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# Advances of health care transition for patients with childhood-onset chronic diseases: International perspectives, volume II

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# Advances of health care transition for patients with childhood-onset chronic diseases: International perspectives, volume II

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# Editorial: Advances of health care transition for patients with childhood-onset chronic diseases: International perspectives, volume II

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healthcare transition, childhood-onset chronic diseases, independence, transition readiness, social participation, family functioning

Editorial on the Research Topic
Advances of health care transition for patients with childhood-onset chronic diseases: International perspectives, volume II

Owing to the advances in pediatric medicine, many children with chronic diseases are now able to survive till adulthood, often without serious sequelae or disabilities (1, 2). However, managing the health care of adult patients with childhood-onset chronic diseases (APCCD) is a challenge in contemporary pediatric practice; consequently, there is considerable discussion around the world regarding the state of health care transition for these patients.

In 1993, the American Academy of Adolescence and the American Academy of Pediatrics issued a joint statement on the medical care of adolescents with chronic conditions and defined transition as the "purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented health care systems" (3). Earlier, a transition was to be accompanied by a voluntary transfer to adult-oriented care, meaning that the patient actively moves on their own will. Thirty years later, patients who find it difficult to become completely independent or are unable to make their decisions are also now eligible for transition and no longer require an accompanying obligatory transfer.

The "Six Core Elements of Health Care Transition™ 3.0" in the Got Transition, the federally funded national resource center on health care transition in the US, classified transition into three types: "transition youth to an adult health care clinician," "transitioning to an adult approach to health care without changing clinicians," and "integrating young adults into adult health care" (4). Since the concept of transition has evolved, we must recognize the transition of different patients in various fields.

Thus, the major issues regarding future transitions are proposed in this Research Topic. For patients who wish to transfer to an adult health care clinician, are independent, and are capable of social participation, future research must focus on institutional support for education and employment, factors associated with successful transition, and assessment of transition readiness.

Sakurai et al. performed a nationwide questionnaire-based survey on the prevalence and possible barriers to healthcare transition in Japan for APCCD in 2020. They stated that the top transitional barrier on the patient side were intellectual disability/rare disease and dependence on pediatrics, and lack of collaboration with adult healthcare was as medical/infrastructure factors; these problems seem to persist worldwide. Furthermore, Wakimizu et al. published a

systematic review focusing on pediatric-to-adult healthcare transition interventions and promoting their effectiveness, and stated that enhanced interventions systematically support the transition, patient independence, and social participation.

Scarponi et al. reported on a particularly important part of their experience with the transition from pediatric-to-adult healthcare services for nephrological patients in Bologna–resistance from the hospital staff during the initial stage of transition to adult care. However, the difficulties caused by differences in pediatric and adult care models were resolved through participation in joint meetings and training sessions by both teams. For patients with cognitive deficits, they also contacted and established relationships with the local mental health facility in the patient's area of residence and ensured continuity between the hospital social services and those on the territory for families with social problems.

Biagioli et al. systematically reviewed the literature regarding self-care for improving the quality of life in children and young adults with chronic diseases. They found that both disease-specific and common instruments of self-care maintenance are being developed for various chronic diseases, with a special focus on treatment adherence. Instruments for self-care and self-monitoring of patients with chronic diseases may serve as important components to ensure a smooth transition as well as the success of a well-planned transition program.

Kobayashi et al. investigated the factors associated with the employment status and academic performance of childhood cancer survivors. Patients aged ≥18 years who participated in this single-center cohort study underwent comprehensive health check-ups for cognitive status, quality of life, transition readiness, and family function. The authors concluded that intellectual quotient, transition readiness, and family functioning were associated with employment status. Long-term follow-up of childhood cancer survivors should ensure comprehensive care to improve health, readiness to transition to self-care, and family functioning.

Interestingly, Takeuchi et al. conducted a narrative review of effective interventions to improve transition readiness in adolescents and young adults using the transition readiness assessment questionnaire, a widely used assessment tool for transition readiness. They identified 261 reports to extract and analyze three articles; all three interventions included were effective in improving transition readiness, particularly web-based and nurse-led organizational interventions.

There are two primary issues encountered in the recent transition-related research that require special mention. First, the question of what should be done about the transition of patients with severe physical and intellectual disabilities to adult care who cannot decide on the transition autonomously. Ishizaki et al. conducted a questionnaire-based survey of healthcare professionals involved in the care of adult patients with the 5p-syndrome, a chromosomal disorder with severe intellectual disability and various physical complications. Regarding support and welfare, all study participants had an experience of receiving consultation about care for the siblings of patients and only 15% of them believed the patient was on their way to the transition of patients with rare diseases and severe intellectual disabilities. This situation would be similar for other patients with severe disabilities due to chromosomal abnormalities.

Second, as a new topic, Kato et al. addressed the history behind the transition of heart transplant patients in Japan. They pointed out that paternalism in clinical settings that exists in Japan hinders the independence and decision-making process of the patients and their guardians. Although they describe it as a problem unique to Japan, the underlying ideas may be universal and the debate could be useful in addressing the problems faced by heart transplant patients across the globe.

There is a range of articles covering a broader perspective on this topic concerning patients with chronic diseases. We recommend that the ideal process of transition should be deliberated based not only on the diagnosis, but also on the patient's circumstances and characteristics, such as cognitive function, workability, and family function.

## Author contributions

Main text was written by YI. All authors contributed to the article and approved the submitted version.

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ORIGINAL RESEARCH
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# Different Reaction Patterns of Caregivers of Children With Imperforate Anus: A Latent Profile Analysis

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**Aim:** This study aimed to explore how different dimensions of caregivers' reaction shape their caring experience, and the factors associated with different reaction patterns.

**Design:** A second analysis of a multisite cross-sectional study were conducted. Caregivers of children with imperforate anus (IA) were enrolled in three tertiary children's hospitals in Eastern China between November 2018 and February 2019.

**Methods:** The caregiver's experience, stigma feeling, social support level and perception of uncertainty were assessed by Caregiver Reaction Assessment, Parent Stigma Scale, Social Support Scale and Parent's Perception of Uncertainty Scale accordingly. The demographic information of caregivers as well as the children's clinical data were collected. Latent profile analysis was conducted to determine different patterns of caregiver's reaction, and logistics analysis was used to explore the associated factors of the reaction pattern.

**Findings:** A total number of 229 caregivers (median age = 30, quartiles: 28, 36) were included. Three distinguishable caregiving reaction types were identified (Class 1: low burden and high benefit, 4.8%; Class 2: moderate burden and benefit, 48.9%; Class 3: high burden and low benefit, 46.3%). In logistics analysis, the Class 1 and Class 2 were combined as one group due to the low population in Class 1. The marital status of caregiver (OR = 0.067, 95% CI: 0.006, 0.700, $P = 0.024$), IA type (OR = 1.745, 95% CI: 1.198, 2.541, $P = 0.004$), children aged > 2 years (OR = 3.219, 95% CI: 1.364, 7.597, $P = 0.008$), social support (OR = 0.907, 95% CI: 0.865, 0.951, $P < 0.001$) and perception of uncertainty (OR = 1.054, 95% CI: 1.026, 1.083, $P < 0.001$) were associated with different caregiver reaction patterns.

**Conclusion:** Nearly half of the caregivers of children with IA experience reaction of high burden and low benefit, but considerable proportion of caregivers could benefit from the caregiving rather than burden from. Married caregivers may have more negative reaction, especially when children > 2 years and diagnosed with intermediate or high type of IA. However, increasing caregiver's social support and reducing perception of uncertainty may have the potential to modify their reaction pattern.

**Keywords: imperforate anus, caregiver, caregiving reaction pattern, latent profile analysis, cross-sectional study**

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# INTRODUCTION

Imperforate anus (IA) is one of the most common type of anorectal malformation, which is defined as newborn baby without normal opening in the anus area, or only fistula remained (1). With an incidence of 1/5000-1/2000 (2), and difficulties in prenatal diagnosis (3), IA has a higher incidence in developing countries (4), laying high medical burden on national health care.

IA could be divide into three categories according to Wingspread classification, namely low, intermediate and high according to height of the deformity (5). Although Krickenbeck classification has been widely adopted in western countries due to the careful consideration of the anatomical and prognosis features (6, 7), the Wingspread classification remained the mainstream that been used by most children's hospital in developing countries like China (8). Children diagnosed with IA usually need to receive at least one operation (anoplasty). The higher the deformity location is, the more difficulty the treatment is (9). For the intermediate and high type of IA, the three-staged operation usually adopted, including a colostomy, anoplasty and colostomy closure (10). After anoplasty, a long period of dilation is needed to improve the prognosis (11). Despite the advances in operation technology, complications like constipation and incontinence are still common to see in a large number of affected children, as high as 90% children need bowel management (2).

Caring for children with IA could put a lot of burden on the family members, especially the caregivers, who take the most caring tasks. A study showed that, the caregivers were usually under greater pressure than the affected children, and in high risk of getting mental disorder (12). Nearly half of caregivers of children with IA reported impaired life quality (13). However, in despite of the negative feelings from caring for a child with IA, some caregivers could also benefit from the experience of caregiving, and get a sense of self-worth (12, 14). The various feelings related to caregiving could be called caregiver reaction (15).

Caregiver reaction is the perception of the caregiving experience, and caregiver's feelings toward caregiving could be affected by diverse factors. Negatively speaking, caring for a child with IA costed a lot of time and energy with disturbed daily life (16). Moreover, the treatment usually put stress on the family's finances, even causing some families into debt (17). The relationships among family members also be influenced during caregiving, either closer or estranged from each other. Particularly in the case of IA, a disease related to sensitive part of the body, often cause the negative feelings such as embarrassment (12), and such feeling could distorted the family member's attitude toward the affected children (18, 19), thus cause possible deviation.

But from positive prospective, the connection between family members could also be strengthened due to the responsibility and attachment toward the care of ill children (20), which could be beneficial to the caregivers. Moreover, some caregivers could also benefit from caregiving experience. Studies reported that during the process of care, caregivers may cherish the present, improve their personal abilities and enhance their perception of various supports (21).

The different of reactions of caregivers not only influence their personal status, but also have an effect on the quality of caregiving, further influence the prognosis of the children with IA (22, 23). Caregivers of children with IA as independent individual, have their own patterns of reaction. To identify the caregiver's reaction patterns is critical to adaptation and effective coping (24, 25), and help medical staff to understand the caregiver's experience and further design targeted interventions.

But, study related to the different reactions of caregivers of children with IA was lacking. Most studies focused on the care burden of caregivers (26), the complexity of caregiver reaction was overlooked. Thus, in this study, we aimed to identify different patterns of caregiver's reaction by categorized individuals according to their Caregivers Reaction Assessments (CRA) scores, and explore the factors associated with different reaction patterns.

# METHODS

## Data Source

The study design, enrollment criteria and hospitals involved were published before (27). The whole project was aiming to explore the caregiving reaction of caregivers of children with imperforate anus using both quantitative and qualitative methods. In this paper, the classification of caregivers reaction and associated factors were identified.

## Measurements

### Latent Variable: Caregiver Reaction

The caregiver's reaction were collected by Chinese Version of CRA (28), which was developed by Given, and widely used to assess caregiver's burden and benefit (15). The scale comprises 24 items, and each item is rated on a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree). The scale consisted five dimensions-impact on health, impact on finances, lack of family support, impact on schedule and caregiver's esteem. The former four dimensions referred the burden of caregivers, and higher score suggested heavier care burden; the last one was the measurement of positive reaction of caregiving, and the higher scores indicated the higher perception of benefit (28). In this study, the Cronbach's Alpha was 0.772 for the scale, and ranged from 0.649 to 0.822 for each dimension.

### Independent Variable

#### *Stigma*

The stigma was measured using Chinese version of Parent Stigma Scale (27). It is a one-dimension scale with five items, and each item was rated from 1 (strongly disagree) to 5 (strongly agree), and high scores indicate strong feeling of stigma (29). The Cronbach's Alpha was 0.883 in this study, and the total scores was used as an independent variable.

#### *Social Support*

In this study, social support was measured by Social Support Scale developed by Xiao (30), the 10-item scale comprising three dimensions as subjective support, objective support and social support utilization. Four items in this scale were rated by four

point (1–4), and other items were calculated by the number of chosen option. The high scores the caregivers got, the higher social support level they had. In this study, the Cronbach's Alpha was 0.814 and the total score was used as an independent factor.

### *Perception of Uncertainty*

The Chinese revised version of Parent's Perception of Uncertainty (PPUS) was used to measure caregiver's uncertainty feelings in this study (31). The 28-item scale included four dimension as ambiguity, lack of clarity, lack of information, unpredictability. Each item was ranked by the Likert 5-point scale, from 1 (strongly disagree) to 5 (strongly agree), and higher scores indicated higher perception of uncertainty (31). The Cronbach's Alpha was 0.844 in this study. The total scores of the scale was used as an independent variable.

### *Demographic and clinical information*

The demographic information and clinical data were collected by self-designed questionnaire, for detailed please to found our previous study (27).

## Data Collection Procedure

The data collection procedure was available in the previous publication (27).

## Data Analysis

Continuous data was expressed by mean and standard deviation. The differences between groups were analyzed using Student's *t* test. Categorial data were expressed by frequencies and proportions and analyzed using Chi-square test. The α would be corrected ($\alpha' = \frac{\alpha}{N}\ N = \frac{n(n-1)}{2}$, n: number of groups) (32) when multiple comparisons presented. Dependent variables would be enrolled in logistics regression analysis when $P < 0.25$ (33), clinical significant were also considered before analysis. The analysis was performed in SPSS version 21.0 (IBM Corporation, Armonk, NY, USA).

Patterns of caregiver's reaction were determined using latent profile analysis (LPA). LPA aims to identify clusters of individuals based on a series of continuous variables (34). In this study, the five dimensions of CRA were used as basis for the analysis of latent profile that generate the different reaction pattern. The two-step strategy was used to analyze the data. Firstly, to identify the best-fit model with an initial assumption of one class, and increase the number of classes in sequence, in order to find the best-fitted model. The model fit was also assessed, and typically a relative high Entropy, and a low Bayesian information criterion (BIC) or adjusted BIC (aBIC) indicated good classification (35). The Lo-Mendell-Rubin (LMR) (*P*) and bootstrapped likelihood ratio test (BLRT) (*P*) were used to help determine best class solution, and $P < 0.05$ indicate that the number (n) of classification is better than n-1 (35). The optimal choice of class solution was also evaluated by the interpretability and clinical judgement. This step was conducted using Mplus version 7.1 (Muthén & Muthén, Los Angeles, CA). Secondly, the outcome of selected classification was used as independent variable, and logistics regression analysis was used to determine the associated factors of different classes (conducted by SPSS version 21.0). $P < 0.05$ was considered statistically significant.

**TABLE 1 |** Measurement of CRA and PPUS.

| | Total score (range) | Item average score (range) |
|---|---|---|
| **Dimensions of CRA** | | |
| Health | 10.74 ± 2.63 (4.00–18.00) | 2.69 ± 0.66 (1.00–4.50) |
| Finance | 8.77 ± 2.77 (3.00–15.00) | 2.92 ± 0.92 (1.00–5.00) |
| Lack of Family Support | 11.22 ± 3.19 (5.00–22.00) | 2.24 ± 0.64 (1.00–4.40) |
| Schedule | 18.00 ± 3.60 (5.00-−25.00) | 3.60 ± 0.71 (1.00–5.00) |
| Caregiver's Esteem | 29.01± 3.20 (20.00–35.00) | 4.14 ± 0.46 (2.86–5.00) |
| Perception of Uncertainty | 72.60 ± 14.28 (29.00–102.00) | 2.59 ± 0.51 (1.04–3.64) |

*CRA, Caregivers Reaction Assessment; PPUS, Parent's Perception of Uncertainty.*

## Ethical Approval

The study was approved by the ethical review committee (2018-IRB-081). Informed consents were obtained from each participant which referred that they had entirely understood the study.

# RESULTS

The demographic and clinical information of sample, and the results of stigma and social support were available in previous publication (27). The scores of five dimensions of CRA and PPUS were presented in **Table 1**.

## Classification of Caregiver's Reaction Patterns

The analysis of patterns of caregiver reaction was done based on the results of five dimensions of CRA. The Entropy and BIC indicate that four-class model fitted well, while the LMR test showed that, the four-class model was no better than three-class model. The advantage of four-class model was trivial compared with three-class model, and the Entropy of three-class model is 0.781, indicating the three class model also had high classification certainty. According to our clinical judgement, the three-class model was found to fit a meaningful clinical interpretation, and it was chosen as the final classification model. The statistics of model fit indices were depicted in **Table 2**. **Figure 1** showed the results of three-class model, giving the characteristics of the five dimensions, the former four dimension could defined as caregiving burden, and the last dimension could view as sense of benefit. When comparing the three classes, the label of 3 classes could be defined as low burden and high benefit (Class 1, 4.8%), moderate burden and benefit (Class 2, 48.9%) and high burden and low benefit (Class 3, 46.3%). In Class 1, esteem got the highest scores, followed by schedule, lack of family support, finances and health. In Class 2, esteem got the highest scores as well, followed by schedule, finance, health and lack of family support. In Class

**TABLE 2 |** Model fit indices.

| Classes | k | Log (L) | AIC | aBIC | Entropy | LMR test | BLR test |
|---|---|---|---|---|---|---|---|
| 1 | 10 | −1147.088 | 2314.176 | 2316.820 | — | — | — |
| 2 | 16 | −1064.555 | 2161.109 | 2165.339 | 0.708 | 0.0002 | <0.001 |
| 3 | 22 | −1043.691 | 2131.382 | 2137.198 | 0.781 | 0.0194 | <0.001 |
| 4 | 28 | −1033.495 | 2122.990 | 2130.393 | 0.815 | 0.0892 | <0.001 |

*AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; LMR, Lo-Mendell-Rubin; BLR, bootstrapped likelihood ratio.*

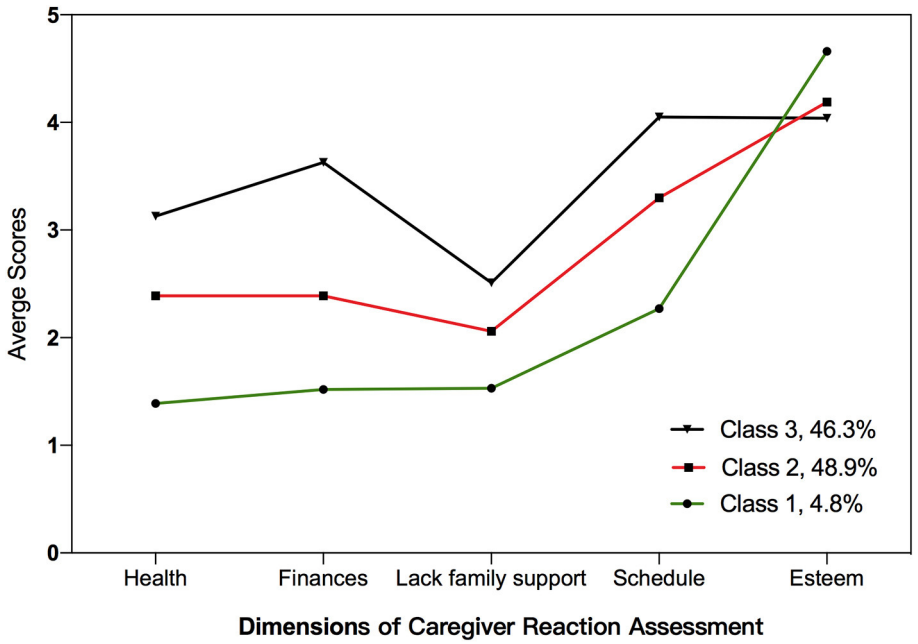


**FIGURE 1 |** Dimension of caregiver reaction assessment.

**TABLE 3 |** Descriptive statistics for five dimensions of CRA in three classes.

| | Class 1 | Class 2 | Class 3 |
|---|---|---|---|
| Health | 1.39 ± 0.38 | 2.39 ± 0.44 | 3.13 ± 0.50 |
| Finances | 1.52 ± 0.55 | 2.39 ± 0.63 | 3.63 ± 0.62 |
| Lack of family support | 1.53 ± 0.39 | 2.06 ± 0.52 | 2.51 ± 0.65 |
| Schedule | 2.27 ± 0.76 | 3.30 ± 0.57 | 4.05 ± 0.46 |
| Esteem | 4.66 ± 0.27 | 4.19 ± 0.42 | 4.04 ± 0.47 |

*Class 1, low burden and high benefit, 4.8%; Class 2, moderate burden and benefit, 48.9%; Class 3, high burden and low benefit, 46.3%.*

3, schedule got the highest scores, followed by esteem, finances, health and lack of family support (**Table 3**).

## Associated Factors of Different Reaction Patterns

In the logistics regression analysis, due to the small number of population in Class 1, the Class 1 was combined with Class 2 as one category, defined as low burden and high benefit group, the Class 3 remained as high burden and low benefit group. The stepwise method were also used to determine the independent associated factors derived from univariate analysis (**Table 4**). The results showed that marital status, IA type, children's age, social support and perception of uncertainty were factors that associated with different reaction patterns (**Figure 2**).

# DISCUSSION

This study aimed to identify different reaction patterns of caregivers of children with IA during follow-ups, and explore associated factors that determined different types of reaction. The results showed that three distinguishable patterns were identified as Class 1 (low burden, high benefit), Class 2 (mediate burden and benefit) and Class 3 (high burden, low benefit). About 46% of the population experienced high burden and low benefit compared to others. Got married, children aged > 2 years and diagnosed with higher type of IA, less social support and perception of uncertainty may negatively affect the caregiver's reaction. To better understand the different reaction patterns and the influencing factors, could not only instruct the medical staff

**TABLE 4 |** Univariate analysis of different reaction patterns.

| Item | Class 1 | Class 2 | $\chi 2/t/z$ | *P*-value |
|---|---|---|---|---|
| **Caregiver** | | | | |
| **Age (years)** | | | 1.079 | 0.583 |
| <30 | 55 | 45 | | |
| 30–40 | 58 | 48 | | |
| >40 | 10 | 13 | | |
| **Gender** | | | 0.125 | 0.724 |
| Male | 21 | 20 | | |
| Female | 102 | 86 | | |
| **Marital status** | | | ——– | 0.127 |
| Married | 117 | 105 | | |
| Other | 6 | 1 | | |
| **Education level** | | | 2.816 | 0.421 |
| Primary school or below | 7 | 10 | | |
| Junior high school | 33 | 35 | | |
| High school | 25 | 20 | | |
| University/college or above | 58 | 41 | | |
| **Occupation** | | | 16.148 | <0.01 |
| Part-time job | 11 | 21 | | |
| Full-time job | 59 | 25 | | |
| Unemployed | 53 | 60 | | |
| **Relationship with patient** | | | 0.581 | 0.446 |
| Mother | 98 | 80 | | |
| Father and other | 25 | 26 | | |
| **Residence** | | | 7.679 | 0.022 |
| City | 42 | 19 | | |
| Suburban | 37 | 39 | | |
| Countryside | 44 | 48 | | |
| **Household structure** | | | 0.159 | 0.690 |
| Extended family | 82 | 68 | | |
| Nuclear family | 41 | 38 | | |
| **Religion** | | | 0.106 | 0.745 |
| Yes | 37 | 34 | | |
| No | 86 | 72 | | |
| **Children** | | | | |
| Age (years) | | | 5.123 | 0.024 |
| ≤2 | 108 | 81 | | |
| >2 | 15 | 25 | | |
| **Gender** | | | 0.588 | 0.443 |
| Male | 80 | 74 | | |
| Female | 43 | 32 | | |
| **IA type** | | | 19.335 | <0.01 |
| Low | 82 | 42 | | |
| Intermediate | 20 | 21 | | |
| High | 21 | 43 | | |
| **Time since diagnosis (years)** | | | 3.744 | 0.053 |
| <1 | 76 | 52 | | |
| ≥1 | 47 | 54 | | |
| **Medical insurance** | | | 4.764 | 0.029 |
| Yes | 100 | 73 | | |
| No | 23 | 33 | | |
| **Concealment** | | | 0.023 | 0.879 |
| Yes | 87 | 74 | | |
| No | 36 | 32 | | |
| Stigma | 13.68 ± 4.68 | 16.48 ± 4.55 | −4.583 | <0.01 |
| Social support | 43.40 ± 7.83 | 36.77 ± 7.52 | 6.520 | <0.01 |
| Perception of uncertainty | 67.37 ± 13.28 | 78.63 ± 12.47 | −6.615 | <0.01 |

*Class 1, low burden and high benefit/moderate burden and benefit; Class 2, high burden and low benefit.*

to provide caregivers with specific interventions, but also help the children and their families to get better transition from initial years into the adulthood period.

There was some similarity among the three classes of reaction pattern. Each pattern shared a relative high esteem score compared to other dimensions, which referred that the caregivers of children with imperforate anus could experience much positive feeling during care. When comparing different classes, the population could be mainly divided into two groups as low burden and high benefit group and high burden and low benefit group, because in Class 1 and Class 2, the esteem all top the five dimensions of caregiver reaction assessment, which presented that the caregivers in these two groups perceived more positive feelings than negative ones, and these population could accounted for 53.7%. Thus, it is important for us to notice the positive feelings that caregivers experienced. The positive reaction from caregiving, could not only impact the caregiver's motives to provide high quality care for the children with IA, but also could reduce the sense of guilty of the children when they grow-up with self-conscious.

The positive feelings, sometimes called benefit finding, was generated from the process of disease coping (21). Benefit finding is a common phenomenon to see in the caregivers of children with chronic illness (14). Because caregivers usually have close relationships with the ill children, they will attach themselves with great possibility to give the children best care, which could also foster the caregivers to find positive meaning during care (24). Therefore, in the long-term of caregiving, it was important for the clinical medical staff to guide the caregivers to treat the illness objectively, especially share the benefit findings with their children, and lead their attitude toward positive side. Interventions like writing disclosure, encouraging the caregivers to spend 20 min a day to record the positive feeling during caregiving (36), could be taught to the caregivers to enhance sense of benefit, which could finally help reduce their care burden, and increase the care quality for children with IA. These could also benefit the children from learning the experiences in the procession, which could facilitate the transition into adulthood.

As for the care burden, impact on schedule in three patterns all top the dimensions of negative reaction, indicated that caregivers suffer most from the disturbed daily arrangement. That is the treatment of IA is a long period, during which, the caregivers need to adjust their daily schedule and decrease their social activities to spend more time to care the children (16). To reduce the negative impact on schedule, on one hand, the caregivers could learn more nursing skills to improve their efficiency of care or ask family members at home for help (37). On the other hand, they could empower the children with self-care ability, along with other living skills in their growth. With the self-care skills, the children with IA could better deal with the chronic disease and make a smooth transition into adulthood.

To our surprise, the married caregivers had more possibility to experience negative pattern of reaction, which referred that they usually burden negative effects and benefit less compared to unmarried caregivers. The possible explanation may be that, the unmarried caregivers have less pressure from spouses (38), because when someone take the responsibility of care, others will take for grant that the children should be cared well. If

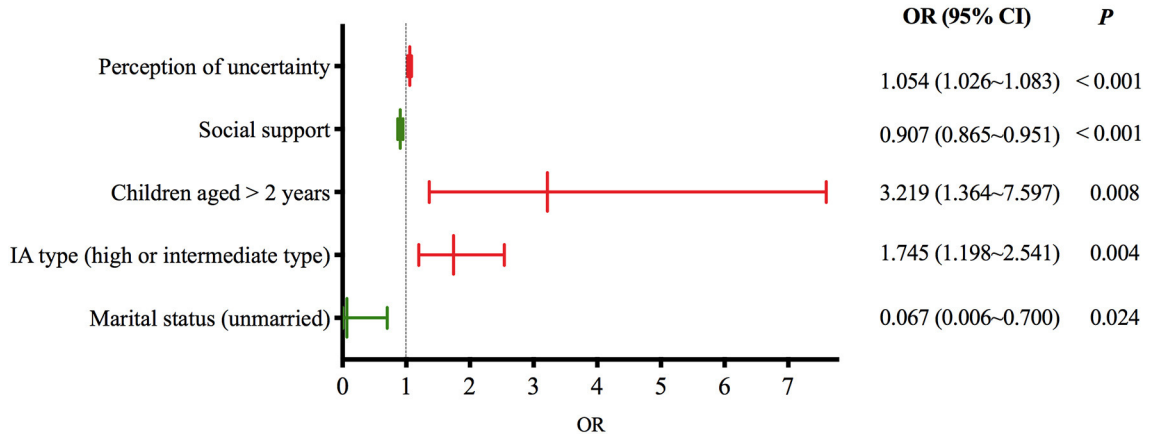


**FIGURE 2 |** Associated factors of different reaction patterns.

there is something wrong with the children, the caregivers will be blamed as careless. Especially in the case of mother, who accounted the majority (77.7% in this study) of the caregivers, even the incidence of IA could be attributed as their fault, and this phenomenon was evident in the results of qualitative part of our study (17). In clinical practice, we should view the children's family as a unit (26), not only caregivers need to know the knowledge and nursing skills for children's, but also other family members. This could help the families of children with IA to care the children together, or at least, enhancing their understanding of the hard caring tasks may help improve their attitude toward caregivers, thus modifying the caregiver's reaction during caring.

In this study, young children aged > 2 years was found to be an factor that caused caregivers react negatively toward caregiving. That is, although most treatment were performed in the initial years, frequent follow-ups were still needed when children grown up with self-awareness (11). Also, the unexpected complications such as soiling and constipation (11) may play a part in shaping their negative reaction pattern. So special care should be paid for the caregivers of children aged > 2 years. Useful materials should be provided to assist the caregivers cope with the chronic situation and regular follow-ups through telephone may be help.

The IA type was also important in determining different reaction patterns. Caregivers of children diagnosed with intermediate or high type of IA usually experience more burden and less benefit from caregiving. That is, compared with low type IA, the other two types needed more complex treatment and longer time of recovery (39). For example, after colostomy operation for intermediate or high type IA, the caregiver need to nurse the colostomy careful to avoid skin injuries and other complications. Moreover, the higher the malformation is, the relative poor prognosis the children will be (39). As the children of intermediate or high type of IA usually have poor-developed interior sphincters, as well as the later reaction of nerve reflexes (40). This could negatively affect the quality of life of children with IA, and the caregivers reaction will be negative correspondingly. To promote caregiver's understanding of characteristics of different IA types may help them to accept the reality they need to face after discharging from hospital, and adjust their anticipation for the children's prognosis, further modify their reaction when caring. With reasonable anticipation, the caregivers could better help the children to accept the possible prognosis they may encounter during their growth into adulthood.

In this study, higher level of social support and less perception of uncertainty could positively affect caregiver's reaction. It was consistent with other studie's results that social support and reduction of uncertainty has the potential to reduce caregiver's burden. Therefore, medical staff should offer sufficient information before they discharging, which could help to alleviate the caregiver's uncertainty feelings during care.

Normally, the perception of uncertainty could cause anxiety, increase caregiver's burden and reduce their sense of benefit (41). However, the effect of uncertainty could be both beneficial or harmful depending on one's view (42). Because uncertainty could also be viewed as possibility of getting a better result (43). Thus, besides providing detailed explanations for the caregiver's concerns, it is also crucial to guide them think positively about the prognosis when something unexpected happened. This could aid in the improvement of caregiver reaction, as well as inspire the caregivers to cultivate the optimistic character of children with IA.

Social support is an important protective factor of improving individual's well-being (44), thus it also should be used to elevate caregiver's sense of benefit during care. Moreover, peer support is also matters (45) other than the support from family members and medical staff. To invite former patients who had successful transition experiences to adulthood, especially those

with positive attitude may help the caregivers to sense more benefit in caring and enhance their perception of social support (30). These success examples could also encourage the children to have a better transition toward adulthood. The results of social support measurement in this study showed that, the objective social support that caregivers got was the highest among three dimensions, however, their subjective social support, especially social support utilization was relative low, which indicated that the caregivers of children with IA may not make full use of their social support. Therefore, medical staff could encourage the caregivers to keep a gratitude dairy to appreciate the help they have received (46), thus increase their perception of social support and make full use of it. This could help them to reduce care burden and promote their sense of benefit.

## CONCLUSION

The caregivers of children with IA could experience high level of benefit during care, but also take a lot of burden like disturbed schedule. According to their reaction pattern, the caregivers could be mainly divided into two groups, namely low burden, high benefit group and high burden, low benefit group. Unmarried caregivers have greater possibility to experience positive reaction pattern. However, when children $>$ 2 years and diagnosed with intermediate or high type of IA, the caregivers may have negative reaction pattern. But, increasing caregiver's social support level, exploring more social support resources, as well as enhancing their perception and utilization of the support they have received, could help them modify their reaction. Moreover, guiding the caregivers to view positively about the fact they faced, and take the uncertainty as possibility may also help them to improve their reaction patterns.

## LIMITATION

There were several limitations in this study. Firstly, the measurement of benefit finding of caregiving was not enough to illustrate the situation. Only one dimension of CRA was used may not stand for the benefit finding of caregivers, and we performed a qualitative research as complement to study more about the benefit finding of this population. Quantitative exploration of benefit finding of caregivers are needed in future studies. Secondly, the nature of cross-sectional study could not help us to determine the direction of correlation, for example, the different reaction patterns may also affect caregiver's perception of uncertainty, and we could not capture the changes of reaction patterns with time as well. In addition, although three categories were identified in LPA, but due to the small number of the sample size, limited members distributed in Class 1, which combined with Class 2 as one category in the logistics analysis. Larger sample size are needed in future study to explore the specific influencing factors associated with distinctive and refined reaction patterns. Lastly, this study did not include the clinical outcome of the children with IA, such as complications, hospitalization time, follow-up frequency and so on. Further explorations could be performed to see the relationships between caregiver's reaction patterns and the clinical outcome of their children, which could provide more evidence of nursing interventions.

## 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 human participants were reviewed and approved by Ethics Committee Board of Children's Hospital of Zhejiang University, School of Medicine. The patients/participants provided their written informed consent to participate in this study.

## AUTHOR CONTRIBUTIONS

HX made the contribution to conception and design. DW, KL, JT, YJ, and WG made substantial contribution to design, acquisition of data, analysis, and interpretation of data. DW draft the manuscript. XC and FL revising it critically for important intellectual content. Each author gave the final approval to the submitted version.

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SYSTEMATIC REVIEW
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# Instruments Measuring Self-Care in Children and Young Adults With Chronic Conditions: A Systematic Review

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Children and young adults (CYAs) with chronic conditions need to engage in self-care to improve their quality of life. This study aimed to retrieve the literature on instruments to assess self-care in CYAs living with chronic conditions and evaluate the psychometric proprieties of the instruments retrieved. A systematic literature review was conducted on six databases to identify peer-reviewed papers that described or used an evaluation instrument of self-care in CYAs with chronic conditions. Twenty-three articles describing 11 instruments of self-care were identified. Five instruments (45.45%) were developed for specific diseases, while six (54.54%) for various chronic illnesses. Most of the instruments were focused on treatment adherence within self-care maintenance (i.e., behaviors to maintain illness stability), excluding the monitoring of clinical parameters or the management of exacerbations. This review provides an overview of available instruments that measure self-care in CYAs with chronic conditions, which health professionals could use for patient education.

**Keywords: self-care, self-management, instruments, chronic disease, pediatric, adolescent, young adult, parent**

## INTRODUCTION

Chronic diseases are defined broadly as conditions that last for a year or longer and require ongoing medical attention or limit activities of daily living or both (1). The prevalence of pediatric-onset chronic diseases is gradually increasing around the world (2), contributing to both morbidity and mortality (3). The number of children and young adults (CYAs), children aged 0–24 years (4, 5), living with a chronic condition is growing due to higher survival rates (6). In the United States, 25% of the pediatric population is affected by a chronic condition and 5% by multiple chronic conditions (7). In Europe, in 2016, 16% of the population aged between 16 and 29 had a long-standing health problem (8). In Italy, 91.8% of children aged 0–14 are in good health, 9.6% have one or more chronic conditions, 1.6% suffer from two or more chronic illnesses (9). In addition, children with complex conditions have to deal with multiple transitions across providers and care settings (10), and those

requiring technology support and home care bear even higher costs (11–13). Furthermore, long-term chronic conditions have a strong impact on wellbeing and require ongoing management over a period of years or decades (14).

In the pediatric population, the most common pediatric chronic conditions, including those with medical complexity (15), are asthma, cystic fibrosis, type 1 diabetes mellitus, and chronic lung disease (16). In particular, children with the highest levels of medical complexity are estimated to be about 0.4–0.7% of all US children (17). Therefore, it is important to promote the quality of life of CYAs with chronic conditions and their family members. This requires a life-long process of self-care or self-management to preserve and improve personal wellbeing, to maintain a good health-related quality of life, and to reduce health costs (18, 19).

The concepts of self-care and self-management have been used with considerable overlap and interchangeably among scholars (20). Self-management refers to the process that individuals with a health problem intentionally use to gain control of their disease, in partnership with health professionals (21). Self-care is a more encompassing concept, referring to patients' ability and performance of activities to achieve, maintain, and promote optimal health and wellbeing, including monitoring and managing acute and chronic health conditions (22, 23). WHO defines self-care as "the ability of individuals, families and communities to promote health, prevent disease, maintain health, and to cope with illness and disability with or without the support of a healthcare provider" (24). According to Riegel and Dickson (25), self-care is a naturalist decision-making process based on patient experience (25).

In particular, the Middle-Range Theory of Self-Care of Chronic Illness identifies behaviors of self-care maintenance, characterized by those actions performed to maintain chronic condition stable (e.g., taking medications as prescribed); self-care monitoring, concerning all those behaviors performed to keep signs and symptoms under control (e.g., monitoring weight); and self-care management, concerning the reaction to symptoms when they occur (e.g., call the healthcare provider in case of fever) (26, 27). However, this Middle-Range Theory was developed for adults. In the pediatrics, especially for CYAs, few theoretical models have been described, such as the new comprehensive model of self-care in CYAs (28). This model emphasized that self-care is a very broad concept since it not only includes personal skills but also healthcare actions provided by others. Others include informal caregivers (parents, relatives, friends, volunteers) who play a crucial role in chronic patient care, but also formal caregivers (healthcare professionals) who provide specific professional support to families in terms of care management (28). Healthcare professionals cooperate with the patient and/or the family who maintain, if possible, the responsibility for their own care (29).

Self-care and quality of life, distress, and depression are interrelated (18). On the one hand, better self-care is associated with positive outcomes, such as more adequate disease control, greater patient safety, higher quality of life, and better personal development, which may lead to lower depression and distress (28, 30). On the other hand, psychological aspects can also be considered as influencing factors; for example, if CYAs are depressed, then they are more likely to neglect self-care behaviors (31, 32). Moreover, healthcare systems admit that self-care has a positive impact on reducing chronic diseases and on reducing health costs (33). Indeed, in general, chronic diseases requires a great amount of human and economic resources (34). Managing chronic diseases requires specialized professional competences and health facilities suited to the health care pathways. Therefore, the chronic diseases during childhood have a strong social impact (35).

In addition, the health consequences are related to the child's age at the onset of chronic alteration (36). Children with chronic diseases occurring during childhood showed a different outcome compared to those in which the diseases onset during their adolescence. Indeed, many aspects of adolescent daily life require a life-long process of self-care such as the need for precisely scheduled daily medications, consumption of special dietary products, regular physical exercise, regular visits to healthcare providers and monitoring of blood glucose levels (37).

Furthermore, adolescents with a chronic disease may deal with the burden of independence incapability and the need to ask for support from parents and other caregivers for most of their daily activities (37). Parents should encourage adolescents to develop self-esteem and avoid an excessively protective attitude (38). Adolescence is a key development period for establishing lifelong health-related behaviors (39). Furthermore, patients with complex chronic diseases, along with developmental changes in adolescence, face challenges related to their health-related quality of life (40).

There is evidence that self-care actions have a positive impact on the health of CYAs with complex chronic diseases, such as diabetes and fibrosis cystic (28, 41). Therefore, it is essential that these patients perform self-care (38, 42). The higher educational level of the population has generated a higher demand for specific information and education regarding healthcare topics (43). This demand has caused an increase of CYAs' care competency for their own health and wellbeing (43). Assessing self-care in the pediatric population with chronic diseases may contribute to improve self-care activities and address any deficiencies.

Therefore, the aims of this study were: (a) to retrieve and describe the literature on instruments (scales or questionnaires) that assess self-care in CYAs living with chronic conditions; and (b) to evaluate the psychometric proprieties of the retrieved instruments that assess self-care in CYAs with chronic conditions.

# METHODS

## Search Strategy

A systematic review was conducted to explore studies that described self-care scales for pediatric patients with chronic diseases. Search procedures followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for writing systematic reviews (44). The review was conducted through six databases: PubMed, Scopus, CINAHL, Embase, PsycInfo, and the Cochrane Library. In addition, a

manual search was carried out to broaden the search. The study selection was conducted in July 2021. The main keywords were "self-care," "self-management," "Scale," "Questionnaire," "Chronic Disease," "Pediatric," "Adolescent," "Young Adult," "Parents." Boolean operators—NOT, AND, OR—were also used to narrow and widen the search. The search was conducted by two reviewers independently. The search strategy is described in **Supplementary Material**.

## Eligibility Criteria

The review included all types of peer-reviewed papers with no limits of time or language. Eligible studies for inclusion had to meet the following criteria: (a) any study published on a peer-reviewed journal; (b) patients with chronic diseases or complex chronic diseases; (c) patients aged between 0 and 24 years; (d) studies that described or used a self-care evaluation scale; (e) studies describing self-care in children or young adults and/or the parental role; (f) studies in any language describing self-care evaluation instruments.

The exclusion criteria were: (a) papers that did not include instruments that evaluated self-care; (b) self-care scales not developed for the population included in this review; (c) unavailable full-texts; (d) scales that did not describe self-care activities; (e) papers published in journal that were not peer-reviewed; (f) scales did not include at least one of the self-care dimensions (self-care maintenance, self-care monitoring, self-care management); (g) studies that evaluated only self-efficacy.

## Study Selection

Firstly, duplicate records were identified and removed. Secondly, titles and abstracts were screened by two independent authors. The full texts of potential eligible studies were read to determine if the papers were eligible. In case of disagreement between the two authors, a third author was involved to make the final decision.

## Data Extraction and Synthesis

The following data were extracted: authors and year of publication; country where the study was conducted; aim;

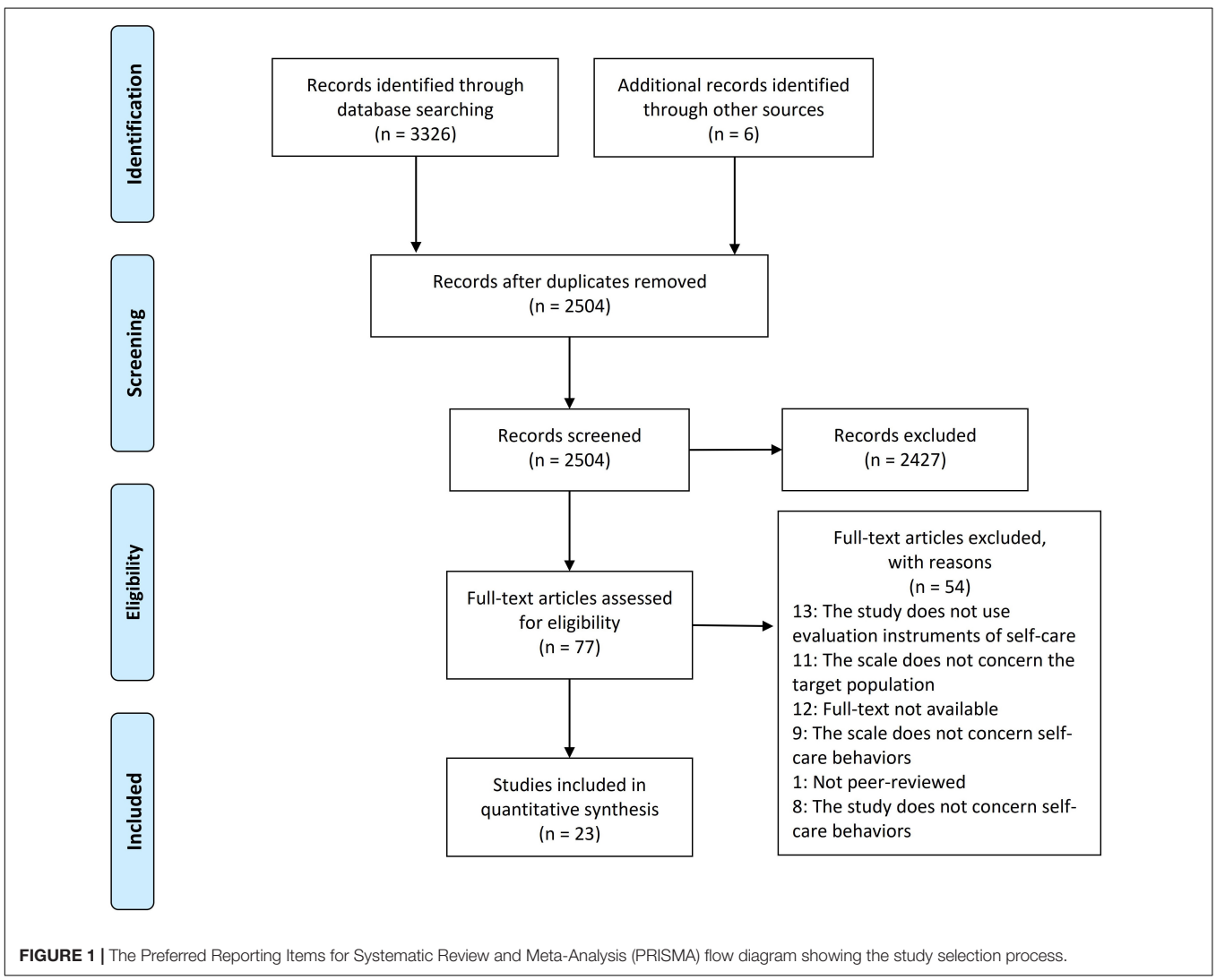


**FIGURE 1 |** The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram showing the study selection process.

study design; population (patient and/or parents age); type of chronic diseases and if mental diseases were included; scales or questionnaires; administration method; timing of administration; whether the instrument was validated; and findings. To describe and synthesize information on every instrument included in this review, the included papers were examined by focusing on the following information: name of the scale; description of the scale or part of it; original author and year; authors who included the scale in their paper; whether the scale was original or adapted; language; whether the entire scale or only one of its dimensions were used; patients' age; chronic diseases; self-care maintenance, self-care monitoring, self-care management; the population that responded to questionnaire (patients, parents, or both), the way the scale and/or questionnaire was administered, and the conceptual model (25). The psychometric characteristics of each included instrument were analyzed using the COSMIN criteria (45). In addition, two researchers independently investigated the dimension of self-care reported in each scale (self-care maintenance, self-care monitoring, and self-care management) according to the Middle-Range Theory of Self-Care of Chronic Illness (26).

# RESULTS

The study selection process is shown in **Figure 1**. The initial search identified 3,326 records across the six databases and six articles after a manual search. After removing the duplicates, 2,545 articles were reviewed by reading the title and abstract and 2,468 were excluded because they did not meet the inclusion criteria. The full texts of the remaining 77 articles were read and, of these, 23 papers were included in the final review and analysis. The reasons for the exclusion of 54 papers are reported in **Figure 1**.

## Characteristics of the Included Studies

Most of the 23 studies included in this review were published in the last decade ($n$ = 20; 86.95%) and mainly conducted in North America ($n$ = 15; 65.21%), followed by Asia ($n$ = 5; 21.73%), Europe ($n$ = 2; 8.69%), and Mexico ($n$ = 1; 4.34%) (**Table 1**). Seven studies (30.43%) used a cross-sectional approach, two (8.69%) were pilots, one (4.34%) was a longitudinal observational study, one (4.34%) used a qualitative design, and 12 (52.17%) did not report their study design. The age of the study samples ranged from two to 28 years, including children, adolescents and/or young adults. The samples of six of the 23 included studies (26.08%) included both children and their parents, whereas one study (4.34%) only the parents.

Nine studies (39.13%) developed or used self-care instruments only for one type of chronic condition: spina bifida ($n$ = 1; 4.76%) (46), type 1 diabetes ($n$ = 3; 14.28%) (47–49), epilepsy ($n$ = 2; 9.52%) (50, 51), asthma ($n$ = 1; 4.76%) (52), cystic fibrosis ($n$ = 1; 4.76%) (38), and congenital heart disease ($n$ = 1; 4.76%) (40). Ten studies focused on multiple chronic conditions such as kidney disease, systemic lupus erythematosus, inflammatory bowel disease, hypertension, renal transplant, and systemic lupus erythematosus (2, 29, 53–61). Four studies did not specify the chronic condition of their sample (57, 62–64).

A total of 13 studies (56.52%) considered neurodevelopmental and/or mental disorders (according to the DSM 5 classification) as an exclusion criterion; two studies (8.69%) included also patients with neurodevelopmental and/or mental disorders, eight studies (34.78%) did not specify whether these disorders were considered exclusion criteria.

Twenty-two of the studies included in this review reported the administration method of the instruments. The authors of four studies (18.2%) specified that the questions were asked by an assistant researcher. With regard to data collection, seven studies (69.56%) used paper-and-pencil instruments administered in hospital settings, nine studies (39.13%) used online or telephone or mail interviews, while seven studies (69.56%) did not specify this. Most of the selected papers included information about the validity and reliability of the instruments ($n$ = 20; 86.9%), while in three papers this information was not provided because they were based on previous validation studies.

## Characteristics of the Self-Care Instruments

Overall, 11 self-care instruments focusing on pediatric patients with chronic conditions were described in the studies included in this review (**Table 2**). Seven instruments were adapted, translated or modified from previous instruments developed by other authors (2, 40, 47, 51, 53, 55, 61). Five (45.45%) of the 11 instruments were specifically used to assess self-care of pediatric patients during the transition process from pediatric to adult care (29, 55, 59–61, 65). Five (45.45%) instruments were published in English (38, 46, 52, 58, 59); one instrument was available in English and Spanish (9.09%) (56); one was published both in English and German (9.09%) (65); two were available in English and Chinese (18.18%) (29, 49); one instrument was both in English and Italian (9.09%) (62), and one is available in English and Malaysian (9.09%) (50). Five (45.45%) instruments were entirely in line with the purposes of this review (38, 49, 58, 62, 65). Indeed, every dimension of the instruments included the concept of self-care and thus were analyzed in every part. The remaining instruments ($n$ = 6; 54.54%) were analyzed only for those dimensions that were relevant to the aim of this review.

