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Research on COVID-19 and air pollution: A path towards advancing exposure science

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ABSTRACT

The COVID-19 pandemic has resulted in an extraordinary incidence of morbidity and mortality, with almost 6 million deaths worldwide at the time of this writing (https://covid19.who.int/). There has been a pressing need for research that would shed light on factors – especially modifiable factors – that could reduce risks to human health. At least several hundred studies addressing the complex relationships among transmission of SARS-CoV-2, air pollution, and human health have been published. However, these investigations are limited by available and consistent data. The project goal was to seek input into opportunities to improve and fund exposure research on the confluence of air pollution and infectious agents such as SARS-CoV-2. Thirty-two scientists with expertise in exposure science, epidemiology, risk assessment, infectious diseases, and/or air pollution responded to the outreach for information. Most of the respondents expressed value in developing a set of common definitions regarding the extent and type of public health lockdown. Traffic and smoking ranked high as important sources of air pollution warranting source-specific research (in contrast with assessing overall ambient level exposures). Numerous important socioeconomic factors were also identified. Participants offered a wide array of inputs on what they considered to be essential studies to improve our understanding of exposures. These ranged from detailed mechanistic studies to improved air quality monitoring studies and prospective cohort studies. Overall, many respondents indicated that these issues require more research and better study design. As an exercise to solicit opinions, important concepts were brought forth that provide opportunities for scientific collaboration and for consideration for funding prioritization. Further conversations on these concepts are needed to advance our thinking on how to design research that moves us past the documented limitations in the current body of research and prepares us for the next pandemic.

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1. Introduction

In the brief time since the onset of the COVID-19 pandemic, studies quickly emerged that addressed the complex relationships among transmission of SARS-CoV-2, air pollution, and human health. These investigations, commentaries, and reviews explored changes in human behavior (e.g., public health lockdowns), air pollutant levels, and the effects of air pollution on the probability of developing or having a worse prognosis from COVID-19. For example, some studies have linked poorer air quality with higher COVID-19-related morbidity and mortality (e.g., Paital and Agrawal, 2020; Pozzer et al., 2020; Wu et al., 2020a). Other studies have examined the effects of lockdown and increased stay-at-home behaviors on air pollution levels; however, regional and chemical-specific results have been inconsistent (Bar et al., 2020; Bekbilir et al., 2021; Collivignarelli et al., 2020; Debven and Semple, 2020; Gautam, 2020; Liu et al., 2021; Varotsos et al., 2021). There have been calls for more scientific rigor as we navigate the next era of research related to COVID-19 and future pandemics, more generally (Brandt et al., 2020; Bray et al., 2020; Heederik et al., 2020).

For example, the robustness of the early research has been limited by ecological study design, underreporting of health outcomes, lack of spatially resolved air pollution data, lack of accounting for regional variations in outbreak timing, and deficient COVID-19 data quality (Villeneuve and Goldberg, 2020; Wu et al., 2020b). This is an opportune time for collective, creative thinking to strengthen methodologic approaches to assessing exposures to air pollutants and respiratory pathogens, which would in turn lay the foundation for improved studies of exposure-outcome associations. This is essential for the current pandemic, and for pandemics still to come.

In-person workshops, focus groups and seminars are ideal means to foster creative discussion on approaches to advancing the science. Considering pandemic restrictions, we conducted an informal on-line exercise in which we queried epidemiologists, exposure scientists, and other researchers with relevant expertise. The goal of this effort was to gather ideas and opinions from fellow scientists regarding their thoughts on aspirational study attributes - for use by scientists and sponsors - to be able to better understand infectious agent and air pollution impacts on exposure and health. Here we briefly describe the questions posed and the ideas, perspectives and recommendations derived from this exercise.

2. Materials and methods

An informal set of 15 questions was developed to obtain input on priorities for research into air quality and respiratory pathogens and recommendations on study design; six of the questions were related to research ideas and recommendations and the remainder were on participant information. The questions were pilot tested by colleagues and revised based on feedback. The questionnaire was provided using the online platform SurveyMonkey via email invitations between September 24 and October 25, 2021 (see Supplement A). Additional comments were allowed via free-form text. Responses to all questions were optional.

