

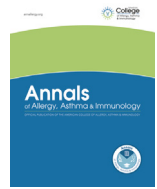


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Review

Reflecting on prediction strategies for epidemics

Preparedness and public health response

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Key Messages

- Successful management of epidemic response depends on the development of preventive and preparedness strategies, surveillance, and interventions.
- Because treatment or pharmaceutical interventions are typically limited early in an epidemic, nonpharmaceutical interventions can be effective in reducing severe outcomes.
- Pharmaceutical and nonpharmaceutical interventions have the ability to reduce the impact of an epidemic if they are implemented efficiently and effectively, with appropriate targeting and prioritization (eg, considering age, underlying health conditions, or access to care) and with limited resources.
- The potential long-term health impact of epidemics for high-risk populations, for example, those with chronic respiratory diseases, further highlights the importance of developing and implementing prevention, preparedness, and intervention strategies.

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ABSTRACT

Objective: To provide an overview of the literature on respiratory infectious disease epidemic prediction, preparedness, and response (including pharmaceutical and nonpharmaceutical interventions) and their impact on public health, with a focus on respiratory conditions such as asthma.

Data Sources: Published literature obtained through PubMed database searches.

Study Selections: Studies relevant to infectious epidemics, asthma, modeling approaches, health care access, and data analytics related to intervention strategies.

Results: Prediction, prevention, and response strategies for infectious disease epidemics use extensive data sources and analytics, addressing many areas including testing and early diagnosis, identifying populations at risk of severe outcomes such as hospitalizations or deaths, monitoring and understanding transmission and spread patterns by age group, social interactions geographically and over time, evaluating the effectiveness of pharmaceutical and nonpharmaceutical interventions, and understanding prioritization of and access to treatment or preventive measures (eg, vaccination, masks), given limited resources and system constraints.

Conclusion: Previous epidemics and pandemics have revealed the importance of effective preparedness and response. Further research and implementation need to be performed to emphasize timely and actionable

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strategies, including for populations with particular health conditions (eg, chronic respiratory diseases) at risk for severe outcomes.

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Introduction

The continuing spread of coronavirus disease 2019 (COVID-19) worldwide has heightened the awareness about infectious disease pandemics and the need for better preparedness^{1,2} and response^{3–5} to minimize the negative public health, economic, and societal impact.

The Middle East respiratory syndrome and severe acute respiratory syndrome (SARS) were caused by coronaviruses, similar to the novel COVID-19. Like SARS, COVID-19 began spreading in China. After a sudden increase in COVID-19 cases, it was classified as an epidemic. Because the disease then spread across several countries and affected many people, it was classified as a pandemic.

Infectious diseases often contribute to the development or exacerbation of respiratory conditions, including asthma and allergies.^{6,7} Approximately 339 million people worldwide were affected by asthma in 2016.⁸ By 2025, it is expected that this number will rise to 400 million worldwide.⁹ In the United States, the condition affects an estimated 8% of the population¹⁰ with a cost of more than \$80 billion annually in medical expenses and days missed from work and school.¹¹ Owing to asthma exacerbations during a pandemic, the economic impact could be even more devastating.

In history, one of the most disastrous pandemics was the 1918 influenza pandemic.¹² It is estimated that one-third of the world population is infected (500 million) and 50 million people died,¹³ which caused social and economic disruptions. The Asian flu began in 1957, during which 116,000 people died in the United States.¹⁴ It was the first time that surveillance¹⁵ was comprehensively used to track the burden of the disease. However, interventions to reduce spread were not considered, and vaccine distribution was slow and without prioritization.¹³ In 1970, the Hong Kong flu spread extensively owing to air travel.¹⁶ As a result of lack of public health intervention strategies, the hospitalization rate was reported as 150%¹⁷ in some areas. Previous pandemics and epidemics have revealed the importance of preparedness of the health care systems and society.

Preparedness and response for epidemics involve a wide spectrum of activities, such as identifying populations at risk (eg, owing to age, economic status, or underlying health conditions), understanding the disease transmission patterns in different communities, surveillance and prediction of the geographic spread of the disease, and managing interventions and policies.^{18–20}

Infectious disease spread surveillance and predictions inform both pharmaceutical interventions (PIs) also called disease mitigation strategies, such as targeted prophylactic use of antiviral drugs,²¹ and nonpharmaceutical interventions (NPIs) also called community mitigation strategies, such as the use of face coverings, physical distancing,²² and public health response activities such as education about the disease and management of resources for mitigating morbidity, mortality, and costs to society.² Intervention and response efforts can be tailored to address specific needs and vulnerabilities of at-risk populations, for example, those with respiratory conditions.

Disease spread projections need to align knowledge, data, and expertise from multiple areas, including biological sciences, epidemiology, population and public health, health systems, health care access, modeling, data analytics, among many others. This review article focuses on infectious disease spread prediction and evaluation of pharmaceutical and nonpharmaceutical

intervention strategies in the context of public health response during an epidemic, emphasizing the connection to respiratory conditions.

This review was developed by overviewing published literature obtained through PubMed database searches and from the authors' expertise in the related fields of research. The primary search criteria focused on PIs and NPIs and public health responses during epidemics. The authors' expertise covers areas such as clinical expertise in respiratory conditions, disease transmission and modeling, access to health care, data analytics, prediction strategies, and public health services research. This review is not comprehensive, thus not covering these areas in depth, but underlines the challenges and the potential solutions in addressing population and public health during respiratory infectious disease epidemics.

