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Investigating exposures and respiratory health in coffee workers

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Published in
Frontiers in Public Health

ISSN 1664-8714
ISBN 978-2-83250-260-0
DOI 10.3389/978-2-83250-260-0

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Investigating exposures and respiratory health in coffee workers

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Citation

Virji, M. A., Cummings, K. J., Cox-Ganser, J. M., eds. (2023). *Investigating exposures and respiratory health in coffee workers*. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-83250-260-0

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frontiers | Frontiers in Public Health

TYPE Editorial
PUBLISHED 08 September 2022
DOI 10.3389/fpubh.2022.1026430

OPEN ACCESS

EDITED AND REVIEWED BY
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SPECIALTY SECTION
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

RECEIVED 23 August 2022
ACCEPTED 25 August 2022
PUBLISHED 08 September 2022

CITATION
Virji MA, Cummings KJ and Cox-Ganser JM (2022) Editorial: Investigating exposures and respiratory health in coffee workers. *Front. Public Health* 10:1026430. doi: 10.3389/fpubh.2022.1026430

Editorial: Investigating exposures and respiratory health in coffee workers

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KEYWORDS

coffee workers, respiratory diseases, α-diketones, dust, engineering controls intervention

Editorial on the Research Topic
Investigating exposures and respiratory health in coffee workers

Workers in the coffee industry face a variety of inhalational hazards. These range from predominantly organic dust, endotoxin, and green and castor bean allergen exposures in the primary processing factories to dusts, gases, and vapors including α-diketones in coffee production facilities (1–5). Previously documented respiratory health effects include symptoms such as wheeze, cough, and dyspnea, bronchial hyperresponsiveness, reduced spirometric parameters, and chronic lung diseases including asthma and obliterative bronchiolitis (OB) (3, 5–10). Some of these studies are decades old, while some are notable for small size and limited exposure assessments. In this special issue of *Frontiers in Public Health* on "Investigating exposures and respiratory health in coffee workers", a series of articles explores in detail the exposures, emissions, engineering controls, and health consequences across the contemporary coffee industry by describing studies of primary processing in 16 factories in two African countries and coffee production in 17 facilities in the United States.

The article by Bratveit et al. summarizes exposures, health effects and exposure-response relationships in a combined dataset of cross-sectional studies conducted in the previous decade in primary coffee processing factories in Tanzania and Ethiopia. At these factories, green coffee beans are cleaned, hulled, sorted and packaged for shipping. High levels of organic dust and endotoxin exposures were measured that frequently exceeded their respective occupational exposure limits. They also report increased prevalence of chronic respiratory symptoms, lowered forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) that were significantly associated with cumulative organic dust exposures in male workers. They also highlight the importance of increasing health and safety knowledge and competency among health personnel, politicians, and stakeholders for prevention of occupational injuries and diseases in these two developing countries.

Other articles in this issue are based on data collected by the U.S. National Institute for Occupational Safety and Health (NIOSH) at coffee production facilities (11). In these facilities, managers and employees were primarily concerned about the risk of OB in relation to exposure to α-diketones, especially in light of the recommended exposure limits (RELs) for diacetyl and 2,3-pentanedione established by NIOSH in 2016 (12). Previous studies had demonstrated adverse respiratory effects among workers exposed to α-diketones in workplaces manufacturing or handling flavoring chemicals or flavored food products (13).

In the NIOSH evaluations, extensive exposure assessments were conducted for diacetyl, 2,3-pentanedione and volatile organic compounds during coffee handling, roasting, grinding, flavoring, packaging, shipping and work in quality control and cafés (LeBouf, Blackley et al.). These data were used to evaluate exposure determinants and emissions factors to facilitate prioritization of exposure mitigation and to generate metrics of peak, average, and cumulative exposure for epidemiologic analysis (Virji, Cummings et al.; LeBouf, Ranpara et al.). An innovative approach was taken to model diacetyl and 2,3-pentanedione exposure determinants using Bayesian mixed models and a Bayesian model averaging method (Blackley et al.). The authors identified determinants with higher exposures such as grinding or open storage of coffee beans, which may be amenable to modification, and those with low exposures such local or general exhaust ventilation, whose use can be encouraged. They highlight some challenges including effectively assessing complex mixtures of chemicals, historical exposure characterization, and collecting more refined exposure determinants.

The health assessment articles report a range of upper and lower respiratory symptoms, respiratory abnormalities and asthma in these coffee production workplaces, including a case of OB in a worker exposed to flavoring chemicals (Harvey, Fechter-Leggett et al.; Harvey, Blackley et al.). The authors suggest that the patterns of symptoms and lung function abnormalities may be indicative of early disease markers or subclinical disease. Decrements in percent predicted FEV_1 and FVC and small airway abnormality on impulse oscillometry were associated with various metrics of exposure to diacetyl, 2,3-pentanedione and the sum of the two α-diketones (Virji, Fechter-Leggett et al.). These effects were strongest among flavoring workers but were also observed in non-flavoring workers. Although the health assessment and exposure-response analysis were extensive, the authors report certain challenges and limitations such as modeling mixed exposures, potential for healthy worker survivor effect, recruitment bias, and few cases of abnormal spirometry.

The article by Johns et al. discusses the impact of various factors and assumptions of risk assessment such as the choice of health effect, use of human or animal studies, quality of exposure assessment, inter-species extrapolation and uncertainty factor that have resulted in a wide range of suggested exposure limits. The authors emphasize the need for transparency in assumptions and methods used to understand the variability in the proposed exposure limits. While additional data are gathered to fill in knowledge gaps in risk assessment, mitigating exposures to α-diketones in coffee production offers the best opportunity to prevent adverse respiratory health outcomes (Stanton et al.) (14). Indeed, the findings of Stanton et al. demonstrates that installing ventilated enclosure on grinding equipment significantly reduced α-diketone exposures near grinders by 75–95%, and in the rest of the facility by 15–61%. Installing engineering controls was also recommended in the study of primary coffee processing.

In both the coffee processing and production studies, standardized data collection enabled data aggregation, facilitating the detection of exposure-response relationships that were otherwise inconsistent between Tanzania and Ethiopia or may not have been observed in individual U.S. production facilities. Given the large number of small- to medium-sized facilities across most industries, these studies highlight the benefits of standardizing data collection and data pooling to increase sample size and the power to detect subtle exposure-response relationships, achieve a more representative population, and make robust inferences (Virji, Cummings et al.). Indeed, aggregating data across multiple industrial, occupational or disease cohorts has long been conducted to take advantage of increased population size (15–17). There are numerous examples of such epidemiologic data aggregation, a vast majority of which are done in a *post-hoc* manner (18), but include some *a priori* aggregation planned in the study design phase (19). *A priori* aggregation is most desirable because a common approach is used to collect data which minimizes differences among studies.

There are likely overlapping health effects of different respiratory hazards that coffee production workers are exposed to. Similar clinical and functional effects can occur in asthma, OB and other chronic respiratory diseases, making it difficult to distinguish among health outcomes. Advanced machine learning methods now make it feasible to explore underlying patterns in multiple symptoms and lung function tests that may help to classify workers into groups indicative of different health outcomes or different stages of disease (20). Such methods may identify early disease stage which can enable timely intervention to prevent the development or progression of lung disease and protect co-workers.

Modeling exposure-response relationships for mixed exposures is challenging, despite efforts to bring attention, resources, and tools to address mixtures (21). Single chemical models of chemical mixtures do not represent the workplace reality, and statistical approaches may not adequately address highly correlated exposures in the same model. Alternatively, multiple chemicals can be combined to generate an aggregate value based on simple addition as was done in

the NIOSH study or taking into consideration quantitative structure-activity relationships.

The success of these studies is in part attributed to the well-planned, standardized data collection combined with comprehensive, high-quality health and exposure assessments that led to robust results. The articles in this series enhance knowledge of exposure-response relationships for α-diketones and show efficacy of well-designed controls. A highlight of this research is the integration of exposure and health characterization for evaluating exposure determinants and risk factors for adverse health outcomes, risk assessment tools, and the efficacy of engineering controls. This approach fits within the paradigm of translational research framework for environmental health science aimed to maximize public health benefit of research studies (22, 23). Such an integrated approach can lead to more accurate health risk estimates and appropriate and targeted exposure mitigation recommendations, ultimately resulting in a reduction in the burden of adverse respiratory health outcomes for workers.

Author contributions

MV, KC, and JC-G contributed to the conception and design of the study. MV wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

Acknowledgments

The authors thank the workers for participating in the NIOSH Health Hazard Evaluation Program and members of the NIOSH field teams for their contributions to data acquisition. The authors acknowledge Dr. David Weissman for his review of the manuscript.

Conflict of interest

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

Publisher's note

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frontiers in Public Health

PERSPECTIVE
published: 11 November 2021
doi: 10.3389/fpubh.2021.705225

A Strategy for Field Evaluations of Exposures and Respiratory Health of Workers at Small- to Medium-Sized Coffee Facilities

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Coffee production is a global industry with roasteries throughout the world. Workers in this industry are exposed to complex mixtures of gases, dusts, and vapors including carbon monoxide, carbon dioxide, coffee dust, allergens, alpha-diketones, and other volatile organic compounds (VOCs). Adverse respiratory health outcomes such as respiratory symptoms, reduced pulmonary function, asthma, and obliterative bronchiolitis can occur among exposed workers. In response to health hazard evaluations requests received from 17 small- to medium-sized coffee facilities across the United States, the National Institute for Occupational Safety and Health conducted investigations during 2016–2017 to understand the burden of respiratory abnormalities, exposure characteristics, relationships between exposures and respiratory effects, and opportunities for exposure mitigation. Full-shift, task-based, and instantaneous personal and area air samples for diacetyl, 2,3-pentanedione and other VOCs were collected, and engineering controls were evaluated. Medical evaluations included questionnaire, spirometry, impulse oscillometry, and fractional exhaled nitric oxide. Exposure and health assessments were conducted using standardized tools and approaches, which enabled pooling data for aggregate analysis. The pooled data provided a larger population to better address the requestors' concern of the effect of exposure to alpha-diketones on the respiratory heath of coffee workers. This paper describes the rationale for the exposure and health assessment strategy, the approach used to achieve the study objectives, and its advantages and limitations.

Keywords: data pooling, harmonization, coffee roasting and packaging, alpha-diketones, respiratory health, exposure assessment

OPEN ACCESS

Edited by:
Henri Heussen, Cosanta BV, Netherlands

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Magne Bråtveit, University of Bergen, Norway
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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: *04 May 2021*
Accepted: *13 October 2021*
Published: *11 November 2021*

Citation:
Virji MA, Cummings KJ and Cox-Ganser JM (2021) A Strategy for Field Evaluations of Exposures and Respiratory Health of Workers at Small- to Medium-Sized Coffee Facilities. Front. Public Health 9:705225. doi: 10.3389/fpubh.2021.705225

INTRODUCTION

Coffee production is a global industry with roasteries located throughout the world. Production involves receiving green (raw) beans, roasting green beans, grinding roasted beans, in some facilities flavoring roasted ground or whole beans, weighing and packaging roasted and ground, flavored or unflavored coffee, and shipping (1). Workers in this industry are exposed to complex mixtures of gases, dusts, and vapors including carbon monoxide, carbon dioxide, coffee dust, allergens, alpha-diketones, and other VOCs (1). Adverse respiratory health outcomes such as respiratory symptoms,

decreased pulmonary function, asthma, and obliterative bronchiolitis (OB), a rare, irreversible lung disease, can occur among exposed workers (2). OB is found among workers exposed to flavoring chemicals in a variety of food processing and flavoring-manufacturing industries (3). Inhalation exposure to alpha-diketones including 2,3-butanedione (diacetyl) and 2,3-pentanedione (acetyl propionyl) in flavorings or natural sources is associated with the development of OB, based on human epidemiologic and animal studies. Mitigating these exposures offers the best opportunity to prevent these adverse respiratory health outcomes (4, 5).

Between 2008 and 2012, two cases of OB were identified in coffee production co-workers exposed to flavoring chemicals (6). Subsequently, three additional cases were diagnosed in former flavoring room workers of the same facility (7). These five cases of OB prompted a request in 2012 to the National Institute for Occupational Safety and Health (NIOSH) to conduct a health hazard evaluation (HHE) to investigate exposures and respiratory effects during coffee production (7, 8). Subsequently, NIOSH received 17 additional HHE requests during 2015–2017 from small- to medium-sized coffee workplaces throughout the United States. HHE requestors expressed concerns about exposure to alpha-diketones and the potential respiratory health effects. The HHE investigations were conducted with a focus on quantifying exposures and adverse respiratory health, evaluating exposure-response relationships and identifying opportunities for exposure mitigation.

HHEs are public health responses to emerging health and safety issues in workplaces mandated by the Occupational Safety and Health Act of 1970 and the Mine Safety and Health Act of 1977, with advantages and some limitations. Their narrowed focus on a particular workplace issue facilitates in-depth investigation that can lead to a resolution of the issue that triggered the investigation, however, the information generated may not always be generalizable knowledge that can be applied more broadly for prevention. Moreover, HHE investigations are constrained by time and resources dedicated to any one investigation. In the coffee industry (North American Industry Classification System code 311920) in 2016, 93% of the establishments were small- (<20 workers) to medium-sized (≥20–<500 workers) workplaces employing 48% of the workforce (9). Individually, these facilities would not have a large enough workforce to provide sufficient power to detect subtle health risks; pooling data across facilities could provide a large enough population to explore exposure-response relationships.

Harmonization of data collection is challenging (10–15) but is required to enable pooling of data for aggregate analysis. A primary challenge is the balance between recording data unique to a particular worksite and collecting data that fit into predetermined standardized categories. With greater standardization and uniformity of data collection, the uniqueness and specificity of each facility may be lost, resulting in exposure or health misclassification, causing loss of any potential gain in statistical power from increase in sample size. There are many examples of successful pooling of data from multiple sources for epidemiologic or exposure studies within an industry, such as the studies in the asphalt and rubber manufacturing industries that pooled exposure data from several European countries (16, 17). However, pooling data across industries is challenging, as highlighted by the numerous calls and proposals over the past three decades for standardization and the development of exposure surveillance databases (18–26); these efforts have failed to gain traction in part because of the complexity and number of data elements to be uniformly collected (27). Within the NIOSH HHE Program, there are some examples of data pooling such as in the microwave popcorn industry where health and exposure data were combined from six plants (28). Additionally, a noise exposure dataset was created by pooling data from 77 HHE reports across various industries, and a dataset of exposure to three solvents, methylene chloride, 1,1,1-trichloroethane, and trichloroethylene was created by pooling data from 63 to 89 HHE and 6-22 Industry Wide Studies reports for the different solvents, which included data elements such as industry, job, hearing protection use, activity, ventilation, and sampling details (29, 30). Some of the variables in the solvents dataset were created after data collection from details in the reports such as the process condition, proximity to source, and ventilation. To ensure systematic collection of contextual information, data elements can be gathered in a tiered approach from more general information collected for all investigations in the first tier that can be pooled across investigations, to more specific information collected in higher tiers targeting nuanced aspects of each facility, and may not always be amenable to pooling, or may be standardized post collection. Such a tiered approach ensures standardized data collection for some basic variables to enable pooling, at the same time enabling the collection of facility specific details to achieve the objectives of the investigation.

PROJECT OVERVIEW AND OBJECTIVES

NIOSH conducted HHEs at 17 coffee facilities in several geographical locations across the United States during different seasons in 2016–2017. After the HHE investigations were completed and facility-specific reports issued, data from the 17 investigations were pooled to better address HHE requestors' primary concern of whether exposure to alpha-diketones was associated with adverse respiratory effects. At each facility, all workers were invited to participate; 229 (35%) workers participated in the exposure survey and 384 (58%) participated in the health investigation. The analysis of the pooled data was approved by the NIOSH Institutional Review Board (IRB). The specific objectives of the pooled analysis were to (1) quantify full-shift, short-term task-based, and instantaneous exposures to alpha-diketones, (2) identify and quantify factors affecting short-duration and full-shift exposures to alpha-diketones, (3) characterize the respiratory health of workers including pulmonary function and symptomology, (4) evaluate exposure-response relationships with exposure metrics and surrogates such as tasks or proximity to process, and (5) evaluate emission sources and recommend exposure control options.

The objective of this paper is to describe the rationale for the exposure and health assessment strategy, the approach used to achieve the study objectives, and its advantages and limitations.

METHODS AND DISCUSSION

Approach

The investigations focused on characterizing both long-term average exposures and high-intensity, short-duration "peak" exposures to diacetyl and 2,3-pentanedione, because these exposures may be associated with small airways damage related to OB; peak exposures can potentially overwhelm the capacity of normal defense mechanisms and induce adverse health effects (31, 32). Peak exposures to diacetyl have been documented in the microwave popcorn industry and at the sentinel coffee facility and may have contributed to disease in OB cases with relatively lower average exposures (28, 33, 34); the role of peak exposure is asthma is also well recognized (35), though relevant exposure to asthmagens such as green coffee dust and allergens could not be assessed quantitatively due to limited time and resources.

Exposure Measurement Strategy

To understand personal exposures and characterize emission sources, both personal and area sampling was conducted for alpha-diketones (1). Personal full-shift, short-duration task, and instantaneous peak exposures were collected to better understand their influence on the disease process, while full-shift and instantaneous area samples were collected to identify sources of emissions to prioritize opportunities to control exposures. Instantaneous samples were also analyzed for 18 additional VOCs including: acetaldehyde, acetonitrile, ethanol, isopropyl alcohol, acetone, n-hexane, chloroform, methylene chloride, methyl methacrylate, benzene, ethylbenzene, toluene, styrene, m, p-xylene, o-xylene, a-pinene, and d-limonene. Repeat measurements were collected for all sample types whenever possible to better capture exposure variability. This sampling and analysis approach enabled: (1) characterization of exposure variability through repeated measurements, (2) quantification of multiple alpha-diketones to evaluate their individual and combined effect on respiratory health, (3) development of multiple current or worklife exposure metrics to test different hypotheses of the effect of peak, average, cumulative exposure or exposure duration on health, (4) identification of mixed exposures, albeit limited to VOCs, and their role in the disease process, (5) better understanding of factors affecting exposures by collecting contextual information as described in the next section, and (6) characterization of emission sources to better guide various exposure mitigation strategies. Although the exposure monitoring was comprehensive, it was time and resource intensive to collect five different types of samples, i.e., personal full-shift, short-duration tasks, and instantaneous samples, and area full-shift and instantaneous samples, but necessary to achieve the investigation objectives.

Exposure Factors, Database Development, and Modeling Exposure Determinants

An integral component of exposure assessment is evaluating exposure variability and understanding factors affecting exposures. Statistical modeling of exposure factors requires the collection of both exposure measurements and detailed contextual information on workplace characteristics such as: processes, control measures, environmental conditions, jobs, tasks, source materials, worker activities, and other relevant work environment factors (18, 36–40). The source-receptor model is a conceptual model that describes the physical pathway of exposure from its generation at the source through different transport compartments and mechanisms to the route of entry at the receptor, and provides a framework to systematically evaluate and collect information on potential micro-level exposure determinants (36–38). At each stage, numerous factors can influence exposure which have been well documented in the literature and should be considered for data collection (36, 40). These within-facility micro-level factors explain differences in exposure caused by tasks or source characteristics. However, differences in exposure can also arise from differences among facility characteristics not directly associated with the physical path of exposure, i.e., higher level factors such as size of the facility, number of workers, production volumes, worker health and safety training, facility safety culture and other organizational factors (37, 38). These higher-tiered factors are particularly important when data are pooled across workplaces or multiple industries. Some factors may be constant within a facility and gathered anytime during the exposure survey (such as general exhaust ventilation parameter), while others may vary in time requiring collection during air sampling (such as tasks, tools, amount of time in different locations) (41). Whereas, attempts to standardize the collection and storage of contextual information have not gained traction (15, 18, 21, 22, 25, 26, 41, 42), numerous studies have successfully collected and used contextual information specific to their research to better understand the causes of variation or to predict exposures (41–43).

In this study, collecting the desired information on exposure determinants during sampling was challenging because of limited time, staff, and resources available to conduct the assessments at each facility. **Table 1** presents a list of the key determinants along the source-receptor pathway and some higher-level facility related factors that were collected. Information on facility level determinants which did not vary within a worksite was systematically collected on forms prior to or at some point during the site visit. However, only a handful of time varying factors were gathered during the survey mostly as notes, but which may have the greatest potential for explaining exposure variability within a facility. Determining a priori the time-varying factors to systematically capture during sampling was challenging as there were numerous short-lived activities which would require continuous observation of the monitored workers to capture accurately. The workers performed numerous tasks and were highly mobile making their continuous observation not practicable. Nevertheless, the contextual information collected will be used in multiple regression models of full-shift and task-based diacetyl and 2,3-pentanedione exposure using advanced Bayesian methods that simultaneously account for repeated measures, measurements below the limit of detection, correlation among predictor variables, variable selection for multiple regression modeling and model averaging of multiple final models (44).

TABLE 1 | Data elements collected during the 17 HHEs to describe exposures.

Variables	Value and description
Facility level information	
• Region	• US geographical region of facility
• Total employees	• Total number of employees on site
• Production employees	• Number of production employees on site
• Building size	• Size in square feet
• Production ares size	• Size in square feet
• Building type	• Production, café, administration
Source characteristics	
• Production rate/capacity	• Amount of material processed per day or capacity
• Percentage source material	• Percent whole bean or ground coffee
• Exposure sources	
• Open containers	• Number of sources within 10 ft
	• Number of open containers of products stored
• Flavoring	• Flavoring added to coffee beans or ground coffee
Work organization	
• Department	• Department or work unit
• Location/work area	• Worker or area sampler location
• Job title	• Worker job title sampled
• Shift	• Work shift and shift hours
• Task/activity	• Task or activity sampled
Sampling and analysis	
• Date	• Sampling date
• Season	• Sampling season
• Sample type 1/ 2	• Area, personal/full-shift, task-based, instantaneous
• Sampler type	• Silica gel tube, canister
• Method	• Analytical methods numbers
• Analyte	• Analytes quantified, e.g., diacetyl, ethanol, etc.
• Concentration/unit	• Concentration value and units
• LOD	• Limit of detection concentration and sample ID
• Duration	• Sample duration or duration of tasks
Exposure controls	
• Process isolation	• Isolated area or process from other areas
• Natural ventilation	• Open windows or doors
• GEV	• General exhaust ventilation present and working
• Makeup air	• Mechanical makeup air
• Fans	• Fans used
• Machine LEV	• Local exhaust ventilation of machines/processes
• Machine enclosure	• Enclosure of machines/processes
• Automation	• Automation of machines/processes
• Cleaning method	• Vacuum, dry sweep, compressed air, wet cleaning
• PPE	• Type of respirator used

Exposure Modules and Job/Task Exposure Matrix

Exposure assessment is a critical component of epidemiologic studies, but can present a significant challenge (45, 46). Many epidemiologic studies use exposure proxies such as job or task exposure matrices (J/TEM), expert judgment, or self-reports (47, 48). Poor exposure characterization can lead to exposure misclassification and attenuation of exposure-response relationships (49) and improper intervention (50). Although personal exposure data are rare in epidemiologic studies, exposure measurements and their determinants collected for jobs or tasks on a subset of workers can be used to create quantitative J/TEM. The J/TEM can be combined with frequency and duration of job or task reported in a questionnaire to calculate exposures for individual study participants (51–53). This approach has been used successfully in several studies (54–56). In situations where job-related exposures are highly variable and depend on tasks performed, a TEM may be preferable (57–59). Under these circumstances, TEMs can result in stronger associations with respiratory health outcomes in different industries compared to JEMs (60–63). Thus, combining worker-specific data (e.g., frequency and duration of tasks performed) from a questionnaire with a J/TEM can result in more accurate estimate of worker exposures compared to a generic J/TEM as it takes into account worker-specific exposure circumstances (64–66). Quantitative exposures are essential to minimize exposure misclassification and obtain quantitative exposure-response relationships to support the development of exposure limits and design of optimal prevention strategies (67).

In this study, information on jobs performed and tenure in the coffee or flavoring industry was gathered in the work history questionnaire. The exposure module elicited information on the frequency and duration of tasks performed in current job, which captures and reflects worker-specific exposure circumstances (**Table 2**). However, the duration and frequency of tasks performed in previous jobs was not gathered because of the potential for error or bias in recalling such detailed information about tasks in past jobs (68). Full-shift and task-based exposure measurements enabled the construction of JEM and TEM. Furthermore, J/TEM cells included average (the minimum variance unbiased estimator of arithmetic mean) and 95th percentile (P95) job or task exposures as well as measures of peak exposures (P95) from instantaneous sampling. The exposure profiles from multiple tasks and jobs held by workers can be summarized to obtain current or worklife highest, average, and cumulative exposure summary metrics to explore multiple hypotheses about exposure-response relationships. Specifically, these metrics include: the highest instantaneous P95 exposure for current activities; the highest P95 and the average short-duration exposures for current tasks, weighted or unweighted by task duration and frequency; the highest (P95) and average full-shift exposure for current job; and highest (P95), average and cumulative exposures for all jobs as worklife metrics. Worklife metrics based on task-based sampling could not be calculated as historical task information was not gathered. These summary metrics can be calculated for the measured alpha-diketones, as well as their combination as a sum of total alpha-diketones concentration. Additionally, information on the frequency and duration of current tasks can be used as qualitative or quantitative surrogate of total exposure experienced during a task, which includes the combination of alpha-diketones, other VOCs, dusts and allergens depending on the task. The frequency and duration

of task information can be combined to obtain the hours per week a task is performed. Performing the task of handling green coffee beans can be a surrogate for exposure to dust and allergens that were not quantified. These wide range of metrics offer the opportunity to fully examine the effects of current or worklife exposure to specific alpha-diketones and their sum, other VOCs, dust, and allergens, peak or cumulative exposure metrics on various respiratory health outcomes of interest ranging from current symptoms to lung function parameters.

Health Assessment Strategy

Cross-sectional surveys were conducted to investigate evidence of OB, asthma and other respiratory diseases using a combination of novel and established methods described in detail by Harvey et al. (2). The questionnaire included modules on irritation, upper and lower respiratory symptoms, disease diagnoses, smoking history, work history, and exposure modules; the respiratory health questions were based on validated survey instruments. Spirometry testing was conducted following American Thoracic Society (ATS) guidelines (69) to identify functional respiratory abnormalities, and obstructive, restrictive and mixed pattern were recorded. Impulse oscillometry (IOS) was conducted according to manufacturer instructions and published experience to augment spirometry as a more sensitive metric of small airways dysfunction that may serve as an early indicator by identifying abnormalities in workers with normal spirometry (70, 71). Bronchodilator was administered for those with abnormal spirometry or IOS to evaluate whether these abnormalities were fixed or reversible. Testing for fractional exhaled nitric oxide (FeNO) was conducted following ATS guidelines (72) to identify those with eosinophilic airway inflammation, commonly seen in allergic or Immunoglobulin E mediated asthma.

The health effects of concern in the coffee production facilities include asthma and OB, which may manifest with a range of overlapping respiratory symptoms and functional abnormalities. The objective of the health investigation was to assess the burden of respiratory abnormalities, in particular early markers of disease that could inform prevention. For instance, spirometry provides objective measures of functional abnormalities and their severity, but may be normal in early OB or mild asthma on account of insensitivity to changes in the small airways (73–75). The addition of IOS was thus intended to capture small airways dysfunction that can occur in both OB and asthma and may precede spirometric detection. For those participants with functional abnormalities, performing lung function testing before and after administration of bronchodilator can help identify workers with reversible abnormalities likely related to asthma from those with fixed abnormality likely associated with OB. Test of FeNO may further distinguish those with allergic asthma from those with irritant asthma (72).

IOS is not a new technology (76), but more recent portable units facilitate its use beyond the pulmonary function laboratory, including field studies of the workplace. IOS measures the mechanical properties of the respiratory system including upper and intrathoracic airways, lung tissue and chest wall, specifically respiratory impedance, and is thought to be sensitive for dysfunction of the small airways (77, 78). Histopathological changes in small airways of workers exposed to alpha-diketones are characterized by bronchiolar wall fibrosis, leading to luminal

TABLE 2 | Questions used in the exposure module of the questionnaire to assess exposures.

What is your current job? Job title, tenure years, hours worked/day, days worked/week
What are your past jobs in this facility? Job title, tenure years, hours worked/week, tasks performed
What are your past jobs in other coffee or flavoring facilities? Facility, job title, tenure years
Production area work or by-stander Location, hours in the area/week, production area worker or passer-by
Do you work with green beans?
Do you work in the warehouse or where finished goods are stored? Location of warehouse (on site/off site)
Do you roast coffee beans? Number of days/week, number of hours/day, roaster ID, collect roast sample and smell beans
Do you grind coffee beans? Number of days/week, number of hours/day, grinder ID, grind flavored/unflavored beans
Do you move roasted beans or ground coffee? Number of days/week, number of hours/day
Do you flavor coffee (whole bean or ground coffee)? Number of days/week, number of hours/day, use liquid/powder flavoring, flavor whole bean/ground coffee
Do you package coffee (whole bean or ground coffee)? Number of days/week, number of hours/day, packaging machine/ by hand, machine ID, package machine ID, package flavored/unflavored, repackage faulty packaging
Do you clean containers of roasted coffee? Number of days/week, number of hours/day, clean storage container/roaster/grinder/packaging machine
Do you perform maintenance on coffee production machines? Number of days/week, number of hours/day
Do you perform any quality control activities? QC green beans/roast beans, number of days/week, number of hours/day
Do your grind coffee beans as part of quality control? Number of days/week, number of hours/day, grind flavored/unflavored coffee, flavor coffee
Do you flavor coffee as part of quality control? Number of days/week, number of hours/day, use liquid/powder flavoring, flavor whole bean/ground coffee
Do you perform quality control checks such as brewing, cupping, and tasting? Number of days/week, number of hours/day
Do you work in the café? Number of days/week, number of hours/day
Do you grind coffee beans in the café? Number of days/week, number of hours/day, grind flavored/unflavored beans
Do you flavor brewed coffee in the café? Number of days/week, number of hours/day, use liquid/powder flavoring
Are you ever within an arm's length of these locations/units? Coffee roaster, cooling bins of roasted coffee, grinder, hoppers or containers of roasted coffee, coffee being packaged, packaged coffee, flavoring is being added or mixed

narrowing and obliteration that obstructs airflow (79). A growing body of literature, particularly from the experience with lung transplant patients and survivors of the World Trade Center disaster, indicates that oscillometry can detect this small airway obstruction at an earlier stage than spirometry (73, 80).

Despite these advantages, IOS does pose challenges. Normative values to aid in the interpretation of IOS parameters are not robust and available for only select small sub populations (74, 81). Additionally, little to no research has explored the underlying patterns in the IOS parameters that may identify new markers of early pathophysiologic changes that may be linked to different disease outcomes. There is a potential wealth of information locked in the numerous IOS parameters and flow and volume parameters from spirometry that are not regularly used, such as forced expiratory volume in 3 s (FEV3). If these IOS and spirometry parameters are combined with symptoms, disease diagnoses, demographics, and exposure data to explore patterns, they may provide invaluable insights into early markers of adverse health outcomes (82). Underlying patterns in these complex set of variables can be brought to light by advanced machine learning methods, which may help identify subgroups of workers at different stages of disease development (83), and enable timely intervention to prevent progression of adverse respiratory health outcomes. The combination of these tests along with advanced data analyses will be used to potentially separate those with asthma from those with effects consistent with OB and to potentially identify early markers of adverse health outcomes.

The health assessment strategy, while extensive and thorough, has several limitations with some that are inherent in the nature of HHE mechanism including: (1) inability to assess longitudinal change in symptoms or lung function because of the cross-sectional nature of the study, (2) potential for healthy worker survivor effect because of enrolling current workers only, (3) potential for bias if differential participation by health status occurred as participation was not 100%, and (4) potential for underestimation of exposure and respiratory health burden in the industry as the HHE requests were often made by management at facilities without known health problems. Additionally, despite the extensive respiratory health evaluations, additional medical testing such as collecting blood samples for immune response to allergens and potential novel biomarkers of early pathophysiologic changes, radiographic imaging that may be more sensitive than lung function for small airway diseases and performing challenge testing to assess for airways hyperresponsiveness could result in better characterization of respiratory health.

Exposure-Response Modeling

A variety of standard and advanced statistical models will be fit for the various outcome measures of interest with the many quantitative exposures to alpha-diketones and quantitative and qualitative metrics of task exposure surrogates. Least-square regression will be used to fit models for continuous outcomes from FeNO, spirometry and IOS parameters. Logistic regression models will be used to model polytomous outcomes from multiple categories of IOS, spirometry, asthma and subgroups identified by machine learning, and binary outcomes from symptoms, chronic disease diagnoses, and other asthma variables. All models will include adjustment for age, sex, race, body mass index, height, weight, smoking status, allergic status, and tenure as appropriate. Model with continuous exposure metrics will be evaluated for non-linearity through fitting restricted cubic splines (84). The various tasks as exposure surrogates are not mutually exclusive thus not independent and cannot be modeled separately or put in the same model due to correlation among tasks. These associations will be explored using advanced statistical methods to account for the effects of multiple correlated exposures and their interactions (85–88).

Anticipated Outcomes of the Study

The exposure assessment strategy facilitates several exposure metrics to be generated to explore multiple questions on the nature of the exposure-response relationships. The respiratory health outcomes include upper or lower respiratory symptoms, disease diagnoses, spirometry and IOS parameters, and FeNO values. Thus, a spectrum of adverse health effects can be explored, including those that may be related to flavoring chemicals and those that may be related to allergen and irritant exposures such as green coffee bean and dust exposures. The analyses using machine learning methods may identify underlying patterns of various health measures parameters that may represent new markers of early health effects. The various exposure-response relationships can address: (1) the relevance of peak, average, cumulative intensity or duration of exposure, (2) the role of individual or combined alpha-diketones or mixed VOC and dust exposures, and (3) the shape of the exposure-response relationship for the various health outcomes.

Results of exposure modeling can identify the effects of contextual information on full-shift and task-based exposures to enable identification and prioritization of exposure mitigation options. The use of the advanced Bayesian modeling method facilitates the evaluation of all determinants that make it into the numerous (could be as high as one thousand) final models which are then averaged to summarize the importance (% presence in final models) and effect (parameter estimate) of each variable; in traditional modeling, such decisions are made based on a single final model fit using a statistically convenient strategy of forward selection or backward elimination (44). The set of important exposure determinants can inform controls selection by identifying factors with the greatest potential impact on exposure to prioritize.

Challenges, Limitations and Reflections on the Approach

With any approach, there are trade-offs and limitations of selected study design or strategy. Primary limitations of exposure assessment were: (1) not measuring exposure to dust and allergens that are important for asthma outcomes (though exposure surrogate of the task of handling green beans may provide some insights), (2) difficulty in collecting adequate detail on time-varying contextual information during exposure monitoring, and (3) impracticality of collecting task duration and frequency information for historical jobs. Job titles in

the coffee workplaces were often non-specific and did not clearly distinguish among workers and their tasks. Task-based sampling offers the opportunity to directly identify high exposure tasks for targeted controls, may provide more precise estimates of the long-term average exposures for epidemiologic studies under some circumstances when exposures are highly variable (57, 89, 90), can be used to compare calculated full-shift exposure to exposure limits through full or partial period consecutive or grab samples (91), and can provide a range of exposure metrics from average to peak exposure that can be summarized to cumulative, average or highest exposure summary metrics for epidemiologic analysis. Despite some advantages, there are a number of challenges associated with task-based sampling, including task definition, extensive sampling effort, accurately collecting information on the frequency and duration of current and historical tasks, and collecting adequate mass for quantification (68, 92–94). Personal real-time monitoring of alpha-diketones and other VOCs would have been ideal, but currently available technology, e.g., a portable Fourier Transform Infrared Spectrometer is an area sampler not suited for personal monitoring (95). With advances in sensor technologies, real-time wearable sensors may be available in the future to capture instantaneous, short-duration and full-shift exposures with one sampler to greatly reduce monitoring effort.

Collecting contextual information is challenging as it entails accounting for time over which innumerable factors may change causing measured exposures to vary considerably. Collecting time-varying contextual information requires direct observation or worker-recording of tasks, duration or frequency, and other factors along the source-receptor pathway, which is challenging and time and resource intensive (56, 96–98). Factors that are constant within a facility and do not vary over time are easier to collect but may explain limited within-facility variability. Contextual variables for task-based samples taken over a shorter period can be short lived and highly variable, and may be best recorded as present or absent to minimize error in estimating duration. New sensor technologies may make it easier to capture contextual information in real-time more accurately without having to continuously observe workers (99). For example, the Dutch Institution of Applied Science, TNO is piloting the use of sensors to detect and record proximity of workers to different sources of exposure, or placing sensors on tools or machines to record their operational information such as vibration sensors on tools or machines to indicate when in use.

While the health assessment was extensive, a comprehensive health assessment is time and resource prohibitive and not practicable for HHEs. Additionally, some potential biases could have been minimized by including former workers and recruiting additional worksites with potentially more varied burden of respiratory disease and exposure experiences, but this was not feasible. Likewise, longitudinal follow-up study design would be ideal but not typical within the HHE Program context. Nevertheless, the combination of several tests with advanced machine learning methods holds promise for the potential identification of early markers of respiratory effects.

CONCLUSION

The overall goal of the study was to characterize exposure conditions, respiratory health, and exposure-response relationships among coffee production workers, ultimately leading to exposure mitigation and prevention of adverse respiratory health outcomes. To achieve these goals, extensive exposure and health assessments were conducted within the confines of the HHE Program. Data were pooled to provide a large enough population to explore exposure-response relationships to address one of the requestors' primary concerns about the effect of exposure to alpha-diketones on the respiratory heath of coffee workers. Strengths and limitations of the approaches used are discussed. It must also be emphasized that when use of secondary data from individual HHEs is deemed to constitute human subjects research, all regulations governing human subjects research must be followed including approval from the NIOSH IRB.

DATA AVAILABILITY STATEMENT

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

AUTHOR CONTRIBUTIONS

MV, KC, and JC-G contributed conception and design of the study. MV wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

FUNDING

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

ACKNOWLEDGMENTS

The authors thank the workers for participating in the NIOSH Health Hazard Evaluation Program and members of the NIOSH field teams for their contributions to data acquisition. The authors acknowledge Drs. Reid Harvey and Brie Hawley Blackley for their review of the manuscript.

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frontiers in Public Health

REVIEW
published: 20 September 2021
doi: 10.3389/fpubh.2021.730201

Dust Exposure and Respiratory Health Among Workers in Primary Coffee Processing Factories in Tanzania and Ethiopia

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OPEN ACCESS

Edited by:
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Reviewed by:
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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: *24 June 2021*
Accepted: *23 August 2021*
Published: *20 September 2021*

Citation:
Bråtveit M, Abaya SW, Sakwari G and Moen BE (2021) Dust Exposure and Respiratory Health Among Workers in Primary Coffee Processing Factories in Tanzania and Ethiopia. Front. Public Health 9:730201. doi: 10.3389/fpubh.2021.730201

Introduction: In primary coffee factories the coffee beans are cleaned and sorted. Studies from the 80- and 90-ties indicated respiratory health effects among the workers, but these results may not represent the present status. Our aim was to review recent studies on dust exposure and respiratory health among coffee factory workers in Tanzania and Ethiopia, two major coffee producing countries in Africa.

Methods: This study merged data from cross-sectional studies from 2010 to 2019 in 4 and 12 factories in Tanzania and Ethiopia, respectively. Personal samples of "total" dust and endotoxin were taken in the breathing zone. Chronic respiratory symptoms were assessed using the American Thoracic Society (ATS) questionnaire. Lung function was measured by a spirometer in accordance with ATS guidelines.

Results: Dust exposure among male production workers was higher in Ethiopia (GM 12 mg/m^3; range 1.1–81) than in Tanzania (2.5; 0.24–36). Exposure to endotoxins was high (3,500; 42–75,083) compared to the Dutch OEL of 90 EU/m^3. The male workers had higher prevalence of respiratory symptoms than controls. The highest symptom prevalence and odds ratio were found for cough (48.4%; $OR = 11.3$), while for breathlessness and wheezing the odds ratios were 3.2 and 2.4, respectively. There was a significant difference between the male coffee workers and controls in the adjusted FEV1 (0.26 l/s) and FVC (0.21 l) and in the prevalence of airflow limitation (FEV1/FVC <0.7) (6.3 vs. 0.9%). Among the male coffee workers, there was a significant association between cumulative dust exposure and the lung function variables FEV1 and FVC, respectively.

Conclusions: The results suggest that coffee production workers are at risk of developing chronic respiratory symptoms and reduced lung function, and that the findings are related to high dust levels. Measures to reduce dust exposure should be targeted to factors identified as significant determinants of exposure.

Keywords: coffee workers, dust exposure, respiratory symptoms and lung function, endotoxin, exposure assessment

INTRODUCTION

Before coffee beans are brought to the primary coffee processing factories, they are processed at the farm to remove the outer layers of the coffee cherries. In the primary factories the beans are mechanically cleaned of debris, hulled to remove the hard cover, and then sorted by size and weight. Damaged and discolored coffee beans may also be removed by handpicking. Finally, the green coffee beans (GCB) are packed for transportation. Only a few of the primary processing factories include the roasting process. Roasting mostly takes place in the countries the coffee is exported to. Several studies describe aspects of work and health in coffee roasting facilities. Jones et al. (1) found significantly lower residual FEV1 among US workers handling green coffee, with long work duration, while in Germany, Oldenburg et al. (2) did not find an association between the level of coffee dust exposure and lung function impairment. Cross-shift reductions in lung function were found among Yugoslavian coffee workers (3). Sensitization to allergens in GCB might be one of the factors involved in workers respiratory effects, including work-related asthma (4, 5).

Only a few older studies have been conducted in primary coffee factories, although numerous workers are engaged worldwide in this part of the coffee production process. Studies in primary factories in Papua New Guinea and Uganda that processed both Arabica and Robusta coffee, showed levels of total dust exposure ranging 0.7–10 mg/m^3 and 1–58 mg/m^3 (6, 7). It has been indicated that the exposure to coffee dust is likely to cause acute and chronic respiratory symptoms (7, 8). A higher prevalence of acute respiratory symptoms was found among primary coffee factories workers in Uganda and Sri Lanka compared to controls (7, 8). Furthermore, reduced lung function was found among primary coffee factory workers in Papua New Guinea (6), indicating that the coffee workers might develop a non-specific chronic lung disease due to dust exposure at work. Exposure to organic dust may also lead to increased levels of fractional exhaled nitric oxide (FENO) (9, 10), and might be an indicator of airway inflammation.

Coffee types and the processing method differ between countries, and results from previous studies on dust exposure and respiratory health may not represent the status in the present coffee processing factories. The largest coffee exporting countries in 2016 were Brazil and Vietnam with over 1.5 million tons (11), while in the present study, the focus is on two of the major coffee producing countries in Africa, Ethiopia and Tanzania. Knowledge and practice regarding health and safety is marginal in many developing countries, particularly in Africa. As a result, many countries have limited legislation and few guidelines to protect workers. This is also the situation in Tanzania and Ethiopia. In both these countries, industrial activities are increasing, and the number of occupational injuries and diseases is increasing as well. There is a lack of a political mechanism that translates this information into action, as there is minor competency in occupational health among health personnel, politicians, and stakeholders. However, both these countries have started small projects on competence building in occupational health at their main universities, and the projects included in the present study have developed from this activity (12).

The main production processes are similar in Tanzania and Ethiopia. The work tasks are mainly performed by men, including reception of coffee beans from the farms, feeding of hoppers, precleaning, hulling, grading, bulking, and packing. However, primary coffee factories may also provide an extra quality check of the coffee beans, called "hand picking." This process is performed by women only; they remove low quality, discolored beans by hand. However, there are differences in coffee types and in preprocessing of the coffee cherries at the farm before they enter the factory. These two countries were selected due to their systematic studies in coffee production, performed in cooperation with Norwegian researchers. Ethiopia and Tanzania are the world's fifth (384,000 tons) and 18th largest (48,000 tons) exporters, and number one and four in Africa, respectively. About 15 million people in Ethiopia depend on coffee production directly or indirectly for their living (13), while in Tanzania, the number of workers in the coffee sector is estimated to be above 2 million (14). The association between dust exposure and lung function was not found to be consistent when analyzing the studies from Tanzania and Ethiopia separately (15, 16) Thus, it is of interest to merge these studies to increase the study power.

The aim of this research was to review and summarize the results from studies the past 10 years on dust and endotoxin exposure, as well as on respiratory health among production workers in primary coffee factories in Tanzania and Ethiopia. Thus, the three studies from before year 2000 were not included in further analysis. We also aimed to identify determinants of dust exposure in order to suggest measures to reduce dust exposure.

MATERIALS AND METHODS

This article presents results from reanalysis of data from cross-sectional studies in primary coffee processing factories in Tanzania and Ethiopia conducted in the years 2010–2019. The included studies are on personal dust exposure in Tanzania (17) and Ethiopia (18) and respiratory health in Tanzania (15, 19–21) and Ethiopia (16, 22). Similar design and methodology were used in these studies in the two countries. Thus, personal dust samples were taken with the same sampling method, lung function was measured with identical instruments and the same standardized questionnaire were used for demographic information and chronic respiratory symptoms. When merging the data from the studies the variables from the original datasets were used with no transformation or with calculations of new variables. In both countries contextual information including characteristics of the factories, practices in processes, design of machines, and task performed by the workers during sampling was obtained by an observational checklist. The measured dust levels were presented separately for the two countries and were not merged for development of dust exposure models since there were some differences in potential determinants of dust exposure between the countries.

Settings

The research in Tanzania was done in in four primary coffee factories, each with 30–65 production workers and an annual output of about 5,000 to 19,500 tons. In Ethiopia, 12 primary coffee processing factories were included with 60–422 production workers, and an annual production of about 1,200 to 38,000 tons. The factories and the source population were the same for all outcomes; Dust exposures, respiratory symptoms, and lung function. The main production processes are quite similar in the two countries (**Figure 1**). However, while Tanzania grows both Arabica and Robusta coffee types, Ethiopia produces only Arabica coffee. In Tanzania, Arabica coffee is mostly wet preprocessed at the farm whereas Robusta coffee is dry preprocessed. In Ethiopia, Arabica coffee were either dry or wet preprocessed.

Dust and Endotoxin Measurements

Repeated personal full-shift samples of "total" dust (Tanzania; $n = 193$ and Ethiopia; $n = 360$) and endotoxin (Tanzania; $n = 154$) were taken by closed-faced 25 or 37 mm conductive cassettes at a rate of 2 l/min from the breathing zone of the production workers. Samples were analyzed gravimetrically, and a subset of samples from Tanzania was analyzed for endotoxin by kinetic chromogenic Limulus amebocyte lysate (LAL) Assay. In addition, the same methodology was used to take personal total dust samples from female hand-pickers of coffee (Tanzania; $n = 9$ and Ethiopia; $n = 115$). The results were compared to the Norwegian Occupational Exposure Limit (OEL) for organic total dust of 5 mg m^{-3} (23). For endotoxin we have used the Dutch health-based recommended occupational exposure limit of 90 EU/m^3 as a reference value (24).

Cumulative dust in the coffee factories was calculated for each worker as a product of the geometric mean (GM) of the total dust of each respective factory and the number of seasons worked in that particular factory. Workers who had worked in coffee factories other than those included in this study had additional cumulative exposure calculated as a product of the number of seasons worked in those factories and the overall GM for total dust in the measured factories. Since identical sampling methods and strategies were used in the two countries the cumulative dust variable were merged. Cumulative dust was not calculated for the control group because these workers have different types of dust exposure.

Respiratory Health Examinations

Respiratory Symptoms

We assessed chronic respiratory symptoms (yes/no) using the American Thoracic Society (ATS) standardized questionnaire among the coffee production workers from two factories in Tanzania ($n = 140$) in comparison with a control group from a beverage factory ($n = 120$) (19). The same questionnaire was used in 12 coffee factories ($n = 115$) and in three water bottling factories ($n = 110$) in Ethiopia (18).

Lung Function

Lung function was measured by a portable spirometer (SPIRARE 3 sensor model SPS 320) in accordance with ATS guidelines for spirometry in Tanzania ($n = 140$ coffee workers/120 controls)

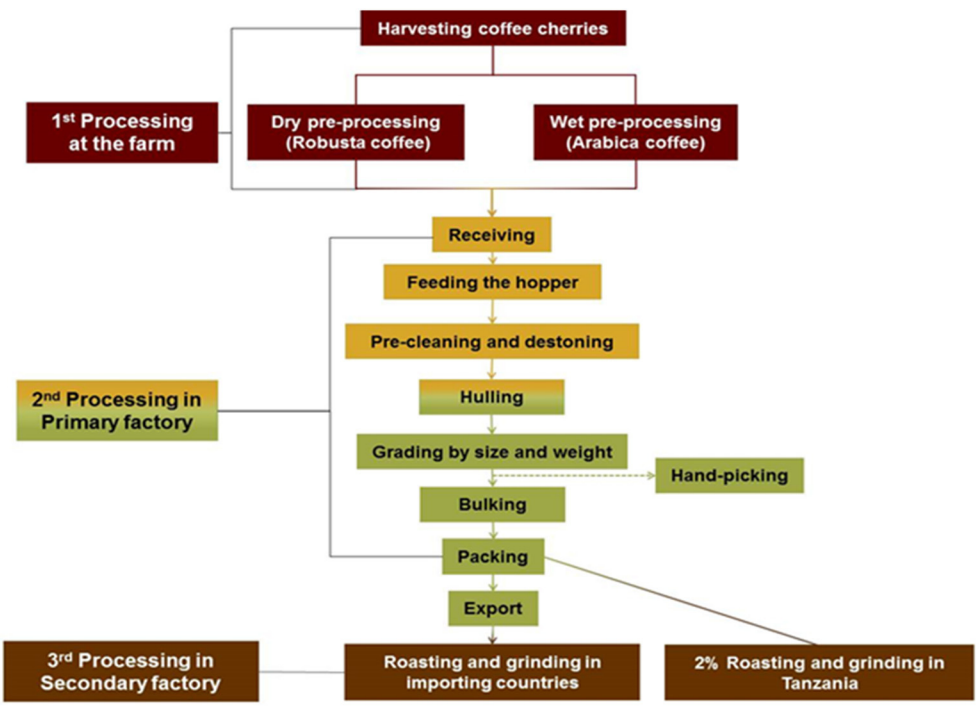

FIGURE 1 | Schematic diagram for coffee processing in Tanzania (21).

TABLE 1 | Personal full-shift exposure to total dust and endotoxin among coffee production workers in Tanzania and Ethiopia.

	Total dust (mg/m^3)					Endotoxin (EU/m^3)				
	Nw	**Ns**	**AM**	**Range**	**GM (GSD)**	**Nw**	**Ns**	**AM**	**Range**	**GM × 10^4 (GSD)**
Tanzania										
Production workers[a]	97	193	3.69	0.24–36.00	2.50 (2.44)	69	154	8,200	42–75,083	0.35 (4.36)
Arabica coffee[a]	71	124	3.69	0.24–36.00	2.10 (2.79)	43	85	3,556	42–75,083	0.14 (3.58)
Robusta coffee[a]	26	69	3.70	1.20–6.67	3.42 (1.52)**	26	69	13,900	1,913–46,964	1.08 (2.12)
Hand pickers[b]		9		0.3–1.7	0.9 (0.5)		9		29–372	183 (119)
Ethiopia										
Machine room workers[c]	60	117	17.47	1.12–77.28	12.54 (2.37)					
Transporters[c]	59	113	17.46	2.51–81.61	12.30 (2.32)					
Hand pickers[d]	60	115	1.55	0.12–9.74	1.08 (2.42)					

*Nw, number of workers sampled; Ns, number of samples; **$p < 0.01$.*
[a] *Sakwari et al. (17).*
[b] *Moen et al. (20).*
[c] *Abaya et al. (18).*
[d] *Abaya et al. (22).*

and Ethiopia ($n = 115$ coffee workers/110 controls) (15, 18). Of these 17 controls and 16 coffee workers were excluded from further analysis of lung function due to unacceptable spirograms. The spirometer tests were performed at any time during the day shift in all studies, and in the same time periods as the dust and endotoxin measurements. The recorded lung function parameters were; Forced expiratory volume in 1 s (FEV1 in L/s), Forced vital capacity (FVC in L) and the ratio FEV1/FVC (in %).

Statistics

Data were analyzed by using IBM SPSS Statistics 25 for Windows, Version 25.0 (Armonk, NY: IBM Corp.). Statistical analysis was performed using Chi-square and Fischer exact test for categorical data, and independent *t*-test for continuous data. Logistic regression was used to determine odds ratio (OR) of the different respiratory symptoms (yes/no) between coffee workers (1) and controls (0) while adjusting for age (years) and current smoking (yes/no). Mixed effects models were developed for analyzing differences in lung function between coffee workers and controls, and for analyzing the association between cumulative dust exposure and lung function variables. Separate linear mixed-effects models were developed with the lung function variables FEV1, FVC, and FEV1/FVC (%) as dependent variables and age, height, current smoking, and either exposure group (coffee workers/controls) or cumulative dust exposure (in mg/m^3 · year) as fixed effects. To account for repeated measurements taken in Tanzania and Ethiopia, country was viewed as a random effect. Years at school was considered as a proxy for socioeconomic status, but as it correlated significantly with age, only age was used in the models. The percentage of total variance explained by the fixed effects (age, height, current smoking, and exposure) in the respective models was calculated as the percentage change in the sum of between-country variance and within-country variances from the random model to the mixed effects model.

RESULTS

Dust Exposure

Personal exposure to total dust among the coffee production workers was considerably higher in Ethiopian than in Tanzanian coffee factories (GM 12 mg/m^3; range 1.1–81 vs. 2.5; 0.24–36) (**Table 1**). About 84 and 17% of the samples exceeded the OEL of 5 mg/m^3 for total organic dust in the two countries, respectively. The majority of coffee workers did not use any type of respiratory protective devices (16, 19).

Personal exposure to endotoxins in the Tanzanian factories was high (GM = 3,500 EU/m^3; range 42–75,083) compared to the Dutch OEL of 90 EU/m^3, with only two of the samples below this limit (**Table 1**). There was a significant correlation between exposure to total dust and endotoxin ($r = 0.62$, $P < 0.001$, $n = 149$). It was not analyzed for endotoxins in the Ethiopian factories. In Tanzania total dust and endotoxin exposures were significantly higher in Robusta than in Arabica coffee factories (**Table 1**), and when handling dry pre-processed coffee compared with wet pre-processed coffee (not shown). The pre-processing method of the Ethiopian Arabica coffee, dry or wet, had no impact on the exposure to total dust. The exposure for the female hand pickers did not differ between the two countries, and it was considerably lower than for the male production workers (**Table 1**).

Demographic Data on Participants in the Respiratory Health studies

The studies on respiratory health among the coffee workers comprised one cross-sectional study from Tanzania and two from Ethiopia (**Table 2**). All coffee production workers and their respective control groups were men whereas all hand pickers and their controls were females. The response rate varied between 88 and 100% (**Table 2**). No difference was found between coffee workers and controls regarding weight, height, BMI, and past respiratory diseases (15, 16). In all studies the mean age among coffee workers were 4 years higher than among the controls.

TABLE 2 | Demographic information on the participants in the three studies of respiratory health among male coffee workers in Tanzania and Ethiopia.

	Tanzania[a]		Ethiopia[b]	
	Controls[c] $n = 120$	Coffee workers $n = 140$	Controls[d] $n = 110$	Coffee workers $n = 115$
Response rate (%)	100	88	94	
Age (years); AM (range)	29 (19–51)	33 (19–65)**	31 (18–68)	35 (18–68)**
Years at school; AM (range)	9 (0–15)	7 (0–16)**	9 (0–16)	7 (0–16)**
Years of current work; AM (range)	5 (0.2–23)	5 (0.2–35)	3 (1–6)	7 (1–30)**
Current smokers; *n* (%)	14 (12)	52 (37)**	4 (3.6)	3 (2.6)
Cumulative dust (mg/m^3·year); AM (range)		19 (0.5–120)		129 (4–595)

[a]*Sakwari et al. (15).*
[b]*Abaya et al. (16).*
[c]*Water bottling (n = 60) and fish factory (n = 60) workers.*
[d]*Water bottling workers; **p < 0.01.*

TABLE 3 | Prevalence and odds ratio for chronic respiratory symptoms among male coffee workers and controls from Tanzania and Ethiopia.

Chronic respiratory symptom	Tanzania[a] and Ethiopia[b]		
	Controls[c] $n = 229$ *n* (%)	Coffee workers $n = 252$ *n* (%)	Odds ratio$^d_{adj}$ OR (95% CI)[b]
Cough	16 (7.0)	122 (48.4)**	11.3 (6.4–20.1)
Cough with sputum	6 (2.6)	60 (23.8)**	10.3 (4.3–24.6)
Breathlessness	18 (7.9)	56 (22.2)**	3.2 (1.8–5.7)
Chest tightness	18 (7.9)	60 (23.8)**	3.5 (2.0–6.3)
Wheezing	14 (6.1)	41 (16.3)**	2.4 (1.2–4.6)

[a]*Sakwari et al. (15).*
[b]*Abaya et al. (16).*
[c]*Water bottling and fish factory workers.*
[d]*Adjusted for age and current smoking;*
***p < 0.01 in Chi-square test.*

The controls had more education than the coffee workers. In the Tanzanian study the prevalence of current smokers among coffee workers was higher than among controls (**Table 2**), but the mean number of cigarettes smoked per day was low, five vs. three cigarettes per day among coffee workers and controls, respectively (15).

Respiratory Symptoms

When merging the studies from Tanzania and Ethiopia, the male coffee workers had higher prevalence for all recorded chronic respiratory symptoms than the controls, also when adjusting for confounders (**Table 3**). The highest symptom prevalence among the coffee workers was found for cough (48.4%), while the highest odds ratios were for cough and cough with sputum, followed by chest tightness, breathlessness, and wheezing (**Table 3**).

Lung Function

The mean FEV1, FVC, and FEV1/FVC for coffee workers were significantly lower than among controls (**Table 4**). In mixed effects models, adjusting for age, height, and current smoking there was still a difference between coffee workers and controls for FEV1 and FVC, but not for FEV1/FVC. The adjusted difference in FEV1 and FVC between coffee workers and controls were 0.26 l/s and 0.21 l, respectively (**Table 4**). The prevalence of airflow limitation (FEV1/FVC <0.7) was significantly higher ($p = 0.002$; Fischer exact test) among coffee workers ($n = 15$; 6.3%) compared to controls ($n = 2$; 0.9%).

