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The Adverse Health Effects of Air Pollution from Sugarcane Burning: A Scoping Review of Observational and Experimental Evidence

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Background: Sugarcane burning is an agricultural practice that is implemented to increase sugar yields. However, sugarcane burning produces air pollutants associated with adverse health outcomes. This review summarizes the current knowledge of the defined exposures and health effects associated with sugarcane burning and identifies research gaps.

Methods: A scoping review was conducted using PubMed, Scopus, and Web-of-Science to identify peer-reviewed literature on health and exposure investigations associated with air pollution from burning sugarcane. Studies were eligible if they included both an air pollution measurement and a health outcome assessment in human workers and surrounding communities or animal studies associated with sugarcane burning.

Results: A total of 24 studies passed our inclusion criteria, including 19 observational and five experimental studies. All observational studies were conducted in Brazil or the United States with the majority focused on respiratory (65%, 15/24), cardiovascular (13% 3/24), and renal (13%, 3/24) health outcomes. The most frequently assessed air pollutants were particulate matter [with aerodynamic diameter $\leq 2.5\ \mu m$ ($PM_{2.5}$) and with aerodynamic diameter $\leq 10\ \mu m$ (PM_{10})] and total suspended particulates (TSP). Of the observational studies, 42% (8/19) were prospective cohorts, and 58% (11/19) employed an ecological design and applied variable exposure assessment methods. The experimental studies all used rodent models with varied exposure routes and pollutants.

Discussion: This review supports a well-documented link between air pollution from sugarcane burning and adverse health effects in workers and neighboring communities with respiratory, renal, and cardiovascular health effects; however, several knowledge gaps were identified, including the need for expansion of studies geographically, application of more advanced exposure science to characterize and quantify sugarcane emission components, probing of emerging health effects (i.e., kidney disease) and associated biomarkers, and evaluation of vulnerable populations that neighbor sugarcane operations. Furthermore, pairing exposure measurements and health assessments in the same study would increase our knowledge and better inform policies to improve the health of workers and communities impacted by sugarcane burning. https://doi.org/10.1289/EHP14456

Introduction

Exposure to air pollution is one of the major causes of premature mortality globally and significantly contributes to the development of chronic diseases, especially in lower-middle-income countries (LMICs).[1,2] Air pollution is a complex mixture of particles, chemicals, and gases that are emitted from natural and anthropogenic sources. The combination of solid particles and liquid droplets, commonly referred to as particulate matter (PM), is highly linked to several negative health outcomes. Emissions from the agricultural sector are an important source of air pollution worldwide,[2] with the global food system accounting for $\sim 22.4\%$ of mortality attributed to poor air quality in 2018.[3] The combustion of crop residues, including sugarcane, has been identified as an important contributor to agricultural emissions in varied geographical regions.[2]

Sugarcane is among the world's most important and highly produced commodities, second only to cereal production.[4] Brazil, India, and mainland China are the top three sugarcane-producing countries.[4] The main byproducts of the sugarcane plant are cane tops, bagasse, filter mud, and molasses, which have many end-uses as components of sugar, rum, biogas, paper, ethyl alcohol, yeast, and citric and acetic acids, among others.[5] The use of sugarcane for bioethanol production has received significant attention because it replaces fossil fuels or petroleum-based gasoline for powering motor vehicles.[6]

The growing season for sugarcane varies by location but generally ranges from 10 to 16 months.[7,8] Typically, harvesting occurs once per year by either burnt cane or green cane harvesting.[9] Burnt cane harvesting entails setting the field on fire and burning off excess leafy material before harvest.[9] This process is reported to maximize sugar recovery at the mill, reduce transportation costs, and diminish the need for pest control.[9,10] Green cane harvesting is usually performed with mechanical harvesters that separate the sugarcane leaves and tops from the sugar-bearing stalk.[9] The purported benefits of this approach include improvements in water and soil conservation, weed control, and reduction in pollutant emissions.[9] Burnt harvesting has been discontinued in many parts of the world due mainly to health concerns associated with air quality impacts. However, it is still practiced in many of the top producing sugarcane producing countries, including India and the US. More than 50% of sugarcane harvesting operations in the US still rely on burnt harvesting methods.[9–11]

Compared with other types of plant-based food production in the US, recent estimates indicate that particulate matter with aerodynamic diameter $<2.5\ \mu m$ ($PM_{2.5}$) emissions from sugarcane production contribute the largest mortality burden to humans as a result of the burning process.[12] Interestingly, the estimated health impacts of sugarcane emissions to both animals and humans have been largely based on the contribution of PM of various size fractions, most commonly $PM_{2.5}$[13–19] and particulate matter with aerodynamic diameter $<10\ \mu m$ (PM_{10}),[18,20–23] whereas few studies have probed the role of other pollutants (e.g., gases) in associated health outcomes.

Burning sugarcane releases a mixture of elemental and organic carbon, minerals, particulates, and gaseous pollutants into the air.[24] Some of the most common air pollutants include fine and

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coarse PM, aluminum, silicon, manganese, potassium, sulfur, benzopyrene (BaP) and other polycyclic aromatic hydrocarbons (PAHs), trace metals, and several gasses, such as carbon monoxide, carbon dioxide, and methane.[25] The health outcomes associated with exposure to these pollutants as a result of sugarcane burning have been primarily linked to the respiratory system, such as asthma, lung cancer, and hospitalization requiring inhalation therapy.[25–28] Recent epidemiological data suggest a link between exposure to air pollution from sugarcane burning and acute renal dysfunction,[16] which may contribute to the growing focal epidemics of chronic kidney disease of unknown etiology (CKDu) in sugarcane workers, globally.[29–31] Much of the research aimed at understanding the health impacts of exposure from burning sugarcane emissions through inhalation has focused on workers during harvest and nonharvest seasons. Exposures have included organically formed complex emissions and select components of air pollution. For example, data show that workers are exposed to as much as 56,000 silicate fibers$/\mathrm{m}^3$ and a three-fold increase in PM levels during harvesting compared to nonharvest seasons.[9,32] In another example, increased PAH levels in ambient air during sugarcane harvesting in Brazil have been associated with an increased cancer risk.[32]

Over the past decade, there have been several excellent reviews on the health effects associated with the sugarcane industry.[33,34] This scoping review was performed to determine the current state of knowledge on exposures to air pollution emissions from sugarcane burning and the linkage with adverse health outcomes so that we may better understand the long-term health impacts. Distinct from other reviews, our approach focused on studies that contained both an exposure measurement and addressed a health outcome in the same study. Furthermore, we included as our populations of interest sugarcane workers and neighboring communities. The findings from this review would help to inform future areas of research, methodological approaches, and health promotion practices for critical stakeholders.

Methods

A literature review was performed on the exposure to air pollution emissions from sugarcane burning (biomass burning) and the associated adverse health effects. With the variability in the literature concerning the types of pollutants, health effects studied, and methodological approaches used, we employed a scoping review. By definition, a scoping review includes broad search strategies by design while fostering reproducibility, transparency, and reliability of the current literature.[35] Therefore, the 5-stage framework proposed by Arksey and O'Malley and supplemented by Levac et al.[35–37] was employed which included the following steps:

1. Identification of the research questions
2. Identification of relevant studies
3. Selection of relevant and reliable studies
4. Data extraction and charting
5. Collecting, summarizing, and reporting the findings

Research Questions

This review aims to synthesize the current state of knowledge on the exposure assessment and health effects associated with air pollution emissions from the practice of sugarcane burning. The following research questions were proposed: What data has contributed to our current understanding of the exposure–response relationship between air pollution derived from burning sugarcane and the associated adverse health outcomes *a*) within the same study design and *b*) in workers and surrounding communities? What scientific advancements have been made in the field? What research gaps still remain?