Infectious Disease and Respiratory Conditions

Those with comorbidities of chronic respiratory disease, such as asthma, can be affected by respiratory infections, potentially triggering or worsening their asthma symptoms.²³

The effect of an infection depends on its type and frequency, an individual's genetic susceptibility, or other factors such as age, atopy, and the microbiome. Here, we review possible susceptibilities of asthma caused by specific viral infections. This may lead to patients with asthma being a riskier population in pandemics caused by these respiratory infections.

Studies have revealed that viral infections trigger up to 85% of asthma exacerbations in school-aged children and up to 50% of exacerbations in adults.^{24,25} Human rhinovirus (RV) is the predominant pathogen identified in school-aged children and adult patients with acute asthma exacerbations.²⁶ Several other viruses have been found to be considerable triggers as well, including syncytial virus, human metapneumovirus, influenza, coronaviruses, and parainfluenza. Viruses such as respiratory syncytial virus and rhinovirus may cause wheezing and predispose infants and young children to the development of asthma later in life.^{6,7}

Although patients with asthma are not known to be more susceptible to contracting viral illnesses compared with healthy controls, they typically have a more severe viral-induced respiratory illness and longer duration of symptoms,²⁷ with the possibility of asthma exacerbation. Both children and adults with asthma are at greater risk of hospitalizations and morbidity from respiratory complications from acute influenza infections. During the H1N1 pandemic in 2009, children with asthma were particularly susceptible to increased intensive care unit admissions and pneumonia.²⁸ During 2010 to 2018, seasonal influenza epidemics were associated with an estimated annual 4.3 to 23 million medical visits, 140,000 to 960,000 hospitalizations, and 12,000 to 79,000 respiratory and circulatory deaths in the United States.²⁹ A recent study estimated that 291,243 to 645,832 seasonal influenza-associated respiratory deaths occur annually worldwide.³⁰

It is notable that there is no clear evidence that patients with asthma were at a higher risk of being infected or becoming severely ill with severe acute respiratory syndrome coronavirus 2, although recent reports from the United States and the United Kingdom suggest that asthma is more common in children and adults with COVID-19 than was previously reported in Asia and in the first surveys in continental Europe.³¹ The prevalence of several

underlying conditions identified in US hospitalized patients with COVID-19 was similar to that for hospitalized influenza patients during influenza seasons 2014 to 2019, regarding chronic respiratory diseases (29%–31%).³²

Evidence reveals that particular viruses can cause a prolonged, more severe course for those with underlying respiratory illnesses such as asthma or even contribute to the development of asthma. It is not certain, but coronaviruses lead to asthma exacerbations in both children and adults and cause chronic bronchitis in adults, as reported from earlier outbreaks of SARS and the Middle East respiratory syndrome.³³ Hence, the potential long-term health impact of epidemics and pandemics further highlights the importance of developing and implementing intervention strategies.

Interventions and Public Health Response

During respiratory infectious disease epidemics, mitigation strategies can be used to slow the spread of the disease. Disease mitigation can be accomplished through PIs, mitigating the spread of the disease, which alter the course of the infectious disease, cure the disease with medications, or prevent the condition with vaccination. In the absence of medications or vaccines, community mitigation strategies, more broadly, NPIs, are the first line of defense against highly transmissible infectious diseases.³⁴ Table 1 summarizes the mitigation strategies typically practiced during respiratory infectious disease epidemics.

Pharmaceutical Intervention Strategies for Asthma

PIs for asthma focus on controlling symptoms and minimizing future risks of asthma including exacerbations, poor lung function, and adverse effects of medications.^{35,36}

Pharmacologic therapy is determined by the degree of asthma severity and asthma control, including avoidance of triggers such as viral infections. Asthma-control medication is based on the severity; treatment approaches by severity have been described in the previous section. Asthma treatment medications include inhaled corticosteroids, short-acting beta-agonists, long-acting beta-agonists, biologic therapies, and oral medication such as leukotriene receptor antagonists and systemic steroids.^{35,36}

Asthma does not seem to be a risk factor for acquiring COVID-19, although poorly controlled asthma may lead to medical complications for those with COVID-19.³⁵ Therefore, those with asthma should make every effort to avoid exposure to the severe acute respiratory syndrome coronavirus 2, and all regular medications necessary to maintain asthma control, including inhaled glucocorticoids, oral glucocorticoids, and biologic agents, should be continued during the pandemic.^{36–38}

For patients who contract COVID-19, there is no good evidence that inhaled glucocorticoids have an adverse effect on the disease course; hence, these medications can be continued. Long-term oral glucocorticoids should also be continued, as abruptly stopping can lead to serious consequences. Inhaled asthma medications should be given to infected patients by inhaler rather than nebulizer when possible to avoid aerosolizing the virus and enhancing disease spread.³⁹ For patients with asthma exacerbations, usual guidelines should be followed for prompt initiation of systemic glucocorticoids, regardless of infection status.³⁶ The current recommendation of the Centers for Disease Control and Prevention (CDC) is to continue the proper use of control medications, including biologic agents (anti-immunoglobulin E, anti-interleukin 5, etc) if they started before COVID-19,⁴⁰ and to keep up with asthma action plans if the asthma conditions are getting worse.^{41–44}

Community Mitigation Strategies

Mitigation strategies in communities or NPIs focus on limiting the spread of the virus (eg, travel screening and restrictions, contact tracing and quarantining exposed or sick people, physical distancing), reducing an individual's risk for acquiring or spreading the infection (eg, hand hygiene, face coverings), reducing the environmental risk of transmission (eg, sanitizing, air ventilation), and communicating risk and best practices to the public.^{12,45–47}

