.6, 49.5)	0.67 (0.08, 1.26)
Other respiratory diseases	962 (176)	928 (125)	−35 (−122, 53)	0.4	−3.5 (−12.2, 5.1)	−0.21 (−0.79, 0.36)
China						
URTI	586 (241)	124 (89)	−461 (−567, −356)	**<0.001**	−78.8 (−85.9, −71.8)	**−2.46 (−3.22, −1.70)**
LRTI	72 (29)	11 (8)	−61 (−74, −49)	**<0.001**	−84.7 (−89.9, −79.6)	**2.76 (−3.56, −1.96)**
Influenza-like illness	14 (17)	<1	−14 (−21, −6.9)	-	-	-
Asthma	11.9 (5.2)	9.0 (6.3)	−3 (−6.3, 0.40)	0.083	−24.4 (−49.6, 0.9)	−0.50 (−1.09, 0.07)
COPD	12.8 (5.8)	12.4 (6.7)	−0.33 (−4.0, 3.4)	0.9	−3.1 (−30.6, 24.3)	−0.50 (−0.62, 0.52)
Respiratory allergies	92 (25)	42 (24)	−50 (−64, −36)	**<0.001**	−54.3 (−66.1, −42.6)	**−2.00 (−2.70, −1.30)**
Other respiratory diseases	189 (48)	59 (30)	−130 (−153, −107)	**<0.001**	−68.8 (−76, −61.6)	**−3.14 (−4.0, −2.29)**
Norway						
URTI	58,628 (15,284)	31,607 (22,865)	−27,021 (−38,802, −15,240)	**<0.001**	−46.1 (−63.6, −28.6)	**−1.40 (−2.04, −0.76)**
LRTI	22,937 (7,141)	10,894 (8,470)	−12,043 (−16,701, −7,384)	**<0.001**	−52.5 (−69.3, −35.8)	**−1.52 (−2.18, −0.87)**
Influenza-like illness	9,302 (10,003)	1,214 (848)	−8,088 (−12,060, −4,116)	**<0.001**	−86.9 (−93.5, −80.4)	**−1.05 (−1.67, −0.44)**
Asthma	9,316 (1,880)	8,697 (2,181)	−620 (−1,829, 589)	0.3	−6.6 (−18.9, 5.6)	−0.30 (−0.88, 0.27)
COPD	8,272 (1,015)	7,034 (1,204)	−1,238 (−1,900, −576)	**<0.001**	−15 (−22.3, −7.6)	**−1.10 (−1.72, −0.49)**

(Continued)

TABLE 2 (Continued)

Country	Pre-pandemic	Pandemic	Change in monthly mean visits between pandemic and pre-pandemic periods			
	Mean (SD)	Mean (SD)	Absolute mean change (95% CI)[1]	*P*-value[1]	Relative mean change % (95% CI)	Standardized mean difference (95% CI)[2]
Respiratory allergies	4,881 (3,793)	5,846 (4,331)	964 (−1,449, 3,378)	0.4	19.8 (−31.9, 71.5)	0.23 (−0.34, 0.81)
Other respiratory diseases	15,961 (3,421)	10,996 (4,873)	−4,965 (−7,506, −2,424)	**<0.001**	−31.1 (−45.3, −16.9)	**−1.18 (−1.81, −0.56)**
Peru						
URTI	443,498 (72,828)	214,486 (67,005)	−229,012 (−277,751, −180,273)	**<0.001**	−51.6 (−59.3, −44.0)	**−3.22 (−4.23, −2.21)**
LRTI	42,873 (8,372)	29,356 (8,702)	−19,310 (−25,955, −12,665)	**<0.001**	−31.5 (−42.5, −20.5)	**−1.97 (−2.78, −1.15)**
Influenza-like illness	495 (61)	608 (481)	112 (−108, 333)	0.3	22.8 (−19.4, 65.1)	−0.30 (−0.38, 0.97)
Asthma	13,561 (2,590)	6,154 (1,353)	−7,407 (−8,934, −5,879)	**<0.001**	−54.6 (−60.7, −48.5)	**−3.69 (−4.80, −2.60)**
COPD	4,601 (862)	1,635 (401)	−2,965 (−3,467, −2,464)	**<0.001**	−64.5 (−69.5, −59.4)	**−4.58 (−5.84, −3.32)**
Respiratory allergies	15,423 (3,321)	7,454 (2,698)	−7,969 (−10,106, −5,832)	**<0.001**	−51.7 (−60.8, −42.5)	**−2.62 (−3.53, −1.71)**
Other respiratory diseases	30,821 (2,317)	47,779 (8,871)	16,958 (12,773, 21,142)	**<0.001**	55 (41.4, 68.7)	2.38 (1.50, 3.25)
Singapore						
URTI	18,985 (2,323)	6,527 (1,661)	−12,459 (−13,617, −11,300)	**<0.001**	−65.6 (−69.7, −61.6)	**−5.94 (−7.27, −4.61)**
LRTI	203 (29)	60 (34)	−143 (−162, −124)	**<0.001**	−70.4 (−77.8, −63.1)	**−4.46 (−5.53, −3.39)**
Influenza-like illness	624 (171)	135 (66)	−489 (−562, −416)	**<0.001**	−78.4 (−83.4, −73.3)	**−3.55 (−4.46, −2.63)**
Asthma	813 (70)	579 (58)	−234 (−271, −197)	**<0.001**	−28.8 (−32.6, −25.0)	**−3.55 (−4.47, −2.63)**
COPD	108 (15)	73 (10)	−35 (−42, −27)	**<0.001**	−32.4 (−37.7, −27.1)	**−2.62 (−3.40, −1.84)**
Respiratory allergies	852 (144)	447 (145)	−405 (−490, −320)	**<0.001**	−47.5(−55.6, −39.5)	**−2.76 (−3.56, −1.96)**
Other respiratory diseases	839 (181)	184 (72)	−655 (−732, −577)	**<0.001**	−78.1 (−82.2, −74.0)	**−4.47 (−5.54, −3.40)**
Sweden						
URTI	1,715 (462)	722 (381)	−993 (−1,237, −748)	**<0.001**	−57.9 (−68.3, −47.5)	**−2.28 (−3.02, −1.54)**
LRTI	314 (85)	69 (38)	−245 (−282, −208)	**<0.001**	−78.0 (−83.7, −72.4)	**−3.51 (−4.43,-2.60)**
Influenza-like illness	40 (56)	3 (7)	−37 (−59, −14)	**0.002**	−92.5 (−101, −84.0)	**−0.85 (−1.45, −0.25)**
Asthma	506 (135)	507 (152)	1.4 (−84, 86)	>0.9	0.2 (−16.1, 16.5)	0.00 (−0.57, 0.58)
COPD	282 (69)	233 (72)	−49 (−91, −7.8)	**0.021**	−17.4 (−30.7, −4.1)	−0.69 (−1.28, −0.09)
Respiratory allergies	111 (91)	123 (75)	12 (−37, 60)	0.6	10.8 (−34.0, 55.6)	0.14 (−0.44, 0.71)
Other respiratory diseases	466 (88)	320 (85)	−146 (−197, −95)	**<0.001**	−31.3 (−40.5, −22.1)	**−1.65 (−2.32, −0.98)**
United States						
URTI	1,053 (593)	263 (107)	−790 (−1,029, −552)	**<0.001**	−75.0 (−81.9, −68.2)	**−1.72 (−2.39, −1.04)**
LRTI	202 (113)	48 (18)	−154 (−199, −109)	**<0.001**	−76.2 (−82.5, −69.9)	**−1.77 (−2.45, −1.09)**
Influenza-like illness	120 (203)	3 (4)	−117 (−198, −37)	**0.006**	−97.5 (−99.6, −95.4)	−0.75 (−1.35–0.16)
Asthma	302 (46)	239 (78)	−63 (−102, −24)	**0.003**	−20.9 (−32.8, −8.9)	**−0.99 (−1.60, −0.38)**
COPD	346 (101)	161 (64)	−184 (−233, −136)	**<0.001**	−53.5 (−63.7, −43.3)	**−2.08 (−2.80, −1.37)**
Respiratory allergies	340 (132)	178 (54)	−162 (−219, −105)	**<0.001**	−47.6 (−57.9, −37.4)	**−1.52 (−2.17, −0.86)**
Other respiratory diseases	333 (118)	155 (63)	−178 (−232, −124)	**<0.001**	−53.5 (−63.7, −43.3)	**−1.78 (−2.46, −1.10)**

[1]Welch Two Sample *t*-test. [2]Hedges'g effect size statistics. The magnitude is assessed using the thresholds provided by Cohen (22): <(+/−)0.2 "negligible," <(+/−)0.5 "small," <(+/−)0.8 "medium," (+/−) > 0.8 "large". Bolded values denote statistical significance at the 95% confidence level or a standardized mean difference of large magnitude.

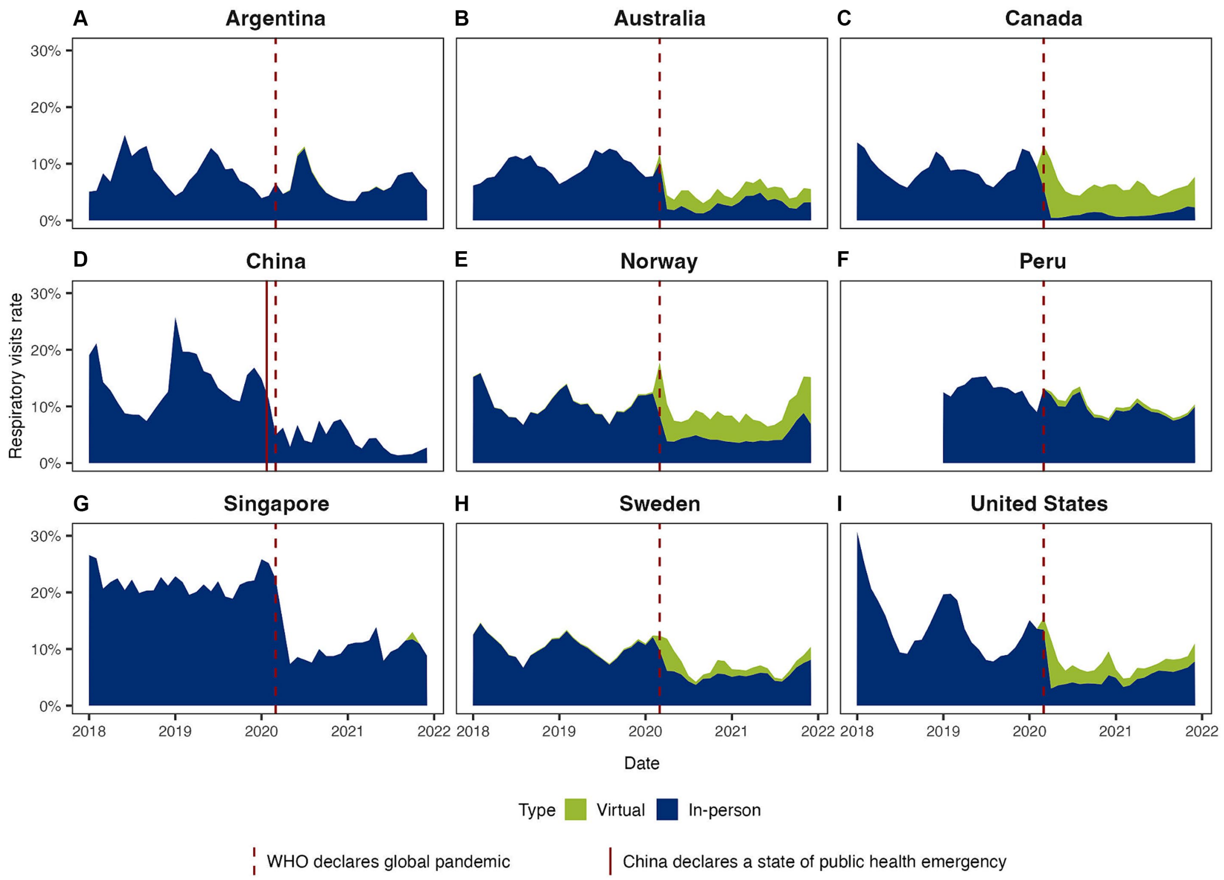

FIGURE 4
Respiratory visit rates by visit modality (virtual vs. in-person) in **(A)** Argentina, **(B)** Australia, **(C)** Canada, **(D)** China, **(E)** Norway, **(F)** Peru, **(G)** Singapore, **(H)** Sweden, and **(I)** United States. Area graphs illustrate respiratory visit rates by modality of care. The rates were calculated by dividing the number of respiratory visits by the total visits to primary care services within each month and are expressed as percentages (%).

example, respiratory illness accounted for 21.8% of visits in Singapore before the onset of the COVID-19 pandemic. This rate dropped below 10% of visits in the first few months of the pandemic and slowly levelled out at just over 10% of visits, with very few attributed to COVID-19. Prior to COVID-19, there was seasonal variation in Canada, with peaks near 15% of primary care visits attributed to respiratory illness. While there was an overall decrease in the rate of respiratory illness, it still hovered around 5%, with a significant number of COVID-19 patients. Our results were similar to those found in the United Kingdom, showing a marked decline in acute respiratory illness with flattening of seasonal variation while maintaining the usual incidence and seasonal variation associated with allergic rhinitis (24).

The variation in respiratory illness visits across countries also highlights differences in the location of COVID-19 infection care within our study population. Reflecting the diverse healthcare landscapes and pandemic responses globally, the dominant sites of COVID-19 care varied significantly. These variations encompass the dominant sites of COVID-19 care, including primary care versus other facilities, and align with the fluctuating waves of COVID-19 infections across the globe. Huston et al. studied the primary care and public health response to COVID-19 in 6 countries in early 2020 at the start of the pandemic (6). They found that COVID-19 assessment centers were the dominant location for triage of potential COVID-19 cases. In accordance with the Houston et al. study, neither their analysis nor our study identified primary care practices as the predominant COVID-19 testing and assessment locations in Australia, Canada, or the United States. Devi and colleagues reported that the majority of patients in their multi-country study had seen a health professional during the pandemic (63%) (25). This was even higher in Argentina, the only country that overlaps our research, which may explain the smaller drop in overall visit volume seen in this country.

4.3 Impact of COVID-19 pandemic on infectious respiratory illnesses

There is evidence that many infectious respiratory illnesses were much less common during the first 1–2 years of the COVID-19 pandemic (26, 27). Stephenson reported that while overall ambulatory visits dropped by just 5% between 2019 and 2020, the number of "common cold" visits dropped by 51% (3). Rodgers et al. reported that during the first few months of the pandemic, respiratory visits to the emergency department (ED) were twice the pre-pandemic rate; however, by the end of 2020, ED respiratory infections were below pre-pandemic rates (28). Liu et al. found lower rates of most respiratory pathogens among

TABLE 3 Site of assessment of potential COVID patients among INTRePID countries.

Country	Virtual	Primary care offices	Assessment centers	After-hours clinics	Emergency departments	Home visits
Argentina						
2020	Common	Sometimes	Common	Sometimes	Common	Sometimes
2021	Common	Sometimes	Common	Occasional	Common	Common
Australia						
2020	Common	Occasional	Common	Sometimes	Sometimes	Occasional
2021	Common	Occasional	Common	Sometimes	Sometimes	Occasional
Canada						
2020	Sometimes	Sometimes	Common	Sometimes	Common	Occasional
2021	Sometimes	Sometimes	Common	Sometimes	Common	Occasional
China						
2020	Never	Occasional	Common	Sometimes	Common	Never
2021	Never	Sometimes	Common	Sometimes	Common	Never
Norway						
2020	Common	Sometimes	Common	Common	Occasional	Occasional
2021	Common	Sometimes	Common	Common	Occasional	Occasional
Peru						
2020	Sometimes	Occasional	Common	Never	Common	Sometimes
2021	Sometimes	Sometimes	Common	Never	Common	Occasional
Singapore						
2020	Never	Common	Common	Common	Common	Never
2021	Sometimes	Common	Sometimes	Common	Sometimes	Never
Sweden						
2020	Common	Sometimes	Common	Sometimes	Common	Occasional
2021	Common	Occasional	Common	Sometimes	Common	Occasional
United States						
2020	Common	Occasional	Common	Occasional	Sometimes	Occasional
2021	Sometimes	Common	Sometimes	Sometimes	Occasional	Occasional

hospitalized children with lower respiratory tract infections (29). Lockdowns, social distancing, and mask mandates may have contributed to protection from COVID-19 (30, 31) and many other endemic and seasonal infections such as respiratory syncytial virus (RSV), influenza and other common rhino and adenoviruses (32, 33). The lower rate of respiratory infections seen among INTRePID participants may indicate the response to robust public health measures aimed at minimizing the spread of contagious illness. With the reduction in COVID-19 mitigation efforts in 2021, there was a resurgence in common respiratory infections (34, 35). Most recent evidence from December 2022 in the United States and Norway revealed major increases in RSV and influenza (36). Renati and Linder reported that a majority of acute respiratory infections may not require a clinical consultation (37). The additional fear of transmission and the restrictions in place in many healthcare settings may have been enough to keep patients with mild to moderate COVID-19 infection away from the clinic. Bullen et al., in a 9-country survey, found that 60% of physicians and pharmacists reported patient "reluctance to visit a healthcare setting." (38).

Insights gained from previous pandemics provide crucial context for understanding the dynamics of viral interactions during outbreaks. For instance, the emergence of influenza A (H1N1) pandemic in 2009 had a significant impact on the circulation of other respiratory viruses between 2009 and 2011 (39). Studies observed unusual patterns in virus activity following the influenza A (H1N1) pandemic peak. Research conducted in France suggested a delay in the circulation of respiratory syncytial virus (RSV) during the 2009–2010 season, compared to previous years (40). Similarly, a study conducted in the United Kingdom found that some cases initially diagnosed as influenza during the summer outbreak were actually caused by other respiratory viruses (41). These findings underscore the interplay between dominant strains like the influenza A (H1N1) during the 2009 pandemic and other respiratory viruses. While our study focused on acute respiratory visits without examining the specific viruses involved, similar dynamics were observed during the COVID-19 pandemic (39).