Identification of Relevant Studies

We identified journals, abstracts, dissertations, reports, and conference proceedings up to May of 2024 to obtain a full scope of the work. Peer-reviewed literature published in English were identified using a systematic search from three electronic bibliographical databases, Scopus, PubMed (Medline), and Web of Science (WoS). These databases were utilized due to their global scope of work and inclusion of journals from important sugarcane-producing counties like Brazil and China. The subject–action–outcome framework, a method taught through the University of Florida's Health Science Library, was used to develop our full search strategies (Table S1). Our initial process to refine our search terms is described in detail in the supplemental data section and includes search terms (Table S2). Briefly, the search terms included the following: "Sugarcane" OR "Sugar cane" OR "cane" AND "burn" OR "Smoke" OR "Ash" OR "pm" OR "Particulate matter" OR "air poll*" OR "Environmental toxins" OR "Bagasse Ash" OR "emission" OR "Environmental Dust." Additional terms were added to this core group of terms that were relevant to four organ systems defined as respiratory ("pulmonary" OR "respiratory" OR "Asthma" OR "COPD" OR "Chronic Obstructive Pulmonary Disease" OR "restrictive lung disease" OR "Pneumonia" OR "Acute Respiratory Illness" OR "Inhalation therapy" OR "Lung Cancer" OR "allerg"), renal (Acute Kidney Injury" OR "Hypertension" OR "Chronic Kidney Disease" OR "Nephritis"), cardiovascular ("cardio" OR "heart" OR "Hypertension" OR "High Blood Pressure"), and other ("Disease" OR "Infection" OR "health" OR "illness" OR "Risk Factor" OR "occupational effect" OR "health risk" OR "genotoxicity" OR "carcinogen" OR "hazard"). Tailored Boolean search terms and operator terms were employed to the defined databases and identified in article titles and abstracts (Table S3).

Selection of Relevant Studies

Two reviewers (A.M. and K.C.) experienced in air pollution and occupational health and safety research, screened the articles during the selection process. The reviewers independently screened the title and abstract of each article for mentions of a health-related outcome and/or an exposure outcome related to sugarcane burning. In the instance of disagreement on an article, both reviewers discussed their rationale and if a disagreement persisted, the article was included in the full screening process. This was done to address any uncertainties. Exclusion and inclusion criteria were set for the full screening process. Human and animal (*in vivo*) studies were included if a health assessment measurement and an air pollution measurement related to sugarcane burning were identified. Animal studies were included if they clearly linked their exposure to an air pollutant (dose) directly associated with air pollution from sugarcane burning and measured a health outcome as described in the study. Animal and human studies allowed us to characterize the health effects from exposure to air pollution from sugarcane burning in organisms by simulating real-world exposure scenarios that sugarcane workers and neighboring communities receive. In the case of animal studies, this was evaluated under controlled settings. Having both a health assessment measurement and an exposure measurement within the same study helped to strengthen our understanding of exposure–response relationships between pollutants from sugarcane burning and adverse health outcomes. Of note, all forms of air pollution measurements were included, including ground-level, spatial interpolation, and satellite remote sensing measurements. Studies were excluded if they met any of the following criteria: the study only addressed either a health outcome or air pollution measurement but not both, the full text was not available in English, review articles and book chapters, and articles that exclusively used an *in vitro* approach. *In vitro* studies were excluded as the goal of this scoping review was to focus on whole organism exposures and effects, although we refer to *in vitro* works, highlighting their importance in supporting mechanistic studies, in the discussion.

Data Extraction and Charting

The data were extracted by each reviewer and combined and organized into a Microsoft Excel file. Extracted information included authors, publication title, year published, location where study was performed, population of focus, study design, health outcomes, anatomical systems explored, methods for evaluating health outcomes, biomarkers measured, exposure assessment methods, pollutants measured, and a summary of key findings. Separate tables were developed to calculate the number and type of pollutants; type of air monitoring employed, including specific equipment; clinical biochemistry blood markers; and blood, ocular, and urinary biomarkers (Table S4–S7). Data were summarized and charted using GraphPad Prism 10.2.2.

Summarizing and Reporting Findings

PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) guidelines were followed, and descriptive characteristics were used to summarize and report the findings.[35,38] An analysis of the final set of studies that passed inclusion criteria was performed to classify the number of studies that were observational and experimental. Trends in the findings and identification of methodologies employed were noted. Health outcomes were thematically synthesized for each of the following organ systems: respiratory, renal, cardiovascular, and others, and populations studied qualified as workers or surrounding communities or both. Exposure findings included reference to the exposure type, source, concentration, and timing.

Results

The search through three electronic bibliographical databases (PubMed: 134, Scopus: 603, and WoS: 299) yielded 1,036 total articles that had their titles and abstracts analyzed, with 672 articles being selected after removing all duplicates ($n = 364$). A total of 101 full texts were retrieved after meeting the abstract and title-relatedness criteria (Figure 1). Of these, 77 articles were excluded due to missing health outcome data ($n = 31$), missing air pollution measurements ($n = 28$), missing both exposure and health outcome measurements ($n = 10$), being a review article ($n = 4$) or book chapter ($n = 1$), failure to find the full text ($n = 2$), and failure to find a complete English translation ($n = 2$). In total, 24 peer-reviewed articles remained for further analysis.

General Description of the Studies

The 24 articles span the timeframe from 1994 to January 2024, with more than half of the papers ($n = 16$) published during the past ten years. All studies focused on sugarcane burning in Brazil ($n = 20$) and the US ($n = 4$). Nineteen studies were observational in design (Table 1), whereas only five studies were considered experimental and consisted of controlled rodent exposures (Table 2). Of the observational studies, 11 were considered ecological, with the remaining eight being cohort studies. More than 34 air pollutants were studied across the reports, including individual toxicants and aerosols generated from burned sugarcane materials (Figure 2A). These included sugarcane ash (2/34), other aerosols (1/34), sugarcane smoke (2/34), gasses [sulfur dioxide (SO_2) (1/34), ozone (O_3) (2/34), and nitrogen oxides (NO_x) (3/24)], and particulates and fibers [asbestos (1/34),

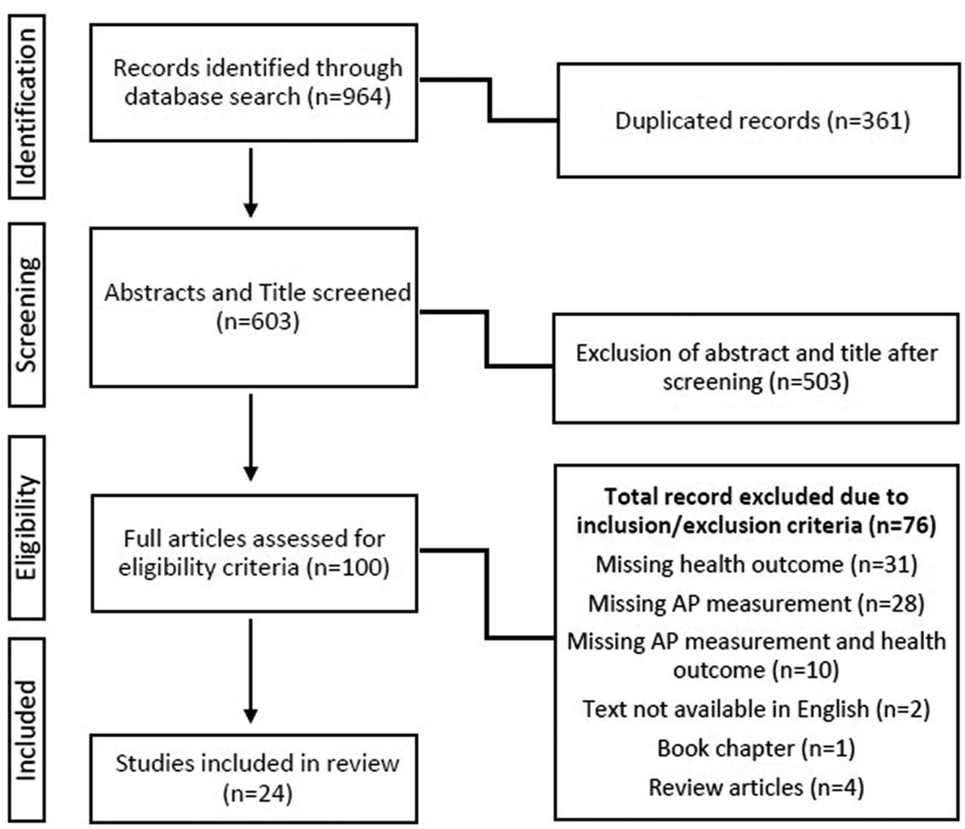

Figure 1. PRISMA-ScR flow chart of the article selection process. AP, air pollution; PRISMA-SrC, Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

Table 1. Complete list of the search terms used in the scoping review. All terms were searched with the operator term for [title/abstract].