Routine cleaning of frequently used surfaces, effective use of air-ventilation systems, and physical barriers can reduce circulating particles possibly containing the disease pathogen. Environmental NPIs play an essential role in controlling the spread in places with a high volume of people in close contact, such as workplaces, schools, airports, or hospitals.^{48,49} Personal NPIs are preventive actions in everyday life which include the use of protective equipment, such as masks and gloves, and other efforts to improve hand hygiene, such as frequent hand washing and using hand sanitizers.^{46,50} Organizations and communities reduce the spread of disease adopting or promoting physical distancing. Large gatherings, such as entertainment activities and conferences, may be canceled, and schools and workplaces could implement temporary closures.⁴⁵

Promotion of large-scale testing strategies is the key in improving early detection⁵¹ of disease-positive cases. Testing is essential in identifying infected individuals. Decisions on how to allocate limited testing resources may dynamically change as the disease spreads and more information or resources become available over time. For example, individuals with symptoms can be prioritized for testing when the capacity is severely limited. When more resources become available, testing efforts can expand for early detection, surveillance, or increase understanding of the natural history and transmission patterns, for example, by screening asymptomatic individuals without known exposure to infection.⁵¹ Other NPIs also support early detection. Contact tracing can be used for controlling further spread of the disease. People are notified if they may have had contact with an infected individual, monitored for early detection of disease, and recommended to follow physical distancing practices such as staying at home or self-quarantine.⁴⁷

For a global epidemic, travel restrictions could be recommended.⁴⁵ Internal travel restrictions are specifically preferred to control localized epidemics. Border closures help limit international spread.⁵²

Most of the interventions are recommended to the public, but their compliance may vary.² Educational programs or guidelines could suggest improvements in the adoption of interventions and understanding of the disease. Educational programs are not only suggested for specific epidemics but also intended for controlling chronic diseases during epidemics.⁵³ Specifically, for high-risk patients such as those with asthma and other respiratory conditions, NPIs are strongly recommended to prevent the severe health outcomes of chronic diseases, for example, promoting strategies for asthma self-management education to control asthma exacerbations.⁵⁴ The importance of NPIs, which are suggested in the daily lives of patients with asthma, such as avoiding asthma triggers and improved hygiene of asthma delivery devices (eg, not sharing with anybody else), further increases during epidemics.

There is no evidence that wearing a mask or face covering reduces oxygen level⁵⁵; however, if the patient cannot wear a mask because of severe asthma or breathing distress, they should comply with other NPIs (eg, staying at home, avoiding crowding).⁵⁶

Self-quarantine reduces exposure to environmental allergens, and social distancing prevents the person-to-person transmission of respiratory viruses. Society-based NPIs help patients with asthma to avoid from potential triggers and improve their overall

Table 1
Prediction Studies Evaluate the Effectiveness of Public Health Interventions of Respiratory Infectious Disease Epidemics (Pharmaceutical, Nonpharmaceutical, or Combination)

Pharmaceutical interventions						
Reference	Pandemic or epidemic	Intervention	Population	Outcome measure	Effects of intervention	Relation to patients with asthma or outcomes
Balicer et al ²¹ (2005)	Avian influenza	Antiviral drugs (oseltamivir), postexposure prophylactic treatment	All patients vs high-risk patients only (Israel)	Costs to economy and direct health care costs	Compared with the baseline; antiviral use strategies are cost saving.	Stockpiling is also directly cost-saving to the health care system, if oseltamivir use is limited to treating patients at high risk.
Doyle et al ³ (2006)	Influenza epidemic	Influenza vaccination and antiviral prophylaxis treatment (oseltamivir)	Age and risk groups (France)	Deaths	2000-86,000 deaths could be avoided, depending on the population targeted and intervention.	For high-risk groups, antiviral treatment seems more feasible and cost-effective than prophylaxis.
Du et al ⁹⁹ (2020)	2017-2018 flu epidemic	Antiviral (baloxavir) treatment	Treatment is given to 30% of infected cases within 48 h after symptom onset (US)	Influenza incidence, percentage of cases treated, and mortality	22 million infections and >6000 deaths could be averted.	Treatment within 24 h would almost double the impact to reduce complications.
Gani et al ⁹⁰ (2005)	1918 (3 waves), 1957, 1968	Antiviral (neuraminidase inhibitors) treatment	Different ages and risk groups (UK)	Hospitalizations	50%-77% reductions in hospitalizations	Treating only the at-risk groups is the most efficient (37% reduction).
Lee et al ¹⁸ (2011)	H1N1	Vaccine	Washington, DC, metropolitan region (US)	Daily measurements of new influenza infections, total infections	106,429 new infections per day at the epidemic's peak (day 48) and 2,825,888 infections overall, which amounted to 38% of the total population of the region.	Poorer counties tend to have more high-risk people per household, resulting in greater risk for worse influenza outcomes. Vaccine prioritizations based on household income are tested.
Milne et al ⁸⁹ (2010)	H5N1	Vaccine	Actual community of approximately 30,000 people in a developed country (Australia)	Illness attack rate	12%-30% reduction of the attack rate	Vaccine prioritization strategies based on the vulnerability of patients are tested.
Trogdon et al ¹⁰⁰ (2010)	Seasonal flu	Vaccine	Adult patients with asthma (US)	Hospitalization, cost of use, and medication	4.4 percentage points less likely to have an inpatient stay owing to ACRC. Influenza vaccination was associated with a \$492 decrease in annual ACRC nonprescription expenditures and a \$224 increase in annual ACRC prescription expenditures.	Results are related to adult patients with asthma.
Yildirim et al ¹⁰¹ (2020)	Seasonal flu	Vaccine	Pediatric patients with asthma (US)	Primary care physician, medication prescriptions, cost of use and medication	Up to 6% reduction of probability of primary care physician. 15% of the cost of asthma medications and 14%-16% of asthma use cost reductions.	Results are specific to children with asthma.
Nonpharmaceutical or combination of nonpharmaceutical and pharmaceutical interventions						
Reference	Pandemic or epidemic	Intervention	Population	Outcome measure	Effects of intervention	Relation to patients with asthma or outcomes
Bolton et al ⁵ (2012)	Influenza pandemic	Travel restrictions, school closure, generalized social distancing, quarantine, antivirals	Mongolia	Attack rate	Early social distancing measures decreased the mean attack rate from 10% to 7%-8%.	Chronic conditions, which are potential risk factors in pandemics, are common in Mongolia.

