What Now? Epidemiology in the Wake of a Pandemic

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Abstract

The COVID-19 pandemic and the coming transition to a post-pandemic world where COVID-19 will likely remain as an incident disease present a host of challenges and opportunities in epidemiologic research. The scale and universality of this disruption to life and health provide unique opportunities to study phenomena, and health challenges, in all branches of epidemiology, from the obvious infectious disease and social consequences, to less clear impacts on chronic disease and cancer. If we are to both take advantage of the largest natural experiment of our lifetimes, and provide evidence to inform the numerous public health and clinical decisions being made every day, we must act quickly to ask critical questions and develop new methods to answer them. In doing so we should build on each of our strengths and expertise, and try to provide new insights rather than becoming yet another voice commenting on the same set of questions with limited evidence.

Key Words: epidemics; coronavirus; epidemiologic methods

Abbreviations: HIV: human immunodeficiency virus; COVID-19: coronavirus disease 2019; US: United States

As the world confronts the threat of COVID-19, epidemiology is having a moment in the spotlight. This focused attention brings both praise and criticism, and has highlighted the role of epidemiology, particularly infectious disease epidemiology. However, while epidemiology's role in combating an emerging infectious disease is well defined, as this disease transitions to endemicity and as we enter the post pandemic period, epidemiology will be no less important, but have a fundamentally different role.

Despite vast differences in scale between the COVID-19 pandemic and other infectious disease outbreaks, infectious disease epidemiologists and virologists have adapted a standard playbook (1) to learn rapidly about the characteristics and transmission dynamics of SARS-CoV-2, the virus that causes COVID-19. For example, after the report of a novel coronavirus cluster in China's Hubei province on December 31, 2019 and subsequent cases in China, Thailand, and beyond, researchers used early data to estimate the number that each infected person was likely to infect (2), the time from becoming infected to transmitting disease or developing symptoms (3), the proportion of those infected who end up dying due to COVID-19 (4,5), and the probability of transmission from asymptomatic infected individuals (6). These estimates continue to be refined as more data become available, and, as the outbreak has progressed, epidemiologists have turned attention to strategies to prevent infection and study the clinical course of disease.

This work on the disease itself is critical, but the scale of both the COVID-19 pandemic and the global response mean its broad effects will extend far into the future. We know from the global

response to the emergence of HIV in the 1980s that epidemiologic research into a novel pathogen can go in unexpected directions as we respond to unforeseen challenges, that often require new methods and data sources. Here, we explore the opportunities and challenges for epidemiology in the wake of the COVID-19 pandemic as deal with the aftermath of mass infection, death and social disruption.

Every Epidemiologist is now a COVID-19 Epidemiologist

We are in the midst of a massive public health crisis. As of the end of June, 2020, over 10 million cases of COVID-19 have been reported worldwide, resulting in over 500,000 deaths, and cases and deaths continue to rise in many areas (7). Because testing has been uneven and incomplete, the actual scope of the pandemic is known to be much larger (8). Moreover, in the United States, early research into the distribution of infections and mortality has revealed a woefully unprepared public health system and deep inequalities, particularly by race (9). These issues have profound consequences for the current moment, and are the subject of intense epidemiologic research and heroic public health efforts. But the scope of the COVID-19 pandemic means that it will have a sustained impact on health and society, even after transmission is brought under control.

Moreover, the pandemic response has prompted governments to take extraordinary actions in disease control that have wide ranging impacts. The social distancing measures taken represent the largest natural experiment in epidemiology in modern times, and the impact on health will

be far ranging, touching on areas ranging from other infectious diseases, to mental health and chronic diseases. In the United States, at the peak of the lockdown in spring of 2020, 83% of the population was under state-wide stay at home orders (Figure 1) (10). Similar, and often more aggressive, stay at home orders were implemented around the world. These orders were accompanied by longer term closures of schools, restaurants, and recreational areas, etc. These disruptions had an immediate economic toll, but their long-term effects on public health are not yet understood.