Subject	Action	Outcome: Respiratory	Outcome: Renal	Outcome: Cardiovascular	Outcome: Other
"Sugarcane"	"Burn*"	"Pulmonary*"	"Acute Kidney Injury"	"Heart*"	"Disease"
"Sugar cane"	"smoke"	"Respiratory*"	"Chronic Kidney Disease"	"Cardio*"	"Infection"
"Cane"	"Ash*"	"Asthma"	"Nephritis"	"Hypertension"	"Health*"
	"PM*"	"COPD"	"Renal*"	"High Blood Pressure"	"illness"
	"Particulate matter"	"Chronic Obstructive Pulmonary Disease"			"Risk Factor"
	"Air poll*"	"Restrictive lung disease*"			"Occupational*"
	"Environmental toxins"	"Pneumonia"			"Health risk*"
	"Bagasse Ash"	"Respiratory Function"			"genotoxicity"
	"Emission*"	"Acute Respiratory Illness"			"Carcinogen*"
	"Environmental Dust"	"Inhalation therapy"			"hazard"
		"Lung*"			
		"allerg*"			

Note: COPD, chronic obstructive pulmonary disease; PM, particulate matter; *, truncation operator. Truncation (wildcard) operators are used to include alternative forms of the word.

silica (2/34), black carbon (1/34), PM_{10} (4/34), total suspended particulates (TSP) (5/34), $PM_{2.5}$ (10/34), and trace metals (1/34)]. Five anatomical systems of interest (Figure 2), including respiratory (63%, 15/24), cardiovascular (13%, 3/24), renal (13%, 3/24), reproductive (8%, 2/24), and others (4%, 1/24) were identified (Figure 2B). A total of 11 articles included the study of people/communities other than workers (i.e., children).

Geographical Locations of Observational Studies

All of the observational studies investigated air pollution exposure and its effects on sugarcane workers in Brazil and the US, with Brazil being the most highly represented ($n = 17$). All of the studies were conducted in Brazil in São Paulo State. The Brazilian studies consisted of seven prospective cohorts[15–19,41,44] and 10 ecological studies.[13,14,17,20–22,26–28,39,43] Four of these studies performed a time-series analysis.[22,26,27,43] The ecological studies investigated the population of the municipalities of Araraquara ($n = 4$),[26–28,43] the entire state of São Paulo ($n = 2$),[13,39] pregnant women in the state of São Paulo ($n = 2$),[20,21] adults and the elderly with cardiovascular disease in Presidente Prudente ($n = 1$),[22] and children and the elderly in Piracicaba ($n = 1$).[14] The cohort studies that included sugarcane workers were in an undisclosed location in São Paulo state ($n = 4$),[16,17,19,44] Mendonça ($n = 2$),[15,18] and Cerquilho ($n = 1$).[41] Two observational studies were conducted in the US, including a health impact assessment[40] and one cohort study.[42] The ecological health impact assessment focused on the general population of 20 counties in South Florida, including those found in the sugarcane growing region (SGR).[40] The prospective cohort study focused on sugarcane workers in Hawaii.[42]

Exposure Assessment Methods

Observational studies. The prospective cohort studies evaluated air pollution exposure from sugarcane burning using personal exposure monitoring ($n = 3$)[17,42,44] and stationary monitoring methods ($n = 5$).[15,16,18,19,41] Personal exposure assessments included the following three approaches: *a*) $PM_{2.5}$ measurements were performed for 2 days during the preharvest season and 3 days during the harvesting periods[44]; *b*) work-shift measurements of biologicals, silica, and asbestos[42]; and *c*) work-shift measurements of $PM_{2.5}$ for 2 to 3 days during both harvest vs. nonharvest periods.[17] Personal exposure monitoring was performed using a DustTrak 8533 air monitor[17,44] and passive sampling with a filter at the breathing zone (Table S7).[42]

Exposure assessments with stationary air monitors employed in the prospective cohort studies consisted of five different approaches that included: *a*) $PM_{2.5}$ for 6 h per day for three consecutive work shifts during harvesting and nonharvesting periods[41]; *b*) daily sampling of $PM_{2.5}$ and PM_{10} for 15 consecutive days during harvest and nonharvest periods during April, July, September, and October[16]; *c*) nonconsecutive daily average measurements of ambient $PM_{2.5}$ collected during the harvesting season and 35 consecutive days during the nonharvesting season[18]; *d*) three 6-h periods for three consecutive days during the harvest period and the cutting and weeding of nonburnt sugarcane in the nonharvest period[19]; and *e*) daily measurements of ambient $PM_{2.5}$ at a sugarcane field and urban residence.[15] Exposure monitoring was performed using a DustTrak 8520,[15,19,41] an ill-defined DustTrak monitor,[18] and one study did not describe the device used for air monitoring (Table S7).[16] Each ecological study used various ambient air pollution measurement approaches to assess sugarcane burning exposure ($n = 11$). These assessments consisted of seven distinct approaches including: *a*) modeled daily ambient PM_{10}, nitrogen oxide, and ozone ($n = 2$)[20,21]; *b*) monthly average of aerosol optical depth ($n = 1$)[39]; *c*) monthly measurements of $PM_{2.5}$, SO_2, and total suspended particles ($n = 1$)[24]; *d*) daily measurements of total suspended particles (TSP) ($n = 3$)[26,27,43]; *e*) daily measurements of total smoke particles ($n = 1$)[28]; *f*) daily measurements of PM_{10} and NO_2 ($n = 1$)[22]; and *g*) daily measurements of $PM_{2.5}$, PM_{10}, and trace metals ($n = 1$).[14] Ambient air pollutant monitoring was performed using stacked filter units,[14] plastic receptacles with 1.5 L of water,[28] ground-level government-operated monitors,[13,20,22,40,21] Energetica's Handi-Vol sampler,[26,27,43] remote sensing data,[20,21,39] and satellite data (Table S7).[40]

Experimental studies. The experimental studies evaluated the toxicity to rodents of different air pollutants associated with sugarcane burning aerosols (PM_{10},[23] TSP,[45] silica nanoparticle (SiNPs),[46] smoke,[47] and sugarcane ash[48]) through three distinct exposure routes, including nasal instillation,[23,45,48] whole-body inhalation,[47] and oropharyngeal aspiration.[46] The exposure periods ranged from acute (1–14 d single dose) to subchronic (30–90 d) based on US Environmental Protection Agency (EPA) definitions of repeated or continuous exposure by inhalation routes.[49] Exposure regimens consisted of 1-d exposure[45]; twice a week for 13 wk[46]; 5 d per week for 13 wk[48]; continuous daily exposure for 1 d, 7 d, and 21 d[47]; and daily for 7 d.[23] Four studies employed Wistar rats, whereas one study used BALB/c mice (Table 3).

In the study that used BALB/c mice, the animals were exposed to 15 µg (1µg/1µl) TSP in distilled water intranasally.[45] The TSP samples were collected from ambient air sampling in Araraquara, Brazil on days when sugarcane burning occurred. In another study, Wistar rats were exposed to suspended PM_{10} intranasally for 7 days.[23] To generate the particulates, PM_{10} was captured onto paper filters (10-µm pore) by burning sugarcane residue in a custom-designed oven that operated with a vacuum pump.[23] Ten-gram portions of the sampling filters were suspended in 100 mL 0.9% NaCl

Table 2. Descriptive characteristics of observational (human) studies ($n = 19$).