Participant recruitment was neither random nor systematic, but instead was based on personal networks and identification of authors (via PubMed searches on air pollution and COVID-19) in the fields of epidemiology, exposure science, air pollution, infectious disease and/or risk assessment. An exact breakdown for areas of expertise of the invitees is not possible as many researchers are multi-disciplinary. Invitations were emailed to 150 individuals from numerous countries, with additional invitations based upon recommendations from participants. A single incentive to participate was offered in the form a gift valued at $80; the recipient was chosen via a random lottery from among those who elected to provide contact information with their responses; otherwise, responses were uncompensated and anonymous.

We examined the results qualitatively, as this exercise was designed to be an information-gathering activity from which to derive suggestions for advancing pandemic- and air pollution-related research. Information was extracted and organized around the following themes: consistency of terminology regarding societal restrictions to aid in future exposure assessments; general viewpoints on air pollution/COVID-19/health outcome issues; factors important for exposure assessments of air pollution and infectious agents and impact(s) on health; and research needed to better explore co-exposures to air pollutants and respiratory pathogens.

3. Results and discussion

Thirty-two experts in pre-determined areas of interest participated. The respondents were approximately equally distributed among early, mid-, and late stages of career (N = 11, 9, 11, respectively) and broadly represented fields of exposure science (N = 18), epidemiology (N = 16), risk assessment (N = 13), toxicology (N = 6), occupational health (N = 1), and engineering (N = 1). Note that the respondents were permitted to select more than one area of expertise. Half of the respondents were employed by academic institutions and most (N = 26) resided in the US. Participants were also employed by industry, government, nongovernmental organizations, and consulting practices (N = 5, 5, 2, and 1, respectively).

3.1. Consistency of terminology regarding societal restrictions to aid in future exposure assessments

The pandemic resulted in societal and behavioral changes that have impacted exposures to SARS-CoV-2 and air pollutants, both indoors and outdoors (Ravindra et al., 2022; Sharma et al., 2022). A large body of research has emerged over a short timeframe examining the impact of governmental or business sanctions or requirements on societal activities. These sanctions have been described by such terminology as “lockdown,” “mask wearing,” “social distancing,” “quarantine,” “curfew,” and “stay-at-home.” However, the definitions, requirements, and enforcements varied widely from locale to region to country, and by the stages of the pandemic. Thus, research on the impact of these societal changes on indoor and outdoor air pollution levels across or even within a geographic area may be difficult to interpret due to inconsistent definitions. The differences may contribute to varying results and conclusions of studies examining restriction-related associations with air pollution levels (Brioz-Déron et al., 2022; Liu et al., 2021; Sarmadi et al., 2021; Vega et al., 2021).

Participants were queried about the value in developing common definitions regarding the extent and type of lockdown. Most respondents (84%) found value in developing a set of common definitions regarding the extent and type of lockdown. It was also noted that achieving concordance across agencies will likely be difficult. Recommendations were offered regarding definitional elements, including:

- Detailed descriptions of activity restrictions (for example, to whom the restrictions apply [e.g., the general public, exclusions for certain occupations, essential trips], activities permitted, time allowed outdoors
- Dates of restrictions
- The extent to which restrictions are enforced (e.g., mandatory, voluntary)
- Geographic extent and duration of restrictions
Given the interest in understanding the impact of pandemic-related societal changes on exposure to air pollution and infectious agents, and the potentially large impact in exposures and health effects related to those changes, developing an approach to achieving the goal of concordant terminology is worthwhile and recommended.

Value was seen in the development of a “pandemic dictionary,” with locale-specific definitions for terminology related to restrictions and enforcement in mobility as part of regional and national health departments’ pandemic response programs. This could then be used as a foundation for dialogue on developing concordant terminology across regions. To be clear, the use of a common lexicon should in no way prevent localities from utilizing tailored approaches to responding to outbreaks.