The self-care instruments were developed for patients ($n$ = 4; 36.36%) (49, 56, 58, 65), for parents ($n$ = 5; 45.45%) (38, 50, 52, 59, 62), or both ($n$ = 2; 18.18%) (46, 65). The target population of the instruments were adolescents/young adults ($n$ = 4; 36.36%) (29, 46, 49, 56, 58, 65), children/adolescents ($n$ = 4; 36.36%) (29, 50, 58, 59), children ($n$ = 1; 9.09%) (52). One instrument (9.09%) (62) did not describe the target population. Five instruments (45.45%) were developed for specific conditions. In particular, these instruments were: the Self-Care Independence Scale (SCIS) for cystic fibrosis (38), FAMSS (38, 46, 49, 50, 52) the Pediatric Epilepsy Medication Self-Management Questionnaire (PEMSQ) (50), Self-Management of Type 1 Diabetes in Adolescence (SMOD-A) (49), the Adolescent Self-Management and Independence Scale II (AMIS II) (46). The remainder ($n$ = 6.54; 54%) were developed for non-specific

**TABLE 1 |** Characteristics of the articles included in the review.

| Author-Year and Country | Aim of the study | Study design | Population (patient\ parents, age) and chronic condition | Neuro developmental and/or mental disorder* | Measurement tool | Administration method and data collection | Results |
|---|---|---|---|---|---|---|---|
| Klinnert et al. (52) United States | This paper presents an assessment tool, the Family Asthma Management System Scale (FAMSS), evaluating the effectiveness of the family asthma management system | NR | 30 mothers of children with asthma | NR | Family Asthma Management System Scale | Pediatric psychologists rated the audiotapes of the interviews using the FAMSS Rating Scales | The FAMSS is a good measure of the family's ability to manage a chronic illness effectively |
| Patton et al. (38) United States | To describe the development and psychometric properties of a survey tool designed to evaluate children's level of independence in treating their cystic fibrosis (CF) | NR | 76 patients with cystic fibrosis (age = 4–17 years) | NR | Self-care Independence Scale | Self-administered, via mail and phone | The SCIS has acceptable internal consistency and good test-retest reliability. The construct validity of the SCIS was supported by positive correlations between patient age, number of years since diagnosis, and SCIS total scores. |
| Schilling et al. (49) United States | To report the development and testing of a new self-report measure to assess self-management of type 1 diabetes in adolescence (SMOD-A) | Qualitative descriptive study | 515 adolescents with type 1 diabetes (age = 13–21 years) | NR | Self-Management of Type 1 Diabetes in Adolescence (the SMOD-A) | Self-administered, participants approached in clinic waiting rooms | The SMOD-A was a reliable, stable, and valid measure of self-management of type 1 diabetes in adolescents. Content validity (CVI = 0.93), acceptable subscale reliability ($\alpha$ = 0.71–0.85) |
| Modi et al. (50) United States | To describe the development and validation of a Pediatric Epilepsy Medication Self-Management Questionnaire (PEMSQ) for caregivers of children 2–14 years | NR | 119 children with epilepsy (age = 2–14 years) and their families | NR | Pediatric Epilepsy Medication Self-Management Questionnaire | Self-administered, participants approached during follow-up clinic appointments | The PEMSQ showed strong psychometric properties, including good internal consistency across scales and construct validity with objective and subjective measures of adherence. |
| Giardini et al. (62) Italy | To present the Adherence Schedule in Transplantation (ASiT, in its three versions: ASiT-A, Adults; ASiT-PA, Proxy Adult and ASiT-PC, Proxy Child) | NR | 56 adult patients, transplant recipients (liver, heart, lung, and kidney) and parents of children | NR | Adherence Schedule in Transplantation-Proxy Child (ASiT-PC) | Self-administered, participants approached in different hospital units | Within a clinical context the schedule tool could be foster communication about adherence and enhance patients' personal limits and resources. |
| Sawicki et al. (65) United States | To develop the TRAQ, a measure of readiness for transition from pediatric to adult healthcare | NR | 192 youths with special health care needs (age = 16–26 years) | Autism Spectrum Disorder or mild mental retardation; attention-deficit hyperactivity disorder, learning disabilities, behavior disorders, bipolar disorder | Transition Readiness Assessment Questionnaire —TRAQ | Self-administered, online through 2 sites | The TRAQ is a reliable measure for assessing skills in self-management and self-advocacy. The TRAQ may also be useful for YSHCN*, their caregivers, and clinicians as a tool to identify areas for patient education and track progress throughout the transition process.<br>Each domain had a high internal consistency. |
| Ferris et al. (56) United States | To describe the development of the University of North Carolina (UNC) TRxANSITION Scale that measures the health-care transition and self-management skills in youth with chronic health conditions | NR | 185 adolescents and emerging adults with different chronic illnesses (age = 12–22 years) | NR | UNC TRxANSITION Scale (Version 3) | Semi-structured, clinically feasible interview tool administered by trained professionals | The UNC TR(x)ANSITION Scale is a reliable and valid tool that has the potential to measure health-care transition skill mastery and knowledge in a multidimensional fashion. Inter-rater reliability was strong ($r$ = 0.71) and item-total correlation scores were moderate to high. Content and construct validity were satisfactory. |

*(Continued)*

**TABLE 1 |** (Continued)

| Author-Year and Country | Aim of the study | Study design | Population (patient\ parents, age) and chronic condition | Neuro developmental and/or mental disorder* | Measurement tool | Administration method and data collection | Results |
|---|---|---|---|---|---|---|---|
| Guo et al. (47) China | To assess diabetes self-management, depressive symptoms, quality of life and metabolic control in a cohort of youth with type 1 diabetes in mainland China. | Cross-sectional study as part of a multi-site longitudinal descriptive study. | 136 youths with type 1 diabetes (age = 8–19 years) | NR | Chinese Version of Self-Report Measure of Self-Management of Type 1 Diabetes for Adolescents (C-SMOD-A) | Self- administered, by telephone | Self-management (Diabetes Care Activity subscale of C-SMOD-A) varied by socio-demographic characteristics. Girls had higher care self-management levels than boys ($p = 0015$), as did youths in two parent families ($p = 0028$). Youths who dropped out of school reported lower diabetes self-management levels than those still in school ($p = 0003$). Youths on intensive insulin treatment regimens had significantly better self-management compared to those not on intensive insulin treatment ($p < 0001$). Youths who were recruited from the CSU diabetes center had significantly better self-management than youths recruited from other hospital sites ($p = 0001$). |
| Sawicki et al. (60) United States | To assess Health care transition readiness using the TRAQ to understand associations between self-care beliefs, HCT readiness skills, and reports of HCT preparation among adolescents/young adults. | NR | 79 youths with cystic fibrosis, diabetes and myelodysplasia/ spina bifida (age = 16–25 years) and 52 parents | NR | TRAQ | Self- administered, data pooled from 2 surveys | High confidence in self-care espoused by youths and parents was belied by low reported readiness to manage many of the discrete tasks necessary for autonomous care, and by exceedingly low levels of preparation and planning for transition. |
| Cantú-Quintanilla et al. (53) Mexico | To provide further validation of UNC TRxANSITION Scale™ Version 3 in a Spanish version among Mexican youths with Chronic Kidney Disease or End-Stage Kidney Disease. | NR | 163 youths with chronic kidney disease or end-stage kidney disease (age = 10–22 years) | NR | Spanish version of UNC TRxANSITION Scale™ Version 3 | Administered by a trained psychologist | The Spanish Version of the UNC TRxANSITION Scale™ version 3 is a brief, reliable and clinically applicable tool that is easy to administer and has demonstrated initial validity in Mexican youths with CKD or ESKD. |
| Cohen et al. (54) United States | This paper examines the validity of the STARx Questionnaire, and includes examination of concurrent, predictive, and discriminant types of validity. | NR | 252 AYA with different chronic conditions | NR | STARx Questionnaire (Successful Transition to Adulthood with Therapeutics) | Self- administered, via online survey or via paper-and-pencil formats | The strong validity of the STARx Questionnaire, in tandem with its strong reliability, indicated adequate psychometric properties for this generic self-reporting measure. These strong psychometric properties should contribute to the STARx being a viable measure of health care transition for both research and clinical purposes. |
| Ferris et al. (29) United States | The Self-Management and Transition to Adulthood with Rx = Treatment (STARx) Questionnaire was developed to collect information on self-management and HCT skills | Pilot study | 194 youths, AYAs, with different chronic conditions, and their parents | NR | STARx | Self- administered, via paper and pencil or on-line | The STARx Questionnaire is a reliable, self-report tool with adequate internal consistency, temporal stability, and a strong, multidimensional factor structure. It provides an additional assessment strategy to measure self-management and transition skills in AYAs with chronic conditions. |
| Moynihan et al. (58) Canada | To refine and psychometrically test the Am I ON TRAC for Adult Care questionnaire. | Descriptive cross-sectional study. | 200 adolescents with different chronic conditions (age = 12–19 years) | NR | Am I ON TRAC | Self- administered | Factor analysis of the knowledge items identified a 14-item unidimensional scale. Knowledge and behavior sub-scale scores increased with age, with a stronger relationship between knowledge and age. Psychosocial maturity correlated with both sub-scale scores, but had a stronger association with behavior. Psychosocial maturity and age had a weak but significant correlation suggesting age is a loose proxy for maturity. |

*(Continued)*

**TABLE 1 |** (Continued)

| Author-Year and Country | Aim of the study | Study design | Population (patient\ parents, age) and chronic condition | Neuro developmental and/or mental disorder* | Measurement tool | Administration method and data collection | Results |
|---|---|---|---|---|---|---|---|
| Karahroudy et al. (48) Iran | To determine the relationship between demographic characteristics and self-management in adolescents with type 1 diabetes. | Descriptive-analytical cross-sectional study | 426 adolescents with type 1 diabetes (age = 13–18 years) | NR | Self-Management of type 1 Diabetes in Adolescence (SMOD-A) | Self-administered, in the hospital or at home | The results showed that the presence of another diabetic member in the family leads to higher levels of self-management in some dimensions, including problem-solving, communication, and goals, yet to lower levels in some others, including collaboration with parents and diabetes care activities |
| Nazareth et al. (59) United States | To improve reliability and generalizability of the STARx and report initial reliability data on the STARx-P Questionnaire | NR | 341 parents (89.4% mothers) and 455 children with kidney disease, inflammatory bowel disease, diabetes, cerebral palsy, sickle cell, and cystic fibrosis (mean age = 12.28 ± 2.53) | NR | STARx (Successful Transition to Adulthood with Therapeutics) STARx P | Self-administered, via e-mail | The current study shows the same factor structure for a parental version (STARx-P) with good internal reliability. Age was significantly correlated with all factors as well as the total score for the AYA patient reported STARx scores, while the parent report STARx-P was only significantly related to age for Factor 2: Self-management |
| Sawin et al. (46) United States | The purpose of this psychometric study was to evaluate the reliability and validity of the 17-item generic Adolescents Young Adult Self-Management and Independence Scale II (AMIS II). | NR | 201 adolescents - young adults with spina bifida (age = 12–25 years) and 111 parents | NR | AMIS II | Structured interview rated by health care providers, via in-person or telephone interview | Exploratory factor analysis of parent data supported the Condition Self-Management and Independent Living Self-Management. CFA of AYA data confirmed these two factors and an overall scale with good fit statistics (GFI and CFI = 0.86 to −0.95; RMSEA = 0.057). Internal reliabilities ranged from o: = 0.72–0.89. Intraclass correlation analysis supported the stability of the instrument (ICC* parent report = 0.82, AYA report = 0.84). Concurrent validity was supported with low to moderate correlations IO six related but distinct variables. |
| Sheng et al. (2) China | To explore the relationships between FM, self-management and transition readiness, and quality of life (QoL), and identify the potential CYP or family factors influencing the relationships. | Cross-sectional design | 268 patients, CYP, with diabetes, rheumatic disease, or renal disorder (age = 8–18 years) and their caregivers | NR | STARx | Self-administered, paper and pencil | This study was unique in that it identified FM*-related facilitators and barriers to CYP's self-management and transition readiness skills and explored optimal mechanisms for the provision of family-focused transition support in health-care settings. |
| Zhong et al. (61) United States | To evaluate the roles of key individual, family, and illness characteristics on the levels of and gains in longitudinal healthcare transition readiness | Longitudinal observational study | 566 adolescents and young adults with different chronic conditions (age = 12–31 years) | NR | The TRxANSITION Index | Administered by trained providers during routine visits or follow-up | Studies have shown that many AYAs rely on their caregivers for disease management, regardless of care setting, possibly explaining why they do not master these skills until an older age. |

*(Continued)*

**TABLE 1 |** (Continued)

| Author-Year and Country | Aim of the study | Study design | Population (patient\ parents, age) and chronic condition | Neuro developmental and/or mental disorder* | Measurement tool | Administration method and data collection | Results |
|---|---|---|---|---|---|---|---|
| Culen et al. (55) Austria and Germany | To cross-culturally adapt and to pilot-test a German version of the Transition Readiness Assessment Questionnaire (TRAQ 5.0) and to provide a tool that can be applied broadly during the HCT process of YSHCN. | Pilot study | 172 patients, YSHCN, with different chronic conditions (age = 14–23 years) | NR | TRAQ-GV-15 | Self-administered, during routine clinical care | The German version of the TRAQ has a direct benefit for YSHCN. The administration of the TRAQGV−15's inevitably led to transition centered communication with health professionals, encouraged caregivers to enhance AYAs' autonomy and sensitized YSHCN for transition specific issues. |
| Shackleford et al. (40) United States | To examine the relationship between the three innate needs of Self-Determination Theory (SDT), self-management of care and adherence to treatment, and the relationship with health-related quality of life (HRQOL) for adolescents with congenital heart disease (CHD). | Experimental, cross-sectional, correlational study | 92 patients with congenital heart disease (age = 13–18 years) | Autism, DiGeorge Syndrome | UNC TRxANSITION Scale | Self-reported | Better family and social support have been associated with better treatment adherence in adolescents with chronic illnesses, including those with renal, liver, heart, and lung transplants. Also, better peer support has been associated with improved adherence in adolescents with diabetes and asthma |
| Tan et al. (51) Malaysia | To assess medication self-management among parents of children with epilepsy and its association with sociodemographic data, clinical characteristics, antiepileptic drug (AED) regimen complexity, and parent self-reported AED adherence. | A cross-sectional survey | 166 parents of children with epilepsy (age ≤ 18 years) | NR | Pediatric Epilepsy Medication Self-Management Questionnaire (caregiver version) | Self-administered, in hospital | The degree of medication self-management among parents of children with epilepsy was satisfactory. A more complex regimen was associated with poorer medication self-management. Barriers to treatment, including disliking taste, parent forgetfulness, and swallowing difficulties, should be addressed to empower parents in achieving better medication self-management. |
| Hart et al. (63) United States | To develop and evaluate a disease-neutral, parental report of their own health knowledge regarding their youth's condition and a parental proxy assessment of youth HCT readiness to be used in parents of youth with chronic health conditions and verified against the medical record by adapting the TRxANSITION Index. | NR | 93 parents of children with different chronic conditions (age = 12–25 years) | NR | TRxANSITION Index–Parent Version | Administered via personal interview and verified against the medical record | The TRxANSITION Index–Parent Version shows promise as a means of assessing parent knowledge of a youth's illness and may provide an accurate proxy assessment of a youth's HCT readiness skills. |
| Ma et al. (57) China | To translate, culturally adapt and evaluate the reliability and validity of the Chinese version of the Self-Management and Transition to Adulthood with Rx = Treatment Questionnaire | Multicenter cross-sectional | 471 children and young people/ adolescents with different chronic conditions (age = 8–18 years) | NR | Star X—C | Self-reported | Four major factors were identified in the Chinese version of the questionnaire, and it had a good fit to the target population. Validity was analyzed through EFA using principal component analysis with varimax rotation and CFA. |

**According to the DSM 5 classification; NR, Not Reported; SCIS, Self-Care Independence Scale; TRAQ, Transition Readiness Assessment Questionnaire; CSU, Central South University; HCT, Health Care Transition; AYA, Adolescent and young adult; SHCN, Special Health Care Needs; GFI, Goodness of fit index; CFI, Comparative Fit Index; RMSEA, Root Mean Square Error of Approximation; ICC, Intraclass Correlation; CYP, Children and Young People; YSHCN, Youth with Special Health Care Needs; USA, United States of America.*

**TABLE 2 |** Characteristics of the self-care measurement tools retrieved from this review.

| Name of the measurement tool, Original/Adapted | Author and Year | Description of the tool or subscale | N. Included items | Languages | Complete tool or dimension | Target population and Chronic condition | Patient age (year) | Administration method | Conceptual model |
|---|---|---|---|---|---|---|---|---|---|
| Family Asthma Management System Scale (FAMSS) Original | Klinnert et al. (52) | The FAMSS evaluates the effectiveness of the family asthma management system. | 11 subscales | English | 4/11 dimensions: Adherence with asthma medications, Adherence with environmental recommendations, Assessment of child's symptoms, Appropriateness of action plan and emotional response to asthma symptoms | Parents of children with asthma | 6–9 | Administered by research assistants | Family asthma management system |
| Self-Care Independence Scale (SCIS) Original | Patton et al. (38) | The SCIS evaluates children's level of independence in their cystic fibrosis treatment. | 44 | English | Complete scale | Parents of children with cystic fibrosis | 4–17 | Self-reported | NR |
| Self-Management of Type 1 Diabetes in Adolescence (the SMOD-A) Original | Schilling et al. (49)† | The SMOD-A evaluates self-management in youths with type 1 diabetes. | 33 | English/Chinese‡ | Complete scale | Patients with type 1 diabetes | 13–21 | Self-reported | NR |
| Pediatric Epilepsy Medication Self-Management Questionnaire (PEMSQ) Original | Modi et al. (50) | The PEMSQ evaluates medication self-management in children with epilepsy. | 15 of 27 | English/Malay§ | 2/4 dimensions: Adherence to medications and clinical appointments, Barriers to treatment | Parents of children with epilepsy | 2-14 | Self-reported | NR |
| Adherence Schedule in Transplantation-Proxy Child (ASiT-PC) Original | Giardini et al. (62) | The ASiT-PC evaluates the cognitive relational antecedents of adherence to treatment and the self-efficacy in disease management in patients before and after transplantation. | 11 | Italian¶ | Complete scale | Parents of children, solid-organ pre and post-transplant recipients | NR | Self-reported | NR |
| Transition Readiness Assessment Questionnaire (TRAQ) Original | Sawicki et al. (65)mm | The TRAQ evaluates readiness for healthcare transition among youth with special healthcare needs. | 20 | English/German* | Complete scale | Patients with special health care needs and their parents | 16–26 | Self-reported | Transtheoretical model |
| (UNC) TR(x)ANSITION Scale Original | Ferris et al. (56)# | The (UNC) TR(x)ANSITION Scale evaluates self-management and health care transition skills in adolescents and young adults with chronic conditions. | 13 of 33 | English/Spanish♦ | 3/10 dimensions: Adherence, Nutrition, Self-management skills | Patients with chronic conditions | 12–22 | Administered by the transition coordinator through an interview | A report of academy of science and self-determination theory |
| Successful Transition to Adulthood with Therapeutics = Rx (STARx) Questionnaire Original | Ferris et al. (29)° | The STARx questionnaire evaluates health transition readiness in young people with chronic diseases. | 9 of 18 | English/Chinese■ | Section 1 of 3 | Patients with chronic conditions | 8–25 | Administered individually online | NR |

*(Continued)*

**TABLE 2 |** (Continued)

| Name of the measurement tool, Original/Adapted | Author and Year | Description of the tool or subscale | N. Included items | Languages | Complete tool or dimension | Target population and Chronic condition | Patient age (year) | Administration method | Conceptual model |
|---|---|---|---|---|---|---|---|---|---|
| ON Taking Responsibility for Adolescent/Adult Care (ON TRAC) Adapted from Williams et al. (92) | Moynihan et al. (58) | The revised ON TRAC evaluates youths' capabilities in performing life skills required to actively participate in their health care and function independently as adults. | 25 | English | Complete scale | Patients with chronic conditions | 12–19 | NR | Holistic model |
| The Parent STARx Questionnaire (STARx-P) Adapted from Ferris et al. (29) | Nazareth et al. (59) | The STARx-P Questionnaire evaluates parents' perspective on their child's health care transition readiness. | 5 of 18 | English | 1/3 dimension: self-management | Parents of children with chronic conditions | 6–17 | Self-reported, online | NR |
| Adolescent Self-Management and Independence Scale II (AMIS II) Original | Sawin et al. (46) | The AMIS II evaluates the adolescent's increasing responsibility for and implementation of self-management behaviors. | 5 of 17 | English | 2/8 dimensions: Self-management medications, Preventing complications | Patients with spina bifida and their parents | 12–25 | Structured interview rated by healthcare providers | NR |

†*The same scale is used by Karahroudy et al. (48) (Author of included study);* ‡*The Chinese version is C-SMODA by Guo et al. (47) (included study);* §*The Malay version is by Tan et al. (51) (included studies);* ¶*Translated in English; The same scale is also used by Sawicki et al. (60) (included study);* **The German version is TRAQ G.V 15 by Culen et al. (55);* #*The same scale is also used by Shackleford et al. (40) and Zhong et al. (61) (included studies);* ◦*The same scale is used by Cohen et al. (54)* ◆ *The Spanish version is C TRxANSITION Scale*™ *Version 3 by Cantú-Quintanilla et al. (53) (included study);* ■ *The Chinese version is by Sheng et al. (2) and Ma et al. (57) (included studies).*

chronic conditions (29, 56, 58, 59, 62, 65). Five of the 11 instruments were self-administered (45.45%) (38, 49, 50, 62, 65), three instruments were administered by others, such as the research assistant (27.27%) (29, 46, 52, 56, 59) and one (9.09%) did not specify this (58).

Four of the 11 instruments (36.36%) described the conceptual models of reference, the other seven instruments (63.63%) did not refer to any conceptual model. In particular, the UNC TRxANSITION scale used the self-determination theory as reference model (56), the TRAQ scale used the Transtheoretical model (65), the Family Asthma Management System Scale (FAMMS) was developed according to the Family asthma management system model (52), and the ON Taking Responsibility for Adolescent/Adult Care (ON TRAC) used the Holistic model (58). *Psychometric characteristics of the tools (Validity and Reliability).*

The 13 studies reported in **Table 3** explored the psychometric characteristics—validity and reliability—of the 11 measurement tools included in this review. Content validity was tested for five instruments (46, 49, 56, 57, 65), following the COSMIN taxonomy (45). Construct validity was verified through Exploratory Factor Analysis (EFA) for six instruments (29, 49, 50, 57–59, 65), and through Confirmatory Factor Analysis (CFA) for two instruments (46, 57). Only for the Star-x instrument the construct validity was verified both through EFA and CFA (57). With regard to criterion validity, concurrent validity was used to analyze four instruments (38, 46, 54, 58), and among these instruments, predictive validity was verified only for StarX and TRAQ (54, 65). The Known-groups validity was tested for the TRAQ instrument (65). Furthermore, the correlation/regression between self-care and child age was explored in seven instruments (29, 38, 50, 54, 56–59, 65).

Regarding reliability, internal consistency was verified in 11 instruments (29, 38, 46, 49, 50, 52, 56–59, 65). Test-retest reliability was tested in four instruments (29, 38, 46, 49), and inter-rater reliability was also verified for the SCIS e the AMIS II scale (38, 46). With regard to the FAMSS and the UNC TRxANSITION Scale, inter-rater reliability was verified in addition to internal consistency (52, 56). Lastly, responsiveness and non-differential validity were not reported for any instruments.

## Self-Care Aspects of Each Instrument

In this review, the self-care aspects/areas reported in the 11 instruments were described according to Riegel's self-care theory focusing on the aspects of each of the three self-care domains (self-care maintenance, self-care monitoring, self-care management) by Riegel (**Table 4**). As regards to self-care maintenance, all the 11 instruments included the aspect/area of medication adherence and only the (UNC) TR(x)ANSITION Scale and The Parent STARx Questionnaire (STARx-P) included the aspect of treatment adherence (56, 59). Feeding was explored in three instruments: the UNC Tr(x)ansition scale, Transition Readiness Assessment Questionnaire (TRAQ) and Adherence Schedule in Transplantation-Proxy Child (ASiT-PC) (56, 62, 65). The aspect of lifestyle was examined only in the TRAQ (65), whereas the prevention aspect was included in two instruments:

**TABLE 3 |** Psychometric characteristics of the self-care tools.

| | | | VALIDITY | | | | | | RELIABILITY | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **References** | **Measurement tool** | **Face and Content validity** | **EFA** | **CFA** | **Known-groups validity ($p < 0.05$)** | **Correlation/ Regression Self-care with child's age ($p < 0.05$)** | **Concurrent validity** | **Predictive validity** | **Internal consistency** | **Test-retest** | **Inter-rater** |
| Klinnert et al. (52) | Family Asthma Management System Scale (FAMSS) | NR | NR | NR | NR | NR | NR | NR | Cronbach's alpha for FAMSS Summary Score was 0.91. | NR | Inter-rater reliability was assessed based on 15 (50%) interviews. Intraclass correlation for was high ($r = 0.97$). |
| Patton et al. (38) | Self-care Independence Scale (SCIS) | NR | NR | NR | NR | Scores correlated positively with child's age ($r = 0.67$, $P < 0.001$). | Scores were related to children's treatment knowledge and level of dependence in non-illness activities. | NR | Cronbach's coefficient alpha: 0.93. | 35 parents completed the SCIS twice over a 4-week period ($r = 0.81$, $P < 0.001$) | Interrater reliability, was good for both the total knowledge score ($r = 0.93$, $P < 0.001$) and individual treatment domain levels ($r = 0.73$–$0.96$, $P < 0.01$). |
| Schilling et al. (49) | Self-Management of Type 1 Diabetes in Adolescence (SMOD-A) | Assessed by multiple groups of experts. | EFA revealed five subscales | NR | NR | NR | NR | NR | Cronbach's alphas for the five subscales ranged from 0.71 to 0.85. | Over 3 months it was 0.67 for the total scale and ranged from 0.34 to 0.47 for the 5 subscales | NR |
| Modi et al. (50) | Pediatric Epilepsy Medication Self-Management Questionnaire | NR | Principal axis factoring | NR | NR | No significant correlations were found with child's age and Pediatric Epilepsy Self-Management scales. | NR | NR | Cronbach's alphas ranged from 0.63 to 0.93. | NR | NR |
| Giardini et al. (62) | Adherence Schedule in Transplantation-Proxy Child (ASiT-PC) | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| Sawicki et al. (65) | Transition Readiness Assessment Questionnaire—TRAQ | Content/face validity by youths and experts | Principal component exploratory factor analysis. | NR | TRAQ scores differed based on the respondent's primary diagnosis, age, and sex. | Older age was associated with higher scores ($p < 0.001$) | NR | Multivariate linear regression | Cronbach's alpha for the entire questionnaire was: 0.93. | NR | NR |

*(Continued)*

**TABLE 3 |** (Continued)

| References | Measurement tool | Face and Content validity | VALIDITY | | | | | | RELIABILITY | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | EFA | CFA | Known-groups validity ($p < 0.05$) | Correlation/ Regression Self-care with child's age ($p < 0.05$) | Concurrent validity | Predictive validity | Internal consistency | Test-retest | Inter-rater |
| Ferris et al. (56) | UNC TRxANSITION Scale | Determined with national experts, clinicians, and patients. | NR | NR | NR | The total score increased with the advancing of age at univariate linear regression ($\beta = 1.08$, $p < 0.0001$). | NR | NR | Each of the items significantly correlated in a moderate to strong fashion ($r > 0.42$) with their respective domains (item-total correlations). | NR | Two independent members of the research team assessed the extent of agreement of the responses to the items ($\kappa = 0.71$, 95% CI: 0.64, 0.77). |
| Ferris et al. (29), Cohen et al. (54) | STARx | NR | EFA identified six factors that accounted for about 65% of the variance: Medication management, Provider communication, Engagement during appointments, Disease knowledge, Adult health responsibilities, and Resource utilization. | NR | NR | Participant age and STARX total score were positively correlated ($r = 0.396$, $p < 0.001$). | The STARx and its subscales positively correlated with the scores of the UNC TRxANSITION Scale™ and the TRAQ. | The STARx was correlated positively with the literacy, self-efficacy, and adherence measures. | Alpha coefficient for the overall scale: 0.80. | 26 participants had two different test observations with 365 days: strong correlation between the first and second total score ($\beta = 0.704$, $p < 0.001$) | NR |
| Ma et al. (57) | STARx, Chinese version | The overall S-CVI/Ave of the expert content validity scores was 0.96 | Four major factors were identified at EFA using principal component analysis with varimax rotation. | The CFA model indicated that there was a good fit. | NR | The *t*-test revealed that the scores of three factors and the overall scale were lower in the 8–11 than the 12–18 years age group. | NR | NR | Cronbach's $\alpha = 0.812$. | NR | NR |

*(Continued)*

**TABLE 3 |** (Continued)

| References | Measurement tool | Face and Content validity | VALIDITY | | | | | | RELIABILITY | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | EFA | CFA | Known-groups validity ($p < 0.05$) | Correlation/ Regression Self-care with child's age ($p < 0.05$) | Concurrent validity | Predictive validity | Internal consistency | Test-retest | Inter-rater |
| Nazareth et al. (59) | Parent STARx | NR | The factors of the STARx-P were confirmed using the same PCA method that was used to determine the underlying structure of the STARx. | NR | NR | The STARx-P self-management subscale was correlated positively with child chronological age. | NR | NR | Cronbach's alpha coefficient was moderate to good ($\alpha = 0.545–0.759$). | NR | NR |
| Moynihan et al. (58) | Am I ON TRAC | NR | EFA using PCA identified a 14-item unidimensional scale. | NR | NR | Knowledge and behavior sub-scale scores increased with age. | The Psychosocial Maturity Inventory had significant moderate correlations with the ON TRAC scores. | NR | For Cronbach's alpha coefficient was 0.84. | NR | NR |
| Sawin et al. (46) | AMIS II | Content validity was conducted using health care professionals, parents, and AYA. | EFA, using principal axis analysis with an oblique rotation, conducted on parent data, supported two related self-management factors. | CFA of AYA data confirmed the two factors and an overall scale with good fit statistics. | NR | AYA age had low but significant correlations with Condition Self-Management ($r = 0.24$ and 0.30 for parent and AYA report) but higher relationships to Independent Living Self-Management ($r = 0.047–0.54$ for parent and AYA report). | Higher self-management behaviors were correlated with less severe SB (sacral lesions), better self-care, higher decision-making participation and maturity, participation in higher number of chores, and higher adolescent responsibility for overall condition management. | NR | Cronbach's alpha for the scale and subscales was 0.78–0.82. Cronbach's alphas for parent and adolescent was 0.87–0.89 for the total scale. | 43 parents-AYA pairs, at a 2–3 week interval: ICC for parent total scale was 0.82, and for the AYA total scale was 0.84. | Inter-rater reliability with the first author was established ($r = 0.88$). Periodical confirmation of inter-rater reliability ($r = 0.85$). |

*AYA, Adolescent and young adults; RMSEA, Root Mean Square Error of Approximation; GFI, Goodness of fit index; CFI, Comparative Fit Index; EFA, Exploratory factor analysis; PCA, Principal Component Analysis.*

FAMSS and ON TRAC (52, 58). The knowledge of health-care services was explored in two instruments, the Parent STARx Questionnaire (STARx-P) and TRAQ (59, 65).

With regard to self-care monitoring, the area of vital signs monitoring was explored only in the Adherence Schedule in Transplantation-Proxy Child (ASiT-PC) and in the Adolescent Self-Management and Independence Scale II (AMIS II) (46, 62). The signs and symptoms aspect was treated in the Self-Management and Independence Scale II (AMIS II) (46).

For the self-care management domain, only one aspect (i.e., consulting) was described in four instruments: Successful Transition to Adulthood with Therapeutics = Rx (STARx) Questionnaire, (UNC) TR(x)ANSITION Scale, ON TRAC and The Parent STARx Questionnaire (STARx-P) (29, 56, 58, 59).

## DISCUSSION

In this literature review, 11 self-care instruments addressing CYAs with chronic diseases were identified. These instruments differ for pathologic contexts and age range. The instruments providing more valid psychometric measurements were AMIS II and STARx. These are also the instruments published more recently (46, 57).

Although all the identified instruments included at least one of Riegel's self-care domains, only one instrument, the SMODA, investigated all of the three self-care domains: self-care maintenance, self-care monitoring, self-care management (49). Every instrument included in this review explored self-care maintenance, focusing particularly on medication and treatment adherence. The importance attributed to autonomy in medication administration might be associated to the advantage of reducing use of healthcare services (66). However, few instruments focused on monitoring vital signs and symptom management. Concerning self-care monitoring, only one instrument investigated signs and symptoms monitoring, an important aspect to detect important health status changes. As regards the self-care management area, the instruments explored mostly the consulting aspect, leaving very little space for the management of complications or acute exacerbations through spontaneous self-care strategies. Overall, the medical management of a chronic condition is not new, probably along with paternalistic and directive guidance in the relationship between healthcare providers and families (67), often associated with the passive decision-making of families allowing the provider to choose the course of action (68, 69). This aspect might reflect the persisting belief in the monopoly on health of the healthcare providers (70), and a great trust assigned to healthcare professionals of reference, such as the nurse case managers (71).

Studies showed that also self-care monitoring and self-care management is important. For example, Riegel et al. (27) describe how symptom monitoring affects self-care behaviors, underling the importance of symptom detection, interpretation and response as fundamental elements of the self-care process (27). Sawin et al. (46) found that when CYAs monitored their signs and symptoms they achieved independence much earlier than others (46). Also Nazareth et al. (59) found that

**TABLE 4** | Self-care dimensions and aspects of each measurement tool.

| | | Self-care maintenance | | | | | Self-care monitoring | | Self-care management |
|---|---|---|---|---|---|---|---|---|---|
| **Name of the measurement tool** | **References** | **Medication adherence** | **Treatment** | **Nutrition** | **Life style** | **Prevention** | **Knowledge of health-care services** | **Clinical parameters** | **Symptoms/ Signs** | **Consulting** |
| FAMSS | Klinnert et al. (52) | X | | | | X | | | | |
| SCIS | Patton et al. (38) | X | | | | | | | | |
| SMODA | Schilling et al. (49) | X | | | | | X | X | | X |
| PEMSQ | Modi et al. (50) | X | | | | | | | | |
| ASiT-PC | Giardini et al. (62) | X | | X | | | | X | | |
| TRAQ | Sawicki et al. (65) | X | | X | X | | X | | | |
| (UNC) TR(x)ANSITION Scale | Ferris et al. (56) | X | X | X | | | | | | X |
| Rx STARx | Ferris et al. (29) | X | | | | | | | | X |
| ON TRAC | Moynihan et al. (58) | X | | | | X | | | | X |
| AMIS II | Sawin et al. (46) | X | | | | | | X | X | |
| STARx-P | Nazareth et al. (59) | X | X | | | | X | | | X |

*TRAQ, Transition Readiness Assessment Questionnaire; SCIS, Self-Care Independence Scale; ASiT-PC, Adherence Schedule in Transplantation-Proxy Child; FAMSS, Family Asthma Management System Scale; PEMSQ, Pediatric Epilepsy Medication Self-Management Questionnaire; Rx STARx Questionnaire, Successful Transition to Adulthood with Therapeutics; STARx-P, The Parent STARx Questionnaire; ON TRAC, ON Taking Responsibility for Adolescent/Adult Care; SMODA, Self-Management of Type 1 Diabetes in Adolescence; C SMOD-A, Chinese Version of Self-Report Measure of Self-Management of Type 1 Diabetes for Adolescents; AMIS II, Adolescent Self-Management and Independence Scale II.*

when CYAs responded promptly to signs and symptoms of exacerbation they became more knowledgeable about their disease management (59).

Specific instruments were developed for the most common chronic diseases. In particular, the SMOD-A scale was developed for diabetes, SCIS for cystic fibrosis, FAMSS for asthma, PEMSQ for epilepsy, and AMIS II for spina bifida (38, 46, 49, 50, 52). The decision to have an instrument for a specific disease might be due to the large prevalence of these diseases, mostly diabetes and asthma, in the CYA population (72, 73). However, even though having instruments for assessing self-care in CYAs with specific chronic diseases is fundamental, there are also many other chronic and sometimes rare conditions to take into consideration. Therefore, the development of a non-specific instrument for the CYA population with different chronic conditions, considering the main age stages, might represent a useful innovation.

Furthermore, in this review, two instruments were found to be more generic [i.e., (UNC) TR(x)ANSITION Scale and TRAQ)] designed for chronic diseases in general or young adults with special healthcare needs (56, 65). However, these two instruments were focused on the skills required during the healthcare transition from pediatric to adult care services. Transition readiness reflects all the indicators (e.g., disease-specific knowledge, scheduling appointments) that young adults can begin, continue, and finish the transition process, including those skills influencing self-care (74–77). Therefore, self-care might be considered an integral part of transition readiness in the context of a challenging transfer to the adult health care system. To our knowledge, no instrument is currently available to assess self-care behaviors among CYAs of all ages aimed at exploring the shift of agency from family to autonomous self-care, regardless of the patient care context.

Moreover, also complex chronic diseases need to be considered. According to Cohen et al. (15), these conditions in childhood are characterized by four domains: (a) family-identified healthcare service needs, (b) one or more chronic clinical conditions, either diagnosed or unknown, (c) severe functional limitations, and (d) highly projected utilization of health resources. CYAs with complex chronic conditions need standardized approaches, tools and more effective competence to manage the complexity of these diseases (78). Therefore, it would be useful to develop a specific self-care instrument for CYAs with complex chronic conditions.

Furthermore, the present review analyzed also the methods used to administer the instruments. Five instruments were self-reported since the respondents were in school-age or adolescents (38, 49, 50, 62, 65). Four instruments asked also the parents to fill in the questionnaire. This aspect might show how the family maintain a central and vital role in supporting both the children—during the pre and scholar age—and adolescents/young adults (79, 80).

Another aspect analyzed in the current review was the conceptual model underpinning each instrument. The conceptual models were specified in four instruments, such as the self-determination theory, the transtheoretical model, the holistic model, and family management of specific diseases such as asthma. Having instruments based on a theoretical framework, as the models reported above, is fundamental to obtain sounder and valid instruments (81). Recently, a self-care model has been developed for complex chronic conditions (28). This model includes the affecting factors, self-care behaviors and outcomes, highlighting that the more the patients are engaged in self-care behaviors, the more the results are positive.

## Implications for Practice

The findings of this review may help researchers identify instruments to assess the level of self-care in CYAs living with chronic conditions for research purposes, as outcome measures for interventional studies, or as a basis for further validation studies. Moreover, we recommend the use of self-care instruments in clinical practice. Although clinicians recognize the importance of promoting self-care in CYAs with chronic conditions, they need standardized approaches and psychometrically sound tools (78). Measuring a patient's level of self-care using an assessment instrument represents, for the clinician, the first step to identifying educational gaps and factors hindering the engagement process (82). Healthcare providers play an important role in fostering autonomy using educational strategies that take into consideration developmental stages and family support (83–85). Educational interventions have resulted in improvements in health outcomes, knowledge related to the chronic condition, quality of life, attendance at school, participation in social activities, and a decrease in health service interactions (86–88). In a second step, the patient could assume greater responsibility for managing their health alone or with the help of parents and healthcare professionals (89).

## Limitations

The findings of this review should be considered in light of some limitations. Firstly, the current review explored the instruments that concerned self-care in CYAs in every context. However, these contexts were found to be very broad and the concept of self-care may overlap with other concepts such as healthcare transition from pediatric to adult clinical setting (56). Therefore, the instruments found could not be considered totally comparable.

Secondly, the search strategy of this review did not include gray literature. Therefore, unquantifiable instruments might have been missed. Thirdly, studies measuring self-care in CYAs with neurocognitive impairment and in those living with cancer were not included in this review. Although the authors of this review believe that these patients deserve specific considerations, important features of the self-care process may have been missed.

Another limitation was the voluntary exclusion of the studies that assessed self-efficacy. Indeed, the aim of this review was to identify the instruments that evaluate self-care behaviors (maintenance, monitoring, management) rather than assessing confidence in self-care (90). However, future quantitative studies could investigate the confidence aspect since the process of self−care implies that self−care confidence (in patients and caregivers) influences the entire process of self−care across the three dimensions of self−care maintenance, monitoring, and management (91).

## CONCLUSION

This review analyzed 23 studies that described 11 self-care instruments for CYAs. Only one instrument assessed each aspect of self-care (maintenance, monitoring, and management) according to our definition. In particular, most of the instruments were focused on treatment adherence within self-care maintenance and ignored the aspects of prevention, feeding, and lifestyle. Less attention was given to vital signs and symptoms monitoring, and to responses to exacerbations of chronic conditions. Therefore, it would be useful to investigate how health professionals are focused on these self-care dimensions while providing education to patients and their families. Furthermore, future research may develop a comprehensive instrument measuring all the dimensions of self-care across all chronic conditions, also including those with medical complexity. Future instruments might be based on "The comprehensive model of self-care in CYA with chronic conditions" (28). This model could guide to a global evaluation of self-care in relation to developmental age, also considering the parent's contribution and shift of agency.

## 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/s.

## AUTHOR CONTRIBUTIONS

GS, VB, and VK made substantial contributions to the conception and design of the systematic review, conducted the literature search, data extraction, and drafted the manuscript. RM gave a substantial contribution to the translation of the text, moreover, critically reviewed and revised the manuscript. AL and GM contributed to evaluated the psychometric proprieties of the tools retrieved, updating the reference list, critically reviewed, and revised the manuscript. OG, MS, EV, and ET helped in results analysis, drafting and critically revising the manuscript. ID'O conceived and supervised all the phases of the systematic review, drafted and critically revised the manuscript for important intellectual content. All authors approved the final version of the manuscript as submitted and agreed to be accountable for all the aspects of this study.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fped.2022.832453/full#supplementary-material

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# Efficacy of a Transitional Support Program Among Adolescent Patients With Childhood-Onset Chronic Diseases: A Randomized Controlled Trial

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It is recommended that patients with childhood-onset chronic diseases (CCD) be transferred from pediatric to adult healthcare systems when they reach adulthood. Transitional support helps adolescents with CCD transition smoothly. Transition readiness is one of the key concepts to assess the efficacy of transitional support programs. This study aims to investigate the effect of a transitional support program on transition readiness, self-esteem, and independent consciousness among Japanese adolescents with various CCD using a randomized controlled trial. Adolescents with CCD aged 12–18 years participated in a randomized controlled trial evaluating the efficacy of a transitional support program. The patients in the intervention group visited transitional support outpatient clinics twice. They answered questionnaires regarding their disease and future perspectives to healthcare professionals and independently made a short summary of their disease. All the participants answered the questionnaires four times. Eighty patients participated in this study. Among those in the intervention group, transition readiness within one, three, and 6 months after interventions, and self-esteem within 1 month after interventions were higher than that of the control group. The scores on the "dependence on parents" subscale at 6 months after interventions were lower for the intervention group as compared to the control group. This program is expected to help patients transition smoothly from pediatric to adult healthcare systems.

**Keywords: transitional support, transition readiness, childhood-onset chronic diseases, adolescent patients, randomized controlled trial**

## INTRODUCTION

The number of patients with childhood-onset chronic diseases (CCD) such as congenital heart disease, childhood cancer, diabetes, and epilepsy has increased, along with advancements in medical and surgical care (1, 2). The mortality rate of patients with CCD aged 1–19 years was 10.46 (per 100,000 population) in 1975 and 3.12 (per 100,000 population) in 2008 (3). However, these patients often develop complications in adulthood due to age-related changes in the treatment region, decline in treatment adherence, and development of lifestyle-related diseases (4–6). Therefore, they need to continue visiting the hospital regularly from childhood to adulthood, and transfer from pediatric to adult healthcare systems based on their age and physical and mental development (7).

Transitional support has been the focus for facilitating a smooth transfer from pediatric to adult healthcare systems. Patients with CCD tend to stop regular hospital visits, based on their own judgment, during the transitional period. Previous studies indicated that 39–65% of patients with congenital heart disease stopped visiting the adult cardiology outpatient clinic in the transitional period (8–10). The reasons included confusion and concern associated with moving to a different healthcare system (11), insufficient explanation by healthcare professionals, and patients' poor understanding of the importance of regular and long-term hospital visits (12). Patients cannot receive optimal medical care and appropriately-timed interventions if they stop regular hospital visits, which may lead to a worsened prognosis (12, 13). Providing transitional support for patients, assessing their readiness for transfer to adult healthcare systems, and judging whether they can adapt to change before the transition is necessary to prevent a worsened prognosis owing to transfer from pediatric to adult healthcare systems.

Healthcare professionals should provide transitional support to enhance patients' "transition readiness." Transition readiness is the concept used by healthcare professionals to assess patients' readiness to transfer to adult healthcare systems and to judge whether they will adapt to the change. This includes an acceptance and understanding of their own disease, and active disease management (14). It is suggested that improvement in transition readiness leads to a better ability to adapt to adult healthcare systems (14–16). A framework for youth with type 1 diabetes during their emerging adulthood transition indicated that transitional events related to various changes that a patient experienced during development directly affected health, developmental, and behavioral outcomes. Furthermore, it showed that these outcomes predicted a successful transition (17). According to this framework, the transitional support program as a transitional event is expected to improve patients' transition readiness, a behavioral outcome predicting a successful transition.

Several previous studies have reported that transitional support programs improved transition readiness and various psychosocial outcomes among patients with CCD. A study of adolescents with congenital heart diseases revealed that face-to-face and online education by nurses about the disease and communication with healthcare professionals improved transition readiness and disease knowledge (18, 19). Another study with inflammatory bowel disease and type 1 diabetes patients also showed the improvement of their transition readiness, self-esteem, and patient-led communication through education by healthcare professionals *via* the Internet (20). Thus, transitional support programs based on disease-specific education by healthcare professionals with detailed disease knowledge have been developed and verified for efficacy. However, in situations where the facilities providing transitional support do not receive compensation from the medical system (such as in Japan), these validated programs, which are customized for a specific disease are unlikely to be accepted because of the lack of personnel for providing transitional support (21, 22).

Self-esteem and independent consciousness are also important psychological outcomes among patients with CCD in the transitional period. High self-esteem was related to high disease management among patients with CCD (23). Additionally, getting more information about the disease increased patients' adaptation to society and improved their self-esteem (24). Among the adolescents and young adults with CCD, independent consciousness was lower and dependence on parents was higher than that of healthy peers (25). Several studies have also suggested lower independence among patients with CCD regarding disease management, including taking medicine and visiting hospitals (26, 27). Thus, self-esteem and independent consciousness are important aspects in patients with CCD in the transitional period and are expected to improve according to the change in transition readiness.

Adolescents' independence is influenced in different ways by cultures and environments. A comparative study of parent–child relationships showed that Japanese youth experienced higher maternal control than their United States counterparts, owing to which the Japanese youth tended to be limited in their independence (28). Therefore, we need to support adolescent patients to be independent in their disease management, including their ability to communicate with healthcare professionals and visit doctors. Considering these difficulties in the capacity to provide transitional support as well as in the characteristics of patients, we need a transitional support program that can meet the needs associated with various CCD, can be managed with limited manpower and costs, and focuses on patients' independence to enable an effective and sustainable support system.

The aim of this study was to investigate the effect of a transitional support program on transition readiness, self-esteem, and independent consciousness among Japanese adolescents with various CCD using a randomized controlled trial (RCT). We expected that the intervention of this study will improve the patients' self-management skills by encouraging them to seek information about their disease and imagining future perspectives.

# MATERIALS AND METHODS

## Study Design

This study used a non-blinded randomized controlled trial design.

## Eligibility Criteria

We recruited adolescent patients with CCD from a single university hospital in an urban area of Tokyo from July 2017 to January 2018. The inclusion criteria were as follows: (1) 12–18 years old, (2) able to converse with the researchers and answer questionnaires in Japanese, (3) visiting the pediatric outpatient clinic at the study facility regularly (every 1 month to one year), (4) able to assent to participate, and their guardian(s) provide consent to participate. People were excluded if: (1) they were judged by their attending doctor to have difficulty participating in the study because of mental vulnerabilities independent of intellectual or developmental disabilities, or acute physical symptoms and (2) were not informed of their diagnosis.

## Recruiting and Allocation

The patients who met all the inclusion criteria and their guardian(s) were invited to participate in the study by their attending doctor during a regular appointment. The researchers then explained the study purpose and obtained written informed assent from patients and informed consent from their guardian(s). If the patients visited alone, the researchers obtained only their written assent and asked them to pass on the research explanation and consent document to their guardian(s). The consent document signed by their guardian was returned to the researchers by mail. After obtaining informed consent, the patients were randomly allocated into the intervention or control group through a cloud-based program that can be allocated by participants through the generation of random numbers by a computer. We adopted a permuted block method (block size 4) using age and sex as allocation factors.

## Procedure

Participants answered questionnaire surveys including the Japanese version of the TRANSITION-Q, Rosenberg Self-Esteem Scale, Independent Consciousness Scale, and demographic information at four different time periods: T1 (within 1 month after agreeing to participate in this study), T2 (intervention group: within 1 month after intervention [the second transitional support outpatient clinic]; control group: 4 months after T1), T3 (3 months after T2), and T4 (6 months after T2). While the time periods of T1, T3, and T4 were uniform between the two groups that of T2 was different between the two groups. We could not keep the timing of T2 uniform in the intervention group because it depended on the schedule of the second transitional support outpatient clinic of each patient; it was based on the schedule of their regular visits to their attending doctor. We defined the periods because we expected an average duration between T1 and the second transitional support outpatient clinic to be 3 months based on our experience. Patients who failed to return questionnaires or provide answers online were reminded *via* letters or e-mails after two- and four-week intervals. As part of usual care, all participants received a leaflet describing the overview and importance of transition between T1 and T2. The leaflet described the explanation, importance, and timing of transition, and information on who would support patients' transition.

## Intervention

A transitional support team consisting of pediatricians, nurses, psychologists, and nursing researchers reviewed and planned the intervention program. Contrary to previous RCTs validating transitional support programs, which included teleconference, Skype, web-based, and text-delivered interventions for participants, this study limited interventions to face-to-face consultations with healthcare professionals (18–20). In addition to regular visits to their attending doctor (usual care), the patients in the intervention group participated in transitional support outpatient clinics twice that were 20–30 min in duration. The transitional support program in this study included three important aspects: (1) the patients attended a transitional support outpatient clinic without their guardian(s), (2) healthcare professionals asked the patients questions using a common inquiry sheet, (3) the patients were asked to make "my health passport" to summarize the information of their disease after the first visit. The two visits were tailored to coincide with the patients' regular appointments to avoid additional absence from school. At both the clinic visits, pediatricians and nurses asked them questions relating to their basic information, diagnosis, treatments, daily life, and future perspectives, using a common inquiry sheet. We expected that in answering these questions, the patients would reflect on their understanding of the disease, its self-management, and imagine their future. If patients could not answer a question, we encouraged them to ask or consult with their attending doctor about the question before the next visit. In the first clinic visit, patients were asked to fill "my health passport" at home and bring it to the second clinic visit. My health passport consisted of three sections: basic patient information, information about the disease, and things they want people around them to help with. The basic patient information included the patient's date of birth, address, hospital and its contact information, the name and department of their attending doctor, emergency contact information, and information on the social security system or disability certificate. Information about the disease included the patient's diagnosis, treatment received in the past, treatment currently being received, precautions in daily life, and precautions to be taken in the future. In the last column, the patients were asked to describe how they would like the people around them to respond to their disease and treatment (e.g., what they would like them to do in the event of seizure). The above information was directly filled out by the patient on a sheet of paper. At the second transitional support outpatient clinic, we asked the patients how they had gathered the information to complete their "my health passport" and whether they had any difficulties completing it. We asked the

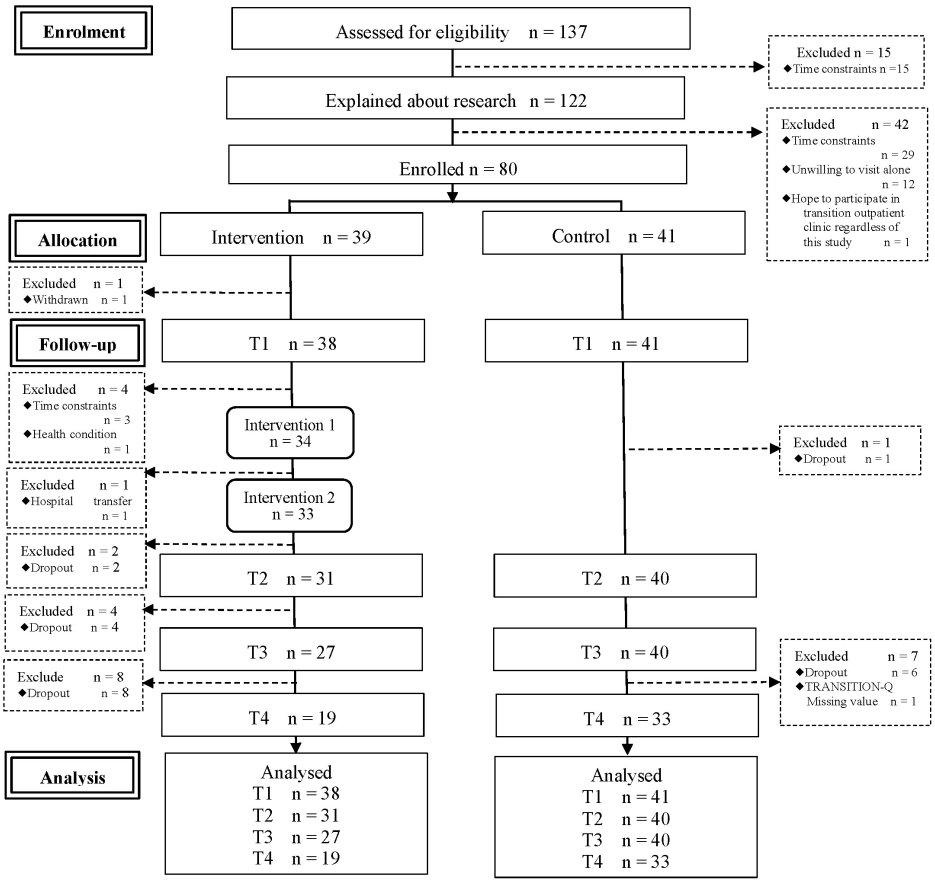


**FIGURE 1 |** Flow diagram of the progress through the phases of a parallel randomized trial of two groups.

patients to confirm with their attending doctor whether the information they completed was correct.

## Outcome Measures

The primary outcome of this study was transition readiness at T2 which indicated the immediate effect of the transitional support program.

### Transition Readiness

Transition readiness was measured with the TRANSITION-Q-J, the Japanese version of the TRANSITION-Q (16, 29). TRANSITION-Q-J was validated and comprises two subscales: communication and self-management and examination behavior (29). The scale includes items such as, "I ask the doctor or nurse questions" and "I contact a doctor when I need to." Responses are rated on a three-point Likert scale (2 = always to 0 = never). The total score is converted to a 0–100-point scale using the score chart (which is based on the Rasch theory) originally calculated by the author and developer of TRANSITION-Q. Higher scores indicate higher transition readiness. In this study, Cronbach's α was 0.84 for the TRANSITION-Q-J scale, 0.81 for the communication and self-management subscale, and 0.79 for the examination behavior subscale.

### Self-Esteem

We used the 10-item Rosenberg Self-Esteem Scale (RSES) to assess patients' self-esteem. Self-esteem was defined as "the sense that evaluates and trusts oneself as worthy of existing" and measured using a validated Japanese version of RSES (RSES-J) (30, 31). Examples of items in this scale are "I feel that I am a person of worth" and "I wish I could have more respect for myself." A four-point Likert scale (1 = strongly disagree to 4 = strongly agree) is used to measure responses; higher total scores indicated higher self-esteem. In this study, Cronbach's α for the RSES-J was 0.76.

### Independent Consciousness

The Independent Consciousness Scale is a validated measure and comprises three subscales: independence, dependence on parents, and resistance and confusion. It evaluates the transition from dependence to independence among adolescents and young adults (32). The independence subscale comprises 10 items (e.g., "I can take responsibility for my own judgment") including five items that are reverse scored; dependent on parents (e.g., "I want to depend on my parents when I am in trouble") and resistance and confusion (e.g., "I often feel inferior to adults") comprise five items each. A five-point Likert scale (1 = strongly disagree to 5 = strongly agree) is used to measure

responses. In this study, Cronbach's α was 0.79, 0.78 and 0.64 for each subscale.

## Participant Demographics

We collected data on sex, age, disease, school, medical treatment at home, and the frequency of the patients' regular visits to their attending doctor using questionnaires and medical record surveys.

## Sample Size Calculation

We calculated the sample size for a two-group comparison without considering the effect of covariates because data predicting the effect of covariates were unavailable. The mean TRANSITION-Q total score was 52.74 ± 12.40 in patients with childhood-onset chronic diseases aged 12–18 years, who did not receive a transitional support program (16). In addition, based on a randomized controlled trial of a transitional support program, we estimated that the score in the self-management domain of the Transition Readiness Assessment Questionnaire (TRAQ), a measurement to assess transition readiness that is different from the TRANSITION-Q, increased by approximately 0.7 SD after intervention (19). A total of 66 participants in both groups were calculated to increase the TRANSITION-Q-J score by 8.7 points (0.7 SD), with a power of 80 and an alpha of 0.05 (two-sided test), using R version 1.37 (R Foundation for Statistical Computing, Vienna, Austria). The dropout rate in previous studies ranged from 5.0 to 11.5% (19, 20); we predicted a higher dropout rate than previous studies because the design of this study required two visits to the transitional outpatient clinic to participate in the program. Finally, we set the sample size as 40 participants in each group, with a total of 80 participants.

## Statistical Analyses

R Version 1.37 (R Foundation for Statistical Computing, Vienna, Austria), IBM SPSS 25.0 J for Windows (SPSS, Chicago, IL, United States), and IBM SPSS Amos ver. 25.0 (SPSS, Chicago, IL, United States) were used for analyses, and $p < 0.05$ (two-tailed) was considered significant. We included data from patients who deviated from the study protocol but did not include the data from patients who dropped out. Descriptive statistics were calculated for the demographic and disease variables. We compared the intervention group and control group using Mann–Whitney's *U* test and Fisher's exact test. For each outcome, we compared the two groups at each time using analysis of covariance (ANCOVA), as the baseline was covariate. In the event of an interaction between the independent variable (group) and covariate (at baseline) by parallelism test, we compared the groups using analysis of variance (ANOVA).

## Ethical Considerations

This study was approved by the Ethics Review Committee of the University of Tokyo, School of Medicine and registered at the University Hospital Medical Information Network Clinical Trials Registry (UMIN000028997). Both the patients and their guardian(s) provided oral and written consent. All participants received a leaflet describing an overview of transition, along with elaborating on its importance, to reduce the potential disadvantages for the patients in the control group. In addition, researchers explained to the patients in the control group that they could withdraw their assent for this study and participation in the transitional support outpatient clinic at any time.

# RESULTS

## Participants' Characteristics

Of the 137 eligible candidates, 122 were provided details about this study from the researcher after their visit to their attending doctor. Eighty agreed to participate (participation rate 65.6%): 39 patients were allocated to the intervention group and 41 to the control group (**Figure 1**).

Demographic data are presented in **Table 1**. The participants' mean age was 14.7 ± 1.8 years in the intervention group and 14.4 ± 2.1 years in the control group. The major disease categories were cardiology: 34 (43.0%); hematology and oncology: 15 (19.0%); neurology: 13 (16.5%); nephrology: 8 (10.1%); pediatric surgery: 4 (5.1%); allergy and immunology: 3 (3.8%); and endocrinology: 2 (2.5%). Two (2.5%) participants had a developmental disorder and two (2.5%) had an intellectual disability. Sixty-one (77.2%) participants were taking medication (**Table 1**). Despite randomization, all four patients with developmental disorders or intellectual disabilities were included in the intervention group. Furthermore, at T2, where primary outcomes were assessed, there were no significant differences in patient' backgrounds between participants who continued to participate in the study and those who dropped out.

The interval between T1 and T2 was 4.8 months for the intervention group and 4.2 months for the control group. There was no significant correlation between the interval from T1 to T2 and the difference in scores on TRANSITION-Q-J at T1 and T2 ($\rho = 0.150$, $\rho = 0.216$, respectively).

Of the 31 participants who attended the second transitional support outpatient clinic, 6 did not bring their "my health passports" with them and consequently filled them in during the session.

## Transition Readiness

There were no significant differences between the two groups in the total and subscale scores of TRANSITION-Q-J at T1. The total score of the intervention group showed an increase at T2, which was maintained until T4. In contrast, the score of the control group remained constant at all-time points. The total score of the intervention group was significantly higher than that of the control group at T2 ($F = 8.45$, $p = 0.005$; $\eta^2_p = 0.11$), T3 ($F = 4.08$, $p = 0.048$, $\eta^2_p = 0.06$), and T4 ($F = 4.90$, $p = 0.032$, $\eta^2_p = 0.09$; **Table 2**, **Figure 2**). This was also true for the communication and self-management subscale score at T2 ($F = 9.07$, $p = 0.004$, $\eta^2_p = 0.12$), T3 ($F = 4.77$, $p = 0.033$, $\eta^2_p = 0.07$), and T4 ($F = 4.17$, $p = 0.049$, $\eta^2_p = 0.08$). However, no significant differences were found in examination behavior between the two groups at T2, T3, and T4.