Citation	Year	Location	Population	Methods	Anatomical system	Major exposure findings	Major health findings
Cançado et al.[14]	2006	State of São Paulo, Brazil (Piracicaba)	Elderly individuals (65 years of age and older) and children (under 13 years of age) from the population of Piracicaba who were admitted to the hospital for respiratory diseases between April 1997 and March 1998	Ecological study	Respiratory	Increase mean levels of PM_{10}, $PM_{2.5}$, black carbon, aluminum, silicon, potassium, manganese, and sulfur by two to four-fold during the sugarcane burning season compared to the nonburning season.	The increase in rates of all-cause respiratory hospital admissions in children and the elderly during the harvesting season is higher compared to the nonharvesting season.
Uriarte et al.[13]	2009	State of São Paulo, Brazil	Elderly individuals (60 years of age and older) and children (10 years of age or younger) who accessed a hospital system in São Paolo State for respiratory disease in 2010	Ecological study	Respiratory	Burning of sugarcane fields lead to greater concentrations of pollutants associated with fires such as smoke, $PM_{2.5}$, and TSP (<50 mm).	Municipalities with >50% of land use for sugarcane had a percentage of hospital cases attributed to current fires increased to 15% and 12% for elderly and children, respectively.
Paraiso and Gouveia[39]	2015	State of São Paulo, Brazil	Population of 345 municipalities in São Paulo State in 2010	Ecological study	Respiratory	—	An increase in the number of points of burning outbreaks and hospitalizations for respiratory diseases for children under 5 years old.
Nowell et al.[40]	2022	Florida, United States	The Population in Broward, Charlotte, Collier, Miami-Dade, DeSoto, Glades, Hardee, Hendry, Highlands, Indian River, Lee, Manatee, Martin, Monroe, Okeechobee, Osceola, Palm Beach, Polk, St. Lucie, and Sarasota	Health impact assessment (ecological study)	Respiratory	Growing regions experienced elevated levels of $PM_{2.5}$ during harvest compared to other regions in Florida, which experienced a reduction in $PM_{2.5}$ levels during the harvest season and when compared to the nonharvest season. Sugarcane fires were estimated to contribute up to $1.0\ \mu g/m^3$ to the annual mean $PM_{2.5}$ concentration.	$PM_{2.5}$ produced by sugarcane fires across 20 counties in south Florida was estimated to contribute to 2.5 deaths per year, 0.16 death per year in the sugar-growing region. Sugar growing region has a 0.4 death per 100,000 individuals per year compared to 0.04 deaths per year in South Florida.
Arbex et al.[28]	2000	State of São Paulo, Brazil (Araraquara)	Patients who received inhalation therapy from two medical systems in Araraquara.	Ecological study	Respiratory	Positive exposure–response for a two-day moving average of sediment weight.	Dose-dependent relationship between the weight of smoke sediment and inhalation therapies.
Arbex et al.[26]	2007	State of São Paulo, Brazil (Araraquara)	Individuals who were admitted to the hospital for asthma in Araraquara main hospital from 23 March 2003 to 27 July 2004	Ecological time-series study	Respiratory	Mean TSP concentrations were twice the value during the burning period compared to nonburning.	Increases in TSP concentrations are associated with asthma hospital admissions. Positive exposure–response for TSP concentrations for a 2-day to 7-day moving average and a positive lag response from 0 days until 7-day lag.

Table 2. (*Continued.*)

Citation	Year	Location	Population	Methods	Anatomical system	Major exposure findings	Major health findings
Arbex et al.[27]	2014	State of São Paulo, Brazil (Araraquara)	Individuals who visited the emergency department for pneumonia in one of the main hospitals in Araraquara from 1 February 2005 to 31 July 2007	Ecological time-series study	Respiratory	TSP concentration was 2.5 times higher during the burning period than during the nonburning period. Temperature was negatively correlated with TSP concentrations for both periods.	Positive association with increases in TSP concentrations and pneumonia emergency department visits (PEDV). Acute effect on PEDV that began on the day of exposure and continued for 2 days. Positive effects on PEDV for a 2-day cumulative exposure
Prado et al.[18]	2012	State of São Paulo, Brazil (Mendonça)	The study included healthy, nonsmoking males 20 to 40 years of age, comprising 113 sugarcane workers and 109 individuals from the general population	Longitudinal cohort study	Respiratory	Exposure to $PM_{2.5}$ is significantly greater for both groups during the harvesting season ($23.5\ \mu g/m^3$ urban and $61\ \mu g/m^3$ sugarcane plantation).	Sugarcane workers and residents experienced an increased incidence of respiratory symptoms during the harvesting season, with the incidence being greater for sugarcane workers. Lung function scores decreased for both groups during the harvesting season. Urinary 1-hydroxylysine, a PAH metabolite, is 11 times greater in sugarcane workers during the harvest seasons. Sugarcane workers experience increased MDA levels and decreased antioxidant enzyme activity during the harvesting season.
Trevisan et al.[17]	2019	State of São Paulo, Brazil	67 sugarcane workers with no preexisting chronic lung diseases	Longitudinal cohort study	Respiratory	The period of 3 months into the harvest season is characterized by the highest concentration of $PM_{2.5}$ ($111.5\ \mu g/m^3$), compared to 6 months ($63.2\ \mu g/m^3$) into the season and nonharvesting ($27.0\ \mu g/m^3$) in the field of sugarcane.	Sugarcane workers have a higher prevalence of rhinitis symptoms and increased IL-6 concentrations in nasal lavage. The prevalence of rhinitis symptoms was greatest at 3 months (53.4%) compared to 6 months (20%) and nonharvesting (26.7%).
Goto et al.[41]	2011	State of São Paulo, Brazil (Cerquilho City)	30 male sugarcane workers between the ages of 21 and 45 irrelevant of smoking status	Longitudinal cohort study	Respiratory	Concentrations of $PM_{2.5}$ were greater in the farm area during harvesting ($87.00\ \mu g/m^3$) compared to nonharvesting ($50.00\ \mu g/m^3$).	Sugarcane harvesting after biomass burning is associated with alteration to nasal mucus properties, impairments of nasal physiological parameters, and is harmful to the upper airways.

Table 2. (*Continued.*)

Citation	Year	Location	Population	Methods	Anatomical system	Major exposure findings	Major health findings
Leite et al.[33]	2018	State of São Paulo, Brazil	78 male sugarcane cutters between the ages of 18 and 60 years old, who worked a previous harvest season	Longitudinal cohort study	Respiratory	The median and interquartile ranges of $PM_{2.5}$ concentrations were increased during the harvesting period [101.8 (31.0–139.50 $\mu g/m^3$) when compared to preharvesting 27.0 (23.0–33.0 $\mu g/m^3$)].	Exposure to sugarcane burning is associated with reduced plasmatic and urinary CC16. There is an increase in inflammatory blood biomarkers and a decrease in RBC over long-term exposure and after a work shift.
Sinks et al.[42]	1994	Hawaii, United States	355 sugarcane workers from two sugarcane plantations on the islands of Maui and Hawaii	Longitudinal cohort study	Respiratory	Workers are exposed to biogenic silica fibers (BSF) primarily during harvesting. More than 80% of the fibers measured had physical dimensions that pose the greatest risk of asbestosis and lung cancer.	Age and time working in the sugarcane industry were associated with pleural plaques and decreases in the mean FEV1 percent and FEV1/FVC ratio. The study did not find a relationship between BSF exposure and fibrotic lung disease or adverse respiratory health in sugarcane workers in Hawaii.
Arbex et al.[43]	2010	State of São Paulo, Brazil (Araraquara)	Individuals who were admitted to the hospital for hypertension in Araraquara main hospital from 23 March 2003 to 27 July 2004	Ecological time-series study	Cardiovascular	Twice the concentrations of TSP were found during the burning period compared to the nonburning period.	Increases in ambient TSP concentration caused by sugarcane burning are associated with hypertension-related hospital admissions, with the greatest effects present at 1-day and 2-day lag exposure periods.
Pestana et al.[22]	2017	State of São Paulo, Brazil (Presidente Prudente)	Adults (19 years of age or older) who were admitted to the hospital for cardiovascular disease in Presidente Prudente from January 2009 to December 2012	Ecological time-series study	Cardiovascular	The average NO_2 concentration (113.11 $\mu g/m^3$) exceeded the WHO acceptable daily limit.	Same-day exposure to elevated NO_2 levels increases the risk of hospitalization for all adult CVD patients.
Barbosa et al.[19]	2012	State of São Paulo, Brazil	28 healthy Caucasian males between the ages of 18 and 50 years old who worked in a sugarcane and ethanol mill	Longitudinal cohort study	Cardiovascular	$PM_{2.5}$ concentrations were higher during the harvesting period.	Exposure to physical overload, hot conditions, and $PM_{2.5}$ changes during the harvest period are related to changes in cardiovascular and blood biomarkers in sugarcane workers that pose a risk for the development of CVD.