As we transition from the current moment, defined by the emergence and early waves of the pandemic, to the future, defined by sustained transmission and recovery, the decisions faced by policy makers and the critical epidemiologic questions will change. Early in the pandemic, we focused on learning about the virus, identifying patterns of transmission, and modeling future incidence of various intervention scenarios to inform control measures. In the next stage, a new, broader, set of questions will take priority. Just because every epidemiologist is now a COVID epidemiologist does not mean that all interesting questions will be about infectious diseases or COVID-19 itself. Rather, the ripple effects of the COVID-19 pandemic will touch every other issue considered by epidemiologists. Below we give a few examples.

How do we optimize care for survivors of COVID-19?: Given the vast numbers (and significant proportion of the world's population) likely to be infected by this disease, understanding the long-term effects of exposure to and infection with SARS-CoV-2 is critically important. For example prior infection with SARS-CoV-2 may increases risk from other infectious or chronic

diseases. We will also need to understand the effects of multiple exposures to SARS-CoV-2, especially at later ages, and on immunity and the clinical response to later infections. Moreover, improving the long-term response to COVID-19 will require a robust understanding the sequelae of disease among children because, though not thought to be a major driver of transmission or a major source of morbidity or mortality at the moment, as the disease moves towards endemicity we expect the average age of infection to shift towards younger individuals.

What are the implications of endemic COVID-19 for other infectious and chronic diseases?:
In addition to learning how to manage patients who have already had COVID-19, epidemiologists and public health practitioners will be faced with decisions about how best to continue routine preventative health services and care and treatment for other infectious and chronic diseases in a world with endemic COVID-19. Early evidence suggests that engagement with routine services, like vaccinations and prenatal care, as well as care and treatment for chronic diseases, like HIV, cancer, and cardiovascular disease, may be suppressed even after severe social distancing measures end due to sustained caution about interacting with the healthcare system. In addition, the threat of endemic COVID-19 may increase complexity in the management of other chronic diseases related to unknowns about whether specific treatments interact with or increase susceptibility to COVID-19 (11,12) and whether treatment for COVID-19 ought to be modified in the presence of other chronic diseases and vice versa.

What can we learn from the largest natural experiment in modern times?: The pandemic marks a natural experiment on a scale that many of us have never seen. With this experiment comes the opportunity to learn about the epidemiology of many different phenomena. For example, introduction of SARS-CoV-2 into a completely susceptible population provides opportunities to learn about the population-level implications of being challenged with a novel pathogen, particularly at older ages. It also allows examination of the effects of social disruption, which may provide insight into the importance of various types of social interaction, educational milestones, and physical activity. In fact, it is unlikely that any disease, chronic condition, or social phenomenon will remained untouched by the COVID-19 pandemic or its response. While the high burden of disease and the social and economic impacts of the response have been devastating, both offer opportunities to learn about factors that will become important as we emerge from the pandemic.

Now is the time to start searching for answers

The pandemic and its aftermath will give rise to many fundamental scientific questions about both the impact of social disruption and the spread of novel pathogens. These questions will take time to answer, and their immediate public health implications may be unclear. Likewise, there are many decisions in public health, clinical medicine, and policy that must be made immediately as we emerge from the pandemic, and these decisions need to be grounded in epidemiologic evidence whenever possible.

The timeline to answer both types of questions may be short. Some decisions will be made with or without scientific knowledge as a guide, while others may wait for evidence but be less effective if delayed. Likewise, the window to answer some deep scientific questions might close if studies are not begun, or at least planned, before we enter the post pandemic period.

Asking the right questions is the first, and most critical step in finding answers that improve public health. Epidemiologists should be central to shaping, asking, and answering both types of questions. Asking good questions cannot wait until we feel prepared to answer them. Rather than asking questions that seem answerable with available data, we should be at the forefront of discussions on what we need to learn, while acknowledging that answering these questions may require new data sources and methods.