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Table 1 (continued)

Pharmaceutical interventions						
Carrat et al ⁹² (2006)	Influenza pandemic	Vaccination, treatment prophylaxis with neuraminidase inhibitors, quarantine, and closure of schools or workplaces	France (community-level individuals no vaccination, no use of antiviral drugs, and no preexisting herd immunity)	Infected individuals	If vaccination started immediately, 4% of the population would be affected by the epidemic. The affected will be 17% of the community if there was a 14-d and 36% if there was a 28-d delay of the vaccine. Closing schools would be very effective when half of the population has an infection.	The model includes individuals, which have the risk of influenza virus infection based on their age, treatment, and vaccination status.
Colizza et al ⁹² (2007)	H5N1 avian influenza virus	Vaccination, travel restrictions, and therapeutic and prophylactic use of antivirals	Global, 3100 urban areas, located in 220 different countries	Average cases, average peak time	Average antiviral supply is sufficient to treat approximately 2%-6% of the population. Even the high use of supplies leaves 30%-50% of the people infected.	Asthma in the US may seem more often in urban neighborhoods.
Eikenberry et al ⁵⁰ (2020)	COVID-19	Mask	US	Daily death rate, peak death reduction	80% adoption of 20%, 50%, and 80% effective masks reduces cumulative relative mortality by 1.8%, 17%, and 55%, respectively, in New York. In Washington, relative mortality reductions are varying from 65%-95%.	COVID-19 can affect respiratory tract and cause an asthma attack.
Ferguson et al ²² (2006)	Pandemic influenza	Border restrictions or internal travel restrictions, school closure, vaccine, antivirals	Great Britain and US	Attack rate	School closure during the peak of a pandemic can reduce peak attack rates by up to 40%; case isolation or household quarantine could have a substantive impact. Given enough drugs for 50% of the population and reactive school closure could reduce clinical attack rates up to 50%.	Outcomes, such as reduced transmission and peak attack rate.
Giordano et al ⁴ (2020)	COVID-19	Social distancing, contact tracing	Italy	Cumulative infected, total infected, recovered, and deaths	Reduction of deaths of 45,000.	People with moderate to severe asthma may be at higher risk of getting very sick from COVID-19. COVID-19 can affect the respiratory tract and cause an asthma attack.
Gojovic et al ⁸⁰ (2009)	H1N1	Vaccination, school closure, and antiviral drug strategies	London, Ontario	Attack rate	Closure of schools and daycares effectively reduced the attack rate even in the no vaccination group (4.5% with a closure vs 21.7% with no closure). Considerable reductions in the attack rate were found with only vaccination without school or daycare closure (vaccination 4.0% vs no vaccination 21.7%).	Early action on vaccine deployment is effective in reducing the attack rate.

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Table 1 (continued)

Pharmaceutical interventions						
Halder et al ⁷² (2010)	H1N1	Vaccine, school and daycare closure	Australia	Final infection rate, peak daily incidence rate, peak attack day	Antiviral drug treatment of 50% of symptomatic cases reduced the attack rate by 6.5%. Treatment of diagnosed individuals combined with additional household prophylaxis reduced the final attack rate to 19%. School closure has minimal effect on reducing the overall illness attack rate.	Outcomes relate the high-risk group, such as decreased attack rate.
Keskinocak et al ⁴⁷ (2020)	COVID-19	Social distancing	US	Number and percentage of cumulative and daily new and symptomatic and asymptomatic infections, hospitalizations, and deaths; COVID-19 –related demand for hospital beds, ICU beds, and ventilators	Shelter-in-place followed by voluntary quarantine substantially decreases COVID-19 infections, health care resource needs, and severe outcomes; delay the peak. Peak time is projected to differ across locations.	People with moderate to severe asthma may be at higher risk of getting very sick from COVID-19. COVID-19 can affect the respiratory tract and cause an asthma attack.
Shi et al ¹⁹ (2010)	H1N1	Mass gatherings and holiday traveling	US	Peak prevalence and the total attack rate	Mass gatherings that occur within 10 d before the epidemic peak can result in up to a 10% relative increase in the peak prevalence and the total attack rate.	Encouraging attendees from high-risk groups to postpone their participation in the event.
Wessel et al ²⁰ (2011)	Influenza pandemic	Drug treatment and isolation of ill individuals	General	Spread of infection	When large-scale use of treatment combined with isolation, the spread of the infection decreases but leads to the emergence and spread of resistance.	Intensive use of these interventions during the early stages of the epidemic could delay the spread of disease.

Abbreviations: ACRC, acute and chronic respiratory conditions; COVID-19, coronavirus disease 2019; ICU, intensive care unit; UK, United Kingdom; US, United States; Washington, DC, Washington, District of Columbia.

health.⁵⁷ A recent study reveals that, during COVID-19, children reduce their asthma-related emergency department visits.⁵⁸

Social Determinants of Health in Epidemics

“Pandemics are more of a social problem than a healthcare problem.”⁵⁹ Pandemics intertwine with economic, social, and health care disparities resulting in inequalities in the short and long terms.