Table 2. (*Continued.*)

Citation	Year	Location	Population	Methods	Anatomical system	Major exposure findings	Major health findings
Santos et al.[16]	2015	State of São Paulo, Brazil	28 randomly selected males from a group of 112 sugarcane workers between the ages of 19 and 39 years old	Longitudinal cohort study	Renal	$PM_{2.5}$ values were (median and IQR) 61 (41–87) $\mu g/m^3$ at the sugarcane plantation versus 24 (11–39) $\mu g/m^3$ in the city during the harvest.	Burnt sugarcane harvesting caused both an acute and significant decrease in the eGFR and an increase in serum Cr that were compatible with acute kidney injury in healthy male workers. Sugarcane workers reported having greater frequent cramps during the harvesting season (39.3%) when compared to the nonharvesting period (7.1%).
Rangel and Vogl[20]	2019	Brazil	Expecting mothers from 13 sugar-growing municipalities resulting in 287,506 live singleton births	Ecological study	Reproductive	Fires that occur upwind differentially increase PM_{10} and O_3.	Late-pregnancy smoke exposure decreases birth weight, gestational length, and *in utero* survival. Dose–response relationship between pollutants from fires and adverse birth outcomes even at low pollution levels.
Rangel and Vogl[21]	2016	Brazil	Expecting mothers from 13 sugar-growing municipalities resulting in 287,506 live singleton births	Ecological study	Reproductive	Fires that occur upwind differentially increase PM_{10} and O_3.	The causal pathway from smoke exposure in the last 3 months of gestation to reduced birth weight and increased risk of fetal death. Dose–response relationship between pollutants from fires and adverse birth outcomes even at low pollution levels.
Matsuda et al.[15]	2020	State of São Paulo, Brazil (Mendonça)	Sugarcane workers ($n = 78$) and residents ($n = 32$) of adjacent towns that were healthy adult males between 19 and 44 years old	Longitudinal cohort study	Sensory	Temperature and $PM_{2.5}$ levels were higher in the sugarcane field (61.00 $\mu g/m^3$) than in the town after the harvest (21.00 $\mu g/m^3$). In the town area, $PM_{2.5}$ was significantly higher after the harvest season (21.00 $\mu g/m^3$) when compared to prior to the harvesting season (8.0 $\mu g/m^3$).	Sugarcane harvesting is associated with abnormalities in mucus quality and content and changes in mucin mRNA on the ocular surface.

Note: —, no data; BSF, biogenic silica fibers; CC16, Clara cell secretory protein 16; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; FEV1, forced expiratory volume in 1 s; FEV1/FVC ratio, ratio of force expiratory volume in 1 s over the forced vital capacity; IQR, interquartile rage; MDA, malondialdehyde; PEDV, pneumonia emergency department visits; $PM_{2.5}$, particulate matter ≤ 2.5 μm in diameter; PM_{10}, particulate matter ≤ 10 μm in diameter; RBC, red blood cell; serum Cr, serum creatinine; TSP, total suspended particulates.

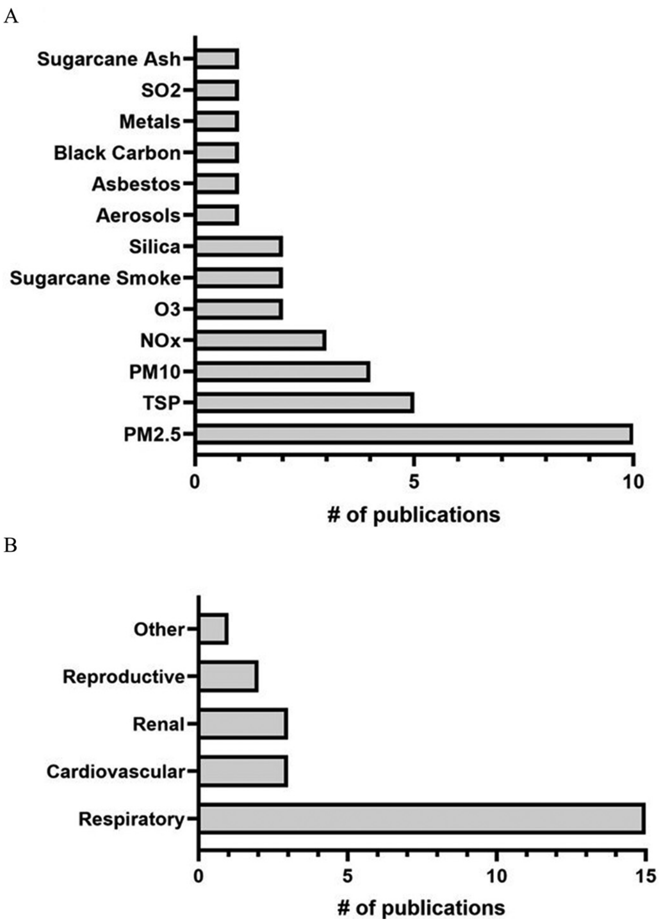

Figure 2. The number of publications that evaluated (A) distinct pollutants and (B) health effects associated with anatomical systems (Tables S3 and S4). $PM_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 µm; PM_{10}, particulate matter with aerodynamic diameter ≤ 10 µm; TSP, total suspended particles.

and then sonicated for 20 min and refiltered using a 10-µm porous membrane.[23] In a separate research study, Wister rats were exposed for 2 h to residual inhalation of a continuous stream of smoke generated in an incineration chamber for 1, 7, or 21 d to represent the subchronic exposure workers receive during the harvesting season.[47] The smoke was generated by burning 200 g of sugarcane straw in a portable combustion chamber with an extraction device that provided a steady stream of aerosols to the animals (whole body exposure).[47] The third study with Wistar rats exposed them to SiNPs. The animals received 200-nm or 300-nm particles suspended in distilled water twice a week for 13 wk by oropharyngeal aspiration.[46] The SiNPs used were synthesized by nanoComposix (San Diego, CA).[46] The final animal study exposed Wistar rats intranasally to 5 mg of sugarcane ash in 100 µl of Millipore water 5 d a week for 13 wk.[48] The ash was collected from a sugarcane field in Leon, Nicaragua.[48]

Health Outcomes

Respiratory effects. Longitudinal studies concluded that sugarcane workers experience an exacerbation of symptoms and increased medical diagnoses related to the respiratory system. A higher incidence of symptoms was reported in workers during sugarcane harvest seasons that included wheezing, coughing, sneezing, and breathlessness.[17,18,42] Abnormal diagnosis included lower lung function scores,[18] abnormal radiographs,[42] and decreased mucociliary clearance and nasal mucus properties.[41] The study by Sinks et al.[42] showed a lack of association between the development of fibrotic lung disease or adverse respiratory function in workers exposed to biological silica fibers and asbestos; however, those who worked for more than 10 years experienced lower lung function scores.[42]

Ecological studies that did not stratify by age concluded that, in general, enhanced air pollution attributed to sugarcane burning is associated with increases in respiratory hospital admissions and mortality and exhibited a time-lagged exposure–response relationship. Arbex et al.[28] concluded that for every 10 mg of sediment weight increase in ambient air from sugarcane burning during the harvesting season, there was a 9% higher risk for inhalation therapy which increased to 20% when the sediment data was stratified by quartiles. A follow-up report found a positive exposure–response association between TSP concentrations and asthma hospital admissions with a lagged exposure–response effect from 0 d until 7 d and cumulative exposures ranging from 0 to 7 d.[26] An increase of $10\,\mu g/m^3$ in TSP concentrations in a 7-d cumulative exposure period represented twice the effect observed on the day of the increase and the day after.[26] Similarly, higher ambient TSP concentrations during the sugarcane harvesting period compared to the nonburning period in Araraquara were associated with a 70% increase in pneumonia-related emergency department (ED) visits and a 6% increase in pneumonia-related ED visits for a 2-d cumulative exposure period.[27] In Florida, modeled ground-level $PM_{2.5}$ concentrations were highest in the sugarcane growing region (SGR) compared to counties outside of these areas.[40] Additionally, $PM_{2.5}$ produced by sugarcane burning was estimated to contribute to 0.4 deaths per 100,000 individuals per year in the SGR compared to 0.04 deaths per year in nonSGR in South Florida.[40]

Several studies suggested that children and the elderly are at the highest risk for adverse respiratory outcomes when exposed to sugarcane burning emissions. Cançado et al.[14] supported this by demonstrating that increases in $PM_{2.5}$ ($10.2\,\mu g/m^3$) and PM_{10} ($42.9\,\mu g/m^3$) associated with sugarcane burning were associated with an increased rate of hospital admissions for respiratory issues in children by 21.4% and in the elderly by 31.03%. In another study, municipalities in São Paulo state with >50% of their land allocated to sugarcane harvesting had an increased predicted rate of hospitalizations by 15% and 12% for the elderly and children, respectively.[13] An ecological study found that the standard mortality ratio for hospitalization for respiratory diseases in children under five was higher by 0.0008% during sugarcane burning for each increment of a point of burning outbreak.[39]

The experimental animal studies showed that exposure to various components of burned sugarcane caused pulmonary inflammation, cellular changes, and tissue damage in the respiratory system. Sugarcane ash was associated with the reduction of subadjacent conjunctive tissue in the trachea, lung inflammation, and reduction of alveolar spaces in exposed rats.[23] In another study, rats exposed to daily (2 h) smoke emissions from burning sugarcane straw (200 g) for 7 days showed enhanced pulmonary inflammation, whereas a longer exposure (21 d) led to angiogenesis in the lung parenchyma, necrosis of the trachea and lung tissues, and collagen deposition in tracheal tissues, findings commonly associated with fibrosis.[47] BALB/c mice exposed to suspended particulates from sugarcane burning via intranasal instillation experienced an increased fraction area of alveolar collapse and polymorphonuclear (PMN) cell influx into the lung parenchyma.[45] This study found similar respiratory effects from traffic-derived particles and biomass burning but concluded that biomass burning was more toxic, as it produced more significant increases in respiratory mechanics based on increased resistive/airway pressure.[45] An increase in restrictive pressure occurs when the difference between peak and plateau pressure expands and if severe enough can limit

Table 3. Descriptive characteristics of experimental (animal) studies ($n = 5$).