Answering important questions in "unprecedented" times

The state of the world during (and beyond) the COVID-19 pandemic is often described as "unprecedented." The "newness" of the situation permeates many of the actionable questions we would like to ask, from questions about the novel pathogen itself to questions related to immunology and clinical consequences of infection, to questions about the social and behavioral consequences of control measures. At the same time, decisions about how to deal with the ripple effects of COVID-19 and social disruption are being made every day, and delaying a decision to wait for more data is a decision in and of itself with real public health consequences.

The canonical approach to epidemiologic research is to design a study, collect all the data on any actions taken (e.g., which treatment was prescribed) and what happened (e.g., patient outcomes), analyze the data, combine results with other studies to meta-analyze the findings, and then make tepid policy recommendations. As we respond to and emerge from the pandemic, we do not have the luxury of this process. Decisions will be made rapidly, with or without our input. For example, because the first known patients with COVID-19 were infected only about 6 months ago, clinicians making decisions about how to treat survivors of COVID-19 must do so without knowledge of long-term outcomes under any possible treatment strategies. Because the world has not seen global lockdown measures like those imposed since March in recent times, we cannot look to historical examples to determine the consequences of such actions. Moreover, while the pace of data collection for COVID-19 studies is accelerating, currently available data are limited in geographic scope and population coverage, meaning that data are not yet available for many geographic areas and population subgroups that would be affected by various types of public health decisions. To base these decisions on the best available evidence, we will need to find ways to synthesize what we know from various sources.

Answering timely questions in this new era will require thoughtful application of existing epidemiologic methods and innovative new approaches. As in all epidemiologic endeavors, a primary impediment to learning will be missing information (13–15). New approaches to build off existing methods to handle various forms of incomplete or missing information will be critical. These may include borrowing approaches from infectious disease modeling (and other

fields) that allow researchers to combine knowledge on disease mechanism with limited available data to strengthen inferences and predictions; using quantitative approaches to generalize or transport results from a setting with available data to one without (16,17); developing new approaches to data fusion (18) to combine inferences from more than one data source; applying new two-stage study designs that leverage available, but imperfect, data sources while collecting key pieces of new information through small, targeted studies (19–21); and developing new analytic approaches to learn from imperfect "natural experiments" like COVID-19 where many factors evolve simultaneously.

Using available, but incomplete, information to inform decision making can be uncomfortable for epidemiologists acutely aware of potential for bias and uncertainty. But learning does not end once decisions are made. Rather, we should participate in the cycle of decision making such that we provide results based on the best information available, observe which decision is made and how events unfold, and update our knowledge accordingly such that, at the next decision point, we stand armed with stronger evidence and updated conclusions.

Working together while not following the crowd

Just because every epidemiologist is a COVID-19 epidemiologist does not mean every epidemiologist must address the same questions or use the same data. Epidemiology is a diverse field, and its many areas of expertise are a strength when confronting a worldwide event like COVID-19. Despite the tens of thousands of scientific papers published on COVID-19

to date, many important questions remain unanswered or have yet to be identified. Epidemiologists from all disciplines have the opportunity to shape the next phase of life as we emerge from the pandemic by identifying and answering questions related to their areas of expertise. While partnerships and collaborations with clinical colleagues and policy makers have long been a hallmark of epidemiologic research, this new era offers opportunities for new types of cross pollination of ideas that will strengthen our collective ability to respond to urgent questions as we emerge from the COVID pandemic and beyond.

Conclusions

Despite having a clear role during the emergence of a new infectious disease, the role of epidemiology in the next phases of the COVID-19 pandemic is still evolving. We contend that epidemiology has a role in shaping and prioritizing the questions that are asked and developing new methods, study designs, and data sources to answer these questions in light of the challenges posed by the massive upheaval caused by the pandemic.

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Figure 1. Proportion of the US population under state-wide stay-at-home or shelter-in-place orders due to the COVID-19 pandemic between March 15, 2020 and June 15, 2020.