

Mechanisms of VOC Pollution-Induced Respiratory Dysfunction: A Review

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ABSTRACT

Air pollutants are the largest documented environmental cause of death. A global increase in wildfire prominence has further exacerbated this problem. The specific mechanisms by which certain pollutants directly create adverse respiratory outcomes are incompletely understood. Improving this understanding of respiratory dysfunction becomes an especially important endeavor amid the ongoing COVID-19 pandemic and its associated respiratory complications. Volatile organic compounds (VOCs) play a major role in the production of harmful pollutants such as particulate matter and ozone. In this study, a systematic review was conducted to synthesize the current published medical literature on how volatile organic compounds (VOCs) directly affect respiratory function. We found a strong association of VOC pollution to respiratory dysfunction, but insufficient conclusions on causal mechanisms relating VOC-induced pollution to adverse health. To clinical and environmental ends, the development of new sensors to measure VOCs is also discussed.

KEYWORDS: COVID-19, Respiratory Dysfunction, Air Pollution, Respiratory Failure, Systematic Review, Sensors, VOCs

INTRODUCTION

Amid the ongoing COVID-19 pandemic, much of the academic discourse surrounding the prevention and treatment of respiratory dysfunction has been brought to center stage. Higher concentrations of particulate matter increase viral transmission, as well as exacerbate the susceptibility and severity of disease symptoms (Comunian et al., 2020). Additionally, in the wake of an endemic rise in wildfires, including areas such as Siberia, Australia, the western United States, among others, concerns regarding air quality and corresponding public health are of paramount interest.

Volatile organic compounds (VOCs) play a role in the formation of ozone and NO_x pollutants and are also related to atmospheric aerosol (particulate matter) concentrations. VOC is an umbrella term for a large class of compounds with thousands of unique species (Atkinson and Arey, 2003). Nearly every single activity involving biological organisms releases trace amounts of various organic species to the atmosphere, and VOCs are primarily removed through chemical oxidation by either OH, O₃, NO₃, or halogen radicals, and to a lesser extent through photolysis and deposition (Koppmann, 2007). While primary organic aerosols (POA)

may be directly released through fuel combustion and forest fires (for example, soot), VOCs are responsible for production of secondary organic aerosols (SOA), nucleations resulting from the oxidation of various gas-phase organic compounds (Griffin, Cocker and Seinfeld, 1999). Upon release or emission, VOCs are oxidized in the atmosphere and form low volatility products (Henze and Seinfeld, 2006). These are formed from successive oxidation of organic chemicals until their vapor pressure reduces sufficiently to partition partly or solely to the particle phase. Upon condensing, these products then form particulate matter. Globally, between 20% and 90% of fine aerosol (under 1 μm) is organic carbon based (Jimenez et al., 2009). Generally, the larger VOCs (i.e., sesquiterpenes vs terpenes or isoprenoids) yield more SOA per carbon atom (up to 67% more for sesquiterpenes) (Kanakidou et al., 2005).

Autooxidation of VOCs forms nearly half of secondary organic aerosols indoors, and VOCs are a major source of particulate matter pollution outdoors (Fenger, Hertel and Palmgren, 1998; Pagonis et al., 2019). Within urban areas, emitted VOCs are typically from transportation, industry, and increasingly, consumer products (Fenger, Hertel and Palmgren, 1998; McDonald et al., 2018). Consumer products, such as different cosmetics, paints, cooking products, and building materials have increasingly become the dominant source of VOCs, and thus may represent a new sector that may need further regulations to achieve further reductions in air pollution (Leung, 2015; McDonald et al., 2018). Furthermore, VOCs emitted by consumer products are typically more reactive than those emitted industrially or by automobiles, leading to a larger contribution of secondary organic aerosols formed from the total aerosol budget (McDonald et al., 2018). A larger component of the public health burden of disease due to air pollution is consequently becoming decentralized, which will complicate effective regulatory measures.

The greatest environmental risk to human health is air pollution, which adds the largest burden of disease (Schraufnagel et al., 2019). Globally, particulate matter air pollution reduces life expectancy by approximately one year on average, with reductions of nearly two life years in polluted countries in Asia and Africa (Apte et al., 2018). In the United States, a decrease of 10 micrograms per cubic meter in the concentration of fine particulate matter ($\text{PM}_{2.5}$) is associated with an average life expectancy increase of 0.61 years (over 7 months) (Arden Pope III, Ezzati and Dockery, 2009). Consequently, reductions in air pollution can account for up to a 15% overall increase in life expectancy (Arden Pope III, Ezzati and Dockery, 2009). This direct link between life expectancy and particulate matter pollution, which is directly measured, provides clear justification and motivation for regulations to limit and decrease emissions of particulate matter, both primary and secondary sources. Besides particulate matter, other air pollutants, such as ozone, further contribute to the total mortality burden and life years lost due to air pollution (Lippmann, 1989; Anenberg et al., 2010). Globally, estimates range from 2.9 to 4.2 million premature deaths occurring annually directly due to outdoor air pollution alone (Lelieveld et al., 2015; Schraufnagel et al., 2019). Around 3.8 million more deaths occur annually due to indoor air pollution, and the resulting pulmonary diseases are the 4th leading cause of death globally (Ferkol and Schraufnagel, 2014; Schraufnagel et al., 2019). Most of the burden of mortality is due to ozone and fine particulate matter pollution, among other compounds such as NO_2 , SO_2 , and CO (Folinsbee, 1992; Silva et al., 2016). Additionally, VOCs are a direct health hazard, besides their role in forming hazardous ozone and particulate matter pollutants (Ten Brinke et al., 1998; Kim, 2011).

