VIEWPOINT

COVID-19: BEYOND TOMORROW

Reopening Society and the Need for Real-Time Assessment of COVID-19 at the Community Level

Frederick J. Angulo, DVM, PhD
Medical Development and Scientific/Clinical Affairs, Pfizer Vaccines, Collegeville, Pennsylvania.

Lyn Finelli, DrPH, MS
Center for Observational and Real-World Evidence, Merck & Co Inc, Kenilworth, New Jersey.

David L. Swerdlow, MD
Medical Development and Scientific/Clinical Affairs, Pfizer Vaccines, Collegeville, Pennsylvania.

Corresponding Author: David L. Swerdlow, MD, Pfizer Vaccines, 500 Arcola Rd, Collegeville, PA 19426 (david.swerdlow@pfizer.com).

Through May 13, 2020, approximately 1.39 million cases of coronavirus disease 2019 (COVID-19) have been reported in the United States (by the Centers for Disease Control and Prevention) and more than 4.3 million cases of COVID-19 have been reported from 188 countries.[1] There is an urgent need for COVID-19 data, including community-level incidence, spectrum of disease, diagnostic test penetration, and proportion of the community with protective immunity to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (herd immunity). These data are vital to understanding where communities are on the continuum of COVID-19 cumulative incidence and prevalence and how nonpharmaceutical interventions can be titrated to reopen business and society. Real-time incidence and seroepidemiologic data are also essential to plan scenarios for the development of COVID-19 vaccines and therapeutics. Cross-sectional community surveys combined with seroepidemiology can help inform the present and help navigate the path forward.

Determining Where a Community Is Now

Rapid community surveys have been widely used by the World Health Organization and other groups to rapidly assess health conditions such as immunization coverage or to conduct demographic surveys.[2] Although other sampling methods have been used, 2-stage cluster sampling design is commonly used in rapid community surveys. Balancing precision and speed, these surveys frequently include 7 households randomly selected from each of 30 clusters, with the clusters selected from the community using "probability proportionate to size" sampling. In a rapid community COVID-19 survey, selected individuals would be queried for a designated recall period and asked if they or their household members have or had COVID-19 symptoms; have sought care, been tested, been hospitalized, been hospitalized in intensive care, or undergone ventilation; and if household members have died.

If a blood specimen and an upper respiratory tract specimen are collected at the time of the survey, the proportion of the community with antibodies to SARS-CoV-2 and the proportion of the community with symptomatic past and current infections can be estimated. These data are fundamental for determining the effectiveness of previous community mitigation strategies and the direction of future such strategies. Simultaneous rapid surveys in multiple adjacent communities can provide generalizable information across geographic areas to allow synchronization and titration of public health interventions and to allow more seamless societal interaction.

A hypothetical example can be used to illustrate how surveillance data and rapid community and seroepidemiologic surveys can be used to estimate where a community is in the continuum of pandemic disease transmission. In this hypothetical scenario, assume that laboratory surveillance data demonstrate that 3000 laboratory-confirmed COVID-19 cases have occurred in a community of 500 000 persons. Also assume that the community survey reveals that only 10% of respondents with symptoms report that they have been tested for COVID-19; therefore, only one-tenth of patients with suspected COVID-19 have been detected. Extrapolating these hypothetical findings to the larger community would suggest that an estimated 30 000 persons (3000 × 10) in the community likely had symptomatic illness.

The proportion of persons with symptoms from the rapid survey could be compared with serologic results to estimate the proportion of persons that have asymptomatic infection with SARS-CoV-2. With the additional assumption that the serosurvey in this community demonstrates that 20% of the population has antibodies to SARS-CoV-2, extrapolation of these hypothetical data would suggest that an estimated 100 000 people (0.2 × 500 000) in the community have been infected. If the reproduction number, R_0 (the average number of cases of transmission caused by an infected person), for COVID-19 is 2.2,[3] then the estimated proportion of the population who would need to be immune to SARS-CoV-2 to achieve herd immunity (estimated as $1 - 1/R_0$) would be 55%.[4]

The results of community and seroepidemiology surveys (indicating that 20% of the population has antibodies to SARS-CoV-2) would suggest that herd immunity has not been achieved and that an additional 35% of the population would need to be infected before there is herd immunity. The results of the seroepidemiologic survey also would suggest that this community could expect to have continued SARS-CoV-2 transmission and should implement public health measures accordingly.