Association Between Cumulative Dust Exposure, Lung Function, and Respiratory Symptoms

Arithmetic mean cumulative dust exposure among the male workers was 66 mg/m^3·year (range: 0.5−595 (mg/m^3·year)), and it was higher in Ethiopia than in Tanzania (**Table 2**). **Table 5** shows a significant association between cumulative dust exposure and the lung function variables FEV1 and FVC among the male coffee workers. The mixed effects models adjusting for the fixed effects age, height and current smoking, indicated a significant decrease in the FEV1 and FVC of 0.9 ml/s and 0.9 ml, respectively for cumulative dust exposure of 1 mg/m^3 per year (**Table 5**). This translates into an additional annual decrease in FEV1 and FVC of 15.8 ml/s and 15.8 ml, respectively for a male coffee production worker exposed to the average dust exposure in Ethiopian factories of 17.5 mg/m^3 in a season.

DISCUSSION

The results support that there is an association between dust exposure among the male coffee production workers and respiratory health effects, including both increased prevalence of chronic respiratory symptoms and reduced lung function compared to controls. In both Tanzania and Ethiopia, a considerable fraction of the dust samples (84 and 17%) exceeded the OEL of 5 mg/m^3 for total organic dust, and exposure to endotoxins was also high compared to the health based OEL. These results suggest that control measures should be taken to reduce dust exposure.

TABLE 4 | Lung function among male coffee workers in Tanzania and Ethiopia.

Lung function variables	Tanzania[a] and Ethiopia[b]						
	Controls	Coffee workers	Controls vs. coffee workers; Independent *t*-test;	Controls (0) vs. coffee workers (1); Mixed effects model[c]			
	n = 213	*n* =239	*p*-value	*B*	95%CI		*p*-value
FEV1, L/s, AM (SD)	3.45 (0.58)	3.26 (0.60)	0.001	−0.26	−0.38	−0.15	<0.001
FVC, L, AM (SD)	4.12 (0.70)	3.96 (0.65)	0.013	−0.21	−0.35	−0.08	0.002
FEV1/FVC, %, AM (SD)	84.0 (6.0)	82.4 (7.3)	0.009	−1.65	−3.49	0.19	0.079

[a] *Sakwari et al. (15).*
[b] *Abaya et al. (16).*
[c] *Mixed effects model with age, height, current smoking as fixed effects, and country as random effect.*

TABLE 5 | Linear mixed effects models for the association between cumulative dust exposure and three lung function variables among 239 male coffee workers in Tanzania and Ethiopia (random effect; country).

Variables	B	95%CI		*p*-value
FEV1 (L/s); 39.6%[a]				
Intercept	−0.750	−2.391	0.892	0.37
Age (years)	−0.025	−0.032	−0.018	<0.001
Height (m)	2.908	1.968	3.848	<0.001
Current smoking (yes/no)	−0.030	−0.185	0.125	0.70
Cumulative dust (mg/m^3·year)	−0.0009	−0.0018	−0.0001	0.028
FVC (l); 31.7%[a]				
Intercept	−1.812	−3.584	−0.042	0.045
Age (years)	−0.024	−0.032	−0.017	<0.001
Height (m)	3.940	2.941	4.938	<0.001
Current smoking (yes/no)	0.0006	−0.165	0.166	0.99
Cumulative dust (mg/m^3·year)	−0.0009	−0.0018	−0.00002	0.046
FEV1/FVC (%); 13.2%[a]				
Intercept	104.725	80.036	129.414	<0.001
Age (years)	−0.145	−0.248	−0.042	0.006
Height (m)	−9.936	−24.055	4.184	0.167
Current smoking (yes/no)	−0.637	−2.962	1.689	0.59
Cumulative dust (mg/m^3·year)	−0.010	−0.023	0.002	0.12

[a] *% of total variance explained by the fixed effects (age, height, and current smoking) in the respective models.*

When analyzing the studies from Tanzania and Ethiopia separately the association between dust exposure and lung function was not consistent (15, 16) which might be due to a relatively low study power in each of the studies. In the Tanzanian study, there were no difference in the FVC and FEV1 between coffee workers and controls, as was the case in Ethiopia. After merging of the lung function data from these studies, and thereby doubling the number of study participants, the inverse relationship between cumulative dust exposure and lung function lends further support for the association between dust exposure and lung function among coffee production workers.

The lung function variables FEV1, FVC, and FEV1/FVC were all reduced among the male coffee workers compared to the controls, indicating both obstructive and restrictive lung effects. However, the significantly higher prevalence of airflow limitation (FEV1/FVC ratio <0.70) among the coffee workers (6.3%) than the controls (0.9%) indicates that the findings mainly support an obstructive effect. Cough, wheezing, and breathlessness, symptoms that are associated with development of reduced lung function (25), had odds ratios of 11.3, 2.4, and 3.2 among the male coffee workers when compared to controls. Female hand pickers in Ethiopia were considerably less exposed, and they had lower prevalence of respiratory symptoms than the male processing workers (22). However, the female hand pickers still had higher dust exposure, a higher prevalence of almost all respiratory symptoms, and lower FEF 25–75 (0.4 l/s) than the female controls (22).

The high level of dust exposure among the coffee production workers is probably due to the open design of the process lines from manual feeding of the hopper through the machines for destoning, hulling, grading, bulking, and packing. Several of these mechanical processes have vibrating surfaces which enhance dust emission. In line with this several of the tasks performed by workers operating these machines have been identified as determinants of increased dust exposure such as feeding the hopper, grading at the gravity table, and mixing coffee (17, 18). Another important determinant of dust exposure was pouring of coffee beans from a dropping height (18). These exposure models suggest that the large variability in dust and endotoxin exposure within the exposure groups can partly be explained by difference in tasks performed by the workers. Furthermore, the identified determinants also indicates that variations in the processing methods among the factories lead to significant variability in exposure levels. For instance, the high exposure to endotoxin is associated with the dry pre-processing method used after harvest (17). Dust exposure among male production workers was higher in Ethiopian than in Tanzanian coffee factories. One reason for the difference in dust levels between the two countries might be that the Ethiopian factories were larger, with respect to both annual production rate and number of production workers. Furthermore, in Ethiopia all processing machines were situated

in one hall, whereas in one half of the factories in Tanzania the machines were in different rooms. In agreement with this, Abaya et al. (18) showed that dust exposure increased with the number of coffee huller machines in the production hall. Previous old studies on total dust exposure in primary coffee processing factories presented only the range of exposure, not any central tendency of the data, which makes comparison with our studies difficult (6, 7).

The high exposure to endotoxins presumably originates from Gram-negative bacteria which have been isolated from dried and stored coffee beans (26), and might result from poor storage and drying coffee on the ground (15). Sakwari et al. (15) reported an association between exposure to cumulative exposure to endotoxin and reduced lung function among male coffee processing workers in Tanzania. Endotoxins might thus be an important constituent of the coffee dust in the development of adverse respiratory effects. However, there was no association between cumulative endotoxin exposure and asthma symptoms among the coffee workers, or any difference in FeNO levels between the coffee workers (GM = 17.4; GSD = 1.8) and controls (16.5; 1.8) (15). Furthermore, cumulative exposure to total dust or to endotoxin among the coffee workers was not associated with any significant effects on FeNO, indicating no evidence of eosinophilic airways inflammation (15). Sensitization to protein allergens in the GCB might also contribute to the respiratory effects among the coffee workers. In an Italian study the prevalence of sensitization to GCB was significantly higher in workers exposed to GCB (25.8%) than in those exposed to roasted coffee (2.7%) and in white collar workers (4.5%) (5). About 10 years ago the first coffee bean protein allergen was isolated and sequenced (27).

It is a strength of the present study that the methodology used for dust exposure, questionnaires and lung function measurements were the same in the Tanzania and Ethiopia. We used validated questionnaires and standardized methods for spirometry and dust sampling. Although questionnaire-based interviews to assess the respiratory symptoms might result in recall and interviewer bias, similar questions were used to assess the respiratory symptoms in both the coffee workers and control groups. Our analyses were adjusted for factors such as age and smoking habits, which may affect lung function. By using mixed effects models with country as random effect we also took into account possible correlation in lung function within the two countries. Although the same design and methodology were used for investigating the respective outcomes, and the same scientific environment has conducted the studies, care should still be taken when merging data from two countries. Among others there might be cultural and language differences in understanding of the chronic symptoms, differences in the impact of confounders on lung function, and in scoring of contextual information between the countries. Furthermore, weaknesses related to estimation of cumulative exposure based on current dust exposure measurements and work history includes risks of bias which may have impact on the association between exposure and lung function. The factories included in this study are considered as representative for primary coffee processing factories in the two countries in terms of size, machine types, coffee types, and design of the factories. It is difficult to know if the results are valid also in other coffee-producing countries. However, the factories studied are established in low-income countries where the competence in occupational health and safety is minor, and the results are likely to be similar in other low-income countries with a similar situation. However, since the included studies are all cross-sectional we are not able to conclude on a definite causal relationship between the dust exposure and respiratory effect. A longitudinal study should be undertaken to further support the association between dust exposure and lung function reduction, but this might be considered as unethical studies.

In conclusion the results suggest that coffee production workers are at risk of developing chronic respiratory symptoms and reduced lung function. Together with the high dust levels these findings strongly indicate that proper dust control measures are necessary to reduce the dust exposure. Personal respiratory protection which might be considered as a first approach to reduce dust exposure. However, the most effective strategy would be to reduce dust at the source by preventive measures at the machines/work tasks identified as significant determinants of increased exposure. The female hand pickers are less exposed, but they still had more symptoms than the controls, indicating that protective measures should be considered also for these workers.

AUTHOR CONTRIBUTIONS

MB, SA, GS, and BM contributed to conception and design of the study. SA and GS conducted the field work in Ethiopia and Tanzania, respectively. SA, GS, and MB organized the database and performed the statistical analyses. MB wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

FUNDING

This work was supported by the Norwegian Agency for Development Cooperation (NORAD) through the Norwegian Program for Capacity Building in Higher Education and Research for Development (NORHED: Number 13000646) and the Norwegian Programme for Development, Research, and Higher Education (NUFU: Number 2007/10166).

ACKNOWLEDGMENTS

We are grateful to the factory management and the workers for their participation. We are also grateful to the Norwegian Programme for Development, Research, and Higher Education (NUFU) and the Norwegian Agency for Development Cooperation (NORAD) for funding this work. We would like to thank Ass. Prof. Simon Mamuya and Prof. Wakgari Deressa for facilitating and coordinating the resources needed for the studies and for the fruitful and stimulating discussions in the project period.

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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.

frontiers in Public Health

ORIGINAL RESEARCH
published: 18 September 2020
doi: 10.3389/fpubh.2020.561740

Exposures and Emissions in Coffee Roasting Facilities and Cafés: Diacetyl, 2,3-Pentanedione, and Other Volatile Organic Compounds

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OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: 13 May 2020
Accepted: 13 August 2020
Published: 18 September 2020

Citation:
LeBouf RF, Blackley BH, Fortner AR, Stanton M, Martin SB, Groth CP, McClelland TL, Duling MG, Burns DA, Ranpara A, Edwards N, Fedan KB, Bailey RL, Cummings KJ, Nett RJ, Cox-Ganser JM and Virji MA (2020) Exposures and Emissions in Coffee Roasting Facilities and Cafés: Diacetyl, 2,3-Pentanedione, and Other Volatile Organic Compounds. Front. Public Health 8:561740. doi: 10.3389/fpubh.2020.561740

Roasted coffee and many coffee flavorings emit volatile organic compounds (VOCs) including diacetyl and 2,3-pentanedione. Exposures to VOCs during roasting, packaging, grinding, and flavoring coffee can negatively impact the respiratory health of workers. Inhalational exposures to diacetyl and 2,3-pentanedione can cause obliterative bronchiolitis. This study summarizes exposures to and emissions of VOCs in 17 coffee roasting and packaging facilities that included 10 cafés. We collected 415 personal and 760 area full-shift, and 606 personal task-based air samples for diacetyl, 2,3-pentanedione, 2,3-hexanedione, and acetoin using silica gel tubes. We also collected 296 instantaneous activity and 312 instantaneous source air measurements for 18 VOCs using evacuated canisters. The highest personal full-shift exposure in part per billion (ppb) to diacetyl [geometric mean (GM) 21 ppb; 95th percentile (P95) 79 ppb] and 2,3-pentanedione (GM 15 ppb; P95 52 ppb) were measured for production workers in flavored coffee production areas. These workers also had the highest percentage of measurements above the NIOSH Recommended Exposure Limit (REL) for diacetyl (95%) and 2,3-pentanedione (77%). Personal exposures to diacetyl (GM 0.9 ppb; P95 6.0 ppb) and 2,3-pentanedione (GM 0.7 ppb; P95 4.4 ppb) were the lowest for non-production workers of facilities that did not flavor coffee. Job groups with the highest personal full-shift exposures to diacetyl and 2,3-pentanedione were flavoring workers (GM 34 and 38 ppb), packaging workers (GM 27 and 19 ppb) and grinder operator (GM 26 and 22 ppb), respectively, in flavored coffee facilities, and packaging workers (GM 8.0 and 4.4 ppb) and production workers (GM 6.3 and 4.6 ppb) in non-flavored coffee facilities. Baristas in cafés had mean full-shift exposures below the RELs (GM 4.1 ppb diacetyl; GM 4.6 ppb 2,3-pentanedione). The tasks, activities, and sources associated with flavoring in flavored

coffee facilities and grinding in non-flavored coffee facilities, had some of the highest GM and P95 estimates for both diacetyl and 2,3-pentanedione. Controlling emissions at grinding machines and flavoring areas and isolating higher exposure areas (e.g., flavoring, grinding, and packaging areas) from the main production space and from administrative or non-production spaces is essential for maintaining exposure control.

Keywords: coffee roasting and packaging, cafe, exposure assessment, volatile organic compounds, diacetyl, 2,3-pentanedione (acetyl propionyl)

INTRODUCTION

The worldwide demand for roasted coffee and coffee beverages is on the rise. Coffee consumption in the United States increased from 1.43 billion kilograms (kg) in 2013/2014 to 1.55 billion in 2017/2018 (1). The United States is forecast to be the second-largest importer of coffee beans (1.57 billion kg) behind the European Union (2.88 billion kg) in 2019/2020 (2). In 2016, the US coffee industry (NAICS 311920) had 15,911 full-time and part-time employees (3) with 11% in small-sized (<20 employees) businesses representing 73% of establishments, 37% in medium-sized (≥20 to <500 employees) businesses representing 7% of establishments, and 52% in large-sized (500+ employees) businesses representing 20% of establishments (4).

Roasted coffee production and café workers can be exposed to a variety of chemicals at work. Roasted coffee emits carbon monoxide (CO), carbon dioxide (CO_2), and a wide range of VOCs (5–10). Emitted VOCs include alpha-diketones such as 2,3-butanedione (diacetyl), 2,3-pentanedione (acetyl propionyl), and 2,3-hexanedione. Grinding roasted coffee beans produces a greater surface area for off-gassing (sometimes called degassing) of CO, CO_2, and VOCs (11, 12). In addition to occurring naturally in roasted coffee, diacetyl and 2,3-pentanedione are added as ingredients in food flavorings used in some food products, including ground or whole bean coffee to make flavored coffee (13–15). Acetoin and 2,3-pentanedione are common substitutes for diacetyl in flavorings (16).

The National Institute for Occupational Safety and Health (NIOSH) has published full-shift Recommended Exposure Limits (RELs) of 5.0 parts per billion (ppb) for diacetyl and 9.3 ppb for 2,3-pentanedione. The NIOSH short-term exposure limits (STELs) are 25 ppb for diacetyl and 31 ppb for 2,3-pentanedione averaged over a 15 min time period. Short-term peak exposures might be relevant for respiratory health, particularly when tasks are repeated multiple times per day.

The NIOSH objective in establishing RELs for diacetyl and 2,3-pentanedione is to reduce the risk of respiratory impairment (decreased lung function) and the severe irreversible lung disease obliterative bronchiolitis associated with occupational exposure to these chemicals. These exposure limits were derived from a risk assessment of flavoring-exposed workers. At an exposure equal to the diacetyl REL, the risk of adverse health effects is low. NIOSH estimated about 1 in 1,000 workers exposed to diacetyl levels of 5 ppb as a time-weighted average (TWA) for 8 h a day, 40 h a week for a 45-year working lifetime would develop reduced lung function (defined as forced expiratory volume in 1 s (FEV1) below the lower limit of normal) as a result of that exposure. NIOSH predicted that around 1 in 10,000 workers exposed to diacetyl at 5 ppb for a 45-year working lifetime would develop more severe lung function reduction [FEV1 below 60% predicted, defined as at least moderately severe by the American Thoracic Society (17)]. Workers exposed for less time would be at lower risk for adverse lung effects. NIOSH RELs should be used as a guideline to indicate when exposure reduction steps should be taken in the workplace. The American Conference of Governmental Industrial Hygienists (ACGIH®) has a threshold limit value (TLV®) for diacetyl of 10 ppb, as a full-shift time-weighted average exposure and a STEL of 20 ppb. Diacetyl is on the 2020 ACGIH TLV list of chemicals under study. ACGIH does not have a TLV®-TWA or a STEL for 2,3-pentanedione. Occupational exposure limits for 2,3-hexanedione and acetoin do not exist.

Inhalational exposure to diacetyl has been associated with a lung disease called obliterative bronchiolitis (18). Obliterative bronchiolitis is a severe, often disabling, lung disease that involves scarring of the very small airways (i.e., bronchioles). Symptoms of this disease may include cough, shortness of breath on exertion, or wheeze, and do not typically improve away from work (19). Occupational obliterative bronchiolitis has been identified in flavoring manufacturing workers and microwave popcorn workers who worked with flavoring chemicals or butter flavorings (14, 20, 21). A diacetyl substitute, 2,3-Pentanedione, was found to have respiratory toxicity in animal studies similar to that of diacetyl (22, 23). In one animal study, there was evidence that 2,3-hexanedione might also damage the lungs, but it appeared to be less toxic than diacetyl and 2,3-pentanedione (24). Obliterative bronchiolitis has been reported among workers at two coffee roasting and packaging facilities that produced both unflavored and flavored coffee (13, 25, 26). At one of those facilities, all former workers diagnosed with obliterative bronchiolitis had worked in the flavoring area (13). Current workers at that facility had excess shortness of breath and obstruction on spirometry, consistent with undiagnosed lung disease. Respiratory morbidity among current workers was associated with working in areas where coffee was flavored, and areas where grinding and packaging of unflavored coffee occurred (13). However, to our knowledge, no cases of obliterative bronchiolitis have been reported in workers

TABLE 1 | Production characteristics of 17 sampled coffee facilities.

Facility	Production area (m^2)	# Production/ total workers	Annual production roasted coffee (tons/year)	Percentage whole bean coffee (%)	Flavoring during survey (yes/no)	Café	Season during sampling	US Climate region
1	1.0×10^2	4/4	1.6×10^1	90	No	Offsite[a]	Spring	Northeast
2	7.4×10^1	3/6	2.0×10^1	45	Yes	–	Winter	Ohio Valley
3	9.3×10^1	10/19	3.0×10^1	70	No	Offsite	Winter	Northwest
4	2.0×10^2	3/6	3.9×10^1	95	Yes	–	Winter	Southwest
5	2.3×10^2	9/18	4.5×10^1	97	No[b]	Offsite[c]	Fall	Southeast
6	1.1×10^2	4/5	6.0×10^1	75	No	–	Spring	Southeast
7	9.3×10^1	3/9	6.0×10^1	75	No	–	Spring	Southeast
8	4.0×10^2	6/20	9.6×10^1	97	No	Onsite	Spring	Upper Midwest
9	1.0×10^3	13/26	1.3×10^2	95	No	–	Summer/Spring	Upper Midwest
10	2.3×10^2	7/19	1.4×10^2	90	No	Onsite	Summer	Upper Midwest
11	2.9×10^2	5/10	1.6×10^2	97	No	Offsite	Spring	Upper Midwest
12	6.5×10^2	10/49	1.7×10^2	75	No	Onsite	Winter	Upper Midwest
13	9.3×10^2	11/43	2.5×10^2	65	No	Offsite	Spring	Upper Midwest
14	2.1×10^3	6/54	1.4×10^3	35	Yes	–	Summer	Upper Midwest
15	4.2×10^3	20/90	2.6×10^3	73	No	–	Spring	Northeast
16	4.9×10^3	100/120	3.5×10^3	40	Yes	–	Summer	Upper Midwest
17	4.5×10^3	50/150	4.5×10^3	60	No	Onsite	Fall	Southwest

[a] *Two locations.*
[b] *Facility does flavor coffee but did not during survey.*
[c] *Not sampled.*
"–," Café not present.

at coffee roasting and packaging facilities that produce only unflavored coffee.

In an effort to characterize occupational exposures to alpha-diketones and other VOCs, we performed exposure assessments at 17 coffee facilities, some of which included cafés, through the NIOSH Health Hazard Evaluation (HHE) program. The HHE program responds to requests to investigate exposure or health issues in workplaces from employers, employees, or union representatives. One HHE request was from employees and 16 were from employers. The respiratory abnormalities of the workforce at these 17 facilities included nose and eye symptoms, wheeze, and rare abnormal spirometry (5%), and is described in detail elsewhere (27).

MATERIALS AND METHODS

Facility Characteristics

Annual roasted coffee production at the 17 facilities ranged from 14,000 to 4,080,000 kgs per year (**Table 1**). The median number of production workers was seven (range: 3–100). The majority of facilities produced unflavored whole-bean coffee. Four of 17 facilities flavored coffee during the survey; one facility flavored ground coffee and three facilities flavored whole-bean and then ground the flavored beans. One facility flavored coffee on occasion but did not do so during the survey. Eight facilities had either one onsite or one offsite café; one facility had two offsite cafés. Facilities were sampled between July 2015 and September 2017 during a variety of seasons and in a number of geographical locations, which influenced the temperature during sampling and amount of natural ventilation occurring from open doors or windows.

Process and Task Description

The main steps in roasting and packaging coffee are typically: (1) receiving green (raw) beans, (2) roasting green beans, (3) grinding roasted beans, (4) weighing and packaging roasted and ground coffee, and (5) shipping. Some facilities also flavored roasted ground or whole bean coffee with liquid flavoring before packaging or grinding.

Green beans were received in jute or burlap bags from countries around the world and stored in designated areas or in the main production space. Workers moved bags of green beans on pallets using a forklift or carried bags to a storage area. The first step in the production process was weighing and transferring the green beans to a conduction or convection roaster. Some facilities pneumatically fed green beans into the roasters. Some facilities blended green coffee beans before roasting and others blended roasted beans after roasting. A roaster operator monitored roasting time and temperature that depended on the green bean origin and desired roast level (e.g., light, medium, dark). Occasionally, the roaster operator would pull a sample of beans from the roaster to check the color and smell of the beans. In a majority of facilities (16 of 17), the roasted coffee beans were sent to downdraft or updraft cooling drums and mixed by an agitator to accelerate cooling. Cooling systems

exhausted out through the roof or side of the buildings. After roasting, the roasted coffee beans were sent through a destoner (to remove any foreign objects) and transferred to containers or silos. In some facilities, the roasted product was allowed to off-gas in a bin or silo located in a designated roasted bean storage area for 12 to 48 h if the product was to be packaged in a bag without a one-way valve. At three of the four facilities that flavored coffee, the flavoring and cooled roasted coffee were measured and added to a bucket with a lid or a plastic bag that was sealed. The worker then shook the flavored coffee container by hand. At the fourth facility, a dedicated flavoring room received whole beans through a pneumatic system. The flavoring room attendant manually mixed the liquid flavorings in an 18-kg pail, then poured it into an automatic ribbon blender, which mixed the flavorings with the whole beans or ground coffee. Some coffee was ground before packaging. Grinders were manual 0.45-kg (1-lb) to 2.3-kg (5-lb) machines or automated machines capable of grinding up to 318 kg per hour. Whole-bean and ground coffee were manually packaged into bags (with and without one-way valves) or other containers, or automatically packaged using weighing and packaging lines. These lines were monitored to assure quality of packaging. In the event of packaging defects, some re-work of product was required. Re-work involved manually cutting open defective packaging and returning coffee to a packaging line. Bags were generally heat-sealed to complete the finished product.

During the production process, companies tested green and roasted beans to ensure quality. The facilities had quality control areas where roasted beans and brews were prepared and assessed. Upon receipt, a worker profiled the green beans to determine the best roast temperature and time. Green beans stored in silos were monitored over time as they aged and roasting specifications were adjusted to account for any changes in the green beans. Within each specific type of roast, the beans were generally packaged in the order they were roasted to ensure freshness.

Various cleaning techniques were used throughout the production areas. Workers used brooms to sweep the production floor, wet or dry wipes on tabletops and equipment surfaces, and compressed air to remove coffee bean dust from surfaces and equipment. In some facilities, maintenance workers maintained and repaired production equipment and customers' coffee roasting equipment (roasters, grinders, and espresso machines) as needed.

Tasks performed by workers during the production process included miscellaneous production (e.g., moving, loading, or scooping green beans; making labels; and moving pallets of coffee), roasting coffee beans, pulling samples of beans during roasting, quality control, moving roasted beans or ground coffee (e.g., scooping roasted whole bean coffee into packaging machine, pouring whole beans into buckets to hand blend, pouring beans into storage bins, etc.), grinding coffee beans, flavoring coffee, packaging coffee, packaging rework, cleaning machines, maintenance of machines, and miscellaneous café tasks (**Supplementary Table 1**). Suspected sources of emissions included roasting, roasted coffee, roasted coffee in bag, roasted coffee in container, roaster cooling drum, roaster door, sampler roaster, QC grinder, miscellaneous QC, ground coffee, heat sealing bags, packaging roasted coffee, flavoring, flavored coffee, café grinder, and miscellaneous café (**Supplementary Table 2**).

Workers were not required to wear company uniforms or protective clothing. We did not observe workers wearing respiratory protection for chemicals. In three facilities, dust masks were occasionally used while working with green beans. In six facilities, hearing protection was available for voluntary use.

Work Area and Workforce Description

The work areas and workforce were divided into three main groups of activities and site: production (e.g., administrative production, roaster, production, production support, quality control, grinder, flavoring, and packaging), non-production (e.g., administrative non-production), and café (e.g., barista and other café) to segregate the exposure groups into general areas of roasted coffee production, administration and support activities, or cafés, respectively. Work areas within these main groups were consistent regardless of whether the facility flavored coffee during the survey (**Supplementary Table 3**). Consistent work areas among facilities were roasting, grinding, packaging, shipping, and storage, with differences among facilities arising from individual facility layouts and level of segregation of processes. Some additional work areas were only present in flavoring facilities (e.g., flavoring). Workers duties necessitated movement throughout the facility to perform tasks in different areas, or the facility was small and open, meaning workers had the opportunity to be exposed to multiple emissions sources during their shift. Many facilities were small to medium size based on total number of production and non-production workers (range: 4–150) and had facility designs with occasional segregation of production/non-production spaces and shared general exhaust ventilation. No local exhaust ventilation was intentionally used for controlling exposures, but the roasting machines had exhausts that were sent outside the building; most facilities had downdraft cooling bins for roasted beans that also incidentally contributed to exposure mitigation. Administrative areas were sometimes within the main production area especially for smaller facilities with little to no separation of workspaces. Industrial hygienists, who were present during the sampling, assigned the workforce to job exposure groups (administrative non-production, administrative production, barista, flavoring, grinder, other café, packaging, production, production support, quality control, roaster) based on job title, job description, and whether they spent a majority of their time in the production area of the facility (**Supplementary Table 4**). Job exposure groups were assigned to group workers with similar job duties and potential for exposure. Workers who could not be assigned to a single job group because they performed multiple jobs were assigned to the generic production job exposure group.

Sampling Approach

Monitoring at each facility was initiated by an HHE request. Outdoor full-shift area samples for alpha-diketones were collected to ensure ambient air was not contributing to workplace air. At each facility, workers were asked to voluntarily participate in the exposure assessment. Some workers were monitored

multiple times over the course of the sampling campaign, which lasted 2 to 4 days depending on the facility. Repeat samples were collected for full-shift (over multiple days), task (on the same day and over multiple days), and instantaneous samples (on the same day and over multiple days) whenever possible. Personal sampling of the worker's breathing zone consisted of full-shift, task-based, and instantaneous samples for diacetyl and 2,3-pentanedione to identify tasks and processes that contributed to exposures. Area samples were located throughout the facility to assess chemical air concentrations in work areas using full-shift samples and from emission sources using instantaneous samples. Full-shift area samples were collected using area baskets placed at breathing height. Short-duration task samples were collected over several minutes and instantaneous samples over seconds to identify peak exposures and sources of diacetyl and 2,3-pentanedione. We collected one field blank per 17 samples and we extracted one media blank per 20 samples.

Full-Shift and Task-Based Air Sampling and Analysis

We collected 415 personal and 760 area full-shift air samples for diacetyl (CAS No. 431-03-8), 2,3-pentanedione (CAS No. 600-14-6), 2,3-hexanedione (CAS No. 3848-24-6), and acetoin (CAS No. 513-86-0) on silica gel sorbent tubes (SKC, Inc., Eighty Four, PA). Samples were collected and analyzed according to the modified OSHA Sampling and Analytical Methods 1013/1016 (28–30). Two glass silica gel sorbent tubes were connected with tubing and inserted into a protective, light-blocking cover and sampled at a flow rate of 50 mL/min. For full-shift sampling, we collected two consecutive 3 h samples and calculated the time-weighted average (TWA) concentration, assuming the total 6 h monitoring results reflected a full work shift (8 h) TWA exposure. We refer to these samples as "full-shift samples" throughout this paper. We also collected 606 personal, short-term, task-based samples in the same manner over a median of 15 min (range: 2–86 min), at a flow rate of 200 mL/min as detailed in OSHA Methods 1013/1016 (28, 29).

Sample analyses were performed in the NIOSH Respiratory Health Division's Organics Laboratory. The samples were extracted for 1 h in 95% ethanol:5% water containing 3-pentanone as an internal standard. Samples were analyzed using an Agilent (Santa Clara, CA) 7890/7001 or 7890/5977 gas chromatograph/mass spectrometer (GC/MS) system operated in selected ion monitoring mode for increased sensitivity compared with the traditional flame ionization detector used in OSHA Methods 1013 and 1016 (30).

The median limits of detection (LODs) and limits of quantitation (LOQs) were 0.3 ppb and 1.0 ppb for diacetyl, 0.3 and 1.0 ppb for 2,3-pentanedione, 0.5 and 1.7 ppb for 2,3-hexanedione, and 1.5 and 5.0 ppb for acetoin for a typical full-shift air sample. The LODs and LOQs for task samples were typically three times higher than full-shift sample LOD and LOQ values because the air volumes collected during task samples were lower. Measurements below the LOD represent values that cannot reliably be distinguished from background noise, while measurements between the LOD and LOQ have a false positive probability of ∼1% but the values have more uncertainty than measurements above the LOQ (31).

Instantaneous Air Sampling and Analysis

We collected 35 pairs of pre- and post-shift instantaneous background air samples in the main production space to identify trends in background VOC levels over the workday, 296 instantaneous activity-based, and 312 instantaneous source air samples using evacuated canisters for diacetyl, 2,3-pentanedione, 2,3-hexanedione, and other VOCs in our standard calibration mixture: acetaldehyde, acetonitrile, ethanol, isopropyl alcohol, acetone, n-hexane, chloroform, methylene chloride, methyl methacrylate, benzene, ethylbenzene, toluene, styrene, *m, p*-xylene, *o*-xylene, α-pinene, and *d*-limonene. The sampler consisted of a 450-mL evacuated canister (Entech Instruments, Inc., Simi Valley, CA) equipped with an instantaneous fitting designed for a short sampling duration (<30 s). For activity-based air samples, a NIOSH investigator placed the inlet of the flow controller by the worker's breathing zone while they were performing a work activity. For source air samples, we placed the inlet of the flow controller directly at the source of interest.

Canister air samples were analyzed using a pre-concentrator/GC/MS system, with the following modifications: the pre-concentrator was a Model 7200 (Entech Instruments, Inc.); the GC/MS was an Agilent 7890/5977; and six additional compounds, diacetyl, 2,3-pentanedione, 2,3-hexanedione, acetaldehyde, acetonitrile, and styrene, were included in the calibration (32, 33). The median LODs for all the VOCs quantified are reported in **Supplementary Table 5**, and were 0.6 ppb for diacetyl, 0.8 ppb for 2,3-pentanedione, and 1.4 ppb for 2,3-hexanedione, based on a 1.5-times dilution factor, which is typical for instantaneous samples. However, individual LOD concentrations varied because they depended on the sample volume inside each canister.

Data Analysis

Statistical analyses were performed using R 3.5.2 (R Foundation for Statistical Computing), JMP 12.0 and SAS 9.4 (SAS Institute, Inc., Cary, NC). Data were log-transformed before statistical analysis. The minimum, maximum, mean and coefficient of variation of the difference between pre- and post-shift diacetyl and 2,3-pentanedione instantaneous concentrations (post minus pre) were calculated. The relationship between log-transformed diacetyl and 2,3-pentanedione concentrations in full-shift personal and area samples was evaluated using linear regression modeling. Summary statistics including geometric means (GM), geometric standard deviations (GSD), and 95th percentile estimates (P95) were calculated using a Bayesian approach that simultaneously accounts for censored data (34). Bayesian computations were conducted using RJAGS/JAGS program in R (35). This approach fits a repeated measures analysis of variance (ANOVA) which accounts for repeated measurements collected on workers when at least five workers are present and at least two workers have repeated measurements. To keep the within- and between-subject GSDs in a reasonable range (1.01–50) because of small sample size, the within- and between-subject standard deviations (on the natural log scale) had uniform priors ranging

TABLE 2 | Average difference between pre- and post-shift background diacetyl and 2,3-pentanedione concentrations using instantaneous evacuated canisters (NMAM 3900) by production area.

Production area	Analyte	N	Average difference (ppb)	CV	Minimum difference (ppb)	Maximum difference (ppb)
NON-FLAVOR						
Café	Diacetyl	4	2.4	86.5	0.8	5.5
Café	2,3-Pentanedione	4	2.3	88.4	0.6	5.2
Production	Diacetyl	11	8.4	106.3	0.0	28.4
Production	2,3-Pentanedione	11	4.5	105.3	0.0	16.6
FLAVOR						
Non-production	Diacetyl	1	–	–	2.3	2.3
Non-production	2,3-Pentanedione	1	–	–	3.9	3.9
Production	Diacetyl	19	2.9	337.0	−16.4	22.0
Production	2,3-Pentanedione	19	8.3	111.8	−3.8	24.1

N, number of samples; ppb, parts per billion; CV, coefficient of variation; "–," No mean or CV for one sample.

from log(1.01) to log(50). The prior on the mean was left vague to allow the data to drive the inference, i.e., normal distribution prior mean 0 and variance 1,000,000. When analyzing area measurements including canister measurements, a one-way analysis of variance model was fit for each individual group of interest without the individual level random effect. This model contained the same normal prior on the mean component but had a vague/weakly-informative inverse-gamma prior on the variance component with shape = 0.1 and rate = 0.1, to allow for higher GSDs that are possible in canister measurements. Convergence was immediate for both models. To ensure convergence, we used 20,000 iterations (20,000 posterior samples of each quantity) after 5,000 iterations of burn-in were removed. While the Bayesian method provides distributions of parameters of interest (GM, GSD, P95), we only report the median values in the tables and text for simplicity; additional data on credible intervals for these parameters can be obtained upon request. For exposure groups with fewer than five observed measurements (non-censored), summary statistics were not calculated and only the maximum observation is reported in tables under P95 column heading. The AIHA exposure assessment strategy of comparing group-level P95 exposure estimates to the RELs was used as an approach to identify groups with potential for exposures exceeding the REL thus identifying particular job groups within coffee roasting facilities and cafés that are out of compliance with the REL (36). The P95 applies to all workers within a defined group and represents the exposure distribution of the group as it incorporates the mean and variance of the log-transformed exposures. The fraction of measurements above the NIOSH RELs were also calculated where appropriate. Given similarity in toxicological endpoint of diacetyl and 2,3-pentanedione exposures, the ACGIH® additive mixture formula was used to calculate a mixed exposure index as the summation of the quotients of diacetyl and 2,3-pentanedione exposures to their respective REL ($\text{Concentration}_{\text{diacetyl}}/\text{REL}_{\text{diacetyl}} + \text{Concentration}_{2,3-\text{pentanedione}}/\text{REL}_{2,3-\text{pentanedione}}$). When this index exceeds 1.0, the mixture index has been exceeded (37); we use a generic term mixture index here as NIOSH has not specified an approach to compare exposure mixtures to RELs. A heatmap was generated to display the distribution of the mean concentration (log-transformed ppb) of eight VOCs collected by instantaneous activity or source samples during different production activities.

RESULTS

1013/1016 Field and Media Blanks

Analyte mass detected on the field blanks was low for most tubes (diacetyl <LOD to 0.092 μg/mL; 2,3-pentanedione <LOD to 0.056 μg/mL; 2,3-hexanedione <LOD for all; acetoin <LOD for all but one sample that measured at 5.6 μg/mL and was likely contaminated in the field). Analyte mass detected on media blanks was low (diacetyl <LOD for all; 2,3-pentanedione <LOD for all; 2,3-hexanedione <LOD to 0.16 μg/mL; acetoin <LOD to 0.045 μg/mL). No field blank or media blank correction was performed.

1013/1016 Outdoor Full-Shift Concentrations

Outdoor full-shift samples had low concentrations of diacetyl (<0.3 ppb for all non-flavoring facilities, with 100% below LOD; <0.3 to 14.1 ppb for flavoring facilities, with 46% below LOD; <0.3 to 0.42 ppb for cafés, with 83% below LOD) and 2,3-pentanedione (<0.3 ppb for all non-flavoring facilities, with 100% below LOD; <0.3 to 0.5 ppb for flavoring facilities and cafés with 60% below LOD for flavoring and 83% below LOD for cafés). Outdoor samples were also mostly non-detectable for 2,3-hexanedione (100% below LOD for flavoring and non-flavoring facilities; 93% below LOD for cafés) and acetoin (100% below LOD for flavoring and non-flavoring facilities; 86% below LOD for cafés).

Instantaneous Background Area Concentrations

Background air concentrations of diacetyl and 2,3-pentanedione increased between pre- and post-shift canister samples in cafés and production facilities because of activities during the work-shift (**Table 2**). In cafés, the mean increase was 2.3 ppb for diacetyl and 2.4 ppb for 2,3-pentanedione. In production areas of non-flavoring facilities, the mean increase was 8.4 ppb for diacetyl and

TABLE 3 | Personal TWA exposures to diacetyl, 2,3-pentanedione, acetoin, and 2,3-hexanedione using modified OSHA Methods 1013/1016 by production area.

Production area	Analyte	N	k	GM (ppb)	GSD	P95 or max* (ppb)	%BDL	% Above REL
NON-FLAVOR								
Café	Diacetyl	18	17	3.9	1.8	10	0	44
Non-production	Diacetyl	41	26	0.9	3.1	6	22	9.8
Production	Diacetyl	259	130	5.6	2.5	25	7	62
Café	2,3-Pentanedione	18	17	4.4	1.8	12	0	5.6
Non-production	2,3-Pentanedione	41	26	0.7	3	4.4	27	0
Production	2,3-Pentanedione	259	130	3.6	2.3	14	7	10.8
Café	Acetoin	18	17	–	–	2.7*	89	–
Non-production	Acetoin	41	26	0	15	3.1	88	–
Production	Acetoin	259	130	1	2.1	3.5	63	–
Café	2,3-Hexanedione	18	17	–	–	–	100	–
Non-production	2,3-Hexanedione	41	26	–	–	0.5*	95	–
Production	2,3-Hexanedione	259	130	0.1	3.5	0.5	92	–
FLAVOR								
Non-production	Diacetyl	6	4	11	3.7	92	0	67
Production	Diacetyl	91	52	21	2.2	79	0	95
Non-production	2,3-Pentanedione	6	4	7.1	2.5	33	0	50
Production	2,3-Pentanedione	91	52	15	2.1	52	0	77
Non-production	Acetoin	6	4	12	13	763	17	–
Production	Acetoin	91	52	27	5.3	413	6	–
Non-production	2,3-Hexanedione	6	4	–	–	–	100	–
Production	2,3-Hexanedione	91	52	0.1	4.6	1.5	77	–

TWA, time-weighted average; N, number of samples; k, number of workers; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; max, maximum presented when <5 measurements were above the detection limit; %Above REL, percentage above NIOSH recommended exposure limit; "–," not enough samples above the detection limit to obtain an estimate or no REL.*

4.5 ppb for 2,3-pentanedione. In production areas of flavoring facilities, the mean increase was 2.9 ppb for diacetyl and 8.3 ppb for 2,3-pentanedione. All mean differences in cafés and in production areas were significantly greater than zero ($p < 0.01$).

Full-Shift Personal Exposures

We collected 415 personal full-shift exposures to diacetyl, 2,3-pentanedione, 2,3-hexanedione and acetoin from 227 workers. These exposures were typically higher among production workers than non-production workers and higher among workers in flavored coffee facilities compared to non-flavored coffee facilities (**Table 3**, **Figure 1**). Exposures to diacetyl were lowest in non-production workers of facilities that did not flavor coffee (GM 0.9 ppb; P95 6.0 ppb). Exposures to diacetyl were highest in facilities that flavored coffee regardless of production or non-production status of the worker. For example, exposures to diacetyl were not statistically different (**Figure 1**) between production workers (GM 21 ppb; P95 79 ppb) and non-production workers (GM 11 ppb; P95 92 ppb) in facilities that flavored coffee (**Table 3**). Exposures to 2,3-pentanedione were also lowest in non-production workers of facilities that did not flavor coffee (GM 0.7 ppb; P95 4.4 ppb) and highest in production workers (GM 15 ppb; P95 52 ppb) and non-production workers (GM 7.1 ppb; P95 33 ppb) of facilities that flavored coffee. There was no statistical difference observed between production and non-production workers in flavoring facilities (**Figure 1**). Exposures were above the REL for diacetyl in 95% of the samples and for 2,3-pentanedione in 77% of the samples collected among production workers of flavoring facilities. Exposures to acetoin were mostly non-detectable (≥88% below LOD) in non-flavored coffee facilities, but elevated (GM 27 ppb; P95 413 ppb) in production areas of flavor facilities. Exposures to 2,3-hexanedione were mostly below the LOD (flavoring production 77%<LOD; non-flavoring production 92%<LOD) (**Table 3**).

Flavoring facilities had the highest percentage of full-shift personal exposures exceeding the mixture index (**Table 4**). The flavor/non-production group exceeded the mixture index in 83% of samples compared to 12% in the non-flavor/non-production group. The difference in flavoring status was not as prominent when comparing the flavor/production group (96%) to non-flavor/production (73%). Full-shift exposures from cafés exceeded the mixture index in 67% of samples.

Personal full-shift exposures were higher among job groups that packaged, ground, or flavored roasted coffee such as grinder operator, packaging worker, production worker, and quality control worker (**Table 5**) compared with administrative workers and roaster operators. For flavored coffee facilities, personal full-shift exposures were highest among flavoring workers (GM 34, P95 284 ppb diacetyl; GM 38, P95 348 ppb 2,3-pentanedione) followed by packaging worker (GM 27, P95 54 ppb diacetyl; GM 19, P95 32 ppb 2,3-pentanedione) and grinder operator (GM 26, P95 102 ppb diacetyl; GM 22, P95 76 ppb 2,3-pentanedione).

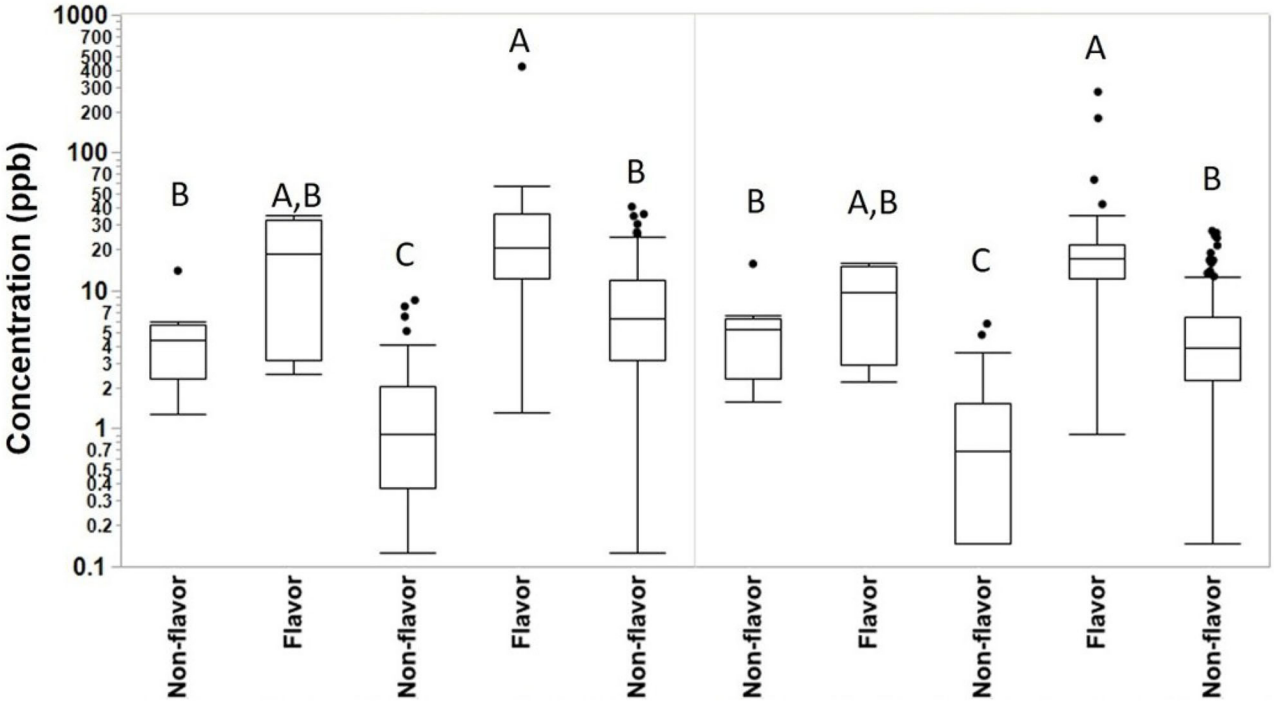

FIGURE 1 | Full-shift TWA personal exposures to diacetyl and 2,3-pentanedione among café, production and non-production workers in flavoring and non-flavoring facilities in samples analyzed using modified OSHA Method 1013/1016. From left to right, number of samples $n = 18$ for café, $n = 6$ for non-production flavoring, $n = 41$ for non-production non-flavoring, $n = 91$ for production flavoring, and $n = 259$ for production non-flavoring. By compound, connecting letters indicate groups not statistically different.

TABLE 4 | Percent of full-shift TWA personal exposures exceeding the mixture index for diacetyl and 2,3-pentanedione using modified OSHA Methods 1013/1016 by production area.

Production area	*N*	k	N (%) exceeding mixture index of 1.00	Median (min, max) mixture indices that exceeded 1.00
NON-FLAVOR				
Café	18	17	12 (67)	1.73 (1.04–4.47)
Non-production	41	26	5 (12)	1.69 (1.08–2.32)
Production	259	130	187 (72)	2.45 (1.00–11.0)
FLAVOR				
Non-production	6	4	5 (83)	7.65 (1.00–8.69)
Production	91	52	87 (96)	6.37 (1.34–114.0)

N, number of samples; k, number of workers; min, minimum; max, maximum.

For non-flavor coffee facilities, personal full-shift exposures were generally lower than in flavored coffee facilities with the highest exposures observed among packaging workers (GM 8.0, P95 26 ppb diacetyl; GM 4.4, P95 12 ppb 2,3-pentanedione), followed by quality control worker (GM 6.4, P95 18 ppb diacetyl; GM 3.8, P95 13 ppb 2,3-pentanedione) and production workers (GM 6.3, P95 24 ppb diacetyl; GM 4.6, P95 18 ppb 2,3-pentanedione). Baristas in cafés had average full-shift exposures below the RELs (GM 4.1 ppb diacetyl; GM 4.6 ppb 2,3-pentanedione) but P95 above the REL (11.0 ppb diacetyl; 13.0 ppb 2,3-pentanedione) and 64% above the mixture index. For non-flavor, administrative non-production workers had the lowest exposures (GM 0.9, P95 4.4 ppb diacetyl; GM 0.6, P95 3.3 ppb 2,3-pentanedione) and the lowest percentage above the mixture index (7.9%). Exposures to acetoin and 2,3-hexanedione by job group are summarized in **Supplementary Table 6**; acetoin exposures were highest among flavoring workers (GM 163 ppb; P95 5,622 ppb). Exposures to 2,3-hexanedione were mostly non-detectable.

Full-Shift Area Concentrations

We collected 760 full-shift area air concentrations for alpha-diketones. Area air concentrations of diacetyl and 2,3-pentanedione were higher in the production and non-production areas of the flavoring facilities compared to non-flavoring (**Table 6**). The non-production area measurements of non-flavoring facilities were the lowest, followed by cafés and production areas.

Proximity to a source such as roasted coffee or flavoring influenced air concentrations of diacetyl and 2,3-pentanedione (**Table 7**). Bakery/Cafés had low (although not the lowest) average area air concentrations of diacetyl (GM 2.5 ppb; P95 15 ppb) and 2,3-pentanedione (GM 2.8 ppb; P95 13 ppb). For production areas of non-flavoring facilities, grinding area had the highest diacetyl GM of 12 ppb but was variable (GSD 3.2) compared with packaging area with a diacetyl GM

TABLE 5 | Personal TWA exposures to diacetyl and 2,3-pentanedione using modified OSHA Methods 1013/1016 by job group.

Job Group	*N*	k	Diacetyl				2,3-Pentanedione				% Above Mixture Index
			GM (ppb)	GSD	P95 (ppb)	%BDL	GM (ppb)	GSD	P95 (ppb)	%BDL	
NON-FLAVOR											
Administrative non-production worker	38	23	0.9	2.7	4.4	21	0.6	2.8	3.3	29	7.9
Administrative production worker	53	25	2.9	3.3	21	19	2.0	3.0	12	17	47
Barista	14	13	4.1	1.9	11	0	4.6	1.9	13	0	64
Grinder operator	3	3	–	–	11*	0	–	–	6.2*	0	67
Other café worker	7	7	4.0	1.9	11	0	3.8	1.6	8.6	0	71
Packaging worker	80	41	8.0	2.0	26	5	4.4	1.9	12	5	84
Production worker	36	24	6.3	2.3	24	0	4.6	2.3	18	0	81
Production support worker	9	4	5.2	3.2	35	11	3.2	1.7	7.5	0	89
Quality control worker	15	5	6.4	1.9	18	0	3.8	2.1	13	0	87
Roaster operator	63	34	5.1	2.6	24	6.3	3.3	2.4	14	7.9	68
FLAVOR											
Administrative non-production worker	7	5	5.1	12	279	14	4.4	4.9	59	0	71
Administrative production worker	6	3	12	2.2	42	0	10	2.0	33	0	100
Flavoring worker	7	4	34	3.7	284	0	38	3.9	348	0	100
Grinder operator	5	2	26	2.3	102	0	22	2.1	76	0	100
Packaging worker	44	27	27	1.5	54	0	19	1.4	32	0	100
Production worker	5	3	4.3	2.4	18	0	4.0	2.7	21	0	60
Production support worker	3	2	–	–	36*	0	–	–	17*	0	100
Quality control worker	4	4	–	–	37*	0	–	–	18*	0	100
Roaster operator	17	7	15	2.8	81	0	9.4	2.4	39	0	88

TWA, time-weighted average; N, number of samples; k, number of workers; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; % Above Mixture Index, percentage above mixture index; max, maximum presented when <5 measurements were above the detection limit; "–," not enough samples above the detection limit to obtain an estimate.*

of 8.6 ppb (GSD 2.1). Flavoring facilities had higher area concentrations of diacetyl and 2,3-pentanedione in production areas than non-flavoring facilities (diacetyl GM 17 ppb vs. 3.0 ppb; 2,3-pentanedione GM 14 ppb vs. 2.0 ppb). Flavoring area had the highest area GMs of 33 ppb for diacetyl (P95 235 ppb) and 49 ppb for 2,3-pentanedione (P95 456 ppb). Acetoin area concentrations were generally higher in production areas of flavoring facilities compared to non-flavoring facilities (GM 29 ppb vs. GM 1.2 ppb; **Table 6**) and highest in flavoring areas of flavoring facilities (GM 304 ppb; P95 9,440 ppb; **Supplementary Table 7**). Area concentrations of 2,3-hexanedione were mostly observed at low concentrations in flavoring areas and in grinding areas within both flavoring and non-flavoring facilities (**Supplementary Table 7**).

Comparison of Diacetyl and 2,3-Pentanedione

Linear regression of log-transformed diacetyl and 2,3-pentanedione air concentrations (n = 1,175, personal and area samples) revealed a positive association with a slope of 1.0, a positive y-intercept of 0.33 and a coefficient of determination of 0.92 (**Figure 2**). The regression indicates diacetyl and 2,3-pentanedione air concentrations track well together. Similar trends and estimates were obtained when the regression model was stratified by facility, flavoring use, or personal vs. area sample type (data not shown). Similar trends were expected among facilities and between sample types because both diacetyl and 2,3-pentanedione are naturally produced and emitted during roasting, grinding and packaging coffee beans. However, differences may arise between measurements of flavored and non-flavored coffee depending on the addition of different flavoring products.

Personal Task Exposures

We collected 606 personal task-based exposure measurements from 134 workers. Exposure to alpha-diketones during short-duration tasks were highest when moving, grinding or flavoring roasted coffee (**Table 8**, **Supplementary Table 8**). Grinding coffee beans had the highest personal task exposure for both non-flavored coffee (GM 26, P95 181 ppb diacetyl; GM 20, P95 109 ppb 2,3-pentanedione) and flavored coffee (GM 30, P95 166 ppb diacetyl; GM 31, P95 205 ppb 2,3-pentanedione) facilities (**Table 8**). Moving roasted beans or ground coffee had the second highest task exposure in non-flavored coffee facilities (GM 20, P95 142 ppb diacetyl; GM 11, P95 80 ppb 2,3-pentanedione). Flavoring coffee had the highest P95 exposures to alpha-diketones (GM 5.4, P95 1,102 ppb diacetyl; GM 45, P95 3,816 ppb 2,3-pentanedione). Packaging coffee task exposures in flavored coffee facilities was higher than in non-flavored coffee facilities for diacetyl (diacetyl GM 25, P95 71 ppb vs. GM 8.6, P95 46

TABLE 6 | Area TWA concentrations of diacetyl, 2,3-pentanedione, acetoin, and 2,3-hexanedione using modified OSHA Methods 1013/1016 by production area.

Production area	Analyte	*N*	GM (ppb)	GSD	P95 or max* (ppb)	%BDL
NON-FLAVOR						
Café	Diacetyl	52	2.4	3.1	15	9.6
Café	2,3-Pentanedione	52	2.7	2.6	13	1.9
Café	Acetoin	52	–	–	5.0*	92
Café	2,3-Hexanedione	52	–	–	0.9*	98
Non-production	Diacetyl	72	1.2	3.0	7.1	22
Non-production	2,3-Pentanedione	72	0.8	2.9	4.7	29
Non-production	Acetoin	72	0.2	4.1	1.8	92
Non-production	2,3-Hexanedione	72	–	–	–	100
Production	Diacetyl	380	4.9	3.5	38	8.7
Production	2,3-Pentanedione	380	3.1	3.2	22	12
Production	Acetoin	380	1.2	2.3	4.7	55
Production	2,3-Hexanedione	380	0.04	4.9	0.6	92
FLAVOR						
Non-production	Diacetyl	32	8.3	3.3	59	0
Non-production	2,3-Pentanedione	32	3.2	7.2	81	19
Non-production	Acetoin	32	5.0	8.9	182	28
Non-production	2,3-Hexanedione	32	–	–	0.5*	94
Production	Diacetyl	224	21	2.5	94	0
Production	2,3-Pentanedione	224	16	2.4	70	0
Production	Acetoin	224	29	6.5	628	4.9
Production	2,3-Hexanedione	224	0.1	6.4	1.1	87

TWA, time-weighted average; N, number of samples; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; max, maximum presented when <5 measurements were above the detection limit; "–," not enough samples above the detection limit to obtain an estimate.*

ppb) and 2,3-pentanedione (GM 15, P95 59 ppb vs. GM 5.3, P95 26 ppb). Exposures to acetoin were higher for tasks in flavored coffee facilities than in non-flavored coffee facilities, which had 60–100% of measurements below the LOD with the exception of packaging rework tasks (25% <LOD) (**Supplementary Table 8**). High acetoin peak exposures, reflected by the P95 estimates (range: GM 2.1–29 ppb, P95 11–8,969 ppb), occurred for multiple tasks in flavoring. Exposures to 2,3-hexanedione for tasks were mostly low with 73–100% of measurements below the LOD for the tasks in flavoring and non-flavoring facilities, except for the task of packaging rework (25% <LOD).

VOC Canister Instantaneous Activity Exposures

We collected 296 instantaneous VOC canister activity air measurements. GMs for diacetyl and 2,3-pentanedione in production ranged from 3.7 ppb (2,3-pentanedione) for roasting coffee beans to 76 ppb (diacetyl) for packaging coffee in flavored coffee facilities (**Table 9**). The highest activity concentrations in flavored coffee facilities were flavoring coffee (GM 62, P95 5,311 ppb diacetyl) and in non-flavored coffee facilities were grinding coffee beans (GM 25, P95 314 ppb diacetyl). The distributions of all additional VOC mean activity exposures are displayed in a heat map (**Figure 3**). The highest measured exposure to additional VOCs was for ethanol during flavoring coffee, which was observed at a GM of 8,765 ppb (P95 263,320 ppb; GSD 8.0) (**Supplementary Table 9**). Acetaldehyde exposures while flavoring coffee varied widely (GM 156 ppb; GSD 8.1) and had a P95 concentration of 4,846 ppb, which is 5.4 times lower than the ACGIH TLV® ceiling of 25 ppm. Acetaldehyde and acetone exposures were generally higher in flavored coffee facilities.

VOC Canister Area Source Measurements

We collected 312 instantaneous source measurements. The highest emission sources of diacetyl and 2,3-pentanedione were roasted whole bean and ground coffee, grinding, and flavoring (**Table 10**). The two highest sources for diacetyl based on GM were ground coffee (GM 488, P95 21,788 ppb) and roasted coffee in a container (GM 225, P95 7,168 ppb), both in non-flavored coffee facilities. The two highest sources for 2,3-pentanedione based on GM were flavoring (GM 1,882, P95 185,446 ppb) and ground coffee (GM 251, P95 12,674 ppb, non-flavored coffee facility). The highest source for diacetyl and 2,3-pentanedione based on P95 was flavoring (P95 354,158 ppb diacetyl; P95 185,446 ppb 2,3-pentanedione). The distributions of instantaneous source means for alpha-diketones and other VOCs are displayed in a heat map (**Figure 4**). Acetaldehyde had highest emissions from ground coffee (GM 987, P95 42,631 ppb) and from roasted coffee in bag (GM 229, P95 52,991 ppb) in non-flavored facilities (**Supplementary Table 10**). Ethanol had highest emissions from flavoring (GM 54,154, P95 1.02 × 10^6 ppb) in flavored coffee facilities (**Supplementary Table 10**). Acetone also had highest emissions from flavoring (GM 341, P95 301,886 ppb) and from ground coffee (GM 477, P95 38,147 ppb) in flavored coffee facilities (**Supplementary Table 10**).