The 1918 Spanish influenza pandemic had revealed inequities in mortality. In Norway, mortality rates were highest among the working-class districts of Oslo; in the United States, they were highest among the unemployed and the urban poor in Chicago.⁶⁰ During the 2009 H1N1 pandemic, positive H1N1 cases were more likely to come from certain ethnic groups compared with test-negative controls.⁶¹ For example, in Utah, it was reported that 29.5% of positive H1N1 hospitalized cases were minorities (those not classified as non-Hispanic Whites), greater than the mean of 22% of hospitalized cases who were minorities during the previous 3 influenza seasons. Pediatric influenza-associated hospitalization was 3 times higher among high-poverty and high-crowding census tracts than in low-poverty and low-crowding census tracts. In

addition, access to vaccine was inequitable during the H1N1 vaccination campaign in the United States at the local level; these inequities were associated with factors including population density and health care infrastructure.⁶²

Children aged less than 2 years, persons greater than 65 years of age, pregnant women, and those with underlying health conditions may be at a greater risk for developing serious complications, potentially resulting in hospitalization and death, during infectious disease epidemics. Traffic-related air pollution is often associated with incident asthma, and asthma was identified as an important risk factor for severe outcomes, including hospitalization.⁶³

Acute inequities are driven by the physical, social, and economic characteristics of the built environment, such as poverty level, education, psychosocial stress, unemployment, inadequate transportation, social networks, access to health care, housing, residential segregation, access to healthy foods, and air quality. Vandalism, illegal drug use, noise, and litter are sources of psychological stress for residents, and psychological stress is known to influence immune function.⁶³ Low health literacy can cause patients difficulty with navigating the complex health care system and understanding medical advice or prescriptions.⁵⁹ Air

pollution has been found to be associated with incident asthma. The CDC has confirmed that individuals with asthma are at higher risk for severe illness from COVID-19.⁵⁹ Empirical findings related to previous epidemics indicated that low educational level, non-White ethnicity, and poor socioenvironmental conditions are typically associated with increased hospitalization or the number of disease outbreaks owing to virus infections.⁶⁴ People in disadvantaged communities are generally more susceptible to occupational exposure to the virus and tend to have higher rates of comorbidities.

Several trends in inequities in the exposure to the COVID-19 virus have been identified during the pandemic. The most vulnerable and most affected by COVID-19 have tended to be more susceptible to occupational exposure. Furthermore, they are susceptible to high exposure in that they tend to commute to work by public transport in which it may be difficult to practice physical distancing.⁶⁵ The prevalence and severity are magnified because of the pre-existing chronic diseases—which are also socially patterned and associated with the social determinants of health.⁶⁰ The CDC has also highlighted multiple factors that contribute to increased risk including discrimination, health care access and use, housing among others. Inequities are further widening because of missing school owing to sickness or school closure during epidemics. This has been particularly a primary concern during the COVID-19 pandemic owing to the extent of school closure throughout the world. School attainment during epidemics is hampered in many ways. Roughly 20%⁶⁶ of students in the United States do not have access to the technology needed for remote learning. Millions of children have lost access to health services through school-based health centers. More than 20 million children rely on school breakfast or lunch.⁶⁷ Abuse and neglect are on the rise.⁶⁸ This is what has been deemed the “COVID-19 slide” in education. As broadly experienced in the COVID-19 pandemic, gender equality and women’s rights take a backseat in epidemics. From health to the economy, security to social protection, the effects are exacerbated for women.

Epidemics in general and the COVID-19 pandemic in particular have had disproportionately negative impacts on populations experiencing social, economic, and political disadvantages throughout the world. This directly and indirectly widens inequities in the health and well-being of people, with consequences that will last for many decades.

Prediction of and Responding to Disease Spread During an Infectious Disease Epidemic

Disease spread surveillance and prediction during respiratory infectious disease epidemics span a broad spectrum of activities, including early diagnosis of those affected,⁶⁹ identifying populations at risk of severe outcomes such as hospitalizations or deaths,⁷⁰ assessing disease spread and transmission over time and geographically,⁷¹ evaluating effectiveness of PIs and NPIs,^{72,73} and understanding prioritization of and access to treatment or vaccination given limited resources and system constraints.⁷⁴ Effective surveillance of the disease and estimating its impact on large populations or at-risk populations involve aligning knowledge about epidemiology, public health, health care system, socioeconomics, and modeling along with data derived from multiple sources, including data for population health and demographics, social networks, peer and family social interactions, among others. In this section, we review the approaches, methodologies, and data for disease spread prediction during respiratory infectious disease epidemics. Figure 1 illustrates the predictive modeling processes in epidemics.

Disease Spread Modeling

PIs and NPIs have the ability to reduce the impact of an epidemic if they are implemented efficiently and effectively, with appropriate targeting and prioritization and with limited resources. Disease spread models (Fig 2) can provide insights regarding how many people could be affected with or without severe outcomes, when and where, potential hot spots, and who could be at risk, under different scenarios (eg, no intervention vs implementing a combination of interventions).