4.4 Role of primary care in pandemic response

Goodyear-Smith and colleagues found that the perceived strength of the primary care system was not associated with a lower

COVID-19 mortality rate (42). However, they also found that the perceived strength of a pandemic plan with robust implementation was associated with lower COVID-19 mortality. Local, regional, and national planning for COVID-19 recovery should also include planning for the management and resurgence of other respiratory infections. Primary care plays a crucial role in vaccination and may need to be part of post-pandemic immunization catchup and annual management (43, 44). Virtual visits may also play an important role in primary care and require further research to maximize their impact.

4.5 Limitations

This research comes with some limitations. First, we collected data from numerous sources with large variations in availability. While some INTRePID countries provided comprehensive national-level data, others provided limited data from a few clinics or regions. For instance, data from Peru (45) include over 8000 primary care practices, representing nearly 70% of the population. Data from smaller samples, such as those from China and the US, may not reflect the regional variation nor the national experience in primary care. Also, the usage of country names to define the regions is primarily for clarity and comprehension purposes rather than a direct comparison between the entire country populations. However, we have at least in part achieved a global footprint in relation to the sampling frame.

Our aim was not necessarily to compare countries to each other but rather to compare pre-pandemic with COVID-19 pandemic time periods among the participating INTRePID countries. We present unadjusted analyses as social and demographic variables were not available among all participant data. As many countries managed COVID-19 outside of the typical primary care setting, the COVID-19-related visits presented here reflect the impact on and role of primary care in the typical primary care settings rather than the full impact of COVID-19 in the community.

Moreover, primary care physicians staffed COVID-19 assessment clinics established outside the conventional primary care settings in numerous INTRePID countries. However, the visit rates for these patients were not accounted for in our data, except in Norway.

Another limitation arises from the reliance on coding systems themselves. For instance, due to the emergence of COVID-19 as a new diagnosis, some coding systems did not differentiate between suspected and confirmed cases. Unfortunately, this limitation in data availability prevented us from making a stratified analysis of suspected and confirmed cases. However, given the widespread epidemic nature of COVID-19, in the midst of a local wave, it is likely that most suspected cases were true COVID-19 infections.

We acknowledge that COVID-19-related visits to primary care do not reflect COVID-19 cases or death rates (20). The results presented in this study do not represent the impact of the global COVID-19 pandemic on primary care. We show the impact of the pandemic within each of the participant countries and particular regions involved.

Telehealth virtual visits are a safe and effective alternative to in-person clinic visits (14). While it has limitations, such as the inability to perform physical exams (46), it allows for efficient triage, effective symptom assessment, and the provision of timely medical advice, especially during times when in-person visits were restricted. Many primary care practices increased their use of virtual telehealth visits throughout the COVID-19 pandemic, particularly in the first year of the pandemic. While the INTRePID data included in-person as well as virtual visits, the rapid shift to virtual visits may not have generated a full encounter in the medical record or billing number in some countries, resulting in a loss of primary care practice visit data. Virtual visits, particularly early in the pandemic, may have been audio only and did not generate a full encounter in some countries' medical or billing records.

5 Conclusion

The COVID-19 pandemic resulted in a major impact on primary care visits and reasons for visits. As expected from widespread physical distancing and mask mandates, there was a decreased rate of respiratory illness presentation in primary care after the start of the pandemic. INTRePID countries exhibited substantial variations. Primary care in all countries continued to provide service, in-person and through virtual telehealth consultation, for respiratory conditions as well as other health needs. Primary care is pivotal in epidemic and pandemic infection management. Understanding the role of primary care may provide valuable information for COVID-19 recovery efforts and planning for future global pandemic emergencies.

5.1 Implications for future research

Future research should explore the long-term impact of the pandemic on primary care utilization patterns and healthcare delivery. Further investigation into the effectiveness of virtual visits and strategies to address the underreporting of encounters is warranted. Moreover, understanding the interplay between pandemic response measures and the resurgence of respiratory infections will inform future public health interventions and pandemic preparedness efforts. This study also identifies the urgent need to consider methods to harmonize and curate data from various sources as a method to conduct robust international primary care research.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: All relevant data is contained within the article. The original contributions presented in the study are included in the article and supplementary files, further inquiries can be directed to the corresponding author. However, data sharing is governed by local regulations, which differ across countries. Individual-level data is not accessible to the public due to research ethics approval restrictions. Analytic code for data analysis is available upon request. Requests to access these datasets should be directed to k.tu@utoronto.ca.

Ethics statement

The studies involving humans were approved by this study received Research Ethics Board approval from the University of Toronto #40943. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

JW: Conceptualization, Investigation, Methodology, Visualization, Writing – original draft. AB: Conceptualization, Formal analysis, Investigation, Methodology, Writing – review & editing. ML: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – review & editing. PZ: Data curation, Investigation, Validation, Writing – review & editing. WW: Data curation, Investigation, Validation, Writing – review & editing. KW: Data curation, Investigation, Validation, Writing – review & editing. WP: Data curation, Investigation, Validation, Writing – review & editing. JS-V: Data curation, Investigation, Validation, Writing – review & editing. LS: Data curation, Investigation, Validation, Writing – original draft. AN: Data curation, Investigation, Validation, Writing – review & editing. J-AM-N: Data curation, Investigation, Validation, Writing – review & editing. ZJL: Data curation, Investigation, Validation, Writing – review & editing. ZL: Data curation, Investigation, Validation, Writing – review & editing. AH: Conceptualization, Writing – review & editing. AL: Data curation, Investigation, Validation, Writing – review & editing. RK: Data curation, Investigation, Validation, Writing – review & editing. CH: Data curation, Investigation, Validation, Writing – review & editing. LG: Data curation, Investigation, Validation, Writing – review & editing. GG: Data curation, Investigation, Validation, Writing – review & editing. SF: Data curation, Investigation, Validation, Writing – review & editing. SL: Data curation, Investigation, Validation, Writing – review & editing. MC-F: Data curation, Investigation, Validation, Writing – review & editing. VB: Data curation, Investigation, Validation, Writing – review & editing. KT: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

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Conflict of interest

JW holds the position of Vice President and is employed by the DARTNet Institute, a non-profit organization specializing in primary care research. AB and ML work for the University of Toronto and part of their salary is supported by grants. WP has received grant funding from NIMCH, sits on the advisory board of AT Still Research Foundation, has stock in Moderna, Johnson and Johnson, Eli Lilly, Novo Nordisk, Styker, Amgen, Novartis, and Pfizer; and received supplies from Boehringer Ingelheim and AstraZeneca. RK teaches at the Swedish advanced training program in quality improvement and owns stocks in the Swedish healthcare company Ambea. SL is the director of the Royal College of General Practitioners (RCGP) Research and Surveillance Center (RSC) as part of his academic post at Oxford. He has received payment to his research group for health services and primary care research from the University of Oxford and the University of Surrey and a wide range of grant funding through his university for vaccine-related research from AstraZeneca, GSK, Sanofi, Segirus and Takeda. MC-F receives honoraria and stocks from the Peruvian Cayetano Heredia University (Universidad Peruana Cayetano Heredia). KT receives a Chair in Family and Community Medicine Research in Primary Care at UHN and a Research Scholar award from the Department of Family and Community University of Toronto. KT received grants from the following organizations in the past 3 years: The Canadian Institutes of Health Research, Rathlyn Foundation Primary Care EMR Research and Discovery Fund, College of Family Physicians of Canada/Foundation for Advancing Family Medicine/CMA Foundation Heart and Stroke Foundation of Ontario, Department of Defense United States of America, St. Michael's Hospital Foundation, Ontario Health Data Platform First Movers Fund, Queen's University CSPC Research Initiation Grant, Diabetes Canada, Heart and Stroke Foundation and Brain Canada Heart-Brain IMPACT Award, CANSSI ICES Data Access Grant, North York General Hospital Exploration Fund, CFPC Janus Grant. All funding sources were not involved in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and the decision to submit the article for publication. The researchers are all independent of funders, and KT, AB, ML had full access to all the data and authors from each country had full access to the country-specific data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2024.1343646/full#supplementary-material

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Assessing the impact of vaccination and medical resource allocation on infectious disease outbreak management: a case study of COVID-19 in Taiyuan City

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Introduction: Amidst an emerging infectious disease outbreak, the rational allocation of vaccines and medical resources is crucial for controlling the epidemic's progression.

Method: Analysing COVID-19 data in Taiyuan City from December 2022 to January 2023, this study constructed a $SV_1V_2V_3EIQHR$ dynamics model to assess the impact of COVID-19 vaccination and resource allocation on epidemic trends.

Results: Vaccination significantly reduces infection rates, hospitalisations, and severe cases, while also curtailing strain on medical resources by reducing congestion periods. An early and sufficient reserve of medical resources can delay the onset of medical congestion, and with increased maximum capacity of medical resources, the congestion's end can be accelerated. Stronger resource allocation capabilities lead to earlier congestion resolution within a fixed total resource pool.

Discussion: Integrating vaccination and medical resource allocation can effectively reduce medical congestion duration and alleviate the epidemic's strain on medical resource capacity (CCMR).

KEYWORDS

COVID-19, carrying capacity of medical resource, vaccination, medical resource allocation, infectious disease outbreak management, China

1 Introduction

"Emerging infectious diseases" typically denote highly contagious and lethal outbreaks that occur within a short timeframe in specific regions (1, 2). The widespread transmission of such diseases poses significant challenges to epidemic control, strains healthcare systems, and triggers public panic, leading to social unrest and crises that threaten national and regional stability and security (3). The COVID-19 outbreak that emerged at the end of 2019 led to numerous infections and hospitalisations (4, 5), severely impacting healthcare systems worldwide. For instance, Bhaskaran et al. (4) discovered that COVID-19 hospital admissions carried significantly higher risks of rehospitalization and death compared to the general population. Additionally, Timothy et al. (5) predicted a peak in COVID-19 hospitalizations from November to April of the following year, which poses challenges for the healthcare system. Therefore, identifying effective prevention and control measures and enhancing the carrying capacity of medical resources (CCMR) during an outbreak are crucial for controlling the spread of COVID-19 (6).

The CCMR is a key indicator for preventive implementation and epidemic response readiness, encompassing two main aspects (7): First, the production and allocation capacity of medical resources, which includes the ability to produce and distribute beds, medications, medical equipment, and related supplies required for patient treatment, reflecting a region's ability to promptly supplement medical resources and its efficiency during an outbreak. Second, the maximum number of available medical resources, which is based on the production and allocation capacity of medical resources and their limited nature indicates the maximum amount of resources that medical institutions can provide promptly. For instance, following the COVID-19 outbreak in Taiyuan City, hospital admissions surged, and departments other than respiratory medicine were repurposed to accommodate COVID-19 patients, maxing out bed capacity across all departments. During the pandemic, as the number of COVID-19 patients increased, the shortage of medical resources and resulting congestion posed significant public health issues in various locations. In a study from Germany, early in the epidemic, to increase the capacity for COVID-19 patients, a reduction of bed and operating room occupancy of $50.8 \pm 19.3\%$ and $54.2 \pm 19.1\%$ was reported (8). The World Health Organization also highlighted that the severe shortage of nursing staff globally could threaten the safety of COVID-19 patients (9). Therefore, during an outbreak, assessing the carrying capacity of the medical resources, preventing the occurrence of medical congestion, shortening the duration of congestion, and developing corresponding prevention strategies are essential.

Vaccination is a pivotal strategy in controlling the spread of infectious diseases. Amidst the COVID-19 pandemic, nations worldwide have prioritised vaccine development and administration (10, 11). In China, governmental and professional institutions such as the Centres for Disease Control and Prevention, have recommended that the public expedite their vaccination process, particularly the administration of the booster doses (12). Studies indicate that completing a three-dose regimen, significantly reduces infection rates (13–17), thereby decreasing the demand for medical resources. Although the efficacy of vaccines in reducing infections has been widely confirmed (18), research on the relationship between vaccination and the CCMR remains insufficient. During the pandemic, quantifying the impact of vaccination on CCMR is paramount for improving local epidemic prevention and control measures.

Infectious disease dynamics modelling is an essential tool for analysing the mechanisms of disease transmission, predicting trends, and identifying influencing factors. Existing research encompasses three main areas. First, the use of infectious dynamic models to analyse the spread of COVID-19 within populations. For instance, Mandal et al. (19) established the SPFEIDR model to predict short-term trends in several severely affected regions in India, identifying that reducing interpersonal contact is key to controlling disease spread. Zhao et al. (20) developed a SUQC model to characterise the COVID-19 dynamics. By fitting it with actual daily incidence data, analysed the outbreak in Wuhan and four first-tier cities in China, predicting the pandemic's end time and the final scale of infection numbers. Second, the assessment of vaccination effects, such as Ali et al.'s (21) SEIIAVR model which mathematically demonstrated that increasing the vaccination rate to over 50% can effectively reduce the infection rate. Paulo and colleagues (22) suggest that to maximise the number of individuals with partial COVID-19 protection, an optimisation model based on SEIR dynamics recommends the optimal delay for the second vaccine dose, considering crucial factors such as the efficacy of a single dose, the anticipated vaccine supply pipeline, and the potential emergence of more virulent COVID-19 variants, which could significantly reduce ICU admissions. Third, the evaluation of the CCMR in different regions. Wang et al. (7) assessed the CCMR of multiple countries post-outbreak using the $SEIARSqTH_1H_2$ model, finding that enhancing medical capabilities and testing in tandem can alleviate the epidemic and prevent excessive pressure on CCMR. Overall, current studies focus on the dynamics of transmission, vaccination rates, and the factors affecting CCMR, while there is a lack of discussion on the impact of different vaccination strategies on epidemic trends and CCMR.

As the capital city of Shanxi Province, Taiyuan boasts convenient transportation and abundant medical resources. Data from sentinel hospitals between December 6, 2022, and January 13, 2023, revealed a COVID-19 mortality rate in Taiyuan below 1/10,000, signifying notable success in pandemic control efforts. This study, taking Taiyuan as a case example, collected vaccination status and incidence data from residents through surveys. Utilising medical resources and patient information provided by sentinel hospitals, an $SV_1V_2V_3EIQHDR$ model simulated vaccination scenarios and epidemic trends during the COVID-19 period. The model assessed changes in hospital bed occupancy, reflecting the impact of different vaccination levels on infection rates, hospitalisations, severe cases, and trends, along with CCMR. This provides a scientific basis for optimising vaccination strategies and medical resource allocation in Taiyuan.

This study categorised the vaccinated population into four groups: those susceptible without vaccination (S), those who have received one dose (V_1), those who have received two doses (V_2), and those who have received three doses (V_3). We use the number of available hospital beds as a quantitative indicator of CCMR. When the number of beds hits zero, the CCMR is deemed to have reached its limit, leading to a medical congestion. The onset, duration, and end time of this congestion serve as metrics for assessing the CCMR. The primary assumptions of the study include:

(H_1) Excludes transmission from asymptomatic infections and those in the incubation period in the model. It is because following the easing of control measures and the discontinuation of nucleic acid testing, it is widely accepted that the propagation of the novel coronavirus is primarily due to individuals exhibiting symptoms of the virus.

(H_2) Individuals exhibiting symptoms of COVID-19 will either be quarantined at home or receive treatment in a hospital.

(H_3) Individuals who have been infected will not contract the infection again within a short span of time.

(H_4) No contagiousness during home quarantine period: Patients are considered not to be infectious during the period of home isolation, given that they are unlikely to trigger community transmission while in home isolation.

(H_5) Provided that there are enough beds, there will also be ample healthcare staff and medical equipment. Even in times of healthcare stress, although there may be difficulties in housing all patients, those admitted to the hospital receive appropriate care.

(H_6) The capacity, contact rate, and severity conversion rate of medical resources will change with the development of the epidemic. Following the initial stage of an epidemic in a region, the rate of infection gradually peaks. A rapid increase in demand for hospital care corresponds to an increase in the demand for medical resources. This signifies the point at which the epidemic reaches its highest level. During this time, social interactions typically decrease as individuals minimise their contact with others. Simultaneously, hospitals see a marked increase in the number of severe and critical cases brought on by the novel coronavirus, compared with earlier levels. Therefore, we propose that the methods used to calculate medical resource capacity, contact rates, and severity conversion rates all change simultaneously.

(H_7) Given that most individuals did not undergo nucleic acid testing following the lifting of restrictions, we consider individuals presenting symptoms similar to those of COVID-19, such as fever or cough, as new cases.

2 Data and method

2.1 Data sources

Taiyuan, the capital city of Shanxi Province, encompasses 10 administrative districts. Each district contains multiple streets, further divided into several communities, typically comprising 1,000 to 3,000 households (23). This study employed a multi-stage random sampling method, selecting two streets randomly from each district and two communities from each street. Finally, 1,200 residents were randomly chosen from each community for a questionnaire survey. The questionnaires were distributed electronically, and the selected residents completed them online. In total, 48,000 questionnaires were distributed, yielding 39,899 valid responses. The analysis provided daily new case numbers and infection rates from December 6, 2022, to January 13, 2023. According to Zhang et al. (24), Taiyuan had a total population of 5,420,957 at the end of 2022. The infection rates obtained from the survey were extrapolated to the entire population of Taiyuan to estimate the daily number of infections citywide. Data on hospitalisations and severe cases were provided by the Shanxi Provincial Health Commission through the sentinel hospital monitoring system.

2.2 Model

To highlight important differences in the separate or combined use of various control strategies within the constraints of limited healthcare resources, we constructed an $SV_1V_2V_3EIQHR$ model, as shown in Figure 1. We categorised the initial population into susceptible populations (S), populations who had received one dose of the vaccine (V_1), populations who had received two doses of the vaccine (V_2), and populations who had received three or more doses of the vaccine (V_3).In the model, E and I represent exposed and infected individuals, respectively, Q represents individuals who are under home quarantine, H represents individuals who are hospitalised and confirmed, Z and D represent the number of patients with severe and critical conditions caused by COVID-19, and the number of deaths among hospitalised patients, respectively, and R represents individuals who have recovered. The detailed definitions of other parameters are given in Table 1.