**TABLE 1 |** Participants' characteristics.

| | Intervention (*n* = 38) | | Control (*n* = 41) | | |
|---|---|---|---|---|---|
| | ***n* (%) or M ± SD** | **Range** | ***n* (%) or M ± SD** | **Range** | ***p*** |
| Sex | | | | | |
| Male | 25 (65.8) | | 25 (61.0) | | 0.816[a] |
| Female | 13 (34.2) | | 16 (39.0) | | |
| Age | 14.7 ± 1.8 | [12–18] | 14.4 ± 2.1 | [12–18] | 0.465[b] |
| Disease | | | | | |
| Cardiology | 16 (42.1) | | 18 (43.9) | | 0.685[a] |
| Hematology and oncology | 7 (18.4) | | 8 (19.5) | | |
| Neurology | 7 (18.4) | | 6 (14.6) | | |
| Nephrology | 2 (5.3) | | 6 (14.6) | | |
| Pediatric surgery | 2 (5.3) | | 2 (4.9) | | |
| Allergy and immunology | 2 (5.3) | | 1 (2.4) | | |
| Endocrinology | 2 (5.3) | | 0 (0.0) | | |
| Frequency of hospital visits | | | | | |
| Every 1–3 months | 32 (84.2) | | 34 (82.9) | | 1.000[a] |
| Every 4 months or more | 6 (15.8) | | 7 (17.1) | | |
| Academic background | | | | | |
| Elementary school | 3 (7.9) | | 3 (7.3) | | 0.862[a] |
| Junior high school | 18 (47.4) | | 23 (56.1) | | |
| High school | 15 (39.5) | | 12 (29.2) | | |
| Vocational school | 2 (5.3) | | 2 (4.9) | | |
| Other | 0 (0.0) | | 1 (2.4) | | |
| Intellectual disability | 2 (5.3) | | 0 (0.0) | | 0.228[a] |
| Developmental disorder | 2 (5.3) | | 0 (0.0) | | 0.228[a] |
| Home medical treatment | | | | | |
| None | 7 (18.4) | | 9 (22.0) | | 0.783[a] |
| Medication | 29 (76.3) | | 32 (78.0) | | 1.000[a] |
| Blood glucose self-monitoring or self-injection | 2 (5.3) | | 3 (7.3) | | 1.000[a] |
| Exercise restriction | | | | | |
| None | 22 (57.9) | | 21 (51.2) | | 0.340[a] |
| Light exercise | 6 (15.8) | | 9 (22.0) | | |
| Moderate exercise | 6 (15.8) | | 3 (7.3) | | |
| Prohibited from exercising | 3 (7.9) | | 5 (12.2) | | |
| Restriction on how they go to school | 1 (2.6) | | 0 (0.0) | | |
| Unknown | 0 (0.0) | | 3 (7.3) | | |

*M, mean; SD, standard deviation; [a]Fisher's exact test; [b]Mann–Whitney's U test.*

**TABLE 2 |** Differences in Transition Readiness as measured by the TRANSITION-Q-J.

| | T1 (Intervention 38 vs. Control 41) | | | | T2 (Intervention 31 vs. Control 40) | | | | | T3 (Intervention 27 vs. Control 40) | | | | | T4 (Intervention 19 vs. Control 33) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **M** | **SD** | ***d*** | ***p*** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** |
| **TRANSITION-Q** | | | | | | | | | | | | | | | | | | | |
| Intervention | 48.05 | 15.50 | 0.04 | 0.859[a] | 55.52 | 14.33 | 0.11 | 8.45 | **0.005[b]** | 55.30 | 15.17 | 0.06 | 4.08 | **0.048[b]** | 55.21 | 14.51 | 0.09 | 4.90 | **0.032[b]** |
| Control | 48.78 | 16.93 | | | 48.20 | 15.10 | | | | 50.02 | 18.15 | | | | 47.15 | 16.05 | | | |
| **Communication and self-management** | | | | | | | | | | | | | | | | | | | |
| Intervention | 10.92 | 3.54 | 0.11 | 0.640[a] | 12.74 | 3.26 | 0.12 | 9.07 | **0.004[b]** | 12.74 | 4.93 | 0.07 | 4.77 | **0.033[b]** | 12.05 | 3.37 | 0.08 | 4.17 | **0.049[b]** |
| Control | 11.34 | 4.13 | | | 10.80 | 3.86 | | | | 11.17 | 4.06 | | | | 10.48 | 4.20 | | | |
| **Examination behavior** | | | | | | | | | | | | | | | | | | | |
| Intervention | 1.55 | 2.37 | 0.15 | 0.238[a] | 2.45 | 2.78 | 0.02 | 1.24 | 0.270[c] | 2.59 | 2.96 | 0.03 | 2.23 | 0.140[b] | 3.05 | 3.22 | 0.03 | 1.28 | 0.264[b] |
| Control | 1.90 | 2.40 | | | 1.90 | 1.91 | | | | 2.10 | 2.78 | | | | 2.24 | 2.61 | | | |

*M, mean; SD, standard deviation; d, Cohen's d;$\eta^2_p$, partial $\eta^2$;[a]Mann–Whitney's U test; [b]Analysis of covariance (ANCOVA); [c]Analysis of variance (ANOVA). ANOVA was adopted for Examination behavior at T2 because the interaction between the independent variable (group) and the covariate (score at baseline) was significant by parallelism test. Bolded values are statistically significant ($p < 0.05$).*

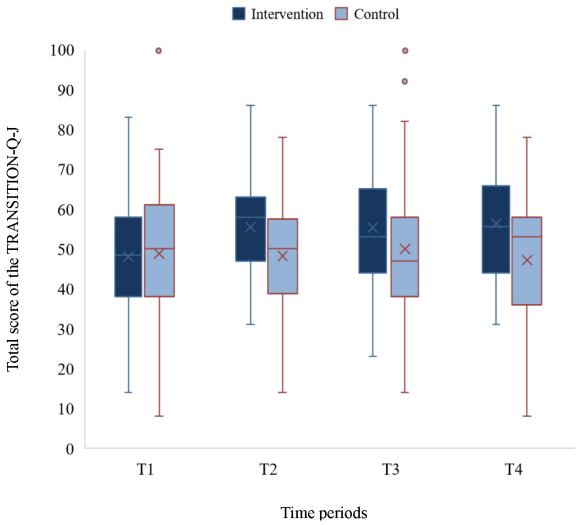


**FIGURE 2 |** A box plot of the score trends.

## Self-Esteem

No significant differences in self-esteem were found between the two groups at T1. However, self-esteem in the intervention group was significantly higher than that in the control group at T2 ($F = 4.54$, $p = 0.037$, $\eta^2_p = 0.07$; **Table 3**). There were no significant differences between the groups at T3 and T4.

## Independent Consciousness

The two groups did not show any significant differences across all three subscales of independent consciousness at T1, T2 and T3. At T4 ($F = 5.18$, $p = 0.027$, $\eta^2_p = 0.10$), the score for the subscale of dependence on parents was lower in the intervention than the control group (**Table 4**).

# DISCUSSION

The current study shows that the two-session transitional support outpatient clinics significantly enhanced and maintained transition readiness. Regarding secondary outcomes, self-esteem at T2 was higher in the intervention group than in the control group, and the dependence on parents' subscale at T4 showed lower scores for the intervention group than for the control group. Our findings support the efficacy of the transitional support program used in this study among adolescents with CCD.

The important aspects of the transitional support program of this study were as follows: (1) patients attended transitional support outpatient clinics without their guardian(s), (2) healthcare professionals asked the patients questions using a common inquiry sheet, and (3) patients made a "my health passport" to summarize the information of their disease. For most participants, this was the first visit to an outpatient clinic without guardians. A patient's transition readiness is enhanced through their own experiences of disease management, which had been handled by their guardian(s) for a long time (33). The intervention in this study provided an opportunity for patients to attend transitional support outpatient clinics without their guardian(s). This opportunity may have evoked awareness of their personal independence and improved transition readiness.

In the common inquiry sheet, we included questions regarding understanding of one's own disease; the status of self-management; and perspectives regarding job selection, marriage, and having a child. There was a positive relationship between having future perspectives and transition readiness (34). Moreover, the support, which focused on their future, addressed their concerns, and encouraged active participation in decision-making improved the transitional process (21, 35). In this study, when patients answered these questions, they reflected on their understanding of the disease, disease self-management, and imagined their future. It was considered that patients thought about their disease in relation to their future perspectives and understood the need for independence and self-management within this context.

Becoming aware of various problems at transitional support outpatient clinics may provoke or increase concern in patients. Indeed, adolescent patients with CCD tend to believe that they have limited job opportunities. They are also likely more anxious about marriage, having a child, and the risk of their children inheriting their disease (36, 37). Therefore, healthcare professionals need to offer follow-up care and consultations to facilitate information processing regarding these issues.

Through the process of filling "my health passport," the patients organized their disease information and realized their insufficient knowledge of the disease. The desire to know more about their own disease arises during adolescence, and by seeking information, adolescents with CCD are better equipped to face the future of living with their condition (37, 38). Further, seeking and selecting information fosters better decision-making and problem-solving skills among individuals living with CCD (38). Making a "my health passport" may also be considered as an experience of facing questions about their disease, which affected the changes in their attitudes. This included actively asking questions from healthcare professionals and seeking more information. The series of changes in the participants' attitude toward their disease may consequently improve their transition readiness.

Most of the existing transitional support programs have deemed disease-specific education to be an important intervention for successful transitions (18–20). Hence, the existing programs need to be specifically designed for each disease or set of diseases, such as congenital heart disease, diabetes, and childhood cancer. Furthermore, these programs require professionals with sufficient knowledge and experience of each disease. Contrary to existing programs, in this study, we proposed a common transitional support program for patients with various diseases and expected to observe changes in patients' information-seeking and examination behavior using a common inquiry sheet and the "my health passport," which were used by adolescent patients with CCD. We established evidence of the

**TABLE 3 |** Differences in self-esteem between groups as measured by the Rosenberg Self-esteem Scale.

| | T1 (Intervention 37 vs. Control 39) | | | | T2 (Intervention 29 vs. Control 38) | | | | | T3 (Intervention 23 vs. Control 38) | | | | | T4 (Intervention 18 vs. Control 33) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **M** | **SD** | ***d*** | ***p*** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** |
| Rosenberg Self-Esteem Scale | | | | | | | | | | | | | | | | | | | |
| Intervention | 24.97 | 4.89 | 0.24 | 0.291[a] | 26.34 | 5.49 | 0.07 | 4.54 | **0.037[b]** | 26.22 | 6.22 | <0.01 | 0.32 | 0.572[b] | 26.33 | 4.89 | 0.03 | 1.54 | 0.221[b] |
| Control | 26.18 | 5.14 | | | 25.37 | 5.36 | | | | 26.37 | 4.58 | | | | 25.48 | 5.67 | | | |

*M, mean; SD, standard deviation; d, Cohen's d;$\eta^2_p$, partial $\eta^2$; [a]Mann–Whitney's U test; [b]Analysis of covariance (ANCOVA). Bolded values are statistically significant ($p < 0.05$).*

**TABLE 4 |** Differences in independence consciousness between groups as measured by the Independent Consciousness Scale.

| | T1 | | | | | T2 | | | | | | T3 | | | | | | T4 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **n** | **M** | **SD** | ***d*** | ***p*** | **n** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** | **n** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** | **n** | **M** | **SD** | **$\eta^2_p$** | ***F*** | ***p*** |
| **Independence** | | | | | | | | | | | | | | | | | | | | | | | |
| Intervention | 37 | 33.11 | 6.70 | 0.05 | 0.818[a] | 29 | 33.59 | 6.18 | <0.01 | 0.04 | 0.852[b] | 23 | 34.17 | 6.52 | 0.01 | 0.55 | 0.461[b] | 18 | 34.33 | 5.91 | 0.02 | 1.04 | 0.313[b] |
| Control | 40 | 33.48 | 7.34 | | | 38 | 33.63 | 7.52 | | | | 39 | 32.74 | 7.33 | | | | 32 | 32.13 | 7.54 | | | |
| **Dependence on parents** | | | | | | | | | | | | | | | | | | | | | | | |
| Intervention | 38 | 17.58 | 3.96 | 0.09 | 0.779[a] | 30 | 17.60 | 3.54 | <0.01 | 0.12 | 0.732[b] | 24 | 17.08 | 3.79 | 0.04 | 2.41 | 0.125[b] | 19 | 16.05 | 4.84 | 0.10 | 5.18 | **0.027[b]** |
| Control | 41 | 17.22 | 4.29 | | | 39 | 17.56 | 4.04 | | | | 40 | 18.53 | 3.88 | | | | 33 | 18.48 | 3.56 | | | |
| **Resistance and confusion** | | | | | | | | | | | | | | | | | | | | | | | |
| Intervention | 38 | 13.50 | 3.63 | 0.05 | 0.802[a] | 30 | 13.47 | 3.76 | 0.01 | 0.75 | 0.391[b] | 24 | 13.33 | 4.16 | 0.01 | 0.39 | 0.533[b] | 19 | 13.68 | 3.27 | <0.01 | 0.18 | 0.673[b] |
| Control | 40 | 13.68 | 4.13 | | | 38 | 14.37 | 4.21 | | | | 39 | 14.13 | 3.84 | | | | 33 | 13.88 | 4.70 | | | |

*M, Mean; SD, Standard deviation; d, Cohen's d;$\eta^2_p$, partial $\eta^2$; [a]Mann–Whitney's U test; [b]Analysis of covariance (ANCOVA). Bolded values are statistically significant ($p < 0.05$).*

efficacy of a new transitional support methodology that does not rely on individual disease-specific education.

Conversely, there is also a need to consider the method of intervention. In the present study, the dropout rate in the control group was 20%, while that in the intervention group was 51%. Notably, dropouts in T2, immediately after the interventions, were higher in the intervention group. In previous studies that introduced online or email-based interventions, the dropout rate ranged from 3–20% (19, 39, 40). While the mandatory face-to-face intervention is a unique and advantageous feature of this program, it is also possible that the manner of intervention was inconvenient for the patients. For adolescents, who have many commitments such as tests and examinations, sporting fixtures, cultural events, family responsibilities, as well as social gatherings and club activities, it is a heavy burden to visit the outpatient clinic for transitional support at a fixed time. Therefore, it is necessary to consider the possibility of visiting the outpatient clinic during school vacations. Furthermore, we need to devise how to evaluate the long-term effects of the intervention, such as allowing patients to respond at their regular outpatient visits in order to reduce the dropout rate.

As previous studies have shown (23, 24), the transitional support program was expected to improve patients' self-esteem by answering questions from doctors and nurses, gathering information regarding their disease, and visiting the clinic without their guardian. Although the self-esteem scores for the intervention group at T2 were significantly higher than that for the control group, the difference in the two mean scores of the intervention and control groups was only 0.97 points. Further, at T2, the score decreased by 0.81 points for the control group. The significant differences between the two groups at T2 may have been affected by this decrease in the score of the control group. Thus, it is difficult to attribute the improvement in self-esteem in the intervention group at T2 to the transitional support received.

At T4, dependence on parents in the intervention group was significantly lower than that of the control group. Parents tended to continue taking initiative regarding their children's disease management, and the patients often had limited independence because of their parents' intervention (41, 42). The experience of getting the information from healthcare professionals by themselves, and that of conveying their understanding of their disease and future perspectives in the absence of their guardians may have enhanced patients' independence.

In many countries including Japan, transitional support from pediatric to adult healthcare systems has not been established as an independent medical domain, and it is difficult to secure related costs and human resources (21). Our study provides a methodology to help establish a sustainable support system.

## Limitations

Although the study has several merits, some limitations must also be discussed. First, the intervention group had several dropouts because of the participants' busy schedule, and only the patients

who were willing to transition were included in the final analysis; thus, the intervention effect may have been overestimated. In the future, it is necessary to examine the timing and method of interventions and devise ways to reduce attrition.

Second, we did not assess the age of onset of the patients' conditions and the duration of the chronic disease or compare it between the two groups even though it could have affected the patients' understanding of their disease and their ability to cope with it. The time elapsed since the chronic disease diagnosis could have had an impact on the efficacy of the intervention.

Third, in this study, we could not uniform the interval from T1 and T2 between the two groups. Though we confirmed no significant correlation between the interval from T1 and T2 and the difference in scores on TRANSITION-Q-J at T1 and T2, the length of the response interval could affect the transition readiness scores since transition readiness is related to patients' age (14–16). Therefore, future studies should uniform the interval of questionnaire surveys between the intervention and control groups.

Fourth, the result of self-esteem needs careful consideration. Although there was a significant difference in self-esteem between the two groups at T2, this difference was minute, and it may have depended on the decrease of the scores in the control group. In future studies, there is a need to investigate other factors related to possible changes in self-esteem.

Finally, as TRANSITION-Q is a scale that evaluates only the skills necessary to maintain health by subjective assessment. We should interpret the results of this study based on the understanding that it was limited to disease management and did not cover the general skills require for adolescents to be independent. Additionally, the efficacy of transitional support program could have been assessed using objective outcomes.

### Conclusion

We conducted a randomized controlled trial to reveal that the transitional support program in an outpatient setting is effective in enhancing transition readiness for CCD. This transitional support program that focused on patients' independence is useful for patients with any disease, as well as for healthcare professionals who do not have specific and sufficient knowledge and experience regarding each disease. Further, this program would be feasible under settings with limited manpower and resources, including such settings in Japan.

## DATA AVAILABILITY STATEMENT

The datasets analyzed in this article are not publicly available because participants of this study did not agree for individual data to be shared publicly. Requests to access the datasets should be sent to the corresponding author.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Review Committee of the University of Tokyo, School of Medicine. Written informed consent to participate in this study was provided by the participants and their legal guardian.

## AUTHOR CONTRIBUTIONS

MM-N contributed to conception, design, intervention, data collection, statistics, and data analysis, and drafted the manuscript. MI, YH, and AS participated in designing the study, intervention, and data collection. SS and AK participated in designing the study, intervention, data collection, and statistical analysis. SK and IS participated in designing the study and statistical analysis. KK and AO supervised the whole study process, from the design of the study and intervention implementation to the completion of the manuscript. All authors participated in the critical revision and read and approved the final manuscript.

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# Hospital Support for Siblings of Children With Illness in Japan

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Recent years have seen increased attention to the needs and support of siblings of children with chronic illness, and reports of intervention studies on siblings are gradually increasing worldwide. In Japan, the basic policy approved by the Cabinet in 2021 of The Basic Law for Child and Maternal Health and Development stipulates promoting support for the siblings of children with chronic illness, medical care, and disabilities. Simultaneously, practical reports are emerging. However, reports on the actual state of sibling support at medical institutions in Japan are limited. This study aimed to describe the actual state of support for siblings of children with illness in Japanese medical institutions using a cross-sectional design. Responses were obtained from 207 of 484 registered training facilities for Board-Certified Pediatricians of the Japan Pediatric Society through anonymous questionnaires investigating the actual state of siblings' support. Descriptive statistics were calculated, and the state of siblings' support was described. Fifty-two participants (25.1%) answered that the entire ward, including two outpatient departments, provided siblings' support, while 37 (17.9%) answered some staff made an effort, and 117 (56.5%) did not. Support mentioned included conversing with siblings, actively speaking to siblings, calling siblings' names, and counseling care through the parents. Of the 45 cases (21.7%) where siblings were invited to events and gatherings, 10 (22.2%) were siblings-centered events. Some cases involved collaboration with local sibling support groups such as non-profit organizations. This study clarified the actual state of siblings' support, and further expansion of this support is required.

**Keywords: children, chronic illness, hospital support, nationwide survey, siblings, children with illness, Japan**

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## INTRODUCTION

Recent years have seen increased attention to the needs and support of siblings of children with chronic illness. Since the concerns and attention of parents and other surroundings are primarily directed to children with chronic illness, their siblings are neglected, threatening their self-esteem (1, 2). Siblings also feel guilt about the capacity to lead healthy and enjoyable lives and the perceived pressure to achieve perfection, not be bothered, and suppress their feelings not to burden parents and other caregivers (3–5).

While long-term survival of children with chronic illness has become possible with developing medical care and attention given to health care transition (6), their siblings also face the risk of psychosocial and emotional difficulties, leading to developmental difficulties and concerns beyond the typical adolescence and young adulthood (7). It is crucial to support them in promoting self-reliance from childhood, vital for personality growth, to prevent or reduce these concerns throughout their lives.

Studies report that health-related quality of life (HRQoL) scores of siblings of children with chronic illness were higher than those of children with chronic illness (8). In contrast, HRQoL among siblings of children with chronic illness were reported to be significantly lower than that of healthy children, including mental health aspects, psychosocial aspects, peers, and financial resource dimensions (9, 10), and they are at increased risk of lower self-esteem (2). These concerns arise from family relationships and social interactions such as friends and school. For instance, siblings are at risk of poor academic performance and peer-related challenges at school (11, 12). Further, the family primarily focuses on the ill child; hence, the siblings cannot rely on their family for support and additionally take on household chores responsibilities. Moreover, because of being worried about their ill siblings, they prefer visiting the hospital over being in school and face a lack of concentration in classes.

Siblings need attention and acknowledgment from loved ones and others, instrumental support, and support available specifically for them (13). To meet these needs, appropriate methodologies, evaluation, and psychological wellbeing interventions for siblings of children and young adults with a chronic illness using group study design with developed and reported effects are gradually increasing worldwide (14). Reports of these interventions, including Sibshops and Sibling Coping Together Group, include community-based and hospital-based organizations (3, 15). However, the grasp of the actual situation of sibling support practiced in daily medical care in hospital settings is limited. Furthermore, the actual situation of siblings' support in daily medical care through collaboration with the resources taken by community-based local support groups and hospitals is little known (16).

In hospitals, some children spend a crucial period in treatment to gain physical recovery, while others are eligible for pediatric palliative care that begins at diagnosis (17, 18). While the patient- and family-centered care philosophy is essential for pediatric palliative care (19, 20), the actual care does not include siblings, which is concerning (21).

Healthcare professionals belonging to medical institutions are aware of the need to support siblings; more integration with community services is needed due to the absence of siblings from hospital settings (22). In Japan, the basic policy approved by the Cabinet in 2021 of The Basic Law for Child and Maternal Health and Development stipulates promoting support for the siblings of children with chronic illness, medical care, and disabilities. Furthermore, the Ministry of Health, Labor, and Welfare indicates the need to expand support for siblings, such as implementing self-reliance support projects for specific pediatric chronic illnesses. Moreover, they must cooperate with non-profit organizations (NPOs) and volunteer groups with comprehensive community care. However, actual support for siblings and collaboration with community-based care in medical institutions are little known.

This study aimed to clarify the actual state of support for siblings of children with illness in Japanese medical institutions.

# MATERIALS AND METHODS

## Design

A cross-sectional study with an anonymous self-administered questionnaire survey was used.

## Participants

Participants were 207 of the 484 registered training facilities for Board-Certified Pediatricians of the Japan Pediatric Society (as of May 13, 2019), whose cooperation was obtained (recovery rate 42.8%).

## Procedure

Based on a list we obtained with the approval of the Japan Pediatric Society, a survey request was mailed to the nursing department directors of 484 registered training facilities for Board-Certified Pediatricians of the Japan Pediatric Society (as of May 13, 2019). The directors were asked to select one chief nurse and hand out the request form and questionnaire. If there were multiple departments engaged in pediatric care, such as the pediatric ward, pediatric outpatient department, and Neonatal Intensive Care Unit (NICU), we requested them to select one participant from one department functioning more or interested in siblings' support. Questionnaires were answered anonymously and retrieved from the participants by mail using a return envelope. The survey period was July–September 2019.

## Questionnaire

Regarding demographics, the survey included details on the type of medical institution, medical service area, number of beds, and departments to which the respondents belonged. For siblings' support, the survey included details on the typically implemented support, whether there are sibling-centered events and content, temporary safekeeping for siblings, method of information-sharing between the staff about the siblings, and implementation of bereavement care. The system for siblings' visitation in the ward and the barriers encountered in the implementation of siblings' support was also included in the survey prepared by the authors for study purposes. All items' implementation status was investigated close-ended by examining whether or not each item was implemented. Besides, free-form answer items were provided in each section, and more specific support content was requested in open-ended questions (**Supplementary Material S1**).

## Analysis

Statistical analysis was conducted using IBM SPSS Statistics 21 (IBM Corp., Armonk, NY, USA). Of the 484 facilities contacted, 207 responded and returned the questionnaires and were included in the analysis. Efforts were made to understand

**TABLE 1 |** Demographics.

| Item | *n* (%) |
|---|---|
| **Form of medical institution** | |
| General hospital | 190 (91.8) |
| Children's hospital | 10 (4.8) |
| Others | 7 (3.4) |
| **Medical service area** | |
| Secondary | 88 (42.5) |
| Tertiary | 115 (55.6) |
| No answer | 4 (1.9) |
| **Department** | |
| Pediatric ward (pediatric internal medicine and pediatric surgery) | 118 (57.0) |
| Pediatric internal medicine ward | 25 (12.1) |
| Pediatric surgery ward | 2 (1.0) |
| Mixed ward for children and adults | 48 (23.2) |
| NICU$^{+}$ | 9 (4.3) |
| Outpatient | 2 (1.0) |
| No answer | 3 (1.4) |

*N = 207.*
$^{+}$*Neonatal Intensive Care Unit.*

**TABLE 2 |** Siblings support efforts in the ward.

| Item | *n* (%) |
|---|---|
| The entire ward (outpatient) makes an effort | 52 (25.1) |
| Some staff make an effort | 37 (17.9) |
| No efforts are being made | 117 (56.5) |
| No answer | 1 (0.5) |

*N = 207 (Including 2 outpatient facilities).*

the status quo by calculating the descriptive statistics of each question.

## Ethical Considerations

This study was conducted with the approval of the Clinical Research and Ethics Review Committee of Ehime University Hospital (No. 1905010).

# RESULTS

## Demographics

The most common medical institution form was "general hospital" (190; 91.8%), followed by "Children's hospital" (10; 4.8%). More than half of medical service areas were "tertiary" (115; 55.6%), followed by "Secondary" (88; 42.5%). Others included an allergy specialty hospital, a rehabilitation hospital, and a treatment and education institution (**Table 1**).

## Actual Siblings' Support

Regarding actual siblings' support, more than half of the participants subjectively answered, "no efforts are being made on siblings support from staff in the ward (outpatient)" (117; 56.6%), about a quarter answered, "All staff in the entire

**TABLE 3 |** Details of siblings' support.

| Item | *n* (%) |
|---|---|
| **Usual direct siblings support (multiple answers)** | |
| Conversing with siblings | 97 (46.9) |
| Actively speaking to siblings | 87 (42.0) |
| Call siblings by their names | 66 (31.9) |
| Playing with siblings | 40 (19.3) |
| Explaining the admitted child's medical condition | 29 (14.0) |
| Giving medals and autograph cards at discharge | 15 (7.2) |
| Reading and introducing books and picture books concerning the sibling's condition | 12 (5.8) |
| Giving orientation about life when hospitalized | 6 (2.9) |
| Exchanging a diary daily with siblings | 2 (1.0) |
| Others | 16 (7.7) |
| **Explanation of the medical and living conditions of the child admitted to the hospital** | |
| All families are asked if they intend to explain to the siblings the situation; the explanation is given based on their decision | 8 (3.9) |
| Explanation given at the family's request | 50 (24.2) |
| Has a track record of providing an explanation in the past | 17 (8.2) |
| No explanation provided | 107 (51.7) |
| No answer | 25 (12.2) |
| **Details of support through parents (multiple answers)** | |
| Intentionally bringing up siblings in the conversation | 124 (59.9) |
| Providing support when the parent explains the medical condition and hospital stay of the ill child to the siblings | 71 (34.4) |
| Reading and introducing books and picture books concerning the siblings | 15 (7.2) |
| Introducing NPO$^{+}$ activities for siblings' support | 7 (3.4) |
| Others | 12 (5.8) |
| **Events and gatherings to which siblings are invited** | |
| Yes | 45 (21.7) |
| Siblings-centered events | 10 (22.2) |
| Events centered on pediatric patients | 34 (75.6) |
| No answer | 1 (2.2) |
| No | 153 (73.9) |
| No answer | 9 (4.3) |
| **System for the temporary safekeeping of siblings** | |
| Yes | 20 (9.7) |
| There are rooms or spaces managed for them in each ward or outpatient department | 6 (50) |
| In one location in the entire medical institution; there is a room or space set aside for siblings | 8 (20) |
| There are no rooms or spaces set aside for siblings | 0 (0) |
| Others | 6 (15) |
| No | 184 (88.9) |
| No answer | 3 (1.4) |
| **Rooms (family room) where the family, including the siblings and inpatient, can gather together (excluding two outpatient facilities)** | |
| Yes | 27 (13.1) |
| No | 176 (85.9) |
| No answer | 2 (1.0) |
| **Long-term stay facilities or similar arrangements that the families, including the siblings, can use** | |
| There is no facility that can be introduced | 143 (69.0) |

*(Continued)*

**TABLE 3 |** Continued

| Item | *n* (%) |
|---|---|
| The facility is inside or in an adjacent location to the medical institution | 36 (17.4) |
| Though not adjacent, there is a facility introduced on a daily basis | 16 (6.3) |
| Others | 6 (4.3) |
| No answer | 4 (1.9) |

*N = 207.*
*+Non-profit organizations.*

**TABLE 4 |** Bereavement support for siblings (multiple answers).

| Item | *n* (%) |
|---|---|
| Pediatric palliative care, including siblings is implemented from the time of diagnosis | 23 (11.1) |
| Support efforts are made when death approaches | 56 (27.1) |
| There are support efforts for siblings' post-bereavement | 15 (7.2) |

*N = 207.*

**TABLE 5 |** Efforts made to share sibling-related matters among the staff.

| Item | *n* (%) |
|---|---|
| Yes, there are instances (multiple answers, *n* = 80) | 80 (38.6) |
| The status of siblings is shared formally, such as in conferences | 59 (73.8) |
| The status of siblings is described and shared in the medical record | 41 (51.3) |
| Staff talk regularly about the siblings' status on a daily basis | 34 (42.5) |
| Others | 0 (0) |
| No | 115 (55.6) |
| No answer | 12 (5.8) |

*N = 207.*

**TABLE 6 |** Visitation between inpatients and siblings in the ward.

| Item | *n* (%) |
|---|---|
| **Visitation has restrictions** | 195 (94.6) |
| **Visiting restrictions based on the age of siblings (*n* = 195)** | |
| High school and above allowed | 70 (35.9) |
| Junior high school and above allowed | 40 (20.5) |
| Elementary school and above allowed | 13 (6.7) |
| Two years old and above allowed | 1 (0.5) |
| Others | 26 (13.3) |
| No age restrictions for siblings | 37 (19.0) |
| No answer | 8 (4.1) |
| **Visiting restrictions based on sibling's health condition (*n* = 195)** | |
| Yes | 183 (93.8) |
| **Method to confirm health condition (multiple answers, *n* = 183)** | |
| Confirming vaccination status with the Maternal and Child Health Handbook | 28 (15.3) |
| Confirming the infection trend at the nursery school or school | 79 (43.2) |
| Confirming the infection trend in the area where the sibling lives | 13 (7.1) |
| Self-declaration by the sibling or parents regarding health condition and signs of infection on that day | 147 (80.3) |
| The medical professionals confirm the health condition and signs of infection on that day | 68 (37.2) |
| Others | 16 (8.7) |
| No | 8 (4.1) |
| No answer | 4 (2.1) |
| **Visiting restrictions based on time (*n* = 195)** | |
| Yes | 164 (84.1) |
| Visitation is allowed 24 h a day | 16 (8.2) |
| No answer | 15 (7.7) |
| **Visitation without restrictions is allowed for siblings of the patient** | 9 (4.9) |
| **No answer** | 1 (0.5) |

*N = 205 (excluding two outpatient facilities).*

**TABLE 7 |** Barriers to implementing siblings support (multiple answers).

| Item | *n* (%) |
|---|---|
| Time | 102 (49.3) |
| Human resources | 136 (65.7) |
| Other barriers | 63 (30.4) |
| Cannot sense any barriers | 17 (8.2) |

*N = 207.*

ward (outpatient) makes an effort" (52; 25.1%), and remaining answered, "some staff in the ward (outpatient) makes an effort" (37; 17.9%) (**Table 2**).

Regarding regular direct siblings support provided (multiple answers), 97 (46.9%) answered "conversing with siblings (Medical staff converse with the siblings)," followed by "actively speaking to siblings (Conveying something from medical staff to siblings)" (87; 42%) and "calling siblings by their names" (66; 31.9%) (**Table 3**). Compared to these three items, the implementation rate of time-consuming interventions such as "playing with siblings" (40; 19.3%) and "explaining the admitted child's medical condition" (29; 14.0%) were low. Many facilities (117) answered "no efforts are being made"; in contrast, 33 (28.2%) answered "conversing with siblings", 21 (17.9%) answered "actively speaking to siblings", and 13 (11.1%) answered "calling siblings by their names".

The highest implementation support was through parents (multiple answers). Furthermore, the highest among all the questions was "intentionally bring up siblings in the conversation" (124; 59.9%). Conversely, implementation of "introducing non-profit organization activities for sibling support" (7; 3.4%) was low (**Table 3**).

Of the 45 facilities (21.7%) implementing events and gatherings to which siblings are invited, the forms of implementation were "events centered on pediatric patients" for 34 facilities (75.6%) and "events centered on their siblings" for 10 facilities (22.2%) (**Table 3**). Of these 10 facilities, no events were held for more than 15 years, and the maximum was "since over 10 years ago" for two facilities (20%); the starting period for most of them was "since over 1 year to at most 5 years" for five facilities

(50%). Additionally, event frequency ranged from "six times a year" for one facility to "once a year" for one facility (10%).

There were 20 (9.7%) who answered "Yes" for siblings' temporary safekeeping. Of these 20, six (15%) responded "Others", unspecific locations such as staff or nurse stations, lounges, and conference rooms were used. Additionally, for the frequency of opening the rooms for siblings' safekeeping, ten (50%) answered "every day", while three (15%) answered "not regularly opened"; for a staff member being present continuously, six (30%) answered "Yes". Furthermore, for efforts made regarding rooms and space (multiple answers), 13 (65%) answered "playing with cards and toys", 11 (55%) answered "conversing with the siblings", and 5 (25%) answered "working on the sibling's homework together".

## Bereavement Support for Siblings

Regarding bereavement support for the siblings, while the response "support efforts are made when death approaches" was the most frequent at 56 (27.1%), 23 (11.11%) answered, "pediatric palliative care, including siblings, is implemented from the time of diagnosis", and 15 (7.2%) answered, "there are support efforts post-bereavement" (**Table 4**). The result from the answers obtained in the free-form description by the respondents of their specific efforts was, "becoming involved with siblings from the time of the pediatric patient's admission makes it easier to provide support even when the patient's condition deteriorates and accept consultation from the parents", suggesting the necessity of interacting with siblings form an early stage. Besides, some facilities also cooperated with local support groups: "we sometimes collaborate with the local community," and "we provide information to the non-profit organization and have them participate in expansion conferences". Further, among the free responses regarding post-bereavement, one responded that "we interact with the school," and another, "we are currently planning a grief workshop with siblings".

## Efforts Made to Share Siblings-Related Matters Among the Staff

Regarding efforts made to share siblings-related matters among the staff, 80 (11.1%) responded "Yes" (**Table 5**). Of these 80 responses (multiple answers), the majority at 59 (73.8%) answered they "share the status of siblings formally, such as in conferences".

## Visitation Between Inpatients and Siblings in the Ward

In results obtained from the responses of 205 facilities, excluding two outpatient facilities, regarding visitations between siblings and inpatients, the majority stated that "visitation has restrictions" (195; 94.6%) (**Table 6**). The details about the restrictions of these 195 facilities concerning age, health condition, and siblings' visitation time are as follows. For siblings' age, most visitations in the ward were limited to "high school and above" with 70 (35%), while 37 (19%) had "no age restrictions". For restrictions on visitation depending on the siblings' health condition, 28 facilities (15.3%) "confirm the sibling's vaccination status with the Maternal and Child Health Handbook", while most were "self-declaration of the siblings or siblings' parents" (147; 80.3%). For the 164 (84.1%) who responded "Yes" to visitation restrictions based on time, most answered that visits were possible between ∼13:00 and 20:00 (UTC+9).

## Barriers to Implementing Siblings Support

Regarding barriers to implementing siblings support (multiple answers), 136 (65.7%) responded with "Human resources" and "time" 102 (49.3%), while those who responded with "others" 63 (30.4%) specified the following barriers: risk of infection and lack of space and staff awareness (**Table 7**).

# DISCUSSION

Since this survey results were obtained from over 40% of the hospitals registered as training facilities for Board-Certified Pediatricians of the Pediatric Society, it may approximately reflect the actual situation of siblings support at facilities representing pediatric practice in Japan. Wiener et al. (23) reported that pediatric psycho-oncology professionals from 63 countries responded that 25% provide individual psychosocial sessions with siblings and 6% provide sibling group sessions. Since this study is not limited to pediatric oncology, it is impossible to make a direct comparison; however, it is expected that the actual situation related to siblings in Japan is not high.

The survey results indicate that even facilities that responded with no efforts toward siblings' support perform actions such as conversing with siblings based on the specific details they provided. Many siblings valued personal contact with physicians and nurses at the hospital and mainly described hospital staff as friendly, helpful, and willing to inform them about the illness (24). Moreover, in Japan, adolescent siblings of children with chronic illnesses answered, "I was happy that medical staff remembered my name" and "The hospital staff spoke to me in the corridor, then we enjoyed playing with cards or some…it was a fun time" (25). Therefore, individual awareness from medical staff such as these actions leads to support and helps establish good relationships with siblings.

Siblings have a strong desire to know and understand their ill sibling's condition. Moreover, information helps siblings' engagement with family and familiarity with hospital environments (26). Moreover, interaction with medical care, system, and staff influence siblings (27). In hospital settings, siblings of admitted children are specifically at risk of unhealthy psychosocial conventions, such as internalizing distress (27). Further, siblings attempt to maintain their usual self, an essential element of children's optimal growth and development, while controlling for internalizing and externalizing complexities (5). However, siblings are largely absent from family-centered care and pediatric healthcare settings (21). Moreover, siblings are often overlooked by clinical staff due to a lack of apparent features in hospital settings (22). To grasp admitted children's siblings' condition and promote appropriate support, healthcare professionals must communicate and build good collaborative relationships with their parents and other caregivers (5). It is challenging for medical professionals to build good relationships with parents for siblings' support. Moreover,

pediatric hospitalization causes psychological distress to their siblings and parents (28).

Some siblings ask for information and believe it should be provided continuously by the healthcare providers (29). Nevertheless, the result indicated that most facilities did not explain the medical and living conditions of the admitted child directly to their siblings. In contrast, information is often directly provided to siblings by their parents (26). Additionally, more than half of the participants in this study answered that they intentionally bring up siblings in conversation with their parents to provide indirect siblings support. Meanwhile, intervention programs for siblings are increasing (30), involving parents for support, and parent-child communication intervention studies are gradually increasing (31, 32). Moreover, siblings desire honest and open family communication (13). Hence, highly accurate programs are required to meet the needs of siblings and their parents that can easily be used by medical professionals at hospitals.

Community resource availability is essential for providing psychosocial support for siblings (33). The study results indicated that few facilities introduce parents to NPO activities for siblings' support. Moreover, some facilities reported collaborating with the local community in the bereavement care process. This collaboration may help with continued support to reach siblings even after the ill child is discharged from the hospital. Integrating hospital-based care with community services may better facilitate the engagement and support of siblings (22). Further, the collaborative approach between hospital-and community-based support may provide psychosocial support to siblings of youth with chronic illnesses (16). In Japan, within the caregiver support project, a self-reliance support project for children with specific pediatric chronic illnesses whose implementing bodies include prefectures, the necessity of siblings' support is firmly stated as safekeeping support for siblings. One recommended project endeavor is to collaborate with specified NPOs and volunteer groups. From this, establishing a collaboration system among prefectures, support groups, and medical institutions may enhance siblings' support circumstances.

School-based social support is valued and related to siblings' emotional, behavioral, and academic adjustments (34). Moreover, Gerhardt et al. (33) suggested partnering with other professionals (such as teachers and community-based providers) to anticipate and address siblings' psychosocial needs. Flexibility in location and care modality is often necessary as contact with siblings may be restricted due to hospital policy or for practical reasons. This is especially true after a child's death. In this study, one responded that they interact with the school about siblings in the post-bereavement process. However, few studies have examined the effect of teachers or peers in providing social support for siblings (11). Siblings give importance to the relationship with teachers in school and their friends. Collaboration between medical professionals such as designated nurses and schools is essential to meet these siblings' needs and implement family-centered care (35, 36). Further collaboration between hospitals and schools must be promoted in the future.

In the United States, to maintain the balance between promoting family-centered care and infection control, the restriction on siblings <12 years old from visiting hospitalized children until the 1980s is now alleviated, and they are encouraged to visit (37). Hence, the benefits of visiting admitted children with chronic illness for their siblings have been reported and well known since (38). In contrast, there are still visitation restrictions for even 13 years above age siblings in Japan to prevent infection. The reasons for these restrictions, other than to prevent infections, are not well known or studied. Despite the benefit and protection of siblings visiting and helping their brother or sister in the hospital (21, 38), the result indicated that almost all facilities have visitation restrictions imposed on siblings' age, health condition, and visitation period. This restriction creates a distance between siblings and medical care; however, the actual situation has not been previously clarified. Moreover, the regulations vary depending on the facility, and no provision as a gold standard. Although there is no clear evidence, many Japanese hospitals have traditionally placed visit restrictions to prevent infectious diseases. A report showed that siblings' visits to the NICU did not increase the viral infection rate (39); therefore, appropriate visitation restrictions must be lifted while investigating verification under various conditions such as pediatric wards. Moreover, these restrictions must be explained, and methods should be considered to better deal with siblings' desire to visit.

Additionally, "staff awareness" was answered in the free-form description; the most rated barrier to implementing sibling support was human resources in this study. Simultaneously, the availability of trained psychosocial staff, staff knowledge concerning siblings, and healthcare providers' access and communication with siblings were barriers to supporting siblings (33). Considering that limited time is subsequent to human resources in the results regarding barriers, sharing siblings matters in daily medical care is required to adequately support staff's learning about siblings issues and practice its implementation.

## Limitations

This survey data was obtained with the consent and free will of each facility. The institutions that do not support siblings may not have been interested in this survey or chose not to disclose their information. Further, if there were multiple departments, we requested selecting one that functions more or is interested in siblings' support. Therefore, the results may have reflected facilities more inclined toward siblings' support. Nevertheless, the results can be used for further developing a siblings' support system.

In this study, only descriptive statistical results were used to represent the situation of siblings' support in the overall medical institutions. The differences in support depending on the attributes must be analyzed and clarified, including between forms of the medical institution, medical service area, or department types, using inferential statistics.

Siblings' developmental stages (such as preschool-age, school-age, and adolescence or young adulthood) are critical for planning and implementing support (40). Siblings are affected

by their brother or sister's type of disease and condition, and the hospital-based approach also has a characteristic influence (9). However, this survey did not analyze whether there are differences in the developmental stage of the siblings or the type of illness or condition of their brother or sister.

While there are studies evaluating the effects of educational interventions of a few days or conducting camps for siblings (14), it is not easy to assess the impact of daily involvement as investigated in this study. Additionally, this study is novel since the influence of pediatric medical care involvement on the siblings transitioning from childhood to adolescence and adulthood has not been previously verified. Future studies must evaluate the effect of actual siblings' support using a long-term longitudinal or retrospective study.

## CONCLUSION

This study clarified the actual state of siblings' support and showed the need for improvements and further expansion of this support in Japan. Some cases involved collaboration with local sibling support groups, such as non-profit organizations and a school.

While it is necessary to raise awareness of medical professionals regarding sibling support, collaboration with hospital-based care, community resources such as local siblings support groups, and school-based social support facilitates engagement and meets siblings' needs. These collaborations may help with continued support to reach siblings even after the ill child is discharged from the hospital, transitioning into adult care, or the contact with medical care becomes low in the future.

## DATA AVAILABILITY STATEMENT

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

## ETHICS STATEMENT

This study was conducted with the approval of the Clinical Research and Ethics Review Committee of Ehime University Hospital (No. 1905010). The patients/participants provided their written informed consent to participate in this study.

## AUTHOR CONTRIBUTIONS

KN, HM, and TH conceived of the present idea. KN, HM, RO, AM, KT, and TH designed this study, performed the survey, and collected and analyzed the data. KN and HM interpreted and analyzed the data. KN drafted the manuscript. HM, RO, KT, NKas, NKak, HT, YI, and TH supervised the entire study process. All authors read and approved the final manuscript.

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## SUPPLEMENTARY MATERIAL

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SYSTEMATIC REVIEW
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# Multidisciplinary Approach for Adult Patients With Childhood-Onset Chronic Disease Focusing on Promoting Pediatric to Adult Healthcare Transition Interventions: An Updated Systematic Review

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**Introduction:** Owing to improved prognosis, the number of adult patients with childhood-onset chronic disease (APCCD) has increased. In this systematic review, we evaluated a multidisciplinary approach toward APCCD, focusing on promoting pediatric to adult healthcare transition interventions and their effects.

**Methods:** We reviewed literature comparing the effects of pediatric to adult healthcare transition interventions in children and adolescents with childhood-onset chronic disease, using PubMed, MEDLINE, and CINAHL, from 2010 to 2021 (keywords: "transition," "children," "intervention," "healthcare," etc.). The inclusion criteria were as follows: (i) original studies, (ii) studies on pediatric to adult healthcare transition interventions in children with chronic disease, (iii) patients including "adolescents" aged 12 and older receiving intervention, and (iv) studies that included the four elements of the PICO model: Patient/ Problem, Intervention, Comparison and Outcome model.

**Results:** After evaluating 678 studies, 16 were selected, comprising topics such as "individual education programs" ($n = 6$), "group meetings" ($n = 6$), "active learning using information and communications technology" ($n = 2$), and "transition clinics" ($n = 2$). The effects obtained varied, depending on the contents and methods of the intervention. Additionally, there was no evidence of adverse outcomes from these interventions.

**Conclusions:** Pediatric to adult healthcare transition interventions provide systematic support for the transition, patient independence, and social participation; thus, they should be adopted based on their expected effects.

**Keywords: childhood-onset chronic disease, systematic review, healthcare transition interventions, multidisciplinary approach, adolescents**

## INTRODUCTION

Due to the rapid progress in the field of pediatric medicine, including fetal medicine and neonatal care, in recent years, the infant mortality rate per 1,000 births in Japan has decreased from 3.2 (2000) to 1.8 (2020), alongside the neonatal mortality rate reducing from 1.8 (2000) to 0.8 (2020); this trend shows that many lives have been saved during the perinatal period (1). Such advances in medical care have led to a reduction in mortality from childhood-onset diseases (2), and a subsequent increase in the number of adult patients with childhood-onset chronic disease (APCCD). Along with this, support for the transition from pediatric to adult medical care is gaining importance. The transition period to adulthood is one in which physical and psychosocial maturity progresses rapidly even in the developmental stage, alongside new problems due to physical maturity, changes in social roles, maturation of the patient's personality, etc. Therefore, it is necessary to provide seamless medical care in pediatric and adult care.

The transition to adult care is defined as "a purposeful and systematic transition from pediatric to adult care, including the process responsible for managing one's own chronic illness" (3, 4). Self-management for transition includes not only management of illness symptoms but also that of medication and consultation appointment, and communication with healthcare professionals (5). Furthermore, studies investigating the transitional experiences and needs of adolescents with chronic illness have identified a variety of needs. These comprise the importance of peer support; future and occupational issues; pathology and insurance and related information; medication (type, dosage, and side effects); disease knowledge, including understanding of genetic predisposition; difficulty in interacting with the doctor; changes in the doctor-patient relationship due to growth and development; taking responsibility for one's own health; and not relying on parents for disease management (6, 7). Therefore, it is necessary to build comprehensive support for various factors regarding the transition of APCCD to adult medical care.

Even in Japan, interest in adult transitional medical support has been high. In 2015, the Ministry of Health, Labor and Welfare developed tools for transitional support and the "Children with Chronic Specific Diseases Child Transitional Medical Support Model Project" (8), the purpose of which was to improve the transitional medical system by holding training at the pertinent medical institutions. The transitional medical support in this project implied "support for the process of transitioning from pediatrics to adult-centered medical care." Its goal was to "provide independence support (autonomous support) to encourage patients to acquire self-care skills and actively participate in decision-making, and to lead to appropriate care in adulthood without interrupting necessary care." Although various adult transition programs aimed at transitional medical support are being developed and evaluated abroad, there are currently no studies that integrate the adult transition programs and their results to evaluate the effectiveness of these interventions.

The PICO (Patient/Problem, Intervention, Comparison, and Outcome) of this study setting was as follows: "Does the adult healthcare transition program for APCCD proceed transition effectively compared with no intervention." Along with the systematic review, it aimed to integrate the transition support program for the medical support of APCCD and its intervention effect in Japan and overseas, evaluating its effectiveness for adult transition in a multidisciplinary manner.

**Abbreviations:** ALICT, Active learning using information and communication technology; APCCD, Adult patients with childhood-onset chronic disease; AYA, Adolescent and young adult; CF, Cystic fibrosis; CFQ-R, Cystic Fibrosis Questionnaire Revised teen/adult version; CHD, Congenital heart disease; CINAHL, Cumulated Index to Nursing and Allied Health Literature; DM, Diabetes mellitus; EA, Esophageal atresia; GM, Group meeting; GSE, General self-efficacy; HRQOL, Health-related quality of life; IBD, Inflammatory bowel disease; IEP, Individual education program; JIA, Juvenile idiopathic arthritis; PAM, Patient activation measure; RCT, Randomized controlled trial; ROBINS-I, Risk of bias in non-randomized studies – of interventions; SCD, Sickle cell disease; T1DM, Type 1 diabetes mellitus; TC, Transition clinic; TCS, Transition competence scale; TRAQ, Transition readiness assessment questionnaire.

## METHODS

### Search for Studies

The search date was September 24, 2021, and PubMed, MEDLINE and Cumulated Index to Nursing and Allied Health Literature (CINAHL) were used as the databases. The search target period was set from 2010 to 2021 in each database. Studies were extracted from January 2010 to May 2021 for PubMed, and from January 2011 to December 2020 for both MEDLINE and CINAHL.

### Search Keywords for the Papers

The search keywords were a combination of "transition/transfer," "care/health care/treatment/therapy," "children/young adult/young people/pediatric," "intervention," "chronic disease/chronic illness/APCCD/disease," and "self-management/selfcare/readiness."

### Inclusion and Exclusion Criteria

Inclusion criteria for this systematic review were as follows: (i) being an original paper; (ii) being a paper on interventions related to adult transition of children with chronic diseases; (iii) including "adolescents," with the intervention target being individuals aged 12 and older; and (iv) papers with a comparison of the results before and after the intervention being shown. Exclusion criteria for the papers were as follows: (i) the participant had difficulty in self-care due to severely handicapped children, chromosomal abnormalities, intellectual disabilities, etc.; (ii) the paper was intended for palliative care; (iii) the fact-finding survey did not involve intervention; and (iv) the intervention included participants under the target age.

### Selection of Target Studies

Excluding duplicate studies from the ones obtained through each database, we perused the titles and abstracts and excluded those that did not fall under P and I of the PICO in this systematic review. We carefully read the entire contents of the papers after the exclusion, eliminated those that lacked pre- and

post-comparisons of the intervention, and finally examined the remaining papers. All the authors worked in consultation during each process.

## Bias Risk Assessment

The Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool (Cochrane | Trusted evidence. Informed decisions. Better health.) was used for the bias risk assessment of the target studies. The tool was capable of measuring confounding, selection, measurement, and missing data, as well as reporting bias, and was ranked low, moderate, serious, no information (NI), and not applicable (NA). The evaluation was conducted independently by the researchers, and the results were shared and discussed among them. Further discussions were held on the suspicions that emerged as a result, and consensus was reached.

## Data Extraction Method

From the target papers, "references," "study design," "interventions," "person or group providing interventions," "participants," "outcomes," "main results," "limits of the study," and "overall risk of bias" were entered in a table prepared in advance, and made into a list. The data were extracted independently by the researchers, and the results were shared and discussed among them. Based on the opinions obtained through the discussion, the extracted contents were added and revised, and a list was created.

# RESULTS

## Breakdown of Analysis Target

Of a total of 678 cases obtained from the keywords, the abstract and text were carefully read. And we selected 17 studies, but one of the studies actually did not meet the PICOs. Because of that, we finally analyzed 16 studies. **Figure 1** shows the process of selecting the target papers.

## Research Report Year

When the 16 papers considered were classified by their reporting years, one study in 2013 (9), two in 2014 (10, 11), one in 2015 (12), one in 2016 (13), two in 2017 (14, 15), four in 2018 (16–19), two in 2019 (20, 21), and three in 2020 (22–24) were obtained. Of the 16 studies, nine had been reported since 2018, accounting for more than half of the studies considered (**Figure 2**).

## Participants

Most of the studies targeted were regarding the late teens, as they were in the process of transitioning from childhood to adulthood. Of the 16 studies, the minimum age of the target population was 11 years, and the maximum was 25 years.

The breakdown of the diseases examined was shown. Diabetes mellitus (DM) was included in six papers, followed by inflammatory bowel disease (IBD) in five, cystic fibrosis (CF) in four, congenital heart disease (CHD) in four, sickle cell disease (SCD) in two, juvenile idiopathic arthritis (JIA) in one, esophageal atresia (EA) in one, and cardiomyopathy in one. There were six studies involving patients with 2–3 diseases rather than a single disease. Additionally, there was one study on patients with common chronic illnesses, involving 1–6 patients for 15 illnesses (**Figure 3**).

## Study Design

As a result of classifying the literature by research design, there were six quasi-experimental studies of one-group pre- and post-test design (9, 12, 17, 19–21), seven studies of randomized controlled trial (RCT) research (10, 11, 13, 16, 18, 22, 23), and three non-RCT studies (14, 15, 24). Since the pure experimental study of one-group pre- and post-test design was not a controlled study, it was difficult to determine to what extent interventions and other factors contributed to self-management, transitional readiness, and improved disease activity. In the non-RCT studies, the intervention and control groups were assigned based on the patients' wishes. Therefore, the possibility of selection bias due to the large number of patients or their families who were more interested in the transition from childhood to adulthood could not be ruled out in the intervention group.

## Bias Risk Assessment

Bias risk assessment was performed using ROBINS-I for the target studies; one study (11) was assessed to be low, 14 (9, 10, 12–23) were assessed to be moderate, and one (24) was assessed to be serious. The latter was more likely to be biased due to loss of data.

## Content of Intervention

The 16 studies analyzed were roughly classified based on the type of intervention. They were classified into four categories: Individual Education Program (IEP) (10, 14–17, 20), Group Meeting (GM) (9, 13, 18, 19, 21, 22), Active Learning using Information and Communications Technology (ALICT) (11, 23), and Transition Clinic (TC) (12, 24) (**Figure 4**). Educational interventions for coping with the disease and self-management were the actions common to all four groups. From the aspect of patient's age, the characteristics of how the programs were used according to the different ages were not mentioned in any of the studies.

## More Specific and Detailed Intervention Content and Its Effects

For each type of intervention, we showed the specific and detailed content of each study and their effects (**Table 1**).

### Individual Education Program

Six studies involved individual programs, in which supporters provided direct face-to-face education, discussions, planning, consultations, follow-ups, etc., according to the requirements of individual patients. The contents of the individual programs were divided into five programs in which supporters provided one-on-one education to patients and their families, and one in which support was mainly provided for planning and implementation. In five education-centered programs, two were conducted as RCT study.