DISCUSSION

To investigate the potential health effects of coffee emissions, we aggregated data from exposure assessments at flavored and non-flavored coffee production facilities and cafés associated with these facilities, through the NIOSH HHE program. The main sources of VOC exposures in coffee facilities and cafés were roasted coffee and flavorings. Roasted coffee contains a complex chemical mixture of over 850 compounds (38). Many of these compounds are VOCs including diacetyl, 2,3-pentanedione, and 2,3-hexanedione, and other chemicals such as CO and CO_2, which are naturally produced when coffee beans are roasted (5–8, 11, 39–41). High CO source emissions were observed where coffee was stored and ground in a number of the facilities, and the results from one facility are discussed elsewhere (12). We observed varying concentrations of diacetyl relative to 2,3-pentanedione in the same air sample in non-flavoring facilities presumably because of differences in green beans and roasting practices among these facilities; coffee roast temperature and time affect aroma formation and VOC profiles (42). The ratio of diacetyl to 2,3-pentanedione concentrations from roasted coffee increases with increasing roasting temperature (400 to 430°F) (43). Volatile constituents are trapped inside the pore structure

TABLE 7 | Area TWA concentrations of diacetyl and 2,3-pentanedione using modified OSHA Methods 1013/1016.

	Diacetyl					2,3-Pentanedione			
Area	**N**	**GM (ppb)**	**GSD**	**P95 (ppb)**	**%BDL**	**GM (ppb)**	**GSD**	**P95 (ppb)**	**%BDL**
NON-FLAVOR									
Administration area	63	1.0	2.8	5.7	19	0.7	2.9	3.8	29
Bakery/café	54	2.5	3.1	15	9.3	2.8	2.6	13	1.9
Breakroom	9	2.2	2.1	7.2	33	1.6	1.9	4.8	33
Green bean storage area	7	0.9	2.9	4.9	14	–	–	2.1*	43
Grinding area	40	12	3.2	81	7.5	7.5	3.0	44	7.5
Packaging area	103	8.6	2.1	29	1	5.0	2.1	17	1
Production area	102	3.0	3.3	22	7.8	2.1	2.8	11	8.8
Production storage area	25	3.6	4.2	38	20	2.0	5.5	33	28
Quality control area	20	2.1	3.1	14	15	1.8	2.4	7.8	15
Roasting area	72	5.2	3.4	39	18	3.3	3.3	23	21
Shipping area	9	2.3	4.1	23	0	0.8	8.4	26	33
FLAVOR									
Administration area	21	8.6	3.6	72	0	6.7	2.9	39	0
Breakroom	7	13	3.1	84	0	8.9	2.5	40	0
Flavoring area	19	33	3.3	235	0	49	3.9	456	0
Green bean storage area	12	14	2.4	60	0	10	2.0	32	0
Grinding area	26	25	2.5	113	0	18	2.3	68	0
Packaging area	87	24	1.8	66	0	19	1.6	43	0
Production area	12	17	2.0	51	0	14	1.7	32	0
Production storage area	35	16	3.3	108	0	5.5	8.0	168	17
Quality control area	7	15	2.4	62	0	10	1.7	26	0
Roasting area	30	13	3.2	90	0	9.2	2.8	49	0

TWA, time-weighted average; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; max, maximum presented when <5 measurements were above the detection limit; "–," not enough samples above the detection limit to obtain an estimate.*

of the roasted coffee bean and rapidly released when coffee is ground because of the greater surface area for off-gassing (11). For flavored coffee facilities, we observed higher exposures to diacetyl and acetoin than 2,3-pentanedione compared to non-flavoring facilities presumably because of the composition of the bulk flavorings used at the time of sampling (**Table 3**). Bulk samples were collected in a number of these facilities, analyzed for diacetyl, 2,3-pentanedione, and other VOCs, and compared to safety data sheets (44). The analysis revealed varying concentrations of diacetyl and 2,3-pentanedione in a flavoring sample and the presence of diacetyl in 81% and 2,3-pentanedione in 58% of samples.

Production and non-production workers in flavoring facilities had higher exposures and percentage of full-shift exposures above the NIOSH REL for diacetyl or 2,3-pentanedione than production workers in non-flavoring facilities or in cafés; café workers had higher exposures than the non-production workers in the non-flavoring facilities (**Table 3**). Full-shift exposures for flavoring/grinding operators (GM diacetyl range 34–26 ppb; GM 2,3-pentanedione range 38–22 ppb) measured in this study were lower than the levels measured for various job titles (GM diacetyl range 69–89 ppb; GM 2,3-pentanedione range 90–130 ppb) in the flavoring room of a flavored coffee production facility previously described by our group (10). Full-shift exposures for packaging worker in non-flavoring facilities (GM diacetyl 8.0 ppb; GM 2,3-pentanedione 4.4 ppb) and were comparable to those observed by McCoy et al. (45) for grinding (1.5 and 9.4 ppb diacetyl) and Pengelly et al. (46) (mean grinding/packing 7.4 ppb and 41 ppb diacetyl; mean 3.3 ppb and 22 ppb 2,3-pentanedione).

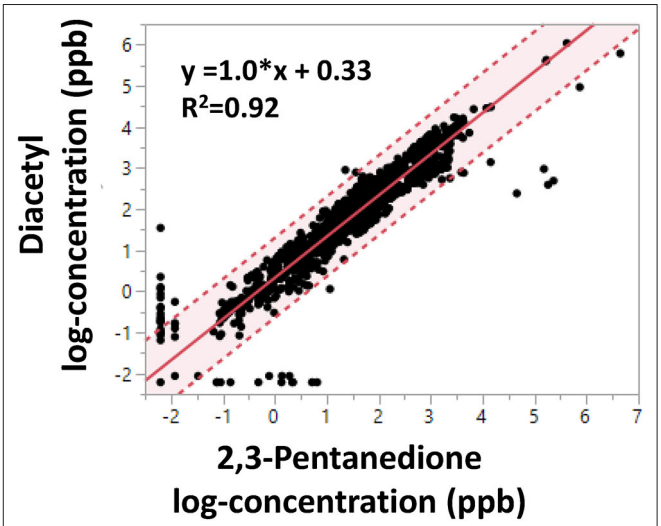

FIGURE 2 | Linear regression of OSHA Methods 1013/1016 diacetyl and 2,3-pentanedione air concentrations (log-concentration in ppb). Shaded area indicates 95% confidence interval. Dotted lines represent 95% confidence limits.

TABLE 8 | Personal task exposures to diacetyl and 2,3-pentanedione using modified OSHA Methods 1013/1016.

Task	Sampling time (min-max)	*N*	k	Diacetyl				2,3-Pentanedione			
				GM (ppb)	GSD	P95 (ppb)	%BDL	GM (ppb)	GSD	P95 (ppb)	%BDL
NON-FLAVOR											
Miscellaneous café tasks	5–16	10	6	2.2	4.5	25	30	3.5	2.5	16	10
Cleaning machines	7–20	9	6	3.4	7.4	89	22	1.7	9.5	59	33
Grinding coffee beans	2–18	58	25	26	3.2	181	5.2	20	2.8	109	1.7
Maintenance of machines	13–15	5	1	–	–	15*	20	–	–	7.8*	20
Miscellaneous production	3–29	9	5	4.0	6.1	78	11	2.2	5.4	34	22
Moving roasted beans or ground coffee	3–25	10	6	20	3.3	142	0	11	3.2	80	0
Packaging coffee	5–53	153	56	8.6	2.8	46	5.9	5.3	2.6	26	7.8
Quality control	4–18	40	9	2.2	6.9	45	33	4.8	2.2	18	2.5
Packaging rework	15–15	4	2	–	–	70*	0	–	–	39*	0
Roasting coffee beans	10–86	152	27	2.6	5.2	39	27	2.4	4.0	24	24
FLAVOR											
Cleaning machines	5–46	27	12	15	2.9	90	7.4	11	2.3	46	7.4
Flavoring coffee	6–18	15	5	5.4	30	1,102	27	45	15	3,816	6.7
Grinding coffee beans	7–32	19	9	30	2.8	166	0	31	3.1	205	0
Miscellaneous production	7–14	3	3	–	–	29*	33	–	–	15*	33
Moving roasted beans or ground coffee	4–15	3	3	–	–	43*	0	–	–	24*	0
Packaging coffee	3–55	46	18	25	1.9	71	2.2	15	2.3	59	8.7
Roasting coffee beans	7–30	43	8	11	3.7	94	16	7.7	3.3	55	21

N, number of samples; k, number of workers; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; max, maximum presented when <5 measurements were above the detection limit; "–," not enough samples above the detection limit to obtain an estimate.*

TABLE 9 | Instantaneous activity exposures of diacetyl and 2,3-pentanedione using evacuated canisters (NMAM 3900).

Activity	N	Diacetyl				2,3-Pentanedione			
		GM (ppb)	GSD	P95 (ppb)	%BDL	GM (ppb)	GSD	P95 (ppb)	%BDL
NON-FLAVOR									
Grinding coffee beans	67	25	4.7	314	0	15	4.7	191	1.5
Miscellaneous café tasks	6	8.6	1.4	15	0	8.5	1.5	16	0
Moving roasted beans or ground coffee	59	9.3	6.7	212	3.4	5.8	7.6	164	17
Packaging coffee	32	18	2.7	90	0	13	3.0	78	0
Pulling sample of beans during roasting	14	8.4	3.0	51	0	5.2	3.0	32	7.1
Quality control	20	22	2.2	79	0	14	2.4	61	0
Roasting coffee beans	16	5.6	4.3	62	6.3	4.4	4.2	47	6.3
FLAVOR									
Flavoring coffee	16	62	15	5,311	6.3	54	7.9	1,594	0
Grinding coffee beans	26	42	6.6	933	7.7	46	3.1	299	0
Moving roasted beans or ground coffee	11	42	2.4	179	9.1	24	2.4	98	9.1
Packaging coffee	7	76	2.5	342	0	39	2.4	158	0
Pulling sample of beans during roasting	6	17	8.2	535	17	–	–	49*	33
Quality control	3	–	–	53*	0	–	–	30*	0
Roasting coffee beans	13	9.3	3.5	73.0	0	3.7	6.1	71	15

N, number of samples; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; max, maximum presented when <5 measurements were above the detection limit; "–," not enough samples above the detection limit to obtain an estimate.*

In the flavored coffee facilities, the highest GM exposures to diacetyl were for flavoring, packaging, and grinding workers, while in the non-flavoring facilities, they were for packaging, QC, and general production workers; 2,3-pentanedione exposures followed a similar pattern with baristas included in the higher exposure group for non-flavoring. However, these average TWA

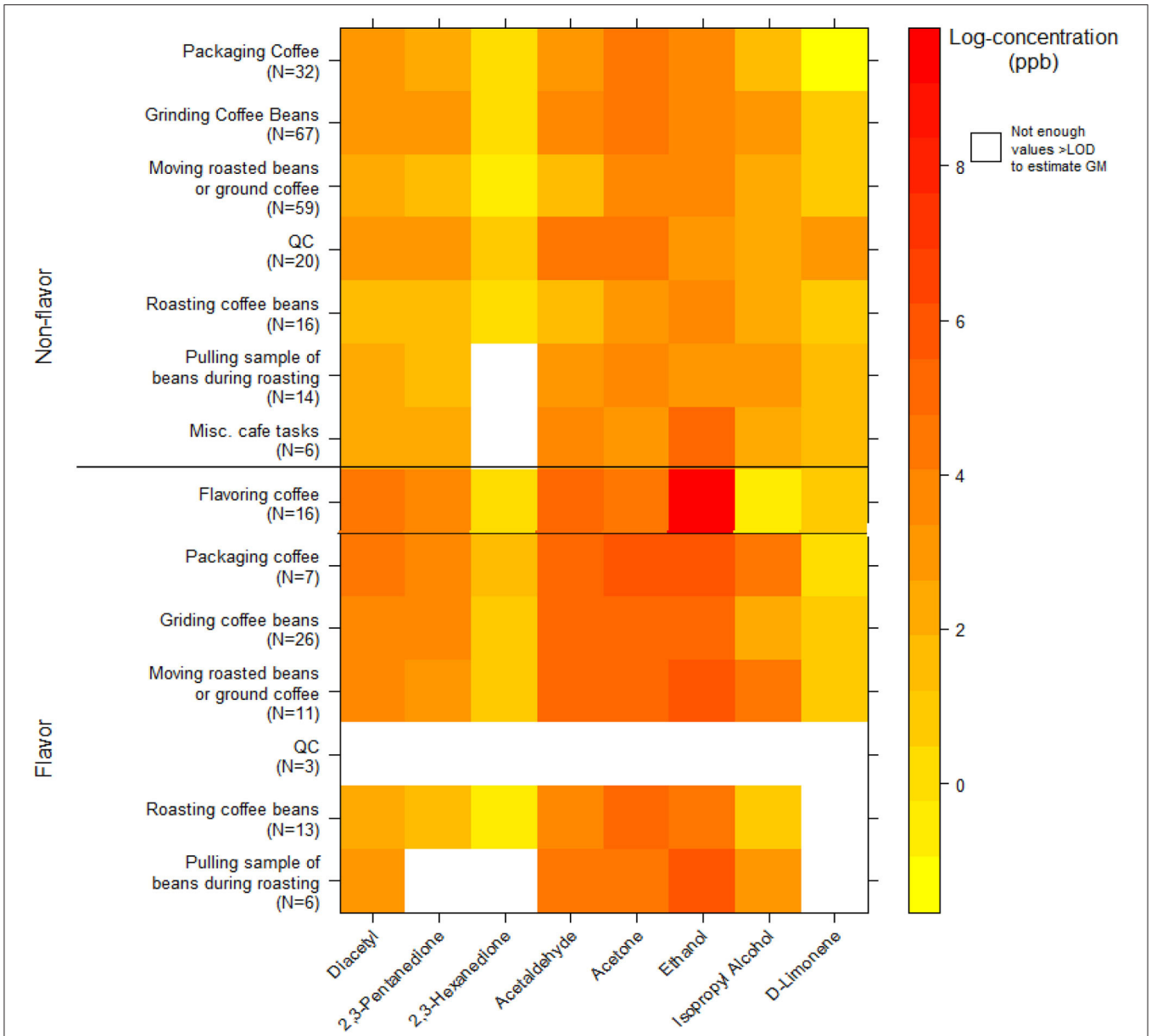

FIGURE 3 | Heatmap of personal instantaneous activity exposures for select VOCs (log-concentration in ppb) using canisters (NMAM 3900).

concentrations do not inform us about short-term exposures, which were orders of magnitude higher and could be relevant to respiratory health, particularly when tasks are repeated multiple times per day. Moreover, average concentrations are not generally as useful as short-term task or source measurements in identifying options for exposure control measures. Given the diversity in facility layouts and process flows, full-shift exposures were likely influenced by multiple sources of exposure when workers were performing tasks in varying areas of the facilities.

The respiratory health risks associated with the full-shift exposures measured in these facilities are higher than NIOSH recommends. For example, geometric mean full-shift personal exposures ranged from 4.3 to 34 ppb diacetyl in flavored coffee facilities and 0.9 to 8.0 ppb in non-flavored coffee facilities (**Table 5**). After a 45-year working lifetime of continual exposure to 50 ppb diacetyl, NIOSH estimated that approximately 12 in 1,000 workers would develop reduced lung function (FEV1 below the lower limit of normal) [Table 5-29 in (18)]. NIOSH predicted approximately 1 in 1,000 workers exposed to diacetyl at 50 ppb would develop more severe lung function reduction [FEV1 below 60% predicted, Table 5-27 in (18)]. FEV1 below 60% predicted is defined as at least moderately severe by the American Thoracic Society (17). The respiratory health risks will change depending on an individual worker's exposure to diacetyl.

TABLE 10 | Area source concentrations of diacetyl and 2,3-pentanedione using evacuated canisters (NMAM 3900).

		Diacetyl				2,3-Pentanedione			
Source	**N**	**GM (ppb)**	**GSD**	**P95 (ppb)**	**%BDL**	**GM (ppb)**	**GSD**	**P95 (ppb)**	**%BDL**
NON-FLAVOR									
Café grinder	7	118	6.5	2,487	0	122	6.4	2,501	0
Ground coffee	52	488	10	21,788	0	251	11	12,674	0
Heat sealing bags	3	–	–	16*	0	–	–	8.8*	0
Miscellaneous quality control	11	27	4.9	366	0	22	5.6	368	0
Miscellaneous café	7	12	2.2	44	0	13	2.5	58	0
Packaging roasted coffee	18	28	4.2	292	0	14	3.9	129	0
Quality control grinding	9	50	6.0	928	0	42	5.7	720	0
Roasted coffee	54	19	4.7	245	0	10	4.6	125	1.9
Roasted coffee in bag	5	76	27	16,456	0	68	19	8,491	0
Roasted coffee in container	53	225	8.2	7,168	0	140	7.9	4,213	0
Roaster cooling drum	12	6.0	3.3	41	0	3.2	4.0	31	8.3
Roaster door	10	8.3	2.2	30	0	4.9	2.7	25	0
Roasting	12	21	6.0	411	8.3	11	4.4	123	8.3
Sample roaster	5	75	7.6	2,059	0	38	12	2,143	0
FLAVOR									
Flavored coffee	8	6.6	100	11,868	38	6.3	71	6,190	38
Flavoring	9	24	381	354,158	44	1,882	17	185,446	0
Ground coffee	17	59	36	20,945	24	143	9.7	6,038	5.9
Miscellaneous quality control	1	–	–	37*	0	–	–	20*	0
Packaging roasted coffee	16	45	4.4	497	13	47	3.6	378	6.3
Roasted coffee	3	–	–	7,386*	33	–	–	1,749*	0

N, number of samples; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; –, not enough samples above the detection limit to obtain an estimate; max, maximum presented when <5 measurements were above the detection limit; "–," not enough samples above the detection limit to obtain an estimate.*

This study is the first to report personal task-based exposure estimates in coffee roasting facilities and cafés. Air samples were collected for short durations ranging from ∼30 s to 86 min to effectively capture high exposures to emitted alpha-diketones. Flavoring coffee, grinding and packaging coffee were the most concerning short duration tasks for exposures to diacetyl and 2,3-pentanedione; flavoring was associated with highest exposures for 2,3-pentanedione, but not for diacetyl. In non-flavoring facilities, grinding and moving coffee had the highest task exposures to diacetyl and 2,3-pentanedione. Gaffney et al. (47) found grinding to be the greatest source of exposure in a roasting facility. In our study, silica gel sorbent tubes were effective at sampling for a few minutes because of a modification to the analytical method that enhanced sensitivity (30). GSDs were higher for some tasks compared to personal full-shift estimates because of inherent environmental variability in shorter term measurements (i.e., environmental variability is dampened in full-shift sampling because of a longer averaging interval). Short duration task exposures were generally over an order of magnitude higher than the full-shift exposures and provided important information on tasks that can be targeted for intervention.

We also collected instantaneous activity exposures from the workers' breathing zones during certain activities, and instantaneous source measurements at the emission source to inform instantaneous peak exposures for activities and at sources. As with short duration tasks, these instantaneous activities and source peak exposures may be important for respiratory health as well as in identifying contributions to emissions. We identified the activity of grinding and the source of ground coffee to be some of the greatest contributors to worker exposures to volatile emissions from unflavored coffee. The source and activity of flavoring coffee were also strong contributors to exposure especially for 2,3-pentanedione, a common diacetyl substitute. The instantaneous source measurements were much greater than the instantaneous activity exposures and provide critical information on options for controlling exposures at the source; information on activity exposures may be useful for planning administrative controls while implementing engineering controls.

Canister sampling was used for instantaneous grab sampling to complement sorbent tube sampling but could have been used for any sampling period. An added benefit of canister sampling was the collection of additional VOC analytes that allowed for quantification of ethanol and acetaldehyde among others. Measured ethanol concentrations are indicative of residual solvent in flavoring formulations. Acetaldehyde is an intermediate in flavoring manufacturing and classified by IARC as possibly carcinogenic to humans (Group 2B) (48) and by ACGIH® as a suspected human carcinogen (A2) (37). Exposures

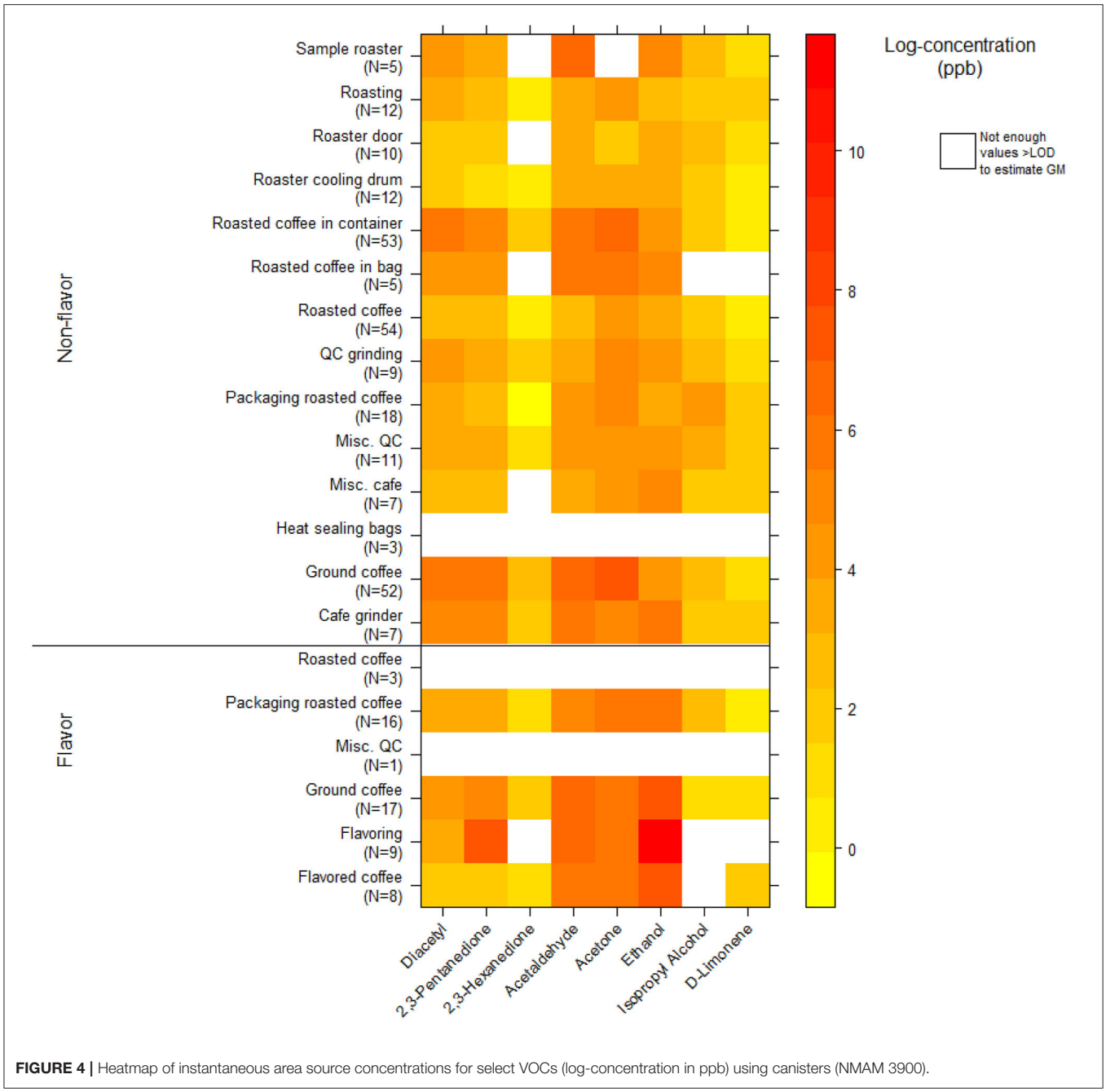

FIGURE 4 | Heatmap of instantaneous area source concentrations for select VOCs (log-concentration in ppb) using canisters (NMAM 3900).

to acetaldehyde were below the OSHA PEL of 200 ppm and less than the ACGIH® TLV® ceiling of 25 ppm, but acetaldehyde emissions during grinding and flavoring should be explored further using standard methods. The ACGIH® TLV® value was set based on eye and upper respiratory tract irritation.

Simultaneous exposure to multiple alpha-diketones as well as exposure to a complex mixture of VOCs, particulate and gaseous exposures occur during coffee processing. In this study, we created a mixture index to account for simultaneous exposure to diacetyl and 2,3-pentanedione using the ACGIH® formula (37). OSHA uses a similar equation of summing the quotients of the components of the mixture to evaluate whether an exposure limit has been exceeded (49). We limited the components to two substances that have been associated with obliterative bronchiolitis and that have exposure limits. Our results show that most job groups in flavored coffee facilities had 100% of measurements above the mixture index, and for non-flavoring facilities only the Administrative job groups had <50% of measurements above the mixture index. To better represent workplace mixed exposures, future epidemiologic studies should consider using a mixed exposure metric or multipollutant model to

address the effects of this complex exposure mixture on respiratory health.

In our assessments, diacetyl and 2,3-pentanedione background air concentrations increased over the workshift indicating a lack of adequate ventilation to keep concentrations to pre-shift levels. To address these potentially harmful levels of alpha-diketones, changes should be made according to the typical hierarchy of controls: eliminate/substitute, engineering controls, administrative controls, and personal protective equipment. This approach prioritizes actions by their likely effectiveness in reducing or removing hazards. In most cases, the preferred approach is to eliminate or substitute hazardous materials. Chemicals known to be hazardous should not be substituted with chemicals of unknown toxicity, which was the case with 2,3-pentanedione prematurely replacing diacetyl in some flavoring formulations. Elimination/substitution is not entirely feasible as diacetyl and 2,3-pentanedione exposures arise not only from the addition of flavorings, but are also generated when roasting coffee beans. Thus, installation of engineering controls should be considered to reduce exposures or shield workers.

Controlling emissions using local exhaust ventilation at sources, such as grinding machines and flavoring stations, might be the most effective means of reducing worker exposures to alpha-diketones. Local exhaust ventilation and enclosures that separate the roasted coffee or flavoring source from the worker should be designed and incorporated at grinding and flavoring areas. Isolating the coffee emission source from the workers by using loose-fitting lids on bins or silos of roasted coffee might reduce exposures by reducing emissions into the workspace, but care should be taken when opening the bins because peak exposures may occur. Isolation of the flavoring room or area from the main production space along with effective ventilation and isolation of the production space from the administrative or non-production space is essential for maintaining pollutant control. Note, however, that isolation of a source or process will increase worker exposures in or from the isolated areas if effort is not made to simultaneously control emissions in the isolated areas using ventilation. We have seen substantial reductions (one to three orders of magnitude) in diacetyl air concentrations by segregating processes and by using local exhaust ventilation at a microwave popcorn plant (14). General dilution ventilation is not recommended to control toxic chemical emissions because they are not effectively removed from the environment, just diluted and dispersed. A well-designed general ventilation system, however, might reduce air concentrations of toxic chemicals such as diacetyl and 2,3-pentanedione by providing outdoor air that is presumably contaminant-free and exhausting contaminants from the indoor air.

The American National Standards Institute (ANSI) and ASHRAE have developed consensus standards and guidelines for general dilution ventilation systems. ANSI/ASHRAE 62.1-2019 recommends outdoor air supply rates that take into account people-related sources as well as building-related sources. There are no specific recommendations in the standard for coffee roasting, packaging and flavoring facilities, or for coffee cafés. However, there are recommendations for similar spaces that can be used as a starting point for dilution ventilation systems. For instance, small to medium coffee production spaces could use the recommendation for sorting, packing, and light assembly areas. Those spaces should receive fresh, outdoor air at the rate of 7.5 cubic feet per minute (cfm)/person for people-related sources, and an additional 0.12 cfm for every square foot (cfm/ft^2) of occupied space to account for building-related sources (50). Medium to large production areas could use the recommendation for manufacturing areas of 10 cfm/person plus 0.18 cfm/ft^2. The recommendations for restaurant dining rooms, café/fast-food dining, and bars and cocktail lounges could be used for coffee cafés. They are recommended to be ventilated at 7.5 cfm/person plus 0.18 cfm/ft^2 (50). Engineering controls should be designed and implemented by qualified ventilation engineers and companies. Process modification or automation to reduce the time workers spend around the emission source are further examples of engineering controls. Modifying work practices that require workers to place their heads near open containers of roasted coffee might reduce exposures. Automatic weighing and mixing of roasted coffee and flavoring of roasted coffee would also reduce exposures.

Administrative controls are next in the hierarchy after engineering controls. An effective administrative control is worker education on potential occupational hazards (e.g., diacetyl, 2,3-pentanedione, CO, CO_2, green bean and roasted coffee dust) and respiratory health consequences of exposure.

Respiratory protection should be the last line of defense, but respirators might be needed as an interim control while permanent engineering and administrative controls can be implemented, and efficacy assessed. If respiratory protection is used, selection of the appropriate respirator should be guided by personal exposure sampling (51) and a written respiratory protection program should be implemented as required by the OSHA Respiratory Protection Standard (29 CFR 1910.134), including training, fit testing, medical evaluation, maintenance and use requirements.

Limitations and Further Research

A potential limitation of the study is exposure misclassification during assignment of job groups in the production area as the administrative job titles were broad. Information obtained during the survey was used to assign these groups based on standardized sample data collection sheets and observations by the sampling team; thus, we expect this misclassification to be minimal. When an exposure is misclassified to an inappropriate job group, the group means and variance can be artificially increased or decreased. The effect of the misclassification will increase with decreasing group sample size. Another limitation of the study is the representativeness of the facilities evaluated and a potential for selection bias. As these investigations were initiated by facility owners or employees through the HHE program, it is not a random sample of facilities; a facility might not volunteer to participate if they have high exposures or if there are currently worker health concerns. While there is a possibility of selection bias, its effect on exposure is likely minimal. The exposure estimates for jobs and tasks reported here are within similar ranges to those reported in other published studies (45–47). A large number of samples were collected from numerous small to medium sized workplaces to characterize exposures to

alpha-diketones associated with tasks, jobs, locations and sources at facilities that roast, grind and package coffee, and represents a valuable resource to estimate exposure for similar activities and workplace settings. Additionally, we could not balance the exposure groups, or the size of the facilities being tested as we had no control over the selection. This analysis did not include large facilities (i.e., >500 employees), where over 50% of employees in the coffee industry work. Most of the facilities in this study were small to medium size based on the total number of workers, which likely affected work processes, production volumes, and exposure levels. Thus, large facilities were not represented in this study and their exposures remain uncharacterized. Some facilities had segregation of production and non-production spaces. Finally, the exposure estimates should be interpreted carefully, especially the estimates of P95 for short-duration and instantaneous tasks, activities and sources due to the large variability (GSD) and censored data, combined with sometimes small sample size. Furthermore, the Bayesian analysis assumes that the priors selected were reasonable. While most priors were left vague to allow the data to drive the inference, we did restrict the GSDs in the repeated measures ANOVA in order to restrict possible GSDs to ranges typically seen in personal time-weighted averages. We also assume that measurements below the limit of detection follow similar trends as the observed measurements (52, 53). Additional assumptions associated with ANOVA include normality of errors, independence of individuals (or observations within a non-repeated measures ANOVA), and constant variances within- and between-workers. The P95 estimates also assume lognormality of exposures. In future analyses, we will assess determinants of exposures for full-shift TWA samples and task-based samples to further elucidate the mechanisms driving exposure concentrations in this industry.

CONCLUSIONS

Obliterative bronchiolitis has previously been observed in the food and flavoring industries (14, 54, 55) and at two coffee facilities that flavored coffee (13, 26). Recently, obliterative bronchiolitis was reported in an individual in India who had worked for 20 years in a coffee facility that roasted and ground coffee; he quit after developing respiratory symptoms (56). Exposure assessments at 17 coffee roasting and packaging facilities revealed exposures to diacetyl above the REL in 95% and to 2,3-pentanedione in 77% of production samples in facilities that flavored coffee. The mixed exposure index for these two chemicals exceeded the mixture index among 96% of production samples in facilities that flavored coffee, 72% in non-flavored coffee facilities, and 67% in cafés. Grinding and flavoring coffee were the main tasks associated with elevated exposures. Controlling emissions at grinding machines and flavoring areas might be the most effective means of reducing worker exposures. Isolating higher exposure concentration areas (e.g., flavoring, grinding, and packaging areas) from the main production space and administrative or non-production spaces is essential for maintaining exposure control. Assessments of diacetyl and 2,3-pentanedione exposures in other coffee facilities is recommended because of the inherent variability in exposures among facilities caused by differences in facility design, workforce, processes, or work flows.

DATA AVAILABILITY STATEMENT

Due to restrictions imposed under the US Privacy Act and the limitations of what participants consented to, the data underlying the analyses presented, beyond what is provided in the paper, are confidential and not available to researchers outside the National Institute for Occupational Safety and Health (NIOSH). For more information about NIOSH's policy regarding sensitive data, see https://www.cdc.gov/niosh/ocas/datahandle.html. Requests to access the datasets should be directed to Ryan F. LeBouf, rlebouf@cdc.gov.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The NIOSH Institutional Review Board reviewed and approved this study (NIOSH Protocol 17-RHD-06XP). All participants provided their written informed consent to participate. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RL, KC, RN, BB, AF, MS, SM, MD, RB, KF, JC-G, and MV contributed to conception and design of the study. AR and DB analyzed the silica gel tube and canister samples. NE and KF organized the database. RL, CG, NE, and MV performed the statistical analyses. RL wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

FUNDING

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

ACKNOWLEDGMENTS

The authors thank the workers for participating in the NIOSH health hazard evaluation program and the members of the NIOSH field teams for their contributions to data acquisition. The authors acknowledge Kevin H. Dunn and Cherie Estill for their review of the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2020.561740/full#supplementary-material

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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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ORIGINAL RESEARCH
published: 23 March 2022
doi: 10.3389/fpubh.2022.786924

Model Predictions of Occupational Exposures to Diacetyl and 2,3-Pentanedione Emitted From Roasted Whole Bean and Ground Coffee: Influence of Roast Level and Physical Form on Specific Emission Rates

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OPEN ACCESS

Edited by:
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Reviewed by:
Pertti Juhani Hakkinen, National Library of Medicine (NIH), United States
Elettra Marone, University of Teramo, Italy
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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: *30 September 2021*
Accepted: *25 February 2022*
Published: *23 March 2022*

Citation:
LeBouf RF, Ranpara A, Fernandez E, Burns DA and Fortner AR (2022) Model Predictions of Occupational Exposures to Diacetyl and 2,3-Pentanedione Emitted From Roasted Whole Bean and Ground Coffee: Influence of Roast Level and Physical Form on Specific Emission Rates. Front. Public Health 10:786924. doi: 10.3389/fpubh.2022.786924

Roasted coffee emits hazardous volatile organic compounds including diacetyl and 2,3-pentanedione. Workers in non-flavored coffee roasting and packaging facilities might inhale diacetyl and 2,3-pentanedione from roasted coffee above occupational exposure limits depending on their work activities and proximity to the source of emissions. Objectives of this laboratory study were to: (1) investigate factors affecting specific emission rates (SERs) of diacetyl and 2,3-pentanedione from freshly roasted coffee, (2) explore the effect of time on SERs of coffee stored in sealed bags for 10-days, and (3) predict exposures to workers in hypothetical workplace scenarios. Two roast levels (light and dark) and three physical forms (whole bean, coarse ground, and fine ground) were investigated. Particle size for whole bean and ground coffee were analyzed using geometric mean of Feret diameter. Emitted chemicals were collected on thermal desorption tubes and quantified using mass spectrometry analysis. SERs developed here coupled with information from previous field surveys provided model input to estimate worker exposures during various activities using a probabilistic, near-field/far-field model. For freshly roasted coffee, mean SER of diacetyl and 2,3-pentantedione increased with decreasing particle size of the physical form (whole bean < coarse ground < fine ground) but was not consistent with roast levels. SERs from freshly roasted coffee increased with roast level for diacetyl but did not change for 2,3-pentanedione. Mean SERs were greatest for diacetyl at 3.60 mg kg^{-1} h^{-1} for dark, fine ground and for 2,3-pentanedione at 3.88 mg kg^{-1} h^{-1} for light, fine ground. For storage, SERs of whole bean remained constant while SERs of dark roast ground coffee decreased and light roast ground coffee increased. Modeling demonstrated that near-field exposures depend on proximity to the source, duration of exposure, and air velocities in the near-field further supporting previously reported chemical air measurements in coffee roasting and

packaging facilities. Control of source emissions using local exhaust ventilation especially around grinding activities as well as modification of work practices could be used to reduce exposures in this workforce.

Keywords: diacetyl, 2,3-pentanedione, coffee, emission rate, occupational exposures, volatile organic compounds

INTRODUCTION

Between 2015 and 2017, the U.S. National Institute for Occupational Safety and Health (NIOSH) received 17 Health Hazard Evaluation requests at coffee roasting and packaging facilities and cafés. As a part of the requests, NIOSH researchers investigated personal exposures and area air concentrations of diacetyl, 2,3-pentanedione, and other volatile organic compounds (VOCs) (1). They found elevated worker exposures to diacetyl and 2,3-pentanedione when working around sources of ground roasted coffee and during grinding tasks (1). Roasted coffee emits VOCs, carbon monoxide, and carbon dioxide at various rates depending on the origin, processing, roast level, physical form, and storage conditions of the coffee (2). Researchers have observed an increase in specific emission rates (SERs) for carbon monoxide with increasing roast level (i.e., darker roasts) and with ground coffee compared to whole bean (3). These researchers also raised concern about storing roasted coffee in unventilated or under-ventilated storage areas because of carbon monoxide accumulation in the space to unsafe levels. The same concerns could be raised for the buildup of hazardous VOCs in storage bins and containers of roasted coffee or in under-ventilated storage areas. Diacetyl and 2,3-pentanedione have also been found in flavoring formulations used to impart a buttery smell or taste to baked goods and in electronic cigarette liquids (1, 4–8). Diacetyl exposure via inhalation has been associated with a debilitating lung disease, obliterative bronchiolitis (9). Like diacetyl, previous studies on animals demonstrated similar respiratory toxicity for 2,3-pentanedione (10).

Coffea arabica and *Coffea robusta* are the two species of coffee commonly used for roasting (11). Roasting green coffee beans at temperatures at or above 200°C (11, 12) produces a myriad of chemicals via the Maillard reaction, Strecker degradation, pyrolysis, and other chemical reactions that give roasted coffee a characteristic aroma (13). Over 800 compounds have been identified from roasted coffee (14). The constituents of coffee emissions include furans, pyrazines, pyrroles, sulfur compounds, aldehydes, and ketones including the alpha-dicarbonyl species: glyoxal, methylglyoxal, diacetyl, and 2,3-pentanedione (14–17). Average concentrations of chemicals in brewed coffee have been measured at 8 μg glyoxal/g, 152 μg methylglyoxal/g, and 19 μg diacetyl/g dry coffee (15). The type of coffee and origin can also affect relative concentration of chemicals formed. Using dynamic headspace analysis to characterize the volatile composition of roasted coffee, a greater concentration of diacetyl and 2,3-pentanedione was measured for Arabica samples (3,235–8,818 μg diacetyl/kg and 3,087–8,853 μg 2,3-pentanedione/kg) compared to Robusta samples (1,959–4,316 μg diacetyl/kg and 341.1–4,701 μg 2,3-pentanedione/kg) (18). Colzi et al. observed a similar trend of greater VOC emissions in terms of type and quantity from Arabica compared to Robusta when attempting to characterize and distinguish species based on volatile profiles using proton transfer time-of-flight mass spectrometry (19). Mayer et al. measured differences in volatile emissions from different varietals of the same species. One research group has found varying concentrations of diacetyl and 2,3-pentanedione in *C. arabica* from different origins (20). Hyong et al. observed espresso coffee samples made using *C. arabica* from Brazil and Ethiopa had a greater concentration of diacetyl than *C. robusta* from Vietnam and India, and the concentration of diacetyl increased with roast temperature and time (21).

The duration and temperature at which coffee is roasted (i.e., roast level) can influence the aroma profile. Roast level has been shown to change the concentration of diacetyl in coffee beans that have been roasted longer. Chemometric analysis coupled with proton transfer time-of-flight mass spectrometry has been used to distinguish organic from regular coffee and espresso from other roast levels (22). The formation of diacetyl begins later in the roasting duration, at a medium roast level (210°C for 14 min) with a peak diacetyl concentration of 2.28 ± 0.07 mg/100 g between 14 and 16 min (23). Chemical reaction pathways change as the roast process continues with early stage roasting generating diacetyl from sucrose (the intact sugar skeleton) followed by sugar fragments later in the roasting cycle (24). Roast level also influences the pore structure of the roasted coffee bean, which can affect mass transport phenomena of aromatic compounds into the surrounding air (25). Bean porosity is increased during roasting because of cell destruction and degradation of the intercellular structure (11).

The physical form of the roasted coffee such as whole bean or ground can affect the rate of chemical release because of increased surface area (26, 27). Migration of coffee volatiles to the bean surface is a relatively slow process and can be limited by accumulation of volatiles into the headspace of the packaging material. Grinding the roasted coffee beans releases trapped aroma compounds and increases the emission rate of chemicals from roasted coffee. Coffee aroma (i.e., chemical emission) decreases over time during storage leading to staleness, a sweet but unpleasant sensory quality of taste and smell (16). Researchers have found that coffee aroma can be maintained when stored ground for ∼2 weeks at room temperature depending on storage conditions (27). The rate of chemical emissions and the storage duration can be used to estimate total mass emitted. This calculated mass value can be compared to a measured value of total content in the bean. SERs estimated from different roast levels and forms of roasted coffee can be used to predict air concentrations of hazardous chemicals based on mass-balance models.

In this study, we employed a near/far field model with a constant emission rate to demonstrate the cyclic, diurnal pattern of high peak exposures when working close to source of emissions (near field) followed by low exposures (far field) and how this profile influences the prediction of full-shift occupational exposures. In laboratory tests, we estimated SERs of diacetyl and 2,3-pentanedione based on degree of roast and physical form to better understand exposure assessments during field investigations in coffee facilities. The aims of this laboratory study were to investigate the effect of roast level and physical form on SERs of diacetyl and 2,3-pentanedione released from freshly roasted and stored coffee, predict air concentrations of these chemicals in hypothetical work environments, and estimate occupational exposures assuming task and job work patterns based on real-world observations and information obtained from coffee roasting and packaging facilities.

METHODS

Coffee Roasting

For each batch, 0.11 kg of green *C. arabica* beans (Colombia La Guamera, Sagebush Unroasted, Chandler, Arizona) was roasted in a BEHMOR Gourmet Coffee Roaster (Incline Village, Nevada) with smoke suppression technology and preprogrammed roast profiles. The roaster has a rotating metal drum cage with heating elements in the rear of the chamber. The roaster was preheated for 1 min and 45 s prior to roasting. During roasting, two distinct stages occur that can be heard by a cracking sound: (1) first crack when steam is rapidly released and the bean expands, and (2) second crack when the bean darkens and structural changes continue to occur. For hard beans, the equipment manufacturer recommends an automatic roast profile setting, P2, which reduces the power to the elements to 25%. Roast levels were achieved by roasting on the P2 setting for ∼11 min (30 s after first crack) for light roast and ∼14 min (30 s after second crack) for dark roast. We use the relative terms light and dark roast levels indicating that light is lighter than dark roast, the latter of which could be classified as medium roast based on a previous report (23). Roasts were visually observed for desired and consistent coloring.

Coffee Grinding and Particle Sizing

The roasted beans were ground using a Cuisinart coffee grinder (DBM-8, Stamford, CT) on the coarsest or finest settings. Roasted coffee was assessed for particle size using ImageJ (public domain software produced at National Institutes of Health, Bethesda, MD). Whole bean or ground coffee was photographed on a piece of white paper with a ruler to set the scale in centimeters (**Figure 1**). Images were independently collected 3 times each for ground particles and 6 times for whole bean. Particles were sized using Feret or caliper diameter, which is the distance between two parallel tangential lines and indicates size along a specified direction.

Experimental Design

Preliminary emission testing was conducted to determine appropriate roasting procedures and experimental set up. Chemical emission data was measured to assess the effect of emission factors of roast level and physical form on average SERs for two conditions: (1) freshly roasted and (2) stored coffee. Testing strategy for each factor depended on the conditions being tested (**Table 1**). For freshly roasted coffee, independently produced batches of coffee were roasted to include the variability associated with multiple roasts. For stored coffee, a single batch of each type of coffee was roasted to assess the impact of storage time on emissions. Storage emission samples were stored as whole bean, coarse ground, or fine ground. Storage emission samples were tested on approximately day 0 (within 4 h), 1, 4, and 10. Immediate roast emission samples were tested within 4 h of roasting and ground immediately before testing. One test was conducted for each freshly roasted sample while two tests were conducted for each stored coffee sample. Samples were stored in resealable, coffee storage bags with one-way valves on a shelf in the laboratory at ∼22°C.

Emission Sample Collection

The emissions test chamber (M-CTE 250; Markes International Inc., Sacramento, CA) was equilibrated for 20–30 min before each trial. Chamber temperature, flow rate, and relative humidity were measured before and after emission testing. Coffee emissions testing was performed using ultra-high purity air at 54.5 ± 11% relative humidity (RH; mean ± standard deviation) and 21.5 ± 2.5°C, measured with a Control Company 4,095 hygrometer/thermometer monitor (Webster, TX). Flow rate was controlled using an in-line rotameter and calibrated using a primary calibration flowmeter (Bios DryCal Defender 530, Mesa Laboratories, Butler, NJ) before and after testing and an average flow rate was used for emissions calculations. The air was humidified using a glass bottle containing 500 mL of water (18.2 MΩ-cm, Millipore Milli-Q system, Billerica, MA). To obtain the desired flow rate and temperature, the chamber system was operated in high-flow mode with the chamber heaters set to 25°C with the cooling fans on. The chamber exhaust air was sampled for diacetyl (2,3-butanedione, CAS# 431-03-8) and 2,3-pentanedione (CAS# 600-14-6) using Universal thermal desorption tubes (Part no. C3-CAXX-5266, inert-coated stainless steel, Markes International, Inc.) at a flow rate of 39.4 ± 2.2 mL/min. The test chamber had a volume of 114 mL, translating to ∼20.7 air changes per hour (N, hr^{-1}) at 39.4 mL/min.

Background air samples were collected from the test chamber for 20 min prior to placing coffee samples in each chamber to make sure the chamber air was clean and free of chemical interferents. Coffee samples were weighed to 5.2 ± 0.18 g (mean ± standard deviation) and placed into one of the four test chambers in the system. Some tests were conducted concurrently in two chambers operated in parallel. Eight sequential air samples were collected from each sample for both storage and roast emission tests at approximate midpoint times of 2, 4, 6, 8, 10, 15, 35, and 60 min. The first five time points were sampled for 30 s to capture rapid changes in chemical emissions. The last three time points were sampled for 1 min.

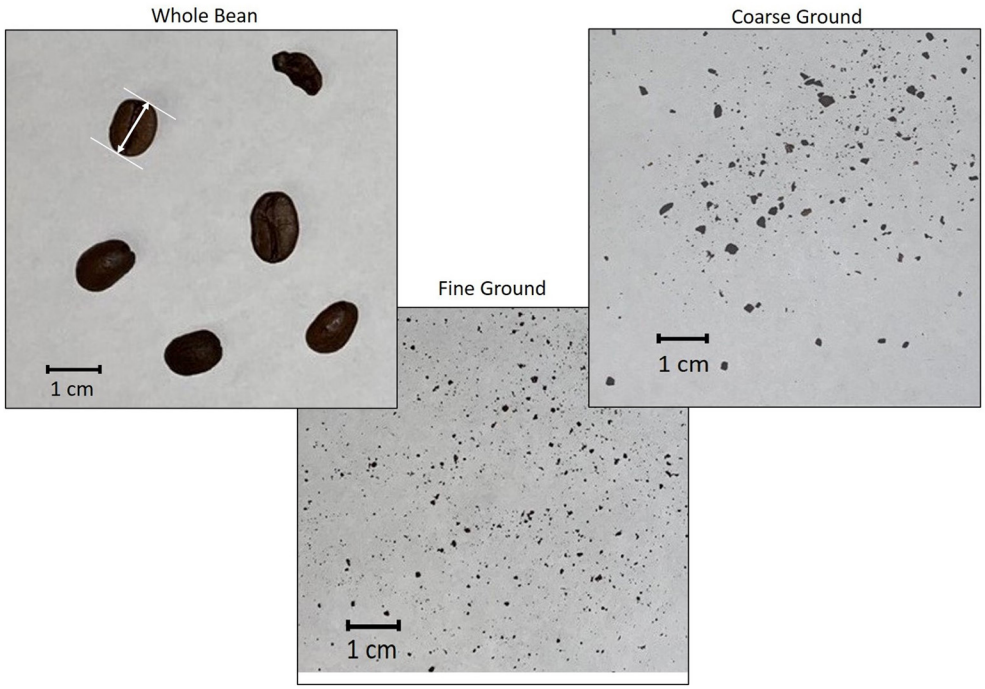

FIGURE 1 | Photographs of the physical forms of dark roasted coffee (whole bean, coarse ground, fine ground). White arrow between two tangential lines is an example of Feret diameter.

TABLE 1 | Emission test conditions for freshly roasted and stored coffee.

		Freshly roasted coffee		Stored coffee	
		Roast level			
		Dark	**Light**	**Dark**	**Light**
Physical form	Whole bean	3 independent roasts ($n = 3$)	3 independent roasts ($n = 3$)	4 time points* 2 replicates per time point ($n = 8$)	3 time points** 2 replicates per time point ($n = 6$)
	Coarse ground	3 independent roasts ($n = 3$)	3 independent roasts ($n = 3$)	4 time points* 2 replicates per time point ($n = 8$)	3 time points** 2 replicates per time point ($n = 6$)
	Fine ground	3 independent roasts ($n = 3$)	3 independent roasts ($n = 3$)	4 time points* 2 replicates per time point ($n = 8$)	3 time points** 2 replicates per time point ($n = 6$)

4 time points: ∼ Day 0 (within 4 hours), 1, 4, and 10.

***3 time points: ∼ Day 0, 4, and 10. Storage emissions samples for light roast were not tested on day 1 because of scheduling conflicts.*

Emission Sample Analysis

Samples were analyzed using a Markes ULTRA-XR, UNITY-XR thermal desorption system attached to an Agilent Technologies 6890 gas chromatograph/5977B mass spectrometer system. The thermal desorption parameters were as follows: internal standards bromochloromethane, chlorobenzene-d5 and 1,4-difluorobenzened added to the tube, split flow 50 mL min^{-1}, flow path temperature of 150°C, desorption temperature of 280°C, purge time 1 min at 50 mL min^{-1}, tube desorption time of 7 min with a flow of 50 mL min^{-1}, and cold trap temperature of 25 up to 290°C during desorption. The gas chromatograph parameters were as follows: 2 mL min^{-1} helium flow, initial oven temperature 30°C (held for 5 min), temperature ramp of 5°C min^{-1} to 170°C, then 20°C min^{-1} to 220°C, with a final ramp of 33°C min^{-1} to 220°C. The mass spectrometer was operated in scan mode from 35 to 350 amu, mass spectrometer transfer line temperature 280°C, source temperature 300°C, and quadrupole temperature 150°C.

Data Analysis

SER estimates were developed using chemical air concentration curves plotted against the midpoint of sampling duration. Curves were fitted using a non-linear regression technique, PROC NLIN, in SAS 9.4 (SAS Institute Inc., Cary, NC). SER models were based

on these concentration curves and ASTM D5116 (28) modified with a steady state SER asymptote (EF_{ss}). We used the first-order decaying source equation to fit the concentration curve data using Equation (1).

$$C(t) = \left[\frac{L(EF_0)\left(e^{-kt} - e^{-Nt}\right)}{N - k}\right] + EF_{ss} \quad (1)$$

where C(t) = diacetyl or 2,3-pentanedione mass concentration, mg m^{-3}, measured at midpoint time t,

L = loading factor (average value 45.6), which is the mass of material for each trial divided by the chamber volume, kg m^{-3},

EF_0 = initial SER (0.1–5 by 1), mg kg^{-1} hr^{-1},

EF_{ss} = steady-state SER (0.1–5 by 1), mg kg^{-1} hr^{-1},

k = decay rate constant (0.1–4 by 1), hr^{-1},

N = air exchange rate, which is the flow rate of air for each trial divided by chamber volume of 114 mL, hr^{-1},

t = midpoint time, which is halfway between the start and end of the sample duration, hr.

Maximum predicted SERs for diacetyl or 2,3-pentanedione were calculated from the maximum concentration predicted that was chosen from the peak of the emission buildup and decay curve generated above. This peak corresponds to the time at which emission of chemical was equal to the removal. Maximum SERs were calculated using Equation (2).

$$EF_{\max} = C_{\max} * \left(\frac{N}{L}\right) = C_{\max} * \frac{Q}{m} \quad (2)$$

where EF_{max} = maximum SER, mg kg^{-1} hr^{-1},

C_{max} = maximum predicted diacetyl or 2,3-pentanedione concentration, mg m^{-3}, from the fitted curve,

Q = volumetric flow rate, m^3 hr^{-1},

m = mass of coffee, kg.

Air exchange rate (N) divided by the loading factor (L) can be reduced to the simpler form of Equation (2) that uses volumetric flow rate (Q) and mass (m). In the beginning of the trial, emission of chemical is greater than removal. The rate of accumulation during the buildup portion of the concentration curve will determine the adjusted maximum EF ($EF_{buildup}$), which may be slightly higher than EF_{max}. $EF_{buildup}$ (mean ± standard deviation) was used for all data analysis. $EF_{buildup}$ was calculated from EF_{max} using the following equation:

$$EF_{buildup} = \frac{EF_{\max}}{\left(1 - e^{-Nt_{\max}}\right)} \quad (3)$$

where $EF_{buildup}$ = adjusted maximum emission factor accounting for buildup, mg kg^{-1} hr^{-1},

EF_{max} = maximum emission factor, mg kg^{-1} hr^{-1},

N = air exchange rate, hr^{-1},

t_{max} = time required to reach maximum predicted chemical concentration, hr.

Particle sizes (Feret diameter) of different forms of coffee (252 whole beans, 7,500 coarse ground particles, 10,819 fine ground particles) are summarized as geometric mean (GM) and geometric standard deviation (GSD) as these particle size distributions are log-normally distributed. Group-wise mean comparison tests on particle sizes for different forms of coffee were conducted on log-transformed data. SERs are summarized as average and standard deviation as these metrics are normally distributed. Minimum and maximum values are also presented. The effect of roast level, physical form, and the interaction between the two on SERs were investigated using a least-squares regression model with Student's *t*-test or Tukey's multiple comparison tests for groups of three or more at a significance level of 0.05 in JMP 13.0 (SAS Institute Inc., Cary, NC).

Emission factors are scalable quantities that can be converted to chemical generations rates based on the mass of material available for emission. These generation rates can then be used to estimate chemical air concentrations in a facility based on room volume and ventilation rates. We estimated chemical air concentrations using emission factors developed here and facility information from the Health Hazard Evaluations as model input.

We used a two-zone well-mixed box model with a constant emission source and IHMOD 2.0 (AIHA, Falls Church, VA, version 2.002, August 2018), a publicly available software, to calculate air concentrations. The near-field and far-field model equations can be found in **Supplementary Material**.

Model assumptions include instantaneously well-mixed concentration within each zone, air flow is limited between zones, cross-drafts (e.g., fans or equipment exhaust) are insignificant, initial chemical concentration in each zone is zero, chemical concentration of the supply air is zero, and the only removal of chemical from the zone is through exhaust (i.e., no losses to surfaces or chemical reactions). Total mass emitted in a certain time can be calculated to compare against known chemical content of material as a *post-hoc* assessment of the model to make sure the model is realistic and not overestimating contaminant transport from the material to the air. We assume that the chemical concentration of the air initially in the zones and entering the zones is zero.

Model inputs not described above in the equations were measured during Health Hazard Evaluation investigations, estimated from information observed during these investigations, or calculated based on laboratory-derived SERs reported here and assumed masses of coffee (**Table 2**). These scenarios represent realistic hypothetical workplace task durations, material quantities, production facility room volume, and ventilation (supply air) rates. Observations during field investigations indicated variable task durations and frequencies, but a cyclic work pattern of alternating proximity to the source was chosen for simplicity. For scenario A, we used air change rates based on measured values (supply air ventilation rates and room area) from a single facility during the Health Hazard Evaluation field investigations. Scenario A values are indicative of a small-scale coffee roasting and packaging facilities. The production room volume and material quantities for Scenario A are smaller than those in Scenario B, a hypothetical medium-scale coffee roasting and packaging facility.

TABLE 2 | Input variables and values for model scenarios.

Input variable	Scenario A values	Scenario B values	Scenario A information	Scenario B information
Production room volume* (m^3)	7,787	31,856	Measured/assumed; fixed value	Same information as A
Supply air (Q, m^3 min^{-1})	65.9–80.5	238.9–292.0†	Measured 73.2 m^3 min^{-1}; uniform distribution with assumed 10% measurement error	Assumed; uniform distribution with assumed 10% measurement error
Generation rate‡ (G, mg min^{-1}), dark roast, fine ground	0.6 ± 0.14	10.9 ± 2.6	Measured/assumed; ±95% confidence interval; normal distribution	Same information as A
Generation rate‡ (G, mg min^{-1}), dark roast, whole bean	0.035 ± 0.24	0.64 ± 0.15	Measured/assumed, ±95% confidence interval; normal distribution	Same information as A
Mass of coffee used for each grinding or packaging task (kg)	10	181.8	Assumed based on small-production volume facility; fixed value	Assumed based on medium-production volume facility with large grinder capacity; fixed value

Assumed 7.6 m height; production room area measured in the field.
†Supply air equivalent to 0.5 air changes per hour used in scenario A, which was based on measured values in the field.
‡Emission rate measured in laboratory tests; mass of coffee assumed.

TABLE 3 | Particle size measured as Feret diameter (cm) for whole bean, coarse ground, and fine ground forms of roasted coffee.