$N = S + V_1 + V_2 + V_3 + E + I + Q + H + Z + D + R$ represents the whole population.

$$
\begin{cases}
\frac{dS}{dt} = \frac{-c(t)\beta SI}{N}, \\
\frac{dV_1}{dt} = \frac{-c(t)\beta_1 V_1 I}{N}, \\
\frac{dV_2}{dt} = \frac{-c(t)\beta_2 V_2 I}{N}, \\
\frac{dV_3}{dt} = \frac{-c(t)\beta_3 V_3 I}{N}, \\
\frac{dE}{dt} = \frac{c(t)(\beta S + \beta_1 V_1 + \beta_2 V_2 + \beta_3 V_3)I}{N} - \omega_1 E, \\
\frac{dI}{dt} = \omega_1 E - \min\{m_1 I, d\max\{H_c(t) - H, 0\}\} - m_2 I - r_I I, \\
\frac{dQ}{dt} = m_2 I - \min\{bQ, (1-d)\max\{H_c(t) - H, 0\}\} - r_Q Q, \\
\frac{dH}{dt} = \min\{m_1 I, d\max\{H_c(t) - H, 0\}\} + \\
\quad \min\{bQ, (1-d)\max\{H_c(t) - H, 0\}\} \\
\quad -\omega(t) r_H H - (1-\omega(t)) r_H H, \\
\frac{dZ}{dt} = \omega(t) r_H H - Z\eta r_{CD} - Z(1-\eta) r_C, \\
\frac{dD}{dt} = Z\eta r_{CD}, \\
\frac{dR}{dt} = Zr_C(1-\eta) + (1-\omega(t)) r_H H + r_Q Q + r_I I.
\end{cases}
\tag{1}
$$

In Model 1, individuals in compartments S, V_1, V_2, and V_3 are infected by I at rates of $c(t)\beta, c(t)\beta_1, c(t)\beta_2$, and $c(t)\beta_3$, respectively, and then enter the incubation period E. E transitions to I after $\frac{1}{\omega_1}$ days. I may recover at a rate of r_2, choose home isolation Q at a rate of m_2, or be hospitalised H at a rate of $\min\{m_1 I, d\max\{H_c(t) - H, 0\}\}$. Here, $m_1 I$ represents the number of people who need to be hospitalised, and $d\max\{H_c(t) - H, 0\}$ is the number of hospital beds that can be allocated to them. For Q, a proportion of r_Q recovers, and a proportion of $\min\{bQ, (1-d)\max\{H_c(t) - H, 0\}\}$ is hospitalised, where bQ represents hospitalisation demand, and $(1-d)\max\{H_c(t) - H, 0\}$ is the number of hospital beds that can be allocated to them. For H, some of $\omega(t) r_H$ become severely ill Z, and a proportion of $(1-\omega(t)) r_H$ recovers. For Z, a proportion of ηr_{CD} dies, and a proportion of $(1-\eta) r_C$ recovers. The parameters are defined in Table 1.

Government policies may change in response to the progression of the epidemic, leading to dynamic fluctuations in hospital medical resources, particularly the number of beds. Following (7), we have

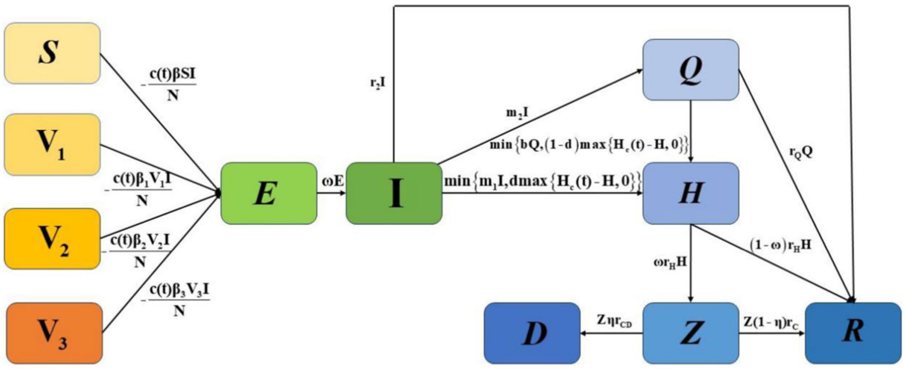

FIGURE 1
Transmission diagram of Omicron.

developed a model to analyse these changes in bed numbers using the logistic growth model:

$$\frac{H_c(t)}{dt} = \delta H_c(t)\left[1 - \frac{H_c(t)}{H_m}\right]. \quad (2)$$

where δ presents the production and allocation capacity of medical resources, and H_m indicates the maximum number of beds available during the epidemic. Hence, these two factors indicate how well equipped the city is to respond to an outbreak of an epidemic. Reference (7) used this formula to simulate the dynamic changes in the number of beds in the study area. In the early stages of an outbreak, the count of hospital beds tends to remain relatively stable. This could be because of a lower demand for hospitalisation or a lack of clear comprehension of the need for hospital beds. Therefore, by solving the previously mentioned logistic equation, we can calculate the daily bed count using the following piecewise function (7).

$$H_c(t) = \begin{cases} H_0 & t \le T_1, \\ \dfrac{H_0 H_m}{H_0 + (H_m - H_0)e^{-\delta(t-T_1)}} & t > T_1. \end{cases} \quad (3)$$

where H_0 represents the initial bed capacity available for COVID-19 patients at the onset of the outbreak, and T_1 represents the pivotal moment at which the city begins to escalate its medical resources, including hospital beds. Therefore, based on actual data, we set $T_1 = 17$ for Taiyuan city. Thus, the daily potential number of empty beds was calculated as $H_j(t) = \max\{H_c(t) - m_1 I - b_1 Q, 0\}$.

When the new policies related to the COVID-19 pandemic were first put into effect on 6 December, restrictions on people's activities were lifted, leading to a marked rise in the rate of contact between individuals. This, in turn, facilitated the swift spread of the COVID-19 pandemic. Subsequently, most individuals started to isolate at home or receive treatment in hospitals, which gradually lowered the contact rates. Hence, we propose that the contact rate is a function that diminishes over time t, as suggested by Wang et al. (7).

$$c(t) = \begin{cases} c_0 & t \le T_1, \\ (c_0 - c_b)e^{-\delta_1(t-T_1)} + c_b & t > T_1. \end{cases} \quad (4)$$

where c_0 represents the contact rate at the initial time. Hence, $c_0 = c(0)$. c_b represents the lowest contact rate given the current control strategies, and $\lim_{t\to\infty} c(t) = c_b$ with $c_0 > c_b$. δ_1 represents how to achieve a reduction in the rate of contact through exponential decline. Wang et al. (7) used this formula to simulate and predict the dynamic changes in the number of infected individuals in the study area.

Considering the progression of the epidemic, it is expected that the number of severe patients will rise in the later stages of the outbreak. Consequently, we use an exponential growth function to represent the conversion rate of hospitalised patients into severe cases:

$$\omega(t) = \begin{cases} \omega_0 & t \le T_1, \\ (\omega_0 - \omega_m)e^{-\omega_2(t-T_1)} + \omega_m & t > T_1. \end{cases} \quad (5)$$

where ω_0 is the initial conversion rate of hospitalisation with $\omega_0 = \omega(0)$, ω_2 denotes how an exponential increase in the conversion rate of hospitalisation is achieved, and ω_m is the maximum conversion rate of hospitalisation under the current situation with $\lim_{t\to\infty} \omega(t) = \omega_m$.

2.3 Analysis method

This study employs the Latin hypercube sampling and Markov chain Monte Carlo (MCMC) simulations to estimate the unknown parameters and fit the reported daily new cases, hospitalisations, and severe patient numbers in Taiyuan from December 6, 2022, to January 13, 2023, with Equation 1. This approach is similar to the methods used in previous studies, such as those by Ma et al; Gamerman and Lopes; Haario et al (25–27). Utilising the ode45 function in MATLAB software, Equations 1, 2 are used to calculate the daily number of available hospital beds and conduct the sensitivity analysis.

3 Result

3.1 Parameter estimation

3.1.1 Estimation of initial value

By the end of 2022, Taiyuan's resident population stood at 5,420,957 (24). The data gathered from the questionnaire survey suggest that the rate of individuals who received one, two, and three doses of vaccines in Taiyuan City are 1.8, 38.39, and 56.02%,

TABLE 1 Parameter definitions.

Parameters		Descriptions
$c(t)$	c_0	Initial contact rate
	c_b	Minimum contact rate after the outbreak of the epidemic
δ_1		Potential decline rate of contact rate
β		Probability of an infected individual transmitting the infection per contact
β_1		Transmission rate of infected individual to vaccinated susceptible population with one dose per contact
β_2		Transmission rate of infected individual to vaccinated susceptible population with two doses per contact
β_3		Transmission rate of infected individual to vaccinated susceptible population with three or more doses per contact
$\frac{1}{\omega_1}$		Average duration of latent period
m_1		Rate at which the non-home isolated individual with symptoms of COVID-19 was required to be hospitalised
d		Rate of the number of hospital beds available for non-home isolated individuals who require medical care
m_2		Transmission rate of infected individuals who choose to quarantine at home
b		Rate at which home-isolated individuals with symptoms of COVID-19 needed to be hospitalised
$\omega(t)$		Conversion rate from hospitalisation to severe and critical illness
η		Conversion rate from severe and critical illness to death
$\frac{1}{r_I}$		Recovery time for the non-home-isolated individual with symptoms of COVID-19
$\frac{1}{r_H}$		Recovery time for hospitalised individuals
$\frac{1}{r_Q}$		Recovery time for the home-isolated individual with symptoms of COVID-19
$\frac{1}{r_Z}$		Treatment time of critically ill patients in the intensive care unit before rehabilitation
$\frac{1}{r_{CD}}$		Average time from severe and critical illness to death
$\frac{1}{r_C}$		Recovery time for severe and critical illness
Initial values		Description
$S(0)$		Initial susceptible population
$V_1(0)$		Initial vaccinated susceptible population with one dose
$V_2(0)$		Initial vaccinated susceptible population with two doses
$V_3(0)$		Initial vaccinated susceptible population with three doses
$E(0)$		Initial exposed population
$I(0)$		Initial infected population
$Q(0)$		Initial home-isolated population
$H(0)$		Initial hospitalised population
$Z(0)$		Initial population with severe and critical illness
$D(0)$		Initial dead population
$R(0)$		Initial recovered population

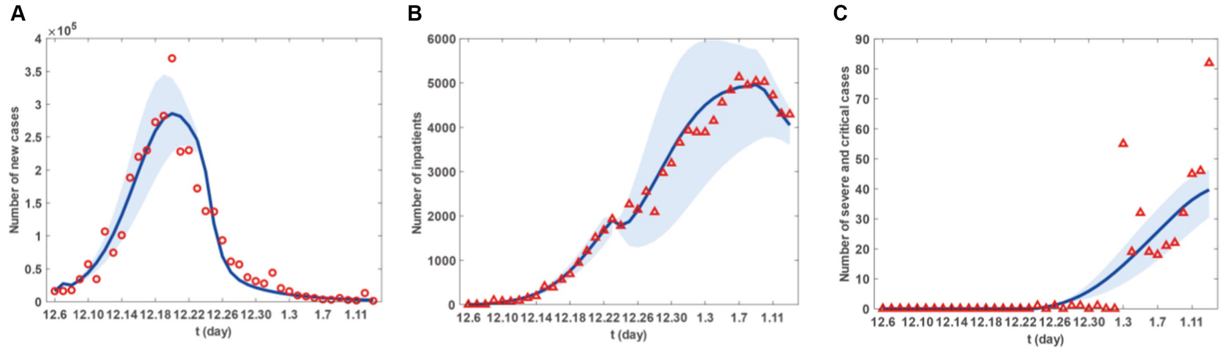

FIGURE 2
Fitting results of new cases, inpatients and sever and critical cases from 6 December 2022 to 13 January 2023 in Taiyuan City. **(A)** The red circles are the number of new cases. **(B)** The red triangle are the number of new inpatients. **(C)** The red triangles are the number of new sever and critical cases. The blue curve in **(A-C)** represents the corresponding estimated new cases, inpatients and sever and critical cases with the shadow areas as the corresponding 95% confidence band.

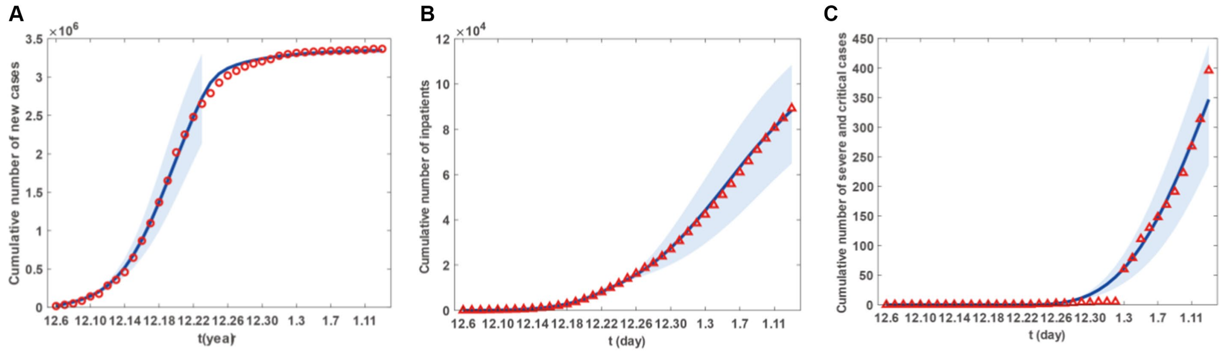

FIGURE 3
Fitting results of cumulative newly cases, inpatients and sever and critical cases from 6 December 2022 to 13 January 2023 in Taiyuan City. **(A)** The red circles are the number of cumulative newly cases. **(B)** The red triangles are the number of cumulative newly inpatients. **(C)** The red triangle are the number of cumulative newly sever and critical cases. The blue curve in **(A-C)** represents the corresponding estimated cumulative newly cases, inpatients and sever and critical cases with the shadow areas as the corresponding 95% confidence band.

respectively. Therefore, we assume $V_1(0) = 97722$, $V_2(0) = 2081151$, and $V_3(0) = 3036854$, respectively. Because there were 16,250 new cases on 6 December, we assume $I(0) = 16250$.

The incubation period of COVID-19 is 1.52 days, about one and a half days. Therefore, we assume $E(0) = 16422 + 17712/2 = 25278$ and thus, $S(0) = 5420957 - V_1(0) - V_2(0) - V_3(0) - E(0) - I(0) = 163702$. Due to the relatively low number of hospitalisations, and severe and critically ill patients, as well as recoveries on 6 December, we assume $H(0) = 0, Z(0) = 0, D(0) = 0, R(0) = 0$.

The current research indicates that hospitalisations primarily occur in secondary and tertiary hospitals. Statistical data reveal that Taiyuan City has a total of 64 secondary and tertiary hospitals (24). As per the China Health Statistics Yearbook (2022), Taiyuan City's medical institutions collectively have 81,400 beds spread across 164 hospitals. Therefore, we estimate that the total number of beds in 64 hospitals in Taiyuan City is $64/164^{*}81400 = 31610$. According to the Introduction to the First Hospital of Shanxi Medical University (28, 29), the number of respiratory beds is no more than $64^{*}123 = 7872$.

3.1.2 Data fitting

Using the parameters and initial conditions provided above and combing with Equations 1, 4, 5, we apply Latin hypercube sampling and Markov chain Monte Carlo (MCMC) simulations to estimate the unknown parameters and fit the data. This approach is similar to the methods used in previous studies, such as those by Ma et al; Gamerman and Lopes; Haario et al (25–27). The results of our analysis are shown in Figures 2, 3 and Table 2.

Figure 2 presents the fitting results for the number of new cases, with Figures 2A–C representing the number of new patients, the number of new hospital admissions, and the number of new severe and critical patients, respectively. Similarly, Figure 3 displays the fitting results for the cumulative number of new cases, with Figures 3A–C representing the cumulative number of new patients, the cumulative number of new hospital admissions, and the cumulative number of new severe and critical patients, respectively. According to the fitting results, illustrated in Figures 2A, 3A, the number of new cases in Taiyuan City began to rise on December 6th, peaked around December 20th, and then gradually declined until January 13th. Figures 2B, 3B show that the number of hospitalised patients started to increase from December 6th, reached a small peak on December 23rd followed by a slight decline, but rose again from December 24th and continued until a decrease began on January 9th, lasting until January 13th. The data in Figures 2C, 3C indicate that the number of severe and critically ill patients remained at zero from December 6th to December 23rd, but began to increase from December 23rd and had not peaked by January 13th.

TABLE 2 Values of parameters.