Air pollution plays a significant role in many ailments, notably being a major contributor to various heart and nervous system diseases, such as heart failure, stroke, hypertension, dementia, and other cognitive impairments (Brook, 2007; Allen et al., 2014; Bos et al., 2014). Several specific examples of common air-pollution induced diseases targeting the respiratory and cardiovascular systems include chronic obstructive pulmonary disease (due to elevated ozone concentrations and particulate matter), acute lower respiratory illness (due to particulate matter), cerebrovascular disease (due to particulate matter), ischemic heart disease (due to particulate matter), lung cancer (due to particulate matter), and sick-building syndrome (due to VOCs) (Ten Brinke et al., 1998; Perez-Padilla, Schilman and Riojas-Rodriguez, 2010; Ferkol and Schraufnagel, 2014; Lelieveld et al., 2015). Better sensing and measurement systems, technical modifications to limit pollutant emission or exposure, and new and increasingly targeted treatment tools all represent necessary components for improving public health concerns regarding air and other environmental pollutants. In fact, reducing these environmental pollutants represents the primary and possibly the most effective way to reduce the burden of all cancers (Danaei et al., 2005). Thus, reducing air pollution is a major opportunity for improving global health and represents a significant and effective disease prevention measure (Ferkol and Schraufnagel, 2014).

Particularly in energy efficient buildings (largely built after the 1970s) in highly developed countries, where the buildings are well insulated (“air-tight”) and consequently air circulation is kept to a minimum, VOCs tend to accumulate to unsafe levels (Ten Brinke et al., 1998; Zhang and Smith, 2003). Consequently, certain diseases, such as sick-building syndrome, can be directly tied to VOCs (Ten Brinke et al., 1998). Health issues arising from exposure to indoor contaminants is one of the most common health concerns people face, with sick-building syndrome becoming an increasingly common concern (Ledford and Lockey, 1994). Sick-building syndrome health ailments are typically non-fatal but can be extremely debilitating (Redlich, Sparer and Cullen, 1997). Consequently, chronic, low-level indoor exposure to VOCs leads to numerous symptoms, the most common including mucous-membrane irritations (eye and throat irritations, cough), neurotoxic effects (headaches, fatigue, lack of concentration), respiratory symptoms (shortness of breath, cough, wheeze), skin symptoms (rash, pruritus, dryness), chemosensory changes (enhanced or abnormal odor perception), and visual disturbances (Redlich, Sparer and Cullen, 1997).

The correlation between VOC pollution and respiratory distress (among other major somatic dysfunctions) has been thoroughly documented (Bentayeb et al., 2013). In this paper, the authors undertake a review of the published medical literature on the nature of the direct causal relationship between VOC pollution and respiratory dysfunction. A synthesized understanding of the direct pathways by which VOC pollutants damage the respiratory system may illuminate treatment of respiratory dysfunction from pollution and other sources, including but not limited to coronavirus-associated respiratory complications. Investigation into causal mechanisms of non-VOC-related pulmonary dysfunction was beyond the scope of this study.

MATERIALS AND METHODS

2.1 Systematic Review

The question of interest in the present review is as follows: “What is currently known about

how VOC pollution proximately affects the respiratory system?” To answer this specific research question, sixteen appropriate search terms, specified to Title/Abstract, were developed. The Sciome Workbench for Interactive computer-Facilitated Text-mining (SWIFT)-Review was used to conduct a systematic review of our search results within the United States National Library of Medicine’s PubMed database (Howard et al., 2016). The principal function of the SWIFT-Review technology was to assimilate and sort search results for centralized manual review. This review adhered to rigorous standards of reproducibility and was conducted using a PRISMA-guided approach (Liberati et al., 2009). The visual workflow representing this systematic effort, as well as the search terms used, are shown in Figure 1.