A multiplier model is a complimentary approach that can be used to assess the current status of community-level disease in the pandemic. Multiplier models use extant surveillance data that are adjusted by survey and other data for underascertainment and underreporting. Surveillance data need adjustment because not all symptomatic persons seek care from physicians or other health care clinicians, not all clinicians or health care centers order tests for COVID-19, test kits and supplies may not be available, and test sensitivity and specificity are less than 100%. A multiplier modeling approach was used early in the 2009 influenza A(H1N1) pandemic to estimate the potential number of cases that had occurred at a time when only laboratory-confirmed cases were being reported in the United States. The model used multipliers based on estimates from general population and community surveys that determined the proportion of persons with influenza-like symptoms who sought medical care, the proportion of those who sought care who had a diagnostic specimen collected, the sensitivity of the tests, and the proportion of laboratory-confirmed cases that were reported to public health. According to this modeling approach, although only 43 677 laboratory-confirmed influenza A(H1N1) cases were reported, an estimated 1.8 million to 5.7 million cases may have occurred during the first 4 months of the pandemic in the United States.[5]

The multiplier approach was also used at the end of the influenza A(H1N1) pandemic to estimate 60.8 million clinical influenza cases in the United States (range, 43.3 million–89.3 million) through the first year.[6] These data, combined with serologic data, estimated that approximately 40% of influenza A(H1N1)–infected persons were asymptomatic[7] and suggested that an estimated 102 million persons in the United States could have been infected with influenza A(H1N1) in 2009-2010, equal to approximately 33% of the US population. Given that the estimated proportion necessary for herd immunity was 41% (an R_0 of influenza A[H1N1] of approximately 1.7),[8] these data suggested that the level of herd immunity in the United States approached the level needed to disrupt sustained transmission of influenza A(H1N1).

Determining Where a Community Will Be in the Coming Months

Projections of likely future COVID-19 scenarios for communities are needed for policy making, public health planning, and intervention development. Communities will need to project future scenarios to adjust intensity of nonpharmaceutical interventions, assuming which specific scenarios and how well they work is known, and to decide when to reopen businesses and schools. In addition, information about baseline levels of immunity are important for planning clinical trials for vaccines and therapeutic agents. Community and seroepidemiologic surveys combined with modeling approaches are useful tools for making projections of future scenarios.

National and local COVID-19 scenario projection models have been developed by a number of groups. Inputs for these models include the number of laboratory-confirmed COVID-19 cases and deaths; underlying assumptions may include the sensitivity of case and death reporting, the number of symptomatic persons tested for COVID-19, and the sensitivity of diagnostic tests. Other model inputs include estimates of the effects of community mitigation efforts and achieving herd immunity on projected declines in COVID-19 incidence. Although these models have been controversial, community and seroepidemiologic surveys can capture data that reduce the uncertainty around underlying assumptions. Repeated seroepidemiologic surveys can provide cross-sectional estimates of the degree of success of nonpharmaceutical interventions and progress toward herd immunity. These data provide iterative inputs for the model to focus model projections and can assist in model validation.

Several groups have initiated ongoing community and seroepidemiologic surveys. A preliminary report of a community serosurvey that was conducted April 3-4, 2020, at 3 drive-through test locations and included 3330 persons invited to participate to be representative of Santa Clara County, California (population, 1.9 million), found a weighted prevalence of 2.5% to 4.2% immunity; with 956 laboratory-confirmed COVID-19 cases on April 1, these data suggest that there are 50 to 85 persons with antibodies for each laboratory-confirmed case in Santa Clara County.[9] However, because the specificity of the serologic assay was less than 100%, there is the potential for false-positives in this low-prevalence population and therefore the multiplier may be lower than estimated. A preliminary report of a community serosurvey conducted in mid-April at 40 locations in 19 counties in New York State (population, 19.4 million) among 3000 persons who were shopping found 13.9% immunity; with 213 779 laboratory-confirmed cases on April 15, these data suggest that there are approximately 13 persons with antibodies for each laboratory-confirmed case.[10]