Parameter	Value of first stage	Value of second stage	Unit	Source
c_0	25	25.2	$year^{-1}$	MCMC/Actual epidemic
c_b	0	5.84	$year^{-1}$	Actual epidemic/ MCMC
δ_1	0	1	$year^{-1}$	Actual epidemic
β	0.089	0.089	$year^{-1}$	Actual epidemic
β_1	0.046	0.046	$year^{-1}$	Actual epidemic
β_2	0.04	0.04	$year^{-1}$	Actual epidemic
β_3	0.01	0.01	$year^{-1}$	Actual epidemic
ω_1	1.52	1.52	$year^{-1}$	(30, 31)
m_1	1.5×10^{-8}	0.65	$year^{-1}$	Actual epidemic
m_2	0.12	0.12	$year^{-1}$	MCMC/Actual epidemic
d	2.24×10^{-5}	3.56×10^{-7}	$year^{-1}$	Actual epidemic
H_0	4,975	4,975	$year^{-1}$	(26)
H_m	31,610	31,610	$year^{-1}$	Actual epidemic
δ	0	0.22	$year^{-1}$	Actual epidemic/ MCMC
r_I	0.0685	0.07	$year^{-1}$	Actual epidemic
b	0.00275	0.0093	$year^{-1}$	Actual epidemic
r_Q	0.06667	0.07	$year^{-1}$	Actual epidemic
ω_0	1.87×10^{-6}	1.87×10^{-6}	$year^{-1}$	Actual epidemic
r_H	0.5	0.183	$year^{-1}$	Actual epidemic
η	0.017	0.322	$year^{-1}$	Actual epidemic
r_{CD}	0.77	0.36	$year^{-1}$	Actual epidemic
r_C	0.03	0.035	$year^{-1}$	Actual epidemic
T_1	17	17	$year^{-1}$	Actual epidemic
ω_2	0	0. 0026	$year^{-1}$	Actual epidemic
ω_m	0	0.18	$year^{-1}$	Actual epidemic

The decrease in the number of hospitalised patients after the small peak on December 23rd, as shown in Figure 2B, was due to the start of resource allocation on that day, as the hypothesis H6 and parameter T_1, where the daily number of new patients requiring hospitalisation exceeded the number of beds available in hospitals. On December 24th, due to limited resource allocation capabilities, the number of available beds was less than the previous day, resulting in a temporary decline. Subsequently, as the number of newly allocated beds increased daily, more patients had the opportunity to be hospitalised, leading to a rise in the number of hospitalised patients until January 9th. The decline starting from January 9th was because, by that time, Taiyuan City had reached the maximum number of beds that could be allocated in the short term. Although a large number of patients still required hospitalisation, no further increase in bed numbers was possible, and new hospital admissions were mainly due to beds vacated by discharged patients.

However, as their condition deteriorates, patients may decide to seek medical help. This situation could trigger a rise in hospital admissions, compelling the government to modify its epidemic prevention strategies, such as augmenting the number of hospital beds and other medical resources to ensure that more patients receive prompt hospital care. It is important to highlight that the peak in hospital admissions did not coincide with the peak in infections but was delayed until early January. This could be because patients might only exhibit severe symptoms that necessitate hospital care some time after being infected. Therefore, there is a certain time gap between the peak of infections and the peak of hospital admissions. Moreover, the transition from hospitalised patients to severe or critical cases also takes a certain amount of time, represented by the parameter ω in the model. This could cause the peak of severe or critical cases to lag behind the peak of hospital admissions.

3.1.3 Calculation of the daily number of available hospital beds

Upon inserting the parameter values from Table 2 into Equation 3 and utilising the plot function in MATLAB software, we generated Figure 4. This figure illustrates a continuous decline in the daily potential number of vacant hospital beds in Taiyuan City from December 6th to December 20th. From December 20th, 2022, to January 24th, 2023, the daily potential number of vacant beds dropped to zero, indicating a possible shortage or overcrowding of medical resources. However, starting from January 24th, 2023, the number of available beds began to increase, suggesting that medical resources are gradually becoming sufficient to meet the demands of epidemic prevention and control. Figure 4 allows us to conclude that the need for hospital beds remained high until 16 January 2023. To manage the surge in hospitalisations, most hospitals in Taiyuan City reassigned beds from other departments to accommodate patients with COVID-19. While this action somewhat mitigated the bed shortage issue, the number of available beds remained at zero, owing to the high demand for hospitalisation from a large number of patients with COVID-19.

3.2 Sensitivity analysis

3.2.1 The impact of different vaccine strategies on the final scale of infections, hospitalisations, and severe cases

First, we analyse the daily cumulative changes in new infections, hospitalised patients, severe cases, and critically ill patients in various scenarios. To highlight the effect of different vaccine doses on the final extent of disease prevalence, we constructed the following three scenarios:

(S1) The first dose of the vaccine is given to individuals who have not yet been vaccinated with the aim of ensuring that all populations have received at least one dose of the vaccine.

(S2) Individuals who are vulnerable or have only been administered one dose of the vaccine are provided with two doses of

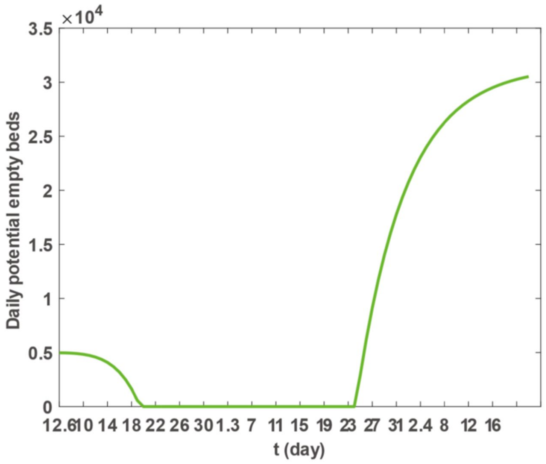

FIGURE 4
Theoretically, the number of daily potential empty beds.

TABLE 3 Final cumulative numbers of new, hospitalised, and critical cases under different scenarios.

	Final cumulative number of scale		
	New cases	Hospitalised cases	ICU/CCU Cases
$CasesC_1$	3,368,646	146,660	1,619
$CasesC_2$	3,255,316	145,397	1,612
$CasesC_3$	3,214,118	144,750	1,606
$CasesC_4$	331,967	17,819	167

the vaccine, ensuring that all populations have received a minimum of two doses of the vaccine.

(S3) Individuals who are vulnerable or have only been administered one or two doses of the vaccine are considered fully vaccinated after receiving three doses of the vaccine. This ensures that all populations have received a minimum of three doses of the vaccine.

Based on Model 1, and incorporating the parameter values from Tables 2, 3, as well as the scenarios described previously, we utilised the ode45 function within Matlab software to generate (Figure 5). The simulation results are outlined in Figure 5 and Table 3. Increasing the count of individuals receiving one or two vaccine doses can marginally decrease the ultimate scope of infections, hospitalisations, and severe cases. However, only in S3 can the ultimate scope be effectively diminished, thus restraining the epidemic's spread. Consequently, for Taiyuan City's inhabitants, merely augmenting the first and second vaccine doses is insufficient to effectively mitigate the epidemic, and the coverage of the third vaccine dose must be expanded.

3.2.2 The impact of different vaccination scenarios on the duration of medical crowding

The data from Figure 5 and Table 3 indicate that ensuring that individuals in Taiyuan City who have received one vaccine dose as well as those who have not been vaccinated update their vaccination status to two doses results in a decrease in the final count of infections, hospitalisations, and severe cases. However, this reduction is relatively minor, and the difference is not significant. In contrast, ensuring that all residents of Taiyuan City receive three doses of the vaccine will significantly lower the number of infections, hospitalisations, and severe cases. Consequently, we further analyse the availability of empty beds in Taiyuan City under various three-dose vaccination strategies, taking into account the actual conditions in Taiyuan City. The specific strategies are as follows:

(SS_1) Prior to 6 December, both the unvaccinated individuals and those who have only received one dose of the vaccine have now completed two doses of vaccination. (All subsequent scenarios are based on this situation).

(SS_2) Prior to 6 December, an extra 500,000 individuals who had previously received only two doses of the vaccine have now completed a course of three doses.

(SS_3) Prior to 6 December, an extra 1 million individuals who had previously received only two doses of the vaccine had completed a third dose of vaccination.

(SS_4) Prior to 6 December, an extra 1.5 million individuals, who had previously only received two doses of the vaccine, had completed a course of three doses.

(SS_5) Prior to 6 December, all individuals who had previously received only two doses of the vaccine had completed a third dose.

Based on Model 1, and incorporating the parameter values from Tables 2, 3, as well as the scenarios described previously, we utilised the ode45 function within Matlab software to generate (Figure 6). The findings presented in Figure 6 indicate that augmenting the third dose of vaccination can effectively postpone the onset of medical resource strain and reduce its duration. This strategy is beneficial in promptly resolving the scarcity of medical resources.

3.2.3 The impact of medical resource related factors on the time of medical crowding

Based on Model 1 and the parameter values listed in Tables 2, 3, we utilise the ode45 function in Matlab software to explore how the maximum number of available beds, the initial number of beds, and the capacity for medical resource allocation affect the timing of medical congestion. The results are presented in Figures 7A–C. Figure 7A demonstrates that by increasing the maximum number of available beds (H_m), the duration of medical crowding can be reduced. However, this does not postpone the onset of medical resource shortages. Furthermore, after the epidemic has passed, there may be some wastage associated with the increased resources. Figure 7B shows that increasing the number of beds at the initial moment can delay the onset of medical resource shortages when the epidemic begins. However, once medical resource shortages occur, it may not bring an earlier end to the shortages. Figure 7C reveals that if the medical resource allocation capacity of Taiyuan City decreases, medical resource shortages will persist for a longer duration. Therefore, the current allocation capacity may be the most cost-effective state.

4 Discussion and conclusion

During widespread outbreaks of acute infectious disease, the strain on medical resources is a common phenomenon and has garnered extensive attention and research from numerous scholars (3, 7, 19, 20, 32–36, 39). Taking COVID-19 as a case study, we investigate the impact of vaccination and resource allocation on

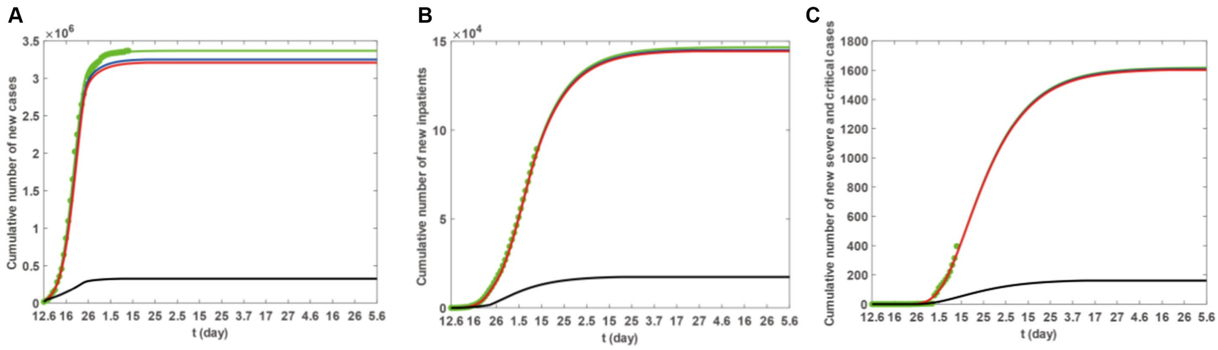

FIGURE 5
The blue, red, and black solid lines represent the cumulative number of new cases under scenarios S1–S3. The green solid line represents the actual fitted situation, and the green dots represent reported case numbers. **(A)** The trend in the cumulative number of new cases. **(B)** The trend in the cumulative number of hospitalisations. **(C)** The trend in the cumulative number of severe cases.

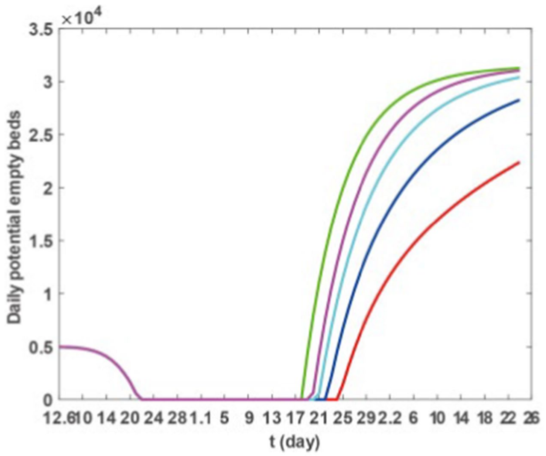

FIGURE 6
Theoretically, the number of empty beds. Green, blue, black, red, and yellow solid lines represent SS1–SS5, respectively.

the epidemic trends and CCMR during such outbreaks. Based on survey data on COVID-19 transmission in Taiyuan, we constructed a dynamic model to fit the daily reported new cases, hospitalised patients, and severe cases (as shown in Figures 2, 3), and estimated parameters (as shown in Table 2), predicting the ultimate scale of the epidemic (indicated by the solid green line in Figure 5). By calculating the trend of remaining bed numbers, we can determine the occurrence and duration of medical congestion. As shown in Figure 2, the peak times for new cases, hospitalizations, and severe cases typically lag in succession. Some existing research (37, 38) can fully support our conclusion. For instance, research by Wang et al. (37) reported that during the COVID-19 outbreak in Wuhan, the median time from the onset of initial symptoms to hospital admission for 260 patients was approximately 8 days; C Dananché and colleagues (38) noted that younger COVID-19 patients tended to have a longer interval between the onset of symptoms and hospitalization. Figure 4 indicates that until January 16, 2023, the demand for hospital beds remained high. To address the sharp increase in hospital admissions, most hospitals in Taiyuan City reallocated beds from other departments to accommodate COVID-19 patients, alleviating the bed shortage, but the continuous high demand for hospitalisation by COVID-19 patients temporarily reduced the number of available beds to zero.

In the sensitivity analysis, we first examined the impact of different vaccination scenarios on the numbers of infections, hospitalisations, and severe cases, as well as the change in the number of availible beds in an ideal vaccination scenario, reflecting the influence of vaccination on medical congestion. We further analysed the specific impact of vaccination on the CCMR. The data from Figures 5 and Table 3 suggests that vaccination can diminish the scope of infections and hospitalisations and reduce severe cases. Figure 6 further illustrates that a vaccination regimen of increasing three doses of vaccine can notably shorten the duration of medical congestion, and enhance the capacity of medical resources. Subsequently, we explored the influence of medical resource-related factors on the duration of medical congestion, as detailed in Figure 7. Figure 7A demonstrates that increasing the maximum number of available beds can end medical congestion earlier. Figure 7B reveals that increasing the number of maximum capacity of hospital beds at the onset of the epidemic can delay medical resource shortages but does not end the shortage earlier. Figure 7C indicates that under a fixed total amount of medical resources, higher efficiency in resource allocation can end medical congestion earlier. In other words, before the outbreak of an epidemic, preparation should begin in advance by increasing the number of beds, equipping medical professionals, and increasing medical supplies. During the outbreak, efforts should be made to accelerate the production and distribution of medical supplies and the deployment of medical professionals.

The capability, quantity, and timing of resource allocation significantly influence the occurrence, development, and closing time of CCMR overload. Thus, a thorough consideration of vaccination and medical resource allocation becomes imperative. In contrast to Wang et al. (7), our research delineates diverse vaccination scenarios and analyses their impact on the CCMR. In contrast to Mandal (19) and Zhao (20), we not only predicted the trend of COVID-19 transmission in Taiyuan but also anticipated potential medical congestion and its duration. Compared to Ali et al. (21), we used the model to validate the effectiveness of

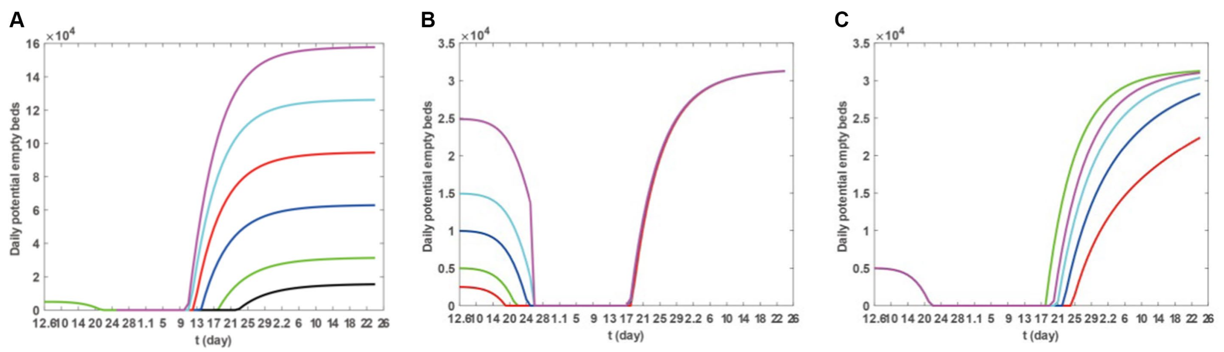

FIGURE 7
Sensitivity of the number of daily potential empty beds to the maximum bed capacity that can be provided, the initial number of respiratory department beds at the beginning and the production capability of medical resources. For **(A)**, the purple, cyan, red, blue, black, and green colours, respectively, represent the number of available beds under the scenarios of 5*Hm, 4*Hm, 3*Hm, 2*Hm, 1.5*Hm, 0.5*Hm, and Hm. For **(B)**, the magenta, cyan, blue, red, and green curves, respectively, represent the scenarios of 5*H0, 3*H0, 2*H0, 0.5*H0, and H0. For **(C)**, the cyan, black, red, blue and green curves, respectively, represent the number of available beds under the scenarios of 0.5*δ, 0.4*δ, 0.3*δ, 0.2*δ, and δ.

vaccination and explore the impact of different dosing regimens on medical congestion. Our study used the number of beds as a quantitative indicator of medical resource capacity. However, the CCMR is affected by multiple factors such as medical staff, ventilators, and patient's hospital preference, which will be addressed in future research. Additionally, our study only considered symptomatic individuals as transmission sources. Future investigations should delve into transmission from asymptomatic and incubation period infections. Therefore, future research may need to consider these factors to improve the accuracy and applicability of the model. Current research focuses primarily on prevention and control strategies for COVID-19 (3, 7, 32–36). Given the constraint of limited medical resources, future research should concentrate on how to combine vaccination and the enhancement of CCMR to alleviate medical congestion and improve local medical resource capacity.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

JG: Conceptualization, Investigation, Methodology, Software, Visualization, Writing – original draft. YL: Data curation, Formal analysis, Investigation, Project administration, Validation, Writing – review & editing. YM: Writing – review & editing. SX: Validation, Writing – review & editing. JL: Validation, Writing – review & editing. TW: Writing – review & editing. LL: Writing – review & editing. LH: Writing – review & editing. HY: Formal analysis, Project administration, Writing – review & editing. JX: Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Influenza vaccination for heart failure patients: a cost-effectiveness analysis from the perspective of Chinese healthcare system

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Purpose: Influenza infection induces cardiovascular events in heart failure (HF) patients, with potential risk reduction through vaccination. This study aims to evaluate the cost-effectiveness of influenza vaccination for HF patients in China.