3.2. General viewpoints on air pollution/COVID-19/health outcome issues

We asked questions related to respondent’s perceptions on the strength of the current evidence regarding whether:

(i) particulate matter in air facilitates spread of infectious disease(s) such as COVID-19;
(ii) the confluence of respiratory disease and air pollution is a risk factor for more severe symptoms and prognosis of COVID-19; and
(iii) pandemic-related societal restrictions led to improved air quality.

Overall, although some earlier literature explored the influence of the spread and susceptibility to the flu virus (Feng et al., 2016; Su et al., 2019), respondents did not feel that, to date, there is strong evidence of a causal relationship that particulate matter facilitates the spread of coronavirus (Supplement B, Fig. B1). It was noted that the importance of this mechanism will be pathogen-specific and will also depend on the characteristics of the particulate matter (e.g., composition, size). It was further noted that this issue is, in general, not well-studied and there are no extant studies that have demonstrated that viable virus is recoverable from particulate matter and can be linked to an outbreak.

In contrast, there was, in general, greater confidence in the science indicating that respiratory disease and air pollution are risk factors for more severe symptoms and prognosis of COVID-19 (Supplement B, Fig. B1). Some respondents expressed the view that the extant epidemiology studies have not been designed to adequately test this relationship (e.g., use of ecological study design, lack of inclusion of important confounders) and therefore there is not yet sufficient evidence on this topic. It was also noted that the concept of a threshold should be considered in future studies; that is, levels of an air pollutant must be sufficiently high to be a risk factor for respiratory disease and in turn produce a more severe COVID-19 outcome.

While most of the respondents agreed that pandemic-related societal restrictions led to improved air quality (Supplement B, Fig. B1), several issues were identified. For example, it was observed that avoidance of public transportation during “shut-downs” resulted in increased traffic in some locations, which could in turn have resulted in higher levels of air pollution. It was also pointed out that increases or decreases in air quality were highly dependent on the specific pollutant, the location and scale of the area of study (e.g., regional, neighborhood), and non-pandemic-related events and activities (e.g., wildfires).

There were mixed views regarding whether particulate matter in air facilitates spread of infectious disease(s) like COVID-19, whether the combination of respiratory disease and air pollution is a risk factor for more severe symptoms and prognosis of COVID-19, or whether pandemic-related societal restrictions led to improved air quality. The lack of agreement on these issues parallels results from current assessments of the literature (Adam et al., 2021; Marqués and Domingo, 2022; Prinz and Richter, 2022; Ram et al., 2021).

3.3. Factors important for exposure assessments of air pollution and infectious agents and impact(s) on health

We queried the respondents regarding their views on socioeconomic factors and sources of air pollution, both factors that can influence research on exposure assessments of air pollution quality, and impact(s) of infectious agents on health. We also asked the respondents to rank their priority topics for funding and research for the next five years. The results from these topics are described here.

3.3.1. Sources of air pollution

Air pollution and SARS-CoV-2 research has generally included assessments of overall measures of air quality, but specific sources of air pollution are not often identified. However, information on sources can lead to identification of modifiable factors which in turn could result in exposure reductions. These sources can include traffic, wildfires, industrial emissions, biofuels, and smoking.

Respondents were asked to rank several sources of air pollution with respect to the importance of their inclusion in future studies (1 = highest, 6 = lowest). As shown in the diagram in Fig. 1, three quarters of the respondents identified traffic and smoking as important sources of air pollution warranting research. Fewer respondents favored prioritizing research on wildfires or industrial emissions as highest priority (Fig. 1). While biofuels were only identified by six respondents as high priority (Fig. 1) for future research, it was acknowledged that this source may be of greater importance in areas where these fuels are used for cooking/heating. Similarly, while no respondents ranked industrial emissions highest priority (7 ranked it as 2nd highest), it was noted that shut-downs could be linked to improved air quality and so may be worth further investigation.

Suggestions for future research on sources of air pollutants also included: incorporation of measures of exposure to bioaerosols, development of an algorithm to characterize exposures to multiple sources of exposure and relative source contributions, collection of indoor air ventilation and filtration data, evaluating indoor and outdoor fires for pleasure (e.g., firepits, fireplaces), measuring outdoor dust, especially in arid regions, creating an index for neighborhood environment, and collection of data on time-activity patterns. Because of general limitations around available research funds, it was further suggested that sponsors prioritize sources that are modifiable.

