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COMMENTARY

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Comment on Ellenberg and Morris: The role of statisticians in vaccine surveillance

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Ellenberg and Morris[1] illustrate nicely the similarities and contrasts between the HIV and COVID-19 pandemics, and the roles of statisticians in related research. The article ends with the exciting news of emergency use authorization for the two new mRNA-based vaccines that appear extraordinarily effective against COVID-19. This news, and the fact that there are now several vaccines either approved or close to being so in several countries,[2] represents one of the most significant differences between the two pandemics.

The delivery and use of coronavirus vaccines present another challenge in which biostatisticians will be implicated in an unprecedented way. We are at the beginning of perhaps the largest vaccine distribution, and therefore the largest vaccine surveillance project, ever undertaken. The worldwide scope and rapidity of the distribution effort means that any research on early vaccines needs to be similarly rapid and of a massive scope, and there are a number of novel aspects of this vaccination effort in which statisticians will be important contributors.

Vaccine surveillance typically works through surveillance of spontaneous adverse events collected by self-report (VAERS), and more focused epidemiologic studies to assess potential causal associations between a specific vaccine regimen and an adverse event.[3] Observational studies of vaccine efficacy can assess real-world effectiveness against endpoints studied in trials, such as severity, but also important endpoints that were not studied in trials, such as the degree to which the vaccines can prevent transmission.

What is novel about the Coronavirus pandemic and vaccine effort? The vaccine effort already includes 10 different vaccines, approved in multiple countries.[2] The size of the effort, and its rapidity (over 160 million doses administered already,[4] with over 10 billion doses and 10 different vaccines promised by the end of 2021[2]) is unprecedented. Finally, vaccines are being administered following a range of dosing strategies. Both the Pfizer and Moderna vaccines were approved for two-dose regimens with the second dose delivered in a fixed time frame. Several countries are considering delaying the second dose, or even single-dose regimens for these vaccines.[4] While there is some evidence that single-dose regimens are effective, and that delaying the second dose does not affect vaccine efficacy, these strategies have not been studied in large-scale randomized trials. Observational studies will be the only way we can assess the safety and efficacy of the various vaccines, and the various different regimens, on a large scale.[3,5,6]

What are the challenges in conducting such surveillance? First, and foremost, systematic data collection are critical. Studies of vaccine safety and effectiveness depend on knowing dosing dates, type of vaccine used, and both history and follow-up. On a large scale, this is only feasible via linkage of accurate vaccine information to health administrative or electronic health record data.[7] This effort will require coordination across jurisdictions and across data sources. Despite the massive scale of the vaccine effort, there still will be rare adverse events that will require very large sample sizes to rule out important associations, and any one country may have insufficient sample size, and/or insufficient variation in vaccine type, to detect differences. Distinguishing between real and spurious associations will likely require data on the worldwide scale. This will certainly require multidatabase efforts involving multiple countries and health care providers. Ensuring that data are standardized across jurisdictions, and analyses are coordinated across databases, will require input from statisticians throughout the process. Measurement and recording of outcomes, study design, assessment and control of confounding, and analysis to assess representativeness and transportability should all be considered.

Many international research groups with expertise in large-scale observational studies in distributed networks have been developed over the past two decades[8-10]; these networks have been primarily focused on safety of pharmaceutical treatments, but the methods developed are easily transferable to the study of vaccines. These networks have evaluated and proposed best practices for design, conduct, and analysis of multidatabase studies.[10-12] The FDA Biologics Efficacy and Safety (BEST) initiative[13] and the Canadian Immunization Research Network[14] are two examples of research groups that have developed protocols for vaccine safety studies on a large scale, which should yield important information about the safety and efficacy of vaccines.

The response to the COVID-19 pandemic has benefited substantially from the contributions of statisticians and data scientists. The continued response, and the success of the vaccine campaign, a key step on the road to a return to normal life, will further depend on such contributions.

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