Methods: We developed a Markov model with a 3-month cycle to simulate the cost-effectiveness of administering the influenza vaccine to patients with HF over a 3-year period. Patients in the model received either the influenza vaccine or a placebo, in addition to standard HF treatment. Cost data, sourced from the China Healthcare Statistic Yearbook and other public records, and effectiveness data from the IVVE (Influenza Vaccine to Prevent Adverse Vascular Events in HF) trial, were incorporated. Specifically, the cost of the influenza vaccine was 75 Chinese Yuan (CNY) (11 USD), the cost of hospitalization for heart failure (HHF) was 9,326 CNY (1,386 USD), and the cost of treatment for pneumonia was 5,984 CNY (889 USD). The study's primary outcome, the incremental cost-effectiveness ratio (ICER), quantifies the incremental cost (CNY and USD) per incremental quality-adjusted life year (QALY). Additional outcomes included total cost, total effectiveness, incremental cost, and incremental effectiveness. We conducted one-way and probabilistic sensitivity analyses (PSA) to assess certainty and uncertainty, respectively. Scenario analysis, considering various situations, was performed to evaluate the robustness of the results.

Results: In the base case analysis, influenza vaccine, compared to placebo, among Chinese HF patients, resulted in a cost increase from 21,004 CNY (3,121 USD) to 21,062 CNY (3,130 USD) and in QALYs from 1.89 to 1.92 (2.55 life years vs. 2.57 life years) per patient. The resulting ICER was 2,331 CNY (346 USD) per QALY [2,080 CNY (309 USD) per life year], falling below the willingness-to-pay threshold based on per capita GDP. One-way sensitivity analysis revealed that disparities in HHF and cardiovascular death rates between groups had the most significant impact on the ICER, while the cost of vaccines had a marginal impact. PSA and scenario analysis collectively affirmed the robustness of our findings.

Conclusion: This study suggests that adding the influenza vaccine to standard treatment regimens for Chinese patients with HF may represent a highly cost-effective option. Further real-world data studies are essential to validate these findings.

KEYWORDS

influenza vaccine, cost-effectiveness analysis, heart failure, cost-utility analysis, influenza infection

Introduction

Heart failure (HF) is a clinical syndrome characterized by structural and/or functional abnormalities of the heart (1), and HF patients exhibit an elevated propensity for vascular adverse events and other critical comorbidities (2). Although mortality rates have declined in recent years, the incidence of HF is increasing globally, placing a heavy burden on healthcare systems (3), especially in developing country. For instance, the age-standardized prevalence of patients with HF aged 25 years and above in China was recorded as 1.10% in 2017, accounting for a total of 12.1 million patients, and the annual cost per-capita for inpatient and outpatient amounts to $4,406.8 and $892.3, respectively (4).

Influenza infection is considered one of the inducing factors for cardiovascular (CV) events in HF patients, augmenting the risk of CV-related mortality, all-cause death, and hospitalization (5, 6). Hence, influenza vaccination may mitigate the risk theoretically, which was also recommended by guideline for decades (7). However, the current clinical evidence remains insufficient. Two meta-analyses suggest that influenza vaccination may reduce the overall mortality risk in HF patients, and one of them found it can also lower CV-related mortality, but both of the included studies were in low certainty of evidence (8, 9).

Furthermore, a recent multicenter, randomized, double-blinded, placebo-controlled trial investigated the efficacy of the influenza vaccine in HF patients across 30 international centers, including six in China, which contributed 13.5% of the total study population, making it the third largest participating country (10). The trial demonstrated that vaccination reduced all-cause hospitalizations (hazard ratio [HR] 0.84, 95% confidence interval [CI] 0.74–0.97, $p = 0.013$) and pneumonia incidence (HR 0.58, 95% CI 0.42–0.80, $p = 0.0006$). Although no significant difference was observed in terms of cardiovascular (CV) events, almost all outcomes in the influenza vaccine group were lower than those in the placebo group. Additionally, studies found that for the older adult, influenza vaccination is associated with direct cost savings and reduced hospitalization rates (11, 12). Therefore, administering the influenza vaccine to HF patients could potentially offer economic advantages as an affordable and straightforward intervention by reducing expenses related to all-cause hospitalizations, incidence of pneumonia, and CV events.

Particularly in China, despite recommendations from the local guidelines, the influenza vaccination rates remain significantly low in most cities (13). Therefore, a cost-effective analysis on the expense in influenza vaccination is needed. Based on the trial, this study aims to develop a mathematical model and assess the cost and effectiveness of influenza vaccination for HF patients in China.

Methods

Model overview

We developed a Markov model to assess the cost-effectiveness for Chinese patients with HF. This Markov model has found widespread application in the pharmacoeconomic evaluation of HF patients (14–16). In simple terms, the model comprised five health states: “New York Heart Association (NYHA) I,” “NYHA II,” “NYHA III,” “NYHA IV” and “Dead.” In our study, patients entered the Markov model starting from the same initial health state as in the IVVE (Influenza Vaccine to Prevent Adverse Vascular Events) trial (10), a randomized controlled trial (RCT) investigating the efficacy of influenza vaccine in HF patients. Patients in the Markov model could experience one of five events in each Markov cycle: “Hospitalization for HF (HHF),” “Pneumonia,” “CV death,” “non-CV death” or “No event.” It was assumed that patients who experienced ‘No event’ had the possibility to transition to a better, worse, or remain in the same NYHA classification during the subsequent Markov cycle. However, those who experienced ‘HHF’ could not transition to a better NYHA classification in the subsequent cycle. For example, if a patient was at a NYHA II state and experienced an HHF in the current Markov cycle, they could transition to NYHA II or NYHA III but not to NYHA I in the subsequent 3 months. However, this does not mean they could never transition to NYHA I; they could do so if their HF condition remained stable for 3 months (a Markov cycle). This assumption was in line with common clinical practice and was also used in other health technology assessments for HF treatment (16, 17). Furthermore, patients who experienced CV or non-CV death were directly transitioned to the “Dead” state, effectively exiting the Markov model.

Our Markov model simulated the 3-year cost and effectiveness for Chinese HF patients, with a cycle length of 3 months. The schematic diagram of the Markov model is shown in Figure 1. Model building and analyses were performed with TreeAge Pro 2022 (Williamstown, MA, USA).

Intervention and control

Over three consecutive influenza seasons, participants were administered either a 0.5 mL dose of inactivated influenza vaccine, or a placebo (saline), intramuscularly once a year. The trivalent vaccine (TIV) consisted of 15 μg of haemagglutinin per 0.5 mL dose for each of the two influenza type A subtypes (H1N1 and H3N2), as well as for an influenza type B/Brisbane/60/2008-like virus. Notably, in China, the influenza season typically spans from November to March. Instead of administering the influenza vaccine within the same month each year, participants were given the option to receive it on the appropriate date aligned with the local influenza season.

Participants in both groups received standard treatment for HF, in addition to either the influenza vaccine or a placebo. The standard treatment regimen for HF outlined in the China National Heart Failure Guideline 2023 encompasses a multifaceted approach, primarily revolving around several key medications. These include angiotensin converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor neprilysin inhibitors, β blockers, diuretics, mineralocorticoid receptor antagonists, and sodium and

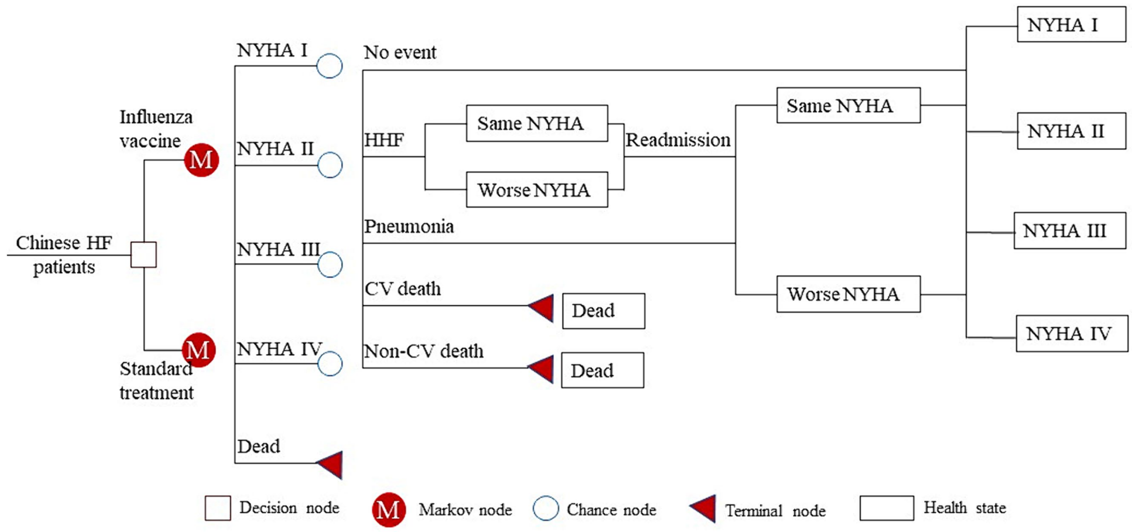

FIGURE 1
Schematic diagram of the Markov model. HF, heart failure; NYHA, New York Heart Association; HHF, hospitalization for heart failure; CV, cardiovascular.

glucose cotransporter-2 inhibitors. Additionally, for specific HF subtypes, adjunctive therapies such as digoxin and soluble guanylate cyclase stimulators may also be prescribed.

Population

The study population comprised Chinese HF patients with baseline characteristics akin to those in the IVVE trial (10). In the IVVE trial, patients had a mean age of 57.2 years, with 51.4% being female, and were predominantly classified as NYHA II (69.5%), with lesser proportions in NYHA III (26.1%) and IV (4.4%). HF with preserved ejection fraction (EF, HFpEF) was observed in 22.6% of patients, while the remaining 77.4% had HF with mildly reduced EF (HFmrEF) or HF with reduced EF (HFrEF). Comparatively, in a study exploring HF prevalence in China, Chinese patients exhibited moderate differences. They were older (63.9 ± 13.2 vs. 57.2 ± 15.3 years) and had higher systolic blood pressure (137.2 ± 22.3 vs. 125.7 ± 23.7 mm Hg) but demonstrated a lower prevalence of hypertension (55.3% vs. 64.9%). However, heart rate, gender distribution, left ventricular function, diabetes, and atrial fibrillation were similar between the cohorts (18).

The patients were randomized to allocate to either the influenza vaccine group or the placebo group in a 1:1 ratio. Regardless of their allocation, all patients received standard treatment. In the influenza vaccine group, patients received an annual intramuscular dose of 0.5 mL of inactivated influenza vaccine, which was recommended for the specific influenza season. Alternatively, patients in the placebo group received a saline injection. It's important to note that the vaccine used during the trial was trivalent, but it is replaced by a quadrivalent vaccine (QIV) currently (10, 19).

Input parameters

Transition probability

The transition probabilities for HHF and CV death were directly obtained from the IVVE trial (10). These probabilities were converted from incidence rates to 3-month transition probabilities using the formula: '3-month transition probability = 1 − exp (−3-month rate).' The 3-month rate was calculated using the formula: '3-month rate = −ln (1 − incidence rate)/Period number (Table 1). Employing the aforementioned formulas, we calculated that the 3-month rate for HHF in the vaccine group was 0.015195761, determined as −ln (1 − 334/2,560)/27.6*3, where 334 represented the HHF events in the vaccine group, 2,560 represented the total patients in the vaccine group, 27.6 represented the follow-up period, and 3 represented the cycle length (10). Subsequently, we obtained the 3-month transition probability for HHF, which was 0.015080888, calculated as 1 − exp (−0.015195761), where 0.015195761 represented the 3-month rate for HHF. Similarly, we derived the remaining transition probabilities for HHF and CV death (Supplementary material).

For the transition probability of non-CV death, it was calculated by multiplying the risk ratio (21), which represented the increased risk of non-CV death in HF patients compared to the general population of the same age, with the background mortality of the general population at the same age (20) (Table 1). The background mortality data for the general population was sourced from the China Health Statistical Yearbook 2022, publicly available (20).

The transition probabilities between NYHA classifications were accessed from a published study (16) (Table 2). Although there are no patients in the NYHA I state at the initial health state in the Markov model, patients in the NYHA II state have a chance to transition to the NYHA I state in subsequent cycles. Therefore, the health state of NYHA I was included in the Markov model, and its utility was also incorporated into the analysis.

Cost

The TIV was priced at 75 Chinese Yuan (CNY) (11 USD), while the QIV costed 138 CNY (21 USD). These prices were determined by the rates negotiated with vaccine manufacturers during collective purchasing by the Chinese government, accurately reflecting the actual cost of influenza vaccines for most Chinese people (23). In our base case analysis, we used the cost of the TIV because the QIV was

TABLE 1 Input parameters in the Markov model.

Parameters	Base case	Range	Source
Transition probabilities (per Markov cycle)			
HHF in vaccine[a]	0.0109	0.0095–0.0122	Ref. (10)
HHF in ST[a]	0.0123	0.0109–0.0138	Ref. (10)
CV death in vaccine[a]	0.0151	0.0135–0.0167	Ref. (10)
CV death in ST[a]	0.0170	0.0153–0.0187	Ref. (10)
Pneumonia in vaccine[a]	0.0026	0.0020–0.0033	Ref. (10)
Pneumonia in ST[a]	0.0045	0.0036–0.0053	Ref. (10)
Non-CV mortality of general population			
55–59 years old	0.0032	/	Ref. (20)
60–64 years old	0.0046	/	Ref. (20)
65–69 years old	0.0074	/	Ref. (20)
70–74 years old	0.0115	/	Ref. (20)
75–79 years old	0.0180	/	Ref. (20)
RR of non-CV death in HF patients	2.50	1.61–4.00	Ref. (21)
Costs, CNY (USD)			
HHF (per time)	9,326 (1,386)	4,663–13,989	Ref. (20)
ST (per year)	7,011 (1,042)	3,506–10,517	Ref. (4)
Pneumonia	5,984 (889)	2,842–13,054	Ref. (22)
Vaccine (per dose)	75 (11)	46–138	Ref. (23)
Administration (per time)	20 (3)	5–40	Local data
Utilities			
NYHA I	0.732	0.695–0.769	Ref. (24)
NYHA II	0.78	0.741–0.819	Ref. (24)
NYHA III	0.715	0.679–0.751	Ref. (24)
NYHA IV	0.66	0.627–0.693	Ref. (24)
HHF or readmission	−0.1	0.08–0.13	Refs. (14–17)
Discount rate in China	0.05	0–0.08	Ref. (25)

HHF, hospitalization for heart failure; ST, standard treatment; CV, cardiovascular; RR, risk ratio; HF, heart failure; CNY, Chinese Yuan; NYHA, New York Heart Association.
[a]The calculation method is detailed in the Supplementary materials.

not available in China at the time of the IVVE trial. Additionally, there was a 20 CNY (3 USD) cost for vaccine administration (Table 1).

When considering HF-related costs, we included the costs associated with HHF and standard HF treatment. The cost of HHF in China, sourced from the China Healthcare Statistic Yearbook, was reported as 9,326 CNY (1,386 USD) per occurrence, representing the comprehensive costs within the country (20). The cost of standard HF treatment was derived from a national survey of over 50 million individuals, which aimed to investigate the prevalence and economic burden of HF in China. According to the survey, the annual cost of standard HF treatment was 892.3 USD in 2016, which, after adjusting for the exchange rate and healthcare consumer price index (CPI) in China, equated to 7,011 CNY (1,042 USD). The CPI values for the years 2015–2022 were: 1.027, 1.038, 1.06, 1.043, 1.024, 1.018, 1.004, and 1.006, respectively (20). For pneumonia treatment, the total cost for community-acquired pneumonia was reported as 5,683 CNY (844 USD), which inflated to 5,984 CNY (889 USD) in 2022 (22). Costs before 2022 were converted to 2022 values using the healthcare CPI, and future costs were discounted at a rate of 5% (range: 0–8%), according to the China Guidelines for Pharmacoeconomic Evaluations (25).

Utility

We obtained the health-related quality of life (HRQoL) values for HF patients from a Chinese domestic study (24). This study determined that the HRQoL utility scores for patients categorized by NYHA functional class were as follows: 0.732 for NYHA I, 0.78 for NYHA II, 0.715 for NYHA III, and 0.66 for NYHA IV. Additionally, the disutility associated with HHF or readmission was recorded as −0.1, a value commonly utilized in published research (15, 16) (Table 1).

Outcome

The primary outcome of the study was the incremental cost-effectiveness ratio (ICER), which represents the incremental cost per incremental effectiveness (measured in quality-adjusted life year, QALY). In the absence of a specific willingness-to-pay (WTP) threshold recommended by the Chinese government, we followed the guidance provided in the China Guidelines for Pharmacoeconomic Evaluations (25), which aligned with the recommendations of the World Health Organization (WHO). In this context, the influenza vaccine was deemed highly cost-effective when the ICER fell below the per capita gross domestic product (GDP), cost-effective if it was between one to three times the per capita GDP, and not cost-effective if it exceeded three times the per capita GDP (2022). The per capita GDP in China stood at 85,698 CNY (12,734 USD) in 2022. Secondary outcomes encompassed total cost, total effectiveness, incremental cost, and incremental effectiveness.

In our base case analysis, we set the starting age at 57 years old to align with the average age in the IVVE trial. Additionally, in the scenario analysis, we considered starting ages of 65, to align with the average age of HF patients in the China Hypertension Survey. Furthermore, we conducted additional scenario analyses to test the robustness of the results. These scenarios involved evaluating the cost-effectiveness of the vaccine in HF patients at the highest price of point and considering an alternative scenario where the HHF rate from the Urban Employee Basic Medical Insurance (UEBMI) scheme was used instead of the data from the IVVE trial (4).