3.3.2. Socioeconomic factors

Air pollution and infectious agent exposures have been shown to be differentially distributed by socioeconomic status (SES) and evidence indicates that lower-SES populations may be more susceptible to each of these insults (WHO, 2010). Respondents were asked which SES factors they felt to be the most important for studying exposures to air pollutants and respiratory infectious agents. They were offered the following options: race, pre-existing respiratory illness (es), culture and/or religious views, caregiver for elderly or infirm, education, essential worker status, ability to choose work location, reliance upon public transit, number of persons in a household, childcare requirement, access to green spaces, distrust of authority, or other. The respondents generally prioritized pre-existing respiratory illness, race, and essential worker status over culture/religion, childcare requirement, access to green spaces, or distrust of authority. The respondents also noted the importance of access to health care, other pre-existing illnesses, income and reliability of that income, and geographic location (e.g., density of population).

3.3.3. Ranked research priorities

Respondents were offered the opportunity to provide input on priority topics for funding and research for the next five years relevant to air pollution and infectious agents. The suggestions were similarly divided among the available options (Fig. 2). Other suggestions included collecting data on bioaerosols in urban areas, time-activity patterns,
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Airborne transmission of SARS-CoV-2, particulate matter and viral transport, doses of air pollutants from indoor air exposures, the extent to which proxies for ventilation quality and air filtration relate to infectious agent disease risks, and re-aerosolization and environmental stability of the pathogen (see Supplement B for additional information on these responses).

In summary, ideas were offered on types of air pollutant sources that could shed light on relationships between exposure, viral exposure, and health. In our view, the concept of prioritizing sources that are modifiable is important. Numerous SES factors were identified as relevant by respondents, with the understanding that these vary by region. Finally, respondents offered wide-ranging recommendations on research focus areas, perhaps reflecting the broad scope of opportunities.

3.4. Research needed to better assess co-exposures to air pollutants and respiratory pathogens

We were interested in gathering input on where limited resources should be directed to minimize study uncertainties and weaknesses and to better prepare for future studies of COVID-19 and other infectious diseases. Thus, participants were asked an open-ended question about their views on research to better assess co-exposures to air pollutants and respiratory pathogens. Most of the recommendations fell into four categories: development of cohort studies, collection of air pollutant data, animal/mechanistic data, and experimental studies (Fig. 3; Supplement B). There were also suggestions for small, focused studies such as clinical trials. Additional focus areas recommended for study were inclusion of areas of varying regional pollution levels (including areas impacted by wildfires), studies focusing on indoor air quality including schools, and studies that closely examine social and socioeconomic factors (e.g., income, proximity to industrial activity/highways, access to healthcare, race, size of household) and how these relate to health outcomes.

More specific suggestions included studies that closely examine time-activity patterns and how indoor air pollutant levels affect the internal dose. Additional recommendations focused on research on - and control of - indoor air quality through ventilation and/or filtration. While the questions in this exercise were focused on exposure, it was noted that under-ascertainment of cases is an important problem impacting the field. Other feedback challenged the concept of air pollution research by

Fig. 1. Sources of air pollution in order of priority for future research. (Ranking: 1 = highest priority, 6 = lowest priority).

Fig. 2. Priority topics for funding and research in the next five years. Values indicate number of respondents who selected the topic as their first or second highest priority.

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Collecting data on determinants of indoor air pollutant levels (ventilation, pollutants, behaviors, particle size, etc.)

Collecting microtemporal and spatial air pollution data

Collecting information on viral transport via particulate matter

Developing a better understanding of the relationship between indoor air pollutant levels and outdoor air monitoring data
recommending instead that time and effort should not be diverted from vaccination and antiviral development. Researchers and sponsors may wish to consider these when planning research and database development.