Of note, 4 different types of models are often used in the literature, which are as follows: (1) differential equations,^{50,75} (2) random graphs,⁷⁶ (3) difference equations,⁷⁷ and (4) simulation (agent-based) models.^{45,73} In differential equation models, individuals are divided into one of the epidemiologic classes (eg, SIR model with susceptible [S], infected [I], or recovered [R] stages) and changes in the number of infected people are calculated based on the cumulative number of people in each step. The difference equations models are similar to differential equation models, but they discretize the time horizon and iteratively predict the spread of the disease for each time period. Random graphs aim

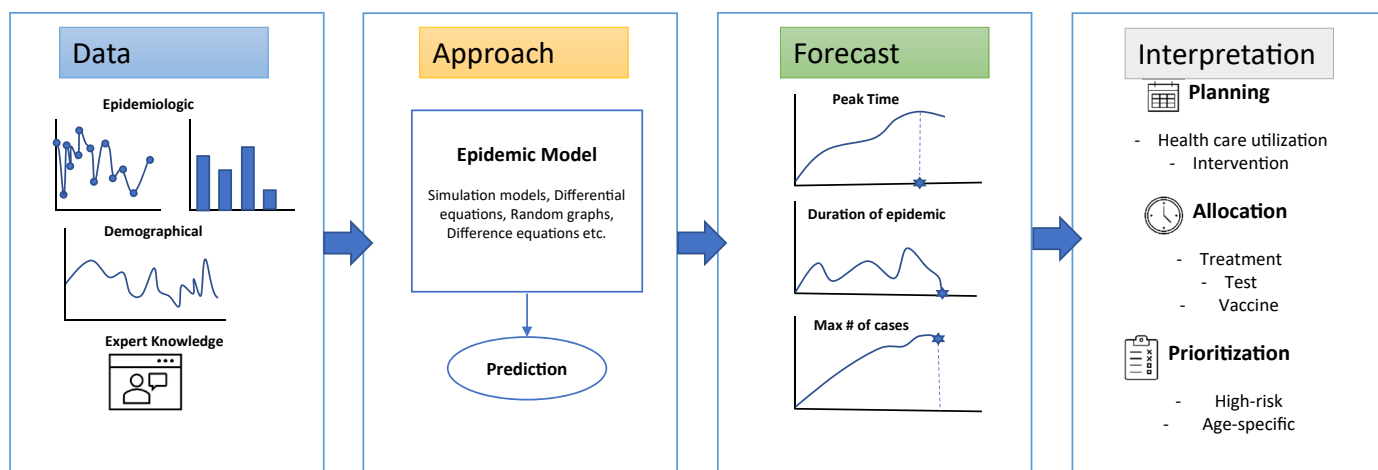


Figure 1. Overview of predictive modeling processes in epidemics.

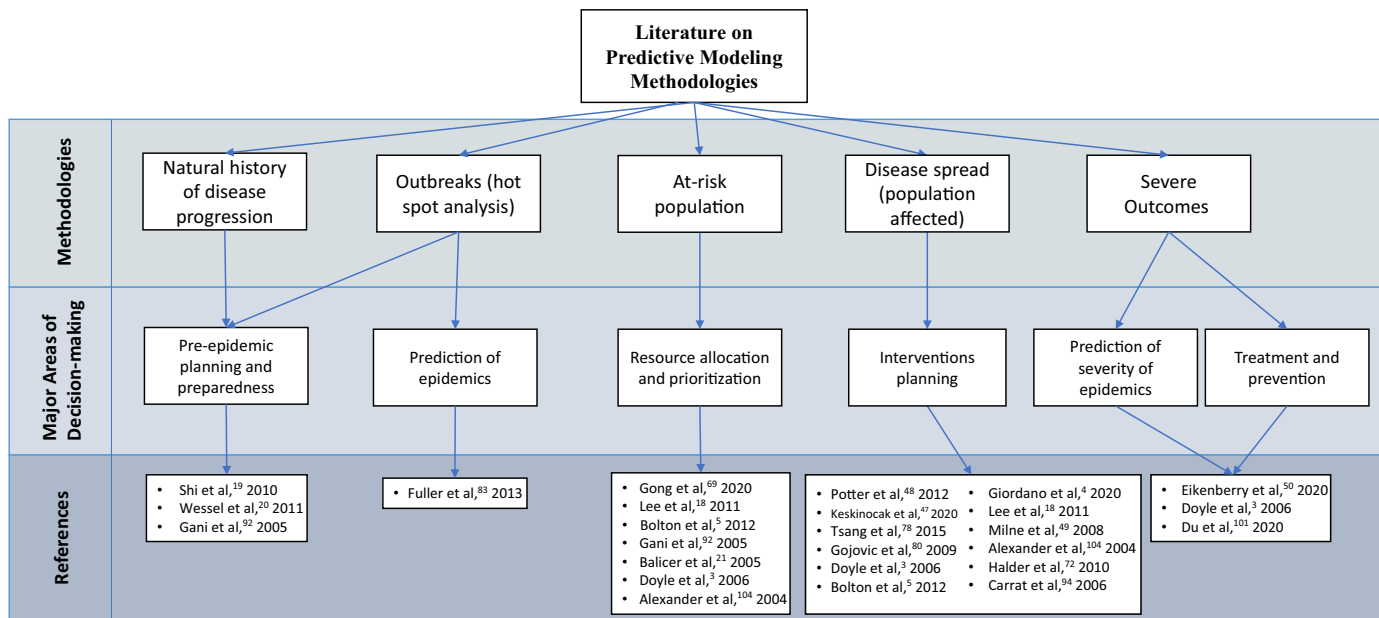


Figure 2. Predictive model methodologies and areas for decision-making in respiratory infectious disease epidemics.