	Feret diameter (cm)			
Physical form	Geometric mean	Geometric standard deviation	Minimum	Maximum
Whole bean	1.1	1.5	0.80	1.38
Coarse ground	0.036	2.0	0.012	0.90
Fine ground	0.032	1.9	0.008	0.26

RESULTS

Particle Sizing

The geometric mean particle sizes for different forms of coffee were 1.1 cm (GSD 1.5) for whole bean, 0.036 cm (GSD 2.0) for coarse ground, and 0.032 cm (GSD 1.9) for fine ground coffee (**Table 3**). A statistical difference was observed between whole bean and coarse or fine ground coffee ($p < 0.001$) but no statistical difference between coarse and fine ground coffee ($p = 0.17$). Minimum and maximum particle size was larger for coarse (0.012; 0.9 cm) than fine ground coffee (0.008; 0.26 cm).

Roast Level and Physical Form Effect on SERs

Mean SERs for diacetyl and 2,3-pentanedione increased with decreasing particle size of coffee form (whole bean << coarse ground < fine ground) (**Table 4**). Whereas, the trend in mean SERs considering roast level (light, dark) was not consistent evidenced by SERs increasing for diacetyl but decreasing for 2,3-pentanedione as the roast level darkened. Mean SERs were greatest for diacetyl at 3.60 mg kg^{-1} h^{-1} for dark, fine ground and for 2,3-pentanedione at 3.88 mg kg^{-1} h^{-1} for light, fine ground. Variability measured as the coefficient of variation was greatest for light roast regardless of chemical when comparing between roast levels of the same ground form. Linear regression modeling for diacetyl revealed a significant effect of physical form ($p < 0.0001$) and of roast level ($p = 0.0067$), while the interaction of form and roast level was not significant ($p = 0.15$). Linear regression modeling for 2,3-pentanedione revealed a significant effect of form ($p < 0.0001$) but not for roast level ($p = 0.82$) nor the interaction of form and roast level ($p = 0.80$). Mean emission rates for physical forms were all significantly different from each other and the same was observed for roast levels, except for roast level comparison for 2,3-pentanedione ($p = 0.82$).

Storage Duration Effect on SERs

When coffee was stored, SERs for diacetyl and 2,3-pentanedione decreased for dark roast (solid black line, **Figure 2**) in coarse ground or fine ground forms. SERs increased for light roast in fine ground forms but were unchanging for diacetyl and decreased for 2,3-pentanedione in coarse ground forms (dashed gray line, **Figure 2**; **Supplementary Table S1**). Dark roast, ground coffee exhibited an initial increase in emission factors on day 1 followed by a decrease. The highest average emission factors were observed on day 1, dark roast for both chemicals: fine ground for diacetyl (7.07 mg kg^{-1} h^{-1}) and coarse ground for 2,3-pentanedione (9.17 mg kg^{-1} h^{-1}). Whole bean emission factors were constant for light roast regardless of chemical and for dark roast for 2,3-pentanedione, but decreased for dark roast for diacetyl, never exceeding 0.64 mg kg^{-1} h^{-1} (**Supplementary Table S1**).

TABLE 4 | Specific emission rates ($n = 3$) for diacetyl and 2,3-pentanedione for different roast levels (light, dark) and forms including whole bean, coarse ground, and fine ground.

			Specific emission rates (mg kg^{-1} h^{-1})				
Compound	**Roast level**	**Physical form**	**Mean**	**Std. dev**	**CV**	**Minimum**	**Maximum**
Diacetyl	Dark	Whole bean	0.21	0.14	67.9	0.09	0.37
		Coarse ground	2.50	0.32	12.8	2.22	2.85
		Fine ground	3.60	0.52	14.3	3.10	4.13
	Light	Whole bean	0.12	0.06	54.7	0.04	0.17
		Coarse ground	1.57	0.69	44.3	0.88	2.27
		Fine ground	2.34	0.77	33.0	1.46	2.92
2,3-Pentanedione	Dark	Whole bean	0.14	0.07	50.7	0.07	0.22
		Coarse ground	2.45	0.43	17.6	2.04	2.90
		Fine ground	3.43	0.58	17.0	2.77	3.88
	Light	Whole bean	0.07	0.05	77.9	0.02	0.12
		Coarse ground	2.33	1.17	50.3	1.34	3.63
		Fine ground	3.88	1.44	37.0	2.59	5.44

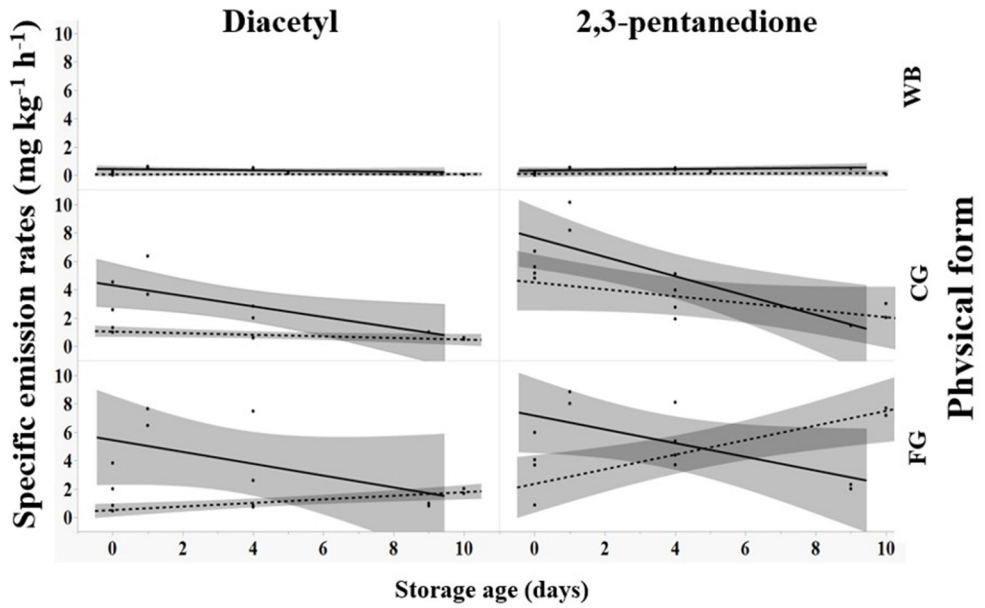

FIGURE 2 | Effect of storage age (days) on specific emission rates for diacetyl and 2,3-pentanedione for different roast levels (— dark, - - - light) and forms of roasted coffee including whole bean (WB), coarse ground (CG), and fine ground (FG). Shaded areas around lines indicates 95% confidence limit of least-squares regression line.

Predicted Air Concentrations and Exposure Profile

Scenario A

Diacetyl emission rates for dark roast, whole bean and fine ground coffee were used to simulate a hypothetical employee exposure for an 8-h workday in a facility representative of one observed during field investigations. In scenario A, a general production worker performs three packaging tasks on whole bean coffee and one grinding task with this cycle of tasks repeated four times. Each task is performed on 10 kg of dark roast coffee (the source) for 15 min. Low exposures (0.04–0.21 ppb) were assumed to be the same concentration as far-field (away from source) exposure estimates in between tasks for 5 min, and during cleaning and labeling tasks for 15 min. Two 15-min breaks and one 30-min lunch are included with no exposure during these periods. The model estimated median near-field exposures at 2.1 ppb (95th percentile 10.9 ppb) during packaging and 7.9 ppb (95th percentile 25.8 ppb) during grinding. Because the 95th percentile encompasses the NIOSH short-term exposure limit (STEL) of 25 ppb, some grinding tasks could have exceeded the STEL. Total emitted mass of diacetyl was 0.53 mg during each packaging task and 9 mg during each grinding task. Diacetyl

time-weighted average (TWA) cumulative exposure reached a maximum of 11.7 ppb after the first grinding task at 75 min and continued to increase and decrease throughout the day because of repeated exposures to diacetyl from roasted coffee sources with grinding having the greatest effect on cumulative exposure (**Figure 3**). By the end of the day, the full-shift cumulative exposure concentration was 1.8 ppb median (95th percentile 7.4 ppb) and might have exceeded the NIOSH recommended exposure limit (REL) of 5.0 ppb considering the confidence interval encompassed this limit.

Scenario B

The same work pattern occurs in scenario B but the grinding activity is assumed to last 1 min because of the quantity of coffee and large footprint of the grinder while the packaging task is 15 min. Packaging and grinding tasks were performed on 181.8 kg of dark roast coffee (the source). Low exposures (0.001–0.03 ppb) were used as far-field (away from source) exposure estimates in between tasks for 5 min, and during cleaning and labeling tasks for 15 min. Two 15-min breaks and one 30-min lunch are included with no exposure during these periods. The model estimated median near-field exposures at 8.3 ppb (95th percentile 28.9 ppb) during packaging for 15-min each and 123.5 ppb (95th percentile 28.9 ppb) during grinding for 1-min each. Total emitted mass of diacetyl was 9.6 mg during each packaging task and 11.4 mg during each grinding task. Assuming 14-min of far-field exposure to 0.2 ppb, grinding for 1-min would expose a worker to a cumulative 15-min TWA exposure of 8.4 ppb and would not exceed the NIOSH STEL of 25 ppb. Diacetyl TWA cumulative exposure was greatest at 8.3 ppb after the first packaging task (**Figure 4**). By the end of the day, the cumulative exposure concentration (i.e., full-shift TWA) was 4.1 ppb (95th percentile 14.2 ppb) and might have exceeded the NIOSH REL of 5.0 ppb considering the confidence interval encompassed this limit. Median short-term concentration excursions up to 4.9-times the STEL (123.5 ppb/25 ppb) occurred four times in this scenario.

Sensitivity Analysis of Inter-zone Air Flow Rate (β)

For 10 kg of fine ground, dark roast coffee, a sensitivity analysis of inter-zone air flow rate between near-field and far-field zones (β) demonstrated a substantial influence of low air flow rates, which are heavily influenced by random air velocities at the boundary (S), on near-field TWA exposure concentrations (**Figure 4**). Near-field TWA exposure concentrations decreased 2.9-fold (1,153–394 ppb) for β from 1.77 to 5.3 m^3 min^{-1} in relatively still air corresponding to air velocities of 1.0–3.0 m min^{-1} and these concentrations asymptotically approached zero as β increased (**Figure 5A**). Near-field TWA exposure concentrations decreased 3.9-fold (200–51 ppb) for β from 10.6 to 42.4 m^3 min^{-1} indicative of typical air velocities from 6.0 to 24 m min^{-1}

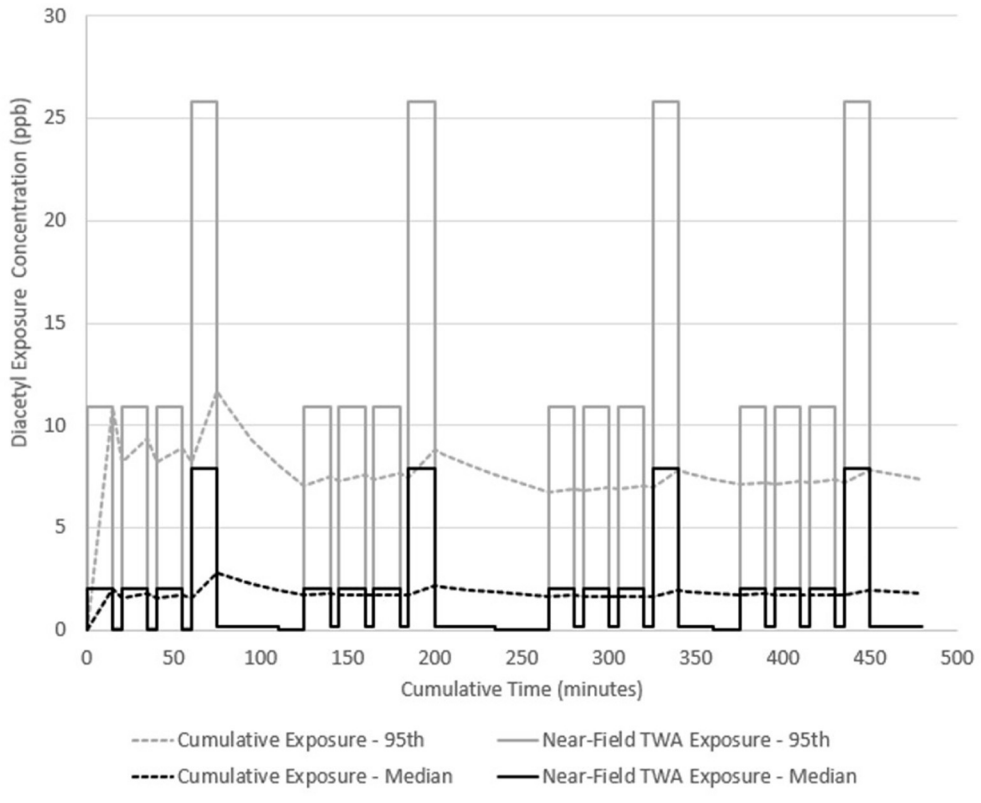

FIGURE 3 | Diacetyl cumulative exposure profile for a general production worker (Scenario A). NIOSH REL 5.0 ppb for diacetyl.

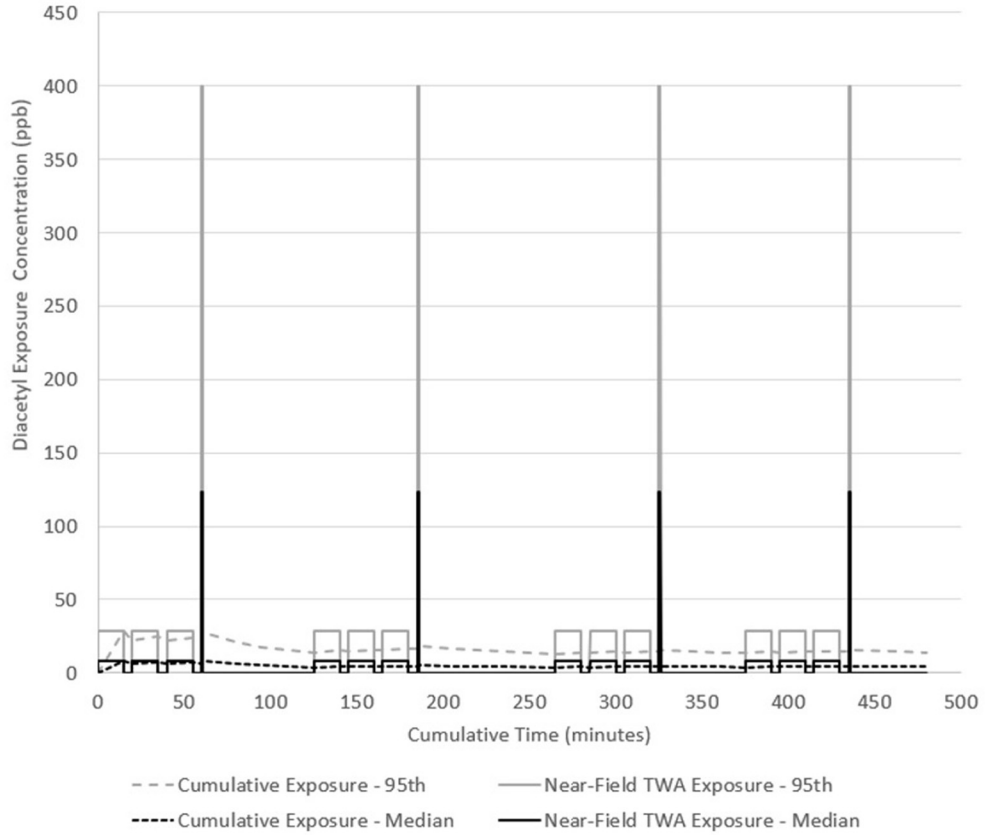

FIGURE 4 | Diacetyl cumulative exposure profile for a general production worker (Scenario B). NIOSH REL 5.0 ppb for diacetyl.

in occupational settings. At air velocities indicative of walking (72–84 m min^{-1}), near-field TWA exposure concentrations decreased 1.1-fold (18.4–16.0 ppb). As we approach steady-state conditions (i.e., t gets large), the near-field concentration can be approximated with a reduced form of Equation S1 (**Supplementary Material**) with no dependence on near-field or far-field volumes or air exchange rates in these fields. Plotting the inverse of β demonstrated a known linear trend from the reduced form of Equation S1 with the slope equivalent to the generation (2040) and intercept equivalent to generation divided by the flow rate (4.78) (**Figure 5B**).

DISCUSSION

Previous reports presented information regarding hazardous chemicals including diacetyl and 2,3-pentanedione and raised respiratory health concerns from exposure to workers at coffee roasting and packaging facilities. Scientific insight to the factors involved in emission of diacetyl and 2,3-pentanedione from roasted coffee, specifically roast level and physical form, and how these factors influence worker exposures has been lacking. Our study provides valuable SER values for these two chemicals from roasted coffee as well as a meaningful link between these emission factors and exposures through modeling based on information from actual workplaces observed during field investigations. The described approach investigates exposure air concentrations and SER depending on emission factors and coffee packaging and grinding tasks but also extends the application to real-world scenarios.

Particle Size and Physical Form Effect on SERs

Although no statistical difference was observed between particle sizes of coarse and fine ground coffee, decreasing the particle size should increase the surface area available for emissions. We did observe a meaningful and statistical difference between chemical emission rates from these physical forms of roasted coffee (fine ground > coarse ground >> whole bean) for both chemicals. Emission rates from whole bean roasted coffee were the lowest because of the trapped gases in the bean pore structure and low surface area available for emissions compared to ground coffee. When the coffee was ground, these trapped gases were released and increased the emission rate for chemicals from the roasted coffee. Increased bean porosity for darker roasts (11) and the influence of this pore structure on emissions (25) likely affected estimates of SERs observed during freshly roasted and storage trials.

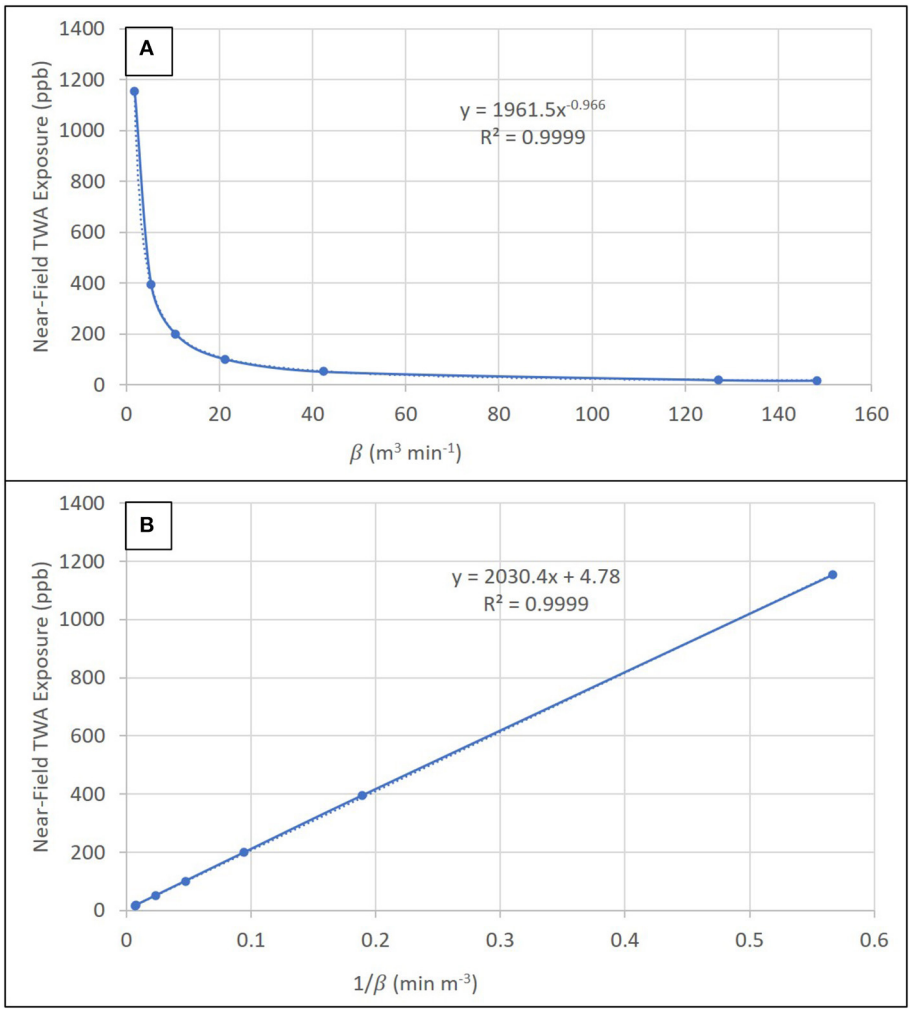

FIGURE 5 | Sensitivity analysis showing the trend in near-field TWA exposure concentration as a function of **(A)** the inter-zone air flow rate (β) and **(B)** $1/\beta$.

Roast Level Effect on SERs

Unlike physical form, we observed a difference in the effect of roast level on chemical emissions that was dependent on the chemical. As the roast level darkened, SERs increased for diacetyl but decreased for 2,3-pentanedione. Schenker et al. observed increasing diacetyl and 2,3-pentanedione concentrations with increasing degrees of roast, with 2,3-pentanedione slightly higher than 2,3-butanedione (13). These researchers also observed 2,3-pentanedione decreasing at the darkest roast level which is similar to the observed drop in SERs observed in this study. Echt et al. also found that diacetyl emissions were the highest for the darkest roast level (French roast) and increased with increasing roast level (29).

Storage Duration Effect on SERs

Longitudinal trends in emission factors during storage tests revealed a decrease for diacetyl and 2,3-pentanedione from dark roast level but an increase from light roast, especially for ground coffee. Emission factors for light roast would presumably decrease if the storage period was measured for a longer period. Pore structure differences between light and dark roast might have influenced emission factors of stored coffee. Increased bean porosity of darker roast may have increased the emission rates of chemicals decreasing the amount of chemical in the sample and decreasing the emission rates of chemicals over time (i.e., steeper slope in the trend line of emission rates vs. storage days). Lighter roast coffee likely had smaller pores decreasing the ability of trapped gases to migrate to the emission surface. Whole bean coffee had the slowest change in SERs over time because of the lack of available surface area for emission compared to ground coffee.

Predicted Air Concentrations and Exposure Profile

Mass-balance models can be used to model air concentrations of chemicals by tracking mass through different zones or boxes. The well-mixed box model with a constant emission source is the simplest model to apply but assumes the chemical concentration

is instantly dispersed throughout the space, which is not likely realistic. However, this simple model underestimates exposure at the source (30). Assessing the potential for occupational exposures to chemicals from an emission source can be more accurately approximated using a two-zone, near field/far field model, which accounts for incomplete mixing of air (31). Peak exposures at the emission source should be considered in epidemiologic and exposure studies because high concentration exposures for short durations can potentially overwhelm the body's natural defense mechanisms against adverse health effects (32). Near field/far field models are more realistic of these peak exposures when considering the employee may be near the emission source and exposed to higher concentrations, then move away from the emission source thus decreasing exposure. This approach still assumes complete and instantaneous mixing within each zone, only mass removal mechanism is through air leaving the zones, and input parameters that need to be measured or carefully assigned based on expert judgment or that require knowledge of the specific workplace scenario.

Model input parameters can be measured or estimated from other parameters but always have an uncertainty associated with them. Measured parameters can include room volume, ventilation rates, and emission rates, although the latter are often not measured and was an impetus to this work. Estimated parameters include inter-zone air flow rate, which can substantially affect near-field zone, and thus, worker exposure. A probabilistic approach to model input assigns an uncertainty bound to the parameter estimate and leads to a range of air concentrations that more accurately represents the variability observed in environmental sampling data (33). Distributions of input parameters are chosen to reflect what is known about the parameter. A uniform distribution, for example, might be chosen if the parameter has a range of values and the likelihood of any of the values is the same. A normal or lognormal distribution might be chosen if the parameter data fit these distributions, which have a measured or known variability (standard deviation or geometric standard deviation). Monte Carlo simulations are performed to sample these distributions multiple times (e.g., 10,000 iterations) and propagate the uncertainty in the input parameters to the model output.

Modeling worker exposures using SERs measured in the laboratory combined with observational data from the field and expert opinion yielded realistic exposure estimates that can be used to screen control strategies prior to implementation. We used a constant generation rate model, which is an appropriate choice given the limited change in emission rates over this time scale (15 min maximum). A modification to the model is available for situations when the emission source strength decreases over time (34). For this study, we only modeled two scenarios as examples of how to use the emission rates to estimate worker exposures. We also restricted the simulations to hypothetical non-flavoring coffee facilities with realistic model inputs based on observations during field surveys. For scenario A, we estimated median exposures to diacetyl of 2.1 ppb for packaging whole bean coffee and of 7.9 ppb for grinding coffee for intermittent short-term durations (15 min) leading to a full-shift exposure of 1.8 ppb for a general production worker performing various tasks and durations used in this simulation. Some exposures would likely exceed short-term STELs and full-shift RELs based on 95th percentile estimates encompassing these limits. For scenario B, we estimated median exposures to diacetyl of 8.3 ppb for packaging whole bean coffee (over 15 min) and of 123.5 ppb for grinding coffee (over 1 min) leading to a full-shift exposure of 4.1 ppb for a general production worker performing various tasks and durations used in this simulation. In this hypothetical scenario, multiple peak excursions above STELs for very short durations produced low estimates of full-shift exposures when averaged over the workday because of dilution from exposure to far-field exposures. Although this fixed cyclic pattern of peak exposures does not likely exist in occupational settings, episodic exposures to elevated concentrations of hazardous chemicals are likely in the coffee industry and depend on the work process and flow as well as individual worker behaviors and proximity of the worker to the source of emissions. Total mass emitted for the tasks in each scenario never exceeded 5% of the total predicted mass in the coffee based on 19 μg diacetyl/g coffee (15) indicating the model was producing reasonable estimates of emission for these chemicals. Modeled exposures presented in this study are similar to measured exposure estimates previously reported. Echt et al. observed median full-shift TWA exposures of 16 ppb diacetyl and 6.9 ppb 2,3-pentanedione among seven workers in a craft roastery (29). Davey et al. measured air concentrations of 0.02–8 ppb diacetyl and 2,3-pentanedione using sorbent tubes and peak excursions of these compounds between 15 and 20 ppb using proton-transfer reaction time-of-flight mass spectrometry (35). McCoy et al. measured two short-term breathing zone samples collected from a grinder operator in excess of 20 ppb (36). Pengelly et al. observed that 40% of full-shift personal samples exceeded 20 ppb but these samples originated from one worksite (37). In 17 coffee facilities, NIOSH researchers observed a comparable geometric mean of short-term task exposures of 8.6 ppb (GSD 2.8) for packaging coffee and 26 ppb (GSD 3.2) for grinding coffee (sampling duration ranged from 2 to 18 min) (1). At these non-flavoring coffee facilities, they estimated a geometric mean of full-shift exposures at 6.3 ppb (GSD 2.6).

Sensitivity Analysis of Inter-zone Air Flow Rate (β)

Sensitivity analysis of inter-zone air flow rate demonstrated a substantial influence of this parameter on modeled worker exposures (i.e., near-field air concentrations). The most rapid change in near-field exposures occurred from 1.77 (relatively still air) to 10.6 m^3 min^{-1} (air velocity 6 m min^{-1}). The choice of air velocity at the boundary between zones is crucial to accurately represent real-world conditions. When the source is stationary (i.e., the air is still), chemical diffusion dominates the estimates for exposure. When air velocities increase because of movement of the source either from process (e.g., automation such as a conveyor belt) or worker movement, the air velocity at the boundary increases leading to worker exposures that can increase or decrease depending on work activities and the orientation and proximity of the worker to the source. Incorporating uncertainty in this input

parameter is paramount to accurately reflect the variability observed in environmental measurements because of irregular worker activities (38). While not assessed here, we note that general ventilation values do not substantially affect near-field source concentration estimates, which are controlled by source emission characteristics (generation) and inter-zone air flow rate (removal).

Emission rates of diacetyl and 2,3-pentanedione and the results of modeled exposures support the need to control source emissions to control worker exposures. Our models indicate that the use of engineering controls such as local exhaust ventilation targeted at grinding machines could be beneficial to reduce exposures because we have shown that ground coffee releases these chemicals at a substantially greater rate than whole bean coffee. If engineering controls are not practicable in a workplace, modification of work practices to reduce the amount of time that the worker is near the source (roasted coffee) could be used to control exposure.

Limitations

We observed an increase in SERs on day 1 for dark roast coffee but we did not measure SERs for day 1 storage on light roast coffee. We are uncertain whether an initial increase in SERs would be observed for light roast like that seen in dark roast. This would not substantially affect the trend observed where SERs increased with increasing storage age for light roast coffee. SERs were generated in this study to investigate the influence of roast level and grind. SERs reported here are limited to the test conditions and material tested. The assessment of particle size using Feret diameter did not accurately capture the decrease in particle size, which we hoped would act as a surrogate for the increase in surface area between coarse ground and fine ground forms of coffee. These results should not be generalized to workplace conditions but can be used to estimate air concentrations. Industrial coffee grinders used in coffee roasting and packaging facilities might grind roasted coffee to a different particle size than the grinder used in this study. Different particle sizes, and effective surface areas, will affect SERs. Future models could incorporate the age of the coffee and storage conditions to better represent the chemical emission rates. We present model scenarios to demonstrate the use of modeling to predict air concentrations and occupational exposures in this industry. Estimated air concentrations or exposures should be confirmed with air sampling. If broadly applicable SERs are desired, a wide range of coffee origins and species as well as roasting profiles should be assessed. SERs were experimentally derived at normal laboratory temperature and a fixed humidity. SERs increase with increasing environmental temperature for most compounds depending on vapor pressures and humidity for polar compounds, such as diacetyl in this study and formaldehyde. For example, a coffee roasting facility in hot, humid environment may have higher SERs than those in cold, dry environments.

CONCLUSIONS

Chemicals including diacetyl and 2,3-pentanedione are emitted from roasted coffee at various rates depending on the roast level and physical form of the roasted coffee. SERs of diacetyl from freshly roasted coffee increased with roast level and grinding. SERs of 2,3-pentanedione did not change with roast level but increased with increasing level of grind. SERs of whole bean coffee remained stable in contrast to those of ground coffee, which decreased over a 10-day period. The exception to this was light roast coffee whose emission rates increased over a 10-day period. SERs developed here coupled with facility information obtained during previous field surveys provided model input to estimate worker exposures during various activities. Modeling demonstrated that near-field exposures depend on proximity to the source, duration of exposure, and air velocities in the near-field further supporting previously reported chemical air measurements in coffee roasting and packaging facilities.

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

RL conceived and designed the study, conducted the data analysis, and wrote the first draft of the manuscript. EF collected the samples. All authors read, reviewed, and approved the final manuscript.

FUNDING

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

ACKNOWLEDGMENTS

The authors would like to acknowledge Callee Walsh and Ju-Hyeong Park for reviewing the manuscript and Michael Aldridge for analyzing samples.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.786924/full#supplementary-material

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ORIGINAL RESEARCH
published: 09 June 2022
doi: 10.3389/fpubh.2022.878907

Determinants of Task-Based Exposures to Alpha-Diketones in Coffee Roasting and Packaging Facilities Using a Bayesian Model Averaging Approach

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OPEN ACCESS

Edited by:
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Reviewed by:
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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: 18 February 2022
Accepted: 19 May 2022
Published: 09 June 2022

Citation:
Blackley BH, Groth CP, Cox-Ganser JM, Fortner AR, LeBouf RF, Liang X and Virji MA (2022) Determinants of Task-Based Exposures to Alpha-Diketones in Coffee Roasting and Packaging Facilities Using a Bayesian Model Averaging Approach. Front. Public Health 10:878907. doi: 10.3389/fpubh.2022.878907

Coffee production workers can be exposed to inhalational hazards including alpha-diketones such as diacetyl and 2,3-pentanedione. Exposure to diacetyl is associated with the development of occupational lung disease, including obliterative bronchiolitis, a rare and irreversible lung disease. We aimed to identify determinants contributing to task-based exposures to diacetyl and 2,3-pentanedione at 17 U.S. coffee production facilities. We collected 606 personal short-term task-based samples including roasting ($n = 189$), grinding ($n = 74$), packaging ($n = 203$), quality control (QC, $n = 44$), flavoring ($n = 15$), and miscellaneous production/café tasks ($n = 81$), and analyzed for diacetyl and 2,3-pentanedione in accordance with the modified OSHA Method 1013/1016. We also collected instantaneous activity-based ($n = 296$) and source ($n = 312$) samples using evacuated canisters. Information on sample-level and process-level determinants relating to production scale, sources of alpha-diketones, and engineering controls was collected. Bayesian mixed-effect regression models accounting for censored data were fit for overall data (all tasks) and specific tasks. Notable determinants identified in univariate analyses were used to fit all plausible models in multiple regression analysis which were summarized using a Bayesian model averaging method. Grinding, flavoring, packaging, and production tasks with ground coffee were associated with the highest short-term and instantaneous-activity exposures for both analytes. Highest instantaneous-sources of diacetyl and 2,3-pentanedione included ground coffee, flavored coffee, liquid flavorings, and off-gassing coffee bins or packages. Determinants contributing to higher exposures to both analytes in all task models included sum of all open storage sources and average percent of coffee production as ground coffee. Additionally, flavoring ground coffee and flavoring during survey contributed to notably higher exposures for both analytes in most, but not all task groups. Alternatively, general exhaust ventilation contributed to lower exposures in all but two models. Additionally, among facilities that flavored, local exhaust ventilation during flavoring processes contributed to lower 2,3-pentanedione exposures during grinding and packaging tasks. Coffee production facilities can consider

implementing additional exposure controls for processes, sources, and task-based determinants associated with higher exposures to diacetyl and 2,3-pentanedione, such as isolating, enclosing, and directly exhausting grinders, flavoring mixers, and open storage of off-gassing whole bean and ground coffee, to reduce exposures and minimize risks for lung disease among workers.

Keywords: task-based, exposure determinants, correlated predictors, coffee, Bayesian model averaging, alpha-diketones, diacetyl, 2,3-pentanedione

INTRODUCTION

Coffee production is a global industry and produced an estimated 23.2 billion pounds (lbs) of coffee in 2020/2021, representing an increase of 15.4 million lbs from the previous year (1). The number of workers employed in the coffee industry in the United States has risen to meet increased demand with an estimated 17,704 workers employed in 2019 representing ∼0.01% of the U.S. workforce (2), up 11% from 2016 (3). Workers in coffee production can be exposed to multiple inhalational hazards associated with negative health outcomes such as carbon monoxide (4–7), green coffee bean and roasted coffee dust (8–10), and volatile organic compounds including the alpha-diketones diacetyl and 2,3-pentanedione (11–14).

Diacetyl and 2,3-pentanedione are naturally occurring in roasted coffee beans and are also found in some liquid flavorings used to flavor coffee (15). Exposure to diacetyl is associated with the development of occupational respiratory disease, including obliterative bronchiolitis, a rare and irreversible lung disease that results in inflammation and narrowing of the bronchioles and symptoms such as cough, shortness of breath, and wheeze (16–18). 2,3-Pentanedione, a structurally similar chemical to diacetyl and often used as a substitute for diacetyl in flavorings, causes airway fibrosis, including obliterative bronchiolitis-like changes in rodents after repeated inhalation exposure (15, 19). To reduce the risk of respiratory impairment and severe irreversible lung disease, the National Institute for Occupational Safety and Health (NIOSH) developed recommended exposure limits (RELs) of 5 parts per billion (ppb) for diacetyl and 9.3 ppb for 2,3-pentanedione for time-weighted average (TWA) full-shift exposures (20). Additionally, NIOSH recommended short-term exposure limits (STELs) of 25 ppb for diacetyl and 31 ppb for 2,3-pentanedione averaged over a 15-min time period.

A cluster of obliterative bronchiolitis was observed among former workers of a coffee roasting and packaging facility between 2008 and 2015 (21, 22). The cluster of obliterative bronchiolitis was publicized in coffee trade magazines and spurred concerns among coffee companies and employees, prompting some to submit health hazard evaluation (HHE) requests to NIOSH. NIOSH performed HHE investigations at 17 coffee roasting and packaging facilities in response to these requests during 2016 and 2017. A summary of full-shift, short-term task-based, and instantaneous exposures to diacetyl and 2,3-pentanedione at these 17 facilities is reported in LeBouf et al. (13). Lebouf et al. observed that 11–77% of personal full-shift diacetyl samples collected at non-flavoring facilities and 62–95% of personal full-shift 2,3-pentanedione samples collected at flavoring facilities exceeded their respective RELs (13). Personal task exposures were orders of magnitude higher than full-shift exposures and had larger geometric standard deviations (GSDs) than many full-shift exposures. Measurements of elevated exposures to diacetyl and 2,3-pentanedione highlighted a need to understand determinants of exposures to alpha-diketones in coffee production facilities such that exposure mitigation strategies can be designed and implemented accordingly.

Statistical modeling of exposure determinants has been used extensively in the field of industrial hygiene to (1) predict exposures for use in epidemiologic studies or for risk assessment and (2) understand factors affecting exposures such as exposure duration, source strength, proximity to sources, and existing exposure controls, to subsequently identify, prioritize, and implement exposure mitigation strategies (23, 24). New approaches using Bayesian statistics have recently been proposed and used to account for parameter uncertainties, censored data, and to take advantage of the ease of Bayesian inferences (13, 25). Specifically, Bayesian model averaging (BMA) methods not only address the uncertainties in model building and variable selection, but also address limit of detection issues, repeated measurements on individuals and provides posterior distribution of parameters for all variables considered. Further, this modeling approach can be easily implemented in R-software using RJAGS and in other Bayesian programs such as OpenBUGS or Stan (26–28).

Despite the need, no previous studies have evaluated factors contributing to elevated task-based exposures to diacetyl and 2,3-pentanedione in coffee production facilities. Here, we expand upon the summary of exposures and emissions in coffee roasting facilities and cafés, reported in LeBouf et al., by identifying (1) tasks, activities, and sources associated with elevated short-term and instantaneous exposures to diacetyl and 2,3-pentanedione, and (2) determinants associated with elevated, or reduced, short-term, task-based exposures to diacetyl and 2,3-pentanedione using a BMA approach.

METHODS

Facility Characteristics

Roasted coffee production at sampled facilities ranged from 16 to 4,500 tons per year and total number of employees ranged from 4 to 150 workers. Air samples were collected between July 2015 and September 2017 across different seasons, in a variety of geographical locations, with differing amounts of natural ventilation occurring from open doors or windows. LeBouf

et al. provides additional information on the facilities, including information relating to production scale and process-related factors [Table 1 of LeBouf et al. (13)].

Sampling Approach

The full sampling approach utilized in the exposure assessment surveys performed at the 17 coffee roasting and packaging facilities was described previously in LeBouf et al. (13). Here, we provide a brief summary of the sampling approach used to collect short-term task-based, and instantaneous activity-based breathing zone and source air samples. Sampling at each facility was initiated by an HHE request. Workers were asked to voluntarily participate in the air sampling surveys, which lasted 2–4 days at each facility, and provided their informed consent prior to participating.

Short-Term Task-Based Air Sampling and Analysis

We collected 606 personal short-term task-based samples in worker's breathing zones during various tasks including roasting ($n = 189$), grinding ($n = 74$), packaging ($n = 203$), QC ($n = 44$), flavoring ($n = 15$), cleaning machines ($n = 36$), moving roasted beans/ground coffee ($n = 13$), miscellaneous production ($n = 17$), miscellaneous café ($n = 10$), and maintenance ($n = 5$). A full description of the various sub-tasks included in each of these 10 task categories can be found in Supplementary Table 1 of LeBouf et al. (13). Repeat samples were collected for tasks on the same day and over multiple days whenever possible.

Short-term task-based samples were collected on silica gel tubes (SKC Inc., Eighty Four, PA) and analyzed for diacetyl and 2,3-pentanedione according to the modified OSHA Sampling and Analytical Methods 1013/1016. Two glass silica gel sorbent tubes were connected with tubing and placed in a protective light-blocking cover and sampled at a flow rate of 200 mL/min. Sample analyses were performed in the NIOSH Respiratory Health Division's Organics Laboratory. The median limits of detection (LODs) were 0.9 ppb for diacetyl and 1.0 ppb for 2,3-pentanedione.

Instantaneous Activity-Based and Source Air Sampling and Analysis

We collected 296 instantaneous activity-based breathing zone samples, and 312 instantaneous source air samples using evacuated canisters for diacetyl and 2,3-pentanedione. A full list of volatile organic compounds (VOCs) analyzed in instantaneous canister samples can be found in LeBouf et al. (13).

Instantaneous canister samples were collected and analyzed in accordance with NIOSH method 3900 (29). The sampler consisted of a 450-mL evacuated canister (Entech Instruments, Inc., Simi Valley, CA) equipped with an instantaneous fitting designed for a short sampling duration (<30 s). For activity-based air samples, the inlet of the canister was opened and held near the worker's breathing zone for <30 s while they performed an activity. For source air samples, the inlet of the canister was opened and held for <30 s directly at the source of interest. Median LODs were 0.6 ppb for diacetyl and 0.8 ppb for 2,3-pentanedione, based on a 1.5-times dilution factor, which is typical for instantaneous samples. However, individual LOD concentrations varied because they depended on the sample volume inside each canister.

Sample-Level and Process-Level Determinants

The source-receptor model described by Tielemans et al. was used to conceptualize factors that might modify inhalational exposure to diacetyl and 2,3-pentanedione during tasks (30). Source-receptor model factors included source strength (e.g., whole bean or ground coffee), transport of the contaminant through different compartments (e.g., process isolation), and loss of contaminants (e.g., local exhaust ventilation). Information on sample-level and process-level factors relating to production scale, sources of alpha-diketones, and engineering controls were collected prior to, during, and after completion of surveys. Descriptions of sample-level and process-level factors can be found in **Supplementary Table 1**.

Task-based sample-level factors included roaster characteristics (e.g., roaster capacity and enclosed/unenclosed), grinder characteristics (e.g., grinder's typical weight of ground coffee processed), coffee characteristics during grinding task (e.g., grinding flavored or unflavored coffee), coffee characteristics during packaging task (e.g., packaging volume), and sampled task type (**Supplementary Tables 1, 4, 7**). Process-level determinants did not vary within a facility and were systematically collected on forms prior to or after sampling. Process-level factors included coffee storage determinants (e.g., sum of all open storage sources present in a facility), general sources determinants (e.g., total number of sources of diacetyl or 2,3-pentanedione), amount of roasted coffee produced (e.g., average roasted coffee production in lbs per day), roast depth (e.g., average roast length in minutes), amount of grinding performed and grinding processes (e.g., average percent of production as ground coffee), flavoring process determinants (e.g., flavor ground coffee and isolated flavoring room), automation of sources (e.g., percent automated sources), isolation of sources (e.g., any isolated sources/processes), enclosure of sources (e.g., any enclosed sources), and mechanical ventilation type [e.g., general exhaust ventilation (GEV)] (**Supplementary Tables 1, 5–7**).

Statistical Modeling

Statistical analyses were performed using R (version 4.0 or greater; R Foundation for Statistical Computing), JMP 15.0 and SAS 9.4 (SAS Institute, Inc., Cary, NC). In addition, all Bayesian analyses were programmed using rjags (27) and data were organized and summarized in figures in R using tidyverse and ggplot2. Diacetyl and 2,3-pentanedione measurements were log-transformed allowing for the use of ANOVA and linear regression-based methods. Repeated measures analyses were used to account for within subject variability when sufficient numbers of workers with repeated measurements ($n > 5$) were included in sample sets.

Bayesian modeling strategies accounting for censored data were used throughout our analyses because up to 24 and 27% of task-based samples for diacetyl and 2,3-pentanedione were below their respective LODs (25, 31). In all cases, priors were

selected to be as weakly informative as possible to allow the data to drive the inference. Specifically, priors for regression coefficients or mean parameters were specified to be a wide normal distribution with mean 0 and variance 1,000,000. Fixed effect models used inverse-gamma priors on the variances [with shape = 0.1 and scale = 0.1 as described in Gelman et al. (32)]. Repeated-measures random effect models used uniform priors on the standard deviations with a range of ln (1.01) to ln (500). Convergence was assessed using trace plots and Markov chain Monte Carlo (MCMC) standard error. Models suggested almost immediate convergence (within 5,000 iterations). Each linear regression model chain with at least one predictor was thinned to keep only every 60th iteration to avoid autocorrelation in the chains. All estimates provided in tables or figures are for the median posterior estimate and the respective credible interval (based on quantiles of the posterior distribution).

Additionally, in all analyses, we assumed independence, linearity, equal variances, and normality of residuals, consistent with linear regressions. Non-linear relationships were not explored. Similarly, lognormality of each chemical was assumed, and other distributions were not explored.

Descriptive Analysis of Task-Based Samples and Instantaneous Activity/Source Based Samples

Exposure estimates for short-term task and instantaneous activity and source exposures were generated using a Bayesian intercept only (ANOVA; no predictors) model. Short-term task estimates further accounted for repeated measures. A total of 20,000 iterations after 5,000 iterations of burn-in were used to develop posterior exposure estimates of the GM, GSD, and 95th percentile for each short-term task and instantaneous exposure distribution. Instantaneous canister samples were summarized for various personal or source activities. Additional details of the methods used in the descriptive analysis of instantaneous samples can be found in the **Supplementary Material**.

Task-Based Univariate Determinant Models

We aimed to identify determinants affecting exposures across all tasks as well as task-specific determinants. Thus, we generated (1) an overall model to identify determinants of exposure across all tasks, and (2) task-specific models to identify additional sample-level and task-process specific determinants. We performed a series of single-variable Bayesian linear regression models with each individual determinant separately to identify important determinants of exposures. Determinants were designated as notable if the 80% credible interval (Bayesian uncertainty interval) for the regression estimate of any slope did not include 0. Additional information on how determinants of short-term task-based exposure to diacetyl or 2,3-pentanedione were created can be found in the **Supplementary Material**.

We conducted a series of single-variable Bayesian regression models accounting for repeated measurements for the overall, roasting, grinding, and packaging models. Facility was not included as a random effect due to too few subjects (<5) observed at many facilities resulting in insufficient information to estimate the variance components in a nested random effect model; thus, we used a model with random effect for subjects only. Additionally, QC ($n = 44$) and flavoring models ($n = 15$) had too few measurements to run repeated measures models. Therefore, we used a simpler fixed effect form of the Bayesian regression models to identify notable determinants. Multiple linear regression models for QC and flavoring were also not developed due to small sample sizes.

Multicollinearity Check

Many determinants were expected to be highly correlated with one another due to many process-based determinants being related to each other. Inclusion of multiple correlated predictors would lead to multicollinearity/collinearity and increased standard errors on the regression estimates. Therefore, to determine collinear combinations of determinants for each model, we calculated Pearson correlations of each pair of notable determinants. We developed Pearson correlations for each category above reference of a determinant using indicators. It is commonly agreed that correlations >0.5 will result in multicollinearity (33, 34). Pairs of determinants with 0.5 level correlation or greater (and in at least one category if a categorical variable) were noted as multicollinear and were excluded from entry into the same models. In addition, some variables were identified as nested when one variable was a subset of another variable. All nested variables were also excluded from entry into the same models to avoid the inclusion of redundant variables in the same models.

Bayesian Model Averaging

To develop estimates of each variable's contribution to exposure for diacetyl and 2,3-pentanedione, we used a BMA approach. BMA performs a set of Bayesian linear regressions that considers all possible combinations of predictors (as fixed effects). The models are then summarized over the regression estimates.

We developed a list of all possible models for each model type (task model and analyte). Each model was developed to account for repeated measures and to account for measurements below the LOD. Then, using information from the multicollinearity check, we removed any models with any multicollinear combination of predictors. Thus, the final BMA approach considered a subset of possible models.

We utilized GSD reduction, calculated as the overall GSD in the null model minus the overall GSD in the models with determinants, as an alternative metric to R-squared to evaluate the need for weighting models. R-squared is avoided in Bayesian methods, especially when Bayesian methods are utilized to estimate values below the LOD, because R-squared statistics could be misleading as they will estimate the variance of the censored measurements to be low at each iteration. After experimenting with weighting models by relative contribution (% GSD reduction), we observed that weighted models did not result in substantial changes to estimates compared to unweighted models which is likely related to a lack in substantial overall GSD reduction (analysis not shown). As a result, we did not weight models when calculating parameter estimates for each determinant.

Each model was run for 10,000 iterations after 5,000 iterations of burn-in (after thinning every 60 iterations). We performed

the averaging process at each iteration of the process for each model containing the determinant providing a full posterior distribution of the average regression parameter estimate across models. Averaging was performed only in the models in which the determinant was included; this was done intentionally to avoid shrinkage toward 0 in the estimates of the coefficients for determinants that were not included in all models (due to collinearity).

The relative magnitude of effect of each determinant on exposure to diacetyl or 2,3-pentanedione was assessed by calculating the percent change (1) for categorical variables compared to the reference category or (2) per x units of a continuous variable. Percent change was calculated based on the following formula: Percent Change = (exp(beta_k × units_k)−1) ×100 where beta_k is the regression coefficient estimate and units_k is the units of measure for the regression coefficient k. We defined a notable or credible difference to be present when the 95% credible interval (CI) for the slope coefficient or the percentage change does not contain 0.

RESULTS

Comparison of Diacetyl and 2,3-Pentanedione Measurements

Log-transformed diacetyl and 2,3-pentanedione air concentrations from task-based samples (n = 606) were positively correlated with a Spearman's correlation coefficient of $rho = 0.507$.

Short-Term Task-Based Exposure Summary

A summary of personal short-term task-based exposures and sample durations (range: 2–86 min) can be seen in **Figure 1** and **Table 1**. Overall, the highest task-based exposures for diacetyl and 2,3-pentanedione across all facilities were measured during grinding (GMs = 27.8 and 22.7 ppb, respectively), flavoring (GMs = 5.4 and 45.1 ppb), and moving roasted beans or ground coffee (GMs = 21.7 and 13.1 ppb). Large variability (GSD = 30.2) was observed for diacetyl exposures during flavoring tasks.

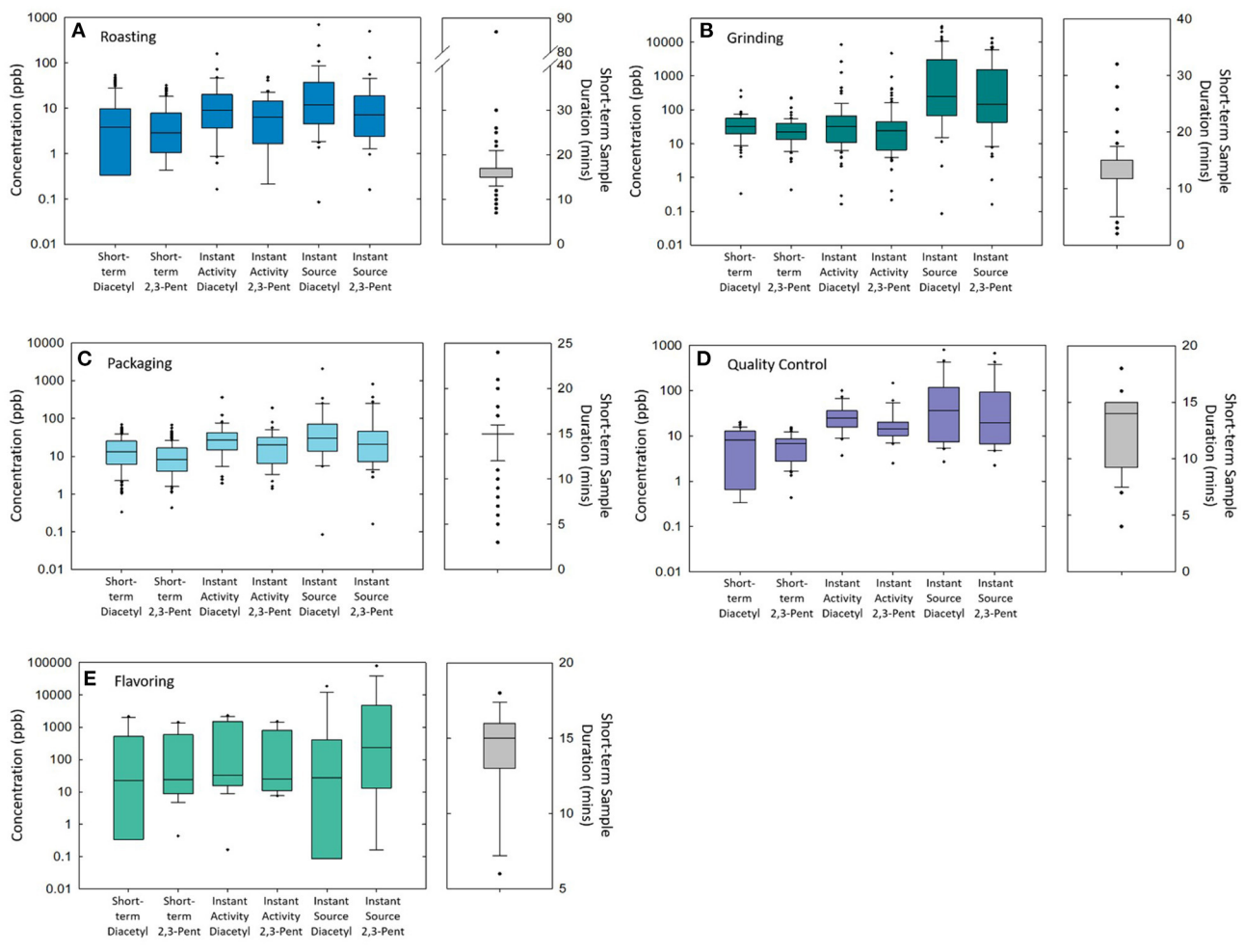

FIGURE 1 | A panel of box plots of diacetyl and 2,3-pentanedione concentrations measured in short-term task-based, instantaneous activity, and instantaneous source samples and short-term task-based sample durations during roasting tasks **(A)**, grinding tasks **(B)**, packaging tasks **(C)**, QC tasks **(D)**, and flavoring tasks **(E)**.

TABLE 1 | Personal short-duration task exposures to diacetyl and 2,3-pentanedione.

Task	Sampling duration (min–max)	*N*	k	Diacetyl						2,3-Pentanedione					
				GM (ppb)	GSD	P95 (ppb)	%BDL	*N* 15 min samples	% >STEL (*N*)	GM (ppb)	GSD	P95 (ppb)	%BDL	*N* 15 min samples	% >STEL (*N*)
Flavoring coffee	6–18	15	5	5.4	30.2	1,102	27%	6	50% (3)	45.1	14.8	3,817	7%	6	50% (3)
Grinding coffee	2–32	74	32	27.8	2.7	147	4%	35	69% (24)	22.7	2.6	112	1%	35	34% (12)
Moving roasted beans or ground coffee	3–25	13	9	21.7	2.7	109	0%	6	50% (3)	13.1	2.6	63	0%	6	0% (0)
Cleaning machines	5–46	36	18	10.3	4.0	102	11%	11	64% (7)	6.5	3.4	49	14%	11	0% (0)
Packaging coffee	3–55	203	74	11.3	2.9	66	5%	136	24% (32)	7.0	2.9	40	8%	136	6% (8)
Misc. production	3–29	17	9	4.7	4.4	52	18%	4	0% (0)	2.7	3.9	25	24%	4	0% (0)
Roasting coffee	7–86	189	34	3.6	5.3	55	25%	70	13 (9)	3.1	4.1	32	24%	70	0% (0)
QC	4–18	44	9	3.9	3.7	33	25%	14	0% (0)	5.5	2.1	19	2%	14	0% (0)
Miscellaneous café tasks	5–16	10	6	2.2	4.5	25	30%	4	0% (0)	3.5	2.5	16	10%	4	0% (0)
Maintenance of machines	13–15	5	1	–	–	15*	20%	4	0% (0)	–	–	7.8*	20%	4	0% (0)

*N, number of samples; k, number of workers; GM, geometric mean; ppb, parts per billion; GSD, geometric standard deviation; P95, 95th percentile; %BDL, percent samples below the limit of detection; N 15 min samples, number of 15 minute samples for comparison to NIOSH STEL; % >STEL (N), percent of 15 min samples greater than NIOSH STEL for diacetyl or 2,3-pentanedione; STEL, NIOSH short-term exposure limit of 25 ppb diacetyl and 31 ppb 2,3-pentanedione; *indicates where maximum is presented when <5 measurements were above the detection limit; –indicates not enough samples above the detection limit to obtain an estimate.*

Of the samples collected for 15 min duration and available for comparison with the NIOSH STELs, 50% ($n = 3/6$) of flavoring tasks, 69% ($n = 24/35$) of grinding tasks, 50% ($n = 3/6$) of moving roasted beans or ground coffee tasks, 24% ($n = 32/136$) of packaging tasks, 13% ($n = 9/70$) of roasting tasks, and 64% ($n = 7/11$) of cleaning machines tasks exceeded the NIOSH STEL of 25 ppb diacetyl (**Table 1**). Additionally, 50% ($n = 3/6$) of flavoring tasks, 34% ($n = 12/35$) of grinding tasks, and 6% ($n = 8/136$) of packaging tasks exceeded the NIOSH STEL of 31 ppb 2,3-pentanedione.

Instantaneous Activity-Based and Source Exposure Summary

A summary of instantaneous activity-based and source samples can be seen in **Figure 1** and **Supplementary Tables 2, 3**. Instantaneous activity and source samples summarized in **Figure 1** are those associated with roasting (**Figure 1A**), grinding (**Figure 1B**), packaging (**Figure 1C**), QC (**Figure 1D**), and flavoring (**Figure 1E**) tasks and processes. Descriptive statistics (GM, GSD, P95) for instantaneous activity-based and source samples can be seen in **Supplementary Tables 2, 3**.

Univariate Analyses of Determinants Contributing to Short-Term Task-Based Exposures

Determinant distributions and univariate model estimates of regression coefficients and 80% CIs are reported in **Supplementary Tables 4–7**. A color-coded heat map of determinants contributing to increased or decreased short-term, task-based exposures in coffee production overall as well as during specific tasks such as roasting, grinding, and packaging can be seen in **Figures 2A,B**. Additionally, univariate model estimates of GMs and 80% credible intervals for diacetyl and 2,3-pentanedione concentrations in each determinant category and each task category (all tasks, roasting, grinding, and packaging) can be seen in **Supplementary Figures S1–S4**. A summary of the univariate analyses for each individual task as well as for all tasks is provided in the **Supplementary Materials**.

Multiple Linear Regression Models of Determinants Contributing to Short-Term Task-Based Exposures

Correlation matrices for all determinants identified in the previous step as notable at the 0.2 level on univariate analyses for each task model can be seen in **Supplementary Figures S5–S8**. BMA results are provided in **Figures 3–6** and **Tables 2–5**. Average regression estimates across all multiple linear regression models and the 95% CI for each determinant that was identified as notable (i.e., 95% CI did not contain 0 for the slope) in single determinant analyses can be seen in **Tables 2–5**. The number and percent of models containing the determinant are also included in **Tables 2–5**. The percentage change in exposures for the given coefficient above reference along with the 95% CI can be seen in **Figures 3–6**. We note that the percent change is judged relative to the reference condition and should be interpreted alongside the intercept reference value for each respective BMA model.