Of the education-centered programs, two RCT (10, 16) and one non-RCT research (14) were programs for CHD patients to gain understanding of diseases, confirmation of the current

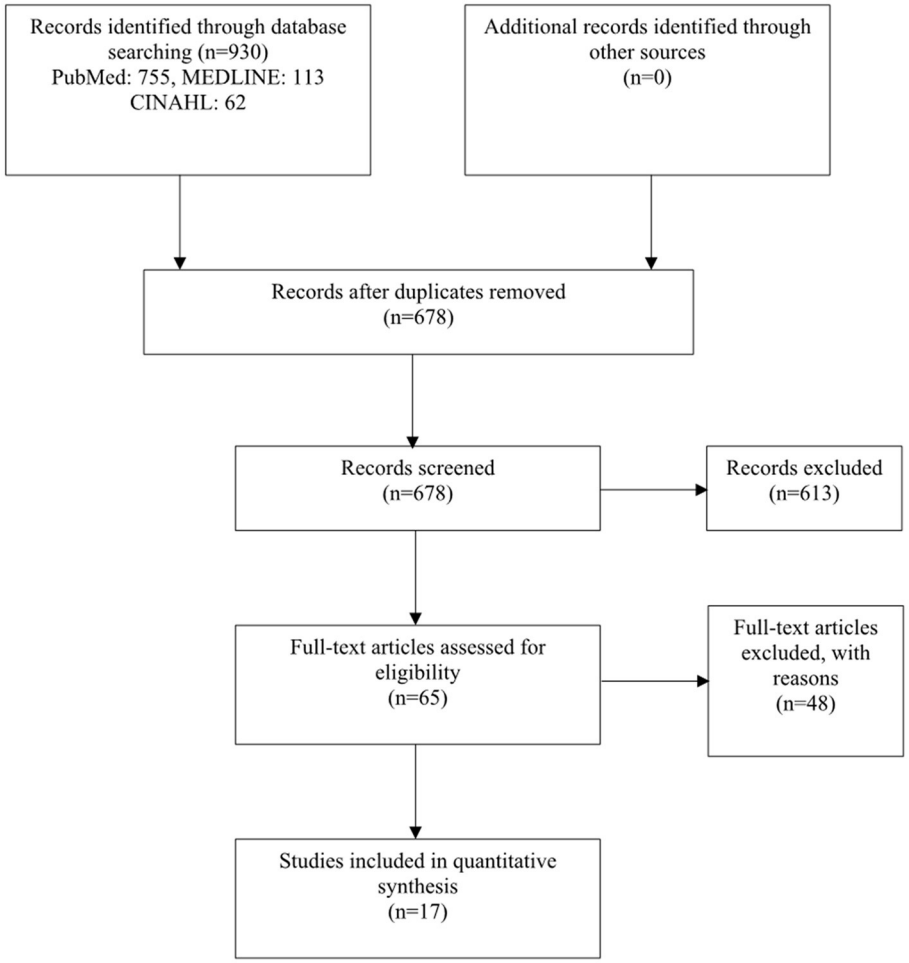


**FIGURE 1 |** Flowchart of the study selection.

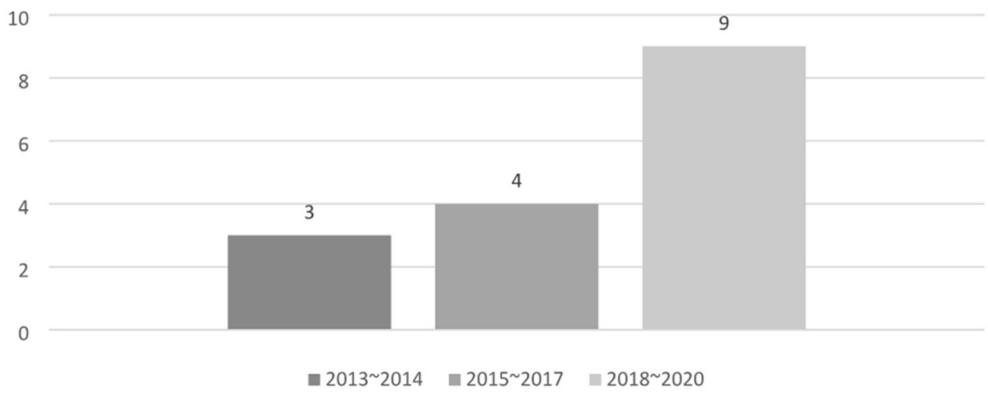


**FIGURE 2 |** Number of papers by year.

situation, points to be noted in future daily life, etc., through the creation of a My Health Passport developed in Canada. My Health Passport specifically included CHD anatomy, treatment history, names/amounts/benefits of medications taken, future complications, names and locations of local adult cardiologists, an introduction to a health care website for young people, case

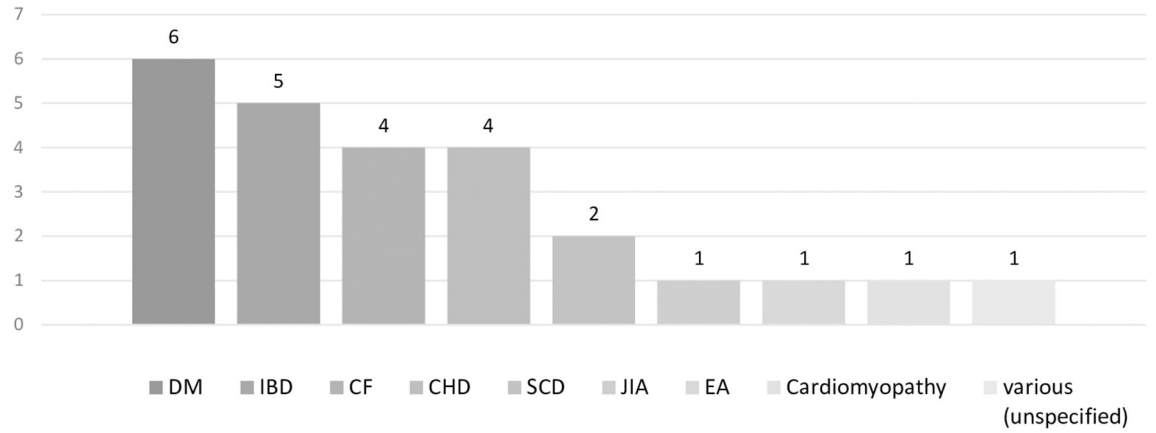


**FIGURE 3 |** Number of papers by disease of the participant.

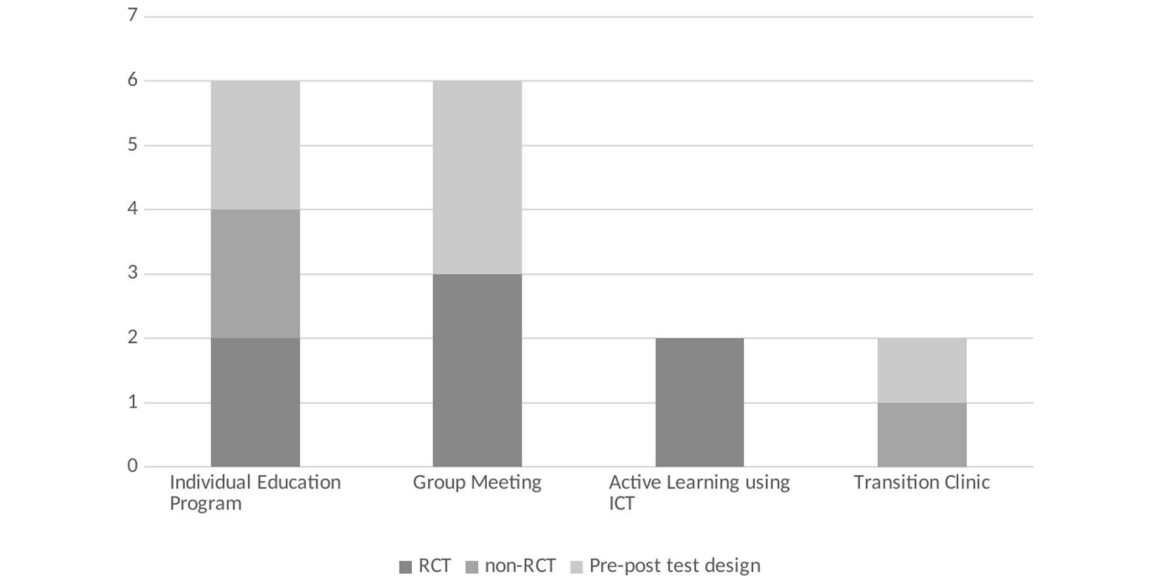


**FIGURE 4 |** Number of papers by the content of the intervention.

study (alcohol, smoking/street drug, sexuality/contraception), introduction to adult CHD clinic consultation, and setting of one education-related goal. The three studies centered on the My Health Passport, including an introduction to adult CHD clinics (16), education on sexually transmitted diseases and substance abuse (10, 14), setting goals for transition, and follow-up (10, 16).

All the three studies found that the intervention group displayed significantly higher knowledge scores for diseases and health than the non-intervention group. In two RCT studies (10, 16) that also included a program with transitional goals and follow-up by healthcare professionals at intervals, self-managed Transition Readiness Assessment Questionnaire (TRAQ) scores were higher than in the non-intervention group in both studies. In addition, compared to the non-intervention group, the transition time from pediatrics to adult specialty was shorter (16), and the self-assertion TRAQ score was higher (10).

A non-RCT study of patients with a history of EA (15) conducted the ModuS-T program developed for patients with type 1 diabetes mellitus (T1DM), IBD, and CF in Germany. Specifically, supporters held discussions with patients and their parents over a 2-day period regarding the changes occurring due to adulthood, examination of changes in the attending physician, health system, stress coping, among others. The study showed improved parental knowledge compared to the non-intervention group, but no significant effect on Health-Related Quality of Life (HRQOL) and self-management ability.

The transition program for patients with CF (17) in Denmark which is conducted as quasi-experimental studies of one-group pre- and post-test design, featured split care for children and

**TABLE 1 |** List of study design and intervention contents of review papers.

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| IEP | Mackie et al. (16) | RCT | A one-on-one session between the nurse and the patient will be held on the appointment date at the clinic and 2 months later (two times in total for 1 h each).<br>1st: Creating a My Health passport (CHD anatomy, treatment history, name/amount/efficacy of medications taken, future complications, name and location of local adult cardiovascular doctor, introduction of health care website for young people, case study on alcohol intake, introduction to adult CHD clinic consultation, setting of one education-related goal, etc.)<br>2nd: Confirmation of goals set in Part 1, watching / discussing short videos on communication with medical professionals, role-playing, related materials/website introduction<br>In both sessions, the contents will be sent from the nurse by email etc. within seven days after the implementation.<br>For all patients, including the control group, the pediatrics sent medical records to the adult clinic, and the adult clinic sent notifications about the date of first visit to the patients. | Pediatric clinic nurses | 121 patients with Moderate or complex CHD, 16–17 years old (58 in the intervention group and 63 in the control group) | Excess time between pediatric and adult CHD treatment: (time interval from the final pediatric visit to the first adult visit)-(recommended time interval for these visits)<br>My Heart Scale<br>TRAQ<br>Williams' self-management scale<br>Assessment of self-management by cardiologist<br>Incidence of cardiac reintervention surgery or catheterization 12 or 24 months after enrollment | At the recommended time of initial booking for adults (excess time = 0), intervention participants were 1.8 times more likely to book within a month (95% CI: 1.1 to 2.9; Cox regression, $p = 0.018$).<br>Intervention participants are 3.0 times more likely to make an appointment within a month when the overtime is 6 months (95% confidence interval: 1.1–8.3).<br>The intervention group had higher scores at 1, 6, 12, and 18 months on the My Heart knowledge survey (mixed models, $p < 0.001$) and TRAQ self-management index (mixed models, $p = 0.032$). | Participants may have had a participant bias of relatively high (or low) knowledge and self-management ability compared to the general population with CHD.<br>It is a nurse-led intervention and variability among nurses is inevitable.<br>Although the grouping is not known to cardiologists and other clinic staff, it is possible that the grouping may be mistakenly known. | Moderate |

*(Continued)*

**TABLE 1** | Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| IEP | Mackie et al. (10) | RCT | About the transition and its importance, Creating a My Health passport (name of heart disease, treatment history, name and purpose of the drug being taken, whether or not there is a need to prevent endocarditis), Confirmation of cardiac anatomy, About three possible heart complications in the future, Confirmation of contact and location of local cardiologist, Distribution of related websites and materials (sexually transmitted diseases and substance abuse), Case study of alcohol intake, etc., Follow-up recommended by nurses by email etc. Control group: Cardiologists or nurses at cardiovascular clinics promote self-management and communication skills and provide non-standardized information about the heart, either verbally or in writing. | One experienced cardiovascular nurse | 58 patients with Moderate or complex CHD or cardiomyopathy, 15–17 years old [(25) in the intervention group and 31 in the control group] | Evaluation of self-management (1) and self-advocacy (2) TRAQ [e.g., (1) filling out prescriptions, making appointments for consultations, (2) communication skills and use of school and local resources] Confirmation of knowledge about heart condition (a unique scale of the study): My Heart Scale (evaluated by a pediatric cardiologist, a cardiologist, a research assistant) | Compare the intervention group with the regular care group at 6 months after the intervention. The average self-managed TRAQ score is 3.59 (± 0.83) vs. 3.16 (± 1.05) ($p = 0.048$, adjusted by baseline score), respectively. The average self-advocacy TRAQ score is 4.38 (±0.56) vs. 4.01 (±0.95) ($p = 0.18$). The average My Heart score is 75% (±15) vs. 61% (±25) ($p = 0.019$). | Inevitable variability among intervention nurses Self-management evaluation is self-reporting Long-term follow-up and intervention at an adult heart clinic should not be evaluated. | Moderate |
| IEP | Ladouceur et al. (14) | Non-RCT (Allocation based on experience of participating in educational programs) | Individual consultation by a specialist nurse at the time of regular consultation in cardiology Discussions on potential cardiac symptoms requiring medical assistance, the importance of long-term and frequent consultations by cardiologists, dangerous behaviors to avoid, health habits and prevention of sexually transmitted diseases, and Osler | Two experienced cardiology nurses | 115 adolescents and young adults with CHD 14–19 years old (22 in the intervention group and 93 in the control group) | Questionnaire with 29 items for boys and 34 items for girls regarding six areas (Knowledge about CHD and heart surgery, heart follow-up and treatment, heart symptoms and self-management, dangerous behavior and healthy lifestyle, insurance and professionalism, recurrence, and | The average value of the overall health knowledge score (out of 20 points) in the education group was significantly higher than that in the comparison group (11.7 ± 3.5 vs. 8.6 ± 3.2; $P < 0.001$). | The number of intervention groups is small. Possibility of selection bias because it is not an RCT. | Moderate |

*(Continued)*

**TABLE 1** | Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| | | | endocarditis, etc.<br>Standard care was provided to all participants, including the control group. Some participants were provided with oral and / or written information at the discretion of the cardiologist. | | | gynecological problems) | | | |
| IEP | Dingemann et al. (15) | Non-RCT (Assign to desired group) | Transition-specific patient/parent education program ModuS-T<br>General purpose module: Consider changes in adulthood, consideration of changes to the attending physician, health system, career development, social connections, stress coping, and specific changes in daily life<br>Symptom Modules: Family Planning, Alcohol, Drugs 12 units 45 min each (2 days)<br>Control group: Normal care (no details) | General-purpose module: 1 psychologist each<br>Symptom Module: Experienced Pediatric Surgeon | Patients with a history of EA and their parents, 14–21 years old (10 in the intervention group and 19 in the control group) | Program satisfaction: ZUF-8<br>Confirmation of knowledge in the program: transition-specific knowledge questionnaires<br>HRQOL:DISABKIDS Chronic Generic Measure-37<br>Adolescents' own health care efforts: German version of the Patient Activation Measure-13D (PAM-13D) | The patient's transitional knowledge was 36% correct before the program, but improved 18% immediately after the intervention, with a 56% correct answer rate ($p = 0.004$). However, there was no change in the control group (54 vs. 52%, n.s.).<br>Parental transitional knowledge did not change after the intervention (correct answer rate 66:67%, ns).<br>There was no detectable effect on HRQOL (intervention group 79.7 vs. control 81.5, DISABKIDS general score) and self-management (intervention group 44.4 vs. control 41.4, PAM-13). | The number of research participants is small<br>Three evaluations were performed before the intervention, immediately after the intervention, and 4 weeks after the intervention, but the follow-up period was short.<br>Since it is not an RCT, the participation rate of those who are interested in research is high. | Moderate |

*(Continued)*

**TABLE 1** | Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| IEP | Skov et al. (17) | Quasi-experimental study of group one pre-post-test design | Divided medical care for parents and children_ Consultation by nurses focusing on life, self-management, psychosocial risk, and resilience (twice a year) Annual parental event (interaction with CF Center, Adolescent Center staff, etc.) | Doctors and nurses | 40 CF patients, 12–18 years old | Preparation checklist (created by researchers) Quality of life related to the health of CF patients: CF Questionnaire Revised teen/adult version (CFQ-R) Height, weight, body mass index, lung function [forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1)] | Preparedness checklist scores increased significantly from an average of 64 points to 76 points at baseline and at 12-month follow-up ($p = 0.002$). However, the number of respondents who answered two points was $n = 15$. In QOL, "role restriction," which indicates the ability to respond to daily life, increased significantly ($p = 0.046$), and "respiratory symptoms" decreased ($p = 0.003$). Lung function was flat. | No one dropped out of the program, but some participants were too busy to complete the checklist. | Moderate |
| IEP | Gray et al. (20) | Quasi-experimental study of group one pre-posttest design | Transition coordinator at regular visits provides 15–20 min interviews with patients and family, customized education on self-management and parent-to-patient responsibility transfer (once a year)_ Follow-up of goals set by phone or email (within 3 months after interview). | Transition coordinators (social workers) | 135 IBD adolescents and young adults and their families, 14–17 years old | Evaluation of self-management skills for health: TRAQ Clinical disease activity: PGA (Physician Global Assessment) Evaluation before (T1) and 1 year after (T2) the transition coordinator's intervention | The TRAQ score was 68.13 points before the intervention, but increased to 74.38 points after the intervention, showing a significant increase in transition readiness and self-management ability. Of the 20 items of self-management ability acquired, it was 7.07 before the intervention, but increased to 8.20 after the intervention, showing a significant increase. | Because it is not a controlled study, it is not possible to determine to what extent the transition coordinator and other factors contributed to self-management, transition readiness, and improvement in disease activity. Self-management evaluation is self-reporting. | Moderate |

*(Continued)*

**TABLE 1** | Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| GM | Markwart et al. (22) | RCT | Educational program consisting of nine modules (transition to adult medical institutions, future plans and occupations, communication about illness with peers and parents, etc.) The control group does not participate in the intervention, but answers the questionnaire at the same time as the intervention group. | Psychologists and pediatricians, adult medicine doctors, young adults with the same chronic illness as intervention participants | 723 patients with chronic disease (T1DM, CF, IBD) Average 16.98 years old, SD = 1.64 (407 in the intervention group and 316 in the control group) | General Self-Efficacy scale (GSE) Transition Competence Scale (TCS) PAM | The intervention group had significantly higher patient empowerment (PE) scores than the control group. | | Moderate |
| GM | Schmidt et al. (18) | RCT | Educational program consisting of nine modules (transition to adult medical institutions, future plans and occupations, communication about illness with peers and parents, etc.) The control group received routine care, including medical care based on individual needs and counseling as needed. | Transition Workshop: Psychologist, Pediatrician. Some modules: Young adults with chronic illness and adult medical professionals. | 285 IBD and DM patients. Average 16.57 years old, SD = 1.31 (125 in the intervention group, 24 in the dropout, 117 in the control group, 19 in the dropout) | Health-related TCS The German short version of the DISABKIDS Chronic Generic Measure The EUROHIS QOL-8 | The intervention significantly improved transitional ability in both groups, but higher in IBD patients. | | Moderate |
| GM | Schmidt et al. (13) | RCT | Educational program consisting of eight modules (transition to adult medical institutions, medical system, future plans and occupations, parting with parents, communication about illness with peers and parents, stress management, resource activation, etc.) The control group received routine care, including medical care based on individual needs and counseling as needed. | Psychologist, pediatricians. In some modules, young adults with chronic illnesses and doctors in the adult field. | 274 adolescents with T1DM, CF and IBD, 13–22 years old. (142 in the intervention group and 132 in the control group) | Health-related TCS GSE PAM13-D Satisfaction with health care (CHS-SUN self) The German version of the EUROHIS QOL-8 A short form of WHOQOL-Bref The German short version of the DISABKIDS Chronic Generic Measure | The intervention group had a significant effect on transition ability, self-efficacy, and satisfaction with school care 6 months after the intervention, but not on patient activation and quality of life. | The failure to show changes in quality of life may be due to the fact that the measurement range is too wide for general QOL measurement methods. | Moderate |

*(Continued)*

**TABLE 1 |** Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| GM | Maslow et al. (9) | Quasi-experimental study of group one pre-post-test design | Discuss diagnosis, how to deal with illness, how to interact with doctors, school problems, friendships, family relationships, etc. while interacting with high school patients and university mentors at a dinner party (2.5 h a month). | Mentors (university students under the guidance of specialized groups), program directors, volunteer staff (pediatrics, psychiatric residents, group discussion facilitators, child life therapists, medical students, etc.) | 20 patients with chronic disease Average 15.4 years, SD = 0.3 years | Connection with society: the University of California Los Angeles (UCLA) Loneliness Scale Competence and confidence: TRAQ Questionnaire to program graduates (high school student participants/university student mentors): Current and past educational experience (high school graduation, degree acquisition, current academic status, etc.) | Loneliness decreased from 46 to 38.5 ($p < 0.001$), and health care self-assertion increased from 3.8 to 4.2 ($p < 0.001$). | It is not an RCT and there is no control group setting. | Moderate |
| GM | Johnson et al. (21) | Quasi-experimental study of group one pre-posttest design | Program in line with transition readiness assessments, prescription medications, guidelines to prevent a pain crisis, and personal care and health care guidelines. Watch video for SCD patients in their teens. Q & A session with four questions of "Incorporating Health Care Transition Services Into Preventive Care for Adolescents and Young Adults: A Toolkit for Clinicians." [(1) Reassurance for your own health management, (2) Timing when primary care or medical examination by a specialist is required, (3) The importance of self-health management such as filling out prescriptions, taking independent medicine, | No information | 10 patients from SCD Pediatric Hematology Clinic. * No details about the age of the target person. * Inclusion criteria 18 years old and over | TRAQ | The total average score for women improved from 3.46 to 4.31, while for men it improved slightly from 3.19 to 3.28 before and after the intervention. For men, there was a slight improvement after the intervention in drug management, schedule management, and understanding of health problems. For women, improved medication management, health problem tracking, medical conversations, and daily life management. | Further investigation by RCTs is needed to address the limitations of the study. | Moderate |

*(Continued)*

**TABLE 1** | Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| | | | carrying insurance cards, and making appointments for consultations, (4) Questions and concerns about changing to an adult clinician]. | | | | | | |
| GM | Essaddam et al. (19) | Quasi-experimental study of group one pre-posttest design | 2–3 h/time group (8–12 people) meetings for children and their families. Introducing and asking questions about the adult team. Distribution of "diabetes health passport." | Pediatric team (doctors, nurses, nutritionists) and adult teams (doctors, nurses, nutritionists, secretaries). | 48 T1DM patients, 14.5–23.2 years old | HbA1c<br>Number of hospital visits<br>Number of hospitalizations | The HbA1c value decreased significantly 1 year after the transition to adulthood, with an average decrease rate of 0.93 $\pm$ 1.69%. The number of people who achieved HbA1c < 7.5% increased to 8%. | It is possible that the group is originally highly motivated because it is a person who wishes to participate in an outpatient consultation / program for more than 2 years. | Moderate |
| ALICT | Huang et al. (11) | RCT | Disease management with MD2Me (eight months).<br>Disease management and communication skills on the website, lifestyle education, case studies by disease (2 months).<br>Short message and question delivery to confirm comprehension (3–5 times/week).<br>2 months later, disease management and information and weekly reminder messages on the website.<br>Providing an automated SMS algorithm to support disease management decisions and a communication portal with the medical team.<br>Control group: Receive monthly messages about common health issues by mail or email. | Medical team | 81 adolescents (ACD) with IBD, CF and T1DM, 12–20 years old. (40 in the intervention group and 41 in the control group) | TRAQ<br>PAM<br>Frequency of patient-led communication.<br>Disease status<br>The Karnofsky Performance Scale, a functional status assessment scale<br>Pediatric Quality of Life Scale (PedsQL)<br>The Test of Functional Health Literacy in Adults | MD2Me participants showed significant improvements in disease self-management, health-related self-efficacy, and patient-led communication at baseline, 2 and 8 months, compared to the control group ($p = 0.02$, $P = 0.02$, $p < 0.001$). | The sample size is relatively small, it is a single facility, and there is a difference in intervention frequency between the intervention group (once a week) and the control group (once a month). | Low |

*(Continued)*

**TABLE 1** | Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| ALICT | Crosby et al. (23) | RCT | Group session (6 weeks), interpersonal booster session. Symptom recording by companion app (iManage). Control group: Education on SCD and general health was conducted by telephone for 6 weeks. | Doctor, two research facilitators (psychologist, psychology fellow, or graduate student in psychology) | 53 AYA patients with SCD, 13–21 years old. (26 in the intervention group and 27 in the control group) | Self-efficacy: PAM-13<br>Self-management skills: TRAQ-5, UNC $TR_XANSITION$ Scale<br>SCD Knowledge: 25 disease-specific knowledge questionnaires<br>Health Motivation: the Treatment Self-Regulation Questionnaire (TSRQ)<br>Health-related quality of life HRQOL: the PedsQL sickle cell disease Module | In the intervention group, there was a significant improvement in self-efficacy (8-point change), with Moderate effect sizes, $P = 0.09$ and $\eta^2 = 0.06$. There was also a statistically significant improvement in self-management skills (tracking health), $P = 0.04$. | The sample size is small. | Moderate |
| TC | Gaydos et al. (24) | Non-RCT The control group was selected from patients who had visited the Pediatric Cardiology Clinic before the transition clinic was opened. | Development of Subspecialty Pediatric Heart Clinic in January 2016 (once a month).<br>Individual education is provided at the transition clinic. First visit: Explanation of transition method and importance, confirmation of understanding of one's disease, introduction of adult cardiovascular clinic, self-management goal setting, interview with adult CHD nurse.<br>Second and subsequent visits: Re-education regarding heart disease, resetting self-management goals, interviews with adult CHD nurses, etc. The control group was a CHD patient who visited the Pediatric Cardiovascular Clinic for 3 months (December 2015–February 2016) and received normal medical care. | Pediatric cardiologists, adult CHD nurses | 54 patients who visited the Pediatric CHD transition clinic, 16–21 years old. (54 in the intervention group and 53 in the control group) | participant "lost to follow-up" rate<br>TRAQ<br>PedsQL 3.0 Cardiac Module | The percentage of "unfollow-up" that improved follow-up rates in adolescents and young adults was 7.3%, significantly lower than in the control group (25.9%, $p < 0.01$). There was no significant difference in the TRAQ score in the follow-up score. | Selection bias is likely to occur because referral by a cardiologist was required. | Serious |

*(Continued)*

**TABLE 1** | Continued

| Content of interventions | References | Study design | Interventions | Person or group providing interventions (supporter) | Participants | Outcomes | Main results | Limits of the study | Overall risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| TC | Staa et al. (12) | Quasi-experimental study of group one pre-posttest design | Transition Clinic/Youth Clinic establishment and transition coordinator, transition protocol setting, regular consultation between pediatric and adult care (including multidisciplinary transition meetings)_Individual Transition Plans<br>Personal consultation<br>Providing information leaflets and websites for young people. | Pediatric and adult medical team | AYA generation patients with T1DM or JIA (T0) At the start, 389 people, 11 to 25 years old (T1) 1 year later (at the time of completion), 430 people (T2) 2 years later, 207 people | The Independent Behaviors During Consultations Scale (IBDCS)<br>General independence during consultations<br>Topics Discussed During Consultations Scale (TDDCS)<br>The Dutch version of GSE<br>On Your Own Feet Self-Efficacy Scale: OYOF-SES) | IBDCS, General independence during consultations, and GSE increased significantly from T0 to T2, and Your Own Feet Self-Efficacy Scale also increased from T1 to T2 (all $p < 0.05$–$0.001$). | There is a lack of information on how the intervention was actually performed and on clinical outcomes. | Moderate |

parents to create an opportunity for the patient to be seen alone. In addition, two of the 12 consultations a year were held by nurses for 60-min consultations, providing opportunities for consultation on life, self-management, psychosocial risks, and resilience. An annual event for parents was also one characteristic of the program along with individual patient interventions. A mini-lecture on how to deal with chronic diseases and adherence by experts, discussions among parents, and a place to share experiences were provided. The study showed a significant reduction in readiness indicators and respiratory symptoms before and after the intervention.

The study targeting patients with IBD in the United States (20) which is also one-group pretest-posttest design research focused on the formulation and implementation of transition plans. Interviews with patients and their families were conducted by a transition coordinator (social worker) at the time of regular visits. Specifically, during a 15–20-min interview, the IBD Self-Management Handbook was used to explain the concept of transition, provide education on the transition of responsibility from parent to patient, and set migration goals for family and patients. Three months after the interview, a follow-up was conducted on telephone or email regarding the status of the goals set at the time of the interview. The study showed a significant increase in TRAQ transition readiness and self-management ability before and after the intervention.

## Group Meeting

The number of studies that involved GMs to promote transition from childhood to adulthood through group education and discussions for patients and parents, was the same as that for IEPs. Among them, by participant, five studies were targeted at children who were patients, and one was targeted at both parents and children.

Of the five studies mainly for children, three RCT (13, 18, 22) were for patients with chronic diseases such as T1DM, CF and IBD in Germany. All programs were offered to four or more patients at a time for two consecutive days, including transition to adult care, health care systems, future plans and professions, illness communication with peers and parents, stress management, etc. The program was primarily conducted by psychologists and pediatricians, and incorporated group-work to facilitate knowledge and information exchange between participants. Of the three studies, in the one on patients with T1DM, CF and IBD (22), and the one on patients with DM and IBD (18), the intervention group had significantly higher empowerment and knowledge scores than the control group. In another study (13) of patients with T1DM, CF and IBD, it was reported that while the transition ability, self-efficacy and satisfaction with school care were significantly higher than in the control group, there was no significant effect on patient activation and quality of life.

Similarly, in a study (9) conducted as one-group pretest-posttest design research in the United States on patients with chronic illness, high school and university students with chronic illness interacted at a dinner party for about 2.5 h every month. After dinner, they were divided into small groups to select and discuss on various topics such as diagnosis, living with illness,

and problems that occur at school. Before and after the program centered on the interaction of patients with the same illness, it was reported that the feeling of loneliness decreased and the self-assertion about health care improved.

In a group meeting (21) centered on patients with SCD, a session was held within the group on four questions regarding their own medical condition, self-management of medicines, reservations for medical institutions, etc., after watching a video created for teenage SCD patients transitioning from pediatric to adult care. From this one-group pretest-posttest design research, it was found that drug management, understanding of health problems, communication with medical staff, and improvement of health management in daily life were clarified.

GMs (19) for children with T1DM and their parents in North Africa were held once or twice a year in the pediatrics department of the hospital during school holidays. The group meeting lasted 2–3 h and was attended by 8–12 patients with their families and the hospital's pediatric team (two doctors, one nutritionist, and one nurse), and adult staff including adult endocrine doctors, diabetic nursing educators, nutritionists, and secretaries. Through group meetings, patients and their families had the opportunity to interact with new care providers and raise concerns and questions. Through the one-group pretest-posttest design research, HbA1c levels decreased significantly and more patients achieved HbA1c $< 7.5\%$ 1 year after the program intervention.

### Active Learning Using ICT

Two programs were identified as ALICT to promote intervention. Both were RCT. There were three specific intervention methods: disease management and learning programs using ICT, and GMs.

Disease management using ICT was conducted in both studies, and it was recommended to provide and use tools for recording symptoms such as the applications "iManage" (23) and "MD2Me" (11). In particular, "iManage," in addition to self-management such as progress report of self-management goals and input of daily pain and mood discomfort, had provisions for exchanging messages with other participants and sharing of a picture diary of weekly events.

Regarding the learning program (11), information on disease management, communication skills, and lifestyle was provided on the website for 2 months, and self-management in adulthood was learned through case studies by disease. A study (11) that combined ICT disease management and learning programs showed improvements in disease self-management ability, self-efficacy, and patient-led communication.

The ICT GM (23) was used in combination with the in-hospital face-to-face GM to hold a 90-min group session by Zoom. In a study (23) conducted in combination with ICT disease management and GMs, the intervention group had higher self-efficacy and self-management ability than the control group.

### Transition Clinic

The TC for the adolescent and young adult (AYA) generation of T1DM or JIA in the Netherlands (12) provided individual intervention conducted with advice from pediatric and adult medical teams for a year, from setting goals to assessing the effectiveness of efforts to improve care. Patients and the medical team discussed with each other about community barriers and shared their experiences in improving adolescent care. In this one-group pretest-posttest design research revealed that the independent behaviors during consultation, general independence, and self-efficacy increased from before the intervention to 1 year after the intervention.

CHD patients in the United States (24) were provided a personalized education program by pediatric cardiologists to assess and promote the preparation and transition of these patients to age-related adult cardiac care. The TC was developed in January 2016 as a monthly subspecialty pediatric heart clinic. Specifically, during the first visit, the method and importance of transition were explained, the degree of understanding of one's own disease was confirmed, an adult cardiovascular clinic was introduced, and goals for self-management were set. During the second and subsequent visits, re-education about heart disease and resetting of self-management goals were conducted. Interviews with adult CHD nurses were also conducted during the intervention. A TC was set up between pediatric and adult care, and the group was recommended for consultation had a higher follow-up rate than the control group. This non-RCT study showed its effectiveness as a program to promote continuous hospital visits and participation in treatment during the transition period.

## DISCUSSION

### Research Characteristics

The purpose of this systematic review was to provide a multidisciplinary assessment of intervention programs and their effectiveness in supporting the transition of children and adolescents with childhood-onset chronic illness. With the increase in APCCD, support for the transition from pediatric to adult medical care has been emphasized (3), and research reports have been increasing since 2018. DM was the most common disease among the participants of this study, followed by IBD, CF and CHD. In a review of adolescents in transition who require continuous care, the diseases covered were similar to those in this study (26).

Of the 16 research designs, seven were RCTs, six were quasi-experimental studies of one-group pre- and post-test design, and three were non-RCTs, more than half of which were non-RCT research designs. Since the pure experimental study of one-group pre- and post-test design was not a controlled study, it was difficult to determine the extent to which interventions and other factors contributed to self-management, transitional readiness, and improved disease activity. In non-RCT studies, the intervention and control groups were assigned based on the patients' wishes. Therefore, the possibility of selection bias due to the large number of patients or their families who were more interested in the transition from childhood to adulthood, could not be ruled out in the intervention group.

In the bias risk assessment using ROBINS-I, one study had a low overall bias risk, one had serious bias risk, and the rest had moderate bias risk. Bias risks in most studies ranged from moderate to severe, and confounding bias and bias in measuring

outcomes were the main factors that underestimated the study quality. The results should, therefore, be interpreted carefully from the study design and bias risk assessment perspective.

The number of RCTs in the four intervention groups was two for IEP, three for GM, two for ALICT, and zero for TC, with no significant differences among the groups other than TC, and the risk of bias in the study design RCTs was Moderate except for one ALICT, which was Low. Based on these results, it was difficult to rigorously estimate which intervention group was more effective.

## Intervention Content and Effect

### Individual Education Program

The most common transition support intervention program was the IEP. Specifically, the content was to directly provide face-to-face education, discussions, consultations, planning, follow-up, etc. by the supporter, according to the requirements of individual patients. The results of this study and previous studies indicate that there is a wide range of childhood-onset chronic conditions that require transition support (26). In addition, the transition period from childhood to adulthood is a period of rapid physical, psychological, and social maturity. Therefore, it is expected that individual differences will be large in terms of physical and psychological development and changes in social roles. In this way, in order to deal with various diseases and individual situations, it is considered that education and planning are carried out according to individual situations. In many studies, follow-up was conducted not only as a one-time intervention, but also for maintaining the effects.

While many studies included patients and their parents for education, planning and counseling, one study featured interventions regarding the split care of children and parents to facilitate the transition. The purpose of transition support was to support patients' independence and social participation, in addition to a smooth shift from pediatric to adult care (3, 27). Both patients and their parents are the targets of interventions because it is a transitional period from childhood, when parents are responsible for treatment selection and disease management, to adulthood, which aims for patient independence and social participation.

The effects of the IEP included increased knowledge scores regarding illness and health, increased transition preparation scores, increased independence behavior indicators, independence, self-efficacy, improvement of physical symptoms, and shortening the period of consultation from pediatrics to adult specialties. However, one study reported no significant effect on HRQOL and self-management ability. The risk of bias in the study was moderate, and the level of evidence was limited.

### Group Meeting

GMs for group education and discussions for patients and parents were the second most common support intervention after IEP. Specifically, discussions were held on disease management, medical care after adult transition, and general life including school life and occupation. While most of the studies were regarding patients only, there was one study which included both parents and children. As an independent support for children with chronic pediatric diseases, it is important to provide a place where patients of the same generation, such as peer groups, can share their worries and exchange information (25, 28). Peers become a primary source of support in mid-adolescence, and peer groups are said to participate in self-selection, self-determination, or social participation through exchanging and sharing experiences, information, and ways of thinking (29, 30). Sharing experiences and information with patients of the same generation having the same disease is considered to be effective for future disease management and life planning.

Similar to the IEP, GMs were attended by pediatric and adult health care providers to interact with new care providers. In addition to doctors and nurses, there were also interventions involving professionals from multiple occupations such as social workers, psychologists, and dietitians. As mentioned above, the objectives of transition support included a smooth shift from pediatric to adult care, and support for patient independence and social participation (3, 27). For a smooth shift from pediatric to adult care, both pediatric and adult health care professionals should participate. In addition, we believe that multidisciplinary interventions are being carried out for a wide range of support, including community life along with disease management.

The effects of GMs have been shown to improve knowledge scores, empowerment scores, self-efficacy, transitional ability, disease management status, and physical status. However, one study reported that there was no significant difference in patient activation and quality of life. The risk of bias in the study was moderate, and the level of evidence was limited.

### Active Learning Using ICT

Under ICT interventions, ICT-based disease management and learning programs, as well as, GMs were held. In addition to recommending records related to disease management using applications, providing information on disease management and lifestyle on the website, and content that allows learning of adult self-management through advanced case studies were set. Alongside one-sided transmission of knowledge and information, active learning was devised by exchanging messages with other target people and holding group meetings using Zoom. In recent years, digital therapy using "therapeutic apps" that can change the behavior of patients when they are not visiting the hospital and their way of thinking by acquiring correct knowledge, has attracted attention as a new treatment method in the United States and Europe (31, 32). With the development of ICT, it has spread rapidly, and medical intervention using smartphone applications that are familiar to university students from adolescence, has shown the possibility of smooth symptom and life management (33, 34). We believe that it is also used in intervention programs related to transition support for the same generation.

As an effect of ICT intervention, an increase in disease self-management ability and self-efficacy was observed, and improvement of patient-led communication was shown by devising interactions such as exchanging messages with other participants. All bias risks were moderate, and the level of evidence was limited. However, the use of ICT and the

incorporation of further interaction suggested the possibility of a transition-promoting effect.

### Transition Clinic

There were two studies in which TCs were set up to assess and promote transition from pediatric to adult care in patients. At the TC, individual education and interviews were conducted by the pediatric and adult health care teams and specialists, such as pediatric cardiologists and adult CHD nurses. Recommendations included assigning doctors with knowledge of transition support to both children and adults, creating teams of specialist nurses, psychological workers, social workers, etc., and establishing organizations for transition outpatients at the American Academy of Pediatrics, the International Society for Pediatric Kidney Disease, etc. (4, 35). Moreover, since many pediatric chronic diseases were highly specific, it was suggested that individual measures should be taken for each disease area, taking into consideration the severity and number of patients (32, 36). Based on these facts, setting up a TC with specialists assigned to each disease area was considered. Although the intervention was shown to be effective in increasing independent behavior, self-efficacy, and continuing hospital visits and promoting participation in treatment during the transition period, the risk of bias was serious and the level of evidence in the study was low.

## Limitations

This study had a few limitations. While we clarified the selection criteria and conducted a comprehensive literature search, there is a possibility that the collection of related literature is insufficient, the search being restricted to those available in English only, and also due to the limited availability of databases. Longitudinal studies without a control group did not show a causal relationship. Moderate risk of bias was also reported in studies with control settings and the results should be interpreted with caution. In addition, it was difficult to accumulate research studies based on a clear definition of transition support intervention programs.

## Suggestions for Research and Practice

As mentioned above, this systematic review lacked the accumulation of studies based on a clear definition of transition support intervention programs. And it was unclear which actions would have a positive effect on which outcomes. The effectiveness of the intervention may also be influenced by the expertise, skills and attitudes of the intervention program provider. Therefore, future studies will require interventions based on a clear definition of transition support intervention programs, evaluation of which actions are effective for which outcomes, and evaluation of program providers.

In some of the studies considered for this systematic review, both pediatric and adult experts were involved in transition support. Specialists in the pediatric and adult fields are medical providers who can provide specialized medical care through different approaches, and it is expected that these two medical providers will provide seamless care (36, 37). In addition, while the number of patients requiring transition support is increasing, the number of medical staff involved in transition support is currently small, and there is an urgent need to expand the education program for transitional medical care for medical staff (35). It is also important to offer personalized support to young people and their parents when assessing the transition readiness, focusing on self-management skills, illness knowledge, and communication with healthcare professionals (38, 39). For these reasons, the future issues in practice are the cooperation system between the pediatric and adult fields, the construction of a seamless medical care system, and the provision and evaluation of educational programs for transitional medical care for the young people, their parents, and medical professionals.

# CONCLUSION

In this study, we reviewed studies of intervention programs for children and adolescents with childhood onset. The results showed that: (i) DM and IBD were common among the diseases suffered by the study participants, (ii) intervention programs were broadly classified into four categories—IEP, GMs, ALICT and TC, and (iii) education, consultation and planning for disease and disease management through IEPs were common, followed by GMs for group education and discussion. Many studies reported improved knowledge of disease and disease management and improved readiness for transition through the intervention program. Most of the study designs were pre/post comparative studies and RCTs, with the risk of bias being moderate in most of them.

Future challenges include the dissemination of programs with individualized measures for each disease area, as well as the establishment of evaluation and educational methods for program providers.

# 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/s.

# AUTHOR CONTRIBUTIONS

RW, KS, MY, and YS: conceived or designed the study. RW, KS, MY, AM, and YS: performed research and wrote the paper. RW, KS, AM, and YS: analyzed data. All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to the article and approved the submitted version.

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MINI REVIEW
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# Toward Improving the Transition of Patients With Congenital Adrenal Hyperplasia From Pediatrics to Adult Healthcare in Japan

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The transition of patients with childhood-onset chronic diseases from pediatric to adult healthcare systems has recently received significant attention. Since 2013, the Japan Pediatric Society developed working groups to formulate guidelines for transition of patients with childhood-onset chronic diseases from pediatric to their disease specialty. Herein, we report on the activities of the Japan Society of Pediatric Endocrinology (JSPE) and the current status of transition medicine for 21-hydroxylase deficiency (21-OHD) in Japan. The JSPE proposed roadmaps and checklists for transition and prepared surveys on the current status of healthcare transition for childhood-onset endocrine diseases. In Japan, newborn screening for 21-OHD started in January 1989; however, there is no nationwide registry-based longitudinal cohort study on 21-OHD from birth to adult. The current status and the whole picture of healthcare and health problems in adult patients with 21-OHD remain unclear. Thus, we conducted a questionnaire survey on JSPE members to clarify the current status of healthcare transition of 21-OHD and discuss future perspectives for the healthcare transition of patients with 21-OHD in Japan.

**Keywords: healthcare transition, congenital adrenal hyperplasia, 21-hydroxylase deficiency, childhood-onset endocrine disease, inter-professional support system**

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## INTRODUCTION

Advances in pediatrics and neonatal medicine have dramatically improved the prognosis of children with chronic diseases, which have consequently increased the number of adolescents transitioning from pediatric to adult healthcare systems. The transition of patients with childhood-onset chronic diseases from pediatric to adult healthcare systems has recently received significant attention worldwide (1). The transition has been defined as a multifaceted, active process that attends to the medical, psychosocial, and educational needs of adolescents as they move from pediatric to adult healthcare systems (2). The number of adolescents undergoing healthcare transition is increasing; therefore, suitable and individually optimized programs are required to integrate the patients into adult-centered care and to help them grow socially and become independent working adults (1).

In Japan, the term "healthcare transition" was introduced in 2006 to replace "carryover," and the Japan Pediatric Society convened a committee for healthcare transition and summarized its statements in 2013 (3). Around the same time, a Research Committee on the Investigation and Refined Policy to Support Social, Medical, and Educational Life of Children with Chronic Disease was appointed by the Ministry of Health, Labour and Welfare of Japan to develop a support guidebook on healthcare transition for pediatricians (4). In response to the statement, subcommittees of the Japan Pediatric Society created working groups for transition and started to formulate guidelines for transition into their disease specialty. In the present review, we report the activities of the transition committee of the Japan Society of Pediatric Endocrinology (JSPE) and the current status of transition medicine for childhood-onset endocrine diseases in Japan, taking 21-hydroxylase deficiency (21-OHD) as an example.

## HEALTHCARE TRANSITION OF PATIENTS WITH CHILDHOOD-ONSET ENDOCRINE DISEASES IN JAPAN

Most childhood-onset endocrine diseases cannot be cured and need lifelong treatment. The statement for healthcare transition of the JSPE advocated that healthcare "transition" does not necessarily equate to "transfer" from pediatrics to adult healthcare (5). Healthcare transition is a lifelong process that should be started at diagnosis and includes education or support suited to each patient's development stage. The transition committee of the JSPE proposed roadmaps and checklists of transition aiming for and supporting self-reliance and autonomy of patients with childhood-onset endocrine diseases, including 21-OHD, type 1 diabetes mellitus (T1DM), combined pituitary hormone deficiency, and Prader-Willi syndrome (6). The transition from pediatric to adult healthcare should be based on transitioning the initiative for treatment from parents to patients themselves with individualized, planned, organized, and multidisciplinary support. Moreover, support systems should be constructed with interprofessional work inside and outside facilities and should be done in cooperation with each community.

Although the significance and necessity of healthcare transition have been widely recognized, the actual condition of healthcare transition of patients with childhood-onset endocrine diseases in Japan remains unclear. Although a person to supervise the transfer of a T1DM patient, i.e., a diabetologist, may be relatively easy to find and access compared with finding someone to supervise the transfer of patients with other congenital or childhood-onset endocrine diseases, there still are no systems for healthcare transition that have been established. A questionnaire survey of pediatric endocrinologists on the current status of healthcare transition for patients with T1DM in Japan revealed that 61.9% of pediatric endocrinologists continue to treat adult patients with T1DM mainly because of the patients' own request (7). Another cohort study indicated that one-fourth of patients over 40 years of age with childhood-onset T1DM received pediatric care (8). Surveys on the current status of healthcare transition of other rarer childhood-onset endocrine diseases are needed, and some of them are being prepared by the JSPE.

## HEALTHCARE TRANSITION OF PATIENTS WITH 21-HYDROXYLASE DEFICIENCY IN JAPAN

The most common form of congenital adrenal hyperplasia (CAH), which is a group of autosomal recessive disorders characterized by cortisol synthesis deficiency, is 21-OHD. Because patients with classical 21-OHD require lifelong steroid replacement, it requires management for each stage of life. Undertreatment leads to adrenal insufficiency and hyperandrogenism, reducing adult height because of premature induction of puberty, while overtreatment leads to obesity and Cushing syndrome and inhibits growth (9). Therefore, it is crucial to control the treatment. Practical administration should be individually dependent on the patient's condition and age (9). During the pediatric period, the main targets for treatment are normal physical growth, normal sexual development, and avoidance of an adrenal crisis. Once growth is completed, a shift in treatment goals from optimal growth and puberty to the prevention of long-term adverse outcomes and optimization of sexual function and fertility is needed. The clinical practice guidelines in the United States and Europe focused on the significance of healthcare transition in the long-term management of patients with CAH, recommended the gradual transition of adolescents to adult care over several years, and suggested the use of joint clinics comprised of pediatric, reproductive, and adult endocrinologists during this transition (10). Indeed, the successful transition to adult endocrinologists from pediatricians is associated with regular medical follow-up and better health-related quality of life in adult patients with CAH (11).

In addition to the classical problems (adrenal failure and androgen excess), recent studies have shown that, in both adolescents and adults with CAH, morbidity is increased and quality of life is decreased by a number of causes, including obesity, hypertension, diabetes mellitus, impaired glucose tolerance, dyslipidemia, osteoporosis, and infertility (11–16). A large cohort study in the United Kingdom revealed a higher hazard ratio for all-cause mortality of 5.17 and a lower mean age at death (54.8 years) in patients with CAH than in the healthy control group (17). Health problems of patients with 21-OHD due to overtreatment or undertreatment, including metabolic and cardiovascular issues, fertility in both women and men, gonadal and adrenal tumors, and bone problems, may have subclinically developed in childhood or adolescence and should be managed in childhood from the aspect of adult healthcare (18); this requires detailed longitudinal patient data that are supported by seamless transition care from childhood to adulthood. However, recent cohort studies on patients with CAH in Europe revealed that many adult patients with CAH (10–50% depending on the study) did not receive follow-up care with an endocrine specialist after transition (19, 20).

The condition is similar in Japan, where newborn screening for 21-OHD started in January 1989 and one per 18,000 to 20,000 infants is found to have 21-OHD (18, 21, 22). Newborn screening promotes early recognition and treatment of infants with classic 21-OHD, consequently reducing morbidity and mortality (10, 23). However, there is no nationwide registry-based longitudinal cohort study on 21-OHD from birth to adulthood. A recent questionnaire survey on JSPE members showed that at least 10% of adult patients with classic 21-OHD after starting the newborn screening were treated by pediatric endocrinologists in Japan (24); however, longitudinal surveys and follow-up on the other 90% who transferred to adult healthcare may be required. The current status and the whole picture of healthcare and health problems in adult patients with 21-OHD remain unclear.

To better understand the current status of the follow-up systems for patients with 21-OHD, we sent cross-sectional questionnaire surveys to all 190 councilors of the JSPE (24). The study consisted of two parts including an opinion survey of pediatric endocrinologists treating adult patients with 21-OHD on healthcare transition and a fact-finding survey on adult patients with 21-OHD who were treated in pediatrics. In the first part of the study, the biggest factor hindering the healthcare transition for 21-OHD (selected by 63% of pediatric endocrinologists who took the survey) was insufficient knowledge and experience of physicians involved in adult healthcare for 21-OHD. The second part of the study focused on 115 patients (53 men and 62 women with a median age of 26). It revealed that half of them continued to be treated in pediatrics at their own request. The prevalence of long-term complications including obesity, osteoporosis, infertility, menstrual disorder, gender dysphoria, and testicular adrenal rest tumor was 27.5, 8.8, 11.1, 26.3, 7.1, and 12.5%, respectively, which is comparable to previous reports (10, 14, 25–30). However, more than half of the patients were not assessed for the presence or absence of osteoporosis and infertility. Although 44 of the 62 female patients had genital reconstructive surgery, more than half of them were not followed up by gynecologists or pediatric urologists in parallel with pediatric endocrinologists.

The major points obtained from the survey are as follows:

(1) Pediatric endocrinologists who treated adult patients with 21-OHD regarded the problems of counterparts as hindrances to healthcare transition; however, the major reason for continuing to be treated in pediatrics was the patient's request.
(2) One-fourth of the adult patients exhibited obesity, and many of them developed obesity in their 20s.
(3) More than half of the adult patients with 21-OHD treated in pediatrics were not checked for infertility and osteoporosis.

The first finding indicates that there is a gap in perception of healthcare transition between the pediatric endocrinologists and the adult patients with 21-OHD treated in pediatrics and suggeststhe necessity of education and psychological support for self-reliance and autonomy of the patients. The second finding suggests that there is a need for tightening the control of treatments to prevent childhood obesity in order to achieve a smooth transition to adult healthcare. The third finding suggests that there is a need not only for the enlightenment of pediatric endocrinologists but also for interprofessional and multidisciplinary cooperation with gynecologists, reproductive or adult endocrinologists, orthopedists, and liaison psychiatry teams. Health problems associated with adult patients with 21-OHD and the prevalence of the problems in the cohort are summarized in **Figure 1** (18, 24).To prevent long-term

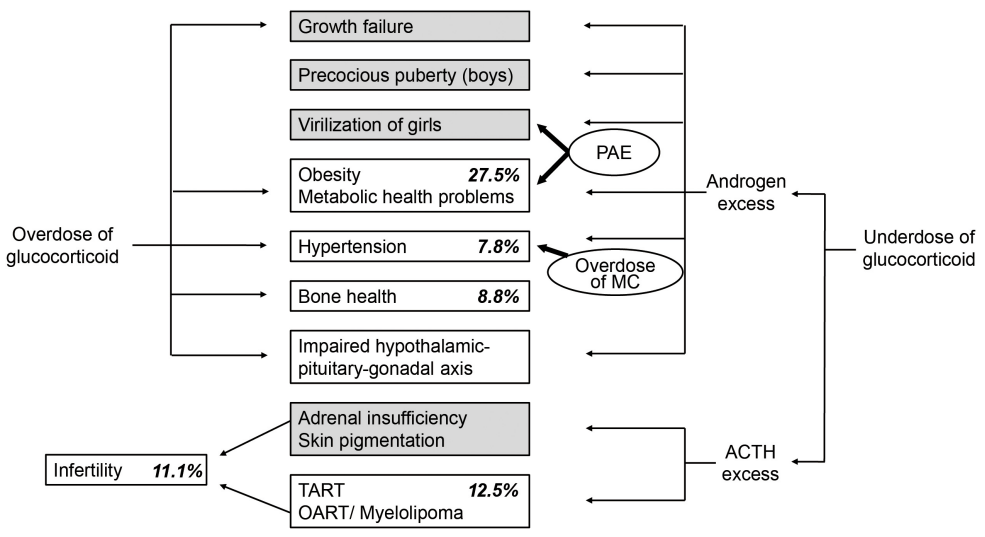


**FIGURE 1 |** Endocrine imbalances in 21-hydroxylase deficiency (21-OHD) (18) and long-term complications of adult patients with 21-OHD treated in pediatrics in Japan (24). *Italic* indicates the prevalence of long-term complications of adult patients with 21-OHD treated in pediatrics in Japan. Gray boxes indicate complications that mainly draw the attention of pediatric endocrinologists. PAE, prenatal androgen excess; MC, mineralocorticoid; ACTH, adrenocorticotropic hormone; TART, testicular adrenal rest tumor; OART, ovarian adrenal rest tumor.

complications including metabolic, gynecological, urological, orthopedic, and psychological problems and improve quality of life and social health, multifaceted and multidisciplinary support systems tailored to regional and individual characteristics are necessary (10, 11, 31). Medical staff of joint clinics with pediatric and adult healthcare have been suggested to optimize communication during the transition from pediatric to adult care (10), although these are not yet available for most patients worldwide (32). Pediatric endocrinologists need to take a more active approach to working with other healthcare workers, their patients, and society as a whole.

## FUTURE PERSPECTIVE OF HEALTHCARE TRANSITION IN 21-HYDROXYLASE DEFICIENCY IN JAPAN

We reviewed the current condition and issues to be addressed in the healthcare transition for childhood-onset endocrine diseases, especially 21-OHD, in Japan and indicated that there is plenty of room for improvement. Prior to, or in parallel with, building interprofessional support systems of health transition tailored to regional and individual characteristics, a more detailed grasp of the actual situations of health transition in 21-OHD from birth to adult is required. Because almost all patients with 21-OHD are diagnosed in the neonatal period by newborn screening, it should be possible to launch a nationwide disease registry and longitudinal follow-up system.