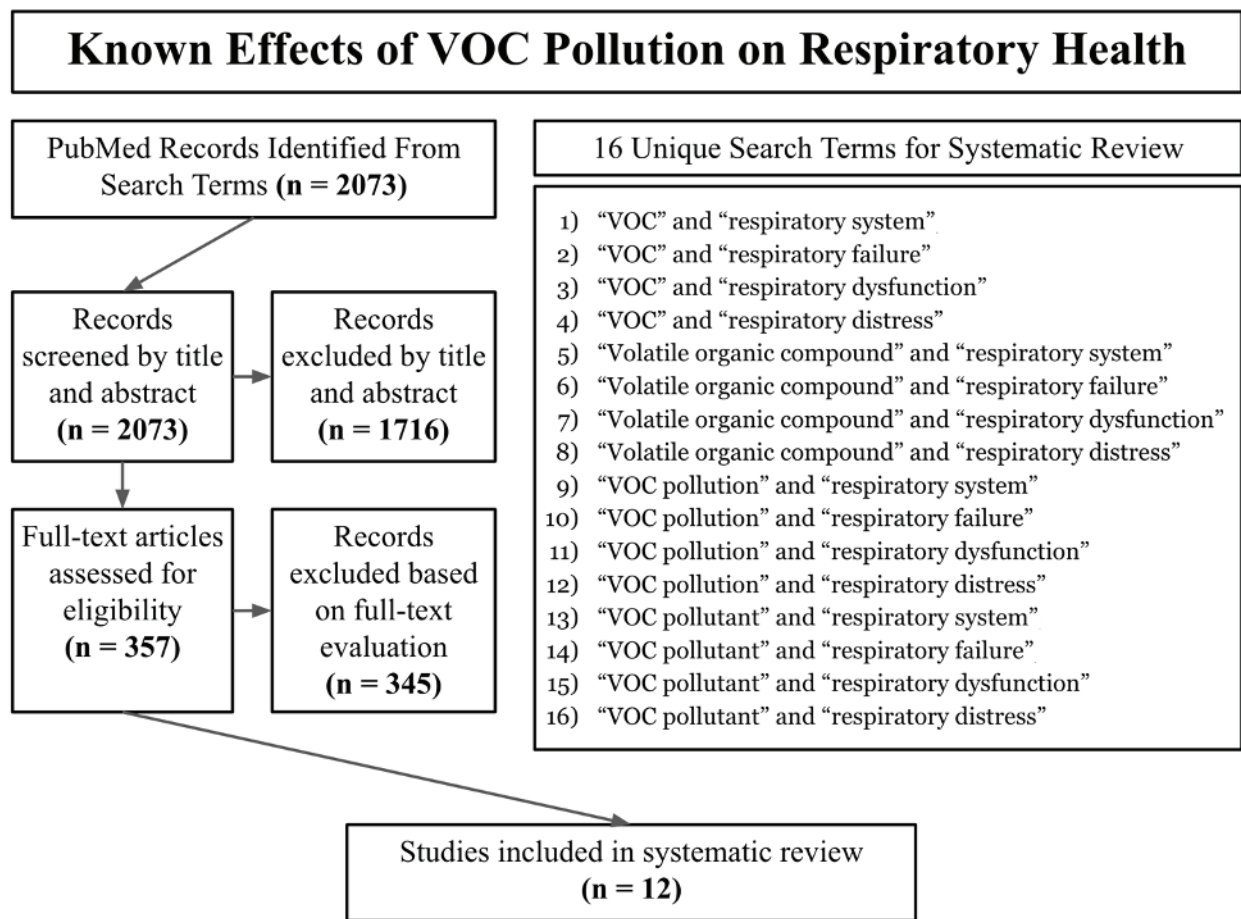


Figure 1. Systematic review workflow (including search terms) investigating the proximate mechanism(s) by which volatile organic compound (VOC) pollution causes respiratory dysfunction.

Duplicates and articles identified as irrelevant to the research question were excluded automatically and manually, respectively. Upon full-text review, only studies in which direct association to a respiratory dysfunction was established or a specific causal mechanism of action was proposed were included. We identified twelve studies whose data fulfilled our investigative criteria.

RESULTS

The review identified twelve papers whose content matched our study criteria by directly addressing the association between VOC pollution and adverse respiratory health outcomes. The robust association between VOC pollution and adverse respiratory outcomes (including but not limited to breathlessness, pulmonary dysfunction, dyspnea, wheezing, upper respiratory symptoms, and asthma) is confirmed by our review (D'Amato, G., Liccardi, G., D'Amato, M., Cazzola, 2002; Delfino et al., 2003; Yoon et al., 2010; Tanyanont, W., Vichit-Vadakan, 2012; Bentayeb et al., 2013; Kim et al., 2015; Gostner et al., 2016; Norbäck et al., 2017; Paciência et al., 2019; Zhao et al., 2019). The results of the review are shown in Table 1.