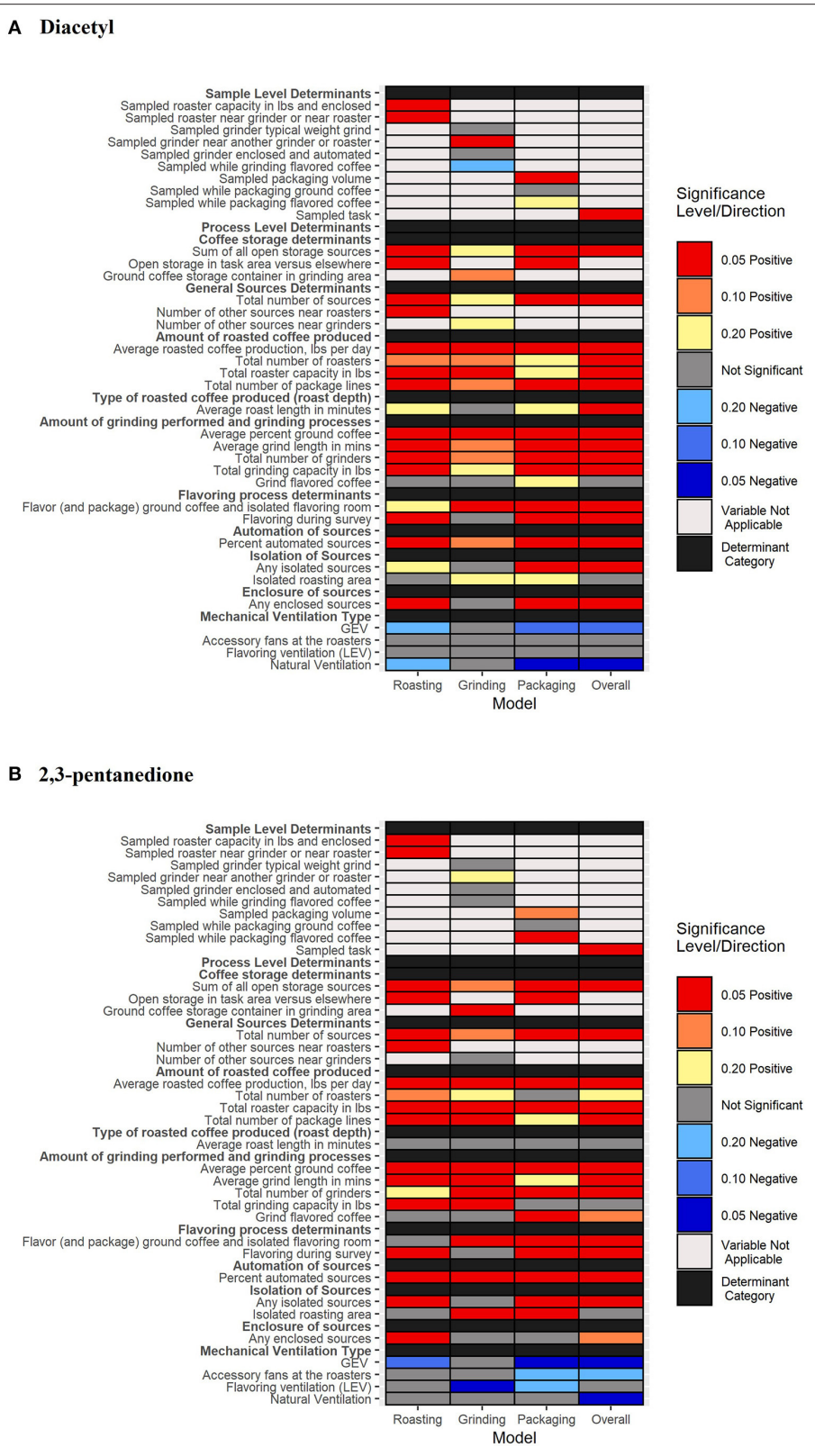

FIGURE 2 | A heat-map of significant determinants identified in univariate analyses considered for models of diacetyl **(A)** and 2,3-pentanedione **(B)** exposure. Notable credible intervals (CIs) are depicted for 80, 90, and 95% CIs. Positive associations are depicted with warm colors (yellow, orange, and red) and negative associations are depicted with cool colors (light blue to dark blue).

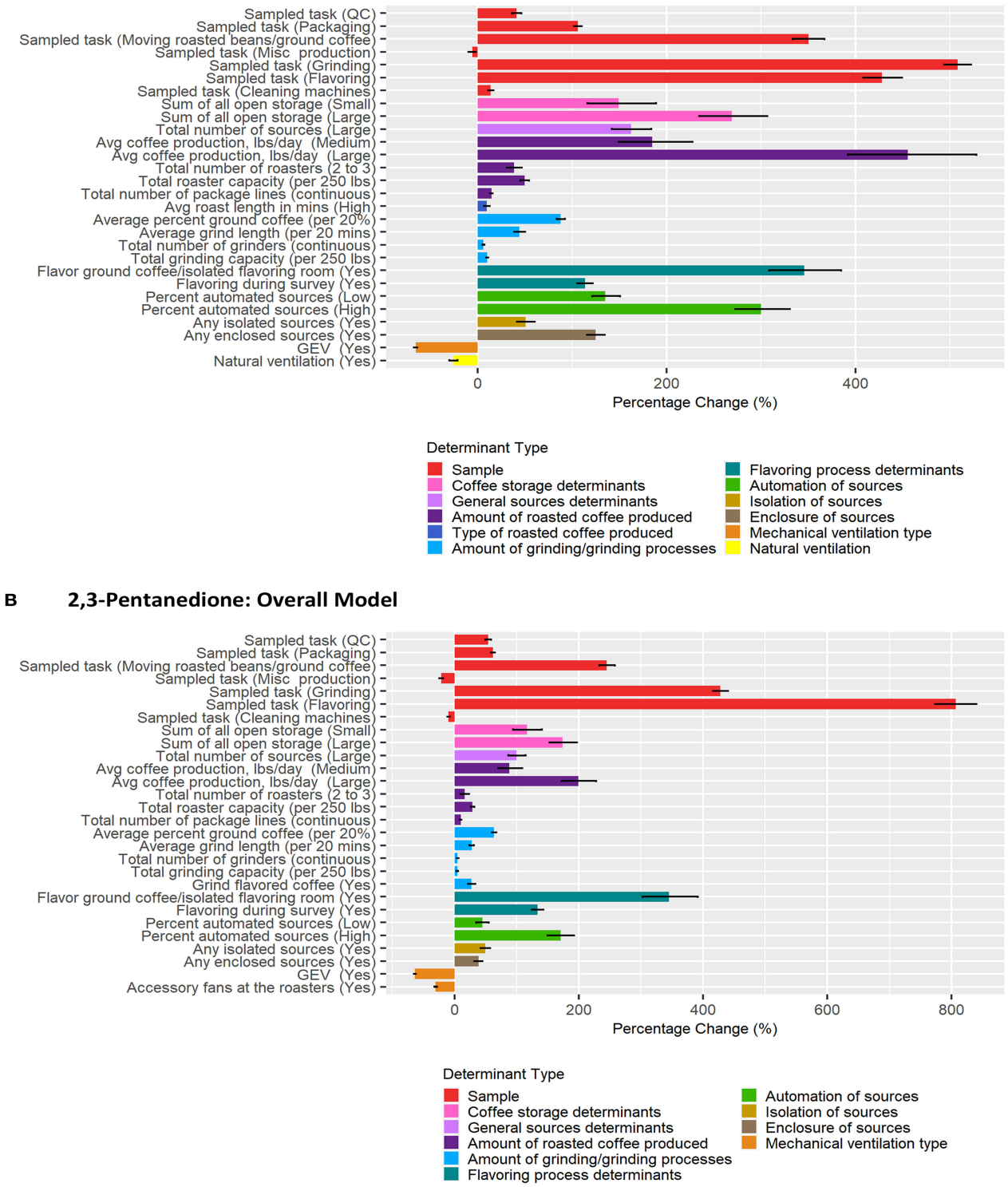

FIGURE 3 | Bar chart of percent change in diacetyl **(A)** and 2,3-pentanedione **(B)** exposures during all tasks (overall model) compared with reference category or per unit change. Each bar represents the estimated percent change for the median posterior estimate with error bars for the 95% credible intervals. Percent change for continuous variables defined as per 1 unit with the exceptions of the following: total roaster capacity and total grinder capacity are calculated per 250 lbs, average percent ground coffee is calculated per increase in 20%, and average grind length in minutes is calculated per 20 min.

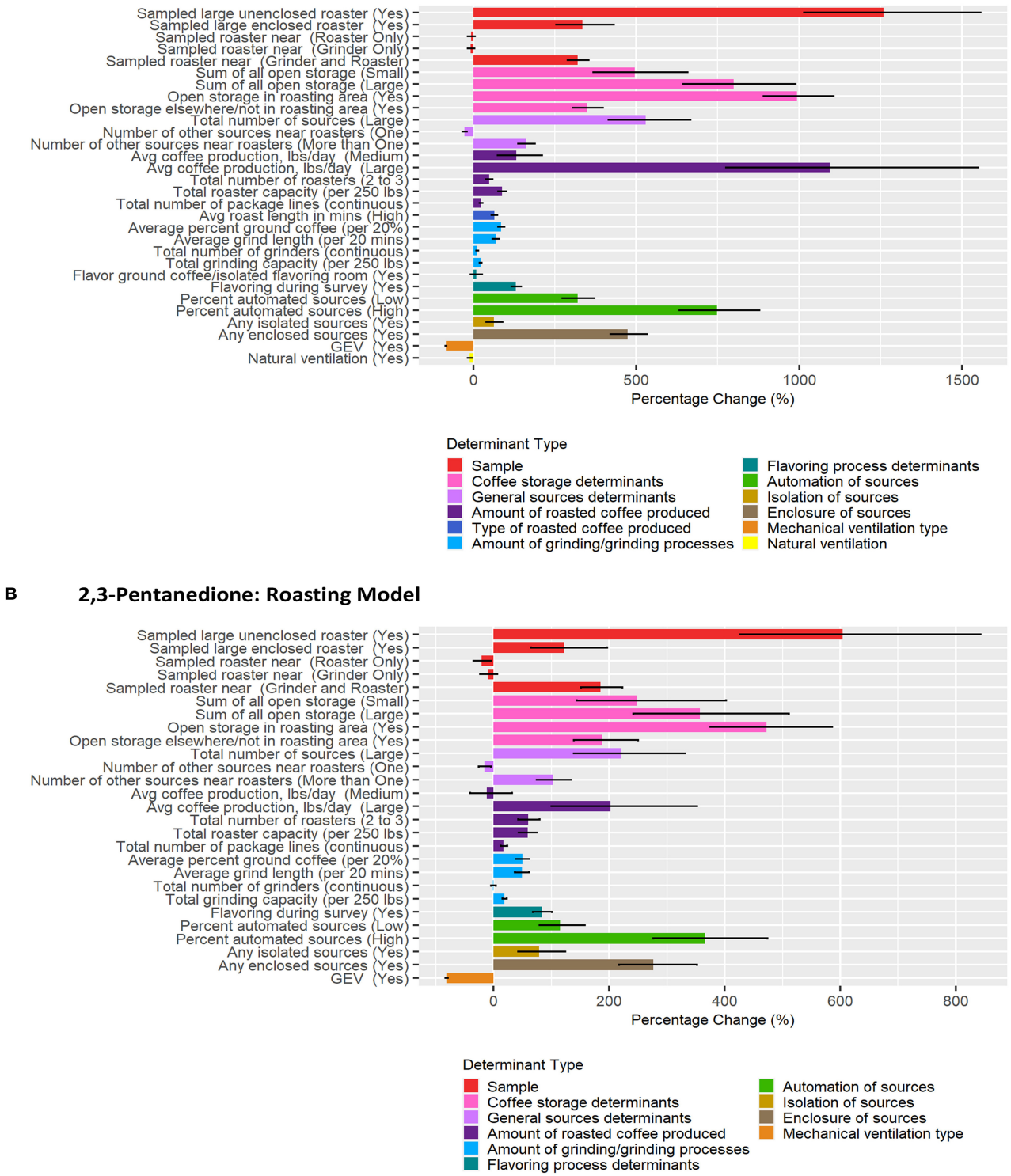

FIGURE 4 | Bar chart of percent change in diacetyl **(A)** and 2,3-pentanedione **(B)** exposures during roasting tasks compared with reference category or per unit change. Each bar represents the estimated percent change for the median posterior estimate with error bars for the 95% credible intervals. Percent change for continuous variables defined as per 1 unit with the exceptions of the following: total roaster capacity and total grinder capacity are calculated per 250 lbs, average percent ground coffee is calculated per increase in 20%, and average grind length in minutes is calculated per 20 min.

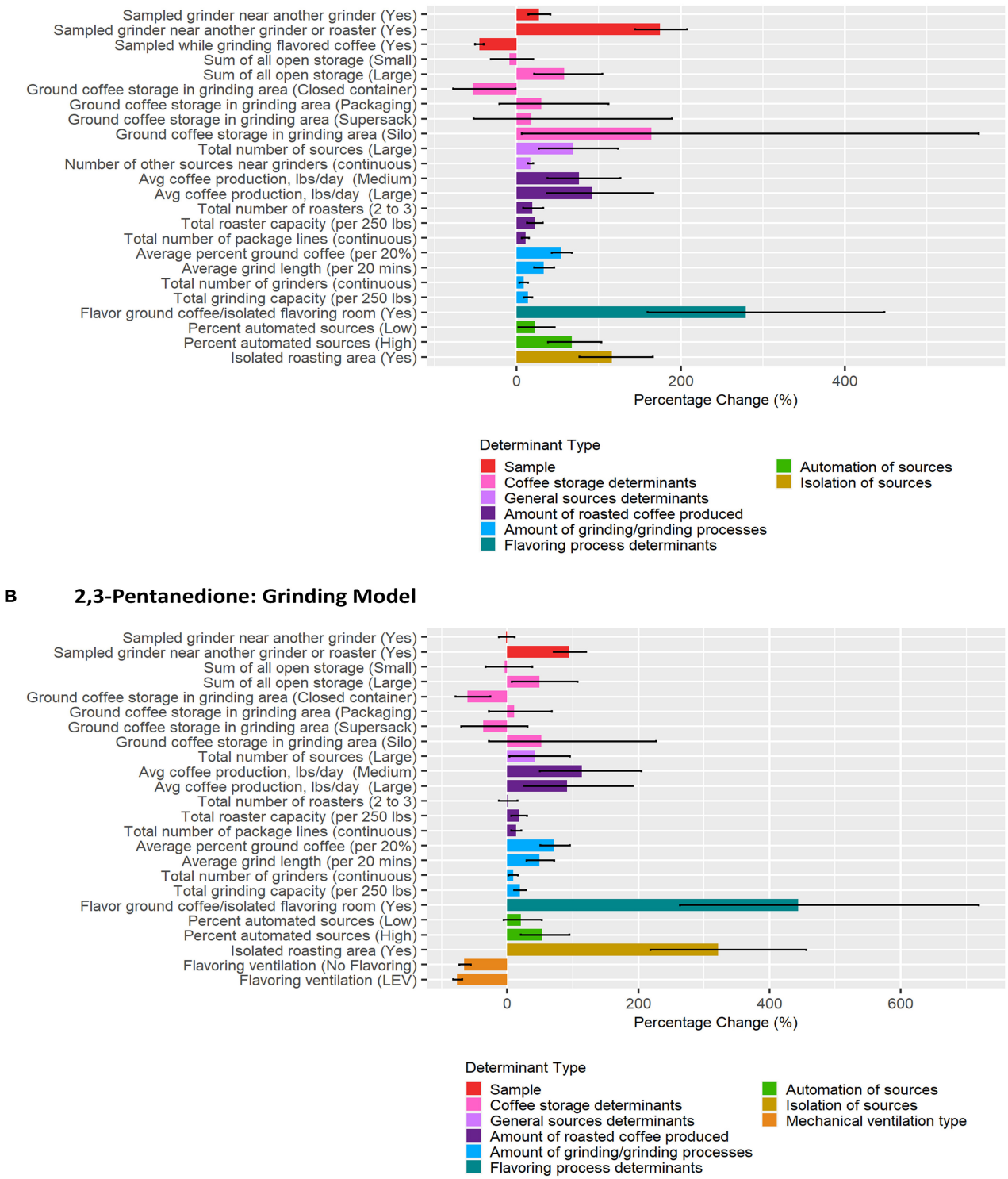

FIGURE 5 | Bar chart of percent change in diacetyl **(A)** and 2,3-pentanedione **(B)** exposures during grinding tasks compared with reference category or per unit change. Each bar represents the estimated percent change for the median posterior estimate with error bars for the 95% credible intervals. Percent change for continuous variables defined as per 1 unit with the exceptions of the following: total roaster capacity and total grinder capacity are calculated per 250 lbs, average percent ground coffee is calculated per increase in 20%, and average grind length in minutes is calculated per 20 min.

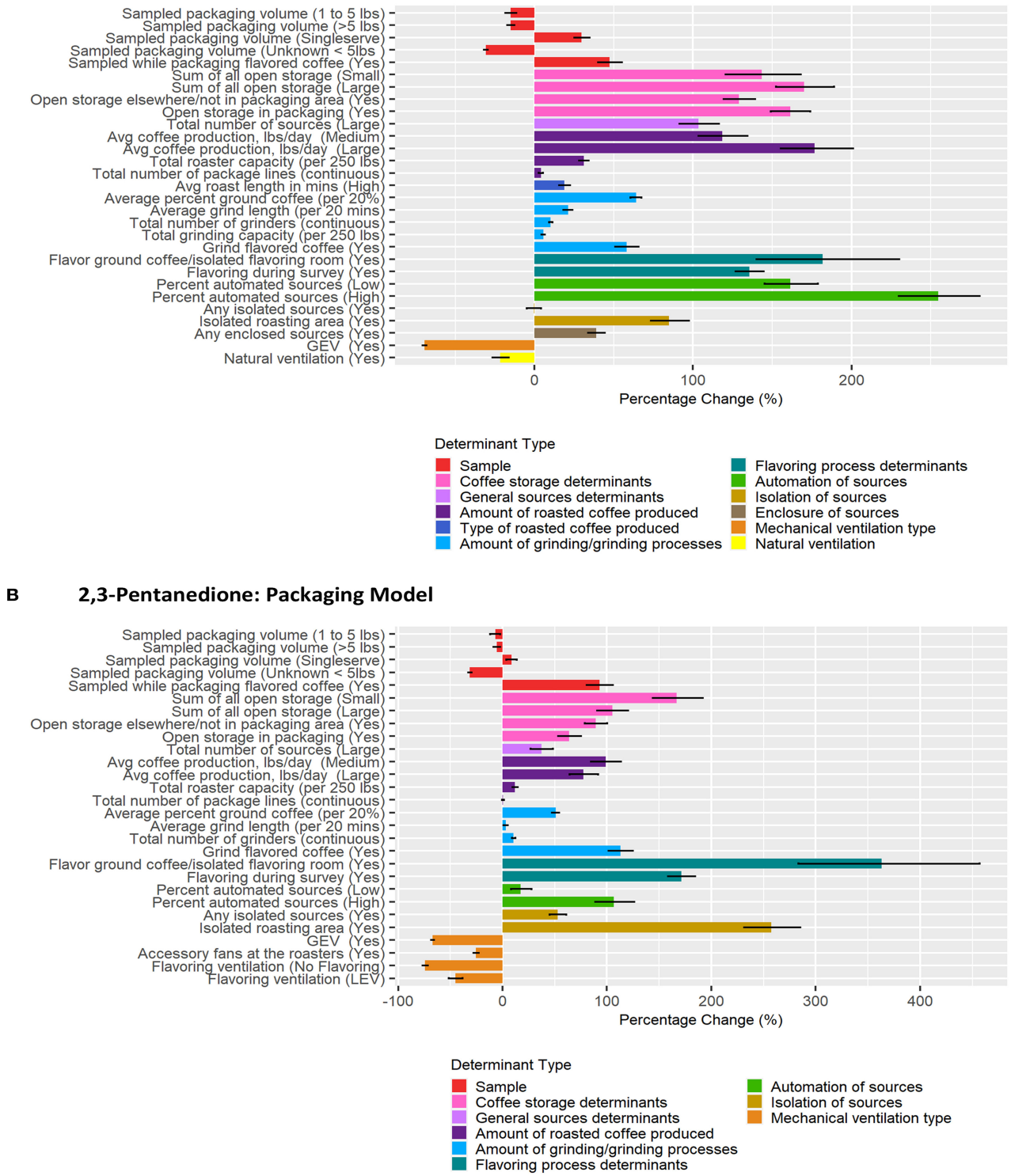

FIGURE 6 | Bar chart of percent change in diacetyl **(A)** and 2,3-pentanedione **(B)** exposures during packaging tasks compared with reference category or per unit change. Each bar represents the estimated percent change for the median posterior estimate with error bars for the 95% credible intervals. Percent change for continuous variables defined as per 1 unit with the exceptions of the following: total roaster capacity and total grinder capacity are calculated per 250 lbs, average percent ground coffee is calculated per increase in 20%, and average grind length in minutes is calculated per 20 min.

TABLE 2 | Bayesian model averaging results for diacetyl and 2,3-pentanedione exposures during all tasks (overall task model).

Determinant	Diacetyl $N_{total} = 483$				2,3-pentanedione $N_{total} = 483$			
	N models	% models included	Median posterior estimate - β	95% CI	*N* models	% models included	Median posterior estimate - β	95% CI
Sample level determinants								
Sampled task (QC)	242	50.1	0.34	(0.31, 0.38)	242	50.1	0.43	(0.4, 0.46)
Sampled task (packaging)	242	50.1	0.72	(0.7, 0.74)	242	50.1	0.48	(0.46, 0.5)
Sampled task (moving roasted beans/ground coffee)	242	50.1	1.5	(1.47, 1.54)	242	50.1	1.24	(1.2, 1.28)
Sampled task (Misc production)	242	50.1	−0.06	(−0.1, −0.02)	242	50.1	−0.24	(−0.28, −0.2)
Sampled task (grinding)	242	50.1	1.8	(1.78, 1.83)	242	50.1	1.66	(1.64, 1.69)
Sampled task (flavoring)	242	50.1	1.66	(1.63, 1.71)	242	50.1	2.2	(2.17, 2.24)
Sampled task (cleaning machines)	242	50.1	0.13	(0.1, 0.15)	242	50.1	−0.1	(−0.12, −0.08)
Coffee storage determinants								
Sum of all open storage (small, 1–2)	16	3.3	0.91	(0.77, 1.06)	24	5	0.77	(0.66, 0.88)
Sum of all open storage (large, >2)	16	3.3	1.31	(1.21, 1.4)	24	5	1.01	(0.93, 1.09)
General sources determinants								
Total number of sources (>7)	24	6	0.96	(0.88, 1.04)	32	6.6	0.69	(0.62, 0.76)
Amount of roasted coffee produced								
Avg coffee production, lbs/day (Medium, ≥1,000 lbs and <10,000 lbs)	16	3.3	1.05	(0.91, 1.18)	24	5	0.63	(0.53, 0.74)
Avg coffee production, lbs/day (Large, >10,000 lbs)	16	3.3	1.71	(1.59, 1.84)	24	5	1.1	(1, 1.19)
Total number of roasters (2, 3)	72	14.9	0.33	(0.27, 0.38)	52	10.8	0.15	(0.09, 0.21)
Total roaster capacity (per 250 lbs)	16	3.3	0.0016	(0.0015, 0.0017)	24	5	0.26	(0.23, 0.28)
Total number of package lines (continuous)	24	4.97	0.13	(0.12, 0.15)	24	5	0.09	(0.08, 0.11)
Type of roasted coffee produced (roast depth)								
Avg roast length in mins (high, ≥15 min)	234	48.5	0.09	(0.06, 0.12)	–	–	–	–
Amount of grinding performed and grinding process determinants								
Average percent ground coffee (per 20%)	72	14.9	0.032	(0.030, 0.033)	84	17.4	0.49	(0.47, 0.51)
Average grind length (per 20 min)	16	3.31	0.018	(0.016, 0.020)	40	8.3	0.24	(0.22, 0.27)
Total number of grinders (continuous)	92	19.1	0.06	(0.05, 0.07)	72	14.9	0.05	(0.04, 0.06)
Total grinding capacity (per 250 lbs)	84	17.4	0.0004	(0.0003, 0.0004)	64	13.3	0.04	(0.04, 0.05)
Flavoring process determinants								
Flavor ground coffee/isolated flavoring room (yes)	108	22.4	1.49	(1.41, 1.58)	66	13.7	1.49	(1.39, 1.59)
Flavoring during survey (yes)	144	29.8	0.76	(0.72, 0.80)	98	20.3	0.85	(0.81, 0.89)
Engineering controls determinants								
Percent automated sources (low, ≤6)	48	9.9	0.85	(0.79, 0.92)	36	7.5	0.37	(0.3, 0.44)
Percent automated sources (high, >6)	48	9.9	1.39	(1.31, 1.46)	36	7.5	1	(0.92, 1.07)
Any isolated sources/processes (yes)	54	11.2	0.41	(0.35, 0.47)	64	13.3	0.4	(0.35, 0.45)
Any enclosed sources (yes)	80	16.6	0.81	(0.77, 0.85)	72	14.9	0.33	(0.28, 0.37)
GEV (yes)	170	35.2	−1.08	(−1.13, −1.03)	216	44.7	−1.02	(−1.05, −0.98)
Natural ventilation (yes)	100	20.7	−0.30	(−0.36, −0.24)	–	–	–	–
Grind flavored coffee (yes)	–	–	–	–	160	33.1	0.24	(0.2, 0.29)
Accessory fans at the roasters (yes)	–	–	–	–	188	38.9	−0.36	(−0.39, −0.34)

N_{total}, total number of models; N, indicates number of models determinant was included in; %, percent; –, determinants that were not applicable (>0.2 on univariate analyses); 95% CI, 95% credible intervals.

TABLE 3 | Bayesian model averaging results for diacetyl and 2,3-pentanedione exposures during roasting tasks.

Determinant	Diacetyl N_{total} = 837				2,3-pentanedione N_{total} = 240			
	N models	% models included	Median posterior estimate - β	95% CI	*N* models	% models included	Median posterior estimate - β	95% CI
Sample level determinants								
Sampled roaster capacity (large) and unenclosed	36	4.3	2.61	(2.41, 2.81)	12	5.0	1.95	(1.66, 2.24)
Sampled roaster capacity (large) and enclosed	36	4.3	1.47	(1.27, 1.67)	12	5.0	0.8	(0.5, 1.09)
Sampled roaster near another roaster	158	19	−0.07	(−0.19, 0.06)	48	20.1	−0.23	(−0.42, −0.05)
Sampled roaster near another grinder	158	19	−0.08	(−0.18, 0.03)	48	20.1	−0.1	(−0.27, 0.06)
Sampled roaster near roaster and grinder	158	19	1.44	(1.36, 1.51)	48	20.1	1.05	(0.92, 1.17)
Coffee storage determinants								
Sum of all open storage (small, 1–2)	24	2.9	1.78	(1.54, 2.03)	8	3.3	1.25	(0.89, 1.61)
Sum of all open storage (large, >2)	24	2.9	2.2	(2.01, 2.39)	8	3.3	1.52	(1.23, 1.81)
Open storage in roasting area	102	12.3	2.39	(2.29, 2.49)	24	10	1.74	(1.56, 1.93)
Open storage elsewhere/not in roasting area	102	12.3	1.5	(1.4, 1.6)	24	10	1.06	(0.87, 1.25)
General sources determinants								
Total number of sources (>7)	24	2.9	1.84	(1.64, 2.04)	8	3.3	1.17	(0.87, 1.46)
Number of other sources near roasters (1)	252	30.3	−0.31	(−0.39, −0.23)	72	30.1	−0.17	(−0.30, −0.04)
Number of other sources near roasters (>1)	252	30.3	0.99	(0.88, 1.10)	72	30.1	0.7	(0.56, 0.85)
Amount of roasted coffee produced								
Avg coffee production, lbs/day (Medium, ≥1,000 lbs and <10,000 lbs)	24	2.9	0.84	(0.56, 1.14)	8	3.3	−0.12	(−0.53, 0.27)
Avg coffee production, lbs/day (large, >10,000 lbs)	24	2.9	2.48	(2.17, 2.8)	8	3.3	1.11	(0.7, 1.51)
Total number of roasters (2, 3)	308	37.1	0.39	(0.32, 0.46)	88	36.8	0.47	(0.36, 0.59)
Total roaster capacity (per 250 lbs)	24	3.8	0.63	(0.57, 0.7)	8	4.4	0.46	(0.36, 0.56)
Total number of package lines (continuous)	24	2.9	0.21	(0.18, 0.25)	8	3.3	0.16	(0.11, 0.21)
Type of roasted coffee produced (roast depth)								
Avg roast length in mins (High, ≥15 min)	416	50.1	0.50	(0.45, 0.55)	–	–	–	–
Amount of grinding performed and grinding process determinants								
Average percent ground coffee (per 20%)	76	9.1	0.62	(0.56, 0.67)	28	11.7	0.40	(0.33, 0.48)
Average grind length (per 20 min)	72	8.7	0.53	(0.47, 0.58)	24	10.0	0.40	(0.32, 0.48)
Total number of grinders (continuous)	96	11.6	0.11	(0.09, 0.14)	24	10.0	−0.01	(−0.05, 0.04)
Total grinding capacity (per 250 lbs)	96	11.6	0.21	(0.19, 0.23)	32	13.4	0.17	(0.15, 0.20)
Flavoring process determinants								
Flavor ground coffee/isolated flavoring room (yes)	144	17.3	0.09	(−0.08, 0.24)	–	–	–	–
Flavoring during survey (yes)	288	34.7	0.84	(0.77, 0.90)	100	41.8	0.61	(0.52, 0.70)
Engineering controls determinants								
Percent automated sources (low, ≤6)	88	10.6	1.44	(1.32, 1.55)	32	13.4	0.77	(0.58, 0.95)
Percent automated sources (high, >6)	88	10.6	2.14	(1.99, 2.28)	32	13.4	1.54	(1.33, 1.75)
Any isolated sources/processes (yes)	60	7.2	0.49	(0.34, 0.64)	16	6.7	0.58	(0.35, 0.81)
Any enclosed sources (yes)	102	12.3	1.75	(1.65, 1.85)	24	10.0	1.33	(1.15, 1.51)
GEV (yes)	292	35.1	−1.83	(−1.92, −1.75)	120	50.2	−1.68	(−1.8, −1.58)
Natural ventilation (yes)	248	29.8	−0.11	(−0.19, −0.03)	–	–	–	–

N_{total}, total number of models; N models, number of models determinant was included in; %, percent; –, determinants that were not applicable (>0.2 on univariate analyses); 95% CI, 95% credible intervals.

TABLE 4 | Bayesian model averaging results for diacetyl and 2,3-pentanedione exposures during grinding tasks.

Determinant	Diacetyl N_{total} = 154				2,3-pentanedione N_{total} = 76			
	N models	% models included	Median posterior estimate - β	95% CI	*N* models	% models included	Median posterior estimate - β	95% CI
Sample level determinants								
Sampled grinder near another grinder	49	31.8	0.24	(0.13, 0.34)	35	46.1	−0.01	(−0.13, 0.11)
Sampled grinder near another grinder and roaster	49	31.8	1.01	(0.89, 1.13)	35	46.1	0.66	(0.53, 0.79)
Sampled while grinding flavored coffee (yes)	68	44.2	−0.61	(−0.7, −0.51)	–	–	–	–
Coffee storage determinants								
Sum of all open storage (small, 1–2)	12	7.8	−0.09	(−0.38, 0.18)	6	7.9	−0.04	(−0.4, 0.33)
Sum of all open storage (large, >2)	12	7.8	0.45	(0.19, 0.72)	6	7.9	0.4	(0.07, 0.73)
Ground coffee storage in grinding area (closed container)	4	2.6	−0.77	(−1.49, −0.01)	4	5.3	−0.94	(−1.57, −0.3)
Ground coffee storage in grinding area (packaging)	4	2.6	0.26	(−0.24, 0.75)	4	5.3	0.1	(−0.33, 0.52)
Ground coffee storage in grinding area (supersack)	4	2.6	0.17	(−0.75, 1.06)	4	5.3	−0.46	(−1.2, 0.27)
Ground coffee storage in grinding area (silo)	4	2.6	0.97	(0.06, 1.89)	4	5.3	0.42	(−0.33, 1.18)
General sources determinants								
Total number of sources (>7)	8	5.2	0.52	(0.24, 0.8)	6	7.9	0.35	(0.03, 0.67)
Number of other sources near grinders (continuous)	49	31.8	0.16	(0.13, 0.18)	–	—-	–	–
Amount of roasted coffee produced								
Avg coffee production, lbs/day (medium, ≥1,000 lbs and <10,000 lbs)	8	5.2	0.57	(0.32, 0.82)	3	3.9	0.76	(0.4, 1.11)
Avg coffee production, lbs/day (large, >10,000 lbs)	8	5.2	0.65	(0.32, 0.98)	3	3.9	0.65	(0.23, 1.07)
Total number of roasters (2, 3)	50	32.5	0.18	(0.07, 0.28)	24	31.6	0	(−0.13, 0.14)
Total roaster capacity (per 250 lbs)	12	7.8	0.2	(0.12, 0.28)	6	7.9	0.16	(0.06, 0.26)
Total number of package lines (continuous)	6	3.9	0.1	(0.06, 0.14)	2	2.6	0.13	(0.06, 0.19)
Amount of grinding performed and grinding process determinants								
Average percent ground coffee (per 20%)	24	15.6	0.43	(0.36, 0.51)	8	10.5	0.54	(0.41, 0.67)
Average grind length (per 20 min)	12	7.8	0.29	(0.19, 0.38)	4	5.3	0.4	(0.26, 0.54)
Total number of grinders (continuous)	9	5.8	0.08	(0.03, 0.13)	6	7.9	0.09	(0.02, 0.15)
Total grinding capacity (per 250 lbs)	12	7.8	0.13	(0.08, 0.17)	4	5.3	0.18	(0.1, 0.25)
Flavoring process determinants								
Flavor ground coffee/isolated flavoring room (yes)	15	9.7	1.33	(0.95, 1.7)	10	13.2	1.69	(1.29, 2.1)
Engineering controls determinants								
Percent automated sources (low, ≤6)	30	19.5	0.2	(0.02, 0.38)	16	21.1	0.19	(−0.06, 0.42)
Percent automated sources (high, >6)	30	19.5	0.51	(0.32, 0.71)	16	21.1	0.43	(0.19, 0.67)
Isolated roasting area (yes)	34	22.1	0.77	(0.57, 0.98)	13	17.1	1.44	(1.16, 1.72)
Flavoring ventilation (NA, no flavoring)	NA	NA	NA	NA	17	22.4	−1.06	(−1.3, −0.82)
Flavoring ventilation (LEV)	NA	NA	NA	NA	17	22.4	−1.45	(−1.74, −1.16)

N_{total}, total number of models; N models, number of models determinant was included in; %, percent; –, determinants that were not applicable (>0.2 on univariate analyses); 95% CI, 95% credible intervals; NA, not applicable; LEV, local exhaust ventilation.

Overall Tasks

A total of 483 overall task diacetyl models and 483 overall task 2,3-pentandione models were generated comprising 19 determinants for both diacetyl and 2,3-pentanedione exposures (**Table 2**). Among sample-level determinants, task type, specifically, performing grinding or flavoring tasks, were associated with the highest increases in diacetyl and 2,3-pentanedione exposures when compared to the reference group

TABLE 5 | Bayesian model averaging results for diacetyl and 2,3-pentanedione exposures during packaging tasks.

Determinant	Diacetyl N_{total} = 927				2,3-pentanedione N_{total} = 631			
	N models	% models included	Median posterior estimate - β	95% CI	*N* models	% models included	Median posterior estimate - β	95% CI
Sample level determinants								
Packaging 1–5 lbs	362	35.5	−0.16	(−0.2, −0.12)	224	35.5	−0.07	(−0.12, −0.02)
Packaging >5 lbs	362	35.5	−0.16	(−0.19, −0.14)	224	35.5	−0.06	(−0.09, −0.02)
Packaging single serve ground coffee	362	35.5	0.26	(0.22, 0.3)	224	35.5	0.08	(0.03, 0.13)
Packaging unknown, <5 lbs	362	35.5	−0.37	(−0.39, −0.35)	224	35.5	−0.37	(−0.4, −0.35)
Packaging flavored coffee (yes)	165	16.2	0.39	(0.34, 0.44)	104	16.5	0.66	(0.59, 0.72)
Coffee storage determinants								
Sum of all open storage (small, 1–2)	42	4.1	0.89	(0.79, 0.99)	48	7.6	0.98	(0.89, 1.07)
Sum of all open storage (large, >2)	42	4.1	0.99	(0.93, 1.06)	48	7.6	0.72	(0.65, 0.79)
Open storage elsewhere/not in packaging area	206	20.2	0.83	(0.79, 0.87)	108	17.1	0.64	(0.58, 0.69)
Open storage in packaging	206	20.2	0.96	(0.91, 1.01)	108	17.1	0.49	(0.43, 0.56)
General sources determinants								
Total number of sources (>7)	52	5.1	0.71	(0.65, 0.77)	34	5.4	0.32	(0.24, 0.39)
Amount of roasted coffee produced								
Avg coffee production, lbs/day (medium, ≥1,000 lbs and <10,000 lbs)	84	8.2	0.78	(0.71, 0.85)	72	11.4	0.69	(0.61, 0.76)
Avg coffee production, lbs/day (large, >10,000 lbs)	84	8.2	1.02	(0.94, 1.1)	72	11.4	0.57	(0.5, 0.65)
Total roaster capacity (per 250 lbs)	40	3.9	0.27	(0.25, 0.29)	44	7	0.11	(0.09, 0.14)
Total number of package lines (continuous)	40	3.9	0.04	(0.03, 0.05)	66	10.5	0	(0, 0.01)
Type of roasted coffee produced (roast depth)								
Avg roast length in mins (high, ≥15 min)	297	29.1	0.17	(0.14, 0.2)	–	–	–	–
Amount of grinding performed and grinding process determinants								
Average percent ground coffee (per 20%)	125	12.3	0.49	(0.47, 0.52)	100	15.8	0.41	(0.39, 0.43)
Average grind length (per 20 min)	65	6.4	0.19	(0.17, 0.22)	92	14.6	0.03	(0.01, 0.05)
Total number of grinders (continuous)	110	10.8	0.1	(0.09, 0.11)	44	7	0.1	(0.09, 0.11)
Total grinding capacity (per 250 lbs)	73	7.2	0.05	(0.04, 0.06)	–	–	–	–
Grind flavored coffee (yes)	222	21.8	0.46	(0.41, 0.51)	140	22.2	0.76	(0.7, 0.81)
Flavoring process determinants								
Flavor ground coffee/isolated flavoring room (yes)	39	3.8	1.04	(0.88, 1.19)	30	4.8	1.53	(1.34, 1.72)
Flavoring during survey (yes)	172	16.9	0.86	(0.82, 0.89)	100	15.8	1	(0.95, 1.05)
Engineering controls determinants								
Percent automated sources (low, ≤6)	92	9	0.96	(0.9, 1.03)	62	9.8	0.16	(0.08, 0.24)
Percent automated sources (high, >6)	92	9	1.27	(1.19, 1.34)	62	9.8	0.72	(0.64, 0.82)
Any isolated sources/processes (yes)	185	18.2	0	(−0.05, 0.04)	144	22.8	0.42	(0.37, 0.48)
Isolated roasting area (yes)	162	15.9	0.61	(0.55, 0.68)	102	16.2	1.27	(1.2, 1.35)
Any enclosed sources (yes)	170	16.7	0.33	(0.29, 0.37)	–	–	–	–
GEV (yes)	410	40.2	−1.18	(−1.22, −1.15)	316	50.1	−1.11	(−1.15, −1.07)
Accessory fans at the roasters (yes)	–	–	–	–	192	30.4	−0.29	(−0.33, −0.26)
Flavoring ventilation (NA, no flavoring)	–	–	–	–	50	7.9	−1.35	(−1.44, −1.26)
Flavoring ventilation (LEV)	–	–	–	–	50	7.9	−0.6	(−0.72, −0.48)

N_{total}, total number of models; N models, number of models determinant was included in; %, percent; –, determinants that were not applicable (>0.2 on univariate analyses); 95% CI, 95% credible intervals; NA, not applicable; LEV, local exhaust ventilation.

of roasting tasks (**Table 2**; **Figure 3**). Across models containing sampled task, grinding was associated with a median increase of 508% in diacetyl concentrations (95% CI: 494–522%) and 428% increase in 2,3-pentanedione concentrations (95% CI: 416–440%) compared to the reference task (**Figure 3**). Similarly, flavoring task was associated with a median increase of 428% in diacetyl concentrations (95% CI: 408–449%) and 806% median increase in 2,3-pentanedione concentrations (95% CI: 774–840%) above the reference group of roasting tasks (**Figure 3**). We note that the highest increases for diacetyl and 2,3-pentanedione (e.g., 508% increase in diacetyl for grinding tasks and 806% increase for flavoring tasks) are large, albeit relative, increases. For context when interpreting percentage change, the intercept reference value across all models was 6.0 ppb diacetyl and 6.3 ppb 2,3-pentanedione.

For process-level determinants, the top five production-level determinants with greatest impact on increasing diacetyl exposures compared to their respective reference categories included (1) >10,000 lbs average daily roasted coffee production, (2) flavor ground coffee, (3) >6% automated sources, (4) >2 sources of open storage, and (5) >1,000 lbs of average roasted coffee production, with 95% CIs of percent increases ranging from (1) 392–528%, (2) 309–385%, (3) 272–330%, (4) 234–307% and (5) 149–227%, respectively (**Figure 3**).

Process-level determinants associated with notable increases in 2,3-pentanedione exposure in the overall task model were similar to those for diacetyl, although the exact order was not the same. Additional determinants identified as notable for 2,3-pentanedione exposures in the overall task model included grinding flavored coffee (reference: grinding only unflavored coffee) (**Table 2**; **Figure 3**). Average roast length in minutes was identified as a determinant associated with notable increases in diacetyl, but not 2,3-pentanedione (**Figure 3**). The top five production-level determinants with the greatest impact on increasing 2,3-pentanedione exposures were (1) flavor ground coffee, (2) >10,000 lbs average daily roasted coffee production, (3) >2 sources of open storage, (4) >6% automated sources, and (5) flavoring during survey, with 95% CIs of percent increases ranging from (1) 303–392%, (2) 173–228%, (3) 153–197%, (4) 150–192%, and (5) 124–143%, respectively (**Figure 3**).

Process-level determinants associated with notable decreases in diacetyl or 2,3-pentanedione exposure in the overall task model included GEV and natural ventilation (**Table 2**; **Figure 3**). GEV was associated with estimated 95% CIs of percent decreases ranging from 64.1 to 67.6% in diacetyl and 62.3 to 65.2% in 2,3-pentanedione (95% CIs, **Figure 3**). Natural ventilation was associated with 95% CIs of percent decreases ranging from 21.5 to 29.9% for diacetyl but not 2,3-pentanedione (**Figure 3**). Additionally, accessory fans at the roasters were associated with 95% CIs of percent decreases ranging from 28.6 to 32.3% for 2,3-pentanedione but not diacetyl.

Roasting Tasks

A total of 837 roasting task diacetyl models and 240 roasting task 2,3-pentanedione models were generated comprising 22 and 19 determinants for diacetyl and 2,3-pentanedione exposures, respectively (**Table 3**). Determinants associated with increases in diacetyl and 2,3-pentanedione exposure during roasting tasks were similar to those identified in the overall task model although the order was not the same. Additional roasting specific process-level determinants associated with increases in diacetyl and 2,3-pentanedione during roasting tasks included open storage of coffee in the roasting area and >1 source near the roasters (**Table 3**; **Figure 4**). Also, unlike the overall model, flavor ground coffee did not contribute to increased diacetyl exposures and total number of grinders did not contribute to increased 2,3-pentanedione exposures during roasting tasks.

Among sample-level determinants, sampled roaster capacity (large) and unenclosed was associated with some of the highest increases in diacetyl exposures compared to the reference category of sampled small unenclosed roasters (**Table 5**; **Figure 4**). This effect was notably larger for large unenclosed roasters (95% CI: 1,014–1,556% increase in diacetyl; 427–843% increase in 2,3-pentanedione) than for a large enclosed roaster (95% CI: 255–431% increase in diacetyl; 65–197% increase in 2,3-pentanedione) (**Figure 4**). Additionally, a sampled roaster being near another roaster and grinder was associated with notable increases of both diacetyl and 2,3-pentanedione (95% CI: 289–354% increase in diacetyl; 151–223% increase in 2,3-pentanedione) when compared to the reference of a sampled roaster not near any grinders or roasters (**Table 3**; **Figure 4**). We note that although an increase ranging from 1,014–1,556% for diacetyl and 427–843% is large, for context, the intercept reference values for diacetyl and 2,3-pentanedione across all roasting models was 3.0 ppb diacetyl and 3.9 ppb 2,3-pentanedione.

Among process-level determinants, the top five with the greatest impact on increasing diacetyl exposures during roasting tasks were (1) open storage of coffee in the roasting area, (2) >10,000 lbs average daily roasted coffee production, (3) >2 sources of open storage, (4) high percent (>6%) automated sources, and (5) large number of total sources (>7), with 95% CIs of percent increases ranging from (1) 890–1,104%, (2) 775–1,548%, (3) 644–988%, (4) 632–878%, and (5) 414–667%, respectively. The top five process-level determinants with greatest impact on increasing 2,3-pentanedione exposures during roasting tasks were (1) open storage of coffee in the roasting area, (2) high percent (>6%) automated sources, (3) >2 sources of open storage, (4) any enclosed source, and (5) 1–2 sources of open storage, with 95% CIs of percent increases ranging from (1) 375–586%, (2) 277–474%, (3) 242–511%, (4) 217–352%, and (5) 144–402%, respectively (**Figure 4**). Some differences were noted between the models for diacetyl and 2,3-pentanedione. Total number of grinders and average roast length in minutes contributed to notable increases in diacetyl exposure but not 2,3-pentanedione exposure.

Process-level determinants associated with decreases in exposure to diacetyl or 2,3-pentanedione during roasting tasks, listed from highest to lowest median percent decreases, included: GEV (included in both diacetyl and 2,3-pentanedione models), natural ventilation (included in diacetyl model) and one source near the roasters (included in both diacetyl and 2,3-pentanedione models) (**Table 3**; **Figure 4**). GEV was associated with estimated 95% CIs of percent decreases ranging from 80.5 to 84.3%

decreases in diacetyl and 79.4 to 83.4% decreases in 2,3-pentanedione (**Figure 4**). Natural ventilation was associated with estimated 95% CI of percent decreases ranging from 3.0 to 17.2% decreases in diacetyl (**Figure 4**).

Grinding Tasks

A total of 154 grinding task diacetyl models and 76 grinding task 2,3-pentanedione models were generated comprising 17 and 16 determinants for diacetyl and 2,3-pentanedione exposures, respectively (**Table 4**). Determinants associated with increases in diacetyl and 2,3-pentanedione exposure during grinding tasks were similar as those noted in the overall task model (e.g., coffee storage determinants, total number of sources, amount of coffee produced, amount of grinding performed, flavoring ground coffee). Some grinding specific determinants were also notable in the grinding model: silo containers for ground coffee storage in the grinding area (reference: open containers) and number of other sources near the grinder were associated with increases in diacetyl but not 2,3-pentanedione exposures (**Table 4**; **Figure 5**). Additionally, isolated roasting area was associated with increased diacetyl and 2,3-pentanedione exposures during grinding tasks but not in the overall model.

Among sample-level determinants, sampled grinder near another grinder and roaster was associated with some of the highest increases in diacetyl (95% CI: 144–208%) and 2,3-pentanedione (95% CI: 70.6–120.2%) exposures during grinding tasks compared to the reference category of the sampled grinder not being near another grinder or roaster (**Table 4**; **Figure 5**). This effect was smaller but also notable for diacetyl exposures for sampled grinders near another grinder only (95% CI: 14–41% increase) (**Figure 5**). For context when interpreting percentage change, the intercept reference values for diacetyl and 2,3-pentanedione across all grinding models was 23.3 ppb diacetyl and 22.7 ppb 2,3-pentanedione.

Among process-level determinants, the top five process-level determinants with the greatest impact on increasing diacetyl exposures during grinding tasks were (1) flavor ground coffee, (2) silo storage containers for ground coffee in the grinding area (reference: open containers), (3) isolated roasting area, (4) >10,000 lbs average daily roasted coffee production, and (5) 1,000–10,000 lbs average daily roasted coffee production, with 95% CIs of percent increases ranging from (1) 159–448%, (2) 5.9–563%, (3) 77–166%, (4) 37–166%, and (5) 37–127%, respectively. Similarly, the top five process-level determinants with the greatest impact on increasing 2,3-pentanedione exposures during grinding tasks were (1) flavor ground coffee, (2) isolated roasting area, (3) 1,000–10,000 lbs average daily roasted coffee production, (4) >10,000 lbs average daily roasted coffee production, and (5) average percent ground coffee, with 95% CIs of percent increases ranging from (1) 263–719%, (2) 219–456%, (3) 49–205%, and (4) 26–192%, and (5) 51–95%, respectively (**Figure 5**).

Multiple sample and process-level determinants were associated with decreases in diacetyl or 2,3-pentanedione exposure during grinding tasks. Sampled while grinding flavored coffee (reference: sampled while grinding unflavored coffee) was associated with decreases ranging from 40.1–50.5% for diacetyl (95% CIs, **Figure 5**). Closed containers for storage of ground coffee in the grinding area (reference: open containers) was associated with 95% CIs of percent decreases ranging from 1.4 to 77.5% for diacetyl and 25.9–79.1% for 2,3-pentanedione, compared to the reference category of open containers (**Figure 5**). Flavoring processes performed with ventilation in the form of local exhaust ventilation (LEV) was associated with 95% CIs of percent decreases ranging from 68.5 to 82.5% for 2,3-pentanedione during grinding tasks, compared with the reference group of flavoring processes performed with no LEV (**Figure 5**).

Packaging Tasks

A total of 927 packaging task diacetyl models and 631 packaging task 2,3-pentanedione models were generated comprising 23 and 20 determinants for diacetyl and 2,3-pentanedione exposures, respectively (**Table 5**). Process-level factors associated with notable increases in diacetyl and 2,3-pentanedione exposure during packaging tasks were similar to those noted in the overall task model (e.g., coffee storage determinants, total number of sources, amount of coffee produced, amount of grinding performed, flavoring ground coffee, flavoring during survey). Some additional determinants associated with increased diacetyl and 2,3-pentanedione exposures included some packaging specific determinants such as open storage of coffee in the packaging area (reference: no open storage). Additionally, isolated roasting area (reference: roasting area not isolated) was associated with increased diacetyl and 2,3-pentanedione exposures during packaging tasks.

The sample-level determinants of (1) sample collected while a worker packaged flavored coffee (95% CIs: 40–55% diacetyl, 81–106% 2,3-pentanedione; reference: packaging unflavored coffee) and (2) single-serve coffee pods of ground coffee (95% CIs: 25–35% diacetyl, 4–14% 2,3-pentanedione; reference: packaging <1 lb coffee) were associated with notably higher exposures to diacetyl and 2,3-pentanedione after controlling for other covariates (**Table 5**; **Figure 6**). For context when interpreting percentage change, the intercept reference values for diacetyl and 2,3-pentanedione across all packaging models was 12.1 ppb diacetyl and 9.8 ppb 2,3-pentanedione.

The top five process-level determinants with the greatest impact on increasing diacetyl exposures during packaging tasks were (1) high (>6%) automated sources, (2) flavor ground coffee, (3) >10,000 lbs average daily roasted coffee production, (4) >2 sources of open storage of coffee, and (5) low (>0%, ≤6%) automated sources with 95% CIs of percent increases ranging from (1) 230–281%, (2) 140–230%, (3) 155–201%, (4)152–189%, and (5)145–179%, respectively. Similarly, the top five process-level determinants with the greatest impact on increasing 2,3-pentanedione exposures during packaging tasks were (1) flavor ground coffee, (2) isolated roasting area (reference: roasting area not isolated), (3) flavoring during survey (reference: not flavoring during survey), (4) 1–2 sources of open storage, and (5) grind flavored coffee, with 95% CIs of percent increases ranging from (1) 284–457%, (2) 231–285%, (3) 159–184%, (4) 144–192%, and (5) 101–125%, respectively (**Figure 6**).

Multiple process-level factors were associated with decreases in diacetyl or 2,3-pentanedione exposure during packaging

tasks. Natural ventilation was associated with 95% CIs of percent decreases ranging from 16.4 to 26.5% for diacetyl (**Figure 6**). GEV was associated with 95% CIs of percent decreases ranging from 68.2–70.5% for diacetyl and 65.8–68.4% for 2,3-pentanedione (**Figure 6**). Accessory fans at the roasters and flavoring processes performed with LEV (reference: flavoring processes performed with no LEV) were associated with percent decreases ranging from 23.0–27.9% and 38.4–51.4% for 2,3-pentanedione, respectively (**Figure 6**).

DISCUSSION

Five cases of obliterative bronchiolitis observed among current and former coffee production workers were first described in 2013 and 2015 (21, 22). Since then, two recent case reports have described additional cases of obliterative bronchiolitis in workers exposed to diacetyl and 2,3-pentanedione in coffee production (12, 35) including a case of obliterative bronchiolitis observed in a current worker at one of the 17 coffee production facilities included in our study here (12). Observed cases of obliterative bronchiolitis among current and former workers in coffee production facilities along with measurements of elevated exposures to diacetyl and 2,3-pentanedione in the 17 facilities surveyed here (13) highlights a need to understand determinants of exposures to alpha-diketones in coffee production facilities such that exposure mitigation strategies can be designed and implemented accordingly.

An understanding of tasks associated with higher diacetyl and 2,3-pentanedione exposures and determinants of elevated task-based exposures is particularly important because elevated short-term exposures to diacetyl and 2,3-pentanedione can potentially contribute to (1) obliterative bronchiolitis and negative respiratory health outcomes (22, 36) and (2) higher TWA full-shift exposures (37–39). Previous studies in various workplace settings describe how specific tasks and processes contributing to high exposures can be overlooked when full-shift sampling is used to guide controls for exposure mitigation (40–42). Quantifying intermittent, task- and process-based exposures is needed for (2) an understanding of short-term or peak exposures, (1) comparison with short-term exposure limits, and/or (3) use as an exposure metric in epidemiological studies (43). Additionally, instantaneous measurements during very brief activities or at specific process-related sources can identify high exposures and emissions that could otherwise also be overlooked in exposure assessments and subsequent exposure control strategies. Further, task-based sampling can be used to develop models that identify determinants of high short-term exposures that can be directly targeted for exposure controls.

Traditional modeling approaches have favored multiple linear regression or linear mixed effects models (24, 37). However several notable limitations exist when making inferences based on these models, including uncertainty and variability associated with model building strategies and the selection of the best final model (44). Different approaches to select the final model can lead to different final models identified by different researchers. Alternatively, model averaging methods incorporate uncertainties of model selection strategies by summarizing a set of contending models to make inferences about the predictors and is widely used in other fields (45). The use of model averaging methods in occupational exposure assessment was first proposed and used by Lavoue et al. in 2009 (44). A model averaging approach is appealing because it can be implemented easily using standard statistical software (45–47). The BMA modeling approach is particularly advantageous because it addresses uncertainties in model building and variable selection, censored data issues, repeated measurements on individuals, and provides posterior distribution of parameters for all variables considered.

In our study, we identified tasks and sources associated with elevated exposures to diacetyl and 2,3-pentanedione. We then used BMA models to identify determinants associated with short-term task-based exposures to diacetyl and 2,3-pentanedione and highlight additional process-level and task-level factors to focus exposure mitigation efforts in coffee production facilities.

Tasks and Sources Associated With Elevated Exposures to Diacetyl and 2,3-Pentanedione During Coffee Production

Grinding, flavoring, packaging ground coffee, and various production tasks with ground coffee had among the highest personal task and instantaneous activity exposures for diacetyl and 2,3-pentanedione (13). Specifically, samples collected during flavoring (50%), grinding (69%), moving roasted beans or ground coffee (50%), packaging (24%), roasting (13%), and cleaning roasting, grinding, packaging, and flavoring machines (64%) tasks exceeded the NIOSH STEL of 25 ppb diacetyl. Similarly, samples collected during flavoring (50%), grinding (34%), and packaging (6%) tasks exceeded the NIOSH STEL of 31 ppb 2,3-pentanedione. Although no exposure limits exist for instantaneous exposures to diacetyl and 2,3-pentanedione, the instantaneous measurements during specific tasks highlight opportunities for exposure mitigation controls. Ground coffee, flavored coffee, liquid flavorings, and off-gassing bins or packages were also identified as the highest sources of diacetyl and 2,3-pentanedione. Elevated task, instantaneous activity, and instantaneous source exposures associated with grinding and flavoring tasks are consistent with the work history of a coffee production worker diagnosed with obliterative bronchiolitis, who performed grinding and flavoring tasks for 7 years prior to diagnosis in the grinding area and flavoring room of one of the 17 coffee and roasting facilities described here (12).

Our results suggest coffee production facilities can consider targeting grinding and flavoring tasks for exposure mitigation. Specifically, facilities can consider isolating flavoring and grinding tasks in a designated area or room and utilizing LEV to directly remove alpha-diketone emissions from these isolated areas and processes. Facilities can also consider enclosing and ventilating grinders for reduction of alpha-diketone emissions from grinders. Another article in this Research Topic collection of articles investigating exposures and respiratory health in coffee workers shares encouraging results which show significant decreases in exposure to diacetyl and 2,3-pentanedione after

enclosing and ventilating grinders. Stanton et al. observed >75% decreases in concentrations of alpha-diketones in the production space after enclosing and ventilating grinders at a large coffee production facility (48). Similar engineering controls such as enclosing and ventilating flavoring mixers can also be considered for flavoring processes (49). We also observed high exposures during moving roasted beans or ground coffee, packaging, roasting, and cleaning machines tasks, indicating additional engineering and administrative controls are needed to mitigate exposures to diacetyl and 2,3-pentanedione in coffee roasting and packaging facilities. Modeling determinants of short-term task-based exposures highlighted additional process-level and task-level factors to focus exposure mitigation efforts and are discussed in greater detail below.