Multiple alternative treatment approaches are being developed with the aim of tailoring therapy for improved long-term outcomes for patients with 21-OHD, including treatments designed to replace cortisol in a physiological manner and treatments with adjunct agents intended to control excess levels of androgen, which thereby enables reduction in glucocorticoid doses, e.g., modified-release hydrocortisone, continuous subcutaneous hydrocortisone infusion pump, 17-hydroxylase inhibitor, hypothalamic–pituitary–adrenal axis suppressors, and cell-based or gene-based therapies (33). These advances in treatment may shed more light on the significance and necessity of healthcare transition.

The very first step toward the establishment of healthcare transition in 21-OHD may be to organize an interprofessional team for adolescent and young adult patients with 21-OHD in each facility or region at the initiative of pediatric endocrinologists while involving physicians or adult endocrinologists. The gradual transition of leadership from pediatric to adult endocrinologists will be fostered through participation and cooperation with activities of interprofessional support teams. Concurrently, it will be required to enlighten medical staff involved in adult healthcare and to promote patient education for health autonomy according to the stage of patient's growth and development as a preparatory step for a gradual transition. Accumulation of interactive cooperation between interprofessional support teams tailored to the characteristic of each facility or region could form the foundation of healthcare transition in 21-OHD in Japan. The missions of pediatric endocrinologists in Japan are to disseminate the significance and necessity of healthcare transition in 21-OHD, attract participants across many different fields into support teams, and take on the role of a hub in interprofessional and multidisciplinary cooperations.

## AUTHOR CONTRIBUTIONS

KT and KK designed and wrote the manuscript. KK supervised the drafting of the manuscript. Both authors contributed to the article and approved the submitted version.

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BRIEF RESEARCH REPORT
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# Factors Surrounding the Healthcare Transition From Pediatric to Adult Care in 5p- Syndrome: A Survey Among Healthcare Professionals

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**Background:** The 5p- syndrome is associated with intellectual disturbance and physical complications from infancy, and patients continue treatment into adulthood. This study aimed to clarify the factors that facilitate and prevent healthcare transition from pediatric to adult care by conducting a questionnaire survey among medical professionals.

**Subjects:** The survey included 81 medical professionals nominated by an association of families of 5p- patients in Japan. The questions involved medical care for 5p- syndrome in adulthood, experience of transition, and factors facilitating a patient's transition. Responses were obtained from 32 participants, with 27 answers eligible for analysis.

**Results:** The questionnaire items involved physical symptoms and concerns regarding support and welfare prompting consult. The most common physical symptom was constipation. Regarding support and welfare, all participants had an experience of receiving consultation about care for the siblings of patients. Three (11.1%) participants had an experience of transition. Regarding the transition of patients with rare diseases or intellectual disturbance, only four (14.8%) believed that progress was being made in the transition.

**Discussion:** Only 11% of the respondents experienced the transition of patients with 5p- syndrome. Because it is difficult for highly specialized adult care providers to deal with multidisciplinary complications of 5p- syndrome and information on prognosis and natural history is not known, it is presumed that the transition of 5p- syndrome did not progress. Factors to improve the transition of patients with 5p- syndrome and are likely to be effective for the transition of patients with other rare diseases or intellectual disabilities.

**Keywords: 5p- syndrome, healthcare transition, physical disability, intellectual disability, siblings**

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## INTRODUCTION

The transition of healthcare from pediatric to adult care in patients with childhood-onset chronic illness can be hindered by factors such as intellectual disturbance, physical complications, consultations with physicians in multiple clinical departments, and inadequate understanding of the disease by physicians in adult care departments. In particular, it is difficult for patients with intellectual disabilities to move to adult centered care (1).

The 5p- syndrome is attributed to a chromosomal abnormality and is associated with developmental retardation. This starts in infancy, but the severe intellectual disturbance and physical complications persist into adulthood (2–5). In 1963, 5p- was first reported as Cri du chat Syndrome by Lejeune et al. (6), and it is currently one of the most common chromosomal deletion syndromes, with an incidence of 1:15,000 to 1:50,000 live births (7). In Japan, Higurashi et al. (8) reported a birth prevalence of 5p- syndrome of 2 out of 21,472 consecutive newborn babies at a large maternity hospital in Tokyo.

The main clinical features of patients with 5p- at birth are low birth weight, microcephaly, round face, and characteristic facial features such as large nasal bridge, hypertelorism, epicanthal holds, low-set ears, micrognathia, and typical cry (2). With age, behavioral problems and linguistic disabilities become prominent (2, 3, 9, 10). The severity and spectrum of clinical features (i.e., phenotype) depend on the size and location of the deletion (i.e., genotypes) (11).

Although the mortality in childhood was about 10% in an early report (12), it has since been improving (2). If no major origin defects or other clinical medical conditions exist, the life expectancy appears to be normal (2). In line with improving prognosis, it is also necessary to consider the healthcare transition of 5p- patients to adult centered care. Since patients with 5p- have various symptoms, it is necessary for them to undergo treatment in multiple clinical departments. Thus, we believe that 5p- syndrome may represent a model of medical care and transition of patients with childhood-onset chronic illness who have physical and intellectual disabilities persisting into adulthood. In this study, we conducted a questionnaire survey of medical professionals who were involved in the medical care of patients with 5p-. This study aimed to clarify the status of the transition of patients with 5p- and the factors contributing to the progression of this transition (especially considering physical disabilities and intellectual delay).

# METHODS

## Subjects

The study population included 81 medical professionals who were nominated by the 5p- Syndrome Association Chamomile. Established in 1995, it is the only association of the families of patients with 5p- in Japan. There are around 110 families throughout Japan, with patients ranging from newborns to 30 years old. The activities of the association include exchange meetings, information provision, and peer counseling. All medical professionals nominated by the association have been involved in the medical care of patients with 5p-.

## Methods

The survey included questions about medical care for patients with 5p-, experience regarding the transition of patients with 5p-, factors facilitating the transition of patients with rare diseases or intellectual disturbance from pediatric to adult health care, and free descriptions. The survey questions were prepared by representatives of the 5p- Syndrome Association Chamomile, pediatricians, and specialists of pediatric genetics based on and academic views. The questionnaire was distributed by a controller, filled out anonymously by the subject, then returned to the controller (**Appendix**).

## Ethics

This research was approved by the Ethics Committee of Kansai Medical University Medical Center (No. 2019129).

# RESULTS

## Characteristics of the Participants

Replies were obtained from 32 medical professionals (return rate; 39.5%), and there were 27 answers eligible for analysis. Of the 27 participants, 23 were doctors and 4 were dentists. Among the respondents, 13 were from the Department of Pediatrics, six were from the Department of Genetics, and eight were from other departments, such as Orthopedics, Ophthalmology, Dentistry, Rehabilitation, Neurosurgery, Psychiatry, Otorhinolaryngology, and Internal Medicine. The length of their clinical experience was 27.6 (standard deviation [SD]: 8.9; range: 12–50 years). In terms of experience, these physicians treated an average of 2.8 (SD: 3.9) patients with 5p-, and 19 performed regular medical examinations for patients with 5p-.

## Medical Care for 5p- Syndrome

**Table 1** summarizes the items answered by the respondents regarding physical symptoms and concerns regarding support and welfare which have prompted consult. The most common physical symptoms were constipation, sleep disorders, and feeding difficulties, followed by hyperactivity and dysphagia. Regarding consultations for support and welfare, all participants answered they were consulted by the families of patients with 5p- about care for the siblings of patients. Other notable concerns were regarding prognosis, schooling, employment, and the diagnosis of disability.

Answers for the questions about the cited difficulties in medical treatment included "shortage of clinical experience" ($N$ = 9, 33.3%), "lack medical information about 5p-" ($N$ = 7, 25.9%), "need to attend multiple clinical departments" ($N$ = 6, 22.2%), and "transitions to the adult centered care" ($N$ = 4, 14.8%).

About visiting multiple departments, 22 respondents (81.5%) said that their patients visited multiple departments. Among these participants, seven (25.9%) reported that they experienced problems in concurrent care with other departments, specifically regarding "increased burden on the patient" ($N$ = 6, 33.3%) and "difficulties in information sharing" ($N$ = 2, 7.4%).

The most common clinical departments the patients consult other than pediatrics were Otolaryngology ($N$ = 11, 40.7%), Rehabilitation ($N$ = 10, 37.0%), Ophthalmology, Orthopedics, Dental and Oral Surgery ($N$ = 9, 33.3%), and Genetics ($N$ = 4, 14.8%). The other departments were General Internal Medicine, Endocrinology, Pediatric Surgery, Orthopedics, Pediatric Cardiology, Neonatology, and even at an epilepsy center.

**TABLE 1 |** Physical symptoms and social support and welfare concerns of patients with 5p- syndrome according to healthcare professionals ($N < 27$, multiple answer).

| | N | % | | N | % |
|---|---|---|---|---|---|
| **Physical symptoms** | | | **Social support and welfare concerns** | | |
| Constipation | 11 | 40.7 | Care for siblings | 27 | 100 |
| Sleeping disorder | 10 | 37.0 | Prognosis | 13 | 48.1 |
| Difficulties of breastfeeding | 9 | 33.3 | Education and employment | 12 | 44.4 |
| Hyperactivity | 7 | 25.9 | Certification of disabilities | 11 | 40.7 |
| Difficulties in chewing | 7 | 25.9 | Medical certificate | 11 | 40.7 |
| Weight loss | 6 | 22.2 | Support for medical costs | 10 | 37.0 |
| Aspiration | 6 | 22.2 | Cooperation with other | 9 | 33.3 |
| Self-harm behavior | 6 | 22.2 | Medical professionals | | |
| Hypotonia | 6 | 22.2 | Recurrence within the family | 8 | 29.6 |
| Hearing sensitivity | 4 | 18.2 | Patient group | 8 | 29.6 |
| Irritation | 4 | 18.2 | Short stay | 6 | 22.2 |

## Transition of Adult Patient With 5p- Syndrome and Patients With Rare Diseases or Intellectual Disturbance

Only three participants (11.1%) reported that they had an experience of transition, whereas 24 (88.9%) did not. None of the respondents reported that they rejected the request of transition nor did their patients reject the transition request.

Regarding the transition of patients with rare diseases or intellectual disturbance, 4 out of 27 participants (14.8%) believed that progress was being made in the aspect of transition care.

When asked about the factors facilitating the smooth transition of patients with rare diseases or disabilities (multiple answers were allowed), 23 physicians (85.1%) answered "provides a summary of information about the disease together," "obtains an informal consent in advance from the physician to whom the patient is to be referred," and "maintains close contact with the physician to whom the patient was referred and accepts referrals." The other common answers were "health care transition from pediatric to adult care is explained to family members" ($N = 22$, 81.5%), "makes a list of information about medical institutions accepting the transition" ($N = 18$, 66.8%), and "provides detailed information about past medical history" (N = 16; 59.3%) (**Table 2**). To solve these problems, participants gave the following answers in the free description portion of the questionnaire: "adult physicians provide comprehensive medical care, like pediatricians," "use of care management guidelines for the relevant disease," "convincing adult physicians of advantages of transition and disadvantages of continued care by pediatricians," "collaboration between pediatric and adult medical institutions," and "making a list of information about medical institutions accepting the transition."

When asked about considerations for patients with rare diseases or disabilities receiving medical care in the community, participants cited the following: "systems for collaboration among medical professionals," "improvements of regional medical networks," "having a summary of medical history and test results," "information sharing in advance, such as susceptibility to infection, means to exercise, and any required medical care," "willingness of accepting and dealing with difficulties in medical care for patients with intellectual disturbance," "availability of paramedical staff capable of dealing with patients with intellectual disabilities," "availability of human resources (divisions) to comprehensively coordinate issues including those related to medical care, welfare, education, and employment," "considerations such as shortened waiting time and space to wait for medical examinations," "flexibility to adjust for characteristics of patients/patient families," and "information sharing at patient/family meetings."

# DISCUSSION

We administered a questionnaire survey among healthcare professionals to clarify the status of the transition of 5p- syndrome from childhood to adult care, as well as the factors contributing to its progression, especially considering physical disabilities and intellectual delay. Notably, out of 27 respondents, more than 66% reported that patients with 5p- syndrome visited multiple clinical departments, 11% experienced the transition of patients with 5p- syndrome from childhood to adult care, and none reported that they or their patients rejected the transition.

As an interpretation of this result, we considered that 11% of the participants had an experience of complete transition. The remaining 89% were actually treating adult patients with 5p- syndrome. Among professionals whose patients were in childhood and adulthood, some of them were looking for a transition goal but had not yet found it or they had tried to move to adulthood but had not succeeded in it and were trying again. It is also thought that there were some participants who did not feel the need for transition to adult care and thought that there was no problem in continuing to see the adult patients in pediatric clinics. At the time of this survey, the eldest patient was in their 30s, and there were no elderly patients in the 5p- Syndrome Association Chamomile in Japan. As a result, majority of the patients were still being assessed in pediatrics and may have had little experience with transitions.

Regarding medical care for patients with 5p-, participants cited the presence of various physical and behavioral symptoms such as constipation, sleeping disorder, difficulties of breastfeeding, hyperactivity, and difficulties in chewing, suggesting that patients with 5p- continuously need different

**TABLE 2 |** Factors facilitating the smooth transition of patients with rare diseases or disabilities (*N* = 27, multiple answer).

| | N | % |
|---|---|---|
| Provides a summary of information about the disease together | 23 | 85.1 |
| Obtains an informal consent in advance from the physician to whom the patient is to be referred | 23 | 85.1 |
| Maintains close contact with the physician to whom the patient was referred and accepts referrals | 23 | 85.1 |
| Healthcare transition from pediatric to adult care is explained to family members | 22 | 81.5 |
| Makes a list of information about medical institutions accepting the transition | 18 | 66.7 |
| Provides detailed information about past medical history | 16 | 59.3 |

aspects of medical care. Regarding social support and welfare, the families of patients most commonly consulted about caring for the siblings of 5p- patients, followed by prognosis, employment, and certification of disabilities.

Mental health problems have been reported in the siblings of children with rare diseases (13), chronic illness (14), and developmental disability (15–17). Hodapp et al. (18), examined the stress-related concerns and responses of families of patients with 5p-; it was found that parents and siblings disagreed on the extent of the siblings' interpersonal concerns. Parents reported that the siblings felt ignored and misunderstood, whereas the siblings themselves rated these concerns at much lower levels. Although this paper was published in the 1990s, sibling care remains a very important issue for the families of patents with 5p-.

Moreover, more than 80% of respondents stated that the transition care of patients with rare diseases or disabilities was not moving forward. These findings are in agreement with those in previous reports regarding the transition of neurological disease patients with intellectual disturbances.

Based on the results of this study, most patients with 5p- syndrome have not transitioned to adult centered care. Since none of the participants reported rejecting/being rejected for transition, it is presumed that no attempt has been made. The reasons may be complex and the following points might be specific to 5p-: (1) 5p- syndrome has multidisciplinary complications, such as cardiovascular, urogenital, musculoskeletal, otolaryngology, ophthalmology, and dentistry, and often requires surgical treatment. Because adult care providers are often specialized and they rarely provide comprehensive medical care like pediatricians, they were not able to handle multidisciplinary complications; (2) Since patients are not accustomed with adult care providers, they do not report their symptoms by themselves due to intellectual disabilities, like those in patients with 5p-; and 3) Little information on prognosis and natural history has been accumulated due to the low incidence of 5p- syndrome.

Not only is 5p- syndrome itself a combination of multiple physical complications and intellectual disability, but the general public also lacks information about the disease. Therefore, disseminating knowledge and social support for this disease may be an effective intervention for improving the rates of transition care. The 5p- Syndrome Association Chamomile, which planned this survey, is promoting a guidebook for patients' families and medical professionals. Such activities may promote the health care transition of patients with 5p-.

The current status of transition for patients with 5p- can be improved by factors such as collaboration between pediatric and adult departments, information sharing, preparation of medical institution lists, disease guidelines, clarification of the benefits of transition to adult departments, and the availability of human resources to coordinate issues comprehensively. Similarly, these can likely be effective as well for the transition of patients with other rare diseases or intellectual disabilities.

## CONCLUSION

Because patients with 5p- can be a representative model for patients with physical and intellectual disturbance, the factors which can improve the transition to adult care can similarly be effective as well for patients with other rare diseases or intellectual disabilities.

## 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 human participants were reviewed and approved by The Ethics Committee of Kansai Medical University Medical Center. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

## AUTHOR CONTRIBUTIONS

YI, MM, KS, and YF were performed the data collection. YI and MM performed the first draft of the manuscript. KS and YF revised it critically for important intellectual content. All authors contributed to the study conception and design, commented on previous versions of the manuscript, and read and approved the final manuscript.

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## APPENDIX

Questionnaire regarding the current status of healthcare transition for the patients with 5p- syndrome

(1). Specialty and experience
  (1) Specialty
  (2) Years of experience

(2). How many patients with 5p- syndrome have you seen in the past? (Yes/No)
  (1) Number of patients seen so far
  (2) Number of patients seen within the last year

(3). Do you see patients with 5p- syndrome on a regular/irregular basis? (Yes/No)
  (1) Regular basis
  (2) Irregular basis

(4). Symptoms of patients with 5p- syndrome
  (1) Please tell us the symptoms of the patients with 5p-syndrome at the time of consultation.

(a). Constipation (b). Sleep disorders (c). Hearing sensitivity (d). Obesity (e). Weight loss (f). Irritation (g). Aspiration (h). Choking (i). Difficulties in chewing (j). Difficulties in breastfeeding (k). Hand tremor (l). Visual impairment (m). Hearing impairment (n). Hyperactivity (o). Impulsivity (p). Autistic tendency (q). Self-harm behavior (r). White hair (s). Regression (t). Hypotonia (u). Hypertonia (v). Early tooth loss (x). Dysmenorrhea

  (2) Please tell us the support or welfare concerns of the patients with 5p-syndrome

(a). Prognosis (b). Recurrence within the families (c). Certificate of disabilities (d). Medical certificate (e). Patient groups (f). Education (g). Employment (h). Respite care (i). Short stay (j). Admission to a medical facilities (k). Group home (l). Medical certificate (m). Care for siblings (n). Pension (o). After the death of parents (p). Cooperation with other clinical departments and medical institutions (q). Others

(5). What difficulties do you face in treating patients with 5p- syndrome?

(a). Nothing in particular (b). Lack of medical information about 5p- syndrome (c). Shortage of clinical experience (d). Not enough time for consultation (e). Frequent visits (f). Many kinds of prescription (g). Various complications (h). Needs of long-term management (i). Need to attend multiple clinical departments (j). Cooperation cannot be obtained from patients due to intellectual delay (k). Difficulties in communication with patients (l). Multiple uses of social welfare (m). Preparing lots of documents (n). Transition to adult centered care (o). Others

(6). Does your patient with 5p- syndrome see other departments? (Yes/No)

(7). Did you ever face any issues with other medical departments? Please describe
  (a). Difficulties in information sharing
  (b). Treatment policy is affected
  (c). Difficult to know the prescription of the other clinical department
  (d). The necessary inspection is omitted
  (e). Increasing medical examination
  (f). Increase burden of the patients

(8). Have you ever experienced a transition from pediatric to adult health care for your patients with 5p- syndrome? (Yes/No)

(9). Have you ever been denied transition of the patients with 5p- syndrome? (Yes/No)

(10). Do you think the transition of patients with rare diseases and disabilities is progressing? (Yes/No)

(11). What are the factors that facilitate the smooth transition of patients with rare diseases and disabilities?
  (a). Provides a summary of information about the disease together
  (b). Obtains an informal consent in advance from the physician to whom the patient is to be referred
  (c). Maintains close contact with the physician to whom the patient was referred and accepts referrals
  (d). Healthcare transition from pediatric to adult care is explained to family members
  (e). Makes a list of information about medical institutions accepting the transition
  (f). Provides a detailed information about past medical history

(12). What kind of consideration do you think patients with rare diseases or lifelong diseases need to take when receiving medical care in the community? (free description)

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# The process of transition from pediatric to adult healthcare services for nephrological patients: Recommendations vs. reality—A single center experience

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Transitional care is an essential step for patients with kidney disease, and it is supported by policy documents in the United Kingdom and United States. We have previously described the heterogeneous situation currently found in Europe regarding certain aspects of transitional care: the written transition plan, the educational program, the timing of transfer to adult services, the presence of a coordinator and a dedicated off-site transition clinic. In line with the transition protocol "RISE to transition," the objective of this paper is to describe the experience of the Bologna center in defining a protocol for the management of chronic kidney disease and the difficulties encountered in implementing it. We apply this model to various chronic diseases along the process of transfer to adult services. It begins when the patient is 14 years old and is complete by the time they reach 18. The family is continuously involved and all the patients in transitional care receive continuous medical care and psychological support. We identified a series of tests designed to measure various criteria: medical condition, psychological state, quality of life, and degree of patient satisfaction, which are repeated at set intervals during the transition process. The organization of the service provided an adequate setting for taking charge of the patients in the long term.

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The transition program implemented by the adult and pediatric nephrology services of the Bologna center has lowered the risk of discontinuity of care and greatly improved the patients' awareness of responsibility for their own healthy lifestyle choices.

KEYWORDS

transitional care, CKD, adolescents, health-related quality of life, disease awareness, self-management skills

## Introduction

The number of young patients transitioning from pediatric to adult renal care has been progressively increasing for some time, mainly due to improvements in antenatal screening for nephrourological anomalies, which have resulted in a growing number of children with chronic kidney disease (CKD) being followed by pediatric nephrologists, and improved management of acute kidney injury with patient survival rates of 85–90% (1–3). From a healthcare perspective, the transfer between different contexts of care (different approaches to the same disease are often seen in pediatric and adult nephrology units) should ideally be a gradual process within a care pathway guaranteeing, on the one hand, coordination and continuity of care and, on the other, the sustained treatment adherence of each adolescent (4). Therefore, such a program should include a revision of logistic and organizational, but also educational, aspects in order to motivate transfer and make sense of the transition experience for all concerned (patients, family members, healthcare professionals) in a simple "handover."

Due to their complexity, the pediatric patients under our care require a dynamic care pathway, from diagnosis, which accounts for the different stages of growth and development and is therefore adaptable according to the patient's age, physical, cognitive, psychological, and social skills, as well as the course of their renal disease *per se*.

The transition process is therefore a reference framework within which the patients, their families, and the healthcare professionals prepare for the passage from adolescence to early adulthood, and from the pediatric to the adult service. Such a model requires healthcare professionals to adopt a more open form of communication, an educational attitude toward the understanding and management of the disease and its treatment by the patient-parent, and an introduction to the adult service (5).

In order to be effective, this process should not begin just before the patient's eighteenth birthday, but well before so as to actively involve youths in their own care pathway (6).

In fact, it is well known that when the transfer from one context of care (pediatric) to another (adult) occurs without adequate prior communication it can cause a sense of disorientation and confusion in patients, which can reduce treatment adherence at the adult service and accelerate dropout (7). As patients will be required to attend less regular visits at the adult unit, an increased risk of clinical and prognostic worsening may be seen (8).

As parents' disease knowledge influences that of their adolescent children, family members must be involved in these phases in order to receive support for encouraging growing disease awareness in their children, favoring adaptive behavior, and facilitating their autonomy in managing their disease (taking medications, booking appointments, etc.) (9). Parents should participate in the educational processes proposed by the clinicians and gradually reduce their involvement in the management of the disease, especially once the patient has reached adulthood (10).

The personnel involved in the transition process must work in close collaboration, and plan a series of meetings before the moment of transfer to promote their mutual knowledge of the patient, from a clinical and relational standpoint. Furthermore, a series of logistical information (who will be responsible for the patient, where the adult service is located, and the relevant contact details) must be supplied and organizational arrangements made in order to identify the most suitable out-patient clinic for each case (11).

As clinicians, we must expect some degree of failure in the transition process, as reported in the literature (12). For this reason, the progress of the process must be monitored by means of accurate reporting of the number of transitioned patients, the number of dropouts, and through sharing the first-hand experiences of the patients and their care-givers, also in terms of their perceived quality of life, even as early as the first follow-up visit after transition.

## Description of the process

Transitional care is an essential step for our patients with kidney disease. We have previously described the heterogeneous situation currently found in Europe regarding certain aspects of transitional care: the written transition plan, educational programs, the timing of transfer to adult services, the presence

of a coordinator and a dedicated off-site transition clinic (13). In order to address the problem of heterogeneity in transitional care models, we have developed an interventional model designed around the available healthcare resources of our hospital.

In line with the transition protocol "RISE to transition," which can be considered a milestone, the Bologna center wants to share its experience in defining a protocol for the management of CKD, and the difficulties encountered in implementing it (14).

We selected personnel from the pediatric and adult services and formulated the transition plan together. The clinicians met to identify and establish the different roles within the team as well as the care plan and its organizational-management aspects (dedicated spaces, timing). The two multidisciplinary structures share the same objectives: the inclusion and empowerment of the patients, continuity of care, the integration of different healthcare interventions. This process was facilitated by the fact that the two services are located near to each other on the hospital grounds.

We chose a pediatric nephrologist as the coordinator responsible for organizing the transition plans for all the patients because they interact with the patient and the family from the beginning of the clinical history, which means they have a full understanding of the patient, their disease, their prognosis, and can therefore provide the psychologist with valid suggestions for finding the best approach. The pediatric nephrologist is the person who interacts with all the other specialists (ophthalmologist, orthopedic doctor, etc.) and healthcare professionals (dieticians, physiotherapists) and therefore has a global understanding of the patient's problems. Thanks to the "imprinting" that is established with the patient and their family they are the professionals who can, more than any other, gradually begin to give the patients information about their disease and initiate detachment from their parents (7). The coordinator works in harmony with the transition team, which comprises all the pediatric nephrologists in the unit, a medical psycho-physiologist, a nurse, and a social worker. It is also possible to consult other specialists if necessary.

Furthermore, our Pediatric Nephrology and Dialysis Unit is the regional reference center for nephrological diseases in children, which means that patients diagnosed at other centers in the Emilia Romagna region may also be included. The project was formally initiated in 2020.

## Study population and inclusion criteria

Given that the number of young patients graduating from pediatric to adult renal care has progressively increased, it was important to clearly define which patients, among those with chronic nephrological diseases, had to be included in our transition process. To date, we have included 83 patients and their families.

Severity of the disease was the first criteria adopted: all kidney transplant recipients (13/83 patients; 15%) and patients with CKD in at least stages II-III (23 pts; 28%), regardless of their primary etiology, were included. We further included all patients with kidney disease at risk of progression toward CKD: chronic glomerulopathies such as systemic lupus erythematosus, membranous glomerulonephritis, C3 glomerulonephritis, vasculitis, etc. (13 pts; 15%) and nephrotic syndrome (11 pts; 13%), genetic diseases, such as atypical hemolytic uremic syndrome (6 pts; 7%), autosomal recessive or dominant polycystic kidney disease and Alport syndrome (9 pts; 11%), tubulopathies (Dent syndrome, Bartter syndrome, etc.), hyperoxaluria, cystinuria, congenital anomalies of the kidney and urinary tract with severe renal dysplasia (9 pts; 11%).

Of note, six of the patients included had syndromes involving the kidney and causing reduced autonomy (Lowe syndrome, tuberous sclerosis, Bardet Biedle syndrome, etc.); these patients are unable to express their ideas autonomously once they reach adulthood, however, they still require more personalized transitional care. We accounted for all of the clinical situations that significantly affect the psycho-neurobehavioral status of the patients and for which it is necessary to adjust the pathway, for example a longer transition time or transition accompanied by a caregiver, without any limitations to the healthcare they receive (7). The COVID-19 pandemic caused reduced and delayed access to out-patient clinics for chronic patients, thus decreasing the activity of the program, which resumed normal activity in 2021. Recently, the transition of 45 new 14-year-old patients with different kidney diseases was initiated; 17 of them have already reached 16 years of age and have therefore met the adult team together with the pediatricians.

## Timing of the process

The process of transfer to adult services begins when the patient is 14 and is complete by the time they reach 18 years of age. During this period, all the patients in transitional care receive continuous medical care and psychological support and their families are involved throughout the entire process. At the beginning of the transition process, all patients are offered a clinical psychology interview, including psychometric assessment. The psychological evaluation consists in a series of clinical interviews in support of the patient and their family focused on managing the difficulties they have in coping with the disease. In addition, we identified a series of tests designed to measure various criteria such as depression and anxiety, quality of life, degree of patient satisfaction, all significantly affected by the status of chronic disease in adolescence (15). These

evaluations are repeated at set intervals during the transition process (Table 1).

When a patient reaches 14 years of age, the doctor and the psychologist inform them and their family about the transition process, the healthcare professionals involved, and the medical appointments they will need to attend. These moments, during which the medical personnel interact with the patient and their family, provide an opportunity to begin investing in the patient as a person who is potentially capable of increasing autonomy. We offer the patient a psychometric evaluation, which involves the administration of age-appropriate tests aimed at assessing anxiety and mood levels (Table 2). The results, which are discussed with the patient and their family, may indicate the need for an actual psychotherapeutic intervention (16).

The clinical psychology interviews take place between 14 and 16 years of age, providing the educational support necessary for encouraging the development of each family unit's compliance and resilience skills. Their main objective is to reduce the fear of the unknown expressed by adolescent patients and to increase confidence and trust in a new medical team (17).

When the patient reaches 16 years of age, a multidisciplinary appointment is organized during which the pediatric team introduces the patient to the adult nephrologist and psychologist responsible for the transition process. In this way it is possible to create an initial shared space, where everyone speaks the same professional language in order to give the family a sense of continuity of care. This set-up remains the same for every follow-up visit until the patient turns 18.

The psychological interviews which take place between 16 and 18 years of age include psychometric evaluation, which is repeated in cases where significant psychological suffering has been previously diagnosed and when the patient has undergone psychotherapy and it is necessary to assess its efficacy in terms of psychological health (Table 2).

Once the patient is 18, at the end of the clinical appointment in the transition clinic, and depending on the disease and/or CKD stage, the patient and their caregivers are provided with the necessary information regarding their first appointment at the adult Nephrology, Dialysis and Transplant Unit. As the adult nephrology unit is located near the pediatric unit, the discomfort linked to a change in settings which are culturally very different is greatly reduced (18).

The adult nephrologist in the transition team initially takes charge of the patient, irrespective of their type of kidney disease. Only subsequently will the patient be assigned to the appropriate out-patient clinic based on their specific nephropathy (genetic diseases, glomerular diseases, CKD, dialysis, transplantation). The initial mode of access to the adult unit is therefore identical for all patients: the date and time of the clinical visit and blood tests is provided at the end of the final appointment in the transition clinic. The timing of the first adult appointment is dictated by the clinical condition of the patient at the moment of transition. In the case of patients who request transfer to an adult nephrology unit at a different hospital, the adult team will organize a meeting with the receiving hospital team to guarantee continuity of care.

Within the first year after transfer to the adult service, the patient is asked to undergo a psychological-psychometric evaluation. The psychometric tools adopted will guide the possible psychological support in keeping with any potential psychological emergencies, even in adulthood.

This initial psychological follow up involves the psychological re-assessment of the patient to which the evaluation of the quality of life perceived by the patient and their caregivers is added (Table 2). This last assessment guides the transition program and its efficacy (19).

## The process in real life

The transition process was defined, in organizational terms, in accordance with the hospital services and, after a careful review of the literature, a model that is currently in line with the available staffing, logistic, and cultural resources was created. The participating specialists were

TABLE 1 Outline of the stages of the transition process from pediatric to adult healthcare.

| Transition process | | | |
|---|---|---|---|
| When | 14 years of age | 16 years of age | 18 years of age |
| Where | PEDIATRIC NEPHROLOGY Clinic | TRANSITION Clinic | ADULT NEPHROLOGY Clinic |
| What | MEDICAL VISIT<br>INTERVIEW WITH PEDIATRIC TEAM<br>PSYCHOLOGICAL ASSESSMENT:<br>• Psychological interview<br>• Tests: Children's depression inventory (CDI), anxiety scale (Busnelli-Dall'Aglio-Farina) | MEDICAL VISIT<br>INTERVIEW WITH PEDIATRIC AND ADULT TEAM<br>PSYCHOLOGICAL ASSESSMENT:<br>• Psychological interview<br>• Test: Beck depression inventory (BDI-II), the state-trait anxiety inventory (STAI-Y) | MEDICAL VISIT<br>INTERVIEW WITH ADULT TEAM<br>PSYCHOLOGICAL ASSESSMENT:<br>• Psychological interview,<br>• Test: BDI-II, STAI-Y, QV |
| Who | Pediatric team | Pediatric and adult team | Adult team |
| For whom | PATIENT with PARENTS/CAREGIVERS | PATIENT with PARENTS/CAREGIVERS | PATIENT and PARENTS/CAREGIVERS |

TABLE 2 Psychometric tests administered during the transition process from pediatric to adult healthcare.

| Transition process psychometric tests | | | |
|---|---|---|---|
| Age | 14 years | 16 years | 18 years |
| Depression | CDI<br>Children's depression inventory | BDI-II<br>Beck depression inventory-II | BDI-II<br>Beck depression inventory-II |
| Anxiety | BUSNELLI<br>Anxiety scale questionnaire for evolutive age | STAI-Y<br>State-trait anxiety inventory Y | STAI Y<br>State-trait anxiety inventory Y |
| Quality of life PATIENTS | / | / | PedsQL<br>Pediatric quality of life inventory version 4.0 generic core scales |
| Quality of life PARENTS/CAREGIVERS | / | / | PedsQL<br>Pediatric quality of life inventory version 4.0 generic core scales |

identified and began planning the transition clinic, a dedicated setting in the pediatric unit. It was necessary to set up the activities of this clinic in parallel with the regular out-patient clinic activities, and on a different time schedule in order to facilitate participation by the multidisciplinary team members. The clinic was set up on a weekly basis. Specific codes identifying the services provided within the transition pathway were established and a shared, personalized electronic patient file was created containing the medical reports submitted by the different specialists involved (6). Therefore, the entire transition history of each patient is documented and immediately consultable by each member of the team (20).

## Difficulties encountered and solutions found

We encountered several difficulties during the initial stages. For example, we were met with some resistance from the hospital regarding the proposed changes to the management of these patients, which we overcame by meeting with hospital administrative staff to discuss, plan and create the organizational model. The problems caused by differences in the pediatric and adult models of care were resolved by selecting a pediatric team and an adult team who participated in joint meetings and training sessions. We reinforced professional networks to promote continuity of care between centers for patients who transfer to an adult unit in a different hospital or city. We contacted and established relationships with local mental health facilities in the residential areas of patients with cognitive deficits, and ensured continuity between the hospital social services and those on the territory for families with social problems. Educational therapy provided support for families when passing from the pediatric to the adult reality, while psychological evaluation and interviews provided clarification and support to patients as they gradually become more autonomous and less dependent on their families. The face-to-face discussions and consultations in the pediatric unit were conducted in order to identify the best communicative approach necessary for establishing a personalized transition support intervention program.

## Adherence to the transition process

Although the pathway is relatively new, we have seen good adherence in such that the families have continually expressed interest in the process, mainly because they were involved well in advance, and appreciation for the educational approach to the whole family adopted by the team. The main difficulty recognized concerned the passage from family-based consultations to adolescent-focused care (21). Nonetheless, the caregivers feel that they have broadened their parent-child relational perspective, recognizing ever-improving self-management skills in their children. The patients were pleasantly surprised by an approach which recognizes their growing autonomy, but were fearful of being accountable for their own health. The patients and their parents requested interviews with the psychologist, both individually and as a group, even after transfer, which is an indication of the trust which developed between the families and the staff and the mutual respect within the families. In order to minimize the difficulties the staff had in finding the correct approach to use with both the families and the adolescents, and to improve their communication style, specific meetings were introduced into the annual training schedule of the dedicated pediatric staff. Various meetings were also held with the adult nephrology team, with the aim of creating a stable network of professionals with the skills necessary for dealing with the transition process. To date, we have had no dropouts.

## Discussion

This paper gives a detailed account of the transition process for patients with kidney disease in our hospital in Bologna, Italy. In our experience, the organization of the transition service, based on the recommendations compiled by the multidisciplinary team and approved by the Parents' Association, has provided an adequate setting for taking charge of the patients in the long term.

The level of satisfaction among patients and caregivers is high, as reflected by the fact that there have been no dropouts so far. The most recognized key points in the process of assessment and accompaniment of the patient in terms of their healthcare-related aspects are the presence of a coordinator, the timing of transfer, the logistics, and the multidisciplinarity of the team. The biggest limitations capable of reducing the applicability of the model in our experience are those clinical situations which require the collaboration of highly specialized professionals not included in the multidisciplinary team (e.g., professionals skilled in communicating with deaf, blind and mute patients), a limited number of dedicated resources in relation to the growing number of patients, and the poor medication compliance of some patients and/or their caregivers.

In assessing the efficacy of the transition program implemented by the adult and pediatric nephrology services of the Bologna center, it is evident that the risk of discontinuity of care has decreased and the patients' awareness of and responsibility for their own healthy lifestyle choices has greatly improved. The implementation of this model aims to improve adherence rates, rejection rates, and quality of life. The results of our study may serve as a basis for further research, which could contribute to further improving the transition experience for pediatric renal patients in Italy.

## Data availability statement

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

## Author contributions

DS and GC contributed to the conception and design of the work and wrote the first draft of the manuscript. APa, GL, and APe contributed to the conception and design of the work and critically reviewed the manuscript. CB, CL, FM, DA, and MB critically reviewed the manuscript. All authors contributed to manuscript revision, read, 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.

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# Prevalence and barriers to health care transition for adolescent patients with childhood-onset chronic diseases across Japan: A nation-wide cross-sectional survey

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Since the Japan Pediatric Society published its "Recommendations on Transitional Care for Patients with Childhood-Onset Chronic Diseases" in 2014, there has been an increased interest in the health care transition of adolescents with childhood-onset chronic diseases in Japan. However, the actual status of healthcare transition was not studied yet. The purpose of this study was to explore the prevalence of transitional support for adolescent patients with childhood-onset chronic disease and the factors hindering their transition. We conducted an anonymous questionnaire survey in August 2020, targeting physicians and nurses involved in health care transition at 494 pediatric facilities in Japan. Survey items included demographic data, health care systems related to transition to adult departments, health care transition programs based on Six Core Elements (establishing transition policy, tracking and monitoring transition progress, assessing patient readiness for transition, developing the transition plan with a medical summary, transferring the patient, completing the transfer/following up with the patient and family), barriers to transition (34-item, 4-point Likert scale), and expectations in supporting transition (multiple-choice responses), which consisted of five items (78 questions); all questions were structured. Descriptive statistics were used for analysis. Of the 225 responses collected (45.5% response rate), 88.0% were from pediatricians. More than 80% of respondents transferred patients of 20 years or older, but only about 15% had took a structured transition process of four or more based on the Six Core Elements. The top transition barriers were "intellectual disability/rare disease" and "dependence on pediatrics" as patient/family factors, and "lack of collaboration with adult healthcare (relationship, manpower/system, knowledge/understanding)" as medical/infrastructure factors. The study provides future considerations,

including the promotion of structured health care transition programs, development of transitional support tailored to the characteristics of rare diseases and disorders, and establishment of a support system with adult departments.

KEYWORDS

childhood-onset chronic diseases, health care transition, transition program, barriers to transition, cross-sectional study, Japan

## Introduction

The health care transition (HCT) of adolescents with childhood-onset chronic disease from pediatric to adult health care systems has recently received worldwide attention. However, Japan is lagging behind other countries, as the concept of HCT was introduced only 10 years ago (1). The number of patients registered in the Research Project for Treatment of Specific Pediatric Chronic Diseases in Japan is approximately 93,000 per year (2). It is estimated that 95.7% of patients with specific pediatric chronic diseases other than malignant neoplasms reach adulthood (3). However, these patients often develop complications in adulthood due to age-related changes in therapeutic areas, poor treatment adherence, and the development of lifestyle-related diseases (4–6). Therefore, there is a need to transition from the pediatric to the adult health care system; a smooth transition of these patients to the adult health care system appropriate to their needs, where they can receive appropriate medical care and the life they desire, is needed. Thus, the implementation of a structured transition program that includes support for patient independence is recommended (7, 8). In Japan, in 2014, the Japan Pediatric Society published a consensus statement on the "Proposal for Transitional Care for Patients with Childhood-Onset Diseases" (9).

Clinical Reporting in Transitional Care, recommended by the American Academy of Pediatrics, the American Academy of Family Physicians, and the American Board of Internal Medicine (7), uses Got Transition® (10). The Six Core Elements of the National Resource Center on Health Care Transitions specifically describe both pediatric and adult health care programs and include the following: (1) establishing the transition policy, (2) tracking and monitoring transition progress, (3) assessing the patient's readiness for transition, (4) developing the transition plan with a medical summary, (5) transferring the patient, (6) completing the transfer and following up with the patient and family. These consist of and define the basic elements in a structured transition process.

Some of the questions in this study were developed based on these six elements. Other countries have reported outcomes of transition support using the Six Core Elements (11, 12). In addition, several literature reviews on health care transitions (13–16) also report measuring and evaluating the outcomes of transition interventions and transition models, describing the effectiveness of implementing structured transition programs. In Japan, transition support using the Six Core Elements was implemented in five hospitals under the Ministry of Health, Labor and Welfare's Transition Support Model Project (17, 18). Later, in FY2019, the Ministry of Health, Labor and Welfare, Research Group created the Six Core Guides for Adult Transition Support (19) based on the Six Core Elements and distributed it to children's hospitals nationwide. However, it is unclear to what extent transition support in Japan is consistent with the programs recommended in the United States and Japan.

In Japan, 62.3% of patients with childhood-onset chronic diseases, aged 20 and older, regularly visited multiple medical facilities, with pediatrics being the primary department of care for about half of them (20), indicating that the transition to adult care is not smooth (21). Patients with childhood-onset chronic diseases are required to transfer from the medical cost subsidy system under the measures for specific pediatric chronic diseases to the designated intractable diseases system if they meet the criteria for disease severity (22). However, patients who do not meet some of the criteria are currently forced to bear the long-term burden of high medical costs or to forgo the best treatment because eligibility for the public medical cost subsidy system ceases after the age of 20 (21).

The age of 20, when the subsidy for medical expenses for pediatric chronic diseases is no longer available, is a major turning point in the lives of patients as they are at a crossroads in terms of employment and higher education. However, studies of Japanese patients with pediatric chronic diseases have reported that patients with chronic pediatric diseases face difficulties in earning a living on their own due to low income and low employment (20). Thus, increased health care costs can be burdensome for those with low levels of education and limited employment opportunities due to pediatric chronic illnesses. Particularly, patients who are unable to cope with these increased health care costs will have no choice but to give up appropriate medical care.

Reported barriers to transition include lack of knowledge of pediatric-specific conditions and understanding of adolescent patients and families by adult departments, fear of losing trust and longstanding relationships with pediatricians, difficulty finding adult providers, fundamental differences between

pediatric and adult care, and negative beliefs and expectations of adult departments (12, 23, 24). In Japan, the high dependence of patients and families on pediatrics, lack of awareness among health care professionals, and anxiety and distrust of adult medicine have been noted (25). In addition, although there have been recent health care provider surveys of general pediatric nurses and adult nurses (26), there is no updated national survey on transition barriers among health care providers who are central to transitional care in Japan. Therefore, we believe that there is an urgent need to understand the actual status of transitional care and investigate barriers to transition nationwide so that all patients with childhood-onset chronic diseases can smoothly transition to adult health care systems and receive appropriate medical care.

We believe that the results of this study will contribute to clarifying the role of such programs, improving the quality of transition support at medical institutions, and establishing a system that can support the transition to independence for patients. To this end, this study aimed to explore the status (prevalence) of transition support for adolescent patients in pediatric institutions and the factors, issues, and challenges in the health care system that hinder HCT.

# Materials and methods

## Definition of terms

Pediatric chronic diseases: chronic diseases that occur in children under 15 years.

Transition support: assistance for transition from the pediatric health care system to the adult health care system.

## Research design

This was a cross-sectional survey study of physicians and nurses providing transition support at pediatric institutions in Japan.

## Setting

The study was conducted between August to November 2020. We sent pen-and-paper questionnaires to 494 medical institutions in Japan that specialize in pediatrics (pediatric specialty hospitals, pediatric cancer center hospitals, hospitals with specific functions that provide pediatric care, university hospitals, general hospitals, hospitals that provide home medical care for children, comprehensive perinatal care centers, regional perinatal care centers, etc.).

## Participants

The eligibility criteria were physicians or nurses working at the above facilities and providing transition assistance at the time of the survey. The facility director selected respondents who met the eligibility criteria and gave them a survey form. Participants were assumed to have completed and directly returned the unmarked questionnaire themselves.

## Variables, data sources, and measurement methods

These items were generated based on a literature review, expert discussion, and interviews with three CNS in pediatrics (27). A Pilot Study was completed by sending the questionnaire to two pediatricians of HCT experts for content validity testing. Face validity was also tested on three similar participants. Alterations were made regarding feedback from the Pilot Study, such as changing the questions that were considered ambiguous. Then we formed the final version of the questionnaire for distribution to participants.

This study was in the initial discovery phase regarding actual transition support. The following data were included:

(1) Demographic data: information about the participant (job title, specialty, position, years of experience supporting transition, location of transition support) and information outlining the institution (type of founding agencies, disease groups treated).
(2) Medical care system for transfer to adult departments: medical care system for adolescent patients with chronic diseases (implementation of adolescent patient transfers, availability of specialized outpatient clinics and dedicated personnel, age at which the HCT program starts, reasons for starting support, collaboration with community family physicians, collaboration with adult hospitals and departments, use of educational and support tools for transition support).
(3) Contents of the HCT program based on the Six Core Elements (10): establishing the transition policy; tracking and monitoring transition progress; assessing the patient's readiness for transition; developing the transition plan with a medical summary; transferring the patient; completing the transfer and following up with the patient and family.
(4) Barriers to transition from pediatric to adult care (13, 18, 19, 23–32): based on 11 items for patients, nine for family members, and 14 for health care providers, the survey respondents' self-reported factors hindering the transition to adult care. A 4-point Likert scale was used for each item with the following response options: not at

all applicable, not very applicable, fairly applicable, and very applicable.

(5) Transitional support for adolescent patients that should be enhanced in the future (14–16, 18, 19, 25, 28–31): the survey provided the possibility of multiple-choice responses for each of the following items: policy and local government (four items); academic institutions (four items); affiliated facilities (eight items); and individuals (eight items).

## Bias

The questionnaire was anonymous to avoid bias in the participants' responses. The participants directly returned the questionnaires themselves.

## Quantitative variables

An average score of 1 (not applicable at all), 2 (not very applicable), 3 (fairly applicable), and 4 (very applicable) was extracted to measure the factors preventing transition to adult care.

## Data analysis methods

Descriptive statistics including frequencies, means, and standard deviations were used in the analysis.

## Ethical considerations

When selecting potential research collaborators, return envelopes were distributed only to research participants to avoid the exercise of coercive power, the disclosure to outside parties of the presence or absence of replies, or the contents of the questionnaire. The questionnaires were unsigned to prevent the identification of the participants, and their responses to the questionnaire indicated that they had agreed to cooperate in the research. This study was conducted after obtaining approval from the ethical review committee of the researcher's institution (No. 19019).

# Results

A total of 494 copies of the questionnaire were distributed, and 225 were collected (45.5% response rate). To address missing data, statistical analyses were conducted using only valid responses in each section.

## Overview of the respondents

The respondents included 199 (88.4%) physicians and 26 (11.6%) nurses, with 22 (9.8%) children's hospital respondents among them. A total of 153 (68.0%) had more than 10 years of clinical experience in transition support, 179 (79.5%) were in administrative positions, and 76 (33.8%) were Specialized Physicians or Certified Nurses/Clinical Nurse Specialists. The following were multiple responses: the places of care delivery for adolescents with chronic diseases included outpatient

TABLE 1 Participants background ($n = 225$).

| | No answer | *n* | % |
|---|---|---|---|
| Sex | 2 | | |
| Male | | 169 | 75.1 |
| Profession | 0 | | |
| Pediatrician | | 199 | 88.4 |
| Nurse | | 26 | 11.6 |
| Hospital | 0 | | |
| Children's Hospital | | 22 | 9.8 |
| Pediatrics other than Children's Hospital | | 203 | 90.2 |
| Administrative Position | 0 | | |
| Yes | | 179 | 79.5 |
| Certified or specialization | 0 | | |
| Specialized physicians | | 64 | 28.4 |
| Certified nurses/clinical nurse specialists | | 12 | 5.3 |
| No | | 149 | 66.2 |
| Total years of experience supporting transition | 5 | | |
| 1< | | 6 | 2.7 |
| 1–3 | | 20 | 8.9 |
| 4–9 | | 41 | 18.2 |
| ≧10 | | 153 | 68.0 |
| Place of care delivery for teens with chronic disease (multiple responses) | | | |
| Specialization clinic | | 5 | 2.2 |
| Center | | 3 | 1.3 |
| Outpatient clinic pediatrics | | 204 | 90.7 |
| Inpatient pediatrics | | 51 | 22.7 |
| Other | | 9 | 4.0 |
| Specialization (multiple responses) | | | |
| Neuro-muscle | | 116 | 51.6 |
| Syndromes involving chromosomal or genetic changes | | 104 | 46.2 |
| Endocrine | | 81 | 36.0 |
| Childhood cancer | | 71 | 31.6 |
| Cardiology | | 68 | 30.2 |
| Respiratory | | 60 | 26.7 |
| Type 1 DM | | 58 | 25.8 |
| Kidney | | 56 | 24.9 |
| Congenital/Inherited metabolic diseases | | 51 | 22.7 |
| Other | | 185 | 82.2 |

pediatrics clinics 204 (90.7%); neuromuscular diseases were the most common with 116 cases (51.6%), followed by syndromes involving chromosomal or genetic changes with 104 cases (46.2%) (Table 1).

## Medical care system for transfer to adult departments

Twenty (10.0%) had a specialty outpatient clinic and 61 (30.5%) had a full-time person in charge. The age at which the HCT program started was stated by 36 respondents (16.0%). Academic/career change and age were the most common reasons for starting support services, with 155 respondents (68.9%), followed by diseases outside the scope of pediatricians, with 135 (60.0%). Regarding collaboration with other agencies and departments, 80 (40.0%) respondents indicated that they collaborated with the local family physician, while 97 (48.5%) indicated that they collaborated with adult hospitals and departments. A total of 159 (79.5%) reported no use of educational and support tools for transition assistance, indicating that the guides were not widely used (Table 2).

TABLE 2 Medical care system for transfer to adult departments ($n = 200$).

| | No answer | *n* | % |
|---|---|---|---|
| Specialized clinic | 1 | | |
| Yes | | 20 | 10.0 |
| Specialist | 33 | | |
| Yes | | 61 | 30.5 |
| Define the age for starting the HCT program | | | |
| Yes | | 36 | 16.0 |
| Not defined | | 163 | 72.4 |
| Other | | 1 | 0.4 |
| Reason to start the HCT program (multiple responses) | | | |
| Academic/carrier change | | 155 | 68.9 |
| Age | | 155 | 68.9 |
| Disease outside the scope of pediatricians | | 135 | 60.0 |
| Patients' preference | | 93 | 41.3 |
| Family's preference | | 73 | 32.4 |
| Psycho-social maturity | | 71 | 31.6 |
| Pediatrician's circumstances | | 67 | 33.5 |
| Stable disease condition | | 62 | 27.6 |
| Collaboration with general practitioner in community | 1 | | |
| Yes | | 80 | 40.0 |
| Adult practitioner | | 69 | 34.5 |
| Child practitioner | | 24 | 12.0 |
| No | | 119 | 59.5 |
| Collaboration with the adult practitioner in the hospital | 0 | | |
| Yes | | 97 | 48.5 |
| Educational/information package for transition | 1 | | |
| Yes original | | 13 | 6.5 |
| Yes use the existing package | | 25 | 12.5 |
| No | | 159 | 79.5 |
| Other | | 2 | 1.0 |

HCT, health care transition.

## Contents of the HCT program based on the six core elements

Two hundred respondents indicated that they transferred adolescent patients to adult departments, with "transferring the patient" being the most common response. Of the transition planning, 155 (77.5%) of the respondents prepared medical summaries. Medical summaries included: disease name with 81 cases (40.5%), examination results with 78 cases (39.0%), treatment summary with 77 cases (38.5%), and prescribed medicine/care with 74 cases (37.0%).

More than 70% responded "No" to all five other content areas: establishing the transition policy with 180 (90%), tracking and monitoring transition progress with 179 (89.5%), assessing the patient's readiness for transition with 143 (71.5%), developing the transition plan with 169 (84.5%), following up with the patient and family with 140 (70%), and patient feedback with 177 (89.4%).

For the combination of the Six Core Elements, 33 (16.5%) practiced only "transferring the patient," 70 (35.0%) practiced "transferring the patient" and "making a medical summary," and 30 (15.0%) practiced four or more elements (Table 3).

## Barriers to transition from pediatric to adult care

The patient factors with the most scores were "very applicable" and "fairly applicable" were "Emotional dependence on pediatrics" with 80 cases (37.7%)/101 cases (47.6%) and "Patient's intellectual disability" with 98 cases (46.2%)/76 cases (35.8%), followed by "rare disease" with 75 cases (35.4%)/96 cases (45.3%) (Figure 1-1). Among family factors, "Emotional dependence on Pediatrics" was the highest at 82 cases (38.0%)/108 cases (50.0%), followed by "Over-involvement of patients" at 50 cases (23.1%)/102 cases (47.2%) and "Lack of information about adult departments" at 40 cases (18.5%)/113 cases (25.5%) (Figure 1-2).

The medical/infrastructure factor with the highest score was "Lack of adult medicine departments" with 86 cases (41.7%)/87 cases (42.2%). The followes were "Lack of understanding of patients and diseases by adult physicians"

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TABLE 3 Contents of the HCT program based on six core elements ($n = 200$).

| | No answer | *n* | % |
|---|---|---|---|
| Combination of healthcare transition process based on the six core elements | 0 | | |
| One element (Only "transferring the patient") | | 33 | 16.5 |
| Two elements | | 85 | 42.5 |
| "Transferring the patient" and "making a medical summary" | | 70 | 35.0 |
| Three elements | | 53 | 26.5 |
| Four elements | | 13 | 6.5 |
| Five elements | | 13 | 6.5 |
| Six elements | | 4 | 2.0 |
| Establishing the transition policy | 0 | | |
| No | | 180 | 90 |
| Yes | | 20 | 10.0 |
| Tracking and monitoring transition progress | 2 | | |
| No | | 179 | 89.5 |
| Yes | | 16 | 8.0 |
| Other | | 3 | 1.5 |
| Assessing the patient's readiness for transition | 0 | | |
| No | | 143 | 71.5 |
| Yes | | 56 | 28.0 |
| Use of assessment tools | 1 | | |
| Yes | | 10 | 5.0 |
| Evaluation Item (multiple responses) | | | |
| Understanding the disease | | 49 | 24.5 |
| Need for the continuation of treatment | | 38 | 19.0 |
| Medication adherence | | 38 | 19.0 |
| Self-management | | 38 | 19.0 |
| Employment and schooling | | 28 | 14.0 |
| Treatment behavior | | 25 | 12.5 |
| Cautionary points in daily life | | 24 | 12.0 |
| Medical care system | | 24 | 12.0 |
| Sexual and reproductive health | | 10 | 5.0 |
| Other | | 1 | 0.5 |
| Developing the transition plan with a medical summary | | | |
| Developing the transition plan | 0 | | |
| No | | 169 | 84.5 |
| Yes | | 30 | 15.0 |
| Other | | 1 | 0.5 |
| Making medical summary for transfer | 1 | | |
| No | | 43 | 21.5 |
| Yes | | 155 | 77.5 |
| Disease name | | 81 | 40.5 |
| Examination results | | 78 | 39.0 |
| Treatment summary | | 77 | 38.5 |
| Prescribed medicine/care | | 74 | 37.0 |
| Emergency contact information | | 32 | 16.0 |
| Explanatory document about the disease | | 31 | 15.5 |
| Patient's self-management evaluation | | 9 | 4.5 |
| Use of my medical history | | 8 | 4.0 |
| Transition summary | | 4 | 2.0 |
| Other | | 1 | 0.5 |
| Transferring the patient | 0 | | |
| Yes | | 200 | 100 |
| Completing the transfer and following up with the patient and family | | | |
| Following up with the patient and family | 0 | | |
| No | | 140 | 70.0 |
| Yes | | 59 | 29.5 |
| Other | | 1 | 0.5 |
| Patient Feedback | 2 | | |
| No | | 177 | 89.4 |
| Yes | | 20 | 10.0 |
| Other | | 1 | 0.5 |

with 67 cases (32.5%)/100 cases (48.5%), "Lack of personnel to coordinate" with 53 cases (25.7%)/101 cases (49.0%), "Lack of collaboration between pediatricians and adult physicians" 47 cases (22.8%)/107 cases (51.9%), and "Lack of a collaborative system" with 51 cases (24.8%)/95 cases (46.1%) (Figure 1-3).