Study	Association?	Mechanism Proposed?
Bönisch et al., 2012	Yes	“Our results demonstrate that exposure to VOCs may increase the allergic immune response by interfering with DC function and by inducing oxidative stress and has therefore to be considered (sic) as risk factor for the development of allergic diseases.”
Bayzar et al., 2019	Yes	N/A
Gostner et al., 2016	Yes	Suggests the investigation of molecular effects of VOCs <i>in vitro</i> .
Kim et al., 2015	Yes	N/A - “In addition, risk assessment recognizes the association between air fresheners and adverse health effects, but the distinct causal relationship remains unclear.”
Paciência et al., 2019	Yes	N/A
Tanyanont & Vichit-Vadakan, 2012	Yes	N/A
Yoon et al., 2010	Yes	“We hypothesised that VOCs impair pulmonary function through enhancing oxidative stress, especially in the elderly population.”
Bentayeb et al., 2013	Yes	“The underlying mechanisms could consist of oxidative stress and irritation damaging the airways mucosa.”
Zhao et al., 2019	Yes	“These findings indicate that VOCs exposure may induce potential pulmonary health risk due to the alteration of gas-liquid interfacial properties of PS.”
D'Amato et al., 2002	Yes	N/A
Delfino et al., 2003	Yes	N/A
Norbäck et al., 2017	Yes	N/A

Table 1. Overview of review results.

The most common causative mechanism linking VOC exposure with the development of pulmonary dysfunction was mentioned by Yoon et al. (2010), Bentayeb et al. (2013), and Bönisch et al. (2012), suggesting that VOC exposure induces oxidative stress, leading to impaired pulmonary function. Also proposed is the suggestion that microinteractions at the gas-liquid interface may be responsible for adverse pulmonary outcomes (Zhao et al., 2019). Beyond these, robust alternative mechanisms were not identified by the authors.

DISCUSSION

Our systematic review demonstrates that the current medical literature provides an incomplete understanding of the respiratory health risks posed by VOC exposure. Both principal proposed mechanisms from the review, as well as hitherto-unproposed hypotheses for the causal association between VOC pollution and respiratory dysfunction, require elevated particle sensing technology to validate or reject and replace. The COVID-19 pandemic has dramatically elevated the importance of understanding respiratory dysfunction risk factors and causative mechanisms as healthcare professionals race to treat respiratory complications in affected patients. Beyond the ongoing pandemic, the rise of pollution-associated pulmonary dysfunction, particularly in industrialized areas, presents a global public health crisis that requires the urgent attention of medical researchers. In particular, we strongly recommend further study into causal mechanisms of VOC-induced respiratory illness. Furthermore, present-day VOC detection capabilities, which may increase our ability to assess their proximate effects on respiratory function, are insufficient. Several opportunities exist for new data collection and VOC measurement.

Novel sensing techniques such as those based on advancing optical particle counters, metal-oxide semiconductors, and photoionization detectors provide exciting perspectives for rapid detection of different aerosols and their precursors. Traditional techniques most commonly used today (such as gas chromatography or mass spectroscopy) require large expensive detectors with slow response times. Thus, new techniques for rapid and widespread testing provide possibilities such as breath diagnostics, highly localized air quality and composition monitoring, and improved forecasting.

Besides new testing technologies, new testing techniques unlock exciting possibilities for air quality measurements. Unmanned aerial vehicles (UAVs) provide an opportunity for dynamic measurements at unprecedented resolutions. Mounting sensor systems to UAVs allows for real time data collection at varying horizontal and vertical scales, potentially autonomously. The same sensor systems, which must be sufficiently portable and lightweight for use on UAVs, may be used by clinicians and other healthcare professionals for disease diagnostics. Measuring environmental factors influencing health through air quality and directly making diagnoses by measuring breath exhalation composition provide rapid and affordable advances in healthcare.

Newly developed photoionization detectors, utilizing tubular electrodes, allow for sub-parts per billion detection of gases such as isoprene (the most common VOC globally). Measuring VOCs permits improved diagnostics not only of the aforementioned VOC-linked health conditions but also of particulate matter. New detection methods help quantify VOCs and

other air pollutants and will help identify their sources.

Portable VOC detectors not only permit high spatio-temporal measurements of primary VOC emissions but also can be directly used to identify health care conditions linked to particular VOCs. Many different diseases, from malaria to tuberculosis to cancers, can be directly tied to specific biomarkers. These biomarkers are released via VOCs either through breath or skin emissions (Poling et al., 2011; Kelly et al., 2015; Sun, Shao and Wang, 2016; Schraufnagel et al., 2019). Measuring these VOCs permits non-invasive and rapid disease diagnostics. Additionally, breath-based diagnostics may complement existing procedures, decreasing risk of misdiagnosis and clinical error.

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