3.5. Strengths and limitations

This exercise has several limitations. On-line questionnaires offer only one-way transfer of information, with no opportunity for follow-up questions or dialogue among participants (as compared to, for example, a workshop). Thirty-two scientists offered their perspectives. While this was fewer than hoped for, the response rate (about 18%) was similar to a recent survey of epidemiologists during the pandemic conducted by the New York Times (response rate of around 8.5%) (Sanger-Katz et al., 2020) and may reflect the impact of pandemic-related time pressures. Additional scientists may have provided different perspectives and research ideas. Further, while invitations were sent to international scientists, most of the respondents were from the US. The insights and recommendations obtained may not be generalizable to other countries. For example, what constitutes important SES factors will vary by region and country. On balance, as noted previously, input was sought on advancing the science in order to be better prepared for future pandemics, and this can occur from the development of one or a few ideas from any region. Questionnaires are useful tools to garner input from colleagues with limited inconvenience, particularly during the pandemic when networking opportunities are limited.

In summary, there were as many study design recommendations offered as there were participants. This speaks to the numerous types of study gaps but also to the need for varied approaches to achieve a better understanding of the combined impacts of air pollution and respiratory pathogens on human health. Research sponsors can benefit from drawing on these research recommendations when developing requests for proposals.

4. Conclusions

The scientific experts participating in this information-gathering exercise provided valuable insights regarding needs for future research on exposure to SARS-CoV-2 and air pollution. We note that the views described here derive from a small group of experts and are not meant to be generalizable to the broader scientific community. Key conclusions and recommendations are given here.

Most respondents agreed that concordance of terminology regarding societal pandemic-related restrictions would aid in assessing changes in exposures to air pollutants and respiratory pathogens. At the same time, the difficulty in achieving this goal was noted. We recommend initiation of a dialogue across localities, regions, and countries that would (i) result in a common language for societal restrictions, and (ii) enable researchers to compare air pollution data by restriction type and enforcement approach. This could be led by an international body such as the World Health Organization.

Participants offered a wide array of input on what they considered to be improved study designs to advance our understanding of exposures. We recommend this input be used to begin conversations among international researchers, regulators, health agency scientists, risk assessors, and sponsors; prioritization of these concepts would be highly valuable for research funding decision-making.

While this exercise was focused on air quality, we note that a better understanding of the impact of behavioral interventions such as social distancing and mask-wearing is needed, including the regional, political and societal influences on their implementation. Similarly, better ascertainment of COVID-19 (and emerging infectious disease) cases is also needed; without this, it is not possible to understand impacts of environmental exposures on pandemic-related illness. Ascertainment of COVID-19 is subject to error due to a variety of dynamics including the regionalization of factors that impact exposure, such as asymptomatic cases, unconfirmed diagnoses, limitations in accuracy of and access to diagnostic testing, emergence of new variants, and the impact of vaccines (different types of vaccines, dosages). In summary, even with the “best” exposure data possible, studies of exposure-outcome associations will only be as good as the outcome data obtained.

The COVID-19 pandemic has resulted in an extraordinary incidence of morbidity and mortality, with almost 6 million deaths worldwide at the time of this writing (https://covid19.who.int/). There has been a pressing need for research that would shed light on factors – especially modifiable factors – that could reduce risks to human health. The
enormous body of research produced in the short time since the start of the pandemic highlights the enthusiasm for conducting research on air pollution and respiratory pathogens. Those who graciously gave their time to participate in this exercise provided important insights into aspects of study design that should be considered moving forward so that we are better prepared for the next pandemic. This input can be used to lead us to study designs that can better examine relationships between exposures to respiratory pathogens and air pollution.

Important concepts were brought forth from this exercise that provide opportunities for scientific collaboration and for consideration for funding prioritization. These results further indicate the need for conversations among risk assessors, research sponsors, public health officials, and scientists from the international community. Inclusion of front-line health professionals from communities with different characteristics such as SES, traffic density, and industrial exposures is needed to advance our thinking on how to design research that moves us past the documented limitations in the current body of research and prepares us for the next pandemic.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper. Carol Burns and Judy LaKind consult to governmental and/or private sectors. The authors retain sole responsibility for the writing and content of this paper, which represent the professional opinions of the authors and not necessarily those of API or its member companies.

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Appendices. Supplementary data

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