Citation	Year	Animal model	Particulate source	Exposure delivery method and dose	Exposure timeframes	Anatomical system evaluated	Major exposure findings	Major health findings
Ferreira et al.[23]	2014	Young Wistar rats	Burned sugarcane residue suspension	Intranasal exposure of a 10-g portion of air sample filtered in 100 mL of 0.9% NaCl	Daily exposure for 7 days	Respiratory	The chemical composition of the ashes from sugarcane residue (PM_{10} suspension) contained phenolic and organic compounds (PAH).	It affected alveolar space and induced an inflammatory response mediated by cytokines.
Matos et al.[47]	2017	28 male Wister rats weighing 250–300 g	Smoke generated through burning sugarcane straw	Residual inhalation of 200 g of burnt sugarcane straw	2-h Continuous daily exposure for 1, 7, and 21 days	Respiratory	—	Exposure to emissions from sugarcane burning was associated with increased inflammation in the trachea and lung tissue and noted lung parenchyma, alveolar, vascular, and bronchiolar changes. Tissue fibrosis was noted in the trachea in the rodents exposed for 21 days.
Mazzoli-Rocha et al.[45]	2008	29 female BALB/c mice weighing 25–30 g	Ambient TSP from Araraquara and São Paulo during the burning season	Intranasal exposure, 15 μg (1 μg/1 μl)	1-day exposure	Respiratory	Particulates from TSP collected during sugarcane burning contained higher metal contents of Fe, Zn, Ni, Mn, Pb, Co, Cd, and Cr than traffic-derived particulates. PAH concentrations were lower from the biomass-derived TSP when compared to traffic-derived TSP.	Significant increase in alveolar collapse, the influx of PMN cells in the lung parenchyma, and increased mechanical parameters. Histology demonstrated acute respiratory inflammation.
Sasai et al.[46]	2022	30 male Wister rats that weighed between 150 and 200 g.	Synthesized by a private firm (nanoComposix)	Oropharyngeal aspiration of 4 mg of 200-nm or 300-nm SiNP in 150 μl of distilled water	Twice a week for 13 weeks	Renal	Chemically digested sugarcane ash collected from sugarcane fields showed that most nanoparticles fell in the 200- to 300-nm range.	Interstitial inflammation in the kidneys is associated with tubular injury and reduction in kidney function. The absence of exposure after 13 weeks did not halt the progression of kidney disease, with significant tubulointerstitial fibrosis developing at 26 weeks. SiNPs were elevated in the urine, suggesting that they pass through the lungs and to the kidney inducing tubular injury and inflammation. Damage caused by SiNPs was only found in the lung and kidneys, with no changes to the spleen and liver.

Table 3. (*Continued.*)

Citation	Year	Animal model	Particulate source	Exposure delivery method and dose	Exposure timeframes	Anatomical system evaluated	Major exposure findings	Major health findings
Roncal-Jimenez et al.[48]	2024	24 Male Wistar rats weighing 400–450 g	Sugarcane ash was collected from Nicaraguan sugarcane field	Intranasal exposure of 5 mg of ash distilled in 100 µl of Millipore water	Five days a week for 13 weeks	Renal	5 mg of sugarcane ash contained about 3.34 mg of silica nanoparticles.	SINP from sugarcane ash was found in the lungs, spleen, liver, and kidneys of exposed rodents. Exposure to sugarcane ash caused low-grade kidney injury characterized by segmental glomerulosclerosis, proximal tubular injury, and chronic tubulointerstitial fibrosis. Kidney injury progress after exposure was terminated.

Note: —, no data; Cd, cadmium; Co, cobalt; Cr, chromium; Fe, iron; Mn, manganese; Ni, nickle; PAH, polycyclic aromatic hydrocarbon; Pb, lead; $PM_{2.5}$, particulate matter <2.5 µm in diameter; PM_{10}, particulate matter <10 µm in diameter; PMN, polymorphonuclear leukocytes; SiNP, silica nanoparticles; TSP, total suspended particulate; Zn, zinc.

airway exchange. Elevated airway pressure can be associated with asthma,[50] a condition that has been linked to inhalation of pollutants found in burned sugarcane.[51]

Silica nanoparticles (SiNPs), component materials of sugarcane burning, were evaluated for their toxicity in rats exposed for 26 wk.[46] Results confirmed lung lesions in the bronchioles with the accumulation of vesicle-filled macrophages consistent with a granuloma, along with local fibrosis, focal areas of inflammation (CD68-positive macrophages), and fibrosis (collagen type III stain). These rats also presented with myofibroblast infiltration, increases in CD68-positive cells, and significant fibrosis in the lungs.[46]

Respiratory biomarkers. Sugarcane workers demonstrated increased levels of oxidative stress and inflammatory biomarkers in blood,[18,44] decreased serum antioxidant enzyme activity,[18] elevated interleukin-6 (IL-6) concentrations in nasal lavage,[17] reduced red blood cell count,[44] and plasmatic and urinary Clara cell protein [Clara protein 16 (CC16)][44] in the harvest period when compared to the nonharvest period. Higher levels of inflammatory [IL-6, IL-1α, IL-1β, interferon gamma (IFN-γ), CC16, C-reactive protein (CRP), neutrophils, and eosinophils] and oxidative stress [creatine kinase (CK), CC16, and malondialdehyde (MDA)] biomarkers were noted in both human and animal models exposed to sugarcane-related compounds compared to those unexposed, indicating the potential for injury or inflammation of the airways.[17,18,23,44,45,47] One study found significant increases in cytokines IL-1α, IL-1β, IL-6, and IFN-γ in lung and trachea tissue from exposed young Wistar rats compared to unexposed.[23] The studies that analyzed human samples also found higher IL-6 and, in addition, IL-4 in nasal lavage. There were higher levels of MDA and CC16 in urine and increased levels of CRP, CK, and immune cell profiles (neutrophils, eosinophils, monocytes, and lymphocytes) in blood samples.[17,18,44]

Cardiovascular effects. Changes in ambient TSP concentration caused by sugarcane burning was associated with a greater incidence of hospital admissions for hypertension, with the most significant effects present at 1-d and 2-d lag exposures.[43] Acute exposure to elevated NO_2 levels associated with sugarcane burning was significantly associated with an increased risk of hospitalization due to cardiovascular disease (CVD) in adults (20–60 years of age) and a greater risk in older adults (>60 years of age).[22] The longitudinal study noted that changes in ambient $PM_{2.5}$ levels, physical overload, and other environmental conditions posed a risk to the development of CVD.[19] Greater serum levels of blood biomarkers, including CK, glutathione peroxidase (GPx), and glutathione transferase (GST), and higher values of clinical outcomes, including 24-h systolic blood pressure, rest-to-peak diastolic blood pressure, and increased sympathetic nerve activity, were observed in male sugarcane workers during harvest in Brazil.[19]

Renal effects. One prospective cohort study found that burnt sugarcane harvesting was associated with an acute and significant decrease in the estimated glomerular filtration rate (eGFR) and increase serum creatinine (Cr) across a work shift during the harvesting season (Figure 3).[16] These two biomarkers have been used to assess kidney function and to diagnose CKDu.[52] Additionally, white blood cells, that included neutrophils, lymphocytes, and monocytes, were higher post-shift male sugarcane workers and can also be compatible with acute kidney injury (AKI).[16] One of the animal studies showed exposure to 200-nm and 300-nm SiNPs, that are morphologically similar to sugarcane-derived silica fibers, caused interstitial inflammation in the kidneys indicating tubular injury along with reduced kidney function.[46] The second animal study using a rodent model demonstrated that exposure to sugarcane ash led to low-grade kidney injury with pathological changes in the kidney, including focal glomeruli with segmental glomerulosclerosis