to mimic social contact networks and transmission of the disease within and across parts of the network. In agent-based simulation models, each individual belongs to different groups in social contact networks (eg, family or household,⁷⁸ small community [schools],⁴⁸ or large population⁴⁷). Simulation studies are often used in evaluating intervention effectiveness; they can be viewed as “policy” laboratories, where policies and interventions can be tested without direct deployment to the public.⁷⁹ The simulated scenarios can cover baseline (no intervention) and individual or combination of interventions (eg, shelter-in-place and school closure) and with different levels of enactment, compliance, or deployment. Decisions on when, how, and where to intervene can further inform by comparing the outcomes from simulated scenarios. Such models rely on structural and parameter estimation

of the disease spread, for example, based on previous or similar outbreaks or use parameters that are continuously updated as new information becomes available about the natural history or the transmission patterns of the disease. For certain diseases, such as seasonal flu, the natural history parameters may change and be updated annually.¹⁹

During the COVID-19 pandemic, several disease spread models have been developed to support decision-making.^{3,47,49,80} Some of these models extensively use data science and machine learning techniques (J. Baek et al, unpublished data, 2020) or an ensemble approach.⁸¹

Despite best efforts, outbreaks may occur, and their timely detection relies on data, geographic systems, and hot spot analysis.⁸² Detection of outbreaks helps prevention, planning

Table 2 Sources of Input Data of the Predictive Models

Category	Data sources	References
Epidemiologic data	Centers for Disease Control and Prevention Surveillance data	Lee et al ¹⁸ (2011), Du et al ⁹⁹ (2020), Yildirim et al ¹⁰¹ (2020)
	Published journal articles	Bolton et al ⁵ (2012), Fuller et al ⁸² (2013)
	Public health reports for recent or previous outbreaks	Keskinocak et al ⁴⁷ (2020), Shi et al ¹⁹ (2010), Wessel et al ²⁰ (2011), Gani et al ⁹⁰ (2005), Potter et al ⁴⁸ (2012), Tsang et al ⁷⁸ (2015), Gojovic et al ⁸⁰ (2009), Doyle et al ³ (2006), Bolton et al ⁵ (2012), Giordano et al ⁴ (2020), Lee et al ¹⁸ (2011), Balicer et al ²¹ (2005), Eikenberry et al ⁵⁰ (2020), Du et al ⁹⁹ (2020), Alexander et al ¹⁰² (2004), Colizza et al ⁹¹ (2007), Halder et al ⁷² (2010)
	Clinical data from health care organizations, hospitals	Gani et al ⁹⁰ (2005), Halder et al ⁷² (2010), Carrat et al ⁹² (2006)
Demographic data	Expert opinion	Tsang et al ⁷⁸ (2015), Balicer et al ²¹ (2005), Gong et al ⁶⁹ (2020), Du et al ⁹⁹ (2020)
	Publicly available data (news, webpages, etc)	Doyle et al ³ (2006)
	Survey	Giordano et al ⁴ (2020), Keskinocak et al ⁴⁷ (2020), Eikenberry et al ⁵⁰ (2020)
	Census	Potter et al ⁴⁸ (2012), Fuller et al ⁸² (2013), Trogdon et al ⁹⁹ (2010)
Demographic data	Survey	Keskinocak et al ⁴⁷ (2020), Shi et al ¹⁹ (2010), Gojovic et al ⁸⁰ (2009), Doyle et al ³ (2006), Lee et al ¹⁸ (2011), Eikenberry et al ⁵⁰ (2020), Milne et al ⁴⁹ (2008), Halder et al ⁷² (2010), Carrat et al ⁹² (2006), Yildirim et al ¹⁰¹ (2020)
	Office for National Statistics, UK	Potter et al ⁴⁸ (2012), Trogdon et al ¹⁰⁰ (2010)
	The US Bureau of Labor Statistics	Gani et al ⁹⁰ (2005)
	Human Mortality Database	Lee et al ¹⁸ (2011)
	School-based data	Lee et al ¹⁸ (2011)
	Central Bureau of Statistics	Gojovic et al ⁸⁰ (2009), Potter et al ⁴⁸ (2012)
	State, local government data	Balicer et al ²¹ (2005)
	Australian Bureau of Statistics, Census Collection Districts	Halder et al ⁷² (2010)
		Milne et al ⁴⁹ (2008)

Abbreviation: UK, United Kingdom; US, United States.

(pre-epidemic, during epidemics), and decision-making (eg, decisions on types and timing of interventions based on outbreak severity).²

Projections of the disease spread, identifying populations at risk, and estimating resource use (eg, demand estimates for hospital beds or ventilators geographically and over time) can inform key preparedness tasks for health care delivery (eg, expanding capacity by building specialized facilities or acquiring certain supplies and equipment) and allocation of limited health care resources, personnel, and supplies¹ to reduce severe outcomes. Disease spread models combined with resource allocation optimization models can inform and improve decision-making, for example, distributing limited quantities of vaccine to populations in need.^{62,74}

Morbidity and mortality owing to an infectious disease epidemic can have a severe impact on the populations and strain all aspects of health care delivery.^{1,83} Mortality varied considerably across previous epidemics; the Asian flu pandemic in 1957 caused approximately 1.5 million deaths, whereas, the 2009 H1N1 pandemic resulted in 151,000 to 575,500 deaths.⁸⁴

The impact of the disease may vary across subpopulations, for example, those with specific conditions such as asthma, pregnant women, or certain age groups.^{27,85} To identify communities for targeted interventions in early diagnosis, prevention, and treatment, methodologies and data from multiple sources need to be used. For example, predictions can be informed by data on disease prevalence of subpopulations affected by the epidemic estimated at the community level. Resources include surveillance data from the CDC,⁸⁶ demographics data from the US Census Bureau,⁸⁷ and recent publications on asthma prevalence.⁸⁸

The effectiveness of interventions varies depending whether deployed for the general population,^{4,50,89} high-risk populations,^{3,21} children, or multiple age groups.⁹⁰ Timing and duration of interventions⁹¹ and decision on the types (pharmaceutical, nonpharmaceutical, or combinations) of the responses^{5,20,22,80,92} possibly affect the outcome of the preventive actions.