## Transitional support for adolescent patients that should be enhanced in the future

The most common item was related to academic institutions, with 166 (73.8%) selecting "sharing knowledge and support methods with adult medicine departments." This was followed by "establishment of transitional care centers by policies and local governments" with 121 respondents (54.3%) and "securing an adult department to treat adolescent patients" with 114 respondents (51.1%), representing more than half of the sample (Table 4).

# Discussion

## Characteristics of the respondents

The survey's respondents were pediatricians and nurses in management positions at major pediatric institutions in Japan,

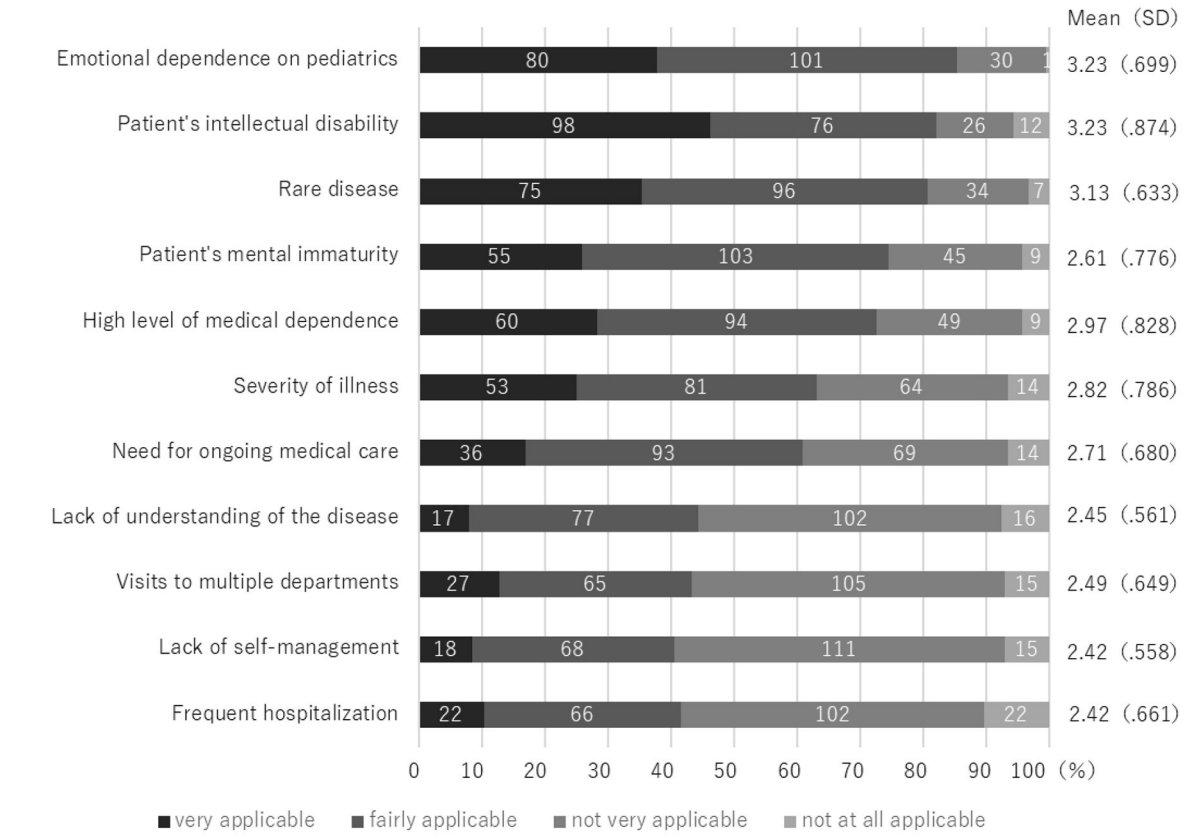


FIGURE 1-1
Barrier to Transition from Pediatric to Adult care: Patient Factors ($n = 212$).

and their views may reflect the principles and conditions of practice applicable to transition of care in adolescents and young adult health care in Japan.

In terms of specialties, "neuromuscular diseases" and "syndromes involving chromosomal or genetic changes" accounted for about half of the cases. Although a systematic approach to transitional support for neurological diseases is currently being developed in the U.S. (33), the current situation in Japan is not yet fully understood and programs must be developed to enhance support in the future.

Compared with previous surveys on HCT (34–37), the response rate for this survey (45%) was standard for national surveys that were not limited to board-certified physicians or medical departments. About half of the facilities that did not respond might understand HCT but did not provide support or did not have a sufficient understanding of the HCT available.

## Status of HCT programs in Japan

The results of this study showed that although more than 80% of adolescent patients were being transferred to adult departments, few departments and people were dedicated to transition support, and educational and informational tools were not being used. Regarding the HCT contents based on the Six Core Elements, the most common is transferring the patient, followed by the making of a medical summary, with 30–40% of the medical summaries containing information on the disease, and <5% related to patient's understanding of their disease or self-management. Regarding the HCT process based on the Six Core Elements, transfers accounted for about half of the cases. The purpose of the HCT program is not limited to transferring, but to provide seamless, high-quality, and developmentally appropriate medical services during the developmental process from adolescence to adulthood to maximize a person's role functioning and potential (29, 30).

Therefore, developing a transition plan with a medical summary in a transition program should not end with simply sending medical information to the adult department, but should include a transition summary (31). In the Transition to Adult Care program for sickle cell disease, the medical summary includes not only medical information, but also social, academic, and emotional content sent by the nurse case manager (38). The medical summary is also used as a tool to engage the patient or family in taking ownership of medical care (39). One method is an initiative that allows patients, pediatricians, and adult

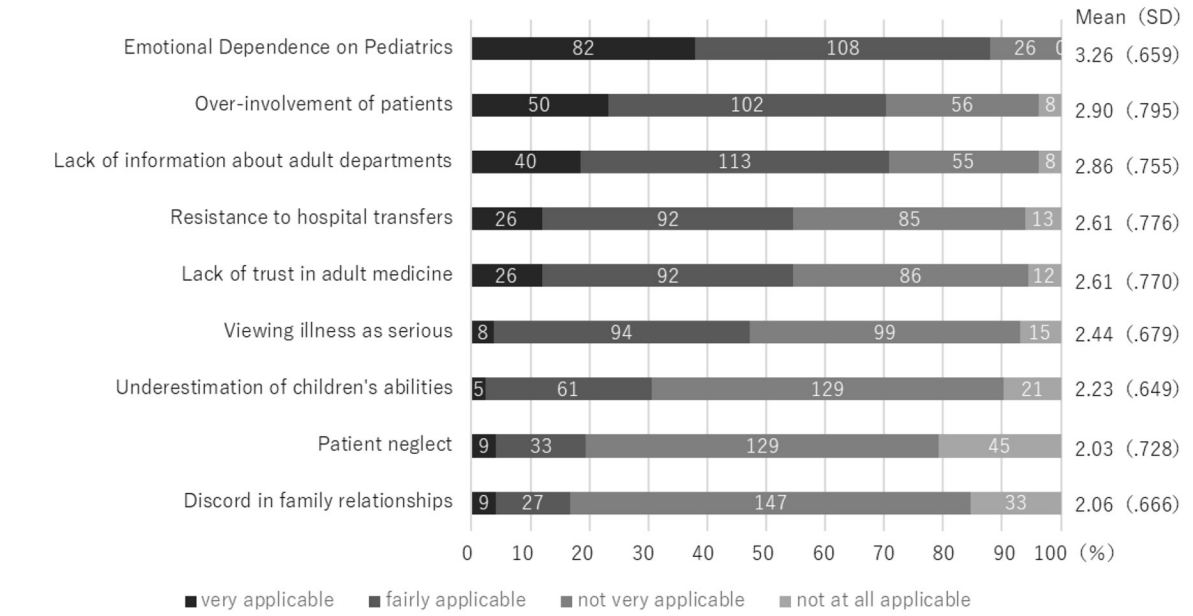


FIGURE 1-2
Barriers to Transition from Pediatric to Adult Care: Parents Factors ($n$ = 216).

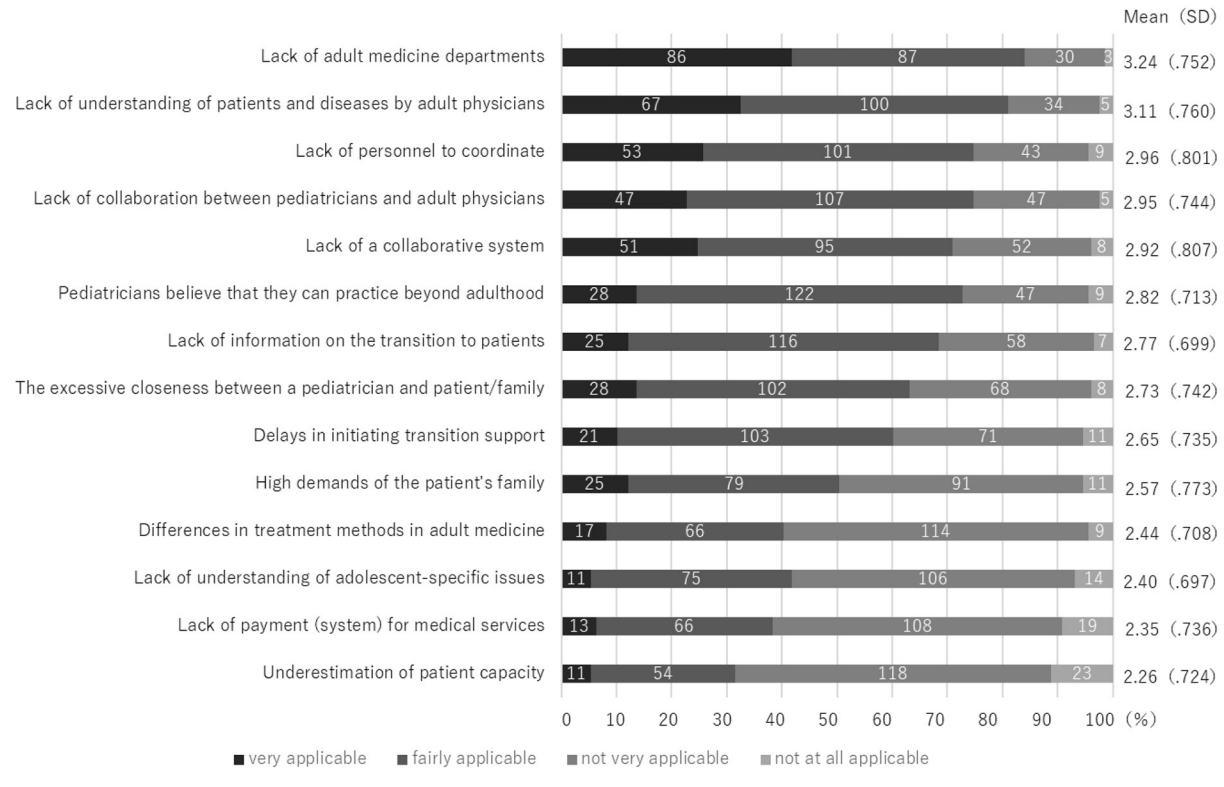


FIGURE 1-3
Barriers to Transition from Pediatric to Adult care: Medical/Infrastructure factors ($n$ = 206).

TABLE 4 Requests for transition support (Multiple Responses) $n = 223$.

| Unit | Content | *n* | % |
|---|---|---|---|
| Academic | Sharing knowledge and support methods with adult medicine departments | 166 | 73.8 |
| | Development of HCT program and guidelines | 91 | 40.8 |
| | Public Awareness Activities | 90 | 40.4 |
| | Advocacy of core concepts | 32 | 14.3 |
| Policy & municipalities | Establishment of transitional care support centers | 121 | 54.3 |
| | Medical expense subsidies for patients | 96 | 43.0 |
| | Revision of medical fees | 90 | 40.4 |
| | Employment support for patients | 87 | 39.0 |
| Institution | Securing an adult department to treat adolescent patients | 114 | 51.1 |
| | Securing human resources | 79 | 35.4 |
| | Creation of departments (divisions) | 69 | 30.9 |
| | Educate and inform patients and families | 52 | 23.3 |
| | Educate and inform staff | 49 | 22.0 |
| | Secure budget | 39 | 17.5 |
| | Sharing the goal philosophy | 17 | 7.6 |
| | Survey of current patient status | 13 | 5.8 |
| Individuals | Communicate and share information with the adult department | 95 | 42.6 |
| | Acquisition of knowledge and expertise in support | 80 | 35.9 |
| | Coordination for transfer to the adult department | 61 | 27.4 |
| | Checking readiness of patient for transition | 53 | 23.8 |
| | Developing a care plan | 34 | 15.2 |
| | Follow up with patients after transfer | 22 | 9.9 |
| | Prepare transition summary | 19 | 8.5 |
| | Evaluation of transition support | 11 | 4.9 |

health care providers to share an electronic medical summary website (40). These may help bridge the gap between pediatric and adult care and are important in achieving a seamless transition. Development and research of tools that can be shared longitudinally and with patient families is needed in Japan.

About 15% of the facilities had HCT programs that combined four or more elements. The Six Core Elements are not a model of care, but a structured process. They can be customized for each hospital's use and can be applied to different types of transitional care models and settings (31). The structured HCT processes have shown positive results in reducing pre-transition patient anxiety and enhancing patients' experiences and satisfaction with their care, and interventions that had positive outcomes were described as having a combination of HCT activities (17, 41–43). These findings indicate a need for more widespread implementation of structured HCT programs in Japan.

## Patient and family factors hindering the transition to adult care

In this study, the top factors that prevented patients from transitioning to adult care were intellectual disability and rare diseases among patient factors and emotional dependence on pediatrics among patient and family factors. Similar findings have been reported in Japan and other countries (25, 38, 44). Patient and family factors in transition barriers are said to include anxiety about transition, inadequate planning, and systemic problems (31), indicating that there are compounding factors. These considerations indicate that a combination of structured processes is needed to provide support.

As for rare diseases and intellectual disabilities, in Japan, the percentage of patients over the age of 20 with congenital metabolic disorders exceeds 35% (45), and children with rare diseases are reaching adulthood. The importance of supporting children with chronic illnesses who require these special considerations and the need for research is described (38), and the needs of patients and families (46, 47), barriers to transition (48), clinical reports on support (49–51), informational sites (52, 53), pediatric and adult department practices, and consensus on pediatric and adult medical care and support have been reported (54). Thus, it is necessary to study the current situation and support patients with special medical needs transitioning to adult care in Japan in the future.

Ochiai, in a survey of patients 15 years of age and older visiting a pediatric cardiology outpatient clinic of a children's hospital, described a lack of information about transfers and the need for continued attendance at a pediatric hospital (32). Based on such surveys, we developed the questionnaire regarding patient/family barriers, but they may not cover all of them.

## Expectations for transitional medical support centers

The results of this survey showed that less than half of the respondents were collaborating with adult health care, and challenges to collaborating with adult health care were identified as a factor hindering transition. Also, the top expectations for transition support were related to collaborating with adult health care. The challenges in collaborating with adult and pediatric departments in Japan included the following: lack of communication/systems, lack of understanding and knowledge

of pediatric care and patient characteristics by adult health care departments, lack of manpower/institution to coordinate, and difficulties in securing an adult department to treat adolescent patients. Research reports on barriers to transition in the health care system include communication and consultation gaps, knowledge and training limitations, lack of personnel and resources, and financial constraints (23, 31, 55, 56), similar to those found in this study.

One way to resolve these issues, at the policy and municipal levels, is to "establish transitional medical support centers." This is a facility that provides comprehensive support for transition, including not only medical care but also welfare. In 2017, a model project was launched by the Ministry of Health, Labor and Welfare requiring each prefecture to secure at least one transitional medical support center (57), but as of 2021, there were only seven such centers nationwide. Their main roles include the following: (1) identification and publication of information on medical departments and medical institutions that can treat patients with chronic pediatric diseases in adulthood; (2) liaison, coordination, and communication support between pediatric medical institutions and adult medical institutions; and (3) promotion of support for patients' independence and autonomy (57). It is expected that the establishment of this support organization will be expanded in the future.

In Japan, various physicians' professional organizations developed guidelines for congenital heart disease (58), renal disease (59), type 1 diabetes (60), rheumatic diseases (61), and various other diseases. In the field of adult congenital heart disease in Japan, close affiliation and interaction with the International Society for Adult Congenital Heart Disease and European meeting in Adult Congenital Heart Disease exists, and a system of medical care and certified physicians has been introduced (62). In other countries, advanced practice nurses in charge can provide care that meets patients' needs (63), and they also improve patient care and family satisfaction (64). Thus, it is necessary to train specialists without being limited to a specific department to ensure that patients receive seamless transition support.

In Japan, few facilities have transition coordinators (36) and pediatricians are responsible for most of them. Although there are some projects and organizations that provide transition coordinator training programs (65) and ongoing training for pediatric nurses (66), there are no systematic educational programs. In other countries, there are already educational systems for pediatric and adult health care providers (67, 68). Therefore, in Japan, it is desirable to harmonize and improve the quality-of-care delivery through education and knowledge sharing in the future.

### Limitations of this study and future issues

The results of this survey were mainly derived from physicians nationwide, and we believe that the status of transitional support in pediatric care is clear; however, because facilities that provide transitional support were more likely to respond, those that did not respond to the survey may not be providing adequate support. Therefore, the full scope of support, including that of adult departments and patients/families, might not have been captured. It would therefore be necessary to continue the survey by expanding its scope and considering specific transitional care and support.

The results of this survey were mainly derived from physicians nationwide, and we believe that the status of transitional support in pediatric care is clear. We found that about half of the facilities do not provide transition support due to barriers or insufficient understanding of specific support. As a future challenge, we believe it is necessary to make new contacts with facilities that did not respond to the survey and learn about their difficulties in promoting a systematic HCT program.

## Conclusions

We sent self-administered questionnaires to pediatricians and nurses in 494 facilities throughout Japan and received responses from 225 facilities, of which approximately 80% had implemented "transitioning patients." However, the structured implementation of transition programs was not standardized. Barriers to transition related to the medical institutions included a lack of coordinators and difficulties collaborating with adult departments due to a lack of adult departments that could handle pediatric conditions. Patient/family-related barriers to transition included delayed independence due to disability and psychosocial factors, as well as lack of information about the HCT. To resolve these issues, it is suggested that transition support be developed according to the characteristics of rare diseases and disabilities, transition medical care support centers be popularized, coordinators be appointed as a support system, and a system of collaboration between pediatric and adult departments be established.

## 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 human participants were reviewed and approved by Saitama Prefectural University

Research Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

## Author contributions

IS, MM, TM, and MH contributed to conception and design of the study. IS organized the database, performed the statistical analysis, and wrote the first draft of the manuscript. MM wrote sections of the manuscript. All authors contributed to manuscript revision, read, 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.

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# Efficacious interventions for improving the transition readiness of adolescents and young adult patients with chronic illness: A narrative review of randomized control trials assessed with the transition readiness assessment questionnaire

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**Objective:** We inspected efficacious interventions to improve the transition readiness of adolescent and young adult patients with childhood-onset chronic illnesses using the Transition Readiness Assessment Questionnaire (TRAQ).

**Methods:** Our narrative review was conducted on randomized control studies assessed with TRAQ for outcome measurement before and after the interventions. We included all patients with chronic diseases. We searched eight electronic database(s): Allied and Complementary Medicine Database (AMED) Allied and Complementary Medicine, BioSciences Information Service of Biological Abstracts (BIOSIS) Previews, Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Cochrane Library, Embase, Ichu-shi, Medline, and Web of Science. The text words for the search of data sources were as follows: "("transition readiness assessment questionnaire" OR TRAQ) AND 2011/01:2022/06[DP] AND (clinical AND trial OR clinical trials OR clinical trial OR random* OR random allocation)." More studies were identified from the references in our reported study. This data set was independently cross-checked by two reviewers.

**Results:** We identified 261 reports and collected three articles. The target diseases were type-1 diabetes, congenital heart disease, cystic fibrosis, and inflammatory bowel disease. All the studies excluded patients with intellectual disabilities. The age of the participants was distributed between 12 and 20 years. Nurse-provided web-based intervention of transition readiness

was constructed using digital resources in two studies. The intervention ranged from 6 to 18 months. All the interventions were efficacious in improving transition readiness assessed with TRAQ scores, except for the self-advocacy score.

**Conclusions:** We obtained three randomized control studies with TRAQ for outcome measurement. In two studies, web-based and nurse-led organized interventions were shown to improve transition readiness.

KEYWORDS

**adolescent, chronic disease, intervention, randomized controlled trial (RCT), review, transition readiness, questionnaires, young adult**

# Introduction

There is a growing concern about what medical care should be for adolescent and young adult patients with childhood-onset chronic diseases around the world. American Academy of Pediatrics, jointly with the American Academy of Family Physicians and American College of Physicians – American Society of Internal Medicine issued a Consensus Statement on Health Care Transitions for Young Adults with Special Health Care Needs in 1992 (1). While most young adults with special health care needs are able to become adults, many patients with severe medical conditions and disabilities — which limit their ability to function and result in complicated social, emotional, or behavioral sequelae — experience difficulty while transitioning from child to adult health care systems (1). Transition readiness is associated with independent self-care behaviors and patient quality of life, in addition to the appropriate shift to adult health care systems. The specific methodology for the transition is summarized in Six Core Elements (2). However, it has not been clarified as to what kind of interventions are effective in promoting self-care skills in adolescents and young adults with chronic diseases. In order to evaluate the efficacy of interventions aimed at transition to adult health care systems, it may be appropriate to examine the transition readiness status by interventions. At the moment, there are 10 kinds of tools to assess transition readiness. Among them, the Transition Readiness Assessment Questionnaire (TRAQ) (3) and TRxANSITION (4) have been verified for enough reliability and validity. Moreover, TRAQ, developed in 2011 (5, 6), has acquired internal validity, construct validity, and internal consistency (7). A higher TRAQ score indicates knowledge of the disease, skill, self-efficacy, positive outlook toward the future, and health-related quality of life (8–11). Conversely, a lower TRAQ score indicates non-adherence to drug therapy (12). In this study, we tried to review high-quality interventional research using the TRAQ for the outcome measurement to identify efficacious interventions and thus improve transition readiness for patients with childhood-onset chronic disease. We targeted randomized controlled studies for high-quality interventional research to avoid selection bias and confounding bias. The aspects to be addressed in this narrative review are as follows: participants, intervention, control, and outcome. We confirmed that increasing the score between the intervention group and control group allows for assessment of the quality of transition readiness. Therefore, employing efficacious interventions can improve the outcomes of the patients.

# Methods

## Study design

All randomized control trials assessed with the TRAQ before and after the intervention were included. Our narrative review was conducted by partially following the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2020 (PRISMA 2020) as a guide for the systematic review and meta-analysis protocol (13).

## Criteria for the included studies

We established eligibility criteria and exclusion criteria before the identification and selection of studies. The eligibility criteria are as follows: (1) research papers and not protocols or reviews and (2) studies assessed with TRAQ. The exclusion criteria are as follows: (1) non-intervention studies and (2) non-randomized studies.

## Patients

We included all patients who were diagnosed with childhood-onset chronic illness.

## Data sources and search strategy

On 18 June 2022, we searched eight electronic databases: Allied and Complementary Medicine Database (AMED)

(14), BioSciences Information Service of Biological Abstracts (BIOSIS) Previews (15), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (16), the Cochrane Library (17), Embase (18), Ichu-shi (in Japanese) (19), Medline (20), and Web of Science (21) for articles from 1st January 2011 to 30th June 2022. The text words used for the search were as follows: "("transition readiness assessment questionnaire" OR TRAQ) AND (clinical AND trial OR clinical trials OR clinical trial OR random* OR random allocation) AND 2011/01:2022/06[DP]." We checked the updates to all the databases through 30 June 2022. Additionally, more studies were identified from the references in our past reports. No limitation was imposed with regard to language. Publication type was limited to research papers of any length.

## Identification and selection of studies

First, we identified eligible studies through electronic searches and excluded duplicates. Second, we identified eligible studies and excluded duplicates of the same study by referring to the study title. Third, two reviewers (JT and YY) independently checked the reports at the title/abstract level and identified potentially relevant studies among the research assessed with TRAQ. Fourth, we assessed the studies and decided whether to include them based on the same eligibility criteria as the aspects of the randomized intervention. Any disagreements were resolved by an additional reviewer (YI).

## Data items and management

Characteristics of the studies, patients, interventions, and outcome measures were collected from each included study. Characteristics of the studies were established as columns in one table, and characteristics of the patients, interventions, and outcome measures were established as columns in another table.

One reviewer (JT) put the above data as variables into a data set in MS Excel. This data set was independently cross-checked by another reviewer (YY). They consulted with an additional reviewer (YI) regarding the variables with missing information. If we could not solve a problem, we employed expert opinion.

## Ethics

This narrative review does not require ethical approval. The data used here are neither individual nor private.

# Results

We searched eight database records identified ($n = 261$) from the following: no study from AMED, 90 studies from BIOSIS Previews, 4 studies from CINAHL, 92 studies from the Cochrane Library, 35 studies from Embase, 10 studies from Ichu-shi (Japanese), 15 studies from Medline, and 15 studies from Web of Science. After removing the duplicates, 147 studies were identified. After checking the reports at the title and abstract level, 47 studies were identified as potentially relevant. The excluded 100 studies were deemed to focus on other research themes. Of the remaining 47 studies, 11 studies were without an abstract or only included an abstract; 10 only included protocols; 3 were reviews; 10 included other questionnaires and not TRAQ; 5 were without intervention, and the last 6 were without randomization; therefore, we excluded these 45 studies. Finally, we included two randomized control studies (22, 23) in our review. An additional study (24) was identified from the references of our previous report (25). Overall, our study included three randomized control studies. The characteristics of the studies are presented in Table 1. All the reports are original articles in English. The collected data are presented in Table 2.

## Patients

The target diseases were type-1 diabetes in two studies, congenital heart disease in one study, cystic fibrosis in one study, and inflammatory bowel disease in one study. All the studies excluded intellectual disability. The subjects ranged in age from 12 to 20 years, with the mean or median age in each study ranging from 15 to 17 years.

## Intervention

In one study (24), the health care provider provided web-based and mobile phone-text-delivered disease management and skill-based interventions. The intervention was an 8-month technology-based disease management program based on Bandura's Social Cognitive Theory.

In the second study (22), nurses provided two nurse-led face-to-face sessions. The sessions comprised individualized 60-min educational sessions: Session 1 was created using the MyHealth Passport app (26). Session 2 reviewed the education-related goals including discussion, role-play, and reviews, with the same materials [short videos, video, scenarios, booklet (27), and website (28)], followed by a text message or e-mail interaction within 7 days.

In the third study (23), a nurse provided two face-to-face structured motivational interviews based on training manuals

TABLE 1 Characteristics of studies.

| No. | Author(s)' name | Protocol | Clinical trial ID | Citation or publication | Year(s) of study | Year of publication | Location | Setting | Number of centers | Type of design | Sample size, *n* | Observation period, months |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Huang et al. (24) | MD2Me - Texting to Promote Chronic Disease Management | ClinicalTrials.gov Identifier: NCT01253733 | PEDIATRICS | October 2010 to March 2011 | 2014 | United States | A tertiary care pediatric academic medical center | Single | A parallel randomized trial of two groups | 80 | 16 |
| 2 | Mackie et al. (22) | The CHAPTER II Study - Congenital Heart Adolescents Participating in Transition Evaluation Research | ClinicalTrials.gov Identifier: NCT01723332 | Journal of the American College of Cardiology | 2012 to 2016 | 2018 | Canada | Outpatient clinics | Multiple (Not described in detail) | A parallel cluster randomized trial of two groups | Not described | 30 |
| 3 | Al Ksir et al. (23) | Motivational Interviewing to Improve Self-Management in Youth With Type 1 Diabetes | ClinicalTrials.gov Identifier: NCT04798937 | Journal of Pediatric Nursing | 2019 to 2020 | 2022 | Tunisia | A pediatric endocrinology clinic | Single | A parallel randomized trial of two groups | 60 | 6 |





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TABLE 2 Characteristics of study patients, interventions, and outcome.

| No. | Type of basal disease | Exclusion criteria for participants | Number of participants at baseline, n | Gender distribution at baseline, n (%) | Mean (SD) or median [IQR], and range of age, years | Type of interventions | | | | | Controls | Type of outcome measure | Time(s) of outcome measurement | Withdraw during intervention periods, n (intervention group) | TRAQ score; means (SD) at baseline | TRAQ score; means (SD) after intervention |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Purpose | Interventionist | Contents | Tools | Amount | | | | | | |
| 1 | IBD, CF, T1D | Cognitive impairment | 81 participants before intervention: CD 23; UC 11; CF 13; T1D 34) | Male 37 (45.7); 17 (42.5) in intervention group | 17 between 12 and 20 in intervention group, 17 between 12 and 19 in control group IBD, 17 [16–18]; T1D, 17 [16–18]; CF 14 [13–16] | Disease management and skill-based interventions. Discussed about self-management constructs of monitoring disease symptoms. | Health care providers | Not face-to-face. Management program based on Bandura's Social Cognitive Theory. | Tailored short messages service and queries; 3–5 messages/ week. Reminder short messages service messages to reinforce previously introduced concepts and skills. | 3–5 messages/ week for 1–2 months. Weekly after 2 months. | The control group: monthly messages via mail or e-mail addressing general health issues | Primary outcome: 1, disease status by using scales developed for each disease; the Pediatric Ulcerative Colitis Activity Index for patients with ulcerative colitis; the abbreviated Pediatric Crohn's Disease Activity Index for patients with Crohn disease; | | | | |

*(Continued)*







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TABLE 2 (Continued)

| No. | Type of basal disease | Exclusion criteria for participants | Number of participants at baseline, n | Gender distribution at baseline, n (%) | Mean (SD) or median [IQR], and range of age, years | Type of interventions | | | | | Controls | Type of outcome measure | Time(s) of outcome measurement | Withdraw during intervention periods, n (intervention group) | TRAQ score; means (SD) at baseline | TRAQ score; means (SD) after intervention |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Purpose | Interventionist | Contents | Tools | Amount | | | | | | |
| | | | | | | | | | | | | the Cystic Fibrosis Clinical Score for patients with CF; the Diabetes Quality of Life Brief Clinical Inventory for patients with T1D 2, health status by using; the Karnofsky Performance Scale and the Pediatric Quality of Life Scale as quality of life | 3 times (baseline, 2, and 8 months) | 6 (2) | Overall score: 3.4 (0.9) in intervention group vs. 3.6 (0.7) in control group 2.9 (0.9) in CF group vs. 3.7 (0.8) in T1D group vs. 3.5 (0.7) in IBD group | Overall score: 3.5 (0.7) in intervention group vs. 3.8 (0.9) in control group, at 2 months; 4.0 (0.8) in intervention group vs. 3.8 (0.8) in control group, at 8 months* |

*(Continued)*





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TABLE 2 (Continued)

| No. | Type of basal disease | Exclusion criteria for participants | Number of participants at baseline, n | Gender distribution at baseline, n (%) | Mean (SD) or median [IQR], and range of age, years | Type of interventions | | | | | Controls | Type of outcome measure | Time(s) of outcome measurement | Withdraw during intervention periods, n (intervention group) | TRAQ score; means (SD) at baseline | TRAQ score; means (SD) after intervention |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Purpose | Interventionist | Contents | Tools | Amount | | | | | | |
| | | | | | | | | | | | | 3, health literacy by using Test of Functional Health Literacy in Adults 4, readiness for transition and assesses performance of chronic disease self-management skills by using TRAQ scores (TRAQ 4.1) 5, managing one's own health and health care by using The Patient Activation Measure | | | | |

*(Continued)*





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TABLE 2 (Continued)

| No. | Type of basal disease | Exclusion criteria for participants | Number of participants at baseline, n | Gender distribution at baseline, n (%) | Mean (SD) or median [IQR], and range of age, years | Type of interventions | | | | | Controls | Type of outcome measure | Time(s) of outcome measurement | Withdraw during intervention periods, n (intervention group) | TRAQ score; means (SD) at baseline | TRAQ score; means (SD) after intervention |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Purpose | Interventionist | Contents | Tools | Amount | | | | | | |
| 2 | CHD | Less than a grade 6 level of reading or comprehension, and those with a heart transplant | 125 | Male 62 (51.2); 26 (44.8) in intervention group | 16.9 (0.6) in intervention group, 17.1 (0.6) in control group, between 16 and 17 | Session 1: inform participants about their heart condition. Session 2: motivate participants to self-manage and self-advocate. | One of two cardiology registered nurses | One-on-one sessions Session 1: creation of a MyHealth passport. Session 2: review of the education-related goal. | Available teleconference or video call in Session 2. Both sessions followed text message and or e-mail interaction. Below materials Session 1: a MyHealth passport. Session 2: 6 short videos, a video, 2 scenarios, a booklet, and a website. | Follow within 7 days Session 1: 1.0 h in a pediatric cardiology clinic visit. Session 2: 1.0-1.5 h for 2 months. | The usual care group: pertinent medical records were sent to adult CHD providers. | Primary outcome: excess time between pediatric and adult CHD care Secondary outcome: 1, change in the CHD knowledge (MyHeart) score 2, 1) change in TRAQ (20 items, version was not described) score; 2) Williams' self-management scale; | 5 times (baseline, 1, 6, 12, and 18 months) | 4 (3) | Self-management score: 2.9 (0.7) in intervention group vs. 2.9 (0.9) in control group Self-advocacy score: 4.0 (0.6) in intervention group vs. 3.9 (0.7) in control group | Self-management score; no numerical description[y] Self-advocacy score; no numerical description[y] |

*(Continued)*







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TABLE 2 (Continued)

| No. | Type of basal disease | Exclusion criteria for participants | Number of participants at baseline, n | Gender distribution at baseline, n (%) | Mean (SD) or median [IQR], and range of age, years | Type of interventions | | | | | Controls | Type of outcome measure | Time(s) of outcome measurement | Withdraw during intervention periods, n (intervention group) | TRAQ score; means (SD) at baseline | TRAQ score; means (SD) after intervention |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Purpose | Interventionist | Contents | Tools | Amount | | | | | | |
| | | | | | | | | | | | | 3) assessment of self-management via a cardiologist questionnaire 3, incidence of cardiac re-intervention | | | | |
| 3 | T1D | A neurological disability (epilepsy, autism) or significant intellectual delay | 66 | Male 33 (50); 17 (51.5) in intervention group | 15.3 (1.65) in intervention group, 15.06 (1.71) in control group, between 13 and 18 | Development of general and disease self-management skills. To motivate the youths' engagement. Self-efficacy in changing his/her behavior. | A nurse | The individual; face-to-face sessions | Web-based videos and brochures. A MyHealth Passport. A calendar -tool. | 20 min long with regular appointment with the pediatric endocrinologist. A 10 min follow-up call every month for the study period by nurse. | The control group: not described | Primary outcome: changes in TRAQ sores (TRAQ 4.1) Secondary outcome: change in HbA1c values | 3 times (baseline, 3, and 6 months) | 0 | Overall score: 2.81 (0.86) in intervention group vs. 2.05 (0.57) in control group | Overall score: 3.53 (0.56) in intervention group vs. 2.11 (0.57) in control group, at 3 months; 4.25 (0.383) in intervention group vs. 2.31 (0.50) in control group, at 6 months |

SD, standard deviation; IBD, inflammatory bowel disease; CF, cystic fibrosis; T1D, type 1 diabetes; CHD, congenital heart disease; HbA1c, Hemoglobin A1c. *Testing repeated-measures models testing the treatment × time interaction, including baseline ($p = 0.02$). †Post-intervention TRAQ self-management scores and TRAQ self-advocacy scores were not listed, only illustrations testing mixed models ($p = 0.03$, and $p = 0.67$). ‡Testing with $t$-tests at 3 and 6 months ($p \leq 0.001$, and $p \leq 0.001$).





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(29, 30). The sessions were conducted as 20-min face-to-face sessions and 10-min follow-up calls every month.

Contents of interventions were provided by digital resources in two studies. The length of the interventions ranged from 6 to 18 months in all studies.

## Control

Usual care was provided in the control groups in two studies; however, the remaining study did not describe the process followed.

## Outcome

The number of outcome types was five, five, and two in each study, respectively. All the outcomes were employed as a means to assess the TRAQ. The outcomes included disease status in all the studies. The outcomes of the two studies included health literacy or disease knowledge, which are not included in the TRAQ. All the interventions were efficacious at 6, 8, and 18 months, except for the self-advocacy score as evaluated by the TRAQ scores.

The mean TRAQ score at baseline was around 2.9 points, ranging from 2.05 to 3.7 in all three studies (22–24). Each chronic disease was shown in the same study (24), with a mean TRAQ score (SD) of 3.7 (0.8) points for patients with type-1 diabetes, 3.5 (0.7) points for patients with inflammatory bowel disease, and 2.9 (0.9) points for patients with cystic fibrosis.

The intervention in the overall TRAQ score showed a 0.6-point increase in the mean of the intervention group compared with a 0.2-point increase for the control group during 8 months for patients with inflammatory bowel disease, cystic fibrosis, and type-1 diabetes (24).

The intervention in the TRAQ self-management score did not have a numerical description but showed a significant increase in the graphic figure during 18 months among patients with congenital heart disease (23). The usual care in the TRAQ self-management score for patients with congenital heart disease did not have a numerical description but showed a significant increase in the graphic figure during 12 months; however, it did not show a significant increase in the graphic figure at 18 months (23). Neither the intervention nor usual care in the TRAQ self-advocacy score for patients with congenital heart diseases have a numerical description and did not show a significant increase in the graphic figure during 18 months (23).

The intervention in the overall TRAQ score showed an increase of 1.44 points in the mean of the intervention group compared with 0.26 points in that of the control group during 6 months among patients with type-1 diabetes (22).

# Discussion

The TRAQ is one of the best assessment tools (5), as it has cross-cultural validity and has thus been translated into many languages (25, 31–35). In our search results, three randomized control trial articles were assessed with the TRAQ. The developer of TRAQ recommends using the mean when it comes to a representative value. However, the authors of the study (24) instructed that acquiring four points or more as a TRAQ summary score can be regarded as starting to acquire the necessary disease management skills.

The target diseases were, of course, chronic illnesses, as the age for starting transition is related to the specific disease. In fact, the mean age in patients with type-1 diabetes was approximately 15 years, and that for patients with congenital heart disease was around 17 years. These differences mean that patients with a younger-onset disease tend to have a later starting transition than patients with an older-onset disease, as patients with a younger-onset disease are not adequately prepared for the transfer to adult care.

Before the discussion of interventions and assessment, we summarize the interventions and assessment, particularly related to the TRAQ for the three studies: In the first study, there was a 2-month intensive web-based and text-delivered disease management and skill-based intervention followed by a 6-month review period, with disease management and self-efficacy assessed with TRAQ (24). In the second, there were nurse-led face-to-face sessions in the intervention, with periods between the end of pediatrics and the beginning of adult medicine as the primary outcome, and change in the congenital heart disease knowledge in the TRAQ as the secondary outcome (22). In the third, 20-min face-to-face sessions were conducted as intervention, with changes in the TRAQ score as the primary outcome, and changes in hemoglobin A1c as the secondary outcome (23).

The intervention tools were applied with digital online devices for intervention staff to communicate with patients in two studies. A nurse was employed for intervention because nurses can work in both pediatrics and adult medicine. They additionally provide medical care for patients with chronic diseases. Nurses can improve the TRAQ scores of patients with nurses' independent support. On the other hand, medical social workers participate in connecting patients with social resources or the local society for transition readiness (2, 36, 37). We could not find a study in which a medical social worker led the intervention, and we hope such a randomized control trial study will be conducted with TRAQ in the future.

Patients with younger-onset disease tended to have lower mean TRAQ scores in the order of highest scores to lowest scores (24). These results indicated that patients with younger-onset diseases tend to have lower scores than patients with older-onset diseases. Sato et al. reported the TRAQ score (SD)

for each chronic disease — 4.2 (0.6) points for patients with kidney disease, 3.3 (1.0) points for patients with congenital heart disease (25), and 4.2 (0.5) points for patients with other diseases (mainly rheumatoid disease) — assessed with the Japanese TRAQ. Thus, we should intensively intervene in patients with younger-onset diseases.

The intervention group showed a 0.6-point increase in the mean of the overall TRAQ score compared with the 0.2-point increase for the control group during 8 months among patients with inflammatory bowel disease, cystic fibrosis, and type-1 diabetes (24). The intervention group showed an increase of 1.44 points in the mean intervention group compared with 0.26 points in that of the control group during 8 months among patients with type-1 diabetes (22). After all, the longer the intervention was continued, the more efficacy was shown. In 2015, a Cochrane review reported that intervention made improvements in transition readiness, but it had low evidence (38). However, we collected novel evidence on transition readiness (22, 23).

Parental knowledge and parent-child discussions about transition are associated with higher TRAQ scores (9). Transition readiness requires intelligence. The three studies indicated some role of intelligence in the exclusion criteria. However, the TRAQ is one of the outcomes that assess transition readiness. However, the TRAQ has some limitations in terms of transition readiness. For instance, the TRAQ scores are not associated with appropriate consultation with medical experts for adults (3). Deliberateness would be required to increase appropriate consultations. Besides, while transitional intervention improves knowledge and transition readiness, it is unclear whether it improves the quality of life (39). We recommend the use of general quality of life scales as well as disease-specific scales for condition assessment (40–42). Disease-specified TRAQ can assess a disease-specific issue (43–45). The status or events of the disease can also be used to assess disease-specific issues from the current studies (22, 23). We require multiple assessments in practice (9, 46). Disease-specific evaluation tools are also recommended based on these results (24).

We try to provide patients with an opportunity to communicate with their guardians and health providers for their transition readiness through TRAQ. Such communication gives them an idea of how to deal with their disease.

In conclusion, both face-to-face and web-based interventions were shown to have the potential to improve transition readiness, as assessed by TRAQ. Nurses were considered to be key players in face-to-face interventions. All three studies intervened with the subjects repeatedly, suggesting that continuous support is efficacious.

## Author contributions

YS, YI, RO, and TN contributed to the conception of the study. JT substantially contributed to designing, searching databases, and drafting the article. JT, YY, AM, and YI contributed to the review of reports. JT, YY, YS, AM, YI, RO, and TN contributed to the critical revision of the article. All authors read and approved the final manuscript.

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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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# Significance of active screening for detection of health problems in childhood cancer survivors

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**Background:** Childhood cancer survivors (CCSs) have a lifelong increased risk of chronic health problems, most of which are associated with the curative therapies. Recent studies have suggested that prospective active screening using comprehensive assessments for CCSs is superior in identifying undiagnosed chronic health problems.

**Methods:** To assess the significance of active screening using comprehensive medical examinations for detecting chronic health problems in multiple organ systems in CCSs, we retrospectively compared the frequency and severity of health problems between two different cohorts of CCSs in a single institution: 110 CCSs who visited the outpatient clinic for regular follow-ups between December 2010 and December 2015 (regular follow-up group) vs. 58 CCSs who underwent comprehensive medical examinations between February 2016 and September 2019 (active screening group). CCSs were defined as patients aged ≥ 18 years who had been diagnosed as having childhood cancer ≥ 10 years before and had survived without cancer for ≥ 5 years.

**Results:** Patient characteristics were similar between the two groups except for primary diagnosis (more brain tumors and embryonal tumors in the active screening group) and treatment history (more alkylating agents used and surgical interventions performed in the active screening group). The prevalence and the median number of health problems were significantly higher in the active screening group than in the regular follow-up group: 93% vs. 67% and 1.0 [0.0–8.0] vs. 2.0 [0.0–7.0] respectively. In term of organ-specific health problems, pulmonary dysfunction, neurocognitive impairment, ocular abnormalities, and dental abnormalities were identified more in the active screening group, partly because these problems had not been assessed in the regular follow-up group. Nevertheless, the prevalence of grade 3–5 health problems was similar between the two groups, except for pulmonary dysfunction.

**Conclusion:** Active screening using comprehensive medical examinations was effective for identifying health problems in CCSs. Although the prevalence of severe problems identified by both approaches was similar, comprehensive medical examinations could detect overlooked problems such as severe pulmonary dysfunction, dental maldevelopment, and borderline intellectual functioning, which might have an impact on quality of life in CCSs.

KEYWORDS

childhood cancer survivor, health problem, late effects, long-term care, screening

# Introduction

Progress in the development of therapies for children with cancer has resulted in a >80% survival rate in developed countries, and children who overcome childhood cancer grow up as childhood cancer survivors (CCSs) (1). CCSs have a lifelong increased risk of chronic health problems, most of which are associated with the curative therapies. Chronic health problems in CCSs include cardiac dysfunction, pulmonary dysfunction, renal impairment, endocrine and reproductive disorders, growth impairment, neurocognitive impairment, and subsequent malignant neoplasms (2, 3). These health problems have previously been evaluated using self-report questionnaires or registry data. Recent studies have shown that prospective active screening using comprehensive systematic assessments for all CCSs was superior in identifying a substantial number of undiagnosed chronic health problems (4, 5). In fact, a large study of active screenings for adult CCSs revealed that the estimated cumulative prevalence of chronic health problems and serious/disabling or life-threatening problems at 45 years of age was 95.5 and 80.5%, respectively (6).

At St. Luke's International Hospital, active screening for late-onset health problems among CCSs was started in February 2016. CCSs aged ≥ 18 years or older who were diagnosed as having childhood cancer at least 10 years before and remained in remission for ≥ 5 years underwent comprehensive medical examinations. Before the active screenings were initiated, patients treated for childhood cancer were evaluated for health problems during regular clinic visits at the discretion of the physician in accordance with the Children's Oncology Group Long-term Follow-Up Guidelines (7) considering cancer type and treatment history.

In the present study, we compared the frequencies and severities of late-onset health problems between different approaches, namely, comprehensive medical examinations and regular clinic-based evaluations. The aim of this study was to assess the utility of active screening using comprehensive medical examinations in detecting chronic health problems of multiple organ systems in CCSs, which might be overlooked at regular clinic visits.

# Materials and methods

## Study design and participants

All data were obtained through the studies approved by the institutional review board of St. Luke's International Hospital. In the present study, CCSs were defined as patients aged ≥ 18 years who were diagnosed with childhood cancer ≥ 10 years before and survived without cancer for ≥ 5 years. Data of 58 CCSs who underwent comprehensive medical examinations between February 2016 and September 2019 were prospectively collected (active screening group). We also reviewed the medical records of 147 CCSs who visited the outpatient clinic for regular follow-ups between December 2010 and December 2015, and their medical records were retrospectively analyzed. Of those 147 CCSs, 37 CCSs were excluded because they also underwent a comprehensive medical examination after February 2016, and were thus included in the active screening group in this analysis. Finally, 110 CCSs were assigned to the regular follow-up group. Written informed consent was obtained from all participants in the active screening group and opt-out consent involving provision of an information leaflet was obtained when the medical records of patients in the regular follow-up group were reviewed.

## Data collection

In the active screening group, participants underwent a comprehensive evaluation as follows: medical history, physical examination, resting blood pressure, complete blood cell count, comprehensive metabolic panel, fasting lipid profile, blood sugar, hemoglobin $A_1C$ level, endocrine–reproductive function (thyroid, gonadal, hypothalamic–pituitary axis function), urinalysis, fecal occult blood test, echocardiography, pulmonary function testing, audiological testing, ophthalmologic evaluation, dental evaluation, neurocognitive testing, bone mineral density testing, gynecological examination (female only), thyroid ultrasonography, abdominal ultrasonography,

and brain MRI. These examinations were selected according to the comprehensive medical checkup system administered in healthy adults in Japan (8) and the St. Jude Lifetime Cohort (SJLIFE) study (6). In the regular follow-up group, medical records and the most recent examination results were reviewed, and information about health problems was extracted. Medical assessments for CCSs in the regular follow-up group were performed at the discretion of the pediatric oncologist in accordance with the guidelines (7) considering cancer type and treatment history. The cost of examinations for CCSs in the active screening group and the regular follow-up group was covered by the research grant and public health insurance, respectively. In both groups, cancer-related information, including type of cancer, cumulative doses of chemotherapy, information on hematopoietic cell transplantation, surgical interventions, and the dose and anatomical location of radiological therapy, was extracted from the medical chart for each patient.

## Definition of health problems and grading

The criteria for positive screening and the grading are shown in **Table 1**. Chronic health problems were classified according to the modified National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, which was also utilized in the SJLIFE study (9). We made additional minor modifications to the SJLIFE-modified CTCAE as follows: obesity was defined as BMI $\geq$ 25 based on Asian criteria; $HbA_1c$ and cholesterol level was used in the evaluation of diabetes mellitus and hyperlipidemia, respectively, because the results of fasting tests were not always available in the regular follow-up group; hypothalamic–pituitary axis dysfunction was diagnosed using growth hormone provocation tests or ACTH (adrenocorticotropic hormone) stimulation tests in children in the regular follow-up group who were positive in screening for insulin-like growth factor-1 or morning cortisol level, respectively; hepatitis B or C virus infections were classified as grade 3 if they were serologically positive.

## Statistical analysis

Health problems were compared between the active screening group and the regular follow-up group. The significance of the presence and the number of health problems per CCS was tested by Fisher's exact test, a non-parametric test, and one-way analysis of variance. Non-parametric variables were tested using the Mann–Whitney test and Kruskal–Wallis test. Data were analyzed using EZR (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) (10); more precisely, it is a modified version of R commander, which is designed to perform statistical functions frequently used in biostatistics.

# Results

## Participant characteristics

The demographic, treatment, and diagnostic characteristics of the 110 CCSs in the regular follow-up group and the 58 CCSs in the active screening group are shown in **Table 2**. The proportion of males (43.6% vs. 46.6%), median age at diagnosis (6 years vs. 6 years), median age at the last follow-up (27.5 years vs. 25.5 years), and median duration of follow-up from diagnosis (19.0 years vs. 18.0 years) were not statistically different between the regular follow-up group and the active screening group. Hematological malignancies were more prevalent in the regular follow-up group than in the active screening group (81.8% vs. 70.7%), whereas the proportion of CNS tumors and embryonal tumors was higher in the active screening group. All CCSs received chemotherapy, but the proportion of CCSs receiving alkylating agents was higher in the active screening group. Nearly half of the CCSs in both groups received radiotherapy, and the main target organ was the brain. The proportion of CCSs who underwent surgical intervention was higher in the active screening group.

## Prevalence of health problems in childhood cancer survivors

The prevalence of any health problems was significantly higher in the active screening group than in the regular follow-up group (93.1% vs. 67.3%; **Table 3**). In addition, the median number of any health problems was also higher in the active screening group than in the regular follow-up group (1.0 [0.0–8.0] vs. 2.0 [0.0–7.0]), and a third of CCSs in the active screening group had 4 or more health problems. In contrast, the prevalence and median number of severe health problems ($\geq$ grade 3) were not significantly different between the two groups. Similar results were obtained from intrapatient comparisons in 37 CCSs who underwent regular follow-up and then active screening (data is not shown).