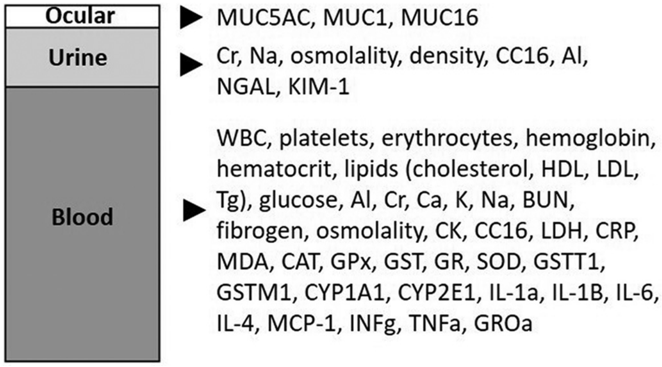

Figure 3. A list of all the biomarkers explored by each type of biospecimen (Table S6).

as well as tubulointerstitial inflammation and fibrosis.[48] Additionally, silica accumulation was found in the lungs, kidney, spleen, lung, and liver of exposed rats.[48]

Other effects. This review identified two other systems that may be adversely affected by exposure to pollutants generated from sugarcane burning that include the sensory and reproductive systems. The study that focused on the sensory system found that sugarcane workers had significantly lower levels of neutral mucus in goblet cells of the bulbar and tarsal conjunctiva and higher expression of MUC5AC, MUC1, and MUC16 when compared to resident of adjacent towns preharvest and after harvest.[41] MUC5AC serves to protect the eye, and MUC1 and MUC16 indicate a greater demand for membrane-associated mucin 24 (Figure 3).[41] The reproductive study noted a strong dose–response relationship between pollutants from fires in sugarcane-rich regions and adverse birth outcomes (low birth weight, prematurity, prenatal hospital admission, stillbirths, and postpartum mortality) even at low levels of PM_{10}, NO_2, and O_3.[20] Another report by the same group identified a causal pathway between smoke exposure in the last 3 months of gestation to reduced birth weight, shorter gestation, and increased risk of fetal death.[21]

Discussion

Global sugarcane production has almost reached 2 billion tons annually.[34] Burning sugarcane as a part of the harvesting process is widely practiced;[26] however, major sugar-producing countries, including Brazil[33] and Thailand,[53] are phasing out or have banned sugarcane burning based on reported pollution and health risks. Research supporting the association between exposure to air pollution from sugarcane burning practices has primarily focused on populations in Brazil and accounted for 83% (20/24) of the studies examined in this review, of which half were published before burnt harvesting was banned in 2017 in São Paulo State.[54] Only four studies (20%, 4/24) focused on US populations despite the high production of sugarcane in Florida, Louisiana, and Texas, which covers nearly 1 million acres.[55] The Americas account for over half (51.2%) of sugarcane production globally, followed by Asia (40.8%,) Africa (5.7%), and Oceania (2.4%).[4] No studies relevant to other major sugarcane-producing countries, including India, China, Thailand, and Central America[4] were identified, likely due to our inclusion criteria that both an exposure measurement and health outcome evaluation was required of each study. A number of studies addressed either a health outcome ($n = 31$) or exposure measurements ($n = 28$), which may have captured a few articles from these regions. These data highlight the lack of research studies that address both measures, indicating a need for more studies that attempt to define the exposure–response relationship of air pollution from sugarcane burning and adverse health outcomes in key geographic regions.

Studying and documenting the health effects of workers and agricultural communities of other primary sugarcane-producing countries would significantly contribute to our understanding of similarities and differences in associated health impacts. This can promote the adoption of green cane harvesting practices that will potentially help to reduce the burden of disease in sugarcane workers and neighboring communities. In the US, it has been shown that burning sugarcane can increase the levels of particulate matter with aerodynamic diameter ≤ 1 μm (PM_1), $PM_{2.5}$, PM_{10}, black carbon, and CO by 10%, 11.6%, 25.3%, 55%, and 67.6%, respectively.[56] Additionally, concentrations of PAH associated with PM_{10} were shown to be up to 15 times higher during the harvesting season compared to the growing season in Belle Glade, Florida (Palm Beach County), a community in the sugarcane growing region.[57] The lack of geographical representation from other leading producers that make up about 50% (Asia, Africa, Oceania) of the sugarcane-producing nations[4] and the US limit the generalizability of the findings.

The evidence of health impacts on Brazilian communities has likely influenced the government's policies to phase out sugarcane burning as the primary harvesting practice in this country. The phase-out supports innovative technologies that promote the processing, use, and recycling of excess leafy material that is removed during burning of sugarcane plants.[5,6] The plethora of byproducts that can be produced from this excess leafy material demonstrates opportunities for new applications and industries in regions with abundant sugarcane production.[5,6] For example, bioethanol production can benefit from sugarcane byproducts derived from green harvesting, bolstering an alternative fuel to help reduce global reliance on fossil fuels and improve the economy of communities that harvest sugarcane.

Preharvest sugarcane burning is well documented to release numerous pollutants including inorganic and organic (i.e., PAHs) chemicals, metals, silicates, gases (i.e., carbon monoxide), and particulates, among others. A recent review by Stem et al.[34] goes into details about the physiochemical properties of preharvest sugarcane burning, highlighting significant health concerns for sugarcane workers and neighboring communities. All of these pollutants have been individually associated with adverse health outcomes,[5,7,8] and there is an abundance of data to support that smaller-sized respirable particulates ($PM_{2.5}$)[15,17,18,26,27,40,41,43,44,45] pose a significant threat to the health of workers and communities near sugarcane plantations. A limited number of studies in this review[13,14] evaluated the mixed emissions produced by combustion of sugarcane that contains numerous pollutants with varied properties. One study found that burning whole sugarcane stalks in a combustion chamber that simulates field burning produced slightly higher emission factors for PAHs [8.18 ± 3.26 (mg/kg)] and carbonyls [942 ± 539 (mg/kg)] compared to burning dry leaves (7.13 ± 0.94 PAHs and 201 ± 39 carbonyls (mg/kg)).[58] Additional emission factors for volatile organic compounds (VOCs), $PM_{2.5}$, organic carbon, elemental carbon, and tracer compounds like levoglucosan were determined to be 942 ± 539 mg/kg, 2.49 ± 0.66 g/kg, 0.16 ± 0.09 g/kg, 0.71 ± 0.22 g/kg, and 7.87 ± 5.42 mg/kg in dried sugarcane leaves, respectively.[58] Aerosols derived from burning sugarcane may also include adsorbed organic chemicals, such as pesticides, herbicides, and fungicides[59] that have been implicated in some of the health effects that are reported in this review. However, most epidemiological models have evaluated health effects attributable to $PM_{2.5}$ exposure based on the bulk mass concentration without consideration of chemical constituents. $PM_{2.5}$ is a heterogeneous mixture of organic and inorganic fractions with a chemical composition that varies spatially, temporally, and by source. Since the composition of $PM_{2.5}$ can be complex, there are long-standing questions about which components are most highly associated with health concerns. Several studies advocate for PM characterization in evaluating toxicity, exposure, and health end points, stressing the need to move away from general assumptions based solely on PM concentration.[60,61] For example, an evaluation of 52 chemical components of $PM_{2.5}$ collected in 187 US counties (2000–2005) showed that samples with a higher content of nickel, vanadium, or elemental carbon had higher $PM_{2.5}$ effect estimates for cardiovascular or respiratory hospitalizations.[60] General assumptions have also been applied to molecular-based studies focusing on oxidative stress and immune markers. A recent study by Forman et al.[62] points out that relying on these biological markers without consideration of PM components could lead to misinterpretation of PM toxicity. This study also underscores the need for superior biological assays and the development of exposure/effect biomarkers that reflect "real world" differences in PM composition that are highly relevant to toxicity.