Access to Preventive Services and Treatment

Epidemics can widen the health disparities among subpopulations owing to inadequate access to early diagnosis, treatment, vaccine, and preventive services.⁹³ Health care access is a complex construct,⁷⁹ affecting populations vulnerable to severe or poor health outcomes through multiple dimensions, including affordability, accessibility, availability, accommodation, and acceptability.⁹⁴ Interventions need to consider all dimensions to achieve equitable, efficient, and effective access to prevention and treatment in epidemics.

Because of the complexity of the health care systems,⁹⁵ intervening to improve access requires system-specific considerations, including different constraints in supply and demand for treatment and prevention, for example, varying prevalence of at-risk or affected populations across communities, limited treatment or vaccine availability, preferences and behaviors depending on demographics, and limited participation of specialized health care providers in public insurance programs. Accounting for such constraints in access to prevention and treatment is critical to reducing the potential health disparities arising owing to the severe health outcomes in epidemics.

Health care access in epidemics is multifold. It spans access to emergency and inpatient care to treatment of severe outcomes⁹⁶ and to specialized health care, for example, for asthma control and targeted prevention.^{54,97} Because of uncertainties and unintended consequences of interventions and outcomes during epidemics, access to mental health care is critical for a healthy transition from epidemics to life-as-usual.⁸³

If treatment or vaccine becomes available, access to treatment requires careful considerations.^{18,89} For example, under limited availability, prioritization strategies based on societal function (eg, essential workers), risk level for disease-related mortality or morbidity, risk level of exposure and transmission, and age need to be implemented.^{89,98} Allocating treatment within a limited time can be tailored using data collected to facilitate forecasting, planning, and logistics.⁷⁴ Importantly, advanced methodologies in evaluating access to treatment are needed to ensure effective and equitable treatment allocation across subpopulations, with a particular focus on reducing health disparities.⁶²

The end point of this synthesis on health care access is to inspire actionable and effective policy, intervention, and practical implementation in epidemics. Appropriate use to health care during epidemics can have multiple contributors to improving health outcomes, including appropriate use of health care resources when most needed and distributions of health care resources where needed.

Data Analytics

Many of the approaches informing prediction strategies in epidemics rely on specifications of a series of parameters representing assumptions and approximations. They are often drawn from a wide range of published documents or input using expert knowledge on the natural history of the disease and the population being affected by the disease. This is common practice because of lack of relevant data needed to make estimates on patients' behaviors and preferences and providers' constraints and network structures, especially early in an epidemic. Therefore, data may come from many sources (Table 2), with different levels of accuracy and aggregation. Identifying the appropriate sources of data and understanding their limitations are overarching aspects of data analytics for decision-making in PIs and NPIs and public health response.

Conclusion

This article provides a high-level overview of strategies relevant to preparing for and responding to respiratory infectious disease epidemics, considering population health, interventions, health care access, methodologies, and data analytics. Key messages include the relevance of targeted interventions for vulnerable or high-risk populations and the importance of establishing both pharmaceutical and nonpharmaceutical interventions to reduce severe outcomes.

Epidemics do not affect everyone in the same manner and can exacerbate health disparities. For example, people with asthma could experience severe health outcomes during a respiratory infectious disease epidemic. When available, treatment or vaccine may not be widely accessible, with vulnerable populations potentially having challenges in access. In turn, this could further widen the gap in health and health care across subpopulations. Infectious disease spread prediction models, especially when combined with resource (eg, vaccines, antiviral treatments, and ventilators) allocation optimization models, can help pinpoint when such disparities may occur and how to overcome them.

PIs (eg, medication, vaccines, or other treatments) are typically not widely available at the beginning of an epidemic, and there are challenges in determining the processes for their most effective use. These factors have increased the need and emphasized the importance of NPIs. The success (eg, public acceptance and compliance, reduction of transmission, and severe outcomes) of public health responses, including NPIs, depends on early planning and timely action, as revealed during the COVID-19 pandemic. As COVID-19 response strategies continue to unfold across the world, some countries have been more successful than others in the adoption and implementation of NPIs.

Infectious disease spread prediction in epidemics relies on extensive modeling and data collection and analytics efforts. Data are collected from multiple sources and observed at various aggregation levels. Strategies informed by data and models for population health, disease transmission, and intervention effectiveness can provide insights on what works, how it works, and for whom. COVID-19 pandemic spurred data-driven analyses of intervention strategies for reducing the disease spread and opened numerous venues for future research.

Importantly, the prediction strategies are actionable if translated into decision-making, by advancing efficient and effective preparedness processes and public health responses for overcoming future epidemics; informing organizations on the costs and potential regulatory practices; and providing the basis of promoting better health and health care for people and helping society in creating an ecosystem that is prepared to provide the care all people need during and after epidemics.

This review has not provided an exhaustive search on preparedness and response strategies for respiratory infectious disease epidemics. It emphasized the relevance of intervention or response strategies for asthma; however, populations with other chronic conditions are often at risk of severe outcomes owing to the viral infection, for example, diabetes, cardiovascular diseases, obesity, among others.

Previous epidemics and pandemics have revealed to the world that they can affect regions, countries, or the world in ways that can reach people, processes, organizations, and societies. Furthermore, they have revealed the lack of preparedness of the health care systems and of the society overall. An important ingredient in successfully understanding and managing the impact of epidemics is deriving strategies and interventions informing public responses. Such strategies need to be timely and actionable. Preparedness and response strategies need to be integrated in the overall ecosystem providing health and well-being to all.

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