Sensitivity and scenario analysis

We conducted a one-way sensitivity analysis to evaluate how individual input parameters influenced the ICER. During this analysis, parameters were systematically varied within their 95% CI or predefined ranges. Specifically, for transition probabilities and utilities, we calculated and incorporated the 95% CI into the sensitivity analysis. Meanwhile, for the cost of the vaccine, we utilized the highest and lowest reported values as the range. Regarding the cost of HHF per time and annual standard treatment cost, due to the absence of reported CI or ranges, we employed 0.5 times and 1.5 times the reported costs as lower and higher bounds, respectively. These values were sourced from reputable references such as the China Healthcare Statistic Yearbook or national surveys, aiming to encompass the typical cost spectrum for Chinese HF patients. The results of the one-way sensitivity analysis were visually represented using a tornado diagram. For the probabilistic sensitivity analysis (PSA), we performed

10,000 Monte Carlo simulations to assess the robustness of our findings. In this analysis, all cost-related parameters were modeled with a gamma distribution, while transition probabilities and utilities were modeled with a beta distribution. Additionally, the relative risk (RR) of non-CV death in HF patients compared to the general population followed a log-normal distribution. The results of the PSA were presented through a scatter plot and a cost-effectiveness acceptability curve.

Results

Base case analysis

In our base case analysis, after a 3-year simulation, each Chinese HF patient in the cohort would accumulate approximately 21,004 CNY (3,121 USD) in costs, resulting in an effectiveness of 1.89 QALYs (2.55 life years) with standard treatment. Alternatively, when administering the influenza vaccine alongside standard treatment, the cost would increase slightly to 21,062 CNY (3,130 USD), resulting in an effectiveness of 1.92 QALYs (2.57 life years) within the vaccine group. Comparing the inclusion of the influenza vaccine to standard treatment alone, the ICER amounted to 2,331 CNY (346 USD) per QALY [or 2,080 CNY (309 USD) per life year], which fell below the WTP threshold based on per capita GDP (Table 3).

Scenario analyses across various conditions yielded consistent results. In scenarios with the highest influenza vaccine costs or a starting age set at 65, the ICER remained below 85,698 CNY (12,734 USD) per QALY. When alternative HHF rates were considered, the influenza vaccine showed reduced costs and increased effectiveness (Table 3).

TABLE 2 Transition probabilities of NYHA classifications in the Markov model (every 3 months).

From to	NYHA I	NYHA II	NYHA III	NYHA IV
NYHA I	0.977	0.019	0.004	0
NYHA II	0.008	0.981	0.010	0.001
NYHA III	0	0.034	0.960	0.006
NYHA IV	0	0	0.055	0.945

Sensitivity analysis and scenario analysis

One-way sensitivity analysis revealed that discrepancies in rates of HHF and CV death between groups had the most significant impact on the ICER, but none of the input parameters resulted in an ICER exceeding the WTP threshold of 85,698 CNY (12,734 USD) per QALY (Figure 2).

Results from the PSA showed that administering the vaccine to Chinese HF patients alongside standard treatment was dominant in 39.9% of cases and highly cost-effective in 56.54% of scenarios. Overall, the vaccine was considered highly cost-effective in at least 96.44% of scenarios (Figure 3). The acceptability curve indicated that at the current WTP threshold of 85,698 CNY (12,734 USD) per QALY, vaccine administration had over 90% acceptability, while standard treatment had less than 10% acceptability (Figure 4).

Discussion

In this study, the ICER of the influenza vaccine compared to a placebo for Chinese patients with HF was calculated at 2,331 CNY

TABLE 3 Results of base case and scenario analysis.

Strategy	Total cost, CNY (USD)	Incremental cost, CNY (USD)	Total effectiveness, QALY/LY	Incremental effectiveness, QALY/LY	ICER, CNY (USD) per QALY	ICER, CNY (USD) per LY
Base case						
Standard treatment	21,004 (3,121)		1.89/2.55			
Vaccine + standard treatment	21,062 (3,130)	58 (9)	1.92/2.57	0.02/0.03	2,331 (346)	2,080 (309)
Scenario 1: Cost of influenza vaccine at the highest price						
Standard treatment	21,004 (3,121)		1.89/2.55			
Vaccine + standard treatment	21,224 (3,130)	220 (33)	1.92/2.57	0.02/0.03	8,869 (1,318)	7,914 (1,176)
Scenario 2: HHF rate from UEBMI						
Standard treatment	34,668 (5,151)		1.75/2.55			
Vaccine + standard treatment	33,476 (4,974)	−1,192 (−177)	1.78/2.57	0.04/0.03	−31,165 (4,631)	−42,905 (−6,375)
Scenario 3: Starting age = 65 years old						
Standard treatment	24,984 (3,712)		1.86/2.51			
Vaccine + standard treatment	25,073 (3,726)	89 (13)	1.89/2.53	0.02/0.03	3,659 (544)	3,266 (485)

CNY, Chinese Yuan; QALY, quality-adjusted life year; LY, life year; HHF, hospitalization for heart failure; UEBMI, urban employee basic medical insurance.

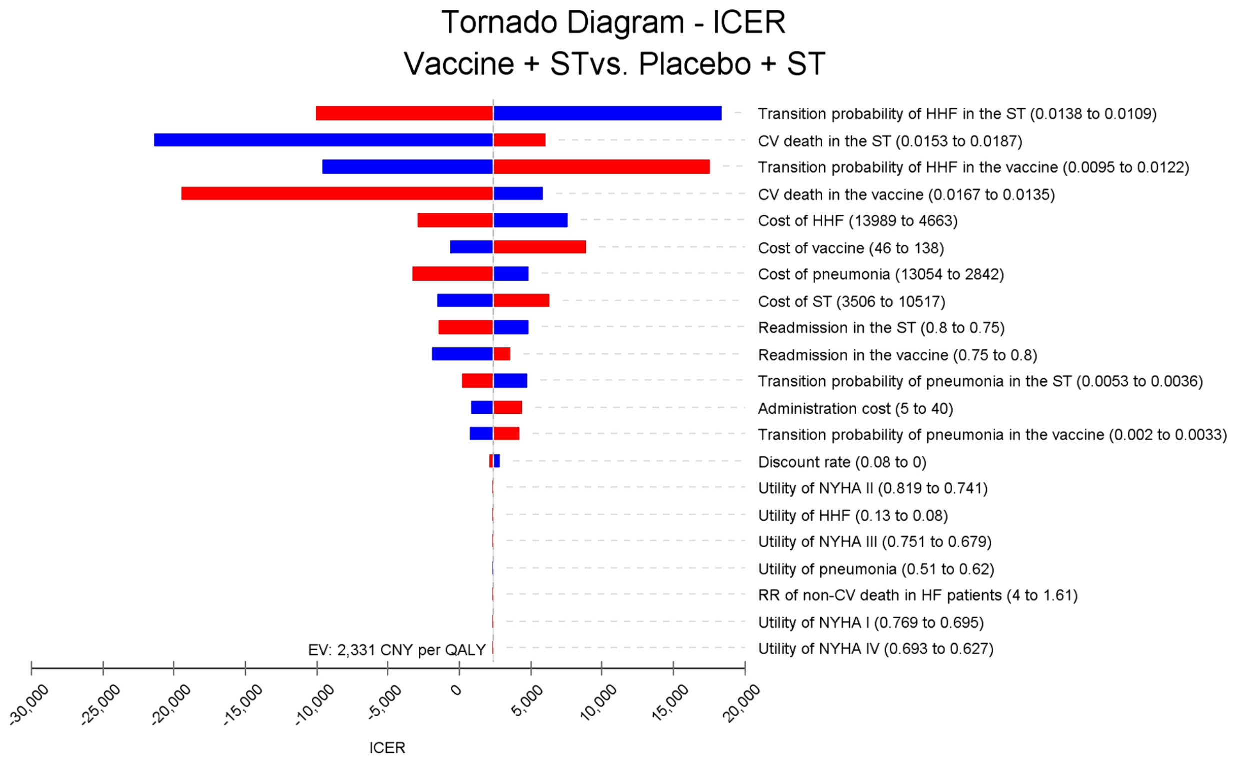

FIGURE 2
Tornado diagram for ICER of vaccine compared to placebo in Chinese HF patients. The disparities in HHF and CV death rates between groups have the most significant impact on the ICER, but do not exceed 20,000 Chinese Yuan (2,972 USD) per quality-adjusted life year. ICER, incremental cost-effectiveness ratio; ST, standard treatment; HHF, hospitalization for heart failure; CV, cardiovascular; NYHA, New York Heart Association.

(346 USD) per QALY [2,080 CNY (309 USD) per life year], falling below the per capita GDP threshold of 85,698 CNY (12,734 USD) per QALY. Additionally, one-way sensitivity analysis revealed that varying parameters within specified ranges did not yield an ICER surpassing the WTP threshold. Moreover, PSA results indicated that incorporating the vaccine into standard HF treatment was highly cost-effective in 96.44% of scenarios. These consistent findings across sensitivity analyses underscore the robustness of this study and underscore the influenza vaccine's status as a highly cost-effective intervention for Chinese HF patients.

In the IVVE trial, although the influenza vaccine did not significantly reduce adverse vascular events throughout the entire trial period, it does not negate the cost-effectiveness of vaccination in this economic evaluation. This could be attributed to several reasons: Firstly, in the original study, nearly all outcomes (including all-cause death, CV death, non-fatal myocardial infarction, non-fatal stroke, all-cause hospitalization, HHF, and pneumonia) except for non-fatal stroke were lower in the influenza vaccine group compared to the placebo group, with only all-cause hospitalization and pneumonia showing statistical significance. These observed synergistic effects may enhance vaccine effectiveness. Secondly, when considering only periods during peak influenza circulation, a significant decrease in all-cause death, CV death, and pneumonia was observed in the vaccine group. On one hand, the reduction of CV events and pneumonia decreased the related costs associated with the vaccine; on the other hand, this reduction also improved effectiveness. These factors collectively contribute to the cost-effectiveness of the influenza vaccine in Chinese HF patients.

Furthermore, it should be noted that the influenza vaccine used in the IVVE trial was a TIV, consisting of two strains of influenza A virus (H1N1 and H3N2) and one lineage of influenza B virus (Yamagata or Victoria). The production of this vaccine was undertaken by Sanofi Pasteur Biologics Co., Ltd. at a cost of 75 CNY (11 USD) per dose. Currently, QIV which included an additional strain of influenza B virus absent from TIV, have demonstrated superior protection and paralleled adverse effects globally (26, 27). Similarly, QIV is recommended by The Chinese Center for Disease Control and Prevention, and likely to be more cost-effective for the elder in China (28). And the QIV produced by Sanofi Pasteur incurs higher cost at 138 CNY (21 USD) per dose. As depicted in scenario 1, the highest price was set at 138 CNY (21 USD) per dose, which currently stands as the most expensive TIV available in China, resulting in an ICER with 8,869 CNY (1,318 USD) per QALY [7,914 CNY (1,176 USD) per life year], lower than WTP. Therefore, if using QIV under current circumstances in China, vaccination is also highly cost-effective even with higher cost.

Currently, the influenza vaccination rate in China was not optimistic. First, vaccination policies have a significant impact on vaccination rates. For instance, in the United States, universal vaccination is recommended for all individuals (29), whereas in most countries, it is only advised for those susceptible to influenza. In China, high-risk groups are defined as individuals aged 60 and above, children under 5 years old, pregnant women, and people with chronic illnesses. In fact, a Chinese national cross-sectional survey conducted in 2014–2015, encompassing a sample of 74,484 individuals aged over 40 years old, revealed that the influenza vaccination rate among

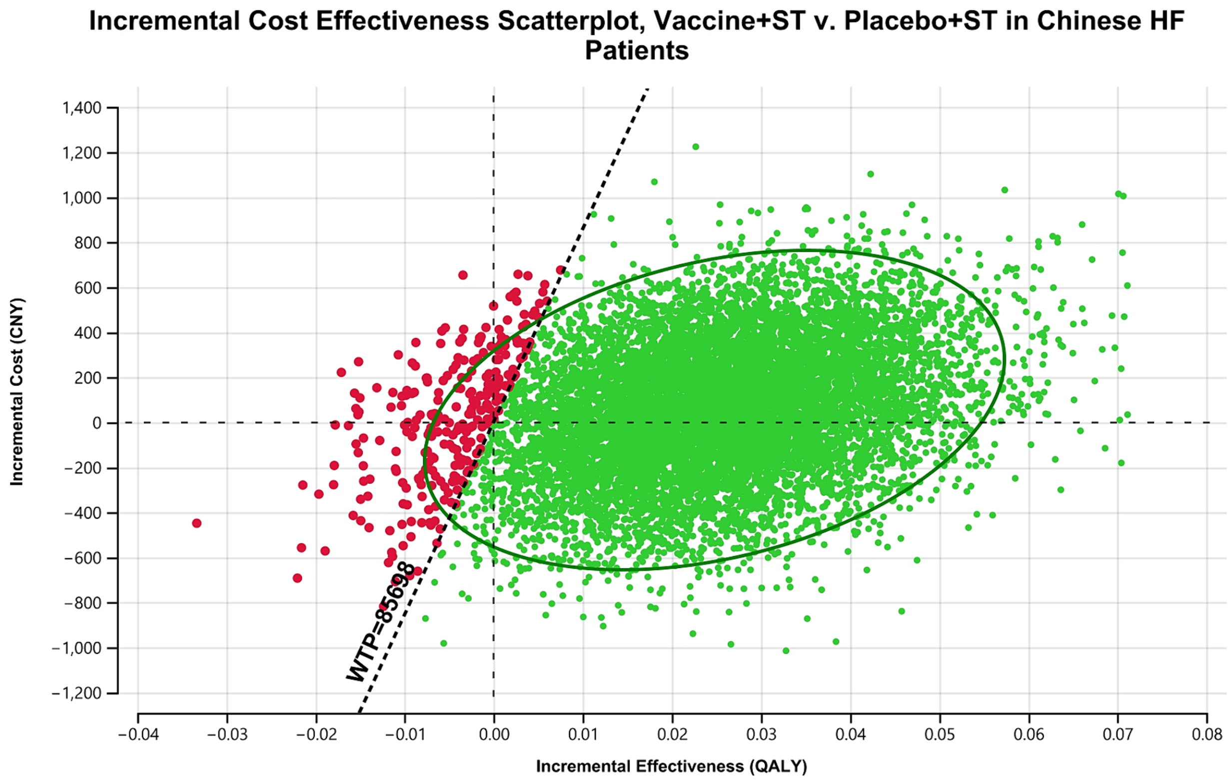

FIGURE 3
Scatterplot analysis of incremental cost effectiveness: influenza vaccine plus standard treatment vs. placebo plus standard treatment in Chinese HF patients. In most occasions, influenza vaccine is dominant or highly cost-effective compared with placebo. ST, standard treatment; HF, heart failure; CNY, Chinese Yuan; WTP, willingness-to-pay; QALY, quality-adjusted life year.

individuals with chronic diseases was merely 4.0% (30). Secondly, there were significant variations in vaccination rates across different regions within China, which were caused by economic gap. For instance, the eastern region exhibited a higher vaccination rate compared to the western region (26.1% vs. 6.7%) (31, 32). In addition, as influenza vaccinations are predominantly not covered by mandatory health insurance schemes, local reimbursement ratio could also influence the vaccination rate (33). Such as Shenzhen city, the government fully covered the reimbursement for influenza vaccination in elder above 60 years old; however, in Guangzhou, a similarly developed city, reimbursement was funded through the surplus of Basic Social Medical Insurance for Urban Employees and the vaccination rate was lower. At the same time, relevant medical authorities have also implemented novel measures to bolster vaccination rates. A study has revealed that video-based education represents an effective and feasible approach for improving older individuals' willingness and uptake of influenza vaccination (34). And interestingly, a pragmatic trial has suggested that a pay-it-forward intervention, which provides complimentary influenza vaccines along with an opportunity to contribute financially toward supporting the immunization of other individuals, could augment influenza uptake (35).

The prevalence of HF patients in China is substantial, imposing a significant burden. It is worth noting that there is a dearth of cost–benefit analyses pertaining to vaccination for HF patients in China. Meanwhile, several studies have conducted cost–benefit analyses on vaccination for older adult individuals in China (36, 37), yielding similar outcomes. Given the considerable overlap between the HF and older adult populations, it could be inferred that vaccination may be cost-effective in HF patients and exhibit enhanced efficacy, which was consistent with our findings. Overall, vaccination is a highly cost-effective intervention for HF patients, and recommended for widespread adoption among the population. Despite the gradual increase in vaccination rates in China over the past years, it remains a formidable challenge for relevant departments to augment vaccination coverage to align with that of developed nations, necessitating further concerted efforts.

This study has several limitations. Firstly, the study employed a simple Markov model based on the IVVE trial. This model considered vaccination as a static process and did not account for varying vaccination rates, timing, herd immunity effects, or adherence to vaccination schedules. Secondly, despite being a multicenter, randomized, double-blind, placebo-controlled trial, the IVVE trial recruited participants from various countries and regions, including Asia. Therefore, the participants in the IVVE trial may not fully represent Chinese patients with HF. Moreover, adverse events in the vaccination group and the control group were also not taken into account, although both groups shared comparable and extremely low incidence of adverse events. Nevertheless, we still hold the belief that this research is useful for policymakers, providing stable and conservative results.