The median number of health problems was high in CCSs with CNS tumors (4.5 [1.0–8.0]; **Table 4**). Radiotherapy (2.5 vs. 1.0), hematopoietic cell transplantation (3.0 vs. 1.0), and platinum agents (3.0 vs. 1.0) were also associated with a higher number of health problems. The prevalence of severe health problems ($\geq$grade 3) was also high in these CCSs: 62.5% in CCSs with CNS tumors, 41.2% in CCSs receiving radiotherapy, 51.9% in transplanted CCSs, and 50% in CCSs receiving platinum agents. The age at diagnosis, age at the last follow-up, and

TABLE 1 Definition of health problems, screening tests, criteria for positive screening, and grading rubric.

| Health problem | Screening test | Criteria for positive screening | Grading rubric (modified CTCAE v4.0) |
|---|---|---|---|
| **Cardiovascular** | | | |
| Cardiomyopathy or Heart valve disorders | Echocardiogram | EF < 50%<br>Detection of presence of valvular sclerosis, stenosis, or calcifications or mild or greater regurgitation | EF<br>1: Not applicable<br>2: Resting EF < 50%–40%<br>3: Resting EF 39%–20%<br>4: Resting EF < 20%; refractory or poorly controlled heart failure due to drop in EF; on medical management; intervention<br>5: Death<br>Heart valve disorder<br>1: Asymptomatic valvular thickening/calcifications with or without mild valvular regurgitation or stenosis by imaging<br>2: Asymptomatic; moderate regurgitation or stenosis by imaging<br>3: Symptomatic; severe regurgitation or stenosis by imaging; symptoms controlled with medical intervention<br>4: Life-threatening consequences; urgent intervention indicated<br>5: Death |
| **Cardiovascular risk factors** | | | |
| Hypertension | Blood pressure | BP ≥ 130/80 mmHg | 1: Systolic BP 130–139 mm Hg or diastolic BP 80–89 mm Hg<br>2: Systolic BP 140–159 mm Hg or diastolic BP 90–99 mm Hg<br>3: Systolic BP ≥ 160 mm Hg or diastolic BP ≥ 100 mm Hg<br>4: Life-threatening consequences; urgent intervention indicated<br>5: Death |
| Dyslipidemia | Lipid panel | Total cholesterol ≥ 200 mg/dl, or<br>LDL-C ≥ 140 mg/dl, or<br>HDL-C < 40 mg/dl | 1: Total cholesterol 200–300 mg/dl<br>2: Total cholesterol 300–400 mg/dl<br>3: Total cholesterol 400–500 mg/dl<br>4: Total cholesterol > 500 mg/dl<br>5: Not applicable |
| **BMI abnormalities** | | | |
| Obesity | BMI | BMI ≥ 25 | 1: Not applicable<br>2: BMI 25–29.9 kg/m$^2$<br>3: BMI 30–39.9 kg/m$^2$<br>4: BMI ≥ 40 kg/m$^2$<br>5: Not applicable |
| Underweight | BMI | BMI < 18.5 | 1: Not applicable<br>2: BMI < 18.5 kg/m$^2$<br>3: Not applicable<br>4: Not applicable<br>5: Not applicable |
| **Pulmonary** | | | |
| Abnormal pulmonary function | Pulmonary function tests | %VC < 80% or<br>FEV1 < 80% predicted | %VC<br>1:%VC: 79–70%<br>2:%VC: 69–60% predicted<br>3:%VC: < 60% predicted<br>4: Not applicable<br>5: Not applicable<br>FEV1<br>1: FEV1 (percentages of observed FEV1 related to its predicted value): 79–70% predicted<br>2: FEV1: 69–50% predicted<br>3: FEV1: 49–35% predicted<br>4: FEV1: < 35% predicted<br>5: Not applicable |
| **Metabolic** | | | |
| Liver dysfunction | ALT, AST | ALT ≥ 40 U/I<br>AST ≥ 40 U/I | 1: AST or ALT > ULN – 3.0 × ULN<br>2: AST or ALT > 3.0–5.0 × ULN<br>3: AST or ALT > 5.0–20.0 × ULN<br>4: AST or ALT > 20.0 × ULN<br>5: Not applicable |

*(Continued)*

TABLE 1 (Continued)

| Health problem | Screening test | Criteria for positive screening | Grading rubric (modified CTCAE v4.0) |
|---|---|---|---|
| Kidney dysfunction | Creatinine, BUN, Urine analysis | eGFR < 60 ml/min/1.73 $m^2$<br>± Abnormal urinalysis | 1: eGFR < LLN – 60 ml/min/1.73 $m^2$<br>2: eGFR 59–30 ml/min/1.73 $m^2$<br>3: eGFR 29–15 ml/min/1.73 $m^2$<br>4: eGFR < 15 ml/min/1.73 $m^2$<br>5: Death |
| **Endocrine or reproductive** | | | |
| HPA dysfunctions | | | |
| GH deficiency | GH provocation testing used to establish diagnosis in regular follow-up<br>Active screening: IGF-1 | GH dynamic testing: GH peak < criteria value<br>Active screening: IGF-1 < -2SD | 1: Not applicable<br>2: Asymptomatic; clinical or diagnostic observations only; intervention not indicated<br>3: Hormone replacement indicated or initiated<br>4: Severe symptoms; limiting self-care ADL; hospitalization indicated<br>5: Not applicable |
| ACTH deficiency | Low dose ACTH stimulation test used to establish diagnosis in regular follow-up<br>Active screening: Morning cortisol | Low dose ACTH stimulation test: Cortisol < criteria value<br>Active screening: Morning cortisol < 5 mcg/dL | |
| Diabetes mellitus | Serum glucose, $HbA_1c$ | $HbA_1C \geq 6.4\%$ | 1: $HbA_1c$ 6.4–6.9%<br>2: $HbA_1c$ 7.0–7.9%<br>3: $HbA_1c > 8.0\%$<br>4: Life threatening consequences, urgent intervention indicated or initiated<br>5: Death |
| Primary hypothyroidism | Serum free $T_4$, TSH | Both: Free $T_4$ below normal range (<1.0 ng/dl) and TSH above normal range (≥4.0 ţIU/ml) | 1: Not applicable<br>2: Asymptomatic; clinical or diagnostic observations only; intervention not indicated<br>3: Hormone replacement indicated or initiated<br>4: Severe symptoms; limiting self- care ADL; hospitalization indicated<br>5: Not applicable |
| Gonadal dysfunction | | | |
| Female | FSH, LH, estradiol | Amenorrhea before age 40 or estradiol < 17 pg/ml, FSH ≥ 30 mIU/ml | 1: Not applicable<br>2: Asymptomatic; clinical or diagnostic observations only; intervention not indicated<br>3: Hormone replacement indicated or initiated<br>4: Severe symptoms; limiting self- care ADL; hospitalization indicated<br>5: Not applicable |
| Male | FSH, LH, testosterone | Receiving testosterone, and/or FSH > 10 mIU/ml, LH > 0.7 mIU/ml, Testosterone < 1.3 ng/ml | |
| **Neurocognitive** | | | |
| Neurocognitive impairment | WAIS | FSIQ < 85 | 1: FSIQ 85–90<br>2: FSIQ 70–88<br>3: FSIQ < 70<br>4: Not applicable<br>5: Not applicable |
| **Neurosensory** | | | |
| Ocular abnormalities | Ophthalmology consultation | Cataract, Intraocular pressure ≥ 21 mmHg, clinically significant abnormalities of retinal pigment, integrity, or vasculature, Low vision (corrected to 20/80 or worse) | 1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated<br>2: Symptomatic; moderate decrease in visual acuity (20/40 or better)<br>3: Symptomatic with marked decrease in visual acuity (worse than 20/40 but better than 20/200); operative intervention indicated (e.g., cataract surgery)<br>4: Blindness (20/200 or worse) in the affected eye<br>5: Not applicable |

*(Continued)*

TABLE 1 (Continued)

| Health problem | Screening test | Criteria for positive screening | Grading rubric (modified CTCAE v4.0) |
|---|---|---|---|
| Hearing loss | Pure-tone audiometry | Measurable hearing loss | 1: ≥ 40 dB at any frequency 6–12 kHz (Chang 1a); > 20 and < 40 dB at 4kHz (Chang 1b)<br>2: ≥ 40 dB at 4 kHz and above (Chang 2a); > 20 and < 40 dB at any frequency < 4kHz (Chang 2b)<br>3: ≥ 40 dB at 2 or 3 kHz and above<br>4: ≥ 40 dB at 1 kHz and above<br>5: Not applicable |
| **Skeletal** | | | |
| Osteoporosis | Dual-energy x-ray absorptiometry | BMD t-score ≤ -1.0 | 1: Radiologic evidence of osteoporosis or BMD t-score -1 to -2.5 (osteopenia)<br>2: BMD t-score < -2.5<br>3: Loss of height ≥ 2 cm<br>4: Not applicable<br>5: Not applicable |
| Dental abnormalities | Dental consultation | Missing teeth and/or microdontia and/or root change | 1: Asymptomatic; hypoplasia of tooth or enamel<br>2: Impairment correctable with oral surgery<br>3: Maldevelopment with impairment not surgically correctable; disabling<br>4: Not applicable<br>5: Not applicable |
| **Infection** | | | |
| Hepatitis virus infection | Hepatitis B surface antigen and core antibody<br>Hepatitis C antibody | Serologically positive | 1: Not applicable<br>2: Not applicable<br>3: Present<br>4: Life-threatening<br>5: Death |
| **Cancer screening** | | | |
| Malignant neoplasms | | Any malignant neoplasms | 1: Not applicable<br>2: Not applicable<br>3: Present<br>4: Life-threatening<br>5: Death |

ACTH, adrenocorticotropic hormone; ADL, activities of daily living; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BP, blood pressure; BMD, bone mineral density; BMI, body mass index; BUN, blood urine nitrogen; CTCAE, Common Terminology Criteria for Adverse Events; eGFR, estimated glomerular filtration rate; FEV1, forced expiratory volume in the first second, FSH, follicle-stimulating hormone; FSIQ, Full scale intelligence quotient; GH, growth hormone; $HbA_1c$, hemoglobin $A_1c$; HDL-C, high-density lipoprotein cholesterol; HPA, hypothalamic-pituitary axis; IGF-1, insulin growth factor 1; LDL-C, low-density lipoprotein cholesterol; LH, luteinizing hormone; LLN, lower limit of normal; SD, standard deviation; TSH, thyroid-stimulating hormone; T4, thyroxine; VC; vital capacity; WAIS; ULN, upper limit of normal; Wechsler adult intelligence scale.

duration of follow-up were not associated with the mean number or severity of health problems.

## Organ-specific health problems in childhood cancer survivors

Table 5 summarizes the prevalence of organ-specific health problems and the proportion of CCSs who did not undergo the screening tests for each health problem. Almost all the health problems were systematically evaluated in the active screening group by comprehensive medical examinations, whereas regular clinic-based evaluations failed to assess several organ-specific health problems, for example echocardiograms (the proportion of "not-tested" CCSs was 79.1%), pulmonary function tests (94.5%), neurocognitive evaluations (88.2%), ophthalmologic examinations (80.9%), audiometry (90.9%), bone mineral density tests (93.6%), and dental examinations (100%). These discrepancies in the frequency of organ-specific evaluations resulted in differences in the prevalence of relevant health problems between the regular follow-up group and the active screening group: pulmonary dysfunction (2.7% vs. 20.7%), neurocognitive impairment (4.5% vs. 22.4%), ocular abnormalities (8.2% vs. 22.4%), and dental abnormalities (unknown vs. 37.9%). However, the prevalence of severe organ-specific health problems (≥grade 3) was the same between the two groups except for pulmonary dysfunction (1.7% vs. 6.9%; $P = 0.049$). In fact, most of the ocular abnormalities reported in the active screening group were trivial (e.g., optic disk cupping, $n = 11$), while cataract was found in 2 CCSs. No CCSs in the regular follow-up group had dental examinations, whereas 54 of 58 CCSs (93.1%) in the active screening group underwent dental examinations and dental problems were reported in 22 CCSs: missing teeth in 14, microdontia in 8, and root change in 8. These dental abnormalities detected in the active screening group were not disabling and could be surgically corrected and were thus classified as grade 1–2. Of 12 patients who showed

TABLE 2 Demographic, treatment, and diagnostic characteristics of CCSs in the regular follow-up group ($n$ = 110) and the active screening group ($n$ = 58).

| Characteristics | | Regular follow-up group ($n$ = 110) | Active screening group ($n$ = 58) | $P$-value |
|---|---|---|---|---|
| Sex | Male (%) | 48 (43.6) | 27 (46.6) | 0.746 |
| Primary diagnosis | | | | 0.025 |
| | ALL | 58 (52.7) | 34 (58.6) | |
| | AML | 13 (11.8) | 3 (5.2) | |
| | Other hematological malignancies | 10 (9.0) | 1 (1.7) | |
| | Lymphoma | 9 (8.2) | 3 (5.2) | |
| | CNS tumors | 3 (2.7) | 5 (8.6) | |
| | Sarcoma | 9 (8.2) | 2 (3.4) | |
| | Embryonal tumors | 6 (5.4) | 10 (17.2) | |
| | Retinoblastoma | 2 (1.8) | 0 (0.0) | |
| Median age at diagnosis [years, range] | | 6 [0–19] | 6 [0–16] | 0.755 |
| Median age at the last follow-up [years, range] | | 27.5 [18–49] | 25.5 [18–42] | 0.503 |
| Median duration of follow-up [years, range] | | 19 [6–37] | 18 [9–39] | 0.413 |
| Treatment exposure | | | | |
| | Chemotherapy | 110 (100) | 58 (100) | |
| | Anthracyclines | 71 (77.2) | 44 (78.6) | 1 |
| | Alkylating agents | 62 (67.4) | 50 (89.3) | 0.003 |
| | Platinum | 12 (13.0) | 12 (21.4) | 0.25 |
| | Radiation | 53 (48.2) | 27 (46.6) | 0.872 |
| | Stem cell transplantation | 18 (16.4) | 9 (15.8) | 1 |
| | Surgery | 19 (17.3) | 20 (34.5) | 0.02 |

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia, CCSs, childhood cancer survivors; CNS, central nervous system.

TABLE 3 Health problems in CCSs in regular follow-ups and active screening.

| Health problems | Regular follow-up group ($n$ = 110) | Active screening group ($n$ = 58) | $P$-value |
|---|---|---|---|
| | No. of CCSs (%) | No. of CCSs (%) | |
| Presence of health problems | | | |
| No | 36 (32.7) | 4 (6.9) | <0.001 |
| Yes | 74 (67.3) | 54 (93.1) | |
| Median [range] of problems per CCS | 1.0 [0.0–8.0] | 2.0 [0.0–7.0] | <0.001 |
| No. of problems per CCS | | | |
| 0 | 36 (32.7) | 4 (6.9) | |
| 1 | 25 (22.7) | 16 (27.6) | |
| 2 | 17 (15.5) | 10 (17.2) | |
| 3 | 15 (13.6) | 9 (15.5) | |
| 4 | 9 (8.2) | 10 (17.2) | |
| ≥ 5 | 8 (7.3) | 9 (15.5) | |
| Presence of ≥ grade 3 health problems | | | |
| No | 82 (74.5) | 37 (63.8) | 0.157 |
| Yes | 28 (25.5) | 21 (36.2) | |
| No. of ≥ grade 3 health problems per CCS | | | |
| 0 | 82 (74.5) | 37 (63.8) | 0.181 |
| 1 | 19 (17.3) | 16 (27.6) | |
| 2 | 10 (9.1) | 5 (8.6) | |
| ≥ 3 | 0 (0.0) | 1 (1.7) | |

CCS(s), childhood cancer survivor(s).

TABLE 4 Prevalence of health problems in CCSs in regular follow-ups and active screening.

| Health problems | Regular follow-up group ($n$ = 110) | | | Active screening group ($n$ = 58) | | | Regular vs. active all grades |
|---|---|---|---|---|---|---|---|
| | Any grades $n$ (%) | Grade 3–4 $n$ (%) | Not tested $n$ (%) | Any grade $n$ (%) | Grade 3–4 $n$ (%) | Not tested $n$ (%) | $P$-value |
| Cardiomyopathy orheart valve disorders | 4 (3.6) | 0 (0.0) | 87 (79.1) | 1 (1.7) | 0 (0.0) | 1 (1.7) | 0.66 |
| Hypertension | 27 (24.5) | 3 (2.7) | 27 (24.5) | 7 (12.1) | 0 (0.0) | 0 (0.0) | 0.069 |
| Dyslipidemia | 40 (36.4) | 0 (0.0) | 6 (5.5) | 25 (43.1) | 0 (0.0) | 0 (0.0) | 0.409 |
| BMI abnormalities | | | | | | | |
| Obesity | 20 (18.2) | 1 (0.9) | 4 (3.6) | 11 (19.0) | 0 (0.0) | 0 (0.0) | 1 |
| Underweight | 15 (13.6) | 0 (0.0) | | 13 (22.4) | 0 (0.0) | | 0.281 |
| Abnormal pulmonary function | 3 (2.7) | 1 (1.7) | 104 (94.5) | 12 (20.7) | 4 (6.9) | 0 (0.0) | <0.001 |
| Liver dysfunction | 9 (8.2) | 0 (0.0) | 0 (0.0) | 6 (10.3) | 0 (0.0) | 0 (0.0) | 0.777 |
| Kidney dysfunction | 6 (5.5) | 3 (2.8) | 1 (0.9) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0.094 |
| HPA disorders | 15 (13.6) | 15 (13.6) | NA | 10 (17.2) | 5 (8.6) | 1 (1.7) | 0.649 |
| Diabetes mellitus | 3 (2.7) | 0 (0.0) | 17 (15.5) | 1 (1.7) | 1 (1.7) | 0 (0.0) | 1 |
| Primary hypothyroidism | 6 (6.5) | 5 (4.5) | 17 (15.5) | 3 (5.2) | 2 (3.4) | 0 (0.0) | 1 |
| Gonadal dysfunction | 20 (18.2) | 10 (9.1) | 20 (18.2) | 7 (12.1) | 5 (8.6) | 0 (0.0) | 0.38 |
| Neurocognitive impairment | 5 (4.5) | 4 (3.6) | 97 (88.2) | 13 (22.4) | 3 (5.2) | 1 (1.7) | 0.001 |
| Ocular abnormalities | 9 (8.2) | 0 (0.0) | 89 (80.9) | 13 (22.4) | 0 (0.0) | 1 (1.7) | 0.015 |
| Hearing loss | 3 (2.7) | 0 (0.0) | 100 (90.9) | 6 (10.3) | 0 (0.0) | 0 (0.0) | 0.065 |
| Osteoporosis | 3 (2.7) | 0 (0.0) | 103 (93.6) | 3 (5.2) | 0 (0.0) | 0 (0.0) | 0.417 |
| Dental abnormalities | 0 (0.0) | 0 (0.0) | 110 (100) | 22 (37.9) | 0 (0.0) | 4 (6.8) | <0.001 |
| Hepatitis B, Hepatitis C virus infection | 7 (6.4) | 7 (6.4) | 22 (20.0) | 5 (8.6) | 5 (8.6) | 0 (0.0) | 0.754 |
| Malignant neoplasms | 5 (4.5) | 5 (4.5) | NA | 5 (8.6) | 5 (8.6) | NA | 0.316 |

BMI, body mass index; CCSs, childhood cancer survivors; HPA, hypothalamic-pituitary axis.

abnormal pulmonary function in active screening group, 11 had restrictive impairment and 4 were classified as grade 3–4.

## Discussion

This report delineates the prevalence and severity of health problems across multiple organ systems in adult CCSs, as assessed by comprehensive medical examinations and regular clinic-based evaluations performed at a single center in Japan. Similar to previous reports, the incidence and severity of chronic health problems were associated with specific clinical factors such as CNS tumors, radiotherapy, hematopoietic cell transplantation, and platinum agents.

Active screening successfully identified more health problems compared with regular clinic-based evaluations (93.1% vs. 67.3%). This result might be attributable to efficient screening using comprehensive examinations to evaluate systemic health problems. In fact, several examinations were rarely performed in CCSs at regular follow-ups: echocardiograms, pulmonary function tests, neurocognitive evaluations, ophthalmologic examinations, audiometry, bone mineral density tests, and dental examination. Active screening revealed that pulmonary dysfunction, neurocognitive impairment, ocular abnormalities, and dental abnormalities were more prevalent than previously thought. In the SJLIFE study, prospective and risk-based systematic screening of health problems among CCSs revealed that the prevalence of newly diagnosed neurocognitive and neurosensory deficits, heart valve disorders, and pulmonary dysfunction was particularly increased, which was almost similar to our study. The examinations administered in the active screening group were selected according to the comprehensive medical checkup system administered in healthy adults in Japan (8) and the SJLIFE study (6). Comprehensive medical checkups allow for early detection of diseases in healthy adults and are widely used in Japan. Considering that this medical program is not covered by public health insurance, the cost-effectiveness of comprehensive medical examinations for CCSs needs to be further evaluated.

Most of the problems overlooked in the regular follow-up group were classified as grade 1–2; however, this may not mean that active screening resulted in overdiagnosis of clinically insignificant health problems in CCSs. For example, grade 1–2 dental anomalies were found in 40% of CCSs in the active

TABLE 5 Health problems by clinical factors.

| Clinical factors | | | CCSs with any health problems (%) | CCSs with ≥ grade 3 health problems (%) | Sum of health problems | |
|---|---|---|---|---|---|---|
| | | | | | Median [range] | *P*-value |
| Primary disease | | | | | | |
| ALL | | *n* = 92 | 72 (78.3) | 21 (22.8) | 2.0 [0.0–5.0] | 0.002 |
| AML | | *n* = 16 | 11 (68.8) | 6 (37.5) | 2.0 [0.0–5.0] | |
| Other hematological malignancies | | *n* = 11 | 9 (81.8) | 3 (27.3) | 1.0 [0.0–3.0] | |
| Lymphoma | | *n* = 12 | 9 (75.0) | 5 (41.7) | 1.0 [0.0–6.0] | |
| CNS tumors | | *n* = 8 | 8 (100.0) | 5 (62.5) | 4.5 [1.0–8.0] | |
| Sarcoma | | *n* = 11 | 4 (36.4) | 1 (9.1) | 0.0 [0.0–2.0] | |
| Embryonal tumors | | *n* = 16 | 13 (81.2) | 6 (37.5) | 2.5 [0.0–7.0] | |
| Retinoblastoma | | *n* = 20 | 2 (100.0) | 2 (100.0) | 3.5 [3.0–4.0] | |
| Age at diagnosis (years) | | | | | | |
| 0–5 | | *n* = 75 | 56 (74.7) | 28 (37.3) | 2.0 [0.0–6.0] | 0.951 |
| 5–10 | | *n* = 37 | 28 (75.7) | 8 (21.6) | 2.0 [0.0–7.0] | |
| ≥ 10 | | *n* = 55 | 43 (78.2) | 13 (23.6) | 2.0 [0.0–8.0] | |
| Age at the last follow-up (years) | | | | | | |
| 18–20 | | *n* = 20 | 15 (75.0) | 4 (20.0) | 1.0 [0.0–6.0] | 0.403 |
| 20–30 | | *n* = 89 | 65 (73.0) | 24 (27.0) | 2.0 [0.0–6.0] | |
| ≥30 | | *n* = 59 | 48 (81.4) | 21 (35.6) | 2.0 [0.0–8.0] | |
| Duration of follow-up (years) | | | | | | |
| <20 | | *n* = 88 | 64 (72.7) | 18 (20.5) | 1.5 [0.0–8.0] | 0.489 |
| 20–30 | | n = 60 | 47 (78.3) | 24 (40.0) | 2.0 [0.0–7.0] | |
| ≥30 | | n = 19 | 16 (84.2) | 7 (36.8) | 2.0 [0.0–6.0] | |
| Treatment exposure | | | | | | |
| Chemotherapy | | | | | | |
| Anthracyclines | Yes | *n* = 115 | 88 (76.5) | 31 (27.0) | 2.0 [0.0–7.0] | 0.537 |
| | No | *n* = 33 | 24 (72.7) | 11 (33.3) | 1.0 [0.0–8.0] | |
| Alkylating agents | Yes | *n* = 112 | 89 (79.5) | 30 (26.8) | 2.0 [0.0–8.0] | 0.074 |
| | No | *n* = 36 | 23 (63.9) | 12 (33.3) | 1.0 [0.0–6.0] | |
| Platinum | Yes | *n* = 24 | 20 (83.3) | 12 (50.0) | 3.0 [0.0–8.0] | 0.007 |
| | No | *n* = 124 | 92 (74.2) | 30 (24.2) | 1.0 [0.0–5.0] | |
| Radiation | Yes | *n* = 80 | 69 (86.2) | 33 (41.2) | 2.5 [0.0–8.0] | < 0.001 |
| | No | *n* = 88 | 59 (67.0) | 16 (18.2) | 1.0 [0.0–6.0] | |
| Stem cell transplantation | Yes | *n* = 27 | 24 (88.9) | 14 (51.9) | 3.0 [0.0–7.0] | 0.017 |
| | No | *n* = 140 | 103 (73.6) | 34 (24.3) | 1.0 [0.0–8.0] | |
| Surgery | Yes | *n* = 39 | 31 (79.5) | 16 (41.0) | 2.0 [0.0–8.0] | 0.209 |
| | No | *n* = 129 | 97 (75.2) | 33 (25.6) | 2.0 [0.0–6.0] | |

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia, CCSs, childhood cancer survivors; CNS, central nervous system.

screening group. Although these dental problems were not disabling and could be surgically corrected, they had potential impact on functional and aesthetic prognoses. Previous studies showed that the prevalence of root abnormalities ranged from 1.3 to 5.6%, and microdontia from 1 to 2% in a population of healthy children (11). The prevalence of hypodontia varies between 4 and 8% depending on the ethnic background (12). Pulmonary dysfunction and neurocognitive impairment were also more prevalent in the active screening group. Considering that the morbidity rate of pulmonary dysfunction was equivalent to that in the SJLIFE study (6) and that 4 of 12 pulmonary dysfunctions found in the active screening group were classified as ≥ grade 3, active screening successfully identified severe underlying pulmonary dysfunctions. Careful follow-up, education, and appropriate intervention such as pneumococcal vaccination should be implemented for CCSs with asymptomatic pulmonary dysfunction to prevent future worsening of pulmonary function. Identification of borderline

intellectual functioning in a substantial number of CCSs in the active screening group is also important because of the potential impacts on quality of life. Further investigation is needed to clarify the significance of early interventions in CCSs with borderline intellectual functioning detected by active screening. The significance of ophthalmological abnormalities found in the present study may be controversial. Eleven of the 13 ophthalmological abnormalities in the active screening group were optic disk cupping, which were asymptomatic and concluded to be a non-specific finding by a more detailed follow-up. Because ocular abnormalities affect quality of life in CCSs, further investigation and analysis are needed to determine the importance of early detection of subtle changes in ophthalmological findings.

Because the prevalence of obesity, hypertension, and several laboratory abnormalities such as dyslipidemia and endocrinopathy did not increase by active screening, routine physical examinations and blood tests were adequate to identify these problems. Despite the low examination rate in the regular follow-up group, the similar prevalence of cardiac dysfunction and osteoporosis between the two groups was surprising. One plausible explanation may be that these problems were appropriately evaluated based on treatment history in the regular follow-up group. Another explanation may be that the follow-up duration of the present study was too short to detect subclinical cardiotoxicity among asymptomatic CCSs with normal ejection fractions. Cardiac dysfunction increases markedly with aging, and as many as 1 in 8 of CCSs treated with anthracyclines and chest radiation therapy will have a life-threatening cardiovascular event within 30 years after treatment (13). Further follow-up using parameters for early detection of subclinical diastolic dysfunction, including strain measurements by speckle tracking, may be required (14).

To our knowledge, this is the first study to prospectively explore systemic health problems in Asian CCSs using comprehensive screening for multiple organs (15). Most previous studies of CCSs in Asian countries have focused on epidemiological research or organ-specific toxicities (15). Health problems in CCSs are affected by a complex of multiple factors. Differences in genetic variations, socioeconomic status, health behaviors, lifestyle, treatment regimens, and clinical practice can be reflected in the prevalence of health problems in CCSs. The relatively low incidence of obesity in our cohort may exemplify the ethnic difference. Differences in genetic variations that influence the incidence of chronic health problems in CCSs between Asian and other populations should be explored in the future.

Several limitations should be considered when interpreting the results of this study. The major limitation is the small sample size. Second, the follow-up period was short, and the participants were relatively young. The health problems of CCSs are known to increase with age (16). Although the number and severity of health problems did not increase with age and from the time since diagnosis of pediatric cancer in this study, continuing active screening is expected to contribute to the prompt identification of health problems in CCSs. In addition, generalizability of our findings may be skeptical because most long-term follow-up clinics cannot afford to do the comprehensive medical testing. We believe that one of the significances of our study is that active screening could identify several overlooked problems, which was not regarded as severe based on CTCAE-based criteria but may affect quality of life in CCSs as described above. We are now planning detailed analyses on these subclinical but important health problems and will propose refined risk-based regular follow-up program including pulmonary function tests, neurocognitive evaluations, and dental examination.

## Conclusion

Our study revealed that active screening using comprehensive medical examinations can identify health problems in CCSs efficiently. Although the prevalence of severe problems was the same between regular clinic-based evaluations based on follow-up guidelines and comprehensive medical examinations, the latter detected several overlooked problems such as pulmonary dysfunction, dental maldevelopment, and borderline intellectual functioning, which might have an impact on quality of life in CCSs. The cost-effectiveness of active screening should be further addressed in future studies.

## Data availability statement

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

## Ethics statement

Written informed consent was obtained from all participants in the Active screening group and opt-out consent involving provision of an information leaflet was obtained when the medical records of patients in the Regular follow-up group were reviewed. This study was approved by the Ethics board of St. Luke's International Hospital.

## Author contributions

YY-S, DH, YH, KK, YI, AM, and MO conceived and designed the study. GS, KN, and MG collected the clinical information and data. YY-S and DH analyzed the data, interpreted the results, and wrote the manuscript. YH, YI, AM,

and MO contributed to the interpretation of the data and revised the manuscript. All the authors reviewed the manuscript and approved the final version of the manuscript.

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# Transition of adult patients with pediatric orthostatic intolerance from child-centered care to adult-centered care

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KEYWORDS

**orthostatic intolerance (OI), cardiovascular deconditioning, psychiatric disorders as a secondary problems, transition, collaboration system between pediatric and adult care**

## Introduction

Orthostatic intolerance (OI) is defined by difficulty tolerating upright posture because of symptoms that abate when returned to a supine position (1). Essential symptoms of OI include lightheadedness, headache, fatigue, weakness, nausea, exercise intolerance, tachycardia, and hypotension (1, 2). OI is caused by autonomic nervous system dysfunction that occurs most often in adolescence. Although symptoms resolve by adulthood in most cases, decreased quality of life has been reported to persist into adulthood for some patients, both in Japan and internationally (1–3). Therefore, the treatment of OI that persists into young adulthood has become an important issue in the field of psychosomatic and behavioral pediatrics (4).

Few studies have examined the transition of adult patients with OI from pediatric to adult medical care. OI has traditionally been considered to be a transient condition that is restricted to children and adolescents. However, recent evidence suggests that OI can present as a major disabling illness in teenagers and young adults, and reduce their quality of life (2). In Japan, OI is generally known as orthostatic dysregulation (OD). Although the Japanese Society of Psychosomatic Pediatrics previously reported that 90% of OD patients improve by age 18 (5), they recently reported that an increasing number of patients exhibit symptoms that persist into adulthood (6). The reason for this phenomenon has not yet been clarified, but may be related to both physical deconditioning caused by changes in the lifestyles of young people, and psychiatric comorbidities such as anxiety, and depression caused by low self-esteem resulting from maladaptation to social activities. To improve the prognosis of adult patients with child-onset OI, it is necessary to develop an approach to transition from child-centered to adult-centered care that focuses primarily on patients' independence.

# Overview of pediatric orthostatic intolerance

## Clinical features

OI is a common disease in teenagers caused by a disorder of the autonomic nervous system that impairs circulatory control during orthostasis, resulting in decreased cerebral blood flow and a range of symptoms: general malaise, headache, dizziness, nausea, and difficulty waking (1). Typical features of OI in childhood and adolescence are divided into three types: orthostatic hypotension, postural tachycardia syndrome, and vasovagal syncope (1, 7). It has been reported that most cases of OI improve between adolescence and adulthood (7), and that symptoms may remain but are typically not problematic for daily living and do not require treatment (8). However, deconditioning and secondary psychiatric disorders have prolonged OI symptoms, increasing the number of adults with OI (1, 9).

## Cardiovascular deconditioning

Cardiovascular deconditioning has been reported to be one of the causes of OI (10). Resulting from myocardial atrophy, cardiovascular deconditioning involves decreased cardiac output, decreased circulating plasma volume, and muscle atrophy in the lower body caused by the microgravity environment, outer space, and reduced physical activity, resulting in circulatory ataxia during standing and reduced orthostatic tolerance (11, 12). Additionally, deconditioning can occur when physical activity in daily life is reduced because of the symptoms caused by OI, and these symptoms may be further aggravated as a result. Deconditioning was reported to occur in healthy children during lockdown in response to coronavirus disease 2019 (13). Thus, prolonged OI caused by deconditioning may be an increasingly important issue because of the lifestyle changes caused by responses to the coronavirus disease 2019 pandemic.

Few pediatricians provide appropriate medical care to patients with prolonged OI, although it is common for physicians to treat patients with deconditioning such as sarcopenia or disuse syndrome (14, 15). It may be possible to improve prolonged OI by improving deconditioning through collaboration with specialists treating disuse syndrome or sarcopenia.

## Psychiatric disorders as a secondary problem

The persistence of OI symptoms over time and the associated limitations on social activities can reduce patients' self-esteem and quality of life. This can result in psychiatric complications such as anxiety disorders and depression (16, 17). In patients with prolonged OI, it is difficult to determine whether physical symptoms are caused by OI, anxiety, or depression. If OI is considered to be an autonomic imbalance associated with growth, it may be reasonable to assume that the physical symptoms in patients approaching adulthood are caused by an anxiety disorder. Patients with psychiatric complications often have difficulty engaging in social activities, including difficulty going out, because of long-term social withdrawal and symptoms such as anxiety. Social withdrawal can lead to a lack of exercise, exacerbating deconditioning, prolonging OI symptoms, and resulting in a vicious cycle.

# Discussion

## Needs and obstacles involved in the health care transition of adult patients with pediatric OI

OI has traditionally been considered as a disease with a high prevalence in childhood and adolescence, with symptoms of OI improving as children grow up. However, a recent study in Japan reported that symptoms of OI have become increasingly prolonged and more likely to persist into adulthood (6) because of complications related to cardiovascular deconditioning and psychiatric disorders as secondary problems. Thus, it is necessary to establish a transition system in OI. However, adult patients with childhood-onset OI may face difficulty adapting to adult medical care because of their immaturity, lack of independence, and lack of social experience. Lack of independence among patients has been reported in cases of transition in other chronic pediatric diseases (18–22), and this is also the case for patients with OI. To improve the prognosis of adult patients with prolonged OI symptoms, an approach toward healthcare transition that focuses primarily on patients' independence may be effective.

The lack of knowledge and experience, and the poor coordination of care between pediatricians and adult care providers can also hinder transitions (21, 23, 24). Adult health care providers are often unfamiliar with the care of complex pediatric patients who are approaching adulthood, and may therefore be uncomfortable managing them (23). Pediatricians should support patients' transition by providing consultation from the adult department during their move and afterwards, as required. Additionally, daily collaboration with acceptable transition sites in the community is considered to be necessary to improve the second concern (6, 25).

## Proposal regarding the process of transition

There is no generally accepted transition system in OI. Therefore, transition models in other chronic diseases should be used as a guide for OI. As a concrete way to start the transition process, the first step is to determine the age of transition. The recommended age for beginning the transition has been proposed to be around the 13th birthday (25), or 14–18 years old (26). In my opinion, the age of 15 years is an appropriate point at which to discuss transition with patients and their parents, because compulsory education in Japan ends at 15 years of age, and parents and their patients are likely to be aware of the termination of pediatric care. In addition, this is an appropriate time to begin preparing patients and their parents for graduation from pediatrics. Around the end of the patient's compulsory education, I always give guidance about the patient graduating from pediatric practice. I suggest that the patient's own choice of treatment is an essential issue regarding independence. The patient's own decision-making, rather than that of their guardians, regarding the proposed treatment plan is important for promoting the patient's independence from their guardians. Patients' experience making their own decisions may improve their self-esteem. This process not only facilitates independence but may also help to prevent secondary psychiatric disorders. In the process of the patient becoming more independent, I recommend using the Transition Readiness Assessment Questionnaire (TRAQ) for assessment of self-management and self-advocacy as a marker for transition readiness (27). I believe that the use of TRAQ enables the health care provider to confirm the progress of transition readiness in adult patients with prolonged OI, as in other types of childhood-onset chronic illness.

The next important step is to choose a model of transition. In OI, a transition system has not yet been established, in Japan and internationally. Several transition programs and guidelines for other chronic diseases are available. I recommend the three types of transition models by Angela et al. (28): "transfer with referral letter," "joint clinic," and the "teenager/transition clinic" mode. The model that best fits regional context should be chosen. Transfer with referral letter is the most convenient method, but transitions may occur without communication between pediatricians and adult physicians. The joint clinic type is based on collaboration between medical institutions. This approach is highly effective for reducing patient anxiety but takes time and financial resources. According to the "teenager/transition clinic" model, Crowley et al. reported that this is one of the most commonly used strategies in successful transition programs (29). I believe that the use of remote interviewing could reduce burdens, and may be helpful in all models. In addition, appropriate transition sites should be considered as adult departments that can treat deconditioning and secondary psychiatric disorders.

## Destination of transition

When deciding on which adult department to transfer the patient to, the most appropriate destination differs depending on whether the main problem is physical symptoms caused by deconditioning or secondary psychiatric disorders. Considering the pathophysiology, the department of cardiology or rehabilitation that created the structured exercise training and rehabilitation plan should be selected as a counterpart for cases with prolonged OI mainly caused by cardiovascular deconditioning. For cases in which secondary psychiatric disorders are the main problem, psychiatrists are the preferred transition destination. In some cases, the patient will need to transition to more than one medical facility. The pediatrician should serve as a link between these multiple medical providers. Although the most appropriate model in OI depends on the local health care system, I believe the "joint clinic" model is most appropriate in OI for the reasons described above.

Finally, I would like to stress the importance of the attitude of the pediatrician. Pediatricians' attitude toward adult patients with OI who have completed the transition should be similar to the attitude of teachers toward students that have graduated. Pediatricians should be available to meet with the patient even if they are no longer directly involved in the consultation, and to congratulate the patient on their progress to adult care. Pediatricians should continue to watch over their patients, similar to the teachers of students who have graduated.

# Author contributions

YY contributed to conception, design of the study, and wrote the first draft of the manuscript.

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# Are we ready for building transition programs for heart transplant recipients in Japan? – Knowing the unique background is the first step for discussion

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## Introduction

Although Japan is a developed country from an economic, educational, and academic viewpoint, certain areas in medicine, such as transplantation and the transition of patients with childhood-onset chronic diseases from pediatric to adult healthcare systems, have fallen far behind the United States (US) or European countries. Especially concerning solid organ transplantation, heart transplantation (HTx) in Japan has a tragic history that hinders active discussion in this field. In this article, we aim to highlight the underlying issues surrounding both HTx and transition medicine in Japan as a preliminary proposal to initiate a constructive discussion to encourage future perspectives.

Blum RW et al. defined transition as the "purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented health care systems" (1). The goal of a transition is to provide uninterrupted, coordinated, developmentally appropriate, psychosocially sound, and comprehensive healthcare for adolescents and young adults (1).

Thanks to advances in surgical techniques and improvements in immunosuppressants, more pediatric solid-organ transplant recipients are surviving to adulthood (2, 3). In general, the period of transition is associated with a risk of non-adherence to medical treatment or lapses in care (4, 5). Such puberty-related non-compliance issues are impactful for transplant recipients, because they directly lead to life-threatening events or graft failure. Transplant recipients tend to be psychosocially immature, and one of the reasons for this is less exposure to their peers during the pre-transplant period (6). Parents' experience with the fear that they may lose their

child to a life-threatening disease may also influence the difficulties in shifting responsibility for care from the parents to the patients themselves. Even so, adolescent and young adult transplant recipients are expected to have the capability to manage their complex medication, independently discuss their condition with their treatment team, and schedule their appointments (7), which can be considered a goal for transition in transplant recipients. In recent years, establishing a successful transition from pediatric- to adult-focused transplant programs has become a topic of special concern, regardless of the type of solid organ (6–11).

The importance of an effective transition program for HTx has been universally recognized recently. The rate of midterm graft loss after HTx is higher in adolescents and young adults than in other age groups (9, 11). More than 50% of institutions in the US employ transition programs, while several pediatric centers continue to follow their patients even after they reach adulthood (11). The barriers to transition for HTx recipients include the requirement of regular inpatient and outpatient follow-up for rejection surveillance with trained transplant physicians possibly leading to unemployment and economic instability, and a sizable number of pediatric HTx recipients have other disabilities associated with congenital heart disease, such as developmental disorders (9). These issues will now be actively reviewed to explore optimal transition programs for HTx recipients worldwide.

Nevertheless, the pediatric-to-adult transition for HTx recipients has gained little attention in Japan to date. The first HTx surgery in Japan was performed in 1968, which was only 9 months after the first human HTx was carried out in South Africa by Bernard in 1967. However, the first case in Japan raised multiple concerns regarding the criminal liability of the surgical team, such as the misdiagnosis of brain death and inappropriate recipient selection (12), causing 30 subsequent years of domestic stagnation in transplant medicine. With the establishment of legal systems, "adult" HTx was re-carried out in 1999 under the Organ Transplant Law, but pediatric patients were still required to go abroad to undergo HTx surgery. The law was amended in 2010, and the first pediatric HTx for recipients younger than 6 years of age was performed in 2012. In recent years, the annual number of HTx surgeries performed in Japan has been about 50–70, including 3 to 17 pediatric cases. In total, 177 Japanese pediatric patients underwent HTx between 1988 and 2020, 124 of which were performed overseas (13). This is highly specific to Japanese pediatric HTx. The primary heart disease requiring HTx is mainly nonischemic cardiomyopathy, regardless of the age group in Japan, and the posttransplant survival rate is excellent, nearly 90% at 10 years (13). The post-HTx follow-up schedule is similar to other countries, requiring weekly visits during the early postoperative period, followed by monthly or bimonthly visits, together with protocol biopsies and surveillance for transplant vasculopathy. The pre- and post-HTx treatment fees are covered by the national health insurance system in Japan, although adult HTx recipients must pay up to 20%–30% of the cost depending on the type of insurance they hold and whether the primary heart disease is a designated intractable disease. For pediatric patients, the Medical Aid for Specific Chronic Pediatric Diseases pays the pre- and post-HTx medical fees until the recipient reaches 20 years old (14). However, as stated above, sizable Japanese pediatric recipients required overseas HTx until recently, of which the cost is out of pocket or fund-raised. Such tremendous costs are indeed a significant burden for parents. This unusual and tragic background of HTx in Japan delayed active discussion on any topic related to transplantation, including transition medicine.

## The road toward a heart transplant transition program in Japan

The Japan Pediatric Society officially announced that patients can be cared for by pediatricians until they reach 20 years old (15), and medical fees for pre- and post-HTx treatments are indeed covered by the government (14). Considering the recommendation from the American Academy of Family Physicians (AAFP) and American Academy of Pediatrics (AAP), which stated that the preparation for a transition plan should be started by age 14 (16), we propose that the actual transition program should be employed around age 15 and gradually adjusted toward the age of 20, according to the developmental stage and intellectual ability of each patient in Japan.

**Figure 1** describes several existing barriers to starting a discussion on the transition program for HTx recipients in Japan and a thinkable roadmap for a successful transition.

First, transition medicine itself in Japan is almost 20 years behind, e.g., the US and European countries (17). The term transition in healthcare was first introduced in Japan in 2006, and it has been only about 10 years since the Japanese Pediatric Society and the government-led committees conducted research or surveys on the healthcare transition in 2013. Since then, the concept of the healthcare transition has spread, and its importance has been recognized by healthcare providers; however, it has not yet reached the area of HTx. Studies related to the transition in Japan were initially driven by pediatric nephrologists (18) and mostly targeted neurology and nephrology, but few studies have included cardiology or solid organ transplantation. Both disease-specific studies and a questionnaire survey by Ishizaki et al. concluded that transition programs are necessary and should be expanded nationwide (19).

Second, the tragic episode of the first HTx in Japan, as described previously, led the Japanese population to begin

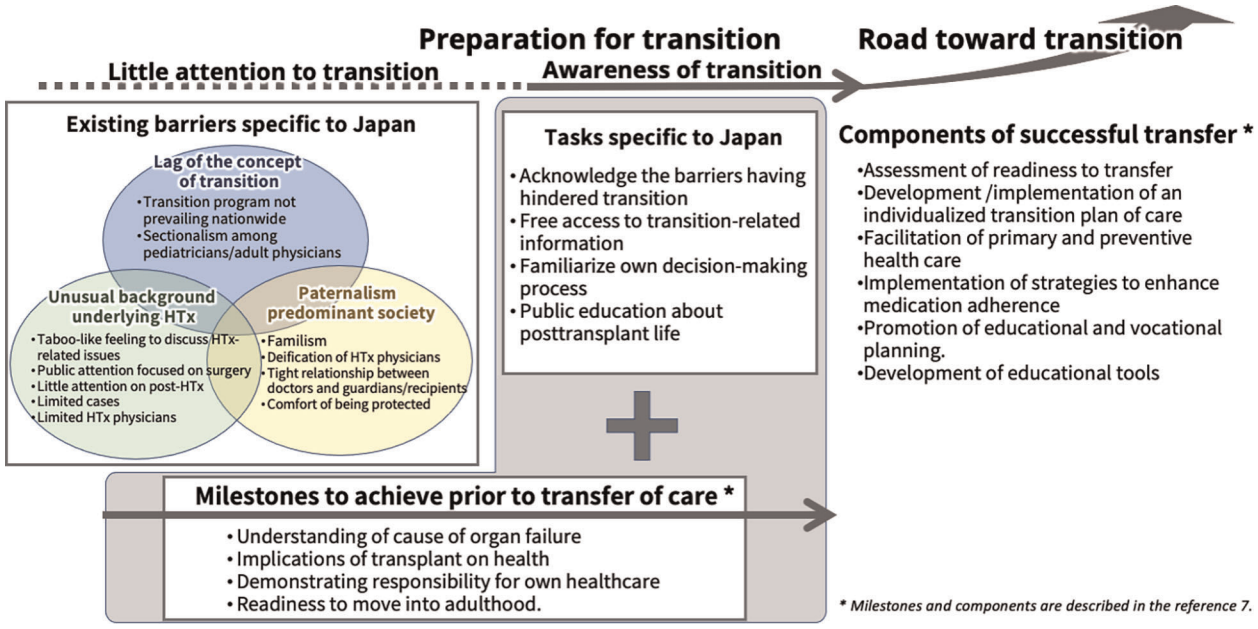


FIGURE 1
The conceptual framework for establishing a transition program for heart transplant recipients in Japan. The transition program has not been fully discussed to date in Japan, and the underlying reasons are described in the three balloons below. The roadmap to a successful transition starts with acknowledging the situation. Critical milestones to achieve and components of successful transfer for young adult patients after solid organ transplantation prior to transfer of care, as described in a consensus conference report (7), are shown in the figure.

considering the concept of HTx "special." Central players, including physicians and recipients, are highly sensitive to any criticism against HTx and have established a strong relationship among each other. On the other hand, non-central players, such as the healthy general population and even healthcare professionals working in the non-transplant field, tend to consider it taboo to participate in discussions related to HTx. In such a society, undergoing HTx surgery itself is the goal, and the recipient's post-transplant life has not received much attention. Indeed, life-stage choices that pediatric HTx recipients will encounter, such as marriage, pregnancy, employment, and actual end-of-life care or re-transplant listing, have not been discussed fully to date in Japan. In addition, the number of cases is small, about one-seventieth of those in the US per capita annually (20). Therefore, it has been difficult to train both pediatric and adult HTx physicians or divide their roles.

Third, paternalism remains predominant in clinical settings in East Asia, including Japan (21), which can hinder the independent and active decision-making process of patients and their guardians. Until recently, it was unusual for Japanese, Korean, or Chinese doctors to convey the truth about a poor prognosis or treatment strategy directly to their patients (22, 23). In other words, patients were commonly left uninformed about their condition (22, 23). Several studies reported that this is related to Confucianism, whose philosophical background is so-called familism (22, 24). Consequently, medical paternalism tends to be a mainstream of clinical decision-making, especially in a process of treating pediatric cases. Besides, the historical background of HTx in Japan further encourages medical paternalism through the deification of transplant surgeons. It is quite understandable that not only recipients but also their guardians feel comfortable being seen by the same HTx physicians for extended periods, regardless of their age, especially when they have created strong relationships with their doctors. The recipients and their guardians feel protected through the behavior pattern of simply following the instructions of healthcare professionals.

Even having considered these barriers, pediatric HTx recipients must eventually stand on their own feet. They require a lifelong self-tailored regimen of post-transplant immunosuppressive drugs and infection prophylaxis, which is a part of recipients' lives on their own. We believe understanding the sociocultural aspects is the first step to starting a fruitful discussion of an effective transition for pediatric HTx recipients in Japan. The critical milestones to achieve and the components of a successful transition for young organ recipients before starting the actual transition are described in the Consensus Conference Report by Bell et al. (7). Irrespective of each society's specific sociocultural background, the milestones and components of successful transfer are universal. The key issues shown in the Consensus Conference Report are also included in **Figure 1** (7).

## Steps for establishing an effective heart transplant transition program in Japan

A report shown in the Cochrane Review assessing the effectiveness of interventions to improve the transition of care revealed that they may be effective in transitional readiness but they led to a little difference in outcome (25). A randomized controlled trial that investigated the feasibility of a transition intervention for young HTx recipients showed it may be efficacious at 3 months, but no differences at 6 months for any outcomes, such as immunosuppressive levels, rejection, or mortality, were identified (26). Both studies were limited by their small sample size and short follow-up duration (25, 26). Still, we believe access to an optimal and effective transition program would vary among countries and firmly depend on their sociocultural background, including the insurance system. A disease-specific approach would be also required. Although the above-mentioned previous studies failed to prove the effectiveness of transition intervention, disease- and country-specific transition programs can produce a favorable effect on the outcome of the very patients being targeted. Therefore, we expect this paper to be the first step in discussing this issue to date for both patients and healthcare professionals in the area of HTx. Issues that hinder or delay discussion of the transition of pediatric HTx recipients to adult programs in Japan are multifactorial, as described above. Even so, it is time to discuss this topic in consideration of the increase in pediatric HTx recipients and the improvement of their survival into adulthood worldwide.

Possible first steps to begin the discussion are as follows: (i) HTx physicians and allied health professionals can recognize both the importance of transition and the risks associated with its process, (ii) HTx physicians and allied health professionals can acknowledge the barriers having hindered transition to date, (iii) HTx recipients and their guardians can freely access information on the transition from domestic and international viewpoints, (iv) HTx recipients and their guardians can recognize the importance of a gradual shift from parent- or physician-directed management to adolescent self-management, and (v) a specialized training program concerning transition for healthcare professionals can be established, including recipient coordinators, which may be the most important and effective step. In addition, (vi) public education to clarify that "HTx surgery itself" should not be the goal, but a joyful and independent post-transplant life, is necessary.

The above proposals seem specific to pediatric HTx in Japan, but the underlying ideas may be universal, and we believe such a discussion would help address the commonality among the issues that transition medicine is facing worldwide. In conclusion, the nurturing of transition programs for pediatric HTx in Japan is warranted. Pediatricians and adult HTx specialists should share these issues and start a discussion, which would promote HTx medicine and ensure better clinical outcomes among HTx recipients in Japan.

## Author contributions

Conceptualization: KTS; Supervision: GH, AY, KA, EHJ, HSA, IT; Visualization: KTS; Writing - original draft: KTS; Writing - review & editing: GH, AY, KA, EHJ, HSA, IT. All authors contributed to the article and approved the submitted version.

## 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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# Content validity of the Japanese version of the health literacy and resiliency scale for youth with chronic illness

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Health literacy, which is the ability to find, understand, and use information as well as services to make informed health-related decisions and actions, is essential for ensuring that youths with chronic diseases adapt to and live with their illnesses. However, in Japan, an appropriate approach for measuring health literacy levels among children is yet to be developed. The Health Literacy and Resiliency Scale for Youth (HLRS-Y) was developed by Kathy Bradley-Klug and her colleagues to assess health literacy, resiliency, and self-advocacy/support among youths aged between 13 and 21 years with chronic illnesses in the United States of America (United States). In this study, we aimed to develop a Japanese version of the HLRS-Y and evaluate its content validity. After receiving approvals from the original authors, four nurse researchers with expertise in pediatric nursing translated the scale into Japanese (forward translation). Afterwards, the appropriateness of each expression was examined by a pediatrician. Next, an English native speaker translated the expressions into English (back-translation). We reported the back-translated version of the scale to the original authors to confirm its accuracy. The scale's content validity index (CVI) was evaluated by health professionals working in the fields of pediatric, transitional, and adult health care. The participants rated the items using a four-point scale. Each item was evaluated for a minimum item-level content validity index (I-CVI) value of 0.78. The scale's total and subscale validities were evaluated using a minimum scale-level content validity index based on an average (S-CVI/Ave) value of 0.90. Eleven participants responded to an online survey for evaluating content validity. Of the 36 items, 34 met the I-CVI criteria. Two items did not exceed the criteria's value, but they approximated it. The values of the S-CVI/Ave were 0.96, thereby satisfying the criteria's requirements. Based on the results, it was confirmed that the Japanese version of the HLRS-Y had good content validity. Future studies should examine the factor validity, known group validity, and reliability of this scale.

KEYWORDS

transition to adult care, health literacy, resiliency, chronic illness, adolescents, young adults, self-advocacy

# Introduction

As the number of youths with special health and medical care needs increases, it is critical for health care providers to maximize the youths' abilities and potential while providing high-quality services appropriate to their developmental stages (1). Achieving this objective requires not only enhancing medical health management but also supporting the development of various abilities, such as health literacy and resiliency.

In 1998, the World Health Organization (WHO) defined health literacy (HL) as "the achievement of a level of knowledge, personal skills, and confidence to take action to improve personal and community health by changing personal lifestyles and living conditions (2)." HL involves the capacity to make sound health decisions, and as one of the health promotion outcomes, it has been attracting attention since the 2000s. HL is a necessary skill for the twenty-first century (3).

Research on HL has developed significantly over the past two decades. Prior studies have shown an association between HL and health outcomes among healthy adults. Low levels of HL are associated with poor health knowledge, noncompliance with medical visit schedules, low rates of medication verification when taking medications, and high rates of hospitalization as well as emergency room usage (4). The acquirement and promotion of HL also results in increased access to adequate health services and health management as well as improved healthcare provider-patient relationships, health-related decisions, and lifestyle choices (5–7).

On the other hand, research on HL among children has been limited owing to the lack of appropriate measurement tools. Although several scales for assessing fundamental HL among children exist, there is no self-administered scale focusing on the independent and subjective evaluation of HL in specific conditions (8). Further research on HL scales that consider various demographic characteristics, such as age, disease patterns, family relationships, social connections, and other factors, is required to ensure that children are respected (9, 10).

In 2017, Kathy Bradley-Klug et al. developed the Health Literacy and Resiliency Scale for Youth (HLRS-Y) to assess HL, resiliency, and self-advocacy/support among 13 to 21-year-olds suffering from chronic ilnesses in the United States (11, 12). The researchers who developed the original scale determined that self-care/management, adaptive coping, and a supportive environment are essential for ensuring that children with chronic illnesses adapt and survive (11, 12). To achieve this objective, they designed the scale to focus on HL (the ability for an individual to make daily decisions regarding their health care and assert their health-related needs) and resilience (self-efficacy, self-regulation, and a sense of connectedness) as essential components aimed at helping children suffering from chronic illnesses adapt and grow (11, 12).

The target population for this scale was defined as youth aged between 13 and 21 years. The items included in the scale were designed to consider the complex and specific situations associated with prioritizing autonomy, building relationships with other individuals outside the family, and integrating identity when dealing with chronic health conditions. This scale comprised 36 items: 10 for HL, 12 for resilience, and 14 for self-advocacy/support, which were rated using a four-point scale (strongly agree, agree, disagree, and strongly disagree). The scale has been verified for factor validity and the Cronbach's alpha coefficients for each subscale were 0.87 for HL, 0.93 for resilience, and 0.79 for support and self-advocacy (11, 12). The strength of this scale is that it is self-administered, and it questions participants about independent health management factors that are necessary for them to live with chronic illnesses without giving them the feeling that they are being tested.

However, currently, in Japan, HL levels among children and adolescents suffering from chronic illnesses are not known, and an appropriate approach for measuring HL levels among such individuals is yet to be developed. Therefore, it was necessary to translate the HLRS-Y into Japanese. Referring to the consensus-based standards for the selection of health status measurement instruments (COSMIN) guidelines (13), first, permission to use and translate the scale was obtained from the authors of the original version. Second, forward translation of the scale was independently performed by four nurse researchers, fluent in English and specializing in pediatric nursing. Afterwards, the contents were reviewed and summarized through discussion. Next, the appropriateness of each expression was examined by one pediatrician. Third, the back-translation into English was performed by an English native speaker. Finally, it was verified whether the Japanese expressions were smooth and easy to understand among youths between the ages of 13 and 21 while still remaining as direct a translation as possible.

Therefore, in this study, we aimed to develop the Japanese version of the HLRS-Y and evaluate its content validity.

# Material and methods

## Content validity index survey

### Participants

Through snowball sampling, 18 experts in the fields of pediatric, transitional, and adult health care were requested to participate in this study. The experts included physicians, nurses, university professors in the fields of nursing and education, social workers, psychologists, and independence supporters for specific pediatric chronic disease. We also

recruited adult patients with congenital heart diseases as well as survivors of childhood cancer.

### Survey method

The survey was conducted using a web-based self-administered questionnaire. The survey period was February 16, 2022 to February 25, 2022.

### Survey contents

To obtain the professional background of the participants, we asked them about their current role, qualifications, and years of experience engaging with patients aged between 13and 21 years with childhood-onset diseases (this included the participants' years of clinical experience, education, and research).

Regarding the content validity of the Japanese version of the HLRS-Y, we asked the participants to rank the validity of the items in each domain (HL, resiliency, and self-advocacy/support) on a four-point Likert scale: 4 = highly relevant; 3 = quite relevant; 2 = somewhat relevant; and 1 = not relevant. Additionally, for each domain, we asked the participants to provide their revisions and comments regarding the items in the free-description section.

### Analysis method

We relied on the item-level content validity index (I-CVI), which is calculated using the number of respondents providing a rating of three or four divided by the total number of respondents for all the items. The criterion value for I-CVI was set at 0.78 (14). We also evaluated the scale-level content validity index based on average (S-CVI/Ave), which is the average of the I-CVI. The criterion value for S-CVI/Ave was set at 0.90 (14).

### Ethical considerations

In compliance with the Declaration of Helsinki, 1964, we considered the protection of human rights (15). The human rights of the individuals were defended. In this study, there was no direct intervention on the participants, and it does not contain any personal information. It was also explained to the participants that they could choose to respond and there would be no disadvantages associated with non-participation.

## Result

### Demographics of the participants

Eleven valid responses were received (valid response rate: 61.1%). The eleven participants were as follows: two specialist physicians (pediatric oncologist and adult cardiologist), one Certified Nurse Specialist in pediatric nursing, one social worker, one university professor of nursing, one university professor of education, one psychologist, one independence supporter for specific pediatric chronic disease, and three patients (one pediatric cancer survivor and two patients with congenital heart disease). The mean level of the years of clinical experience and years of education as well as research involving individuals suffering from chronic illnesses who are aged between 13 and 21 years was 21.0 (SD = 12.5).