A critical knowledge gap identified in the current review is the limited number of studies that included personal exposure monitoring. Of the studies, we evaluated only eight included occupational exposure assessments through stationary monitoring ($n=5$)[15,16,18,19,41] or personal monitoring ($n=3$).[17,42,44] The methods employed in the studies varied for data collection and analysis. For determining personal exposure to $PM_{2.5}$, two studies used the DustTrak 8533 but did not report exposure values using a time-weighted average (TWA), which accounts for the duration of exposure for each participant.[17,44] Furthermore, the utility of the DustTrak 8533 for personal monitoring is limited because it is bulky and, therefore, ill-suited for personal occupational exposure assessment, which may limit the ability to capture exposures across varied and high-exertion work tasks accurately. For instance, PM exposure among sugarcane workers can be highly variable and dependent on their task, such as the initial burning of the sugarcane, treading through burnt cane ash while harvesting the sugarcane stalk, and processing of sugarcane in facilities.[63] Additionally, the placement of the monitoring device would significantly affect its monitoring capabilities for each individual in a workplace setting. The third study measured personal exposure to silica and asbestos using a passive monitoring technique with a filter and electron microscopy.[42] This study was performed using techniques that were suitable for the time period (1994) and was able to demonstrate that sugarcane workers received differential exposure depending on their task.[33] The Ultrasonic Personal Air Sampler (UPAS) is a newer device and an improved option for personal exposure monitoring in occupational settings, as it is lightweight and does not require an external pump or tubing.[64] A version of the UPAS (V2+; Access Sensor Technologies) offers gravimetric sampling at different particulate size fractions that allow for characterization of composition and real-time sensor data for particulates of varied sizes ($PM_{1.0}$, $PM_{2.5}$, PM_4, and PM_{10}) and other measurements (VOC, CO_2, accelerometry, temperature, humidity, GPS location, and differential pressure across the sample filters).[65] These new features are important, as the types of respiratory air pollution hazards posed by agricultural work vary by the specific agricultural sector, farmworker tasks, and related crop.[59,66–68]

It was determined that most studies focused on the respiratory, cardiovascular, and renal health effects associated with short-term (acute) or intermediate exposure to air pollution from sugarcane burning, with only one study investigating the effects of longer-term (subchronic) exposures. These results are not surprising based on the long-standing association between air pollutant exposure and chronic pulmonary and systemic cardiovascular disease.[69,70] The mechanisms driving these health outcomes are still not elucidated, but biomarkers relevant to inflammation and oxidative stress were evaluated in various sample types (blood, urine, and nasal secretions) and shown to be elevated over the long term and across work-shift monitoring.[17,18,44] Laboratory-based rodent studies also supported the induction of inflammation and oxidative stress as a driving factor suggested from the observational study results.[14,15,19,20,23,45] Additionally, biomarkers specific to chronic kidney diseases, such as serum creatinine, estimated glomerular filtration rate (eGFR), KIM-1, and albumin were used to assess kidney function and diagnose CKDu.[52] Application of more advanced technologies, such as "omics," could provide additional mechanistic information from burning sugarcane and relevant injury and disease with a relatively low cost and effort.[71] The identification biomarkers may be useful in developing more high-throughput *in vitro* studies that better define mechanisms of action of sugarcane burning-derived pollutants. The development of complex cell cultures, such as organoids, may be a fruitful avenue to support and advance such work.[72] Furthermore, incorporating biomarkers into a suite of tests, such as pulmonary function tests and health exams, could help explain health stage-specific mechanistic changes associated with the development and progression of diseases.

Recent epidemiological data support the link between burnt sugarcane emissions and the renal system, showing association between $PM_{2.5}$, PM_{10}, ozone (O_3), carbon monoxide (CO), and sulfur dioxide (SO_2) and AKI and the development of CKD.[73,74] While the biological and molecular mechanism remain unclear, there are two main theories on how $PM_{2.5}$ (including SiNP) exposure impact kidney physiology/function.[18,73–76] One theory suggests that inhaled particulates translocate into the bloodstream and reach the kidneys, leading to glomerulosclerosis and tubular damage.[46,48,75] Supporting this notion, a case-report of individuals with CKDu in El Salvadore (a prominent sugarcane producer) demonstrated that high concentrations of amorphous SiNPs were found in renal biopsy of diseased individuals with CKDu that worked in sugarcane when compared to controls.[77] A rodent study showed that exposure to combusted sugarcane-relevant SiNP via oropharyngeal aspiration caused significant tubulointerstitial fibrosis by 26 wk, with elevated levels of SiNP detected in urine and blood, suggesting translocation from the lungs into the bloodstream and the kidneys.[46] Similar results were found in rodents exposed intranasally to sugarcane ash from a Nicaraguan sugarcane plantation that contained 3.3 mg of SiNP.[48] SiNPs were found in the lungs, spleen, liver, and kidney of exposed rodents, and they experienced proximal tubular injury, chronic tubulointerstitial fibrosis, and segmental glomeruli sclerosis.[48] Additionally, an *in vitro* study was able to demonstrate that human kidney proximal convoluted tubule cells exposed to sugarcane-derived silica nanoparticles experience reduced cellular viability, mitochondrial dysfunction and disrupt metabolic activity.[78]

A second theory postulates that pollutants stimulate alveolar receptors, activating the autonomic reflex, causing an imbalance in the autonomic nervous system and neuroendocrine pathways, resulting in increased systolic blood pressure and pulse rate.[75] An epidemiological study in young healthy adults found increases in systolic blood pressure, pulse pressure, and arterial stiffness as well as significant alteration to biomarkers associated with inflammation, oxidative stress, coagulation, endothelial function, lipid transport, and metabolism to be associated with increased exposure to ultrafine particulates.[79] In this review, a study reported an increased incidence of cardiovascular disease and hypertension-related hospital admissions in sugarcane-rich states in Brazil when air pollution (TSP and NO_2) was high during the harvesting season unlike the nonharvesting season.[22,43] Subsequently, a cohort study found that sugarcane workers had significantly higher 24-h systolic and mean blood pressure (BP) during the harvest period during all test stages.[19] Preexisting acute kidney injury in animal models has showed the detrimental interaction of kidney function and BP.[76] Rising and recurring elevations in BP accelerate the progression of kidney function decline.[76] Though, it is postulated that renal damage can occur through endothelial damage, mitochondrial damage, reactive oxygen species, systemic inflammation, immune dysfunction, hypoxia, and thromboembolic events.[73,75,76] However, these mechanisms are yet to be fully elucidated. The contributions of sugarcane burning to kidney function, including CKDu, requires additional research, as it is a novel topic despite the growing epidemic of CKDu in the agricultural sector.

The analysis of the observational studies identified several vulnerable populations, including the elderly, children, pregnant women, and infants as having greater susceptibility to disease. The existing literature supports that infants, children under five, and the elderly (<60 years old) face the most significant risk for adverse health outcomes related to air pollution.[80–82] Five studies[13,14,20,21,39] in this review identified specific effects on infant and child health, indicating greater risk for all-cause respiratory hospitalization,[13,14,39] reduced birth weight, shorter gestational period, and fetal death[20,21] among those exposed to air pollution from sugarcane burning. Three studies highlighted increased risk of all-cause respiratory[13,14] and cardiovascular hospitalizations[22] in individuals over 60 years of age. Findings from this review align with the extensive literature that individuals <60 years old are more susceptible to adverse health outcomes from exposure to air pollution.[13,14,22,83,84] This review confirms the importance of studying vulnerable populations, specific health outcomes, and the level of susceptibility over the life course. Few studies focused on adjacent or nearby communities, which are particularly susceptible to air pollution from sugarcane burning, especially those near workplace emissions.

Limitations

As with any study, there are some limitations. First, there is a heterogeneity of studies with methodological variability exploring different anatomical systems preventing us from performing a quantitative analysis (meta-analysis).[85] However, our scoping review demonstrates that there is sufficient literature regarding the respiratory health effects associated with air pollution from sugarcane burning to support the future conduct of a systematic review with a meta-analysis. A common limitation to performing a meta-analysis is a limited number of similar studies. It is recommended to have at least five studies on the same topic to perform a meta-analysis.[85] For respiratory health, five cohort[17,18,41,42,44] and seven ecological studies[13,14,26–28,39,40] were identified highlighting the possibilities of performing a systematic review with a meta-analysis. The same cannot be said for studies that explored cardiovascular, renal, and reproductive health effects. Second, there is a risk of publication bias with studies only sharing results that support their hypothesis. This scoping review identified one cohort study that found no relationship between biological silica fiber exposure and fibrotic lung disease or adverse respiratory health in sugarcane workers in Hawaii.[42] As with all reviews, although our approach was thorough, publications outside of the scope of the databases that we focused on (PubMed, Scopus, and WoS) could exist.

Conclusion

This review summarizes the state of knowledge of the health effects associated with exposure to air pollution from sugarcane burning and identified significant exposure and health gaps. We identified a need for enhanced personal and occupational exposure assessments that include composition analysis, studies that focus on long-term effects to workers and surrounding communities, and investigations that include the renal system as part of health outcomes of interest. These findings are highly pertinent in the US with the continuation of preharvest sugarcane burning in the south-central and southeastern regions. Additionally, studies that probe sugarcane burning emissions in other top producing countries such as India, Central America, and the US would highlight similarities and differences to the more well-studies communities of Brazil, lending to improving occupational and environmental health and safety.

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