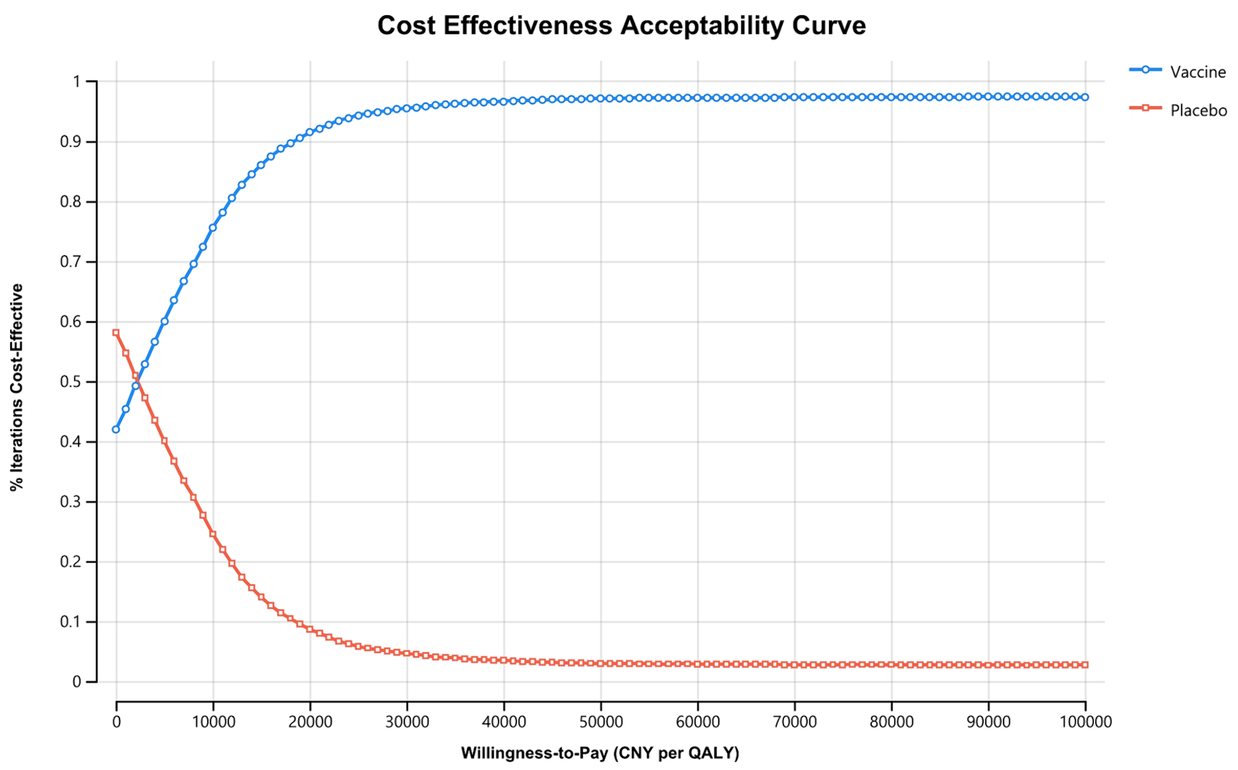

FIGURE 4
Cost effectiveness acceptability curve. The WTP threshold where vaccine is more acceptable than standard treatment in Chinese HF patients falls below 5,000 CNY (743 USD) per QALY, and vaccine is more acceptable under the current willingness-to-pay threshold of 85,698 CNY (12,734 USD) per QALY. CNY, Chinese Yuan; QALY, quality-adjusted life year.

Conclusion

The findings of this study indicate that influenza vaccination is likely to be a highly cost-effective preventive measure for Chinese HF patients, thus warranting its widespread adoption among this patient population.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

MZ: Writing – review & editing, Writing – original draft. FL: Software, Methodology, Investigation, Formal analysis, Data curation, Writing – review & editing. LW: Writing – review & editing, Funding acquisition, Conceptualization, Methodology, Investigation, Formal analysis, Data curation. DC: Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Data curation, Conceptualization.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1348207/full#supplementary-material

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The total joint arthroplasty care patterns in China during the COVID-19 pandemic: a multicenter cohort study

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Background: The COVID-19 pandemic has profoundly affected the care practices of total joint arthroplasty (TJA) throughout the world. However, the impact of the pandemic on TJA care practices has not yet been studied in China.

Methods: This retrospective multicenter cohort included patients aged 18 years or older who underwent TJA between January 2019 and December 2019 (prepandemic period) and January 2020 to December 2021 (pandemic period). Data were obtained from the medical records of 17 Chinese hospitals. Interrupted time series (ITS) analysis was used to estimate differences in monthly TJA volume, hospitalization proportion of TJA, preoperative characteristics, postoperative complications, 30-day readmissions, length of stay (LOS), and costs in inpatients undergoing TJA between the prepandemic and pandemic periods. Multivariate regression and propensity score matching (PSM) analyses were used to assess the impact of the COVID-19 pandemic on hospital complications, readmissions at 30 days, LOS, and costs at the patient level.

Results: A total of 752,477 inpatients undergoing TJA in the prepandemic period, 1,291,248 in the pandemic period, with an average 13.1% yearly decrease in the volume of TJA during the pandemic. No significant changes were observed in the proportion of hospitalizations for TJA. ITS analyses showed increases in the proportion of comorbidities (8.5%, 95% CI: 3.4–14.0%) and the number of comorbidities (15.6%, 95% CI: 7.7–24.1%) in TJA cases during the pandemic, without increasing LOS, costs, complications, and readmission rates. Multivariate and PSM analyses showed 6% and 26% reductions in costs and readmission rates during the pandemic, respectively.

Conclusions: The COVID-19 pandemic was associated with more severe preoperative conditions and decreased volume, costs, and readmission rates in patients undergoing TJA in China. These findings demonstrate that the COVID-19 pandemic did not have a dramatic impact on the TJA care pattern in China, which may have resulted from active and strict strategies in combating COVID-19 as well as a rapid response in hospital management.

KEYWORDS

COVID-19 pandemic, total joint arthroplasty, interrupted time series, healthcare pattern, surgery

1 Introduction

The 2019 coronavirus disease pandemic (COVID-19) has had an unprecedented impact on the global healthcare system, especially surgical care. Many countries have published recommendations on the suspension of non-urgent or elective procedures in response to the increase in COVID-19 cases (1, 2). For example, in the United States, the American College of Surgeons, the Centers for Medicare and Medicaid Services (CMS), and the American Academy of Orthopedic Surgeons advised postponing or canceling elective surgeries at the start of the COVID-19 pandemic (3, 4). Subsequently, total joint arthroplasty (TJA), including total hip arthroplasty (THA) and total knee arthroplasty (TKA), which comprise a substantial share of elective surgeries, has led to a dramatic reduction in resulted in a dramatic reduction in the number of cases, ranging from 30 to 94% (5–8).

Furthermore, it has been reported that the COVID-19 pandemic could affect the clinical outcomes and other practice patterns of TJA, although the results have been inconsistent. A study in India showed that the postoperative complication rate after TJA has increased significantly during the pandemic (9). Studies in the United States did not find an increase in the complication rate but a decrease in length of stay (LOS) (5, 10, 11).

Compared to other countries, China has not enforced policies that restrict or limit the number and arrangement of elective surgeries. Instead, the Chinese government has implemented a series of active strategies to prevent the spread of the virus and protect the wellbeing of citizens, including early detection and reporting of infected cases, contact tracing and quarantine management, strict border control, mandatory mask-wearing, temperature checks, and gathering restriction measures (12, 13). Hospitals designated fever clinics and isolation wards for suspected and confirmed COVID-19 cases. Patients were screened for symptoms, travel histories, and polymerase chain reaction (PCR) tests prior to admission (14, 15). However, surgical practice patterns during the COVID-19 pandemic in China, such as TJA, have never been evaluated. It remains to be clarified whether COVID-19 has had a substantial effect on TJA care in China. Therefore, this study aimed to compare the volume of cases, proportion of hospitalizations for TJA, characteristics, postoperative complications, readmissions at 30 days, LOS, and costs of patients undergoing TJA before and during the pandemic in China.

2 Methods

2.1 Data source and study population

A retrospective cohort study was conducted on adult patients who underwent THA and TKA from January 2019 to December 2021. The study extracted the cover page of medical records from hospital information systems (HIS) in 17 hospitals across various regions of China, including the middle, east, west, north, south, and Beijing (capital). These 17 hospitals adopted an unified HIS and utilized identical fields and data dictionary within the cover page, which included patients' demographic data, diagnosis and procedure information, clinical outcomes, and resource utilization. All inpatients who underwent elective TJA were queried according to the International Classification of Diseases, Ninth Revision, Clinical Modification, Third Volume (ICD9-CM3; THA: 81.51, TKA: 81.54). Elective cases were identified based on the indicators for elective admissions or emergency status. Patients aged $<$ 18 years of age were excluded due to the rarity and distinct characteristics of TJA patients $<$18. This study was exempt from institutional review board approval because all the data were historically de-identified. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

2.2 Study periods

To compare the TJA practice patterns before and during the pandemic, we defined two periods: a prepandemic period from January 1, 2019, to December 30, 2019, and a pandemic period from January 1, 2020, to December 30, 2021. We considered January 1, 2020, the cutoff date because the Chinese government started to implement strict measures to control and prevent the spread of COVID-19 in January 2020. We then divided the TJA patients into two groups based on their hospital admission date.

2.3 Variables and outcomes studied

For patient covariates, we included age, sex, and comorbidities (congestive heart failure, cardiac arrhythmias, and pulmonary circulation disorders). Furthermore, we calculated the Elixhauser score to measure the severity of comorbidities (the method for calculating Elixhauser score was presented in Supplementary Table S1) (16).

As outcomes, we assessed postoperative complications in the hospital, readmission within 30 days, LOS, and inflation-adjusted costs. Complications were determined from the diagnostic codes of the primary and secondary International Classification of Diseases, Tenth Revision (ICD10) and ICD9-CM3, according to the definition proposed by the Centers for Medicare & Medicaid Services (CMS) (17). Additionally, the monthly volume and proportion of hospitalizations associated with TJA, monthly average patient characteristics, and clinical outcomes were summarized to evaluate monthly changes before and during the pandemic.

2.4 Statistical analysis

The characteristics and outcomes of patients before and during the pandemic were described and compared. Continuous variables are expressed as mean (standard deviation) and compared using the *t*-test or Wilcoxon rank-sum test based on the distribution of the data. Categorical variables were expressed as counts (percentages) and compared using the chi-square test. Given the large sample size, the *P*-values for most statistical tests indicated significant differences, as well as effect size (the Cramér V for categorical variables and Cohen *d* for continuous variables), to estimate the difference between the two periods (18, 19).

We performed interrupted time series (ITS) analyses (20) to assess the association between pandemic onset and monthly TJA volumes, the proportion of hospitalizations for TJA, and average patient characteristics. Quasi-Poisson regressions were fitted to estimate the mean percentage change and 95% confidence intervals (95% CI) in monthly TJA volumes and the proportion of TJA hospitalizations between the two periods, adjusted for seasonality. Log-linear regression models were constructed to evaluate whether patient characteristics changed monthly during the pandemic.

To evaluate the relationship between the pandemic and outcomes (including postoperative complications, readmission within 30 days, LOS, and inflation-adjusted costs), we also conducted ITS analyses. Quasi-Poisson regressions were used for monthly in-hospital complications and 30-day readmissions, adjusted for seasonality and monthly patient characteristics. Log-linear regressions were fitted for the monthly average LOS and costs. Furthermore, we constructed multivariate regression models to evaluate the association between the pandemic and outcomes, adjusted for patient-level age, sex, number of comorbidities (Model 1), Elixhauser score (Model 2), and comorbidities (Model 3). Logistic regressions were used to estimate odds ratios (OR) and 95% confidence intervals (CI) of in-hospital complications readmissions within 30 days during the pandemic compared to the prepandemic period, and log-linear regressions were used to estimate the relative ratios and 95% CI. Additionally, propensity score matching (PSM) methods were used to further assess and validate the association between pandemics and outcomes (21). Logistic regression was firstly used to estimate the probability of TJA admission during the pandemic period according to patient age, sex, number of comorbidities of the patient (model 1), Elixhauser score (model 2), and comorbidities (model 3). The TJA cases before and during the pandemic were then 1:1 matched using a greedy matching algorithm. The caliper for matching we set is 0.1 times the standard deviation of the propensity score on the logarithmic scale. Logistic and log-linear regression models were created to estimate the relationships between pandemic and in-hospital complications, 30-day readmissions, LOS, and costs in the matched sample.

A 2-sided $P < 0.05$ was defined as significance. Statistical analyses were performed using R, version 4.0.2 (R Project for Statistical Computing).

3 Results

3.1 TJA volume and proportion of hospitalizations

In total, 2,043,725 adult hospitalizations were identified between 2019 and 2021; 752,477 were from the prepandemic period, and 1,291,248 from the pandemic period. During the prepandemic period, 6,033 of 752,477 (0.80%) patients underwent TJA, and during the pandemic period, 10,486 of 1,291,248 (0.81%) underwent TJA (Figure 1). None of the included cases were infected with COVID-19. The mean volume of TJA cases per year during the pandemic period represented a 13.1% decrease compared to 2019. At the beginning of the pandemic, there was a marked decrease in TJA cases, particularly from February to April 2020, with the monthly volume of TJA dropping by 87.4, 66.8, and 52.8%, respectively, compared to the same period in 2019. Subsequently, the monthly TJA volume gradually increased, reaching prepandemic levels. Based on the ITS analysis, there was a statistically significant difference in the average monthly volume of TJA cases before and during the pandemic period (relative difference: −50.3%; 95% CI: −66.2 to −26.9%; Figure 2A). For the monthly proportion of hospitalizations, the mean monthly proportion of TJA during the pandemic period was not significantly different from that during the prepandemic period (relative difference: 1.3%; 95% CI −19.4 to 27.4%; Figure 2B).

3.2 Patient characteristics

The characteristics of the patients in the TJA group were similar before and during the pandemic, except for the number of comorbidities (Table 1). Although age, proportion of comorbidities, and Elixhauser score in patients who underwent TJA during the pandemic were significantly higher than before, absolute effect sizes were all lower than 0.1 (Table 1). Compared to the prepandemic period, patients who underwent TJA were likely to have more comorbidities (1.61 vs. 1.82), with an absolute effect size >0.1 (Table 1). ITS analyses showed that the average monthly proportion of comorbidity (relative difference: 8.5%, 95% CI: 3.4–14.0%) and many comorbidities (relative difference: 15.6%, 95% CI: 7.7–24.1%) in cases of TJA were significantly higher during the pandemic than during the prepandemic period (Figure 3).

3.3 Clinical outcomes

Based on ITS analysis, the average monthly in-hospital complications, readmissions at 30 days, and LOS during the pandemic period did not differ significantly from those during the prepandemic period (Supplementary Figures S1–S3). There was a minor reduction in monthly average costs during the pandemic period (relative difference: −0.3%, 95% CI: −0.5 to −0.1%, Supplementary Figure S1). In the unadjusted comparisons, readmissions and costs at 30 days during the pandemic period were significantly lower than those during the prepandemic period. In multivariate regression models adjusted for the patient's age, sex, and comorbidities, there was still a 6% reduction in costs (relative ratio: 0.9, 95% CI: 0.9–1.0) and a 26% (OR: 0.7, 95% CI: 0.6–0.9) reduction in the risk of readmissions within 30 days (Table 2, Model 3). The PSM analyses showed results similar to the multivariate regression analyses (Supplementary Table S2).

4 Discussions

Based on the available evidence, this is the first study to compare TJA practice patterns before and during the COVID-19 pandemic in China, where strict measures were implemented to prevent the spread of the COVID-19 virus at the social level, but no strategies were implemented to restrict or suspend the arrangement of elective surgeries at the hospital level. In this

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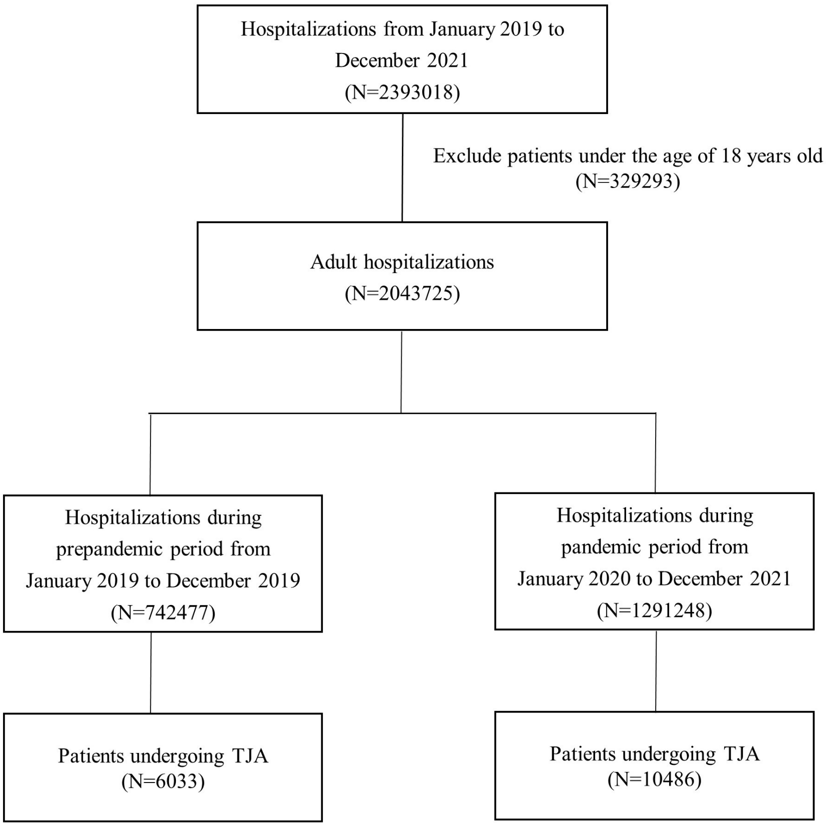

FIGURE 1
Selection flow chart for target population.