Accurate assessment of COVID-19 at the community level requires reliable evidence about the proportion of symptomatic persons tested for COVID-19, the proportion of cases that are asymptomatic, COVID-19 cumulative incidence, the proportion of persons who are hospitalized, and the proportion who die. Serial measurement of antibody levels and population immunity is needed to titrate nonpharmaceutical interventions and for development of COVID-19 vaccines and therapeutics. Integrated community and seroepidemiologic surveys combined with modeling and multiplier approaches to estimate the incidence and prevalence of COVID-19 at the community level are essential to assess the current status of the pandemic, to plan ongoing and future interventions, and to inform decision-making for gradually returning to normal activities within communities.

ARTICLE INFORMATION

Published Online: May 15, 2020. doi:10.1001/jama.2020.7872

Conflict of Interest Disclosures: Dr Angulo reported being employed by Pfizer Vaccines and owning stock and stock options in Pfizer. Dr Finelli reported being employed by Merck & Co Inc and may own stock in the company. Dr Swerdlow reported being employed by Pfizer Vaccines and owning stock and stock options in Pfizer, as well as providing overviews of SARS and Middle East respiratory syndrome epidemiology to a consulting firm for a minimal honorarium.

Funding/Support: This work was supported by Pfizer.

Role of the Funder/Sponsor: Pfizer Inc reviewed the manuscript and approved the decision to submit the manuscript for publication.

REFERENCES

1. Johns Hopkins University Coronavirus Resource Center. Accessed April 24, 2020. https://coronavirus.jhu.edu/map.html

2. Bennett S, Woods T, Liyanage WM, Smith DL. A simplified general method for cluster-sample surveys of health in developing countries. *World Health Stat Q*. 1991;44(3):98-106.

3. Flaxman S, Mishra S, Gandy A, et al. *Report 13: Estimating the Number of Infections and the Impact of Non-pharmaceutical Interventions on COVID-19 in 11 European Countries*. Imperial College London; March 30, 2020. doi:10.25561/77731

4. Fine P, Eames K, Heymann DL. "Herd immunity": a rough guide. *Clin Infect Dis*. 2011;52(7):911-916. doi:10.1093/cid/cir007

5. Reed C, Angulo FJ, Swerdlow DL, et al. Estimates of the prevalence of pandemic (H1N1) 2009, United States, April-July 2009. *Emerg Infect Dis*. 2009;15(12):2004-2007. doi:10.3201/eid1512.091413

6. Shrestha SS, Swerdlow DL, Borse RH, et al. Estimating the burden of 2009 pandemic influenza A (H1N1) in the United States (April 2009–April 2010). *Clin Infect Dis*. 2011;52(52)(suppl 1):S75-S82. doi:10.1093/cid/ciq012

7. Cowling BJ, Chan KH, Fang VJ, et al. Comparative epidemiology of pandemic and seasonal influenza A in households. *N Engl J Med*. 2010;362(23):2175-2184. doi:10.1056/NEJMoa0911530

8. World Health Organization. Mathematical modelling of the pandemic H1N1 2009. *Wkly Epidemiol Rec*. 2009;84(34):341-348.

9. Bendavid E, Mulaney B, Sood N, et al. COVID-19 antibody seroprevalence in Santa Clara County, California. *medRxiv*. Preprint posted April 30, 2020. doi:10.1101/2020.04.14.20062463

10. LaVito A, Brown KV, Clukey K. New York finds virus marker in 13.9%, suggesting wide spread. Bloomberg website. Published April 23, 2020. Accessed May 11, 2020. https://www.bloomberg.com/news/articles/2020-04-23/new-york-finds-virus-marker-in-13-9-suggesting-wide-spread