Determinants of Exposure to Diacetyl and 2,3-Pentanedione During Coffee Production Tasks

No previous studies have reported on determinants contributing to task-based exposures in coffee production, despite a need to understand factors contributing to elevated short-term exposures and design exposure mitigation strategies to reduce short-term and full-shift exposures to minimize risks for respiratory disease. The BMA models for overall task and individual tasks highlighted additional determinants that contributed to higher exposures to both diacetyl and 2,3-pentanedione including sum of all open storage sources, average percent of production as ground coffee, flavoring ground coffee and flavoring during the survey. Flavoring ground coffee was associated with 309–384% increases in diacetyl concentrations and 303–392% increases in 2,3-pentanedione compared to tasks at facilities that flavored whole bean coffee, but not ground coffee. Our results indicate a need for additional engineering controls such as LEV to capture and directly remove emissions from flavored ground coffee during flavoring processes. Additionally, sites that flavor ground coffee should evaluate where and how flavored ground coffee is stored and/or handled, to minimize further emissions during later steps in production. Similarly, any open storage of coffee was associated with elevated short-term exposures to diacetyl and 2,3-pentanedione across all tasks. Our results underscore the importance of reducing exposures across all tasks by storing all coffee in closed containers. Companies that need to store coffee in open containers as part of an off-gassing step in production can consider isolating their open containers of coffee in a space separate from other production processes and implementing source control ventilation designed to capture and remove emissions directly from the open containers. Additionally, surrogates for the amount of ground coffee produced at a site such as average percent ground coffee, total number of grinders, total grinding capacity, and average grind length in minutes were all associated with increases in exposures to diacetyl and 2,3-pentanedione across all tasks. These results highlight the importance of carefully evaluating where and how ground coffee is handled, packaged, and stored in later steps of production and implementing additional engineering and administrative controls to mitigate exposure to emissions from ground coffee.

Unsurprisingly, GEV was associated with decreases in exposures for both diacetyl and 2,3-pentanedione across all tasks, compared with exposures at sites with no GEV. Facilities that do not currently have operational GEV should consider implementing a GEV system designed to create a negative pressure in higher alpha-diketone concentration areas such as flavoring rooms or grinding areas. Pressure differentials can be created by providing GEV supply and exhaust air strategically to different production areas. For example, the exhaust air volume from the flavoring rooms or grinding areas can be designed and operated at slightly greater flow rate than the volume of supply air. A general rule is to design the GEV system with a supply flow rate set at 5–10% less than the exhaust flow rate (49, 50). GEV can also minimize the accumulation of alpha-diketones, and other potential pollutants, in the air of production spaces by diluting contaminants with supply air and exhausting contaminants to the outside (49, 51). Similarly, natural ventilation was observed to decrease diacetyl concentrations across all tasks. However, careful consideration should be taken when utilizing natural ventilation and should be done in accordance with state and local health codes. Opening doors or windows introduces unfiltered air and might contain outdoor air pollutants such as pollen and dust. Further, opening windows and doors can (1) cause imbalances in pressure differentials imparted by ventilation systems designed to mitigate exposures and (2) affect the ability of the heating, ventilation, and air-conditioning (HVAC) system to adequately control temperatures and humidity.

Interestingly, high automation and any enclosed sources were observed as determinants of increased exposure across all tasks. Because high automation and source enclosures were predominantly observed at larger coffee production sites, this observation was likely confounded by production scale. Unfortunately, we did not observe these controls at a sufficient number of small production facilities to evaluate the effect of these controls after accounting for production scale.

Additional determinants identified in the grinding model included storing ground coffee in closed containers in the grinding area which resulted in some of the largest estimated decreases in exposures, indicating that storing ground coffee in closed containers can help further mitigate exposures. Further, if the grinder was located within 10 ft of another grinder or roaster it resulted in increases in exposures during grinding tasks. This effect was markedly higher for grinders near another roaster and grinder, as compared to those near only another grinder. As discussed above, facilities can consider isolating grinding tasks in a designated area or room and increasing general ventilation as well as LEV to directly remove emissions of alpha-diketones from the isolated grinding area. Additionally, some of the highest increases in exposures during packaging tasks were observed when packaging flavored compared to unflavored coffee. Increases in exposures during packaging were also observed when packaging single serve coffee pods of ground coffee. Facilities can consider additional engineering controls to minimize sources of alpha-diketone exposure during packaging tasks such as flavored and/or ground coffee. These results underscore the importance of carefully evaluating when and how

flavored or ground coffee is handled during all production steps and implementing additional engineering and administrative controls to mitigate exposures to emissions from flavored and/or ground coffee. Lastly, although exposures during roasting were among the lowest exposure tasks, there were several roasting specific determinants identified as associated with increased exposures. Some of the highest increases in exposure during roasting tasks were estimated for large, unenclosed roasters, and open storage of coffee in the roasting area. Our results suggest that enclosing roasters, especially roasters with roasting capacity >200 lbs, and storing coffee in closed containers in the roasting area can reduce exposures during roasting tasks.

Sample size for flavoring tasks was too small with too few workers observed to generate multiple linear regression models of determinants of elevated exposures while performing flavoring tasks. However, univariate analyses did identify determinants associated with increases in exposures to diacetyl and/or 2,3-pentanedione during flavoring tasks including amount of roasted coffee produced and amount of grinding performed. Similarly, the sample size for QC tasks was too small with a high degree of censoring to generate multiple linear regression models of determinants. However, univariate analyses identified QC grinding tasks, additional open storage sources, total number of sources, amount of roasted coffee produced, and amount of grinding performed as potential determinants of elevated exposure while performing QC tasks. Additionally, the highest instantaneous activity measurements of diacetyl and 2,3-pentanedione during QC tasks were observed during QC grinding.

Differences in Determinants of Exposure to Diacetyl vs. 2,3-Pentanedione

Scatter plots of log-transformed diacetyl and 2,3-pentanedione air concentrations from task-based samples revealed a positive association with a Spearman's correlation coefficient of 0.507. A positive association was expected because both diacetyl and 2,3-pentanedione are natural byproducts from coffee roasting and are emitted during roasting, grinding, and packaging whole bean and ground coffee. However, differences in emissions of diacetyl and 2,3-pentanedione from freshly roasted coffee have been observed previously, with increased emissions rates of diacetyl, but not 2,3-pentanedione, observed with increasing roast level (52). These differences likely contributed to our observation of roast depth associated determinants (average roast length in minutes) as a notable determinant of increased exposure to diacetyl, but not 2,3-pentanedione, during roasting, packaging, and all tasks. Further, differences exist between diacetyl and 2,3-pentanedione emissions from flavored vs. non-flavored coffee because of differences in the relative amounts of diacetyl or 2,3-pentanedione added to liquid flavorings, with 2,3-pentanedione often used as a substitute for diacetyl in liquid flavorings (53). These differences in concentrations of diacetyl and 2,3-pentanedione were prominent in the task-based samples during flavoring tasks with the GM for 2,3-pentanedione being almost 9-fold higher than diacetyl. Additionally, measurements of diacetyl varied widely during flavoring tasks as indicated by a large GSD of 30.2.

Differences in concentrations observed for diacetyl and 2,3-pentanedione in processes where flavored vs. unflavored coffee was present likely contributed to differences between models for diacetyl and 2,3-pentanedione. For example, grinding flavored coffee was associated with increased exposure to 2,3-pentanedione, but not diacetyl, across all tasks. Additionally, flavoring processes performed with LEV present contributed to lower 2,3-pentanedione, but not diacetyl exposures during grinding and packaging tasks, as compared to these tasks performed at sites with no LEV. Our results suggest that source controls targeting flavoring processes not only reduce exposures during flavoring tasks but also during grinding and packaging tasks. We note that we were not able to directly assess the effect of isolating flavoring processes because an isolated flavoring room was only observed among sites that flavored ground and whole bean coffee.

BMA Modeling Approach to Identify Determinants of Occupational Exposures

Our analyses utilized a sophisticated modeling approach (BMA) to obtain final inferences on a variety of determinants of short-term task-based exposures. Our approach allowed us to understand the (1) impact of each variable when put in models with other non-collinear variables and (2) effect of controlling for other non-collinear variables. This approach also accounted for measurements below the LOD using a Bayesian left-censored framework allowing for inferences. Our modeling strategy also reduced ambiguity present in selecting an ideal final model, because the effects of multiple models are averaged together for final inferences. We also avoided multicollinearity concerns by removing collinear combinations of variables, and subsequently generated reasonable variance estimates and the ability to identify notable differences when those were truly present. It should be noted that not all determinants will go in the models in the BMA process together, so we cannot say that all models controlled for all the other variables. Similarly, the number of models where a determinant is included is a function of how correlated that determinant is with other determinants. For example, determinants could be important but also highly correlated with many other determinants and subsequently included in relatively few models. Therefore, the number of models containing the determinant should not be interpreted as the importance of the determinant in this context. The importance of the determinant should be judged relative to slope value or the percent change. Although our results are focused on determinants of exposure in coffee roasting and packaging facilities, mixed modeling can be used to identify determinants across many occupational settings.

Limitations and Further Research

Flavoring coffee was associated with some of the highest measurements of exposure to alpha-diketones in the surveyed coffee production facilities (13). However, our sample size for flavoring tasks was too small to generate stable models of determinants of elevated exposures while flavoring. The univariate analyses identified amount of roasted coffee produced and amount of grinding performed as potential determinants of elevated exposure while flavoring. However, the small sample

size likely limited our ability to observe other potentially meaningful determinants of exposures during flavoring tasks. Further research with a sufficient sample size to generate multiple linear regression models of diacetyl and 2,3-pentanedione during flavoring tasks is needed to fully assess determinants of exposure to alpha-diketones while flavoring. Additionally, although we were able to generate stable models of determinants of elevated exposures while grinding, our sample size for short-term grinding tasks was relatively small and this contributed to small cell sizes in some categorical determinants, making it difficult to evaluate their effect. For example, small cell sizes in the no GEV category limited our ability to assess the effect of GEV on grinding task exposures. Our smaller sample size for grinding tasks was because grinding was a very brief (<2 min) task at many of the locations surveyed. Because grinding was often performed very briefly, many of the grinding tasks were sampled with instantaneous canisters, and not with short-term task-based samples, and instantaneous canister samples were not modeled in our analyses here.

Not all sample-level determinants were systematically collected during short-term task-based sample collection. Collecting the desired level of detail on exposure determinants for tasks during sampling was challenging because workers performed numerous short-lived activities and were highly mobile making their continuous observation impractical. Some sample-level determinants included unknown values due to not being recorded during short-term task-based sample collection and limited our ability to fully characterize the contributions of each sample-level determinant. Future studies including systematic collection of sample-level determinants would allow for more informed modeling of exposures during short-term task-based sample collection.

Many of our determinants were process-based and at the facility level. Because they were at the facility level, they did not vary by task and potentially directly or indirectly affected all tasks. Additionally, we did not observe determinants across all possible categories and combinations. For example, we only observed some engineering controls such as automation and enclosures at large facilities which made it difficult to evaluate the effect of these engineering controls after accounting for production scale. Future studies designed to evaluate the effect of different engineering controls such as automation and enclosing processes, specifically, are needed. Similarly, having one source near the roasters was associated with lower exposures during roasting tasks. This was an unexpected finding that is likely confounded by an isolated roasting area because we only observed an isolated roasting area at facilities with one source near the roasters. The effect of having an isolated roasting area potentially contributed to the decreased exposures during roasting tasks observed at sites with only one source near the roasters. Unfortunately, we could not evaluate the effect of sources near the roaster on exposures during roasting tasks because we did not observe having an isolated roasting area across all categories for numbers of sources near the roaster. Additional studies designed to evaluate the effect of engineering controls such as source controls, automation, enclosures, and isolation of production spaces are needed to fully assess the effects of these controls on emissions and exposures in coffee production. Our modeling results should be evaluated cautiously and should be used as a guide in decision making in combination with other facility specific information.

Further, as described in LeBouf et al., another limitation of our study is the potential for selection bias (13). Our surveys were initiated by facility management or employees through the HHE program and therefore are not a random sample of facilities. Selection bias is possible. However, the effect on exposure measurements is thought to be minimal as our measurements of exposure during specific tasks are within ranges reported in other studies (11, 14, 54).

Our analyses included task-based samples collected at coffee production facilities with fewer than 500 employees. We did not conduct surveys at large facilities, specifically those with >500 employees. Task-based exposures in larger facilities remains uncharacterized. Results from our study can alert management at larger facilities to potential tasks and sources of elevated exposure to diacetyl and 2,3-pentanedione that can be targeted for exposure mitigation; however, further research is needed to characterize short-term task-based exposures in larger facilities specifically, as their work processes, production volumes, and exposure levels could differ from those observed in our study.

Conclusions

Grinding, flavoring, packaging, and various production tasks with ground coffee were among the highest personal task-based short-term and instantaneous activity measurements for diacetyl and 2,3-pentanedione. Ground coffee, flavored coffee, liquid flavorings, and off-gassing bins or packages were also identified as the highest sources of diacetyl and 2,3-pentanedione. Determinants associated with increased exposure to diacetyl and 2,3-pentanedione across all tasks included sum of all open storage sources and average percent of production as ground coffee. Additionally, flavoring ground coffee and flavoring during survey contributed to higher exposures for both analytes in most task groups. Our results suggest that facilities who aim to reduce exposures to alpha-diketones can consider isolating flavoring and grinding tasks in a designated area or room, adjusting these spaces to negative pressure using GEV, and enclosing and ventilating grinders and flavoring mixers with LEV to directly remove emissions of alpha-diketones from these isolated areas and processes. Additionally, facilities can consider minimizing open storage of roasted coffee, with special attention given to the open storage and off-gassing of ground coffee. Additional LEV can be used to directly remove alpha-diketones from off-gassing coffee where open storage is required for off-gassing procedures and can mitigate exposures near stored coffee as well as throughout the facility.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because of restrictions imposed under the US Privacy Act and the limitations of what participants consented to. The data underlying the analyses presented, beyond what is provided in the paper, are confidential and not available to researchers outside the National Institute for Occupational Safety and Health

(NIOSH). For more information about NIOSH's policy regarding sensitive data, see https://www.cdc.gov/niosh/ocas/datahandle.html. Requests to access the datasets should be directed to BB, bblackley@cdc.gov.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the NIOSH Institutional Review Board (NIOSH Protocol 17-RHD-06XP). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

BB, JC-G, AF, RL, and MV contributed to conception and design of the study. BB, CG, XL, and MV performed the statistical analyses. BB wrote the first draft of the manuscript. All authors contributed to manuscript revisions, read, and approved the submitted version.

FUNDING

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

ACKNOWLEDGMENTS

The authors thank the workers for participating in the NIOSH health hazard evaluation program and the members of the NIOSH field teams for their contributions to data acquisition. The authors would like to acknowledge Kimberly R. Anderson and Matthew M. Dahm for reviewing the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.878907/full#supplementary-material

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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.

frontiers in Public Health

BRIEF RESEARCH REPORT
published: 30 January 2020
doi: 10.3389/fpubh.2020.00005

The Burden of Respiratory Abnormalities Among Workers at Coffee Roasting and Packaging Facilities

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OPEN ACCESS

Edited by:
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Reviewed by:
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William Gwinn, National Toxicology Program Division (NIEHS), United States

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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: *17 October 2019*
Accepted: *08 January 2020*
Published: *30 January 2020*

Citation:
Harvey RR, Fechter-Leggett ED, Bailey RL, Edwards NT, Fedan KB, Virji MA, Nett RJ, Cox-Ganser JM and Cummings KJ (2020) The Burden of Respiratory Abnormalities Among Workers at Coffee Roasting and Packaging Facilities. Front. Public Health 8:5. doi: 10.3389/fpubh.2020.00005

Introduction: Respiratory hazards in the coffee roasting and packaging industry can include asthmagens such as green coffee bean and other dust and alpha-diketones such as diacetyl and 2,3-pentanedione that can occur naturally from roasting coffee or artificially from addition of flavoring to coffee. We sought to describe the burden of respiratory abnormalities among workers at 17 coffee roasting and packaging facilities.

Methods: We completed medical surveys at 17 coffee roasting and packaging facilities that included interviewer-administered questionnaires and pulmonary function testing. We summarized work-related symptoms, diagnoses, and spirometry testing results among all participants. We compared health outcomes between participants who worked near flavoring and who did not.

Results: Participants most commonly reported nose and eye symptoms, and wheeze, with a work-related pattern for some. Symptoms and pulmonary function tests were consistent with work-related asthma in some participants. About 5% of workers had abnormal spirometry and most improved after bronchodilator. Health outcomes were similar between employees who worked near flavoring and who did not, except employees who worked near flavoring reported more chronic bronchitis and ever receiving a diagnosis of asthma than those who did not work near flavoring.

Conclusion: The symptoms and patterns likely represent overlapping health effects of different respiratory hazards, including green coffee bean and other dust that can contribute to work-related asthma, and diacetyl and 2,3-pentanedione that can contribute to obliterative bronchiolitis. Healthcare providers and occupational health and safety practitioners should be aware that workers at coffee roasting and packaging facilities are potentially at risk for occupational lung diseases.

Keywords: coffee roasting and packaging, occupational asthma, obliterative bronchiolitis, flavoring, diacetyl, 2,3-pentanedione, coffee dust

INTRODUCTION

Five cases of obliterative bronchiolitis were diagnosed among former workers of a U.S. coffee roasting and packaging facility during 2012–2015; two cases were confirmed by lung biopsy (1, 2). This cluster of obliterative bronchiolitis was the first identified among workers in the coffee roasting and packaging industry. Obliterative bronchiolitis (also called bronchiolitis obliterans or constrictive bronchiolitis) is a rare and irreversible lung disease characterized by inflammation and fibrotic changes leading to narrowing of the small airways (<2 mm, bronchioles) (3). Symptoms often include cough, exertional dyspnea, or wheeze, typically without a work-related pattern (4). Occupational obliterative bronchiolitis was described in 2002 among workers at a microwave-popcorn production facility that used artificial butter flavoring containing diacetyl (5, 6). Investigations at other microwave popcorn production facilities and in flavoring and food manufacturing facilities that used or produced flavorings containing diacetyl identified additional cases of flavoring-related obliterative bronchiolitis (7–9). Subsequent experimental studies revealed inhalational exposure to diacetyl, caused severe injury to the respiratory epithelium in animals (10–13). Animal studies also demonstrated another closely related compound, 2,3-pentanedione, causes similar toxicity and should therefore not be considered a potential safe substitute for diacetyl by industry (14–16).

The sentinel coffee facility that had employed the former workers who had obliterative bronchiolitis added flavorings that contained the alpha-diketones diacetyl and 2,3-pentanedione to coffee in a separate, enclosed area of the facility; however, diacetyl and 2,3-pentanedione are also naturally produced and released during the coffee roasting process (17). An industrial hygiene investigation based on alpha-diketone levels measured during grinding, packaging, and off-gassing of unflavored roasted coffee, determined sources of diacetyl and 2,3-pentanedione were not restricted to the areas of the facility where flavorings were added (18). Additionally, more workers than expected at the sentinel coffee facility had exertional dyspnea and spirometric obstruction, but not all of these workers were located in the flavoring area of the facility (1). The investigation suggested that natural sources of diacetyl and 2,3-pentanedione might contribute to respiratory disease risk in the coffee roasting and packaging industry, in addition to the known risk from added flavorings.

Workers in the coffee roasting and packaging industry are susceptible to other work-related respiratory diseases in addition to obliterative bronchiolitis, most notably work-related asthma (19). Work-related asthma encompasses both incident occupational asthma and exacerbation of pre-existing asthma (20–22). Symptoms often include shortness of breath, cough, wheeze, or chest tightness that frequently improve away from work. Green and roasted coffee dust, and castor bean dust from contaminated burlap bags used to ship green coffee beans, are established causes of work-related asthma in coffee roasting and packaging (19, 23–27). Work-related asthma can be caused by different mechanisms, including an allergic response to sensitizers like green coffee beans or a non-allergic, irritant induced response to coffee dust (28).

During 2016–2017, the U.S. National Institute for Occupational Safety and Health (NIOSH) evaluated an additional 17 coffee roasting and packaging facilities to address concerns about workplace exposures to diacetyl and 2,3-pentanedione, and other potential respiratory hazards like green coffee beans and dust. Some of the facilities added flavorings to roasted coffee, and others did not. No cases of obliterative bronchiolitis or severe lung disease among workers at these coffee roasting and packaging facilities had been identified prior to our evaluations. We present the combined health evaluations from 17 facilities to describe the burden of respiratory abnormalities among their coffee roasting and packaging workers.

METHODS

During 2016–2017, NIOSH responded to 17 management or employee requests for health hazard evaluations (https://www.cdc.gov/niosh/hhe/default.html) at coffee roasting and packaging facilities to primarily address concerns about potential exposure to diacetyl and 2,3-pentanedione. Each facility was evaluated independently and received its own report of findings and recommendations (available at: https://www2a.cdc.gov/hhe/search.asp). We will present detailed results of the industrial hygiene surveys assessing diacetyl and 2,3-pentanedione in these 17 facilities separately. The NIOSH Institutional Review Board approved this study that pools the data from those 17 public health evaluations (NIOSH Protocol 17-RHD-06XP). All current workers aged 18 years or older at the coffee roasting and packaging facilities were invited to give written informed consent for an evaluation that included an interviewer-administered questionnaire, spirometry, and exhaled nitric oxide. The questionnaire addressed symptoms, diagnoses, work history, work-tasks and exposures, smoking history, and demographic information. Respiratory symptom questions were adapted from validated survey instruments (29–35). We defined work-related symptoms as those reported to be better away from work. For current or former smokers, we calculated smoking pack-year as 20 cigarettes smoked per day for 1 year.

We used a volume spirometer, American Thoracic Society (ATS) criteria for acceptability and repeatability of spirometry tests, and equations for predicted values and lower limits of normal derived from the Third National Health and Nutrition Examination Survey (NHANES) data to define abnormal spirometry (35–37). We defined obstruction as a forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio and FEV_1 less than their respective lower limits of normal (LLN); restrictive pattern as an FVC less than the LLN with normal FEV_1/FVC ratio; and mixed obstruction and restrictive pattern as having FVC and FEV_1/FVC ratio less than their respective LLNs. We used the FEV_1 percent predicted to categorize abnormalities as mild, moderate, moderately severe, severe, or very severe (38). All participants with abnormal spirometry were offered bronchodilator testing to assess for reversibility of at least 12% and 200 milliliters (mL) for either FEV_1 or FVC with albuterol

as the bronchodilator. We used the NIOX MINO® device (Aerocrine Inc., Morrisville, NC) to measure fractional exhaled nitric oxide (FeNO). FeNO concentrations above 50 parts per billion (ppb) were considered elevated (39).

We used participants' narrative descriptions of how work causes or aggravates upper respiratory symptoms (nasal symptoms or sinus problems) and lower respiratory symptoms (wheeze, exertional dyspnea, breathing trouble, cough, chest tightness, asthma attack, or awoken by shortness of breath) to create word clouds using R 3.5.2 (R Core Team, 2019) and the *wordcloud* (v2.6; Fellows, 2018) package. Words or short phrases were sized proportionally to the frequency used to provide graphic representations of keywords used by participants to describe causes or aggravations of symptoms at work.

We compared symptoms, diagnoses, and lung function parameters between participants who reported working near flavoring (within an arm's length of the container when flavorings are being added or mixed with roasted coffee) and participants who did not report working near flavoring. We compared symptoms, diagnoses, and lung function parameters between atopic participants (those with self-reported hay fever, nasal allergies, or eczema) and non-atopic participants. We calculated chi-square values to compare health outcomes between participants who reported working near flavoring and those who did not, and participants who reported atopy and those who did not. We considered $P < 0.05$ to be statistically significant.

We calculated frequencies and standardized morbidity ratios (SMRs) and their associated 95% confidence intervals (CIs). The SMRs compared prevelences of symptoms, diagnoses, and spirometric abnormalities among participants with expected prevelences of a sample of the general U.S. population reflected in NHANES data, adjusting for race/ethnicity (white, black, Hispanic), sex, age ($\leq$39 and $\geq$40 years), and smoking (ever/never) (34, 35). We used the most recent NHANES data available for the specific comparisons, including NHANES III (1988–1994) and NHANES Continuous (select years during 1999–2016).

We compared our study participants to several previous study populations, including the sentinel coffee roasting and packaging facility, sentinel microwave popcorn production facility, and combined data from three other microwave popcorn facilities (1, 7, 18, 40–43). For these comparisons, we categorized the 17 facilities included in our study in to two groups—those that used flavoring or those who did not (non-flavoring). We compared exertional dyspnea, wheeze, cough, percent predicted FEV_1, obstruction, and mean time weighted average (TWA) personal exposure to diacetyl and 2,3-pentanedione. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

We evaluated 384 (58%) of 658 current workers from 17 coffee roasting and packaging facilities in 12 states during 2016–2017. The facilities had a median of 15 participating workers (range: 4–99 workers). Most participants were male (59%) and white (59%), with a median age of 35 years (range: 18–72 years) (**Table 1**). Most participants were never smokers (57%); 43% were current or former smokers with a median of 3.3 pack-years. The median number of years worked at the current facility (tenure) was 2.8 (range: <1–30 years); 79 (21%) participants reported previously working at other coffee roasting and processing facilities or companies that use flavorings, and the median number of years worked at any coffee facility or company that uses flavorings was 3.5 (range: <1–34 years).

Most participants (87%) reported currently working in production areas of a coffee roasting and processing facility where the most common tasks performed included packaging coffee (55%), moving coffee (48%), cleaning equipment (46%), and grinding coffee (42%) (**Table 1**). Sixty (16%) participants roasted coffee. Of the 17 coffee roasting and packaging facilities, 12 did not flavor coffee, while the other five did flavor some of the coffee processed in their facility. At the five facilities that flavored coffee, 23 (16%) of 143 participants who worked in production reported performing the task of flavoring coffee. Eleven (65%) of 17 facilities also included a café; 35 (23%) of 149 participants from facilities with cafés reported working in the cafés, although these employees could have also had other job responsibilities, including production tasks.

TABLE 1 | Characteristics and job tasks of participating workers in 17 coffee roasting and production facilities, $N = 384$.

Characteristic	*n* (%)
Age (years) median (range)	35 (18–72)
Sex	
Male	225 (59%)
Female	159 (41%)
Race/ethnicity	
Non-hispanic white	226 (59%)
Hispanic	112 (29%)
Black	29 (8%)
Asian	7 (2%)
Other, including multi-racial	10 (3%)
Body mass index	
BMI $\geq$ 30	125 (33%)
Smoking status	
Never	220 (57%)
Former	98 (26%)
Current	66 (17%)
Tenure at current facility (years) median (range)	2.8 (<1–30)
Job tasks	*n* (%)
Package coffee	211 (55%)
Move coffee	185 (48%)
Clean equipment	177 (46%)
Grind coffee	162 (42%)
Perform maintenance	105 (27%)
Roast coffee	60 (16%)
Flavor coffee	23 (6%)

Upper respiratory symptoms in the last 12 months were the most commonly reported symptoms (66% of participants); 11% of participants reported their upper respiratory symptoms were work-related (**Table 2**). Participants who reported their upper respiratory symptoms were caused or aggravated by work most commonly implicated dust [55 of (34%) 163 respondents] (**Figure 1A**). Compared with the U.S. adult population, participants were more likely to report a stuffy, itchy, or runny nose in the last 12 months (SMR 1.2; 95% CI: 1.1–1.4) (**Table S1**). Eye symptoms in the last 12 months were reported by 49% of participants; 11% of participants reported their eye symptoms were work-related. Compared with the U.S. adult population, participants were more likely to report watery, itchy eyes in the last 12 months (SMR 1.2; 95% CI: 1.0–1.4).

Lower respiratory symptoms in the last 12 months were reported by 47% of participants; 10% of participants reported their lower respiratory symptoms were work-related (**Table 2**). Participants who reported their lower respiratory symptoms were caused or aggravated by work most commonly implicated green coffee dust [8 (21%) of 39 respondents] (**Figure 1B**). Compared with the U.S. adult population, participants were more likely to report wheeze in the last 12 months (SMR 2.0; 95% CI: 1.6–2.4), and having physician-diagnosed current asthma (SMR 1.4; 95% CI: 1.0–1.9) (**Table S1**). Six (16%) of 38 participants with current asthma reported their asthma was diagnosed after they started working at the coffee roasting and packaging facility (**Table 2**). Participants were not more likely to report exertional dyspnea (SMR 1.0; 95% CI: 0.7–1.2) or cough (SMR 0.9; 95% CI: 0.6–1.4) compared with the U.S. adult population. Participants were more likely to report phlegm for three consecutive months or more in the last 12 months (SMR 1.9; 95% CI 1.4–2.5). Systemic symptoms (flu-like achiness, fever or chills, or unusual tiredness) in the last 12 months were reported by 52% of participants; 13% of participants reported their systemic symptoms were work-related.

Nearly all (96%) spirometry testing met criteria for acceptability and repeatability. Most (95%) participants had normal spirometry (**Table S2**). Of those with abnormal spirometry, seven had an obstructive pattern, nine had a restrictive pattern, and two had a mixed pattern; 16 of 18 participants with abnormal spirometry underwent bronchodilator testing. Seven of nine with obstructive or mixed pattern had bronchodilator testing and five of these seven (71%) participants had a significant improvement in FEV_1 and one (14%) had a significant improvement in FVC. Two participants with severe airways obstruction improved with bronchodilator; one reported pre-existing lung disease prior to employment. Two of three participants with mild obstructive pattern and one of two with moderate obstruction improved with bronchodilator. One participant with a moderate mixed pattern that did not improve following bronchodilator administration was referred to a pulmonologist and diagnosed with obliterative bronchiolitis following an extensive diagnostic evaluation. This participant worked at a coffee production facility for 7 years during which time his job included adding flavoring to coffee; this case is detailed separately (44). The other participant with moderate mixed pattern improved with bronchodilator. Of the nine participants with mild restriction, seven had bronchodilator testing and none had a significant improvement in FEV1 or FVC.

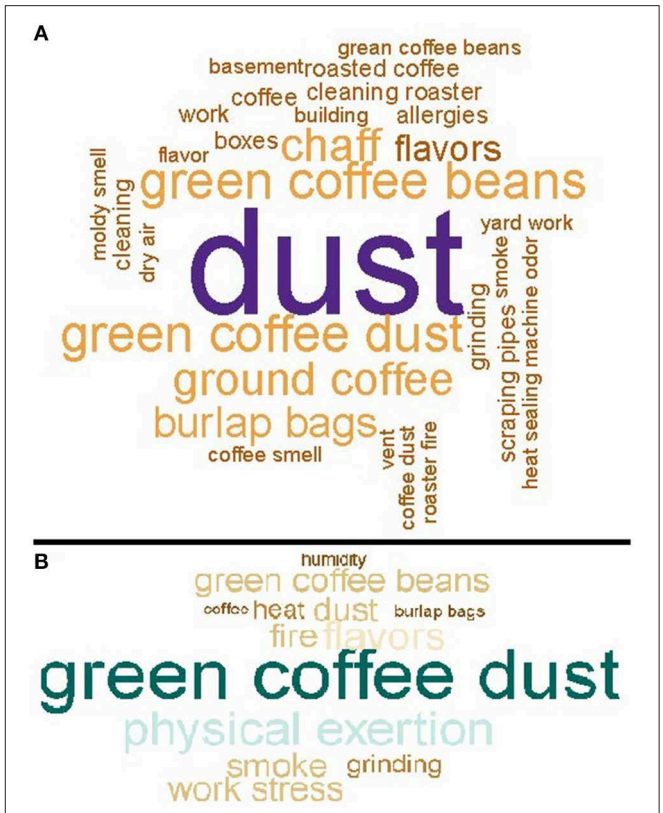

FIGURE 1 | (A) Causes or aggravations of upper respiratory symptoms at work, for workers in 17 coffee roasting and production facilities, $N = 163$. **(B)** Causes or aggravations of lower respiratory symptoms at work for workers in 17 coffee roasting and production facilities, $N = 39$.

Participants' mean percent predicted FEV_1 was 102.3% (range: 39.8–141.1%), mean percent predicted FVC was 103.7% (range: 71.2–143.2), and mean FEV_1/FVC ratio was 80.9% (range: 29.3–99.7%) (**Table S2**). SMRs for abnormal spirometry patterns were not elevated; restrictive patterns were less prevalent compared with the U.S. adult population (SMR 0.4; 95% CI 0.2–0.8) (**Table S1**). Thirty-three (9%) participants had elevated FeNO; participants who reported current asthma ($n = 38$) had an average FeNO of 44 ppb compared with 25 ppb for participants who did not report current asthma ($n = 339$) ($P < 0.05$). Participants who reported current asthma had lower percent predicted FEV_1 (96.2 vs. 103.0%, $P = 0.004$) and FEV_1/FVC (75.8 vs. 81.4, $P < 0.0001$) than participants without current asthma; there was no difference in percent predicted FVC (103.8 vs. 103.7%; $P = 0.98$).

We compared symptoms, diagnoses, and lung function parameters between participants who reported working near flavoring ($n = 44$) and participants who did not work near flavoring ($n = 340$) (**Table S3**). Participants who worked near flavoring reported more exertional dyspnea (24 vs. 14%; $P = 0.08$) and asthma attacks (14 vs. 6%; $P = 0.08$) than participants who

TABLE 2 | Prevalence of reported symptoms and work-relatedness, and self-reported doctor diagnoses and diagnoses post-hire, by workers in 17 coffee roasting and production facilities, $N = 384$.

Symptom(s)	Last 12 months *n* (%)	Last 4 weeks *n* (%)	Work-related *n* (%)
Upper respiratory symptoms (reported at least one of the following)	252 (66%)	152 (40%)	41 (11%)
Nose symptoms*	244 (64%)	145 (38%)	35 (9%)
Sinusitis or sinus problems	105 (27%)	50 (13%)	13 (3%)
Eye symptoms†	187 (49%)	117 (30%)	44 (11%)
Problem with ability to smell	46 (12%)	-	-
Phlegm on most days for 3 months	40 (10%)	-	-
Lower respiratory symptoms (reported at least one of the following)	179 (47%)	82 (21%)	39 (10%)
Chest wheezing or whistling	94 (24%)	36 (9%)	15 (4%)
Exertional dyspnea‡	59 (15%)	-	-
Breathing trouble	79 (21%)	45 (12%)	17 (4%)
Awoke with chest tightness	53 (14%)	13 (3%)	14 (4%)
Usual cough§	40 (10%)	27 (7%)	8 (2%)
Awoke with shortness of breath	28 (7%)	8 (2%)	2 (1%)
Asthma attack	26 (7%)	9 (2%)	2 (1%)
Systemic symptoms (reported at least one of the following)	199 (52%)	94 (24%)	50 (13%)
Flu-like achiness or achy joints	145 (38%)	50 (13%)	17 (4%)
Fever or chills	99 (26%)	22 (6%)	11 (3%)
Unusual tiredness or fatigue	88 (23%)	60 (16%)	30 (8%)
Diagnosis	***n* (%)**	**Post-hire *n* (%)**	
Hay fever or nasal allergies	88 (23%)	17 (4%)	
Eczema	47 (12%)	10 (3%)	
Heart disease	11 (3%)	6 (2%)	
Gastroesophageal reflux disease	30 (8%)	12 (3%)	
Chronic bronchitis	6 (2%)	1 (<1%)	
Asthma (ever)	65 (17%)	6 (2%)	
Asthma (current)	38 (10%)	6 (2%)	

"-" = A 4 week question or work-related question was not asked for the symptom.

**Nose symptoms includes one or both of the following: (1) stuffy, itchy, or runny nose or (2) stinging, burning nose.*

† Eye symptoms includes one or both of the following: (1) watery, itchy eyes or (2) stinging, burning eyes.

‡ This question did not specifically ask about exertional dyspnea within the past 12 months; participants were asked, "Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill".

§This question did not specifically ask about a cough within the past 12 months; participants were asked, "Do you usually have a cough?" If the participants answered "yes," they were then asked, "Have you had a cough at any time in the last 4 weeks?"

did not work near flavoring. Usual cough was reported by 14% of participants who worked near flavoring and 10% of participants who did not work near flavorings ($P = 0.47$). Participants who worked near flavoring reported more chronic bronchitis (7 vs. 1%; $P = 0.02$) and ever receiving a diagnosis of asthma (30 vs. 15%; $P = 0.03$) than participants who did not work near flavoring. There were no substantial differences between the two groups in lung function parameters.

We compared symptoms, diagnoses, lung function parameters, and job tasks between participants categorized as atopic ($n = 119$) and participants categorized as non-atopic ($n = 265$) (**Table S4**). Atopic participants more often reported upper respiratory symptoms, problems smelling, phlegm, exertional dyspnea, trouble breathing, lower respiratory symptoms, and systemic symptoms than non-atopic participants. Atopic participants more often reported gastroesophageal reflux disease and ever receiving a diagnosis of asthma than non-atopic participants. There were no substantial differences in lung function parameters. Atopic participants had a higher mean FeNO than non-atopic participants (31 vs. 25 ppb; $P = 0.04$). More atopic participants reported working with green coffee beans than non-atopic participants (48 vs. 33%; $P = 0.02$).

Symptoms and lung function were similar between participants who worked at flavoring and non-flavoring facilities in our study (**Table 3**). Compared with previous investigations of flavoring-exposed workers, participants in our study had a lower prevalence of exertional dyspnea, cough, and obstruction, and a higher average percent predicted FEV_1. The prevalence of wheeze was comparable with those observed in other flavoring-exposed populations. All study populations included only current workers and no former workers.

The mean TWAs measured for diacetyl and 2,3-pentanedione at the 12 non-flavoring facilities in our study were 7.3 and 4.5 ppb, respectively; the mean TWAs at the five flavoring facilities were 24.9 and 19.1 ppb, respectively (**Table 3**). The mean TWAs measured at the sentinel coffee facility that also flavored were 57.7 ppb for diacetyl and 46.1 ppb for 2,3-pentanedione. The mean TWA for diacetyl at the sentinel microwave popcorn production facility was 19,938 ppb.

DISCUSSION

Our findings demonstrate a burden of respiratory and mucous membrane abnormalities among workers at 17 coffee roasting and packaging facilities. Respiratory abnormalities were characterized by upper respiratory symptoms and wheeze, with a work-related pattern for some participants. The symptoms reported by participants might not represent a single work-related lung disease or condition. Rather, we observed a spectrum of symptoms that could indicate different occupational respiratory diseases including work-related asthma and obliterative bronchiolitis. Our findings likely represent overlapping effects of the different respiratory hazards in coffee roasting and packaging facilities we evaluated, which included

TABLE 3 | Comparison of characteristics for participants from non-flavoring coffee facilities and flavoring coffee facilities to published findings from workers in the sentinel coffee facility, sentinel microwave popcorn facility, and three other microwave popcorn facilities.

	12 non-flavoring coffee facilities ($n = 227$)	5 flavoring coffee facilities ($n = 157$)	Sentinel flavoring coffee facility* (1, 18) ($n = 75$)	Sentinel microwave popcorn facility †‡(7, 42) ($n = 122$)	3 other microwave popcorn facilities(7, 40, 41, 43) ($n = 397$)
Exertional dyspnea (%)	14	17	28	26	26
Wheeze (%)	28	20	20	36	23
Cough (%)	9	13	16	24	24
% predicted FEV_1	102.3	102.5	97.6	90.0	94.2
Obstruction (%)	2 (4 of 214)	2 (3 of 158)	7 (5 of 69)	10 (12 of 16)	4 (17 of 395)
Reversible (%)	100 (3 of 3)	50 (1 of 2)	33 (1 of 3)	11 (1 of 9)	31 (5 of 16)
Mean TWA personal exposure parts per billion (range)					
Diacetyl	7.3 (0.1–40.5)	24.9 (0.1–420.9)	57.7 (4.3–166.0)	19,938 (479–147,170)	328.4 (ND−2,740)
2, 3-pentanedione	4.5 (0.1–27.1)	19.1 (0.2–275.9)	46.1 (<5.2–199.0)	Not measured	Not measured

*Symptoms reported by work area including grinding/packaging, flavoring, and roasting.
†Symptoms reported by job categories including ever mixer, never mixer, packaging non-isolated tanks, and packaging isolated tanks.
‡Area sampling from mixing and packaging areas. ND, Not Detected.

diacetyl and 2,3-pentanedione sources, and other potential hazards such as green coffee bean and other dust.

We found evidence of severe lung disease in only a few workers. Spirometric abnormalities were only present in 5% of those studied, and two classic symptoms of obliterative bronchiolitis, exertional dyspnea and cough, were not in excess. Most symptoms and spirometric parameters were similar for participants who worked near flavoring and those who did not work near flavoring. However, one participant who added flavoring to coffee was diagnosed with obliterative bronchiolitis following referral to a pulmonologist; no cases of obliterative bronchiolitis were identified among workers who did not use flavorings. In addition, we measured higher alpha-diketone exposures in facilities that added flavorings compared with those that did not add flavorings. Thus, risk might be higher in facilities using flavorings, but data are limited. Other limitations are that we studied only current workers, and do not have information about the health status of former workers and whether any left employment because of lung disease. Furthermore, tenure among participants was relatively low, with a median of <3 years. Inclusion of former workers and longitudinal evaluation of longer-tenure workers in facilities that do not add flavorings could help account for the healthy worker effect and shed light on the longer-term risk of naturally occurring diacetyl in these settings.

Our findings are consistent with a burden of work-related asthma among participants. Past studies have demonstrated that coffee roasting and packaging workers were at an increased risk for work-related asthma (23, 28). We found more participants reported asthma than expected compared with the U.S. adult population. Lower respiratory symptoms, many of which are common symptoms of asthma, were frequently reported among participants and frequently with a work-related pattern, suggesting work-related asthma. Green coffee dust was frequently reported as a cause or exacerbator of lower respiratory symptoms. Although our study was not designed to investigate the underlying mechanism causing asthma, green coffee bean dust could have acted as a sensitizer in some workers (1). FeNO was elevated in nearly one in 10 workers, which can be an indication of eosinophilic airways inflammation or poorly controlled asthma (39). Six of the nine participants who had obstructive or mixed pattern on spirometry had significant improvement in FEV_1 post-bronchodilator administration; this would be expected in uncontrolled asthma, and is a higher percentage than a recent study where roughly one-third of adults aged 40 years or older with obstruction improved post-bronchodilator (45).

Upper respiratory symptoms were the most commonly reported symptoms, often with a work-related pattern; eye symptoms were also commonly reported. Nose and eye symptoms were reported more than expected compared with the U.S. adult population. Participants overwhelmingly described dust as the cause or aggravation of their upper respiratory symptoms. Upper respiratory disease such as allergic rhinitis and sinusitis are sometimes associated with lower respiratory symptoms and asthma and might precede the diagnosis of asthma (46–50). Thus, controlling exposures associated with upper respiratory symptoms could ultimately serve to reduce the risk of asthma among coffee workers.

Atopic participants reported more upper and lower respiratory symptoms than non-atopic participants; atopic participants also reported more asthma. Upper respiratory inflammation (e.g., rhinitis, sinusitis) can result in suboptimal control of asthma (48, 49). Interestingly, atopic participants reported working more with green coffee beans. Green coffee dust is thought to be a more potent allergen than roasted coffee dust because roasting destroys some of the allergenic activity (51). N95 disposable filtering-face pieces might prevent symptoms related to green coffee dust and chaff, although are not

protective against diacetyl and 2,3-pentanedione, which would require organic vapor cartridges (52).

Participants reported nearly twice as much wheeze than expected compared with the U.S. adult population, some with a work-related pattern; wheeze was the only lower respiratory symptom reported more than expected for those we could compare to the U.S. adult population. Wheeze is a common symptom of both obliterative bronchiolitis and asthma, and we cannot determine the underlying cause of wheeze among participants in our evaluation. The overlapping effects of different respiratory hazards in roasting and packaging facilities including asthmagens and alpha-diketones likely contributed to the increased risk of wheeze observed among participants.

Compared with workers studied from the sentinel coffee roasting and packaging facility where five cases of obliterative bronchiolitis were identified among former employees, and workers from microwave popcorn production facilities, our population had lower prevalences of exertional dyspnea, cough, and spirometric abnormality likely reflecting a lower risk of obliterative bronchiolitis. The sentinel microwave popcorn facility had fewer participants with reversible spirometric obstruction (11%) than would be expected, perhaps reflecting the greater relative importance of obliterative bronchiolitis as an adverse respiratory health outcome in that setting (45).

Mean diacetyl and 2,3-pentanedione levels from the facilities that flavored in our study were more than three times higher than those from facilities that did not flavor, but still less than half of those measured from the sentinel coffee roasting and packaging facility. However, measurements at the sentinel coffee facility were likely underestimates of exposure to former workers due to improved ventilation and different flavoring formulation that were implemented before sampling occurred (18). Mean diacetyl levels measured from flavoring facilities in our study were far below those from the popcorn facilities where the risk of flavoring-related obliterative bronchiolitis was first described. These exposure differences indicate that for the coffee facilities we studied, particularly those that did not flavor, the risk of obliterative bronchiolitis is lower than the historical risk associated with the microwave popcorn industry and likely also the sentinel coffee facility. Nonetheless, flavoring and non-flavoring facilities in our study had TWAs above the NIOSH recommended exposure limit (REL) for both diacetyl (5 ppb) and 2,3-pentanedione (9.3 ppb) (52).

Our study has several limitations. First, the medical surveys only included current workers; we did not capture former workers who could have work-related health effects. If former workers were included, the prevalence of respiratory symptoms or disease might have been higher; some workers might have left employment prior to our surveys due to work-related respiratory symptoms or disease. Thus, our results were likely influenced by the healthy worker effect, a potential bias caused by workers choosing work environments with lower exposure or leaving work (53). Also, the facilities we evaluated did not have known health concerns before our evaluations and were mostly at the request of management and thus might not have been representative of other settings in the industry. In addition, the participation rate was lower than desired and our findings may not be representative of all workers at these facilities. Finally, our medical surveys were not intended to be diagnostic evaluations; we did not evaluate for airway hyperreactivity or for variability in pulmonary function at and away from work, nor did we assess for Immunoglobulin E (IgE) sensitization to green coffee bean or other workplace allergens. In addition, we did not assess for findings such as air trapping in high-resolution computed tomography (HRCT), which might be more sensitive for small airways disease.

Our findings are not intended to be representative of the entire coffee roasting and packaging industry because of the variation in production processes, including the amount of coffee produced, use of flavoring, size of workforce, automaticity, and use of engineering controls; we observed this large variation in the production processes in the 17 facilities we evaluated. Despite the limitations, this study is one of largest evaluations of coffee roasting and packaging facilities. Combining evaluations from 17 facilities allowed us to evaluate the burden of respiratory abnormalities in a group of coffee roasting and packaging workers.

The burden of respiratory abnormalities we observed, including a range of upper and lower respiratory symptoms, likely reflects the effects of workplace exposures. Our findings indicate occupational respiratory health concerns among coffee roasting and packaging workers are not limited to obliterative bronchiolitis or specific to facilities that use flavorings. The symptoms and patterns we found likely represent the overlapping health effects of different respiratory hazards facing coffee roasting and packaging workers, including green coffee bean and other dust, diacetyl, 2,3-pentanedione, and potentially other respiratory hazards. Public health authorities should be aware of the different potential respiratory health hazards in coffee roasting and packaging facilities, including flavoring and non-flavoring facilities. Healthcare providers should be aware that workers at coffee roasting and packaging facilities are potentially at risk for several occupational respiratory diseases with potentially overlapping symptoms and functional manifestations, including work-related asthma and obliterative bronchiolitis.

DATA AVAILABILITY STATEMENT

Due to restrictions imposed under the US privacy act and the limitations of what participants consented to, the data underlying the analyses presented, beyond what is provided in the paper, are confidential and not available to researchers outside the National Institute for Occupational Safety and Health (NIOSH). For more information about NIOSH's policy regarding sensitive data, see https://www.cdc.gov/niosh/ocas/datahandle.html.

ETHICS STATEMENT

The NIOSH Institutional Review Board reviewed and approved this study (NIOSH Protocol 17-RHD-06XP). All participants provided their written informed consent to participate.

AUTHOR CONTRIBUTIONS

RH, EF-L, RB, KF, MV, RN, JC-G, and KC contributed conception and design of the study. NE and KF organized the database. RH, EF-L, KF, and NE performed the statistical analyses. RH wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

FUNDING

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

ACKNOWLEDGMENTS

The authors thank the workers for participating in the NIOSH health hazard evaluation program and the members of the NIOSH field teams for their contributions to data acquisition The authors acknowledge Dr. Cara Halldin and Ms. Laura Reynolds for their review of the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2020.00005/full#supplementary-material

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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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CASE REPORT
published: 20 May 2021
doi: 10.3389/fpubh.2021.657987

Case Report: Flavoring-Related Lung Disease in a Coffee Roasting and Packaging Facility Worker With Unique Lung Histopathology Compared With Previously Described Cases of Obliterative Bronchiolitis

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Reviewed by:
Victor C. W. Hoe, University of Malaya, Malaysia
Stella Hines, University of Maryland, Baltimore, United States

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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: *24 January 2021*
Accepted: *14 April 2021*
Published: *20 May 2021*

Citation:
Harvey RR, Blackley BH, Korbach EJ, Rawal AX, Roggli VL, Bailey RL, Cox-Ganser JM and Cummings KJ (2021) Case Report: Flavoring-Related Lung Disease in a Coffee Roasting and Packaging Facility Worker With Unique Lung Histopathology Compared With Previously Described Cases of Obliterative Bronchiolitis. Front. Public Health 9:657987. doi: 10.3389/fpubh.2021.657987

Occupational exposure to diacetyl, a butter flavor chemical, can result in obliterative bronchiolitis. Obliterative bronchiolitis is characterized by exertional dyspnea, fixed airflow obstruction, and histopathologic constrictive bronchiolitis, with bronchiolar wall fibrosis leading to luminal narrowing and obliteration. We describe a case of advanced lung disease with histopathology distinct from obliterative bronchiolitis in a 37-year-old male coffee worker following prolonged exposure to high levels of diacetyl and the related compound 2,3-pentanedione, who had no other medical, avocational, or occupational history that could account for his illness. He began working at a coffee facility in the flavoring room and grinding area in 2009. Four years later he moved to the packaging area but continued to flavor and grind coffee at least 1 full day per week. He reported chest tightness and mucous membrane irritation when working in the flavoring room and grinding area in 2010. Beginning in 2014, he developed dyspnea, intermittent cough, and a reduced sense of smell without a work-related pattern. In 2016, spirometry revealed a moderate mixed pattern that did not improve with bronchodilator. Thoracoscopic lung biopsy results demonstrated focal mild cellular bronchiolitis and pleuritis, and focal peribronchiolar giant cells/granulomas, but no evidence of constrictive bronchiolitis. Full-shift personal air-samples collected in the flavoring and grinding areas during 2016 measured diacetyl concentrations up to 84-fold higher than the recommended exposure limit. Medical evaluations indicate this worker developed work-related, airway-centric lung disease, most likely attributable to inhalational exposure to flavorings, with biopsy findings not usual for obliterative bronchiolitis. Clinicians should be aware that lung pathology could vary considerably in workers with suspected flavoring-related lung disease.

Keywords: diacetyl, 2, 3-pentanedione, coffee roasting and packaging, obliterative bronchiolitis, flavoring-related lung disease, case report

INTRODUCTION

Flavoring-related lung disease was first described in 2000 when butter-flavored microwave popcorn production was associated with a cluster of clinical bronchiolitis obliterans, or obliterative bronchiolitis, in former workers (1, 2). Clinical bronchiolitis obliterans will refer to the clinical syndrome and obliterative bronchiolitis will refer to the lung pathology for the purposes of this report. Diacetyl (2,3-butanedione), an alpha-diketone, was determined to be the component of liquid butter flavoring responsible for disease. Unlike other known occupational causes of obliterative bronchiolitis, acute symptoms in these cases did not follow a recognized overwhelming exposure; rather, clinical progression was insidious, marked by exertional dyspnea and airflow obstruction that did not improve significantly following bronchodilation (fixed obstruction). The few cases that underwent biopsy had histopathologic findings consistent with obliterative bronchiolitis (2), typically characterized by concentric fibrosis and destruction of the bronchioles (3). Since the sentinel microwave popcorn plant was identified, additional cases of indolent onset clinical bronchiolitis obliterans have been diagnosed, often without biopsy, in workers in a number of other industries, including flavoring manufacturing, food (other than popcorn) production, and coffee roasting and packaging (4–7).

In 2016, we conducted a National Institute for Occupational Safety and Health (NIOSH) Health Hazard Evaluation that included medical and industrial hygiene surveys following a request from management at a coffee roasting and processing facility that added liquid flavorings to coffee. We describe a case of advanced lung disease in a former coffee worker following prolonged exposure to high levels of diacetyl and the related compound 2,3-pentanedione. The availability of lung tissue in this case provides an opportunity to re-examine the histopathologic consequences of flavoring exposure.

CASE REPORT

In 2009, A 37 year-old male former smoker (1 pack-year history) with no significant medical history began working in the flavoring room and grinding area of a coffee facility that had no respiratory protection requirements or recommendations. He reported mucous membrane irritation, as well as wheezing and chest tightness that worsened with exertion when working in the flavoring room and grinding area beginning in 2010 after several months of employment. Initially, these symptoms resolved after he left those areas of the facility, but his work-related symptoms slowly progressed until there was no discernible work-related pattern. In 2013, he moved to the packaging area but continued to flavor and grind coffee at least 1 full day per week. Beginning in 2014, he developed dyspnea, intermittent cough, and a reduced sense of smell that did not improve when away from work. He reported that during 2014–2016, he experienced frequent upper respiratory infections and was treated with antibiotics several times for presumed pneumonia but received no diagnostic testing.

Our 2016 evaluation of the workforce included pulmonary function testing (8). This worker's spirometry revealed a moderate mixed obstructive and restrictive pattern, and impulse oscillometry was consistent with peripheral airways obstruction; neither the spirometric nor oscillometry measures improved post-bronchodilator (**Table 1**). We recommended the patient seek care from a pulmonologist for evaluation of potential flavoring-related lung disease based on his symptoms, pulmonary function testing, and work history.

The patient was raised in Mexico and reported no childhood history of lung problems. He denied a history before 2010 of frequent respiratory infections, exercise intolerance, frequent cough, or other breathing problems that would indicate asthma or other underlying lung disease. He immigrated to the United States in the late 1990s. He had worked at a hard metal mine in Mexico for <1 year; he had no other work history concerning for lung disease. He reported no notable travel, hobbies, or animal exposures. Pertinent negatives on review of systems included fever, chills, night sweats, weight loss, hemoptysis, and skin rashes. His physical examination findings were unremarkable; lungs were clear to auscultation bilaterally with no wheezes, crackles, or rhonchi. His oxygen saturation was 94% on room air.

Full pulmonary function testing confirmed a moderate mixed pattern on spirometry and demonstrated normal total lung capacity with reduced diffusing capacity (**Table 1**). Inspiratory and expiratory chest high-resolution computed tomography (HRCT) revealed bilateral mosaic attenuation, consistent with air trapping (**Figure 1**). Thoracoscopic lung biopsy revealed focal mild cellular bronchiolitis and pleuritis, including perivascular inflammatory infiltrates (**Figure 2a**; black arrow), and peribronchiolar giant cells/granulomas (**Figure 2b**; black arrow), but no evidence of fibrosis or destruction of the bronchioles. The patient was diagnosed with flavoring-related lung disease and instructed to limit his exposure to diacetyl and 2,3-pentanedione.

The patient's employer moved him from the production area of the coffee facility to an offsite warehouse. He left employment at the coffee facility in 2018. He subsequently worked for a retailer as a custodian and was advised by his pulmonologist to avoid ammonia and floor cleaners during work. He most recently worked in landscaping. He continued to experience dyspnea on exertion and a non-productive cough. He was treated with a 1-year course of azithromycin, followed by a combination of inhaled corticosteroids, beta-agonists, and anticholinergics commonly used for chronic obstructive pulmonary disease. He also received a course of oral corticosteroids for an acute exacerbation in 2018. Periodic spirometry through 2019 (**Table 1** and **Figure 3**), demonstrated persistent mixed pattern without improvement despite cessation of exposure.

NIOSH recommended exposure limits (RELs) are 5.0 parts per billion (ppb) for diacetyl and 9.3 ppb for 2,3-pentanedione for an 8-h workday during a 40-h workweek (11). In 2016, we conducted air sampling for diacetyl and 2,3-pentanedione at the coffee roasting and packaging facility. Full-shift personal air-samples collected on other workers while duties were performed in the flavoring and grinding areas where the patient worked measured elevated levels of diacetyl (41–421 ppb) and 2,3-pentanedione (22–276 ppb) and were 2–84-fold higher than the

TABLE 1 | Lung function testing results of worker diagnosed with flavoring-related lung disease, September 2016–July 2019.

	Reference[€] (9)	August 2016	September 2016	October 2016	June 2017	October 2017	January 2018	July 2019
Spirometry								
FVC*, Liters (% predicted)	4.01	3.22 (80%)	3.05 (74%)	3.28 (80%)	2.39 (58%)	2.60 (64%)	2.96 (73%)	2.68 (62%)
$FEV_1^{\dagger}$, Liters (% predicted)	3.18	2.07 (65%)	1.95 (59%)	1.98 (60%)	1.69 (52%)	1.78 (55%)	1.96 (61%)	1.89 (55%)
FEV_1/FVC (%)	79%	64%	64%	60%	71%	68%	66%	71%
TLC[‡] Liters (%)	5.24	–	–	5.36 (102%)	–	–	–	–
DL_{CO}[£] mL/mmHg/min (%)	27.3	–	–	24.0 (88%)	–	–	–	–
Impulse Oscillometry	Upper limit of normal (10)							
R_5^{**} (cm H_2O/L/s)	3.96	4.59	–	–	–	–	–	–
$R_{20}^{\dagger\dagger}$ (cm H_2O/L/s)	3.20	3.26	–	–	–	–	–	–
Fres[‡‡] (Hz)	12	19	–	–	–	–	–	–
AX[££] (cm H_2O/L/s)	3.60	12.34	–	–	–	–	–	–
R_{5-20}[€€] (cm H_2O/L/s)	0.76	1.33	–	–	–	–	–	–

*Forced vital capacity; †Forced expiratory volume in one second; ‡Total lung capacity; £Diffusing capacity of the lung for carbon monoxide; €Reference values for spirometry derived from National Health and Nutrition Examination Survey (NHANES) III;**R5: resistance at 5Hz; ††R20: resistance at 20Hz; ‡‡Fres: resonant frequency; ££AX: reactance area; €€R_{5-20}: resistance at 5 Hz minus resistance at 20 Hz.*

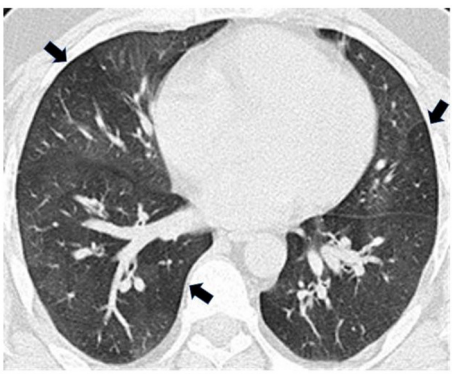

FIGURE 1 | Expiratory high-resolution computed tomography (HRCT) revealed bilateral mosaic attenuation (arrows) consistent with air trapping.