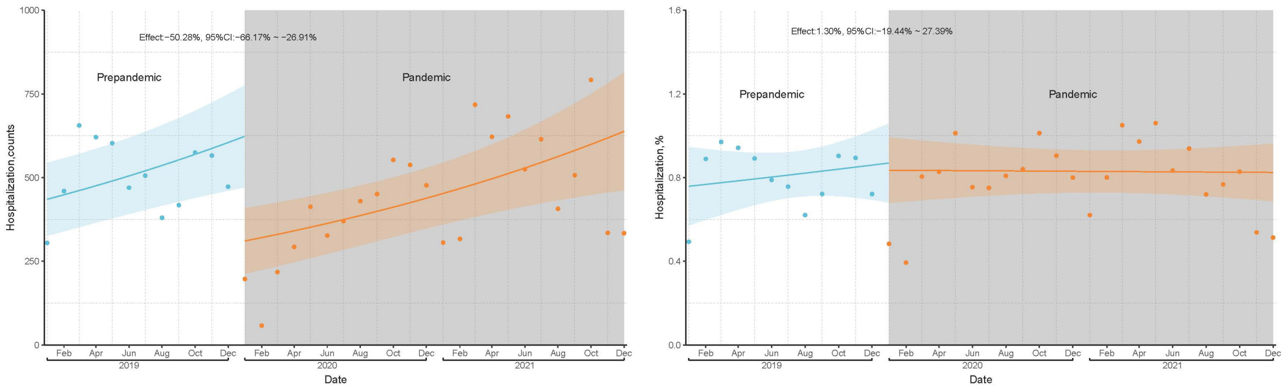

FIGURE 2
TJA volume and hospitalization proportion before and during pandemic based on ITS analyses.

study, we evaluated the TJA care patterns, which account for many elective surgeries during the COVID-19 pandemic in China, evaluating the TJA volumes, the proportion of hospitalizations for TJA, patient characteristics, LOS, costs, in-hospital complications, and readmissions within 30 days.

In this study, a 13.1% annual decrease was observed in TJA volume during the pandemic period, compared directly to that in the prepandemic period. This decrease in hospitalized inpatients who underwent TJA was lower than reported in other countries, which ranged from 30 to 94% (2, 5–8, 22). Similar to other studies, there was also a steep decline in TJA volume during the early stages of the pandemic in China, which showed an 87.39% decrease in February 2020 compared to the same period in 2019. Subsequently, the volume of TJA gradually increased and recovered to prepandemic levels. In 2021, the annual volume in 2021 (6,116) was even higher than that in 2019 (6,033). The return of the TJA volume to prepandemic levels has never been reported in other studies. Heckmann et al. showed that there was also a 31.9%

TABLE 1 Characteristics and outcomes of patients undergoing TJA during prepandemic and pandemic period.

Characteristics/outcomes	Prepandemic period (*N* = 6,033)	Pandemic period (*N* = 10,486)	Effect size*	*P*
Age, mean (SD)	61.18 (12.70)	61.76 (12.68)	0.0457	0.0012
Male,%	2,004 (33.22)	3,487 (33.25)	0.0004	0.9617
Comorbidity,%	4,352 (72.14)	8,081 (77.06)	0.0550	<0.0001
Number of comorbidites, mean (SD)	1.61 (1.62)	1.82 (1.75)	0.1280	<0.0001
Elixhauser score, mean (SD)	0.83 (2.81)	0.95 (3.04)	0.0410	0.0064
Comorbidity				
Congestive heart failure,%	262 (4.34)	474 (4.52)	0.0041	0.5944
Caridiac arrhythmia,%	146 (2.42)	266 (2.54)	0.0036	0.6433
Valvular disease,%	15 (0.25)	25 (0.24)	0.0010	0.8976
Pulmonary circulation disorders,%	2 (0.03)	1 (0.01)	0.0084	0.6277
Peripheral vascular disorders,%	121 (2.01)	274 (2.61)	0.0191	0.0139
Uncomlicated hypertension,%	1,964 (32.55)	3,590 (34.24)	0.0171	0.0276
Comlicated hypertension,%	2 (0.03)	8 (0.08)	0.0084	0.4491
Neurological disorders,%	50 (0.83)	92 (0.88)	0.0025	0.7447
Chronic pulmonar disease,%	98 (1.62)	175 (1.67)	0.0017	0.8290
Uncomplicated diabetes,%	711 (11.79)	1,339 (12.77)	0.0144	0.0647
Complicated diabetes,%	26 (0.43)	42 (0.40)	0.0023	0.7687
Hypothyroidism,%	37 (0.61)	66 (0.63)	0.0010	0.8992
Renal failure,%	48 (0.80)	64 (0.61)	0.0109	0.1623
Liver disease,%	122 (2.02)	272 (2.59)	0.0180	0.0204
Peptic ulcer disease without bleeding,%	28 (0.46)	36 (0.34)	0.0094	0.2288
Metastatic cancer,%	6 (0.10)	6 (0.06)	0.0075	0.5027
Solid tumor without metastasis,%	7 (0.12)	29 (0.28)	0.0166	0.0331
Rheumatoid arthritis,%	281 (4.66)	462 (4.41)	0.0059	0.4521
Coagulopathy,%	17 (0.28)	34 (0.32)	0.0037	0.6358
Fluid and electrolyte disorders,%	29 (0.48)	103 (0.98)	0.0271	0.0005
Blood loss anemia,%	9 (0.15)	38 (0.36)	0.0193	0.0132
Deficiency anemia,%	2 (0.03)	11 (0.10)	0.0123	0.1952
Alcohol abuse,%	72 (1.19)	155 (1.48)	0.0118	0.1301
Depression,%	25 (0.41)	54 (0.51)	0.0070	0.3669
Clinical outcomes				
In-hospital complications,%	26 (0.43)	62 (0.58)	0.0096	0.2122
30-day readmissions,%	141 (2.34)	179 (1.66)	0.0237	0.0021
LOS, mean (SD), days	11.36 (10.56)	11.24 (7.23)	−0.0143	0.9767
Inflated adjusted costs, mean (SD), CNY	81,392.34 (32,147.66)	76,437.41 (31,101.05)	−0.1575	<0.0001

*For categorical variables, Cramér V was used as an effect size measurement for assessing the strength of the association between two categorical variables. Cramér's V ranges from 0 to 1, indicating that it quantifies the magnitude rather than the direction of the association.

decrease in the peak of TJA volume in 2020 compared to before the pandemic (23). Gordon et al. observed that the TJA volume plateaued at 81.5% of the prepandemic baseline (10). Some studies attributed the decrease in TJA volume to fear of exposure to the virus in hospitals, in addition to restrictive policies (2, 24). However, the return of the TJA volume to prepandemic levels shown in our study indicated that strict strategies to prevent the spread of COVID-19 among the population could reduce the fear of contracting the virus in patients. However, the decrease in TJA volume increased to 50.28% when ITS analysis was performed. Unlike previous studies that estimated the reduction in TJA cases based on the assumption that the TJA volume would be stable if

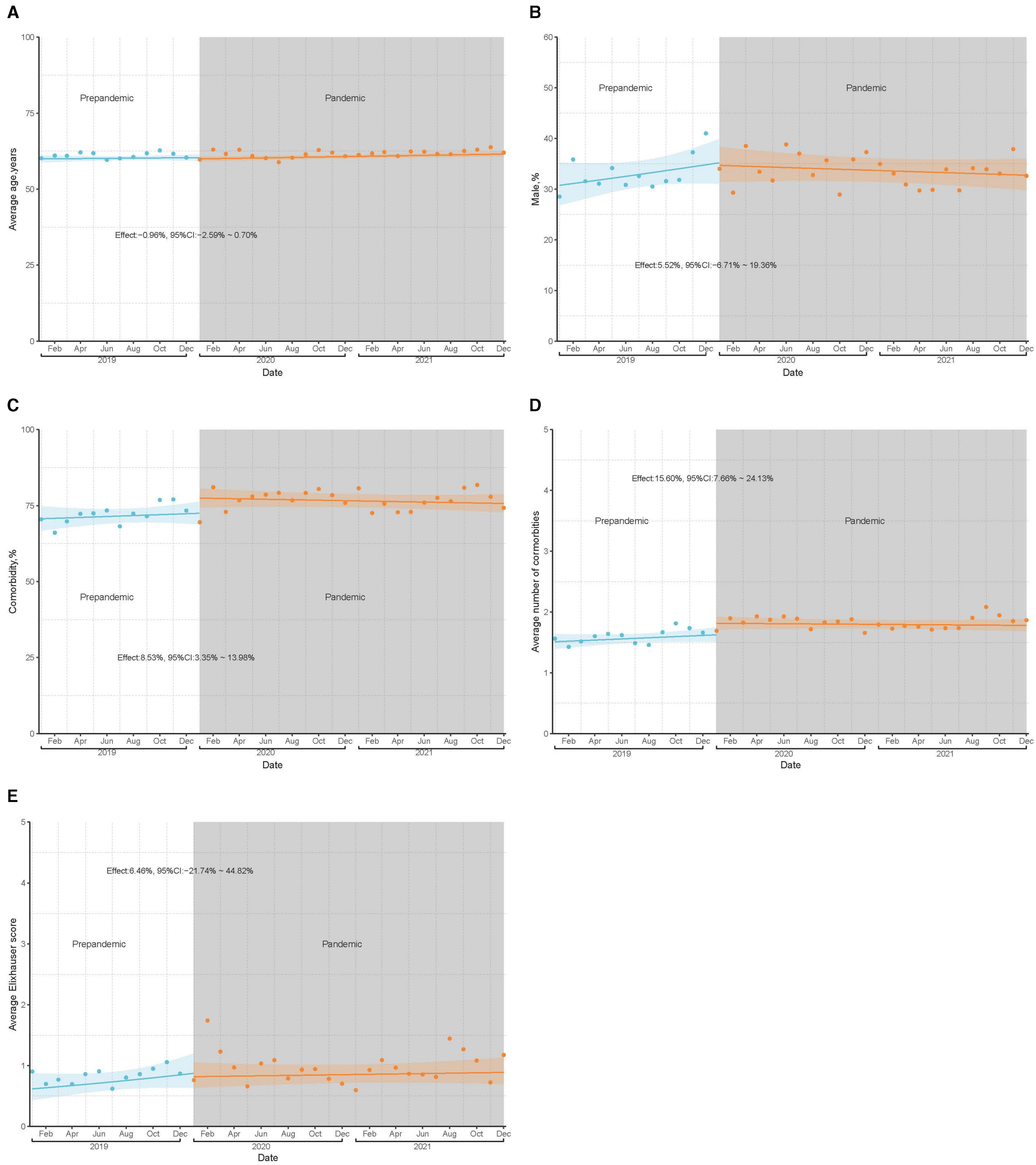

FIGURE 3
Preoperative characteristics of inpatients undergoing TJA before and during pandemic based on ITS analyses. **(A)** illustrates the average age of patients per month before and during the pandemic; **(B)** shows the proportion of male patients per month before and during the pandemic; **(C)** shows the proportion of patients with comorbidities per month before and during the pandemic; **(D)** represents the average number of comorbidities per patient per month before and during the pandemic; **(E)** shows the average comorbidity score (Elixhauser score) per patient per month before and during the pandemic.

there were no pandemic (6, 23, 25), the ITS analyses used in this study evaluated the pandemic effect, controlling for secular trends in the data. The demand and volume of TJA have been reported to increase every year (26). Therefore, the actual reduction in TJA cases would be greater than estimated or reported if the increase in demand for TJA was considered.

This study did not show a change in the proportion of hospitalizations associated with TJA during the pandemic.

TABLE 2 Association of pandemic with outcomes in patients who underwent TJA.

Outcomes	Model 1*			Model 2*			Model 3*		
	Effect size[a]	95% CI	*P*	Effect size[a]	95% CI	*P*	Effect size[a]	95% CI	*P*
Costs	0.94	0.93–0.95	$P < 0.0001$	0.94	0.93–0.96	$P < 0.0001$	0.94	0.93–0.96	$P < 0.0001$
LOS	0.99	0.98–1.00	0.1422	1.00	0.98–1.01	0.8739	1.00	0.98–1.01	0.8913
In-hospital Complications	1.04	0.65–1.67	0.8777	1.17	0.72–1.87	0.5281	1.17	0.73–1.88	0.5213
30-day readmissions	0.73	0.58–0.91	0.0049	0.73	0.58–0.91	0.0054	0.74	0.59–0.93	0.0085

[a]For costs and LOS, effect size were expressed as relative ratio estimated by log linear regressions; For in-hospital complications and 30-day readmissions, effect size were expressed as odds ratio (OR) estimated by logistic regressions.

*Model 1 adjusted for patient-level age, sex, and number of comorbidities; Model 2 adjusted for patient-level age, sex, and Elixhauser score; and Model 3 adjusted for patient-level age, sex, and specific comorbidities.

Although there is a lack of prior research specifically addressing the proportion of hospitalizations during the pandemic, it has been reported there has been a notable shift in TJA cases from hospitalized to outpatient settings in some countries like the United States (5, 10, 24). Therefore, it is reasonable to speculate that the proportion of hospitalized TJA patients may decrease during the pandemic in these countries.

Contrary to previous studies reporting that patients undergoing TJA were younger and healthier during the pandemic period (5, 11), the results of this study indicated that patients undergoing TJA were older and had more comorbidities compared to patients with TJA before the pandemic. The number of comorbidities in patients undergoing TJA during the pandemic period was higher in both direct comparisons with the prepandemic period and the ITA analysis, indicating that Chinese hospitals tended to admit patients with severe disease status during the pandemic period.

Unlike studies conducted in the United States (5, 8, 10), our study did not show a reduction in LOS. Furthermore, the average LOS of patients who underwent TJA was much longer than that reported in the United States during and before the pandemic period. The average LOS in our study was >10 days; however, it was <2 days in studies from the United States (5, 8, 10). This difference may be due to the accelerated shift to outpatient settings and the same-day discharge after TJA in the United States. Whether a shorter LOS could increase the rate of complication in patients undergoing TJA is inconsistent. Therefore, special caution should be exercised to shorten the LOS. Future research is required to evaluate the effect of shorter LOS on the safety of patients undergoing TJA to improve the efficiency and safety of TJA care. Additionally, our study showed a significant decrease in costs among patients undergoing TJA during the pandemic compared to those before the pandemic. The decrease in cost may be due to the Centralized Volume-Based Procurement of High-Value Medical Consumables Policy implemented in China, which aims to reduce the price and expenditure of Medical Consumables (27). The Centralized Volume-Based Procurement of High-Value Medical Consumables was first published in the middle of 2019 and carried out at the end of 2019. Therefore, the effect of this centralized volume-based procurement policy on costs may begin to manifest during the pandemic.

Several studies have assessed the impact of the COVID-19 pandemic on readmission and complication rates in patients who have undergone TJA. A study in India reported an increase in complications in patients undergoing TJA during the pandemic period (9). However, studies conducted in the United States did not produce the same results. Gordon et al. (5) and Abdelaal et al. (24) reported no changes in 30-day complications or readmissions among patients undergoing TJA. A study by Shah et al. revealed that the 30-day readmission rate was lower in the initial period of the pandemic but similar in the later period of the pandemic compared to that before the pandemic (11). However, patients who underwent TJA during the pandemic period in those studies were younger and healthier and had a lower possibility of postoperative complications. In this study, it was observed that there was no change in complication rates and a significant decrease in 30-day readmission rates in patients undergoing TJA, despite their worse conditions during the pandemic period compared to the pre-pandemic period. These findings demonstrated that the quality and safety of TJA care in China were not affected by the pandemic.

In addition to TJA, the COVID-19 pandemic has been observed to have a similar impact on other elective surgical procedures worldwide. Various specialties, including cardiac surgery, endocrine surgery, urologic oncology surgery, and neuro-oncology surgery, have also experienced a decline in surgical volume during the pandemic, particularly at its onset (28–31). A study on cervical spine surgery in the United States observed greater comorbidity burden, which aligns with the observation in this study (32). However, different from our findings, it was noticed an increase in complication rates (32). Further studies are warranted to comprehensively understand the impact of the pandemic on other elective surgical procedures in China.

This study has several limitations. First, the data used in our study were obtained from 17 hospitals and did not cover all TJA procedures performed in China. However, the 17 hospitals were geographically diverse, representing different regions of China, including the Middle, East, West, North, South, and Capital. Therefore, they were representative of Chinese hospitals. The data from these hospitals were useful in determining trends in TJA care. Second, postoperative outcome variables, including complications and readmissions, were limited to in-hospital and 30 days after the operation. Future studies should evaluate long-term follow-up for complications. Finally, this study assumed that the effects observed were directly related to COVID-19 when there were confounding factors that could have influenced clinical practice, such as a centralized volume-based procurement policy. However, we made every effort to control for observable confounders, including secular trends and patient conditions, using ITS, multivariate regression, and PSM analyses.

5 Conclusions

In conclusion, the results of this study revealed a different practice pattern in the care provided to inpatients with TJA in China than in other countries. The volume of TJA procedures experienced a sharp decline at the onset of the pandemic, followed by a gradual increase and eventual return to pre-pandemic levels, with no significant change in the proportion of hospitalizations associated with TJA. Furthermore, it was observed that patients who underwent TJA during the pandemic were generally older and less healthy. However, despite these challenges, there was no increase in complications, readmission rates, length of hospital stay, or costs during the pandemic period. Notably, a significant reduction in costs and readmission rates within 30 days were observed during this period. Our findings suggest that the pandemic has not had a profound negative impact on the care of TJA in China.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: the data presented in this study are available on request from the corresponding author. Requests to access these datasets should be directed to liulihua07@yeah.net.

Ethics statement

The requirement of ethical approval was waived by Research Ethics Committee of Chinese PLA General Hospital for the studies involving humans because this data analyzed in this study was historical de-identified. According to the International Ethical Guidelines for Health-related Research Involving Humans [by the Council for International Organizations of Medical Sciences (CIOMS), 2016], this study did not require ethical approval given that all data were anonymized and the intended use in current study falls within the scope of the original informed consent. The studies were conducted in accordance with the local legislation and institutional requirements. The Ethics Committee/Institutional Review Board also waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because this data analyzed in this study was historical de-identified.

Author contributions

TZ: Conceptualization, Formal analysis, Methodology, Software, Visualization, Writing – original draft. SW: Formal analysis, Investigation, Validation, Writing – original draft. LY: Formal analysis, Methodology, Validation, Writing – original draft. HB: Data curation, Formal analysis, Investigation, Resources, Writing – review & editing. JG: Data curation, Formal analysis, Investigation, Writing – review & editing. JL: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Software, Validation, Visualization, Writing – review & editing. LL: Conceptualization, Formal analysis, Funding acquisition, Project administration, Resources, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1357984/full#supplementary-material

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