Received: 23 January 2021 | Accepted: 13 February 2021

DOI: 10.1002/sim.8931

COMMENTARY

Statistics in Medicine WILEY

Thoughts on "AIDS and COVID-19: A Tale of Two Pandemics and the Role of Statisticians" by Susan S. Ellenberg and Jeffrey S. Morris

Mitchell H. Gail

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, Maryland, USA

Correspondence
Mitchell H. Gail, Division of Cancer Epidemiology Genetics, National Cancer Institute, Rockville, MD.
Email: gailm@mail.nih.gov

Funding information
Intramural Research Program, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health

Abstract

Human immunodeficiency virus and Covid-19 (or SARS-CoV-2) differ in their incubation distributions and in their susceptibility to immunologic defense. These features affect our ability to predict the course of these epidemics and to control them.

KEYWORDS

Covid-19, epidemic model, human immunodeficiency virus, immune response, incubation distribution

Professors Ellenberg and Morris[1] outline key issues for physicians, epidemiologists, medical scientists, and policy makers who confront the devastating HIV and Covid-19 (or SARS-CoV-2) epidemics. Ellenberg and Morris also provide valuable references and highlight the essential role of quantitative thinking and the need for statisticians to pitch in. Although I worked on the clinical epidemiology of human immunodeficiency virus(HIV),[2] my understanding of Covid-19 is secondhand. Nonetheless, I will venture a few observations that are motivated by differences between HIV and Covid-19.

HIV has an incubation period (time from infection to clinical disease) measured in years, and Covid-19 has an incubation period measured in days. The rate of AIDS (acquired immunodeficiency syndrome) incidence is the convolution of the numbers infected at previous times with the incubation distribution. Because the incubation is long, the 19 297 AIDS cases reported in the United States by end of 1985 were indicative of at least 200 000 previously HIV-infected individuals, as estimated by back-calculation.[3] Back-calculation also offered a method to produce reliable projections of AIDS incidence a few years ahead, because near-term AIDS incidence depended mainly on the numbers of subjects infected years before, and not very much on future infections that are hard to predict.[4] In fact, simple extrapolation of AIDS incidence data worked reasonably well.

In contrast, even 2-month projections of Covid-19 clinical disease or death depend mainly on the future incidence of infection. Measured incidence of infection is hard to predict, as it depends on the intensity of testing, local variation in Covid-19 prevalence, reporting delays and anomalies, and variable adherence to protective measures, such as mask wearing, social distancing, and government regulations regarding indoor assembly. Semi-logarithmic plots of detected Covid-19 incidence against calendar time, and the slopes and curvature of such plots, offer useful descriptive statistics, but reliable extrapolations often do not go beyond a few days (eg, Reference 5). Ellenberg and Morris discuss various compartmental models for predicting incidence. Such models identify key parameters that determine incidence, but because projections are so sensitive to these parameters, whose values are uncertain, these models have yielded a wide range of predictions. These models have buttressed arguments for preventive measures such as social distancing to reduce the "reproductive number" and inhibit exponential growth of infections, however.

Based on data from the Centers for Disease Control and Prevention, I estimate that about 723 000 people died from HIV in the United States from 1981 to 2020.[6,7] In recent years, the annual number of deaths fell to between 5000 and 6000.[7] Treatment, drugs that inhibit transmission, and educational programs have played a role in reducing HIV deaths, not vaccination. In the year since February 2020, about 400 000 people died from Covid-19 in the United States. This is comparable to the 655 381 deaths from cardiovascular disease and 599 274 deaths from cancer in 2018 and much more than the 59 120 who died from influenza or pneumonia in 2018. Although there have been improvements in treatment of persons with Covid-19 infection,[1] the ratio of deaths to reported incident cases remains stubbornly near 2%. (Because some asymptomatic persons remain undetected, the case fatality ratio to all infected persons is lower.)

Despite sustained research efforts, no effective vaccine has been developed for HIV. Some of the obstacles to producing antibodies that prevent infection ("neutralizing antibodies") include hypervariability of the virus envelop that leads to many different strains, antibody inaccessibility to conserved regions of the envelop, and chemical instability of "spike" targets on the envelop.[8] Moreover, once HIV invades, it attacks the CD4-positive T-cells that direct much of the immune response, and it establishes itself in sanctuaries that are inaccessible to host immune defenses.[8]

In contrast, stunningly effective mRNA-based vaccines prevent about 95% of clinically diagnosed and PCR-confirmed Covid-19.[9,10] These vaccines evolved from basic research showing that the Covid-19 "spike" glycoprotein binds strongly to angiotensin-converting enzyme 2,[11] facilitating entry of the virus, and that bioengineered spike protein with proline substitutions was more stable than the original spike glycoprotein.[12] These stable bioengineered glycoproteins are antigens that induce neutralizing antibodies. The mRNA vaccines work by instructing cells in the vaccinated patient to produce these bioengineered glycoproteins; the patient subsequently develops a protective immune response to the glycoproteins. These mRNA vaccines and other vaccines directed at the spike protein may thwart this frightening epidemic, while we wait for an effective vaccine against HIV.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID


Mitchell H. Gail https://orcid.org/0000-0002-3919-3263

REFERENCES

1. Ellenberg S, Morris J. AIDS and COVID-19: a tale of two pandemics and the role of statisticians. *Stat Med*. 2021;40:2499-2510.
2. Brookmeyer R, Gail MH. *AIDS Epidemiology: A Quantitative Approach*. New York, NY: Oxford University Press; 1994.
3. Brookmeyer R, Gail MH. Minimun size of the acquired-immunodeficiency-syndrome (AIDS) in the United-States. *Lancet*. 1986;2:1320-1322.
4. Brookmeyer R, Gail MH. A method for obtaining short-term projections and lower bounds on the size of the AIDS epidemic. *J Am Stat Assoc*. 1988;83:301-308.
5. Corona virus 10-day forecast. *Corona virus 10-day Forecast*. Melbourne, Australia: University of Melbourne; 2020.
6. HIV Surveillance Report. *HIV Surveillance Report, 2017*. New York, NY: Centers for Disease Control and Prevention; 2018.
7. Murphy SL, Xu JQ, Kochanek KD, Arias E. *Deaths: Final Data for 2018*. Washington, DC: National Center for Health Statistics; 2020.
8. Koff WC. Accelerating HIV vaccine development. *Nature*. 2010;464:161-162.
9. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med*. 2020;383:2603-2615.
10. Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*. 2020;384:403-416.
11. Wrapp D, Wang NS, Corbett KS, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science*. 2020;367:1260-1063.
12. Hsieh CL, Goldsmith JA, Schaub JM, et al. Structure-based design of prefusion-stabilized SARS-CoV-2 spikes. *Science*. 2020;369:1501-1505.

How to cite this article: Gail MH. Thoughts on "AIDS and COVID-19: A Tale of Two Pandemics and the Role of Statisticians" by Susan S. Ellenberg and Jeffrey S. Morris. *Statistics in Medicine*. 2021;40:2513–2514. https://doi.org/10.1002/sim.8931