NIOSH RELs. Short-term personal air samples collected on other workers during flavoring and grinding tasks were also high and ranged from 521 to 2,173 ppb diacetyl and 345 to 1,445 ppb 2,3-pentanedione during flavoring tasks and 47–81 ppb diacetyl and 21–50 ppb 2,3-pentanedione during grinding tasks. All 15-min samples collected while a worker flavored coffee exceeded the NIOSH short-term exposure limit of 25 ppb for diacetyl and 31 ppb for 2,3-pentanedione.

DISCUSSION

We describe a case of advanced lung disease in a coffee worker following prolonged exposure to high levels of diacetyl and the related chemical, 2,3-pentanedione, with no medical, other occupational, or avocational histories that could account for his illness. Additionally, noninvasive diagnostic test results including lung function testing and HRCT were consistent with previously-described cases of flavoring-related lung disease, including in coffee roasting and packaging workers. Following cessation of exposure to flavorings, his respiratory symptoms and lung function largely stabilized but did not return to normal.

It is notable that lung histopathology in this case was not consistent with obliterative bronchiolitis. Because of the variable findings of noninvasive diagnostic testing, lung biopsy is performed on some workers suspected of having flavoring-related lung disease. The diagnosis commonly associated with flavoring-related lung disease, obliterative bronchiolitis, stems from the pathologic findings from some lung biopsies in workers exposed to flavorings: destruction of the small airways marked by concentric fibrosis of the bronchioles (3). Similar to the noninvasive diagnostic testing, not all lung biopsies on exposed workers demonstrate these characteristic findings. The disease is often patchy, so the findings could be missed because of sampling error (12). The patient's tissue sample seemed to be adequate. Regardless, some evidence indicates that flavoring-related lung disease has a broader histopathologic spectrum. Lung biopsies in some workers diagnosed with flavoring-related lung disease have shown granulomatous inflammation, which is characteristic of other lung diseases including hypersensitivity pneumonitis (2, 6, 7). Pleural proliferation of mesothelial cells and eosinophils also have been observed, as have emphysematous changes and interstitial fibrosis (2, 13, 14). Thus, while this patient's lung biopsy did not demonstrate findings of obliterative bronchiolitis, a precedent exists for ascribing his histopathology to flavorings exposure, supported by his work history, symptoms, and functional and radiographic abnormalities. Furthermore, the cellular bronchiolitis identified could represent an inflammatory stage of the disease preceding development of the concentric bronchiolar narrowing and luminal obstruction classic for obliterative bronchiolitis.

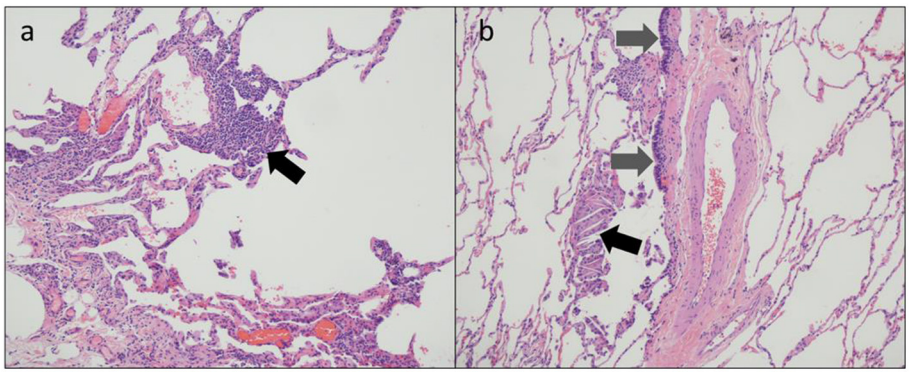

FIGURE 2 | Thoracoscopic lung biopsy from a coffee roasting/packaging facility worker exposed to diacetyl showing **(a)** perivascular inflammatory infiltrates [black arrow] and **(b)** respiratory epithelium [gray arrows] and multinucleate giant cells with cholesterol clefts [black arrow].

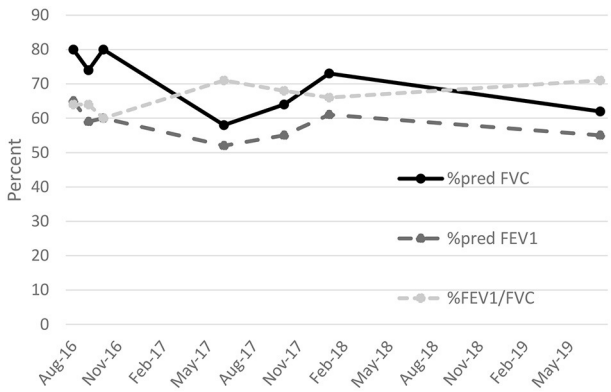

FIGURE 3 | Percent predicted forced expiratory volume in 1 second (%pred FEV_1). percent predicted forced vital capacity (%pred FVC), and ratio of FEV_1 to FVC expressed as a percent (%FEV_1/FVC) for patient diagnosed with flavoring-related lung disease, August 2016 to July 2019.

This patient's functional, radiographic, and histopathologic findings could be attributable to subacute hypersensitivity pneumonitis prompted by a workplace antigen (15). Exposure to coffee dust has been associated with immune sensitization and occupational asthma (16, 17). Exposure to castor beans from cross-contamination of bags used to transport coffee are also associated with asthma in the coffee industry (18). A case of hypersensitivity pneumonitis in a coffee worker was previously reported (19), although the authors subsequently reconsidered this diagnosis when the patient developed rheumatoid arthritis and ultimately attributed his pulmonary disease to autoimmunity rather than coffee dust exposure (20). We are unable to find other reports of hypersensitivity pneumonitis in coffee workers. Notably, diacetyl and its substitutes have been found to stimulate lymphocyte proliferation in a murine model, demonstrating the potential for hypersensitivity responses (21). Thus, it is possible that exposure to flavoring chemicals for this patient caused cellular bronchiolitis and granulomatous changes via an immune-mediated mechanism rather than epithelial necrosis and airway fibrosis via disruption of protein homeostasis (22). Measurements of specific immunoglobulins or lymphocyte proliferation in response to workplace antigens were not available to help distinguish these possibilities.

Patients with flavoring-related lung disease are often diagnosed with more common obstructive lung diseases such as asthma or chronic obstructive pulmonary disease (COPD) before flavoring-related lung disease is correctly diagnosed (23). After developing dyspnea, the patient reported frequent respiratory infections and was prescribed medications for suspected pneumonia before his diagnosis of flavoring-related lung disease. In retrospect, these episodes were likely attributable to his work-related lung disease. Flavoring-related lung disease can be misdiagnosed because of its relatively rare occurrence compared with other obstructive lung diseases, but also because clinical features of the disease can vary. The most common symptoms are shortness of breath, dry cough, and chest tightness with no work-related pattern; however, upper respiratory symptoms including mucous membrane irritation and rhinosinusitis can also occur (1, 24, 25). Although fixed airflow obstruction is a common finding in flavoring-exposed workers diagnosed with clinical bronchiolitis obliterans, spirometry results vary and can include restrictive, mixed, or even normal patterns (5, 6, 25–29); the patient's most common spirometric interpretation was mixed obstructive and restrictive patterns. HRCT findings commonly demonstrate a mosaic attenuation pattern with air trapping in workers diagnosed with flavoring-related lung disease, but HRCT results are often nonspecific and can vary (30); this patient's HRCT findings were consistent with air trapping.

No other workers at the patient's coffee roasting and packaging facility were diagnosed with flavoring-related lung disease following the NIOSH medical survey. Ninety-nine (83%) of 120 employees participated in the medical survey; 15 reported grinding or flavoring tasks and these participants were nearly 4-times more likely to report chest tightness in the last 12 months (odds ratio 3.7; 95% confidence interval: 1.0–13.4) (31). Five (5%) of 98 other participants who completed spirometry at the facility also had abnormal spirometry, including three with mild restrictive patterns, one with a moderate mixed pattern, and one with mild obstruction (31). The most commonly reported symptoms by participating workers were nose and eye symptoms, reported by 46 and 43% of workers, respectively. Wheezing

or whistling in the chest was the most commonly reported lower respiratory symptom (18%), followed by shortness of breath, breathing trouble, and chest tightness (17% each) (31). Some participating workers reported their symptoms were better away from work or caused or aggravated by work. Following the NIOSH health hazard evaluation, the employer instituted a medical surveillance program that included repeating spirometry every 6 months to identify employees who might be developing work-related lung disease (e.g., asthma, flavoring-related lung disease).

Other alpha-diketones, including 2,3-pentanedione and 2,3-hexanedione, have been used as substitutes for diacetyl in some industries after the association of diacetyl and flavoring-related lung disease was observed. However, evidence indicates these substitutes can result in similar pathologic findings as diacetyl and therefore are not safe alternatives (32–34). More recently, another structurally similar compound, methylglyoxal, was toxic at even lower concentrations than diacetyl in animal models (22). Headspace air sampling results from the liquid flavorings sampled at the coffee roasting and processing facility where the patient worked all contained diacetyl (up to 10,741 ppb); most contained 2,3-pentanedione (up to 6,517 ppb); none had detectable levels of 2,3-hexanedione; and we did not test for methylglyoxal (31). A recent study of headspace samples from dozens of liquid flavorings found a majority of the flavorings tested had diacetyl, 2,3-pentanedione, or both as volatile constituents in the headspace. Diacetyl and 2,3-pentanedione were not listed on the Safety Data Sheets of the flavorings tested because of trade secret designations. However, inclusion of diacetyl and 2,3-pentanedione on Safety Data Sheets is vital to protecting downstream users such as coffee roasting and processing facilities that add liquid flavorings, from unrecognized exposure and potential respiratory disease (35). Flavorings from the facility where the patient worked were tested and contained flavoring chemicals that were not disclosed on the Safety Data Sheets.

At the coffee roasting and packaging facility where the patient worked, ∼12 million pounds of coffee were roasted and packaged annually as of 2016, and roughly 60% of the coffee produced was ground. The patient worked in the flavoring and grinding area full-time during 2009–2013, and then at least 20% of the time an additional 4 years. To grind coffee, an automated pneumatic system was used to pull whole beans from a storage silo into either one of two grinders. Both grinders operated on a continuous process and would grind a full silo of roasted coffee in 45–50 min. If grinding a full silo of roasted coffee, the patient would set-up the silo and grinder and then walk away to perform other tasks. Ground coffee was sent through an automated system to another silo for storage until needed for further processing (e.g., flavoring or packaging). To flavor coffee, whole bean or ground coffee was sent to the flavoring room by a pneumatic system that would pull roasted coffee from the silo into the ribbon blender in the flavoring room. The patient would mix a 40-pound pail of liquid flavorings and would manually add liquid flavorings to the ribbon blender while the blender mixed the whole beans or ground coffee with the flavorings. Liquid flavorings were manually added and mixed over a specified time. Once complete, the flavored coffee was emptied into a silo for storage until needed for packaging. The flavoring operation was isolated in a designated flavoring room prior to our investigation. Shortly before our on-site investigation in 2016, employees working in the roasting, grinding, and flavoring areas were required to wear fit-tested half-face or full-face respirators equipped with organic vapor cartridges. Following our investigation, the grinding area was also isolated. Additional engineering control solutions including enclosing and automating the flavoring system and increasing ventilation in the flavoring and grinding rooms were also implemented to reduce potential exposures for workers assigned to duties in these areas.

Our investigation was limited by several factors. While the patient had no known environmental or other occupational exposures attributable to his illness, we do not have a detailed work history and understanding of potential respiratory hazards from his previous work in Mexico before immigrating to the United States in the 1990s. Additionally, no historical air sampling results for diacetyl and 2,3-pentanedione were available from 2009 to 2013 when the patient began working in the flavoring and grinding areas and developed symptoms. Worker participation in the NIOSH health hazard evaluation was good at 83% of current workers, however, our evaluation did not include former workers who could have experienced higher historical exposures. One other current employee was reported to have long-term exposures to flavorings but did not participate in the NIOSH medical survey or respond to several attempts to make contact; it could be possible we missed other cases of flavoring-related lung disease associated with working at this coffee roasting and packaging facility. Additionally, the patient did not undergo laboratory evaluation for connective tissue diseases like rheumatoid arthritis, which can cause bronchiolitis (36). In some cases, lung disease can be the first manifestation of connective tissue disease (37), but notably, the patient did not report joint paint or other symptoms that would suggest rheumatoid arthritis or another connective tissue disease through 2019.

Despite biopsy findings not supportive of obliterative bronchiolitis, medical evaluations, including lung function testing and HRCT, air sampling data, and the lack of other explanatory medical, occupational, or avocational histories indicate this worker developed work-related, airway-centric lung disease, most likely attributable to inhalational exposure to flavorings following years of high exposures to diacetyl and 2,3-pentanedione at a coffee roasting and packaging facility. Clinicians should be aware that lung pathology could vary considerably in workers with suspected flavoring-related lung disease. Public health practitioners should be aware that workers at coffee roasting and packaging facilities, particularly those that add flavorings to coffee, could be at risk for flavoring-related lung disease. Furthermore, if a single case of flavoring-related lung disease is identified, a thorough workplace investigation is warranted to evaluate and reduce exposure to diacetyl and related compounds, as well as identify any additional cases and remove from exposure.

DATA AVAILABILITY STATEMENT

Due to restrictions imposed under the US privacy act and the limitations of what participants consented to, the data

underlying the analyses presented, beyond what is provided in the paper, are confidential and not available to researchers outside the National Institute for Occupational Safety and Health (NIOSH). For more information about NIOSH's policy regarding sensitive data, see https://www.cdc.gov/niosh/ocas/datahandle.html.

ETHICS STATEMENT

The NIOSH Institutional Review Board reviewed and approved this study (NIOSH Protocol 17-RHD-06XP). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RH, BB, RB, JC-G, and KC contributed to the conception and presentation of the case report. EK, AR, and VR provided clinical expertise and interpretations. RH wrote the first draft of the report. All authors contributed to manuscript revision, read, and approved the submitted version.

FUNDING

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

ACKNOWLEDGMENTS

The authors thank the patient for his continued collaboration, workers for participating in the NIOSH health hazard evaluation program, and the members of the NIOSH field teams for their contributions to data acquisition. The authors acknowledge Drs. Marie De Perio and Sara Luckhaupt for their review of the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2021.657987/full#supplementary-material

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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.

frontiers | Frontiers in Public Health

TYPE Brief Research Report
PUBLISHED 12 August 2022
DOI 10.3389/fpubh.2022.966374

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

RECEIVED 10 June 2022
ACCEPTED 18 July 2022
PUBLISHED 12 August 2022

CITATION
Virji MA, Fechter-Leggett ED, Groth CP, Liang X, Blackley BH, Stanton ML, LeBouf RF, Harvey RR, Bailey RL, Cummings KJ and Cox-Ganser JM (2022) Decrements in lung function and respiratory abnormalities associated with exposure to diacetyl and 2,3-pentanedione in coffee production workers.
Front. Public Health 10:966374.
doi: 10.3389/fpubh.2022.966374

Decrements in lung function and respiratory abnormalities associated with exposure to diacetyl and 2,3-pentanedione in coffee production workers

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Coffee production workers are exposed to complex mixtures of gases, dust, and vapors, including the known respiratory toxins, diacetyl, and 2,3-pentanedione, which occur naturally during coffee roasting and are also present in flavorings used to flavor coffee. This study evaluated the associations of these two α-diketones with lung function measures in coffee production workers. Workers completed questionnaires, and their lung function was assessed by spirometry and impulse oscillometry (IOS). Personal exposures to diacetyl, 2,3-pentanedione, and their sum (Sum_{DA+PD}) were assigned to participants, and metrics of the highest 95th percentile (P95), cumulative, and average exposure were calculated. Linear and logistic regression models for continuous and binary/polytomous outcomes, respectively, were used to explore exposure-response relationships adjusting for age, body mass index, tenure, height, sex, smoking status, race, or allergic status. Decrements in percent predicted forced expiratory volume in 1 second ($ppFEV_1$) and forced vital capacity (ppFVC) were associated with the highest-P95 exposures to 2,3-pentanedione and Sum_{DA+PD}. Among flavoring workers, larger decrements in $ppFEV_1$ and ppFVC were associated with highest-P95 exposures to diacetyl, 2,3-pentanedione, and Sum_{DA+PD}. Abnormal FEV_1, FVC, and restrictive spirometric patterns were associated with the highest-P95, cumulative, and average exposures for all α-diketone metrics; some of these associations were also present among flavoring and non-flavoring workers. The combined category of small and peripheral airways plus small and large airways abnormalities on IOS had elevated odds for highest-P95 exposure to

α-diketones. These results may be affected by the small sample size, few cases of abnormal spirometry, and the healthy worker effect. Associations between lung function abnormalities and exposure to α-diketones suggest it may be prudent to consider exposure controls in both flavoring and non-flavoring settings.

KEYWORDS

coffee production, diacetyl, 2,3-pentanedione, spirometry, impulse oscillometry, peak exposures, restrictive pattern, small airways

Introduction

Coffee production workers are exposed to complex mixtures of gases, dust, and vapors such as carbon monoxide, carbon dioxide, coffee dust, green-bean allergens, and α-diketones, including 2,3-butanedione (diacetyl—a commonly used synonym) and 2,3-pentanedione (acetyl propionyl), and other volatile organic compounds (VOCs), including acetoin (1–6). Adverse respiratory health outcomes such as respiratory symptoms, pulmonary function abnormalities, asthma, and obliterative bronchiolitis (OB) can occur among exposed coffee production workers (7–9). OB is a rare, irreversible lung disease characterized by inflammation and bronchiolar wall fibrosis, leading to luminal narrowing of the small airways (i.e., bronchioles) and obliteration that obstructs airflow (10, 11). OB has been found among workers exposed to diacetyl present in flavoring chemicals used in flavoring manufacturing and a variety of food processing industries, including coffee production (11–14). Additionally, exposure to diacetyl is associated with lung function abnormalities including fixed obstructive, restrictive, and mixed patterns on spirometry, as well as longitudinal declines in forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), and FEV_1/FVC ratio, with or without respiratory symptoms (11–13, 15–21). Symptoms can include cough, shortness of breath on exertion, or wheezing, which do not improve away from work (11). Respiratory health risk from exposure to 2,3-pentanedione has not been evaluated in epidemiologic studies, but animal studies report similar toxicity to that of diacetyl (22, 23). In 2016, the National Institute for Occupational Safety and Health (NIOSH) established recommended exposure limits (RELs) of 5 parts per billion (ppb) and 9.3 ppb, and short-term exposure limits (STEL) of 25 ppb and 31 ppb for diacetyl and 2,3-pentanedione, respectively (11).

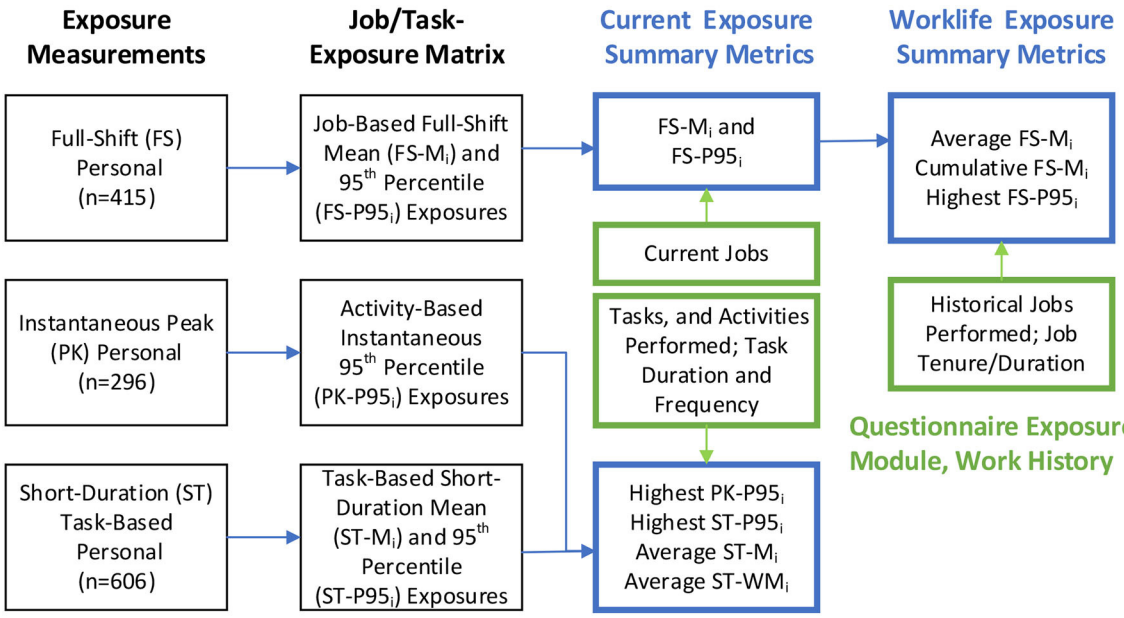
In previous studies of microwave popcorn workers exposed to flavoring chemicals, decrements in lung function, i.e., lower FEV_1 and FEV_1/FVC ratio, were associated with average and cumulative diacetyl exposure (11). At one of these microwave popcorn production facilities, higher cumulative diacetyl exposure (quartiles) was significantly associated with a higher prevalence of airway obstruction (24). Conversely, in a study of flavoring manufacturing workers, higher duration of work in a diacetyl plant was associated with better lung function, i.e., higher percent predicted FEV_1 ($ppFEV_1$), which was attributed to potential exposure misclassification, healthy worker effect, and not accounting for the effect of peak exposure (17). Other studies have reported associations of adverse respiratory health outcomes with proxies of diacetyl exposure such as tenure or type of production activity (13, 18, 25, 26). Although metrics of peak exposure have not been available to evaluate exposure-response relationships, peak exposures to diacetyl have been documented in settings where OB cases have occurred, including the microwave popcorn industry, a flavoring manufacturing facility, and a coffee production facility and may have contributed to disease development with relatively lower average exposures (2, 13, 17, 27).

The goal of this study was to explore exposure–response relationships in coffee production for various lung function measures with a range of exposure metrics including highest, average, and cumulative exposure intensity for individual and combined α-diketone exposures.

Methods

Study design and population

Cross-sectional exposure and health surveys were conducted from 2016 to 2017 in response to health hazard evaluation (HHE) requests received by NIOSH from 17 small- to medium-sized coffee facilities. The plants ranged in size, the number of workers employed, production volume, the type of coffee produced, including flavored, non-flavored, or both, and other characteristics previously described (1). All current employees were invited to participate in the exposure and health assessment surveys, and written informed consent was obtained from each study participant. After the HHE investigations were completed,



$i_{1\text{-}3}$: 1=Diacetyl (DA); 2=2,3-Pentanedione (PD); 3=Sum_{DA+PD}. WM=Duration, Frequency Weighted Mean. FS=Full-Shift; PK=Instantaneous Peak; ST=Short-Duration; FS-M_i=Full-Shift Arithmetic Mean for the α-Diketones; FS-$P95_i$=Full-Shift 95th Percentile for the α-Diketones; PK-$P95_i$=Instantaneous 95th Percentile for the α-Diketones;ST-M_i=Short-Duration Task-Based Arithmetic Mean for the α-Diketones; ST-$P95_i$=Short-Duration Task-Based 95th Percentile for the α-Diketones; Average FS-M_i= Average Job Exposure for the α-Diketones; Cumulative FS-M_i= Cumulative Exposure for the α-Diketones; Highest FS-$P95_i$= Highest 95th Percentile Job Exposure for the α-Diketones; Highest PK-$P95_i$= Highest 95th Percentile Instantaneous Peak Exposure for the α-Diketones; Highest ST-$P95_i$= Highest 95th Percentile Short-Duration Task Exposure for the α-Diketones; Average ST-M_i= Average Short-Duration Task Exposure for the α-Diketones; Average ST-WM_i= Average Short-Duration Task Weighted Mean Exposure for the α-Diketones.

FIGURE 1
Creation of job/task-exposure matrix and summary exposure metrics. Blue text boxes include metrics used in the epidemiologic analyses; green text boxes include information gathered from the questionnaire; black text boxes include exposure data and the summary metrics in the JEM/TEM.

data from the 17 investigations were pooled to increase the sample size to evaluate exposure–response relationships that might otherwise not have been evident within each facility. The study protocol for the secondary analysis of the pooled data was approved by the NIOSH Institutional Review Board (IRB).

Medical evaluations and health outcome measures

A combination of methods was used to characterize the health outcomes, described in detail elsewhere (7). Briefly, a standardized questionnaire was administered that included questions on demographics, symptoms and diagnoses, smoking history, work history, and exposure modules. Spirometry testing was conducted following the American Thoracic Society guidelines, and measurements were compared to their lower limit of normal (LLN) values (28, 29). Obstruction was defined as FEV_1/FVC ratio less than the LLN with normal FVC; restrictive pattern as FVC less than the LLN with normal FEV_1/FVC ratio; and mixed obstruction and restrictive pattern as having FVC and FEV_1/FVC ratio less than their respective LLNs (30). Previously, obstruction was defined as FEV_1 and FEV_1/FVC ratio less than their respective LLNs (7). For data analysis, mixed pattern (n = 2) was combined with restrictive pattern (hereafter referred to as restrictive pattern) because of the small sample size; mixed pattern as indicated by spirometry may indicate a combination of physiological restriction and obstruction, and restrictive spirometry pattern may indicate physiological restriction or be caused by a physiological obstruction such as from air-trapping and small airway disease (15).

Impulse oscillometry (IOS) was performed using the CareFusion IOS system (CareFusion, Hochberg, Germany) according to the manufacturer's instructions. Details of the IOS parameters are described in Supplementary methods. Briefly, IOS parameters include (1) resistance at an oscillation frequency of 5 Hz (total resistance – small and large airways) and 20 Hz (proximal resistance – large airways) (R_5, R_{20}); (2) frequency

dependence of resistance obtained as the difference between R_5 and R_{20} (R_{5-20}); (3) reactance at 5 Hz (distal capacitance – peripheral) (X_5); (4) resonant frequency (f_{res}); and 5) reactance area (AX) calculated as the area under the reactance curve from 5 Hz to f_{res} (31). Percent difference R_5-R_{20} (DR_{5-20}) is calculated as $((R_5\text{-}R_{20})/R_{20})^*100\%$; ppR_5 is the percent predicted R_5. Small airways and peripheral abnormality was defined as ($DR_{5-20} \geq 30\%$) or ($ppR_5 \geq 140\%$, [X_5 predicted – X_5 measured] $\geq$ 0.15 kPa/(L/s) and $DR_{5-20} \geq 30\%$), or ($ppR_5 < 140\%$ and [X_5 predicted – X_5 measured] $\geq$ 0.15 kPa/(L/s)); large and central airways abnormality was defined as ($ppR_5 \geq 140\%$, [X_5 predicted – X_5 measured] $<$ 0.15 kPa/(L/s) and $DR_{5-20} < 30\%$); small and large airway abnormality was defined as ($ppR_5 \geq 140\%$, [X_5 predicted – X_5 measured] $\geq$ 0.15 kPa/(L/s) and $DR_{5-20} < 30\%$); and any IOS abnormality was defined as $ppR_5 \geq 140\%$ or [X_5 predicted – X_5 measured] $\geq$ 0.15 kPa/(L/s) (32, 33). For data analysis, small airways and peripheral abnormality were combined with small and large airway abnormality (hereafter referred to as small airways) to emphasize any abnormality involving small airways.

Job/task exposure matrices and exposure assignment

Job- and task-exposure matrices (JEM/TEM) were created using personal full-shift, short-duration task, and instantaneous activity measurements collected at 17 coffee facilities as outlined in Figure 1 and described in detail in Supplementary materials. Briefly, exposure measurements were summarized overall, as well as stratified by facility, facility size category, and flavoring status, using a Bayesian approach that accounts for censored data and repeated measurements (1). The mean and standard deviation of the log-transformed exposures were obtained from these models and were used to calculate the minimum variance unbiased estimator (MVUE) of the arithmetic means (AM) (34). The 95th percentile (P95) was calculated as (geometric mean) $\times$ (geometric standard deviation)$^{1.645}$. The JEM included the AM and P95 for diacetyl, 2,3-pentanedione, and the sum of the two α-diketones (Sum_{DA+PD}) for all jobs, overall and stratified by the categories as depicted in the second column of Figure 1. The JEM included estimates based on current exposures only, as historical exposure data have not previously been collected at coffee production facilities.

The AM and P95 from the JEM were then assigned to all the jobs reported by each participant in their work history. Past jobs at any facility were assigned current job exposure estimates because historical exposures were expected to be similar to current exposures; facility owners reported that no systematic changes occurred in the past that may impact exposures. The AM and P95 of the most recent job were labeled as the average and highest "current exposure" metrics in parts per billion (ppb—depicted in the third column, first row of Figure 1). The profiles of AM and P95 from multiple jobs held by workers were summarized to obtain worklife (tenure in coffee or flavoring-related work) average, cumulative (AM $\times$ duration in ppb-years) and highest (P95) summary exposure metrics for each worker (depicted in the fourth column, the first row of Figure 1). The P95 metric represents the upper tail of exposure distribution, likely resulting from high exposure tasks within a job, non-routine maintenance activity, or unplanned upset conditions (35). Thus, the highest P95 metric may be considered a surrogate of peak exposure based on full-shift measurements.

A similar approach was used to construct the TEM and assign exposures to participants as described in Supplementary materials.

Statistical analysis

Statistical analyses were conducted using SAS software version 9.4 and JMP software version 15 (SAS Institute, Inc., Cary, NC), and plots were prepared in SigmaPlot 14.0 (Systat Software Inc., San Jose, CA). Summary statistics and correlation coefficients (Spearman rho—ρ) were calculated, and distributions were explored *via* histograms and probability plots for the various exposure metrics and continuous lung function measurements. Multiple linear regression was used to fit models for continuous outcomes, and logistic regression was used to model binary and polytomous outcomes for measures of IOS and spirometry. Metrics of highest, average, and cumulative exposure to diacetyl, 2,3-pentanedione, and Sum_{DA+PD} were fit in separate models due to collinearity among exposure metrics. Models were adjusted for age, sex, race, body mass index (BMI), height, smoking status, allergic status, or tenure as documented in the footnotes of each table. Interactions between exposure variables and tenure or flavoring status were explored to evaluate whether tenure or flavoring status modified the effect of exposure on the health outcome. Covariates were included regardless of statistical significance (11), even though they are partially accounted for in the spirometric and IOS prediction equations, to account for any potential variations from the reference population. Some covariates were dichotomized or excluded from the logistic regression models when they caused a complete or quasi-complete separation of data points (36). Odds ratios (OR) with corresponding 95% confidence intervals (CI) were obtained for the categorical outcomes, and parameter estimates (slope, β) and their 95% CI were obtained for continuous outcomes. To improve interpretability, the model parameter estimates were multiplied by 10, so the effect estimates (i.e., slope and OR) are per 10 ppb of exposure. To evaluate the performance of various exposure metrics for given outcome variables, measures of precision (parameter estimate/standard error—β/SE) and model

10.3389/fpubh.2022.966374

TABLE 1 Summary of respiratory health outcome and exposure characteristics by categories of health and flavoring status.

Health/exposure measure	Health status				Flavoring status	
	Any abnormal spirometry $N = 37$	Any abnormal IOS $N = 104$	Current asthma $N = 38$	No disease/ abnormality $N = 225$	Flavoring job anywhere $N = 71$	Non-flavoring job $N = 313$
Symptoms in the past 12 months: *N* (%)						
Upper respiratory	25 (67.6)	65 (62.5)	33 (86.8)	146 (64.9)	44 (62)	208 (66.5)
Lower respiratory	26 (70.3)	58 (55.8)	37 (97.4)	84 (37.3)	28 (39.4)	151 (48.2)
Breathing trouble	14 (37.8)	22 (21.2)	28 (73.7)	34 (15.1)	11 (15.5)	68 (21.7)
Cough	7 (18.9)	15 (14.4)	10 (26.3)	14 (6.2)	10 (14.1)	30 (9.6)
Wheeze	19 (51.4)	29 (27.9)	29 (76.3)	37 (16.4)	17 (23.9)	77 (24.6)
Chest tightness	4 (10.8)	14 (13.5)	19 (50)	27 (12.0)	7 (9.9)	46 (14.7)
Shortness of breath (SOB)	8 (21.6)	24 (23.1)	19 (50)	20 (8.9)	12 (16.9)	47 (15)
Severe SOB	4 (50.0)	10 (41.7)	9 (47.4)	4 (20.0)	4 (33.3)	14 (29.8)
Awoken with SOB	5 (13.5)	9 (8.7)	12 (31.6)	10 (4.4)	6 (8.5)	22 (7)
Asthma attack	8 (21.6)	9 (8.7)	24 (63.2)	1 (0.4)	6 (8.5)	20 (6.4)
Lung function: Mean (Std) or *N* (%)						
$ppFEV_1$	82.9 (15.17)	96.2 (15.2)	96.2 (11.4)	106.0 (11.5)	101.3 (14.4)	102.6 (13.2)
ppFVC	98.9 (16.6)	99.8 (10.4)	103.8 (10.7)	105.4 (12.1)	103.1 (13.5)	103.8 (12)
$ppFEV_1$/FVC Ratio	84.7 (16.2)	96.1 (11.6)	92.3 (7.5)	100.4 (5.6)	98.1 (9.6)	98.6 (8.5)
Abnormal spirometry	37 (100)	18 (18.0)	9 (25.7)	0 (–)	11 (16.4)	26 (8.7)
Restriction + Mixed	11 (29.7)	6 (6.0)	0 (–)	0 (–)	3 (4.5)	8 (2.7)
Obstruction	26 (70.3)	12 (12.0)	9 (25.7)	0 (–)	8 (11.9)	18 (6.4)
IOS: *N* (%)						
Abnormal IOS	18 (48.7)	104 (100)	13 (34.21)	0 (–)	22 (31.9)	82 (26.5)
Large airways	3 (8.1)	28 (26.9)	3 (7.9)	0 (–)	6 (8.7)	22 (7.1)
Small + small & large	15 (40.5)	76 (73.1)	10 (26.3)	0 (–)	16 (23.2)	60 (19.4)
Exposure (ppb)/duration (years): Mean (Std) or *N* (%)						
P95 Diacetyl	50.9 (76.2)	46.2 (56.1)	33.3 (39.5)	35.3 (37.4)	58.7 (80.9)	33.7 (29.8)
P95 2,3–Pentanedione	46.2 (91.6)	34.9 (64.3)	27.4 (49.3)	23.7 (33.9)	62.4 (102.7)	19.9 (12)
P95 Sum_{DA+PD}	93.4 (165.1)	78.8 (116.6)	53.9 (54.9)	56.7 (65.2)	118.5 (179.5)	50.8 (32.3)
CE Diacetyl	50.5 (66.7)	65.5 (77.8)	43.4 (51.1)	53.1 (74.0)	70.7 (97.7)	56.1 (91.1)
CE 2,3–Pentanedione	36.7 (57.6)	45 (58.8)	35.5 (46.6)	34.5 (49.0)	58.9 (84.4)	33.4 (40.9)
CE Sum_{DA+PD}	86.7 (125.4)	110.9 (135.6)	78.9 (95.9)	86.3 (117.6)	130.3 (183.1)	86.8 (110)
Avg. Diacetyl	13.0 (12.4)	15.5 (13.2)	8.78 (7.1)	12.7 (12.1)	13.4 (11.9)	13 (12.2)
Avg. 2,3–Pentanedione	9.2 (9.3)	9.9 (8.1)	7.7 (9.8)	7.9 (6.6)	10.9 (10)	7.9 (6.6)
Avg. Sum_{DA+PD}	21.7 (21.0)	25.4 (20.9)	16.3 (15.5)	20.4 (18.4)	24.3 (20.9)	20.7 (18.3)
Total tenure (yrs.)	4.3 (3.7)	5.2 (5.4)	6 (5.3)	5.9 (6.1)	6.3 (5.8)	5.7 (6.1)
Flavoring tenure (yrs.)	0.9 (2.2)	0.9 (2.6)	0.95 (3)	0.4 (1.3)	2.8 (3.4)	0 (–)
Flavoring job	11 (29.7)	22 (21.2)	8 (21.1)	36 (16.0)	71 (100)	0 (–)
Demographics: *N* (%) or Mean (Std)						
Ever smoker	21 (56.8)	37 (35.6)	22 (57.9)	95 (42.2)	28 (39.4)	136 (43.5)
Age	37.7 (10.9)	37 (10.5)	38.8 (10.7)	36.6 (11.7)	36.3 (12.2)	37.2 (11.3)
Body Mass Index (BMI)	28.2 (7.4)	31.2 (6.5)	29.3 (6.5)	26.5 (4.8)	28.2 (6.1)	28 (5.9)
BMI $\geq$ 30	12 (32.4)	60 (57.7)	15 (39.5)	48 (21.3)	25 (35.2)	100 (32.1)
Race (White)	25 (67.6)	46 (44.2)	26 (68.4)	142 (63.1)	42 (59.2)	184 (58.8)
Gender (Male)	26 (70.3)	53 (51)	16 (42.1)	145 (64.4)	42 (59.2)	183 (58.5)

CE, cumulative exposure; Avg., average exposure; Severe SOB was assessed by a question on SOB occurring when walking with others of the same age.

fit (Akaike information criterion—AIC) were used to compare models (37).

Results

Demographics, exposure, and health distributions

Participation in the health and exposure assessments ranged from 16 to 100% and 18 to 100%, respectively, by facility. A total of 384 (58%) workers completed the health assessments, and 227 (34%) workers participated in the exposure assessment survey. As reported previously, a majority of the study population was men (59%), white (59%), and never smokers (57%), with a median age of 35 years (range: 18–72 years), median tenure across all coffee and flavoring jobs of 3.8 years (range: <1–34 years), and 35% with a BMI of >30 (7). Among all workers, 10.1% (37/367) had any abnormal spirometry, with nine workers having a restrictive pattern, 26 with obstruction, and two with a mixed pattern. The prevalence of any abnormal IOS was 27.5% (104/378), with 28 having abnormalities in the large and central airways, 18 in the small and large airways, and 58 in the small and peripheral airways. Self-reported physician-diagnosed current asthma was reported by 38/384 (9.9%) workers.

Histograms of the worklife exposure metrics show distributions with right skew; lung function parameters appear to follow a normal distribution (Supplementary Figure 1). Histograms of highest-P95 and average exposure for diacetyl and 2,3-pentanedione show most workers' assigned exposures were above the relevant RELs. The ranges of correlations within and across the different types of metrics are displayed as a heatmap in Supplementary Figure 2. Duration of exposure was negatively correlated with all exposure metrics except cumulative exposure. Metrics based on instantaneous activity were not correlated with any other metrics. Short-duration peak exposures were poorly correlated with other metrics, as were metrics of cumulative exposure. There were some moderate and some high correlations among worklife exposure metrics. Scatterplots of diacetyl vs. 2,3-pentanedione for highest-P95, cumulative, and average exposure show a high correlation within exposure metrics (Supplementary Figure 3).

Bivariate summaries

Table 1 summarizes demographics, symptoms, spirometry, IOS, and exposure values by categories of health outcome and having ever or never held a flavoring job (hereafter referred to as flavoring). Workers who reported current asthma had the highest prevalence of all but one respiratory symptom, followed by those with abnormal spirometry; the latter group had the highest prevalence of more severe shortness of breath. Workers with abnormal spirometry or IOS had the highest exposures across all metrics, while those with asthma had similar or lower exposures compared to the group with no disease or abnormalities. The group with abnormal spirometry was mostly men and white, with the highest prevalence of flavoring jobs. Those with abnormal IOS had the highest prevalence of BMI >30 and the lowest prevalence of white race. Flavoring workers had a higher prevalence of abnormal spirometry and IOS as well as higher exposures across all metrics compared to those who never held a flavoring job; symptoms, spirometric parameters, and demographics were similar between the flavoring and non-flavoring groups.

Figure 2 displays spirometric parameters, selected exposure metrics, and the prevalence of abnormal spirometry and IOS by categories of tenure and flavoring status; tenure categories were selected as ≤1 year representing short-tenure workers (17.5%), >1 to 10 years representing medium-tenure (63.5%) and >10 years representing long-term workers (19%). In the flavoring group, mean $ppFEV_1$, ppFVC, and $ppFEV_1$/FVC values decreased from the low to medium tenure category but increased in the high tenure category. Likewise, the prevalence of abnormal spirometry increased from the low to medium tenure category but decreased in the high tenure category. All exposure metrics, except for the average, show increasing trends with tenure. Similar patterns were observed in the non-flavoring group, albeit less pronounced, with all exposure metrics except cumulative exposure remaining flat across tenure. The prevalence of abnormal lOS decreased from low to medium tenure but increased or remained flat in the high category in both flavoring and non-flavoring groups.

Exposure-response models for worklife exposure metric

P95 exposure

In exposure-response models for spirometry outcomes adjusted for covariates including tenure, the worklife P95 exposure metric for diacetyl, 2,3-pentanedione, and Sum_{DA+PD} was consistently associated with lower spirometric parameters; 2,3-pentanedione and Sum_{DA+PD} were significantly associated with lower $ppFEV_1$ (Table 2). The parameter estimate for $ppFEV_1$ with 2,3-pentanedione indicates a 0.30 percentage point lower $ppFEV_1$ for every 10 ppb increase in P95 exposure. Elevated odds ratios were observed for any abnormal spirometry, FEV_1 <LLN, FVC<LLN and restrictive pattern with P95 exposure for diacetyl, 2,3-pentanedione, and Sum_{DA+PD} in logistic models with covariates (Table 2). The OR (1.19) for the association of restrictive pattern with P95 diacetyl exposure is interpreted as a 19% increase in the odds of having a restrictive pattern for every 10 ppb increase in P95 exposure. Obstruction was not associated with any exposure

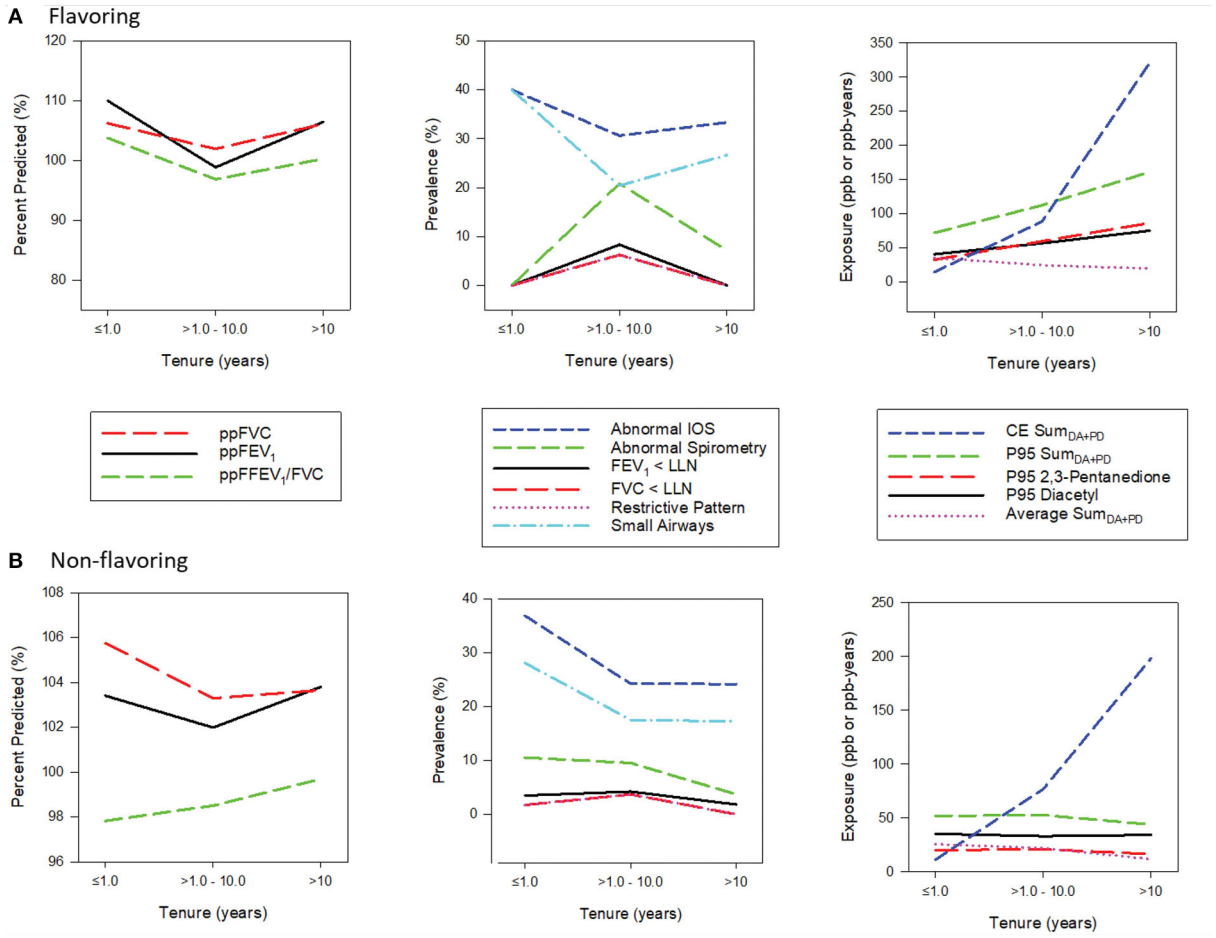


FIGURE 2
(A,B) Panel plots of exposure and health characteristics by tenure stratified by flavoring.

metrics. Significantly elevated odds ratios were observed for abnormality in the small airways with P95 exposure, for diacetyl, 2,3-pentanedione, and Sum_{DA+PD} in logistic models with covariates; overall abnormal IOS followed a similar pattern, albeit with smaller odds ratios (Table 2). The increase in odds for these associations ranged from 3 to 8% for having IOS or small airway abnormalities for every 10 ppb increase in exposure. Large airway abnormality was not associated with any exposures.

Average and cumulative exposures

Average and cumulative exposure to diacetyl, 2,3-pentanedione, and Sum_{DA+PD} were consistently associated with lower ppFVC but not with $ppFEV_1$ and $ppFEV_1$/FVC (Supplementary Table 1). Most notably, FVC<LLN and restrictive spirometric patterns were significant across all exposure metrics. FEV_1 < LLN was significant for 2,3-pentanedione for average and cumulative exposure. Measures of IOS abnormalities, including small and large airway abnormalities, had odds ratios that were much smaller in magnitude with large confidence intervals.

Model covariates

Various covariates were significant for different spirometry and IOS outcomes (Supplementary Table 2) and are described in the Supplementary materials. Model fit and precision metrics are reported in Supplementary Table 3. Duration of exposure (tenure) was positively associated with all continuous spirometry outcomes, indicating significantly higher spirometric values with increasing tenure. Tenure was thus included as a covariate in all the models. There was no interaction between tenure and the exposure metrics. However, a significant interaction was observed between flavoring status and the exposure metrics, thus stratified analyses were conducted.

Exposure-response models stratified by flavoring status

In models stratified by flavoring status, the highest-P95 and cumulative exposure metric for diacetyl, 2,3-pentanedione, and Sum_{DA+PD} were associated with lower $ppFEV_1$, ppFVC, and $ppFEV_1$/FVC in the flavoring group and were significant for the association between highest-P95 and $ppFEV_1$ and ppFVC (Supplementary Table 4). Diacetyl exposures had the largest effect estimates, which were larger than those for the overall model. None of the exposure metrics were associated with $ppFEV_1$ or ppFVC in the non-flavoring group (Supplementary Table 5). Diacetyl, 2,3-pentanedione, and Sum_{DA+PD} were associated with elevated ORs for FEV_1 <LLN, FVC<LLN, and restrictive patterns in the flavoring group, at $p < 0.05$ or $0.05 < p < 0.1$ (Supplementary Table 4). This is likely due to the small sample size in the flavoring group ($n = 71$), with only 11 cases of abnormal spirometry and three with a restrictive pattern. In the non-flavoring group, FVC<LLN and restrictive pattern were associated with elevated ORs for highest-P95 and cumulative exposures at $p < 0.05$ or $0.05 < p < 0.1$ (Supplementary Table 5); there were 26 cases of abnormal spirometry and eight with restrictive pattern in the non-flavoring group of $n = 313$ workers. For IOS in the flavoring group, significant ORs were observed for small airway abnormality with the highest-P95 for diacetyl, 2,3-pentanedione, and Sum_{DA+PD} (Supplementary Table 4); no associations were observed in the non-flavoring group (Supplementary Table 5).

Exposure-response models for current exposure metrics

None of the metrics of current exposures based on full-shift, short-duration task-based, or instantaneous activities were associated with any IOS or spirometry outcomes (data not shown).

Discussion

Association of α-diketone exposures with lung function decrements and abnormalities

Decrements in $ppFEV_1$ and ppFVC were consistently associated with increasing highest-P95 exposure to diacetyl, 2,3-pentanedione, and Sum_{DA+PD} overall or in flavoring. Average and cumulative exposure metrics were also consistently inversely associated with lung function parameters, albeit non-significantly. Elevated ORs for FEV_1 <LLN, FVC<LLN, abnormal spirometry, and restrictive patterns were observed overall, in flavoring, and non-flavoring for highest-P95, cumulative, and average exposure to all the α-diketones. Additionally, the combined categories of small and peripheral plus small and large airway abnormalities on IOS had elevated ORs for highest-P95 exposure to the α-diketones. These associations were observed with worklife exposure metrics but not with current exposures. Highest-P95, a surrogate of peak exposure, seemed to be a more sensitive metric, but cumulative and average exposure was also significant. The association of α-diketone exposures with lung function decrements and abnormalities in a workforce with relatively few lung function abnormalities (7) indicates a potential risk for future occupational lung disease at these facilities with prolonged exposures. Previous studies in flavoring workers have observed increasing symptoms and lung function abnormalities prior to the development of OB (25). Symptoms of chronic respiratory impairment and respiratory abnormalities, one case of OB identified in this workforce (9), and the observed associations with α-diketone exposures in this study may be indicative of early disease markers.

In the past, OB was described as fixed airway obstruction, with spirometry measures focused on obstruction. However, recent studies using spirometry have reported obstruction, restrictive pattern, and mixed obstruction and restriction in popcorn and flavoring manufacturing workers (11, 15, 19). In one flavoring manufacturing facility, abnormal spirometry was mostly restrictive but also included obstructive and mixed patterns (20). Obstruction, restrictive, and mixed patterns on spirometry were also observed in the present workforce, but restrictive pattern was significantly associated with α-diketone exposure metrics. The restrictive pattern is consistent with the findings of small airway abnormalities on IOS (15, 38–40), which was also significantly associated with the highest-P95 exposure to α-diketones.

Exposure–response relationships observed for continuous spirometric outcomes suggest that the effect of exposure on lung function occurs in the entire workforce and is not limited to just the subpopulation with sufficient loss of function to be classified as abnormal. However, continuous outcome variables may be affected by variability in spirometric values, resulting in wider confidence intervals, or nonlinear relationships between lung function values and exposure metrics.

Effect of various exposure metrics for diacetyl, 2,3-pentanedione, and Sum_{DA+PD}

The effect estimates for the associations between various health outcomes and exposure to diacetyl and 2,3-pentanedione when both estimates were significant were similar, but diacetyl had slightly larger effect estimates than 2,3-pentanedione for

10.3389/fpubh.2022.966374

TABLE 2 Associations of lung function with worklife P95 exposure metric for diacetyl, 2,3-pentanedione, and Sum_{DA+PD}.

Health outcome	Diacetyl	2,3-Pentanedione	Sum_{DA+PD}
	slope (95% CI)	slope (95% CI)	slope (95% CI)
$ppFEV_1$	−0.24	**−0.30**	**−0.16**
	(−0.55, 0.07)	**(−0.58, −0.03)**	**(−0.32, −0.01)**
ppFVC	−0.21	*−0.25*	*−0.14*
	(−0.50, 0.08)	*(−0.51, 0.01)*	*(−0.28, 0.01)*
$ppFEV_1$/FVC	−0.05	−0.08	−0.04
	(−0.25, 0.16)	(−0.26, 0.10)	(−0.14, 0.06)
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**
FEV_1 < LLN	**1.11**	**1.11**	**1.06**
	(1.01, 1.21)	**(1.03, 1.19)**	**(1.02, 1.10)**
[a]FVC < LLN	**1.19**	**1.12**	**1.06**
	(1.09, 1.31)	**(1.05, 1.20)**	**(1.03, 1.12)**
FEV_1/FVC < LLN	1.05	**1.06**	**1.04**
	(0.96, 1.14)	**(0.99, 1.12)**	**(0.99, 1.07)**
Abnormal spirometry	**1.08**	**1.08**	**1.04**
	(1.01, 1.16)	**(1.02, 1.14)**	**(1.01, 1.08)**
[a]Spirometry obstruction	1.00	1.04	1.02
	(0.86, 1.11)	(0.94, 1.12)	(0.95, 1.06)
[a]Spirometry restriction +Mixed	**1.19**	**1.13**	**1.08**
	(1.09, 1.32)	**(1.05, 1.21)**	**(1.03, 1.13)**
[b]Abnormal IOS	*1.06*	*1.05*	*1.03*
	(1.00, 1.12)	*(0.99, 1.10)*	*(1.00, 1.06)*
[a,b]IOS Large airways	1.00	0.99	1.00
	(0.88, 1.10)	(0.80, 1.08)	(0.92, 1.05)
[a,b]IOS small + small andLarge airways	**1.08**	**1.06**	**1.04**
	(1.02, 1.15)	**(1.01, 1.12)**	**(1.01, 1.07)**

Covariates, age, BMI, height, tenure, sex, smoke, race, and allergic status; Estimates of slope and their 95% CI are expressed as percentage points per 10 ppb; Estimates of OR and their 95% CI are expressed as odds per 10 ppb; Bold, $p < 0.05$; Italics, $0.05 < p < 0.10$; Models modified to address quasi or complete separation. All logistic and polytomous models used binary race, whites vs. non-whites; [a]sex excluded; [b]height included.

the highest-P95 metric. The converse was true for average and cumulative exposure metrics. There was a high correlation between diacetyl and 2,3-pentanedione for highest-P95 ($\rho_S = 0.89$), cumulative ($\rho_S = 0.97$), and average ($\rho_S = 0.94$) exposure metrics. Therefore, it is not possible to evaluate the independent effect of each α-diketone as the effect estimate reflects the effect of the combination of the two. Because of the high correlation between diacetyl and 2,3-pentanedione, neither remains significant when included in the same model and their interaction (to determine additive or multiplicative effect) could not be evaluated (41). The effect estimate for the sum of the two α-diketones is essentially half of the estimate for diacetyl or 2,3-pentanedione because the range of the exposure estimate has been doubled. The effect estimate reflects the combined effects of the α-diketones; the individual α-diketones underestimate the exposure and therefore overstate the risk, whereas considering the sum of the α-diketones reduces this underestimation of exposures. If the effect of diacetyl is similar to that of 2,3-pentanedione (11, 22), then the effect estimate of the sum of the α-diketones may be more representative of the mixed exposure effect than the individual α-diketones.

Summarizing time-varying historical exposure profiles into summary exposure metrics for use in epidemiologic studies involves assumptions about the relationship between exposure and disease and the time patterns of the effects of exposure (42, 43). Cumulative exposure is the most common exposure index used in epidemiologic studies of chronic effects; however, metrics of peak exposure may be relevant when the association between exposure, dose, and impairment is nonlinear (43, 44). In this study, high to moderate correlations were observed for the highest-P95 and the average exposure ($\rho_S = 0.86$), between average and cumulative ($\rho_S = 0.45$), and highest-P95 and cumulative ($\rho_S = 0.50$) exposure for the sum of the two α-diketones. Although only the highest-P95 was

significantly associated with continuous spirometric parameters, all three, i.e., highest-P95, average, and cumulative exposure metrics, were associated with the categorical spirometric outcomes, perhaps reflecting more complex exposure–response relationships or measurement errors in exposure or outcome variables. Differences in the exposure–response relationship have been observed even when the summary exposure metrics are highly correlated ($r = 0.68$ to 0.88) (45).

Effect of flavoring status

Average values for FEV_1 and FVC were similar between flavoring and non-flavoring groups. However, a significant interaction was observed between flavoring status and exposure metrics. Highest-P95 metric for α-diketone exposures was strongly associated with decrements in the continuous spirometric parameters overall and in flavoring, but not in non-flavoring; the effect estimate was larger in flavoring than overall. All exposure metrics were higher in flavoring compared to non-flavoring, although this is accounted for in the exposure metric used in regression models. There are likely other factors contributing to the difference in effect between the groups, such as other co-exposures in the flavoring group or differences in exposure time needed to experience lung function decrements given the lower exposures in non-flavoring. Abnormal spirometry, including obstruction and restrictive pattern, occurred in both flavoring and non-flavoring groups. Although some of the associations in the flavoring and non-flavoring groups were not significant, these associations are affected by sample size and the number of cases with abnormality, with only three cases of restrictive pattern in flavoring and eight cases in non-flavoring. These findings indicate that α-diketone-related spirometric abnormalities occur in both flavoring and non-flavoring workers.

The effect estimates reported in the NIOSH criteria document for α-diketones are for FEV_1, the ratio of FEV_1/FVC, and obstruction-associated average and cumulative exposure to diacetyl in flavoring (11). In this study, the associations of FEV_1 or the ratio of FEV_1/FVC with average or cumulative diacetyl exposure were not significant. Additionally, obstruction was not significantly associated with any of the exposure metrics. Thus, the present results cannot be directly compared to those reported in the NIOSH criteria document. It is noteworthy that the effect estimates in this study are in units of 10 ppb^{-1}, while those reported in the criteria document are in ppm^{-1}.

Healthy worker effect

The plots of lung function parameters presented in Figure 2 show worsening spirometry going from a low tenure of <1 year to a medium tenure of 1–10 years, followed by improved spirometry in the highest tenure of >10 years. All exposure metrics, except for the average metric, increase with increasing tenure or remained flat (for non-flavoring). Additionally, regression models with tenure as the main effect (without exposures) showed tenure was significantly associated with better spirometry for some outcomes, such as FEV_1 and the ratio of FEV_1/FVC. These findings indicate a potential for a healthy worker survivor effect, and tenure was thus included as a covariate in all the models to account for this positive effect on spirometry. In a study of flavoring manufacturing workers with a higher prevalence of respiratory symptoms, a positive association was also observed between the duration of work in the diacetyl plant and $ppFEV_1$, which was attributed to various causes, including the healthy worker effect (17). This phenomenon is not uncommon in occupational studies where the effect estimate is attenuated in the higher exposure category because of various potential causes, including the healthy worker survivor effect, fewer susceptible workers in the population at high exposure levels, measurement error or exposure misclassification, and the influence of other risk factors that are correlated with exposure (46).