### CVI

Regarding the scale's total validity, the value of the S-CVI/Ave was 0.96, which exceeded the criterion's expected levels (0.90). As shown in **Table 1**, 26 out of 36 items had an I-CVI of 1.00, which is the upper limit. The other four items scored 0.91, each with another four items with a score of 0.82.

There were two items for which the I-CVI values were 0.73, which was less than the criterion's expected levels (0.78). Both of these items (H5 and H9) were related to HL. Regarding H5, "I know the correct amount of medicine for me," the participants who provided ratings of less than three or four were an adult cardiologist, an independence supporter for specific pediatric chronic disease, and a patient with congenital heart disease. The cardiologist commented that "I think the dosage for medication (s) is unnecessary knowledge." Regarding H9, "I understand that illness may affect my relationships with friends in various ways," the participants who provided ratings of less than three or four were a pediatric oncologist, a university professor of education, and a psychologist. The psychologist commented that "It is difficult to answer because the question is not clear."

The I-CVI was above the criterion's expected levels. However, one patient provided a comment regarding R10: "The people around me can help me to laugh about my illness.," stating that the phrase "laugh about my illness" might have a negative connotation in Japanese. For any other items, all the experts did not provide any comments regarding the invasive nature of the expressions to the patients involved in this study.

For some items in the self-advocacy/support criterion, there were comments pointing out that the word "school" might have resulted in difficulty in providing responses because the target population's age was up to 21 years. Additionally, a Certified Nurse Specialist commented, "Not everyone needs support. It is important to be able to ask for support if needed."

## Discussion

In this study, we developed a Japanese version of the HLRS-Y, and its content validity was assessed by eleven experts involved in supporting children with chronic illnesses, including the patients themselves. Previous studies

TABLE 1 Content validity Index of HLRS-Y Japanese version.

| Subscale | No. | | I-CVI | | | |
|---|---|---|---|---|---|---|
| | | | Total ($n = 11$) | Medical expert ($n = 4$) | Psychosocial expert ($n = 4$) | Patient ($n = 3$) |
| Health Literacy | H1 | I know the common symptoms of my illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| | H2 | I can tell if my symptoms are serious or not. | 1.00 | 1.00 | 1.00 | 1.00 |
| | H3 | I understand my illness well. | 1.00 | 1.00 | 1.00 | 1.00 |
| | H4 | I know the medicine I need for my illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| | H5 | I know the correct amount of medicine for me. | 0.73 | 0.75 | 0.75 | 0.67 |
| | H6 | I know what kind of exercise or activities are not good for my health. | 1.00 | 1.00 | 1.00 | 1.00 |
| | H7 | I know when to tell friends and family about things I can't do and things I should be aware of. | 1.00 | 1.00 | 1.00 | 1.00 |
| | H8 | I understand that illness may affect school and workplace activities in various ways. | 0.91 | 1.00 | 0.75 | 1.00 |
| | H9 | I understand that illness may affect my relationships with friends in various ways. | 0.73 | 0.75 | 0.50 | 1.00 |
| | H10 | I am learning about my illness while talking with people who have had the same experience as me. | 1.00 | 1.00 | 1.00 | 1.00 |
| Resiliency | R1 | I am optimistic about my future. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R2 | I accept my illness as one of my characteristics. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R3 | I think about how best to spend my time as I live with my illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R4 | I think positively or humorously about things even in difficult times. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R5 | I try to be optimistic about life. | 0.82 | 0.75 | 0.75 | 1.00 |
| | R6 | I think about ways to enjoy playing with friends and family while living with illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R7 | I think the experience of illness will somehow be useful in the future. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R8 | If you look at someone who is living well with a similar illness, it can be helpful to your own methods of living with illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R9 | I am relieved when I meet or talk with people my age or older who are living with illness. | 0.82 | 1.00 | 0.50 | 1.00 |
| | R10 | The people around me can help me to laugh about my illness. | 0.91 | 0.75 | 1.00 | 1.00 |
| | R11 | Since the people around me enable me to participate in events and activities, I am able to have the same experiences as everyone else. | 1.00 | 1.00 | 1.00 | 1.00 |
| | R12 | Being able to talk to someone about my own experience helps me to live with my illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| Support/Self Adovocacy | S1 | I understand that illness may affect my parents and other people in various ways. | 0.83 | 0.75 | 0.75 | 1.00 |
| | S2 | Teachers at school know about my illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S3 | I tell people around me when I'm feeling unwell. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S4 | I am learning about my disease from medical professionals. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S5 | I limit and adjust daily activities according to my condition. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S6 | I consider my physical condition and when necessary, take breaks or take it easy more than usual. | 0.91 | 1.00 | 1.00 | 0.67 |
| | S7 | I seek the help of family and friends to live with my illness. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S8 | There are people around me who take care of me. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S9 | I seek the help of my school teachers to live with my illness. | 1.00 | 1.00 | 1.00 | 1.00 |

(*continued*)





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TABLE 1 Continued

| Subscale | No. | | I-CVI | | | |
|---|---|---|---|---|---|---|
| | | | Total ($n = 11$) | Medical expert ($n = 4$) | Psychosocial expert ($n = 4$) | Patient ($n = 3$) |
| | S10 | My parents have learned much about my illness and help me live with it. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S11 | There is always someone who cares about whether or not I need help, due to my illness. | 0.82 | 1.00 | 0.75 | 0.67 |
| | S12 | I have family and friends who I can rely on when I have to go to hospital, stay in hospital, go for tests or undergo surgery. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S13 | I am receiving the necessary consideration to be successful in my school life. | 1.00 | 1.00 | 1.00 | 1.00 |
| | S14 | The teachers at school understand the necessities regarding my physical condition. | 0.91 | 1.00 | 1.00 | 0.67 |
| S-CVI/Ave | | | 0.96 | 0.97 | 0.94 | 0.94 |

I-CVI: item-level content validity index.
S-CVI/Ave: scale-level content validity index based on an average.
Medical expert includes physicians, nurse, and university professor in nursing.
Psychosocial expert includes university professor in education, social worker, psychologist, and independence supporter for specific pediatric chronic disease.

recommend the participation of at least five experts in the CVI evaluation (16). The COSMIN Guidelines also recommend the participation of patients during content validity assessments (13). This study meets these requirements and is considered to have achieved a certain level of content validity evaluation. The results of this study were as follows: (1) The CVI of the items of HLRS-Y were above the criterion value, except for two items; (2) Experts, including the patients involved in this study confirmed that the items were not invasive; (3) Some items, such as school-related ones, might require attention in the way the questions were constructed to avoid the inclusion of situations that might not be applicable to some participants. These findings are discussed in detail as follows:

**(1) The CVI of the items of HLRS-Y were above the criterion value, except for two items.**

Overall, the value of the S-CVI/Ave of the HLRS-Y was 0.96, and 34 out of the 36 items met the I-CVI criteria, thereby demonstrating that the scale has good overall content validity. However, two items (H5, H9) did not meet the expected criterion's values. Regarding H5, it could be assumed that H5 did not exceed the criterion values because the experts tended to believe that the importance of medication management was in the name, timing, and effect of the medication rather than in the dosage. Several previous studies suggest that healthcare providers should consider various aspects to ensure that children suffering from chronic illnesses adhere to appropriate medication behaviors (e.g., providing information regarding the type, dosage, duration of use, and common side effects of medications, easy-to-understand medication regimens, creating self-administration plans, and regular consultations with physicians) (17–19). The Transition Readiness Assessment Questionnaire (23 items in total), which is one of the world's most used measures of transition readiness among patients with childhood-onset diseases, includes six items related to adverse medication reactions, appropriate intake, and drug names and dosages (20, 21). Because the HLRS-Y includes more items related to daily life, it has fewer items related to medical care than the TRAQ, with only two items related to medications. Because one of the items (H5) was related to medication dosage, the experts may have thought that there were other items required, such as the names and adverse reactions. On the other hand, the physician commented, "I believe specialized knowledge is unnecessary for understanding health." Additionally, the patients stated, "I believe it depends on the individual," and "As a patient, I believe I understand the bottom line, but it is still not as good as relying on that of the medical professionals." We decided not to modify H5 in the Japanese version of the HLRS-Y because the scale focuses on daily life in general, and several participants commented that detailed knowledge was not always essential.

Regarding H9, the psychologist pointed out that it was difficult to understand the purpose of this question. In this

item, "my health impacts" is assumed to be, for example, that the illness causes limitations in behavior, thereby making it difficult to move at the same pace as a group of friends. However, it could be difficult to understand from the first reading. Although children suffering from chronic illnesses are at a higher risk for emotional and behavioral problems (22), good friendships have been shown to have a positive impact on their psychological and physical health (23). In the Japanese version of the HLRS-Y, H9 was not modified in terms of prioritizing comparability with the original scale.

**(2) Experts, including patients, confirmed that the items were not invasive.**

In this study, the experts did not comment on the invasiveness of the expressions of all the items, except for R10. Regarding R10, one patient pointed out that the expression "laugh about my illness" may have a negative meaning. Therefore, we changed the expression from "humor" to "cheerful," and we modified the item as follows: "People around me are cheerful and help me with my illness."

**(3) Some items, such as school-related ones, might require some attention in the way the questions were constructed to avoid including situations that might not be applicable to some participants.**

There were items that asked about the situations in school. Because the target population for this scale was up to the age of 21 years, some participants might have already graduated from high school and were employed. The school situation was not applicable for them. In fact, patients of the age at which they are eligible for HLRS-Y may not have attended school. Specifically, severely diagnosed patients are reported to have a lower educational background (24, 25), and the more severely diagnosed patients are, the more likely for them to be out of school. However, this also suggests that severely ill patients experience some difficulties in school. Therefore, in the Japanese version of the HLRS-Y, we decided to include items related to school life. However, we shall consider adding "not applicable" as a response option.

## Limitation

The expert panel included only three patients (pediatric cancer survivor and patients with congenital heart disease). When the original version of the HLRS-Y was developed, a wide range of patients was included in the study participants, including those with diabetes and juvenile rheumatoid arthritis (11). Therefore, it is necessary to increase the number of patients and the types of diseases. Guardians should also be included because they are likely to be concerned about whether the scale is invasive for their children.

In conclusion, the Japanese version of the HLRS-Y was found to have good content validity. Future studies should examine the factor validity, known group validity, and reliability of this scale.

# 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/s.

# Author contributions

SS conceived of the present idea; SS, KK, RO and TH designed this study; SS performed the survey and analyzed the data; SS drafted the manuscript; KK, RO and TH supervised the entire study process. 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.

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# Factors related to employment in childhood cancer survivors in Japan: A preliminary study

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**Purpose:** Previous research has revealed vocational and academic difficulties in childhood cancer survivors, and explored impact of survivors' medical history and physical function on vocational and academic status. However, we often encounter survivors with similar diagnoses and late effects but different academic or employment statuses. This raises the question of what affects academic attainment and employment other than treatment or late effects. This study aimed to explore factors associated with childhood cancer survivors' employment status and academic achievement.

**Methods:** Comprehensive health check-up and questionnaire survey were conducted for 69 survivors who were over the age of 18 and participated in St. Luke's Lifetime cohort study. We obtained survivors' biological function using comprehensive health check-up, neurocognitive states, quality of life, transition readiness, and family function. We conducted univariate analysis (Mann–Whitney *U* tests or chi-square tests) to compare the differences between the regular workers/students and non-regular workers/unemployed groups. The variables with *p*-values <0.1 were used as independent variables multivariate logistic regression to explore predictors of employment status and academic attainment.

**Results:** Result of the univariate analysis, intelligence quotient, SF-8 PCS, transition readiness, family function were used for multivariate logistic regression as independent variables. The stepwise likelihood method was conducted; intelligence quotient (odds ratio [OR] = 1.100; 95% confidence interval [CI] 1.015–1.193; $p = 0.021$), transition readiness (OR = 0.612; 95% CI 0.396–0.974; $p = 0.038$), and family function (OR = 2.337; 95% CI 1.175–4.645; $p = 0.015$) were found to be associated with survivors' regular workers/students in the final regression model.

Abbreviations

CI, confidence interval; CTCAE, common terminology criteria for adverse events; FACESKG, family and cohesion evaluation scale at kwansei gakuin; IQ, intelligence quotient; LTFU: long-term follow-up; OR, odds ratio; QoL, quality of life; SF-8, short form-8.

**Conclusion:** Long-term follow-up of pediatric cancer survivors requires the provision of total care, which supports physical, psychological, and social functions to improve health, readiness for transition to self-management, and family functioning.

KEYWORDS

childhood cancer, survivors, employment, self-management, late-effect, transition readiness, academic achievement

# Introduction

The survival rate for childhood cancer has improved, and the survival rates in Japan and Western countries have exceeded 80%. In Japan, the number of survivors of childhood cancer is uncertain, however an estimated 150,000—approximately one in 180 young adults at twenties—is regarded as childhood cancer survivors (CCSs). At the same time, various physical late effects, such as gonadal dysfunction, hypertension, or cognitive dysfunction caused by cancer and its treatment, have been reported (1, 2). As the measures and support for such challenges, there are 15 cancer centers which provide long-term follow-up care based on the guidelines set forth by the Japan Children's Cancer Group.

On the other hand, support for the developmental challenges such as academic achievement and/or low rate of employment which occurred in combination with late effects, long school absences due to treatment, and family factors is under-developed. Previous studies, including a population-based cohort study, have reported that academic attainment is lower in CCSs than in healthy peers; chemotherapy has been identified as a proximate cause of poor educational attainment according to some studies (3–6). The educational background of CCSs with multiple physical conditions is lower than those without those conditions (7). There is evidence that academic achievement is lower in younger-onset cases (8, 9). However, other reports have shown that age of onset is not relevant (10).

In terms of employment, some population-based studies have reported that CCSs are less likely to be working compared with peers (11, 12). French researchers have reported that the rate of CCSs seeking jobs was lower than that of the general French population, and the rate of CCSs having unstable employment was significantly higher (13). CCSs were unemployed for health reasons, and there were no significant differences between CCSs and the general population in terms of unemployment unrelated to health or those in work (14). In central nervous system tumor CCSs who underwent radiation therapy, the lower the age at diagnosis, the higher the number of late effects reported as risk factor for unemployment (7, 11–14). However, there is no existing consensus of risk factors of psychosocial function on academic attainment or employment metrics of Japanese CCSs. Furthermore, since there are large differences in income, social security, and employment stability between regular and non-regular employment in Japan, it is necessary to consider the type of employment when examining predictors of employment.

Empirically, CCSs with similar diagnoses and late effects yet different academic/employment statuses are often encountered. This raises the question of what affects academic attainment and employment other than treatment or late effects. A combination of biopsychosocial functions could influence childhood cancer survivors' academic attainment and employment; therefore, it is necessary to consider survivors' biological and psychosocial functions as influencing factors.

As in the Erice Statement (15, 16), the long-term goal of the cure and care of a child with cancer is that he/she becomes a resilient and autonomous adult with optimal health-related quality of life, accepted in society at the same level as his/her age peers, and to provide systematic support to empower CCSs and their families' adjustment and coping strategies to overcome future challenges in all aspects of life: in education, in work, and in family life. Therefore, the study aimed at ascertaining the factors associated with employment state and academic achievement among CCSs in Japan.

# Materials and methods

## Participants

The participants were 68 CCSs who correspond to all the subjects who participated in the St. Luke's Lifetime Cohort Study. Participants of the St. Luke's Lifetime Cohort Study were those over the age of 18 at the time of the participant, who had completed at least 5 years post treatment, and who knew their diagnosis.

We had calculated sample size using G* power for Mann-Whitney test (effect size = 0.5, $\alpha$ error = 0.05, power 0.95) and logistic regression ($\alpha$ error = 0.05, power 0.80), and it were 92 and 55, respectively. Therefore, it is possible to erroneously determine that there is no difference between the averages of data that are truly different as current study is a preliminary study with small sample.

### The St. Luke's Lifetime Cohort Study

The St. Luke's Lifetime Cohort Study is a study of CCSs who were diagnosed with childhood cancer and treated at St. Luke's International Hospital, or a hospital affiliated with St. Luke's International Hospital. Inclusion criteria were, in addition to

the above, 5 years after completion of treatment, 18 years of age or older, and able to complete a self-administered questionnaire. The St. Luke's Lifetime Cohort Study consists of a comprehensive health check-up with general and survivor-specific health examinations, psychological check-up, and tests to evaluate the state of late-effects and a questionnaire survey, which is conducted every 5 years.

CCSs meeting the inclusion criteria were briefed on the cohort study by a physician. If the survivor agrees to participate, provide written consent. After that, a questionnaire and schedule for a comprehensive health check-up were mailed to the CCSs.

On the comprehensive health check-up day, CCSs answered questionnaire provided prior to the check-up day and underwent a comprehensive medical examination at St. Luke's International Hospital Affiliated Clinic, Center for Preventive Medicine. For psychological check-up, CCSs revisited the hospital for intelligence quotient (IQ) tests on a day different from their health check-up. After the health check-up and IQ tests, all participating survivors received their IQ test results and feedback forms containing recommendations for a healthy lifestyle and long-term follow-up outpatient visits.

## Measurements

All data were obtained from the St. Luke's Lifetime Cohort Study including academic attainment, employment status, medical history, physical condition, and psychosocial condition.

### Dependent variable: state of academic attainment or working status

We divided the CCSs in two sub-groups. One consisted of students ($n = 22$) and regular workers ($n = 37$), another consisted of non-regular workers and unemployed ($n = 9$).

In the questionnaire survey of the St. Luke's Lifetime Cohort Study, the participants stated whether they were currently working, pursuing a degree (graduate school, college, vocational school, or junior college). Those who were working were asked employment type (regular or non-regular), and those enrolled in school asked institution type (graduate school, college, vocational school, or junior college). Classification of schools and employment was based on the census classification of the Ministry of Internal Affairs and Communications (17).

Since financial and social participation are important indicators from the perspective of children's independency. And there are large differences in income, social security, and employment stability between regular and non-regular employment in Japan, it is necessary to consider the type of employment when examining predictors of employment. In adittion to that, academic achievement higher than high school significantly affect getting regular job (18). And attending school as a fulltime student is considered as regular social participatory. Therefore, we combined regular workers and students as one group and non-regular worker was another.

### Physical indicators

#### *Medical history*

We collected medical history data from long-term follow-up summary which was written by the attending physician and was provided by the CCSs. In this study, we include CCSs' diagnosis and treatment (chemotherapy, surgery, radiation, or hematopoietic cell plantation).

#### *Physical condition*

Health condition of survivors were obtained from the comprehensive medical examination of St. Luke's Lifetime Cohort Study, which included tests for lifestyle-related diseases, blood and urine sample tests, an electrocardiogram, physiological tests (hearing test, chest x-ray test), diagnostic imaging (abdominal ultrasonography), and barium-based stomach examination. Additionally, provisions were made for women who wished to undergo gynecological examination, such as cervical screening and pelvic examination.

CCSs' physical conditions were classified based on the National Cancer Institute's Common Terminology Criteria for Adverse Events (the CTCAE) version 4 (19, 20). The CTCAE is a descriptive terminology which can be utilized for Adverse Event reporting (19, 20). A grading (severity) scale is provided for each Adverse Event term. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each Adverse Event based on this general guideline: Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2 Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL). Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL. Grade 4 Life-threatening consequences; urgent intervention indicated. Grade 5 Death related to Adverse Event (19, 20). We developed modified version of the CTCAE to better accommodate the grading of Japanese childhood cancer survivors (21). For this study, we considered survivors who have grades 1 or severe defined were those who have condition.

### Psychosocial indicators

In terms of psychosocial indicators, we collected information regarding IQ, quality of life (QoL), depression as a psychological indicator, and family function as a social indicator.

### *IQ*

The IQ of the participants was evaluated by psychologists using Wechsler Adult Intelligence Scale-IV as an index of neuro-cognitive function. We used the IQ score as continuous variable.

### *Qol*

We used the Japanese version of the Short Form-8 (SF-8) questionnaire (22), a comprehensive health-related QoL scale, which consists of eight items: physical function, daily role function, body pain, overall health, vitality, Social life function, daily role function. The physical health summary score (PCS) and mental health summary score (MCS) of the participants were calculated and compared against national standard scores; 50 points were assigned for each summary score. We used the PCS and MCS scores as continuous variables.

### *Depression*

The Kessler Psychological Distress Scale (23) is a self-administered screening scale for depression developed by Kessler et al. (24) in the United States. It consists of 10 items and a 5-step Likert scale with a cutoff score of 25 points (23). In this study, participants with a cutoff score ≥25 points were considered depressive, and those with a cutoff score < 25 were considered non-depressive.

### *Family function*

The Family and Cohesion Evaluation Scale at Kwansei Gakuin (FACESKG) developed by Tachiki, is a family function evaluation scale based on Olson's Circumplex Model of Marital and Family Systems (25–27). It has two components: family cohesion and family adaptation, with a scoring range of −14.5–19 and range of −13.5–14.5, respectively. Adaptation is interpreted from rigid or structured with lower score to chaotic or flexible with higher score, and cohesion is interpreted as disengaged or separated with low score and enmeshed or connected with higher score (26, 27). We used the scores of adaptation and cohesion as continuous variables.

### *Transition readiness*

The Japanese version of the transition Scale (28) was used to assess the participants' transition readiness. It was originally developed by Klassen (29) and consists of three scales: a cancer worry scale (six items, including: "I worry about my cancer every day"), a self-management skills scale (15 items, including: "I know how to contact a doctor if I need to" and "I book my own doctor"s appointment"), and expectations about adult long-term follow-up (LTFU) care scale (12 items, including: "I expect my parent(s) will be able to see the doctor with me" and "I expect the doctor will become like a friend"). The four response options were categorized as "strongly agree (3)," "agree," "disagree," or "strongly disagree (0)," and the total score of each scale was calculated. For the cancer worry scale and the self-management skills scale, higher scores indicate high worry or self-management skills, respectively. Regarding the expectations about adult LTFU care scale, the low "Expectation for adult LTFU" score indicates recognition of more independent consultation behavior. The scores of each scale was used as independent variable.

## Procedure

The St. Luke's Lifetime cohort study participants were childhood cancer survivors who received cancer treatment at St. Luke's International Hospital and at hospitals to which the collaborators of this cohort study belonged. Candidates were provided with an explanation of this research from their physicians, and in cases where face-to-face explanations were possible, received verbal explanation of the cohort study. We obtained written consent form when survivors agree to participate in our study. The heath check-up date and questionnaire were mailed to survivors who agreed to participate.

## Analysis

We performed univariate analysis to compare the differences between the regular workers/students and non-regular workers/unemployed groups. The Mann–Whitney *U* test was used for continuous variables (including age and IQ and SF-8, Transition Scale, and FACESKG scores). Chi-square tests were performed on nominal variables (sex, employment status, academic achievement, cancer type, treatment history, physical function, and Kessler Psychological Distress Scale score).

Multivariate logistic regression backward stepwise analysis was performed to determine factors affecting employment status and academic attainment. Variables with $p$-values <0.1 in the univariate analysis (Mann–Whitney *U* tests or chi-square tests) were used as dependent variables for the multivariate logistic regression analysis. Considering confounding factors, age and sex were included in the model.

All analyses were conducted using Statistical Package for the Social Sciences 28.0 for Macintosh (IBM). A two-sided $p$-value <0.05 was considered statistically significant.

## Ethical consideration

We obtained approval for our research from the Institutional Review Board of St. Luke's International Hospital.

# Results

## Characteristics and descriptive of the survivors

Characteristics of the survivors are shown in **Table 1**. Of the 68 survivors, 37 (54.4%) were regular workers, 22 (32.4%) were

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TABLE 1 Participants' characteristics and medical histories.

| | Regular worker/Students group | | | | Non-regular worker/ Unemployed group | |
|---|---|---|---|---|---|---|
| | Worker ($n = 37$) | | Student ($n = 22$) | | ($n = 9$) | |
| **Characteristics ($n = 68$)** | | | | | | |
| Age, mean (SD) | 29.0 | (5.9) | 21.5 | (3.1) | 32.1 | (6.5) |
| Gender (Female), *n* (%) | 18 | (48.6) | 9 | (42.9) | 5 | (55.6) |
| Academic achievement, *n* (%) | | | | | | |
| Graduate school | 5 | (13.5) | 2 | (9.1) | 1 | (11.1) |
| College | 19 | (51.4) | 16 | (72.2) | 2 | (22.2) |
| Vocational school/Junior college | 5 | (13.5) | 2 | (9.1) | 3 | (33.3) |
| High school | 6 | (16.2) | 0 | (0.0) | 3 | (33.3) |
| Junior high school | 2 | (5.4) | 0 | (0.0) | 0 | (0.0) |
| **Medical history** | | | | | | |
| Cancer type | | | | | | |
| Leukemia ($n = 41$) | 22 | (59.5) | 11 | (50.0) | 8 | (88.9) |
| Neuroblastoma ($n = 10$) | 5 | (13.5) | 4 | (18.2) | 1 | (11.1) |
| Brain tumor ($n = 6$) | 4 | (10.8) | 2 | (9.1) | 0 | (0.0) |
| Lymphoma ($n = 4$) | 3 | (8.1) | 1 | (4.5) | 0 | (0.0) |
| Others ($n = 7$) | 3 | (8.1) | 4 | (18.2) | 0 | (0.0) |
| Treatment history | | | | | | |
| Chemotherapy ($n = 67$) | 36 | (100.0) | 22 | (100.0) | 9 | (100.0) |
| Surgery ($n = 22$) | 13 | (36.1) | 8 | (36.4) | 1 | (11.1) |
| Radiation ($n = 32$) | 21 | (58.3) | 5 | (22.7) | 6 | (66.7) |
| Over Gr3 ($n = 19$) | 12 | (38.7) | 6 | (35.3) | 1 | (25.0) |
| Hematopoietic cell plantation ($n = 11$) | 4 | (11.4) | 5 | (22.7) | 2 | (22.2) |

students, and 9 (13.2%) were non-regular workers/unemployed. Annual income significantly differed between the regular workers and non-regular workers (Chi-square test, $p = 0.005$).

The most frequently reported physical conditions were dyslipidemia for both the regular workers (14, 35.9%) and non-regular workers/unemployed (5, 55.6%) and followed by dental abnormalities (10, 29.4%; 4, 44.4%, respectively) which is the most frequent for students (8, 38.1%) (Table 2).

Fifty-three survivors in the regular workers/student group (93%) and nine (81.8%) in the non-regular workers/ unemployed group had the SF-8 PCS scores below the national standard score of 50 points. Regarding the MCS, 44 (77.2) and seven (63.3%) participants scored below the national standard score of 50 points (Table 2).

## Univariate analysis

There were no significant differences between the regular workers/student group and the non-regular workers/ unemployed group with respect to age, sex, cancer type, treatment histories, or physical function, which were assessed by the comprehensive health check-up (Tables 1, 2). However, IQ was significantly different between the two groups ($p = 0.012$).

In terms of psychosocial indicators, the mean the FACESKG adaptation score was significantly higher in the regular workers/ student group than in the non-regular workers/unemployed group ($p = 0.005$), indicating that the family function of the regular workers/student group was more structed than that of the non-regular workers/unemployed group. There was a tendency ($p < 0.1$) of the differences between the SF-8 PCS scores ($p = 0.073$), the Transition Scale "Self-management scale" ($p = 0.021$), and the "Expectation of adult LTFU scale" ($p = 0.058$).

## Multivariate logistic regression

We used IQ results, the SF-8 PCS score, two transition scale scores ("self-management scale" and "expectation of adult LTFU"), and the FACESKG adaptation score, which showed significance or the tendency of difference in the univariate analyses as independent variables for the multivariate logistic regression analysis to determine the predictors; We found no strong correlations between these variables (Table 3). There were four steps till model convergence in multivariate logistic regression. The final model included IQ (odds ratio [OR] = 1.100; 95% confidence interval [CI] 1.015–1.193; $p = 0.021$)

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TABLE 2 Participant's health conditions and psychosocial statuses.

| | Regular workers/Students group | | | | Non-Regular workers/Unemployed group | | |
|---|---|---|---|---|---|---|---|
| | Worker ($n = 37$) | | Student ($n = 22$) | | ($n = 9$) | | |
| **Health condition ($n = 68$)** | | | | | | | |
| **Physical condition,** *n* (%) | | | | | | | |
| Body mass index <18.5 | 8 | (22.1) | 7 | (31.8) | 0 | (0.0) | |
| Hypertension | 5 | (13.5) | 4 | (18.2) | 1 | (11.1) | |
| Dyslipidemia | 14 | (35.9) | 8 | (36.4) | 5 | (55.6) | |
| Primary hypothyroidism | 2 | (5.4) | 1 | (4.5) | 0 | (0.0) | |
| Liver dysfunction | 2 | (5.4) | 2 | (9.1) | 1 | (11.1) | |
| Kidney dysfunction | 1 | (2.7) | 0 | (0.0) | 0 | (0.0) | |
| Hepatitis B, C virus infection | 4 | (10.8) | 0 | (0.0) | 2 | (22.2) | |
| Hearing loss | 3 | (8.1) | 1 | (4.5) | 2 | (22.2) | |
| Osteoporosis | 1 | (2.7) | 1 | (4.5) | 1 | (11.1) | |
| Dental abnormalities | 10 | (29.4) | 8 | (38.1) | 4 | (44.4) | |
| Ocular abnormalities | 10 | (27.8) | 4 | (18.2) | 1 | (11.1) | |
| Cardiomyopathy | 0 | (0.0) | 1 | (4.5) | 0 | (0.0) | |
| Gonadal dysfunction | 5 | (13.9) | 2 | (9.1) | 1 | (11.1) | |
| HPA dysfunctions | 6 | (17.1) | 0 | (0.0) | 2 | (22.2) | |
| Growth hormone deficiency | 5 | (13.5) | 0 | (0.0) | 1 | (11.1) | |
| **Neuro-congnitive function, mean (SD)** | | | | | | | |
| IQ (WAIS-IV) | 103.1 | (19.1) | 107.9 | (20.3) | 89.0 | (14.5) | * |
| **Psychosocial status, QoL** | | | | | | | |
| PCS, mean (SD) | 26.7 | (9.7) | 28.5 | (15.4) | 34.1 | (12.5) | * |
| MCS, mean (SD) | 37.5 | (11.3) | 41.7 | (11.3) | 44.7 | (9.6) | |
| Depression (K10 = 25), *n* (%) | 2 | (5.4) | 1 | (4.5) | 1 | (11.1) | |
| **Transition readiness, mean (SD)** | | | | | | | |
| Transition Scale | | | | | | | |
| Self-management | 32.9 | (5.2) | 34.6 | (5.7) | 29.2 | (3.7) | * |
| Expectation of adult LTFU | 16.1 | (6.1) | 15.9 | (4.1) | 19.3 | (2.9) | |
| Anxiety | 5.2 | (3.1) | 4.3 | (3.7) | 4.4 | (3.3) | * |
| Knowledge of treatment | 11.0 | (6.1) | 11.0 | (6.5) | 8.9 | (4.9) | |
| Knowledge of cancer diagnosis | 5.5 | (2.9) | 4.2 | (2.9) | 5.1 | (4.0) | |
| **Family function (FACESKG), mean (SD)** | | | | | | | |
| Adaptation | -.87 | (2.4) | -.60 | (1.3) | −3.1 | (2.5) | * |
| Cohesion | 2.0 | (3.5) | 1.2 | (3.1) | 1.6 | (2.1) | |

*$p < 0.1$, Mann-Whitney *U* test between the regular workers/students group and the non-regular workers/unemployed group.

(Table 4), the FACESKG adaptation score (OR=2.337; 95% CI 1.175–4.645; $p = 0.015$), the "Expectation of adult LTFU" score (OR = 0.612; 95% CI 0.396–0.974; $p = 0.038$), and the "Self-Management" score (OR = 1.279; 95% CI 0.960–1.193; $p = 0.093$).

## Discussion

This study aimed to explore factors associated with childhood cancer survivors' employment status and academic achievement. Although the number of subjects was small, valuable data were obtained, and we found that IQ, transition readiness, and family function associated with employment status and academic attainment.

The St. Jude survey (2) reported that more than 98% of childhood cancer survivors have conditions in their 30 s, while on the contrary, this study observed that around 85% of survivors have these conditions. These differences in frequency may be because the participants in this study were younger than those in the St. Jude survey, and the frequency

TABLE 3 Correlations between independent variables.

| | *n* = 68 | | | |
|---|---|---|---|---|
| | **IQ** | **TS self-management** | **TS expectation** | **FACES adaptation** |
| TS Self-management | 0.115 | | | |
| TS Expectation | 0.021 | −0.212 | | |
| FACESKG Adaptation | 0.029 | −0.073 | 0.011 | |
| QOL PCS | 0.103 | −0.104 | 0.068 | 0.002 |

Spearmans's Rho.
TS, the transition Scale.

TABLE 4 Multivariable logistic regression for employment.

| | | | | | | *n* = 67 |
|---|---|---|---|---|---|---|
| | **Step 1** | | | **Step 2** | | |
| | **OR** | **95% Cl** | ***p*-value** | **OR** | **95% Cl** | ***p*-value** |
| IQ | **1.096** | **1.010–1.190** | **0.028** | **1.100** | **1.015–1.193** | **0.021** |
| SF-8 PCS | 0.951 | 0.873–1.037 | 0.225 | | | |
| TS | | | | | | |
| Self-MGT | 1.281 | 0.955–1.171 | 0.098 | 1.279 | 0.960–1.193 | 0.093 |
| Expectation | 0.637 | 0.401–1.011 | 0.056 | **0.612** | **0.396–0.974** | **0.038** |
| FACESKG | | | | | | |
| Adaptation | **2.419** | **1.159–5.047** | **0.019** | **2.337** | **1.175–4.645** | **0.015** |

Multivariate logistic regression was performed using the stepwise likelihood method.
OR, odds ratio; TS, the transition scale; Self-MGT, self-management.

of associated conditions may increase in this cohort in the future. This study's most frequently occurring late effects were dental abnormalities, low weight, ophthalmic abnormalities, and dyslipidemia, which concurred with previous studies (2). Dental and ophthalmic abnormalities are not usually examined in long-term follow-ups centered on pediatrics and hematology. However, this study revealed that these were common late effects, so regular examinations of these are required with the establishment of an insurance-covered follow-up strategy. Additionally, it is clear that childhood cancer survivors in Japan have late effects similar to that observed in survivors belonging to other countries, and their framework of care is considered more seriously than ever before.

According to the Labour Force Survey 2020 by the Statistics Bureau of Japan (30), the percentage of regular workers aged 25–34 years is 77.6%, while the percentage of regular workers in this study is slightly higher at 81.8%. Similarly, regarding academic attainment, 62.3% of this study's subjects graduated from or were enrolled in university or graduate school, and the achievement is higher than Japanese population rate of 41.9%. However, this result needs to be interpreted carefully. This study was conducted in the metropolitan area of Tokyo, in which many of its subjects lived. The Tokyo metropolitan area is reported to have a higher university enrollment rate than other prefectures, which is 64.7% (31). Therefore, this study's high rate of university enrollment may be related to the region's characteristics. Previous population survey reported lower rate of the survivors' university enrollment than that of the general population. Therefore, it can be said that the employment form and academic achievement of childhood cancer survivors are equivalent to that of the metropolitan area's general population.

In terms of factors related to employment status, we did not find any significant associations with diagnosis, treatment, or physical condition, screened using the CTCAE. The most frequent late effects in our study were dyslipidemia and dental abnormalities. These late effects need condition management or regular clinic visits to prevent their progression; however, these may not substantially impact work or school performance. Therefore, further study is needed to clarify the association of what late effects on employment or academic attainment.

A previous study showed that more adaptive family functioning was associated with better outcomes in brain tumor survivors (32). Our study family function is the strongest variable and showed that more structured family adaptation was associated with better states of survivor employment and academic attainment, so patients' families should handle their affected loved ones' situations consistent way and make decisions according to the survivor's developmental stage. It is often reported that childhood cancer survivors experience parent-child closeness and overprotection. Therefore, family's, especially parental adaptation influences on CCSs's adaptation. It is important to encourage the gradual transfer of clinical decision-making from parents to survivors and help survivors make decisions by providing the necessary information and coping methods with consistent way according to the patients' cognitive functions, such as IQ and developmental stages. Besides support from family and health care providers, interaction with peers or support in the school environment could be significant (33–35); child onset cancer survivors diagnosed before forming peer-group friendships overcome their cancer treatment with their parents' support. Therefore, these patients developed a strong bond and feeling of trust with their parents. In adolescent and young adult survivors, on the other hand, it is reported that talking with peers is an important form of social support (36); therefore, it is possible that interacting with peers allows survivors to gain familiar role models and goals from their peers, and encouraging appropriate interaction with peers may positively affect future employment.

As previous studies, IQ showed the strong association with employment status in this study. It is widely known that

treatment for childhood cancer impairs cognitive function. It has been reported that cognitive impairment affects study, social interaction, employment, and self-management of one's body (37), and this study found that it also affects employment and academic performance achievement. In the multivariate logistic analysis, self-management, readiness of independent medical use (measured by expected for adult medical care), and structured family function contributed to employment and academic achievement. Strengthening consistent family function may have a positive impact on the independence of survivors against treatment-induced decline in IQ. However, this study's sample size was small and did not examine the positive effects of family function on IQ. Further research is needed to explore the positive impact on family function considering various contexts such as IQ levels. In the regular workers/students group, "Expectation for adult LTFU" scores were lower than those in the non-regular workers/unemployed group, meaning that survivors with regular workers/students have different expectations regarding adult medical clinic visits. Thus, the low "Expectation for adult LTFU" score indicates recognition of more independent consultation behavior; in other words, the participants' preparation for the transition from pediatric care to adult care was high. It is thought that such independence and decision-making ability in medical use will function positively for making choices to suit themselves and will have the same positive effect on academic attainment and employment.

Similar to previous research (38), the participants' average QoL scores were below the national standard scores for both PCS and MCS. This shows that childhood cancer survivors experience subjective difficulties with their physical and mental health. Interestingly, we found no differences in QoL scores between the regular workers/students and non-regular workers/unemployed groups, but there was a tendency for lower PCS scores in survivors in the regular workers/students group. Full-time work may impose a physical burden, therefore, further research regarding employment and subjective physical burden will provide additional details and recommendations for continuation of employment measures.

There are some limitations to this study. The first is its small sample size, the primary reason for which was the high cost of providing comprehensive health check-ups. Fortunately, our facility has a preventive health center specializing in these, and we obtained support from multidisciplinary health care providers and several foundations to carry out comprehensive health checks not covered by health insurance. Also, although as strength of this study was its method, which included comprehensive health check-ups, there were time and financial barriers to participation for survivors if they lived far from our hospital. For this reason, we began surveying childhood cancer survivors treated at our institution and gradually expanded the recruitment to subjects treated at other hospitals. However, due to the small number of samples, many subjects were regular workers/students, and the statistical power of our results is limited. In that sense, the results of this study will be strengthened by repeated verifications in the future.

Another limitation is our method of grouping employment type. In this study, we combined childhood cancer survivors in regular workers with those who were students (20 were college or graduate students, and 2 were junior college or vocational college) into one group. Strictly speaking, students are promised to be a regular workers; however, in Japan, about 80% of university graduates and 90% of graduate school graduates work as a regular worker (30). Based on this, we treated these as one group. In addition, our results also showed a relationship between university or graduate school graduation and full-time employment ($p = 0.049$).

This study aimed to gain insight into the perceptions of childhood cancer survivors to obtain suggestions for biopsychosocial survivorship care. Considering its limitations, we think of this as a preliminary study, and we will increase the number of subjects to report the employment status of Japanese childhood cancer survivors with a sufficient number of participants in the future. As mentioned above, we will recruit survivors treated at our hospital and those treated at collaborating institutions.

We examined the employment of childhood cancer survivors and clarified the association of biological and psychosocial functions with employment. Due to the high frequency of physical symptoms revealed by the rigorous health check-ups in this study, comprehensive examinations are required for long-term follow-up and provide complete care for survivors' overall independence. This study clarified the importance of supporting their families and improving patients' readiness for transition to self-management. In Europe, the PanCareFollowUp consortium has been established and is implementing follow-up strategies, including patient-centric care-based lifestyle interventions and coaching (39). The St. Luke's lifetime cohort study also provides feedback of results of health check-up and the necessary guides for long-term follow-up in consideration of individual biopsychosocial state. We believe that it is important to further promote such research and clinical practice in an integrated manner to support better survivorship of survivors.

## Conclusion

We examined childhood cancer survivors' employment and academic status and found that family function showed strongest association followed by IQ with employment status. Furthermore, transition readiness was associated with survivors' employment and academic status. We, therefore, recommend that long-term follow-up provides total care with

support for childhood cancer survivors' physical, psychological, and social functions to improve health, readiness for transition to self-management, and family functioning.

## Data availability

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

## Ethics statement

The studies involving human participants were reviewed and approved by The Institutional Review Board of St. Luke's International Hospital. The patients/participants provided their written informed consent to participate in this study

## Authors contributions

KK, YI, YH, DH, AM, OS, YYS, and MO conceived and designed the study. MG, KN, DH, YH, and MO contributed to subject recruitment and data collection. YYS contributed to screening late effects. KK and MO analyzed the data, interpreted the results, and wrote the manuscript. SO contributed to designing the analysis procedure and analyzed the data. 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.

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# Social independence evaluation index for Japanese patients with childhood-onset chronic diseases

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**Introduction:** This study established an independent evaluation index for patients with childhood-onset chronic diseases in Japan.
**Methods:** From November to December 2020, three Delphi rounds were conducted. Thirty-nine participants completed at least one survey. We asked them about targets of social independence for 10 types of activities (education/labor/finance/acquisition of necessities/housing/transportation/leisure/social relationship/intimate relationships/sexuality). The Delphi technique was to be repeated until a consensus of over 80% of participants was reached.
**Results:** The targets chosen for measuring independence in patients with childhood-onset chronic diseases were as follows: "Graduation from high school," "Labor for livelihood (including temporary turnover)," "Financially independent (including temporary turnover, excluding students)," "Buy or rent a house and buy the daily necessities and get the public services you need to live," "Do housework alone," "Plan alone and use transportation to get around," "Participate in play/recreation/leisure activities on own initiative," "Engage in relationships with other people outside of a limited environment (home, school, office, hospital, etc.)," "Create and maintain intimate or romantic relationships between individuals (couples, lovers, sexual partners)," and "Use or know how to use contraceptives and how to prevent sexually transmitted diseases."
**Conclusions:** We established an independent evaluation index for patients with childhood-onset chronic diseases in Japan through a three-round Delphi process. The assessment of social independence using our independent evaluation index may help plan for and provide appropriate support and assistance to these patients.

KEYWORDS

social independence, activity, transitional care, international classification of functioning, disability and health (ICF), social participation (MeSH), childhood-onset, chronic diseases, delphi technique [MeSH]

Abbreviations
ICF, international classification of functioning; RTP, rotterdam transition profile.

## Introduction

The transition from pediatric to adult healthcare systems has recently garnered attention worldwide (1). Various interventions have been used to improve the transition process and have been reported to improve outcomes in population health, experience of care, and utilization and cost of care (2, 3). However, most previous studies have focused on outcomes of transitional care in patients with specific diseases (2, 3).

The goals of transitional care is reportedly "to maximize lifelong functioning and potential through the provision of high-quality, developmentally appropriate healthcare services that continue uninterrupted as the individual moves from adolescence to adulthood (4)." Thus, one goal of transitional care is to improve the quality of social life when the patient reaches adulthood.

Individuals have increased opportunities to engage in various activities and participate in society as they mature from adolescence to adulthood. Furthermore, a notable shift has been observed from the dependency of childhood to greater independence in a range of social roles (5). However, there is some concern that children and adolescents with special healthcare needs, even with appropriate medical care, may have problems finding employment and building relationships, as they cannot engage in the events and activities necessary for social independence.

Therefore, in this study, we focused on social independence, which is one of the outcomes of transitional care, to establish an independent evaluation index for patients with various types of childhood-onset chronic diseases in Japan, with reference to the Rotterdam Transition Profile (RTP) used for cerebral palsy patients (6).

## Materials and methods

The study was approved by the ethics review board of Chiba Children's Hospital, Chiba, Japan (Approval number, 2019-021).

Initially, the steering committee of the study was organized. The committee consisted of seven members of the transitional care committee of the Pediatric Rheumatology Association of Japan (three pediatric rheumatologists, two non-pediatric rheumatologists, and two transitional care nurses) and two education professionals who specialized in teaching children with chronic diseases.

The items of the RTP was based on the contents of "activity and participation" of the International Classification of Functioning (ICF), Disability, and Health (7). Thus, we also referenced the ICF and made an original draft of targets of social independence for 10 types of activities (education/labor/finance/acquisition of necessities/housing/transportation/leisure/social relationship/intimate relationships/sexuality) appropriate for or expected of adult patients with childhood-onset chronic diseases in Japan (**Table 1**). Furthermore, in line with the ICF philosophy, we decided to evaluate the subjects' performance of activities and participation as well as their capacity to engage in these activities while receiving any support/assistance.

From November to December 2020, three Delphi rounds were conducted. A Delphi consensus survey was performed using an online tool (Google Forms). The survey was disseminated to leading pediatric physicians, leading non-pediatric physicians, transitional care nurses, and members of patient/guardian groups in rheumatology, endocrinology, nephrology, allergology, and cardiology. None of the participants received financial compensation.

The participants were informed that the patients' diseases targeted by this project were not associated with any intellectual disability or severe physical disability that would prevent engaging in social activities, even with appropriate support/assistance. The Delphi technique was to be repeated until a consensus of over 80% of participants was reached.

## Results

Thirty-nine participants completed at least one survey. **Table 2** presents the participant characteristics.

We received responses from 39 participants for Round 1. Participants either expressed agreement with the original draft or—if they disagreed with any point—were asked to present a counter-proposal for each item of social independence. In 6 of the 10 items, more than 80% of the participants agreed with the contents of the draft text. Consequently, the draft text was adopted for inclusion in the social independence evaluation index.

In Round 2, we presented the original draft and all counter-proposals for the remaining four items and asked the participants to select one of each item. We received responses from 34 participants. In "Finance" and "Entrainment," only one answer received more than 20% but not 80% of votes. We therefore asked the participants whether they agreed to adopt the answers in Round 3. In "Education" and "Sexuality," two answers received more than 20% but not 80% of votes. We therefore asked the participants to select one of them in Round 3.

In Round 3, we received responses from 30 participants. In "Finance" and "Entrainment", the leading answers received ≥80% of votes, but "Education" or "Sexuality" did not receive more than 80% of the votes.

Finally, the members of the steering committee discussed the independent evaluation index for "Education" and "Sexuality." As the last two proposals included "graduation from high school," we concluded that "graduation from high school" might be a minimum requirement for independence. In terms of

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TABLE 1 Original draft and voting results in the three Delphi rounds.

| Items | Draft | Leader in the 1st round Leading percentage (%) | Leader in the 2nd round Leading percentage (%) | Leader in the 3rd round Leading percentage (%) |
|---|---|---|---|---|
| Education | Enrolled in or graduated from a vocational school or university/ professional education institution | Draft<br>48.7 | Graduation from high school or vocational school<br>32.4 | • Graduation from high school or vocational school<br>• Graduation from high school<br>50.0 each |
| Labor | Labor for livelihood (including temporary turnover) | Draft<br>89.7 | | |
| Finance | Financially independent (including temporary turnover) | Draft<br>71.8 | Financially independent (including temporary turnover, excluding students)<br>55.9 | Financially independent (including temporary turnover, excluding students)<br>90.0 |
| Acquisition of necessities | Buy or rent a house, buy the daily necessities you need, and get the public services you need to live | Draft<br>87.2 | | |
| Housing | Do housework alone | Draft<br>89.7 | | |
| Transportation | Plan alone and travel using transportation | Draft<br>82.1 | | |
| Leisure | Plan and carry outplay, recreation, and leisure activities | Draft<br>74.4 | Participate in play/recreation/leisure activities on own initiative<br>26.5 | Participate in play/recreation/leisure activities on own initiative<br>96.7 |
| Social relationship | Join relationships with other people outside a limited environment (home, school, office, hospital, etc.) | Draft<br>87.2 | | |
| Intimate relationships | Create and maintain intimate or romantic relationships between individuals (couples, lovers, sexual partners) | Draft<br>87.2 | | |
| Sexuality | Experienced with sexual intercourse or able to use contraceptives and prevent sexually transmitted diseases | Draft<br>59.0 | "Educated about sexual intercourse" or "Can use contraception and prevent sexually transmitted diseases"<br>26.5 | "Educated about sexual intercourse" or "Can use contraception and prevent sexually transmitted diseases"<br>63.3 |

TABLE 2 Participant characteristics.

| | Pediatric physician (*n*) | Non-pediatric physician (*n*) | Pediatric Nursing (*n*) | Non-pediatric Nursing (*n*) | Patient/guardian groups (*n*) |
|---|---|---|---|---|---|
| Rheumatology | 3 | 2 | 1 | 1 | 2 |
| Cardiology | 2 | 1 | 1 | 1 | 2 |
| Nephrology | 2 | 1 | 1 | 1 | 1 |
| Endocrinology | 1 | 1 | 1 | 1 | 0 |
| Gastroenterology | 1 | 1 | 1 | 1 | 0 |
| Allergology | 1 | 1 | 2 | 0 | 1 |
| Transitional care | 2 | 0 | 2 | 0 | 0 |

"Sexuality," it tends to be difficult to discuss an individual's experience in sexual intercourse in clinical practice. We therefore focused on contraceptives and the prevention of sexually transmitted diseases. We finally decided that the independent evaluation index for "Sexuality" in Japan in this study would be "Using or understanding how to use contraceptives and how to prevent sexually transmitted diseases."

## Discussion

This study established a consensus concerning independent evaluation indices for patients with childhood-onset chronic diseases in Japan using a three-round Delphi process. The ability to participate in certain social roles and activities considered to indicate "independence" differs among

countries, and people in different positions have different perceptions concerning this ability. We therefore recruited not only medical doctors but also transitional care nurses and members of patient/guardian groups to discuss the social situation in Japan.

Our independent evaluation index differs from the RTP established in the Netherlands (6) in several respects (**Table 3**). We divided "Education and Employment" in RTP into two items of "Education" and "Labor" because a higher education does not necessarily lead to a higher income, and the support systems that encourage independence differs between these two items. Similarly, we divided "Leisure (social activities)" in RTP into two items of "Leisure" and "Social relationship," as social relationships in non-leisure situations, such as at school or in the office, are also considered important for achieving independence. In addition, we added "Acquisition of necessities," an item included in "activity and participation" of the ICF (7) and considered important for people with disabilities.

Education is essential for learning self-dependence. Education in high school in Japan is considered upper secondary education in the International Standard Classification of Education 2011 (8). This level is defined as the second and final stage of secondary education, preparing for tertiary education, and providing skills relevant to employment. In Japan, the admission rate to high school was 95.8% in 2019, and financial support and special schools were available for students with special educational needs owing to learning difficulties, physical disabilities, or behavioral problems.

Labor force participation is linked with higher rates of social inclusion (9). Therefore, regardless of whether financial independence is achieved, labor is considered an essential part of participation in society.

In addition, being economically independent is also very important. However, patients with chronic diseases have lower incomes than healthy individuals (10). Therefore, future studies should focus on income generation methods, given the declining income of young individuals and the uncertainty concerning social welfare in Japan.

"Acquisition of necessities," "Housing," and "Transportation" are important skills for daily life. We noted no significant difference in the content between the RTP and our independent evaluation index.

Building relationships is essential in life. In both "Leisure" and "Social relationship," building relationships—even with unfamiliar people—is necessary for independence. This is leads to more social activity outside the limited environment (home, school, work, etc.). Interestingly, the independent evaluation index for "Intimate relationships" in this study was similar to that in the RTP, while that for "Sexuality" focused less on sexual relationships than that for the RTP, probably due to differences in customs between countries.

At present, opinions vary regarding the most effective implementation methods of the index in clinical practice, including the age at which the evaluation should be started and the frequency of performing such evaluations. In particular, there are conflicting opinions regarding whether it is acceptable and appropriate to conduct evaluations by including topics such as "Intimate relationships" and "Sexuality" from an early age. A preliminary study is therefore considered to be necessary to determine the most appropriate timing to conduct such evaluations.

Nevertheless, the present study had some limitations. First, because of the SARS-CoV-2 pandemic, we were unable to meet in person to discuss and vote on the Delphi rounds. Thus, we voted *via* the web tool, which might have affected the results of this study. Second, we did not consider the influence of disease-specific disabilities in this study. Therefore, future studies should explore whether the results of this study could be applied to actual individual diseases. Third, because the social environment differs among countries, the events and activities required for

TABLE 3 A comparison of the independent evaluation index established in this study and the RTP.

| | Final consensus on the independent evaluation index in this study | RTP |
|---|---|---|
| Education | Graduation from high school | Paid job, volunteer work |
| Labor | Labor for livelihood (including temporary turnover) | |
| Finance | Financially independent (including temporary turnover, excluding students) | Economically independent: job income, benefit |
| Acquisition of necessities | Buy or rent a house, buy the daily necessities you need, and get the public services you need to live | |
| Housing | Do housework alone | Living independently |
| Transportation | Plan alone and use transportation to get around | Young adult arranges transportation for themselves |
| Leisure | Participate in play/recreation/ leisure activities on own initiative | Young adult goes out in the evening with peers |
| Social relationship | Join relationships with other people outside of a limited environment (home, school, office, hospital, etc.) | |
| Intimate relationships | Create and maintain intimate or romantic relationships between individuals (couples, lovers, sexual partners) | Young adult has a current romantic relationship/a partner |
| Sexuality | Use or know how to use contraceptives and prevent sexually transmitted diseases | Young adult has experience with sexual intercourse |

RTP, rotterdam transition profile.

social independence in patients with chronic diseases might also differ.

In conclusion, we have developed a non-disease-specific independence evaluation index for patients with childhood-onset chronic diseases in Japan through a three-round Delphi process. We believe that the assessment of social independence using the index can be used to support pediatric patients with chronic diseases, and assess patients with different chronic diseases.

## Data availability statement

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

## Author contributions

YI, HU, TM, SN, IS, MM, TT, KT, and TM: Conceptualization; YI: Investigation; YI, HU, TM, SN, IS, MM, TT, KT, and TM: Methodology; TM: Project administration; TT, KT: Supervision; YI: Writing (original draft); HU, TM, SN, IS, MM, and TM: Writing (review and editing). 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.

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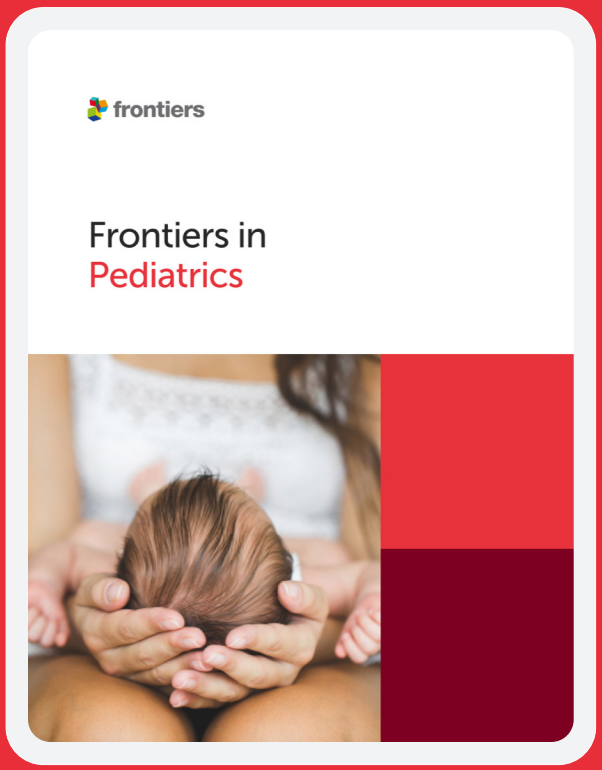


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