Limitations

With any approach, there are trade-offs and limitations of the selected study design or strategy. Some limitations of this study included a lack of historical exposure information; historical job exposures were assumed to be equal to current exposures; historical task information was not gathered; co-exposures to other gases, dust, and vapors in coffee production might also be important but were not collected; a small number of cases of spirometric abnormalities; and other general limitations of cross-sectional study design. Smaller sample sizes may have contributed to the lack of significance found in some of these analyses. Additionally, although the health assessment was extensive, there were several limitations, including the inability to assess longitudinal change in lung function because of the cross-sectional study design, the potential for healthy worker survivor effect because of enrolling current workers only, the potential for bias if differential participation by health status occurred because participation was not 100%, and potential for underestimation of exposure and respiratory health burden in the industry as the HHE requests were often made by management at facilities without known health problems. Some of these challenges could not be avoided within the HHE Program context.

Conclusion

Lung function decrements and abnormalities were consistently associated with various metrics of exposure to

diacetyl, 2,3-pentanedione, and their sum in a workforce of coffee production workers with relatively few workers with lung function changes large enough to be classified as abnormal and a likely presence of healthy worker survivor effect. Although obstruction, restrictive, and mixed spirometric patterns were present, only restrictive plus mixed pattern was significantly associated with α-diketones exposures, consistent with the association for small airway abnormality. The effects of exposure likely occur in the entire population and not just among workers with lung function abnormalities or just in flavoring. Although the highest-P95 summary metric appeared to be more sensitive, average and cumulative exposure metrics are also relevant. An aggregate exposure metric ought to be considered when multiple α-diketones are present. Associations between lung function abnormalities and exposure to α-diketones suggest it may be prudent to consider exposure controls in both flavoring and non-flavoring settings.

Data availability statement

The datasets presented in this article are not readily available because due to restrictions imposed under the US privacy act and the limitations of what participants consented to, the data underlying the analyses presented, beyond what is provided in the paper, are confidential and not available to researchers outside the National Institute for Occupational Safety and Health (NIOSH). For more information about NIOSH's policy regarding sensitive data, see https://www.cdc.gov/niosh/ocas/datahandle.html. Requests to access the datasets should be directed to https://www.cdc.gov/niosh/ocas/datahandle.html.

Ethics statement

The studies involving human participants were reviewed and approved by the NIOSH Institutional Review Board reviewed and approved this study (NIOSH Protocol 17-RHD-06XP). All participants provided their written informed consent to participate during data collection for the HHE.

Author contributions

MV, JC-G, and KC contributed to the conception and design of the study. XL organized the database. MV, JC-G, KC, EF-L, RH, and RB contributed to the interpretation of IOS and spirometry results. MV, BB, RL, and MS contributed to the estimation of exposure. MV, XL, and CG performed the statistical analyses. MV wrote the first draft of the manuscript. All authors contributed to the article and approved the submitted version.

Funding

This study was supported by the National Institute for Occupational Safety and Health (NIOSH) Division Intramural Funds.

Acknowledgments

The authors thank the workers for participating in the NIOSH health hazard evaluation program and the members of the NIOSH field teams for their contributions to data acquisition. The authors acknowledge Drs. Doug Johns and Christine Whittaker for their review of the manuscript.

Conflict of interest

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

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.966374/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Perspective
PUBLISHED 08 September 2022
DOI 10.3389/fpubh.2022.972136

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

RECEIVED 17 June 2022
ACCEPTED 16 August 2022
PUBLISHED 08 September 2022

CITATION
Johns DO, Whittaker C and Cox-Ganser JM (2022) Impacts of risk assessment data, assumptions, and methods: Considering the evidence for diacetyl and 2,3-pentanedione. *Front. Public Health* 10:972136. doi: 10.3389/fpubh.2022.972136

Impacts of risk assessment data, assumptions, and methods: Considering the evidence for diacetyl and 2,3-pentanedione

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The articles published as part of the *Frontiers in Public Health* research topic, "Investigating exposures and respiratory health in coffee workers" present research findings that better characterize exposures to diacetyl and 2,3-pentanedione and inform our understanding of the health risks posed by these exposures. Although various research groups and organizations have conducted risk assessments to derive occupational exposure limits (OELs) for diacetyl, differences in the data used and assumptions made in these efforts have resulted in a wide range of recommended OELs designed to protect human health. The primary drivers of these differences include the decision to use data from human or animal studies in conducting a quantitative risk assessment, and the application of uncertainty factors (UF) to derive an OEL. This Perspectives paper will discuss the practical implications of these decisions, and present additional commentary on the potential role that the recent investigation of human exposures to relatively low concentrations of α-diketones, specifically diacetyl and 2,3-pentanedione, may play in supporting qualitative or quantitative human health risk assessments.

KEYWORDS

risk assessment, occupational exposures, respiratory health, α-diketones, coffee roasting and packaging

Introduction

In 2016, the U.S. National Institute for Occupational Safety and Health (NIOSH) recommended an 8-hour time-weighted average (TWA) occupational exposure limit (OEL) for diacetyl (2,3-butanedione) of 5 ppb. OELs can take various forms, but generally speaking are all science- and health-based upper limits of exposure derived by government and professional organizations to protect worker health. NIOSH's recommended exposure limit (REL) for diacetyl was supported and informed by an extensive and comprehensive review and analysis of the scientific literature, including qualitative and quantitative risk assessments from animal toxicological and human epidemiologic investigations (1). NIOSH also established

a REL for 2,3-pentanedione (acetylpropionyl) of 9.3 ppb, similar but slightly higher to that of diacetyl, owing to their structural similarities while also considering limitations of the analytical method for 2,3-pentanedione. The risk assessments for diacetyl and 2,3-pentanedione were subject to peer and stakeholder review and public comment. Other researchers and organizations have conducted and published risk assessments for diacetyl, prior and subsequent to the publication of the NIOSH criteria document. The authors of these assessments have recommended OELs for diacetyl ranging from 1 to 200 ppb (0.001 to 0.2 ppm) (2–5).

What accounts for this variability between OELs? In truth, such a wide range – greater than two orders of magnitude – is not atypical, and is a function of a number of factors that differ among assessments including: (1) selection of different health endpoints upon which to base an assessment, (2) use of different types of data, such as that from animal laboratory studies vs. data from human observational investigations to derive OELs, (3) methods for estimating exposures in epidemiologic investigations, (4) applying different protocols for interspecies extrapolations – for example, using allometric scaling, incorporating pharmacokinetic information, or using different inhalation dosimetry methods, (5) new data and changes over time in perceived acceptable levels of risk, and (6) efforts to adequately address uncertainty, variability and confounding. Ideally, differences in methods are adequately described in the peer-reviewed scientific literature and will lead to healthy dialogue and scientific debate. Increasing transparency helps to reduce, but does not completely eliminate, confirmation biases of individual scientists – a common tendency to seek answers that support preexisting views or hypotheses (6).

When new high quality data become available or new analytical methods are developed, they may cast doubt or improve the confidence of prior risk assessments. In these cases, risk assessors may conduct additional analyses or new assessments to improve our understanding of health effects resulting from occupational exposures. A recently published series of articles describes investigations of occupational exposures, focusing on α-diketones, and respiratory health among workers employed at small and medium-sized coffee roasting and packaging facilities (7). Diacetyl and 2,3-pentanedione exposures in these investigations were found to exceed the NIOSH REL, particularly among groups of workers whose tasks included grinding, flavoring, and packaging coffee (8). However, these exposures were typically far lower (one to greater than two orders of magnitude) than the exposures observed among microwave popcorn workers upon which NIOSH based its quantitative risk assessment for diacetyl (1).

This perspectives paper will briefly describe published quantitative risk assessments for diacetyl and consider how the recently reported findings of exposures among coffee workers may impact the understanding of occupational risks from exposure to diacetyl as well as 2,3-pentanedione. Note, a list of acronyms used throughout this paper is presented in Table 1 along with their meaning.

TABLE 1 List of acronyms.

Acronym	Full form
EPA	United States Environmental Protection Agency
FEV_1	Forced expiratory volume in 1 s
FEV_1/FVC	Ratio of FEV_1 to forced vital capacity
LOAEC	Lowest observed adverse effect concentration
NIOSH	The National Institute for Occupational Safety and Health
NTP	National Toxicology Program
OEL	Occupational exposure limit
ppb	Parts per billion
ppm	Parts per million
ppm-yr	Parts per million - years
REL	NIOSH recommended exposure limit
SCOEL	European Commission's Scientific Committee on Occupational Exposure Limits
TWA	Time weighted average
UF	Uncertainty factor

Quantitative risk assessments for diacetyl

Several investigators have conducted quantitative risk assessments for occupational exposure to diacetyl, the details of which are briefly summarized in Table 2. The differences in the recommended OELs derived from these risk assessments are largely due to differences in data used and application of uncertainty factors (UF) or extrapolation to an occupational lifetime exposure (e.g., 8 h per day, 5 days per week for 45 years).

Of note, the human-based risk estimates were all lower than the lowest animal-based risk estimates. In the worker exposure-based risk assessments, the European Commission's Scientific Committee on Occupational Exposure Limits (SCOEL) (5) used straightforward extrapolation to a working lifetime (40-year) exposure from Kreiss et al. (9) adjusted for an UF of 2 (after a correction for bias in the exposure assessment). The NIOSH risk assessment used data from Kreiss et al. (9); Kullman et al. (10); Kanwal et al. (11); and Kanwal et al. (12) with risks estimated using regression techniques to extrapolate to a working lifetime (45-year) exposure. Finally, Egilman et al. (3) used data from Lockey et al. (13), extrapolated to a 45-year working lifetime

TABLE 2 Risk assessments based on human and animal studies of respiratory health effects from diacetyl exposure.

Risk assessment citation	Health endpoint	Risk assessment methods and assumptions	Derived OEL
Human based assessments			
SCOEL (5)	Changes in pulmonary function, symptoms, and other respiratory health endpoints in exposed workers.	Using Haber's Law, calculated the 40-year working lifetime concentration corresponding to the lowest observed adverse effect concentration (LOAEC). Corrected for bias in exposure estimation and applied an UF of 2.	0.02 ppm
NIOSH (1)	Changes in pulmonary function, symptoms, and other respiratory health endpoints in exposed workers.	Assumed cumulative exposures over a 45-year working lifetime using regression modeling. Targeted excess risk level of 1 case per 1,000 workers exposed over a working lifetime. No additional UF applied.	5 ppb
Egilman et al. (3)	Changes in pulmonary function in exposed workers (cross-sectional design).	Assumed cumulative exposures over working lifetime of 45 years. Divided exposure estimates by the attributable increased risk to achieve a rate ratio of 1.0 and then extrapolated exposure estimates to working lifetime to estimate safe levels. No additional UF applied.	1 ppb
Risk assessment citation	**Health endpoint**	**Risk assessment methods and assumptions**	**Derived OEL***
Animal based risk assessments			
Maier et al. (4)	Tracheobronchial inflammation in mice after subchronic exposure.	Combined data from 6- and 12-week studies; Estimated excess risk using benchmark dose techniques, extrapolated to human equivalent concentration using EPA regional gas dose ratio method refined with computational fluid dynamics model developed for rats and humans. Applied an UF of 10.	0.2 ppm
NIOSH (1)	Lung inflammation in male rats after subchronic exposure.	Estimated excess risk using benchmark dose techniques, extrapolated to human equivalent concentration using EPA regional gas dose ratio method and pharmacokinetic modeling. Applied an UF of 24.	0.06 ppm*
Beckett et al. (2)	Bronchiolar hyperplasia in rats after chronic exposure.	Estimated excess risk using benchmark dose techniques, extrapolated to human equivalent concentration using EPA regional gas dose ratio method and pharmacokinetic modeling. Applied an UF of 8.	0.2 ppm

*The final NIOSH REL was based on human data and the REL derived from animal data is included for comparison (1).

and applied a safety factor equal to the excess risk rate in the exposed group. The observed differences in risk among the epidemiologic-based risk assessments, then, were driven largely by selection of critical data set and method of extrapolation or selection of UF, which underscores the critical importance of these decisions in characterizing occupational risks.

The three animal-based assessments used three different studies as their primary data source. Maier et al. (4) was based on a 6- and 12-week study with fewer animals than the other two, while NIOSH (1) was based on a subchronic (90-day) study and Beckett et al. (2) was based on a 2-year bioassay. In comparing the proposed OELs from Beckett and NIOSH, the approximate factor of 3 difference between them appears to be almost entirely due to a selection of UF of 8 by Beckett and 24 by NIOSH, corresponding to the difference in primary study length. Beckett selected an UF which comprised an animal to human factor of 2.5 for toxicodynamic differences (also called variability in susceptibility) and an interindividual (human) factor of 3.2 for toxicodynamic differences between individuals, which, when multiplied, equals a composite UF of 8. NIOSH, working from the subchronic study, rather than the 2-year bioassay, applied the identical factors with an additional UF of 3 for the extrapolation from a subchronic study to a lifetime study. The Maier et al. (4) study was based on a smaller study combining a 6-week and 12-week dataset, using an UF of 10.

Several factors may have contributed to the observed differences in the risk estimates for diacetyl, including selection of animal-based or worker-based data sets, and there are advantages and disadvantages to using animal data or human data. In animal studies, there is certainty

about the exposures (although typically higher than human exposures), a homogenous population, and few confounding factors to consider. With human data, exposures are estimated in the species of concern to risk assessors (humans), but exposures are often estimated with wide confidence limits and may be confounded by other exposures and other factors that can influence exposures or health effects of concern. In animal-based risk assessments, uncertainty factors are typically applied to account for interspecies and inter-individual differences in susceptibility and when data on metabolism and disposition of a chemical are not available. When human data are available, risk assessors may apply uncertainty factors to measured exposures or conduct regression analyses to extrapolate risks to working lifetime exposures. In the case of diacetyl, NIOSH used the epidemiological data to estimate the risk of changes in lung function beyond the range of the available data to a working lifetime, assuming that chronic exposure to low levels of diacetyl would result in accumulated and persistent damage. In the absence of evidence to the contrary, this health protective assumption impacts how risks are determined. SCOEL used the summary epidemiology data to derive an OEL by extrapolating to 40 years, adjusting the value for a bias in the exposure assessment and dividing by an uncertainty factor of two. In both cases, the extrapolated critical risk estimates were based on exposures well-below the concentration range of the collected exposure data.

Key findings from coffee roasting and packaging investigations

Virji et al. (14) investigated exposure-response relationships using data from cross-sectional exposure and health surveys from 17 coffee facilities. Personal exposures to diacetyl, 2,3-pentanedione, and their sum were assigned to participants using their work history information and a job exposure matrix developed using data from the exposure surveys (8). Exposure metrics calculated included the highest 95th percentile, cumulative, and average exposures. There was variation in the modeling results with different exposure metrics showing statistically significant associations with different measures of respiratory health. Some key findings for the exposure-response analyses were: (1) metrics calculated using a worker's whole work-history in coffee production showed associations with certain health outcomes; (2) increases in the highest 95th percentile exposure metric were associated with decrements in continuous measures of lung function as well as certain categorical health outcomes; (3) average and cumulative exposure metrics were associated only with categorical health outcomes; (4) both diacetyl and 2,3-pentanedione were associated with certain health outcomes, although not always the same ones; (5) the sum of diacetyl and 2,3-pentanedione captured all the significant associations that were observed in separate analyses of each α-diketone. The α-diketone-related respiratory abnormalities occurred in both flavoring and non-flavoring workers, however in the flavoring workers all exposure metric means were numerically higher, the model coefficients were larger, and the associations were more consistent across both α-diketones. Additionally, Harvey et al. (15) described a case of advanced lung disease in a coffee worker who had worked in the flavoring room and coffee grinding area of a coffee facility for a number of years. Although the biopsy findings were not typical of obliterative bronchiolitis, the authors noted that lung pathology may vary in flavoring-related lung disease. Results of full-shift personal air-samples collected in the flavoring and grinding areas on other workers indicated diacetyl levels of 41–421 ppb and 2,3-pentanedione levels of 22–276 ppb – well-above the NIOSH RELs (i.e., an 8 to 84-fold difference for diacetyl and a 2 to 30-fold difference for 2,3-pentanedione).

Potential to close gaps and revisit assumptions?

Given the varied approaches that have been taken in assessing the human health risk of exposure to diacetyl, it is certainly of interest to consider whether the availability of new exposure and health data in real-world settings may reduce uncertainties and inform assumptions.

As noted above, a primary source of divergence between published final, proposed, candidate or recommended OELs for α-diketones stems from the decision to use animal or human data in conducting quantitative risk assessments. When available, the use of high-quality human data is preferable to animal toxicological data in conducting quantitative human health risk assessments. One of the main arguments raised against using observational epidemiologic data in conducting quantitative risk assessments is uncertainties determining causality based on concomitant exposures to other respiratory hazards or other confounding variables, both recognized and unrecognized. However, there is a compelling argument for the use of human data in the derivation of an OEL for diacetyl given the strong and consistent association between diacetyl exposure and adverse respiratory outcomes in epidemiological investigations. In addition, these associations are supported by animal toxicological studies demonstrating a clear dose-response relationship between diacetyl and respiratory morbidity.

Virji et al. (14) demonstrated a statistically significant association between exposure to both diacetyl and 2,3-pentanedione and decrements in lung function and

abnormalities. Of interest, the most consistent associations between exposure to α-diketones (diacetyl, 2,3-pentanedione and the sum of the two) and lung function abnormalities were observed using the highest 95th percentile exposure during the on-average 4-year work-history, which is described by the authors as a surrogate of peak exposures. Nonetheless, evidence is also presented of significant positive associations between both average and cumulative exposures and lung function abnormalities. These results are generally consistent with previous epidemiological findings from exposures to added flavoring chemicals in which workers were exposed to much higher concentrations of diacetyl over longer periods of time. While Virji et al. (14) posit that the lack of associations between forced expiratory volume in one second (FEV_1) or the ratio between FEV_1 and forced vital capacity (FEV_1/FVC) and average or cumulative exposure in their analysis precludes a direct comparison with the analysis presented in the NIOSH criteria document (1), it is worth noting that among flavoring workers, the authors reported negative associations between cumulative exposure to diacetyl, 2,3-pentanedione and their sum, and the percent predicted FEV_1, albeit with a small sample size ($n = 71$).

Quantitative risk assessments for diacetyl have generally assumed that the adverse respiratory effects of exposure to diacetyl are driven by cumulative exposures over a working lifetime. Although NIOSH also recommended short-term exposure limits at levels 5 times the REL to protect against toxicity from 15-min peak exposures, the criteria document highlights the need to better characterize peak exposures, generally defined as brief or intermittent exposures to high concentrations, that may be relevant to human health risk (1). As previously noted, long-term cumulative exposure is generally the most used predictor of risk for chronic health outcomes; however, observed effects may in fact be more directly related to other dose metrics. For example, health effects may be driven in part by unmeasured peaks over time, particularly for chemicals that are metabolized and/or eliminated without overwhelming homeostatic responses at low levels of body burden. In an evaluation of histopathologic changes to the respiratory epithelium of rats following continuous and short-term pulsed exposures to diacetyl designed to result in similar time-weighted average exposures, Hubbs et al. (16) reported similar effects from both exposure regimens, suggesting that additional studies of short-term exposures is warranted. Epidemiologic investigations used to derive the NIOSH REL for diacetyl measured or estimated full shift TWA exposure concentrations, and did not have sufficient data to investigate the extent to which peak exposure concentrations correlate with the observed associations between exposures to α-diketones and adverse health outcomes. However, these investigations and subsequent analyses do provide some evidence that peak exposures may play a role in the associations observed between cumulative exposure to diacetyl and 2,3-pentanedione and respiratory morbidity. These findings are certainly of interest and merit further investigation, though are far from sufficient to substantially alter the current quantitative risk assumptions that health effects are driven by cumulative exposures.

Discussion

To date, the epidemiologic evidence of associations between diacetyl and respiratory morbidity has largely come from occupational exposures to flavoring additives, while associations between 2,3-pentanedione and respiratory outcomes have not previously been evaluated in epidemiologic investigations. In the studies included as part of this research topic on exposures and respiratory health in coffee workers (7), exposures to diacetyl and 2,3-pentanedione from both flavoring and non-flavoring coffee workers have been characterized, offering the potential to inform our understanding of the impact of both diacetyl and 2,3-pentanedione on respiratory morbidity. These peer-reviewed articles represent a significant contribution to the body of knowledge regarding respiratory effects of exposure to relatively low levels of α-diketones emitted naturally from roasting and grinding coffee as well as from added flavoring chemicals in processing flavored coffee. Beckett et al. (2) posits that an OEL as low as 5 ppb is not practical in protecting health, citing studies that have measured higher concentrations of diacetyl as a result of brewing coffee. It would appear that this assertion is based solely on the observation that some individuals are frequently exposed to concentrations at or above the NIOSH REL, while discounting the possibility that over time these exposures may result in small decrements in lung function among some individuals. The health effects resulting from exposures to the relatively low levels of diacetyl observed in these investigations (average and highest 95% percentile personal TWA exposures below 25 and 100 ppb, respectively) have not been extensively or systematically studied. However, the analyses conducted by Virji et al. (14) have provided evidence that exposures to these levels of diacetyl and 2,3-pentanedione emitted (1) naturally from coffee roasting and grinding, and (2) from flavorings added in processing flavored coffee, may be associated on average with small decrements in lung function and further, in at least one case, with clinical disease as described by Harvey et al. (15).

In evaluating how this information might inform quantitative risk assessment of chronic low exposures, it is illustrative to examine the potential impact on the NIOSH risk assessment. In the NIOSH quantitative risk assessment for diacetyl, the risk to an individual worker exposed to the REL over the entirety of their working life is estimated to be 1 in 1,000 for developing an exposure-induced decrement in lung function as defined as an FEV_1 below the 5th percentile (lower limit of normal). Workers exposed for less than working lifetime are predicted to be at lower risk. One difficulty in conducting

occupational epidemiology is when exposure concentrations are near the REL (5 ppb in the case of diacetyl and 9.3 ppb in the case of 2,3-pentanedione), many workers would need to be studied for a very long time to quantitatively describe the risks, which is rarely feasible; therefore, studies with higher exposures are often used to estimate risks. However, when additional epidemiology studies describe dose-rate effects, such as decrements in lung function associated with peak exposures, this information can be used to expand our understanding of the mechanism of toxicity and can provide some insights into what types of exposures may be critical for workers' health. These considerations would similarly inform other quantitative risk assessments based on cumulative exposures to diacetyl.

There will undoubtedly be differences of opinion in the extent to which this information can or should be used to quantify and/or interpret the risks of exposure to diacetyl and 2,3-pentanedione. In our view, the relatively small sample size with concentrations that are limited to the lower range of exposures may prove inadequate to support a full quantitative risk assessment. Further, the presence of both diacetyl and 2,3-pentanedione exposures makes it difficult to combine this dataset with the human data upon which the NIOSH and SCOEL assessments are based, which included only diacetyl exposure. Nonetheless, the insights gained from this research should be of use to occupational health professionals in evaluating and managing risks from exposure to diacetyl and 2,3-pentanedione, alone or in combination, in coffee processing facilities.

Data availability statement

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

Author contributions

DJ proposed the concept and wrote the first draft. CW summarized details of published risk assessments for diacetyl. DJ, CW, and JC-G contributed to defining the scope of the work and designing the article. JC-G summarized key findings from recent investigations of exposures and respiratory endpoints among workers in coffee roasting and packaging facilities. All authors contributed to manuscript revision and review and approved the final submitted version.

Funding

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

Acknowledgments

The authors gratefully thank Kristin Cummings, M. Abbas Virji, John Piacentino, R. Todd Niemeier, and Frank Hearl for their thoughtful and substantive review of the manuscript.

Conflict of interest

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

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The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

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COMMUNITY CASE STUDY
published: 18 May 2022
doi: 10.3389/fpubh.2022.750289

Case Study: Efficacy of Engineering Controls in Mitigating Diacetyl and 2,3-Pentanedione Emissions During Coffee Grinding

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Exposure to elevated levels of diacetyl in flavoring and microwave popcorn production has been associated with respiratory impairment among workers including from a severe lung disease known as obliterative bronchiolitis. Laboratory studies demonstrate damage to the respiratory tract in rodents exposed to either diacetyl or the related alpha-diketone 2,3-pentanedione. Respiratory tract damage includes the development of obliterative bronchiolitis-like changes in the lungs of rats repeatedly inhaling either diacetyl or 2,3-pentanedione. In one flavored coffee processing facility, current workers who spent time in higher diacetyl and 2,3-pentanedione areas had lower lung function values, while five former flavoring room workers were diagnosed with obliterative bronchiolitis. In that and other coffee roasting and packaging facilities, grinding roasted coffee beans has been identified as contributing to elevated levels of diacetyl and 2,3-pentanedione. To reduce worker exposures, employers can take various actions to control exposures according to the hierarchy of controls. Because elimination or substitution is not applicable to coffee production facilities not using flavorings, use of engineering controls to control exposures at their source is especially important. This work demonstrates the use of temporary ventilated enclosures around grinding equipment in a single coffee roasting and packaging facility to mitigate diacetyl and 2,3-pentanedione emissions from grinding equipment to the main production space. Concentrations of diacetyl and 2,3-pentanedione were measured in various locations throughout the main production space as well as inside and outside of ventilated enclosures to evaluate the effect of the enclosures on exposures. Diacetyl and 2,3-pentanedione concentrations outside one grinder enclosure decreased by 95 and 92%, respectively, despite ground coffee production increasing by 12%, after the enclosure was installed. Outside a second enclosure, diacetyl and 2,3-pentanedione concentrations both decreased 84%, greater than the 33% decrease in ground coffee production after installation. Temporary ventilated enclosures used as engineering control measures in this study effectively reduced emissions of diacetyl and 2,3-pentanedione at the source in this facility. These findings motivated management to explore options with a grinding equipment manufacturer to permanently ventilate their grinders to reduce emissions of diacetyl and 2,3-pentanedione.

Keywords: engineering control, coffee, grinding, diacetyl, 2,3-pentanedione

OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Occupational Health and Safety, a section of the journal Frontiers in Public Health

Received: *30 July 2021*
Accepted: *25 April 2022*
Published: *18 May 2022*

Citation:
Stanton ML, McClelland TL, Beaty M, Ranpara A and Martin SB Jr (2022) Case Study: Efficacy of Engineering Controls in Mitigating Diacetyl and 2,3-Pentanedione Emissions During Coffee Grinding. Front. Public Health 10:750289. doi: 10.3389/fpubh.2022.750289

INTRODUCTION

Identification of obliterative bronchiolitis among former workers of a coffee processing facility that roasted, ground, flavored, and packaged coffee (1) prompted a National Institute for Occupational Safety and Health (NIOSH) Health Hazard Evaluation (HHE) at the facility in 2012. Findings from this evaluation of a flavored coffee production facility demonstrated excess shortness of breath and obstruction on spirometry, and respiratory illness was associated with exposure to elevated levels of diacetyl and 2,3-pentanedione in the flavoring room as well as in other areas of the facility where unflavored coffee was produced (2–4). Dissemination of findings from this evaluation prompted the submission of HHE requests by both owners/management and employees from other coffee production facilities requesting assistance in characterizing potentially hazardous exposures. Between 2016 and 2018, NIOSH completed industrial hygiene and medical surveys at 17 such facilities. Worker exposures above the NIOSH recommended exposure limits (RELs) of 5.0 parts per billion (ppb) diacetyl and 9.3 ppb 2,3-pentanedione (5) were measured in coffee roasting and packaging facilities of varying sizes and production volumes during the NIOSH HHEs (6). Grinding roasted coffee beans was a primary activity resulting in elevated worker exposures to diacetyl (6). In addition to diacetyl and 2,3-pentanedione, emissions of other volatile organic compounds and gases such as carbon monoxide can occur during activities in coffee roasting facilities (3, 7–13). NIOSH researchers provided each facility with results from the comprehensive surveys including recommendations based on the hierarchy of controls. We recommended use of engineering controls to protect employees from exposures associated with grinding. However, certain factors such as various production volumes, sizes of the facilities and associated grinding equipment, facility layouts, and levels of automation made it challenging to recommend a "one-size-fits-all" control strategy.

Solutions for controlling exposures usually follow the principles of the hierarchy of controls. NIOSH researchers often recommend the use of engineering controls to protect workers especially in workplaces where it is not possible to physically remove (eliminate) the hazard or replace (substitute) the hazard with an alternative material that is not hazardous or less hazardous. The NIOSH Engineering Controls Program (https://www.cdc.gov/niosh/programs/eng/default.html) works with a variety of partners to reduce exposures by focusing on engineering control recommendations. This group promoted the use of engineering controls for diacetyl and other food flavorings to industry, regulatory agencies, and consensus standard bodies (14) and in 2015 published a best practices engineering control document (15). This NIOSH Best Practices document (15) included specific engineering control and work practice guidance focused on flavoring production industries. Many of the controls used in the coffee flavoring industry involve ventilation to remove the contaminant and introduce replacement air. Specific considerations included ensuring (1) areas where flavorings are used remain under negative pressure relative to rest of space, (2) air from mixing rooms is not recirculated and is exhausted outdoors, (3) use of ventilated enclosures to collect dusts and vapors, (4) correct positioning of local exhaust ventilation (LEV) hoods, and (5) monitoring of workers' exposures to assess effectiveness of the system. Many of the recommendations NIOSH made in their coffee facility HHE reports were consistent with those in the Best Practices guidance. NIOSH also recommended that facilities implement comprehensive respiratory protection programs in the event respirators were needed until effective engineering and administrative controls were in place to keep diacetyl and 2,3-pentanedione exposures below their respective RELs.

The work described herein demonstrates the utility of ventilated enclosures to reduce grinding emissions at one roasting and packaging facility working to implement workplace changes in response to recommendations made by NIOSH.

CONTEXT

NIOSH researchers contacted facilities where earlier HHEs were conducted to assist with development or evaluation of engineering control solutions to reduce worker exposures to diacetyl and 2,3-pentanedione. We were particularly interested in helping companies implement NIOSH recommendations to further enable the knowledge generated during the HHEs to be transferred into practice that could be utilized throughout the industry. This case study describes work performed at one facility interested in controlling emissions released from coffee grinders. The roasting and packaging facility did not produce flavored coffee products, so all diacetyl and 2,3-pentanedione exposures were from naturally produced sources. NIOSH researchers installed temporary ventilated enclosures around two large coffee grinders in this facility to demonstrate the effect of the control strategy to company management. As described herein, large reductions in airborne diacetyl and 2,3-pentanedione concentrations were obtained in nearly all areas of the facility. The reductions in diacetyl and 2,3-pentanedione concentrations provided sufficient evidence for company management to explore options to either isolate or ventilate the coffee grinders permanently.

Work Area

Production activities including roasting, grinding, and packaging took place in an open area ∼48,000 square feet/4,459 square meters. The green bean storage area was separated from the main production space by a wall with openings on each end. Approximately 50,000 pounds (22,679 kg) of whole coffee beans were roasted per day and ∼55,000 pounds (24,948 kg) were ground over the 3-day period. Coffee was ground using three industrial-scale coffee grinders, each capable of grinding 600–700 pounds (272–318 kg) of roasted coffee beans per hour.

Sampling Approach

We divided the main production area into six work areas: green bean storage, roasting, grinding, packaging, product storage, and shipping. General area air samples were collected and analyzed for diacetyl and 2,3-pentanedione at 29 locations during each of the 3 consecutive days. Three samples were collected from

green bean storage, 15 from roasting, 39 from packaging, three from product storage, three from shipping area, and 18 from grinding. Outdoor area samples were collected in two locations to ensure contaminated outside air was not being re-entrained into the workplace. Area sampling equipment was placed at breathing zone height at each location. According to modified OSHA Method 1013/1016, two glass silica-gel sorbent tubes were protected from light and connected in series to a sampling pump operated at a flow rate of 50 milliliters per minute (mL/min) with analysis by gas chromatography/mass spectrometry (16–18). Two consecutive 3-h samples were collected and a time-weighted average (TWA) concentration for the two combined samples was calculated. We assumed the results from the 6-h monitoring period reflected the average diacetyl and 2,3-pentanedione concentration across a full, 8-h work shift. Area samples collected on the 1st day served to establish baseline concentrations throughout the facility. Paired samples were collected at each of the three grinders to allow for sampling inside and outside enclosures. On the 1st day of sampling and for the third grinder, the paired grinding samples represented duplicate samples. After construction of the grinding enclosures for two of the grinders at the end of day one, the paired samples represented one sampler placed inside, and one outside of the enclosure.

Enclosure Construction

After completion of sampling on the 1st day, NIOSH investigators constructed temporary ventilated enclosures around two of the grinders (A and B) using reinforced plastic film and heavy-duty gaffer's duct tape (**Figure 1**). Each enclosure was fitted with two zippers to allow workers access to the grinder equipment to make necessary adjustments throughout the work shift. Exhaust ventilation from each enclosure was provided using an 8-inch (20-cm) diameter axial fan, typical of those used for confined space entry. One fan per enclosure was placed on the floor directly under the coffee grinders. Airflow inside the grinder A enclosure was 345 cubic feet per minute (cfm) [138 air changes per hour] and inside the grinder B enclosure was 330 cfm [126 air changes per hour]. Flexible ductwork was attached downstream of the fan that passed under the plastic enclosure and up to a large roof-top exhaust fan. This arrangement ensured the exhaust from inside the enclosure was released outside of the facility and not recirculated inside the space. **Figure 2** shows a diagram of the grinder enclosure. No enclosure was constructed around the third grinder (C) because of logistical and space considerations. Grinder C was only operated briefly during sampling on the 2nd day and not operated on the 3rd day. All area samples on the 2nd and 3rd days were collected in the same locations as the 1st day.

Data Analysis

We performed analyses using SAS version 9.4 (SAS Institute, Cary, NC), JMP 15.1.0 (SAS Institute Inc., Cary, NC), and Excel (Microsoft®, Redmond, WA). Diacetyl and 2,3-pentanedione concentrations for general area air samples are reported in parts per billion (ppb) by area location. Percent change concentrations at each grinder and by area location were calculated by subtracting the days 2 or 3 result concentration from day 1 and then dividing by the day 1 concentration.

FIGURE 1 | Images of Grinder B **(A)** front view and **(B)** side view on 2nd and 3rd day of sampling with enclosure in place. One sampler was located inside the enclosure and the second sampler was located immediately outside the enclosure. The yellow and black stripes are the zippers to allow employee access and the yellow flexible tube is a ventilation duct.

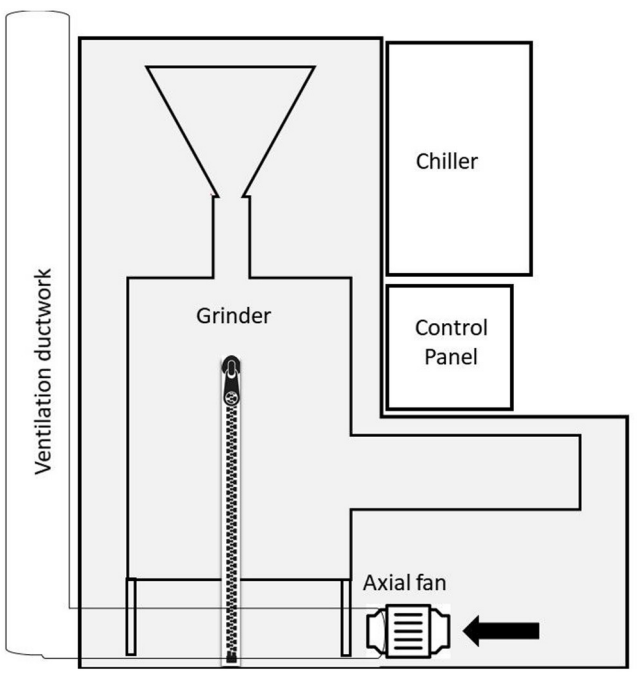

FIGURE 2 | Schematic of ventilated enclosure design. The grinder equipment was enclosed depicted by area shaded in light gray. Both the chiller and control panel were located outside the enclosure. Each enclosure had two zippers to allow access. One axial fan per enclosure was placed on the floor under grinder equipment and connected to ventilation ductwork that was exhausted through the roof.

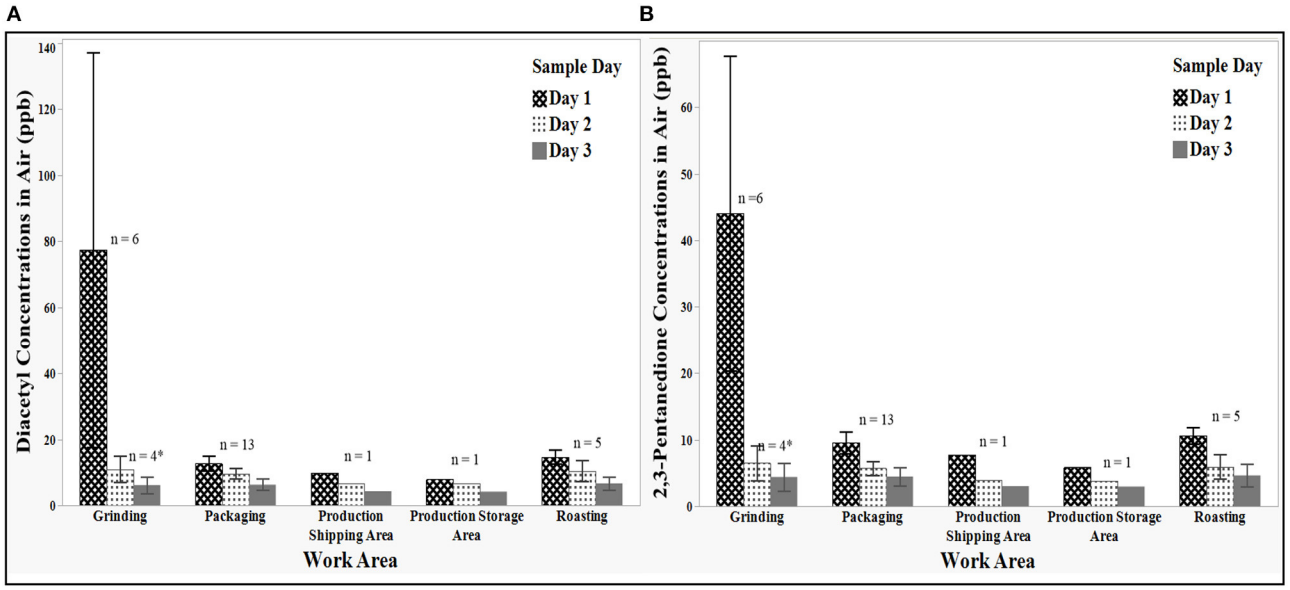

FIGURE 3 | Mean concentrations of diacetyl **(A)** and 2,3-pentanedione **(B)** by sample day and work area. Error bars represent the standard deviation. *After enclosure, the grinding mean concentration on Days 2 and 3 did not include the sample inside the two grinding enclosures.

RESULTS

Diacetyl and 2,3-Pentanedione Concentrations by Work Area

Twenty-nine area samples were collected on the 1st day prior to construction of the grinder enclosures to establish baseline concentrations throughout the main production area. Samples on the 2nd and 3rd day were collected in the same locations with ventilated enclosures around two of the three large grinders. Diacetyl and 2,3-pentanedione concentrations by day are shown in **Figure 3**.

On the 1st day of sampling, mean diacetyl concentrations were the highest in the grinding area at 77.4 ppb (range: 32.5–171.3 ppb). Compared to the grinding area, mean diacetyl concentrations were much lower in the other areas such as in roasting at 14.7 ppb (range: 12.7–17.7 ppb) and packaging at 12.7 ppb (range: 9.6–17.2 ppb). The mean diacetyl concentration in the production shipping area was 9.9 ppb and in the production storage area was 7.9 ppb.

Concentrations of 2,3-pentanedione followed a pattern similar to that of diacetyl on the 1st day of sampling. The highest 2,3-pentanedione concentrations were in grinding at 44 ppb (range: 26.6–87.1 ppb). In the roasting area, the mean 2,3-pentanedione concentration was 10.6 ppb (range: 9.1–12.3 ppb) and in packaging area the mean concentration was 9.6 ppb (range: 7.3–12. 5 ppb). The mean 2,3-pentanedione concentration in the production shipping area was 7.8 ppb and in the production storage area was 5.9 ppb.

On the 2nd day of sampling, diacetyl concentrations decreased in all sampling areas except in green bean storage area where there was a slight increase from 0.9 ppb on the 1st day to 1.0 ppb. The highest diacetyl concentrations were reported in grinding area at 10.9 ppb (range: 6.5–15.3 ppb) and roasting area at 10.5 ppb (range: 6.5–14.0 ppb). The third highest concentration was in packaging at 9.6 ppb (range: 7.1–14.1 ppb). The mean concentration in the production storage area was 6.7 ppb and in the production shipping area was 6.6 ppb.

Concentrations of 2,3-pentanedione on the 2nd day of sampling also decreased in all sampling areas except in green bean storage. The highest 2,3-pentanedione concentration was in grinding at 6.5 ppb (range: 3.9–10.0 ppb). The mean 2,3-pentanedione concentrations in roasting and packaging were similar at 6.0 ppb (range: 3.7–8.2 ppb) and 5.7 ppb (range: 4.3–8.7 ppb), respectively. The 2,3-pentanedione concentration was 4.0 ppb in the production shipping area and 3.8 ppb in the production storage area.

Concentrations of both diacetyl and 2,3-pentanedione continued to decrease on the 3rd day of sampling. Unlike the 1st and 2nd days of sampling, the highest mean diacetyl concentration on the 3rd day was in roasting at 6.6 ppb (range: 4.0–8.8 ppb). Diacetyl concentrations were slightly higher in packaging at 6.3 ppb (range: 2.8–9.0 ppb) than in grinding at 6.1 ppb (range: 3.0–8.3 ppb). The concentration of diacetyl was 4.3 ppb in the production shipping area and 4.2 ppb in the production storage area.

Concentrations of 2,3-pentanedione on the 3rd day trended with diacetyl. Unlike the 1st and 2nd days of sampling, the highest mean 2,3-pentanedione concentration on the 3rd day was in roasting at 4.6 ppb (range: 2.5–6.5 ppb), followed by packaging at 4.5 ppb (range: 1.7–6.2 ppb) then grinding at 4.4 ppb (range: 2.0–6.6 ppb). The concentration of 2,3-pentanedione was 3.0 ppb in both the production shipping area and in the production storage area.

TABLE 1 | Diacetyl and 2,3-pentanedione concentrations in parts per billion (ppb) inside and outside Grinder A & B enclosures.

Location	Diacetyl concentration (ppb)			2,3-pentanedione concentration (ppb)		
	Day 1* No enclosure	Day 2	Day 3	Day 1* No enclosure	Day 2	Day 3
Inside Grinder A enclosure	134.3	721.2	590.2	56.1	335.1	441.2
Outside Grinder A enclosure	171.3	15.3	8.3	87.1	10.0	6.6
Inside Grinder B enclosure	38.1	907.2	418.8	26.6	429.6	303.1
Outside Grinder B Enclosure	51.3	12.9	8.0	35.2	7.0	5.5

One sample collected per day at each location (n = 1 per cell).

**As there was no enclosure on day 1, the inside and outside samples represent duplicate samples. Samples were placed in the same locations once the enclosures were introduced.*

Concentrations of diacetyl and 2,3-pentanedione were lowest in the green bean storage area ranging from 0.9 to 1.0 ppb and < 0.3 to 0.5 ppb, respectively. These results were not shown in **Figure 3**.

Concentrations Inside and Outside of Temporary Grinder Enclosures

Concentrations of diacetyl and 2,3-pentanedione inside and outside of the temporary grinder enclosures are shown in **Table 1**. On the 2nd day of sampling, the concentration of diacetyl inside the grinder A enclosure was 721.2 ppb and the concentration immediately outside the enclosure was 15.3 ppb. The concentration of 2,3-pentanedione inside the grinder A enclosure was 335.1 ppb and the concentration immediately outside the enclosure was 10.0 ppb. At grinder B, the diacetyl concentration inside the enclosure was 907.2 ppb and the concentration immediately outside the enclosure was 12.9 ppb. The 2,3-pentanedione concentration inside the grinder B enclosure was 429.6 ppb and directly outside of the enclosure was 7.0 ppb. At grinder C (no enclosure), diacetyl concentrations from the two side-by-side samples were 6.5 and 8.7 ppb and 2,3-pentanedione concentrations were 3.9 and 5.2 ppb.

On the third day of sampling, the diacetyl concentration was 590.2 ppb and 2,3-pentanedione was 441.2 ppb inside the grinder A enclosure. Immediately outside the grinder A enclosure diacetyl was 8.3 ppb and 2,3-pentanedione was 6.6 ppb. At grinder B, diacetyl inside the enclosure measured 418.8 ppb and 2,3-pentanedione measured 303.1 ppb with 8.0 ppb diacetyl and 5.5 ppb 2,3-pentanedione immediately outside. At grinder C, the diacetyl concentration was 3.0 and 5.2 ppb and 2,3-pentanedione concentration was 2.0 and 3.5 ppb at the two side-by-side samplers on the 3rd day of sampling.

Production Volumes and Percent Change in Diacetyl and 2,3-Pentanedione Concentrations

Total pounds of coffee roasted on the 2nd and 3rd days of sampling were comparable (within 4% compared to day 1). The amount of coffee packaged per day varied by only 8% across the 3 days. The total amount of coffee ground each day showed more variability, largely because of the limited use of grinder C. In total, 12% more coffee was ground on the 2nd day but 67% less on the 3rd day, compared to the 1st day. Compared to the 1st day, grinder A ground 58% more coffee on the 2nd day and 12% more on the 3rd day. The percent changes in diacetyl and 2,3-pentanedione concentrations and production volumes are shown in **Table 2**. Compared to day one, the diacetyl concentration measured just outside the grinder A enclosure showed a 91% decrease on the 2nd day and a 95% decrease on the 3rd day. Concentrations of 2,3-pentanedione decreased by 89% on the 2nd day and by 92% on the 3rd day. Compared to the 1st day, grinder B ground 349% more coffee on the 2nd day and 33% less coffee on the 3rd day. Diacetyl concentrations just outside the grinder B enclosure were reduced by 75% on the 2nd day and by 84% on the 3rd day. Concentrations of 2,3-pentanedione decreased by 80% on the 2nd day and by 84% on the 3rd day. Grinder C ground 73% less coffee on the 2nd day and no coffee at all on the 3rd day, with decreases in diacetyl concentrations of 78 and 88% and 2,3-pentanedione concentrations of 84 and 91% on the 2 days, respectively.

TABLE 2 | Percent change in diacetyl and 2,3-pentanedione concentrations and production volumes across sampling days.

Location	% Change Days 1 to 2		% Change Days 1 to 3	
	Diacetyl/2,3-pentanedione	Production volume	Diacetyl/2,3-pentanedione	Production volume
Outside Grinder A enclosure	−91/−89	+58	−95/−92	+12
Outside Grinder B enclosure	−75/−80	+349	−84/−84	−33
Grinder C (no enclosure)*	−78/−84	−73	−88/−91	−100

**Paired sample results were averaged in calculation.*

Impact of Enclosure in Other Areas

Overall concentrations of diacetyl and 2,3-pentanedione decreased in all sampled areas within the production space after the temporary ventilated enclosures were constructed (**Figure 4**). Diacetyl concentration reductions ranged from 15% in production storage to 33% in production shipping. For 2,3-pentanedione, concentration reduction ranged from 35% in production storage to 49% in the production shipping area.

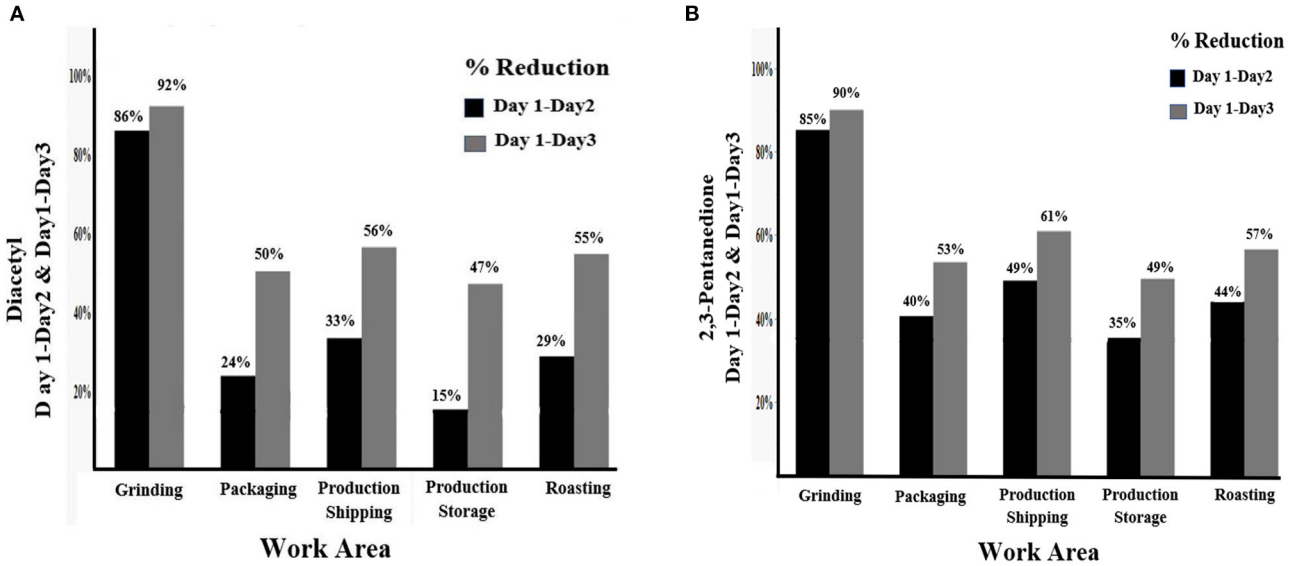

FIGURE 4 | Percent reduction in mean concentrations of **(A)** diacetyl and **(B)** 2,3-pentanedione by work area between Days 1 and 2 and Days 1 and 3.

Both diacetyl and 2,3-pentanedione concentrations had higher reductions from days 1 to 3 than from days 1 to 2. Diacetyl concentration reductions ranged from 47% in production storage to 56% in production shipping. 2,3-Pentanedione concentration reductions ranged from 49% in production storage to 61% in the production shipping area.

DISCUSSION

Grinding is a prominent activity at many coffee roasting and packaging facilities. NIOSH HHE investigations identified the activity of grinding as one of the main sources of emissions for alpha-diketones such as diacetyl and 2,3-pentanedione from both flavored and unflavored coffee that could contribute to worker exposures (6). Controlling exposures typically follows the five-step hierarchy of controls: elimination, substitution, engineering controls, administrative controls, and personal protective equipment. For coffee roasting and packaging facilities, elimination and substitution are typically not feasible because diacetyl and 2,3-pentanedione occur naturally in coffee and are generated during activities such as grinding and roasting. However, elimination and substitution of exogenous flavorings is a possible approach to limiting diacetyl and 2,3-pentanedione exposure related to the addition of flavorings. For this case study, we explored the use of engineering controls including enclosure and LEV at grinding machines as a method to reduce exposure in unflavored coffee production. Sampling results from the 1st day showed diacetyl concentrations at grinders were 5–10 times higher and 2,3-pentanedione concentrations were 4–7 times higher than in other areas of the production facility. Temporary enclosures constructed on two of three large grinders at this facility demonstrated that isolating grinders from the surrounding production space and exhausting that air directly outside can result in meaningful reductions in diacetyl and 2,3-pentanedione concentrations in air throughout the workplace and not just close to the enclosed grinders. The temporary enclosures used in this case study were constructed using plastic sheeting and duct tape, and exhaust ventilation was not optimized. Permanent, well-designed grinder enclosures with appropriate ventilation systems would likely result in more pronounced reductions in airborne alpha-diketone concentrations. To that end and based on the results of this evaluation, management at the facility communicated a desire to incorporate grinder enclosures aimed at reducing worker exposures.

Like previous studies utilizing ventilation control measures, this study measured substantial reductions in inhalational exposures to diacetyl and 2,3-pentanedione concentrations after installing ventilated enclosures. Fransman et al. created a database called the Exposure Control Efficacy Library (ECEL) that included 433 records from 90 peer-reviewed publications to examine efficacy values for six measures (i.e., enclosure, LEV, specialized ventilation, general ventilation, suppression, and worker separation) (19). In their analyses, enclosure and general ventilation had the lowest efficacies at 50 and 43%, respectively, while specialized ventilation and LEV had greater estimated efficacies at 87 and 82%. In the enclosure demonstration presented here, we measured reductions in diacetyl of 92% at the grinders and 79% in the overall production area and for 2,3-pentanedione 90% at the grinders and 77% in the overall production area.

Reductions in airborne diacetyl and 2,3-pentanedione concentrations throughout the plant were substantial after the grinders were enclosed although several factors were not controlled that could make the enclosure performance better than demonstrated here. As discussed, enclosures were

constructed using simple plastic sheeting and duct tape. Although these materials permitted for easy and relatively quick construction, they did not allow for a completely sealed enclosure. Permanent enclosures should be specially designed according to grinder size, shape, and location in the production space, and employee access needs. The ventilation from the temporary enclosures was not optimized. The exhaust from each enclosure was simply the amount of air each fan could move with the ductwork attached and extended to the ceiling exhaust fan. This ventilation scheme was able to keep the enclosures under substantial negative pressure when the zippers were closed. However, it allowed substantial concentrations of diacetyl and 2,3-pentanedione to build up inside the enclosures that could put grinding personnel at substantial risk for exposure upon entry. Permanent enclosures could be designed with the exhaust flow necessary to maintain lower airborne concentrations. It is not clear whether those concentrations could be maintained low enough that workers would not have to wear respiratory protection when inside the enclosure.

This case study aligns with the NIOSH mission of preventing occupational illness by reducing exposures through controlling hazards in the workplace following the Prevention through Design Initiative (20). We were able to engage with company management to explore options for controlling an exposure and demonstrate the utility of process enclosure. Lessons learned during this exercise can be built upon to develop more permanent solutions designed specifically to control emissions in this industry.

Limitations

The temporary enclosures were difficult for employees to enter, and interior space was limited making it hard to maneuver inside to make grinder adjustments. To gain access to the grinders, employees had to unzip the access zipper from the floor until the opening was large enough to enter; ultimately releasing high levels of diacetyl and 2,3-pentanedione into the larger production space, which likely resulted in higher concentrations in these compounds for other area samples taken in the plant. The number of times or length of time the enclosures were opened was not recorded during our sampling so we do not know the impact opening the enclosures may have had on other areas. Grinder operators were observed wearing air purifying half-face respirators fitted with organic vapor cartridges. Although we did not measure personal exposures, depending on concentrations within the enclosure and the amount of time an employee accessed the enclosure, a half-face respirator may not have been sufficient to reduce a 15-min time-weighted average exposure to below the short-term exposure limits for diacetyl or 2,3-pentanedione. The grinders were located on one side of the packaging areas but were not located directly beside each other. Each grinder was slightly different in their input and outlet points. The overall contaminant concentrations throughout the facility likely varied depending on which grinders were operating and for how long. Not being able to construct an enclosure around grinder C limited the ability to assess the full impact of having all the grinders enclosed. However, not having the third enclosure more than likely had a limited effect on results because grinder C was operated sparingly on the 2nd day and did not operate on the last day of sampling. Another limiting variable during this study was not having control of most coffee processing and packaging activities that occurred in the plant during sampling; daily production activities may have increased or decreased the air concentrations measured in this study. Concentrations of diacetyl and 2,3-pentanedione within coffee roasting and packaging facilities are subject to production levels and can vary daily or by time of year such as during holidays when production levels may be greater. Sampling for this scenario was only done for 3 days, which provided a limited number of samples. The results of this study are specific to this worksite and subject to the operating conditions during the 3 days of sampling.

CONCLUSION

To our knowledge, this study was the first attempt to demonstrate the impact of using ventilated enclosures to remove grinder emissions in a coffee roasting and packaging facility. This project clearly showed that controlling airborne concentrations of diacetyl and 2,3-pentanedione released during coffee grinding substantially reduced emissions into the workplace. Controlling hazardous emissions at the source using ventilated enclosures was an effective means of reducing alpha-diketone emissions into the facility where workers could be exposed. These results motivated management to explore options with a grinding equipment manufacturer to permanently ventilate their grinders to reduce emissions of diacetyl and 2,3-pentanedione. This work highlights the utility of a research-to-practice intervention that could be considered at other coffee roasting and processing facilities interested in controlling emissions during coffee grinding.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because, due to restrictions imposed under the US privacy act and the limitations of what participants consented to, the data underlying the analyses presented, beyond what is provided in the paper, are confidential and not available to researchers outside the National Institute for Occupational Safety and Health (NIOSH). For more information about NIOSH's policy regarding sensitive data, see https://www.cdc.gov/niosh/ocas/datahandle.html. Requests to access the datasets should be directed to MS, zfc5@cdc.gov.

AUTHOR CONTRIBUTIONS

MS, TM, MB, and SM designed the study, collected the samples, analyzed the data, and prepared the manuscript. AR analyzed the

samples and assisted with preparation of manuscript. All authors approved the article for publication.

FUNDING

This work was supported by the National Institute for Occupational Safety and Health (NIOSH).

ACKNOWLEDGMENTS

The authors thank the company for allowing us access and for their continued collaboration. The authors would also like to thank the NIOSH Respiratory Health Division's Organics Laboratory staff for samples analyses and acknowledge Aleks Stefaniak and Matt Duling for their review of the manuscript.

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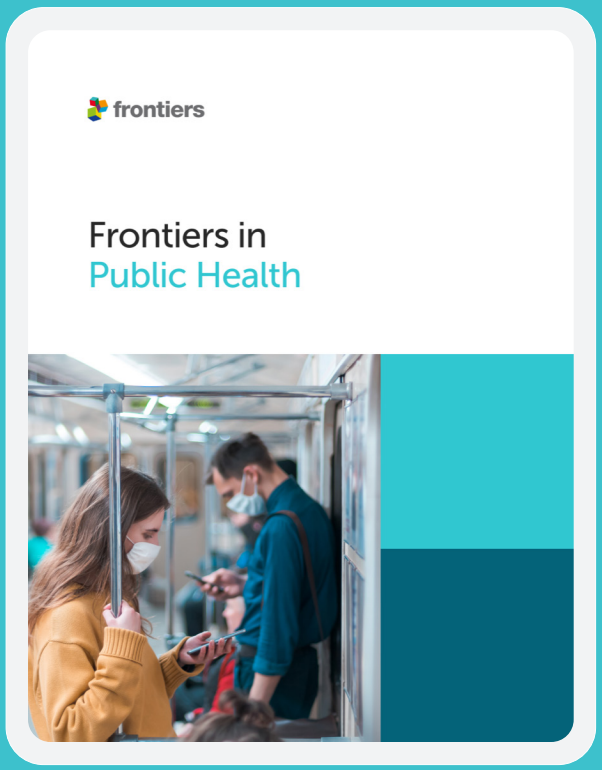

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