Reviewer's report

Title: Patient, Physician, Encounter, and Billing Characteristics Predict the Accuracy of Syndromic Surveillance Case Definitions

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Reviewer: James Buehler

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Major compulsory revisions

The authors are to be commended for their efforts to improve syndrome classification methods for syndromic surveillance by drawing on analogous work in the field of chronic disease surveillance. In addition, their study has been carefully designed and executed. That said, I have several concerns regarding the premise of the study and recommend that greater attention be given to the context of syndromic surveillance practice in describing the rationale for the study and in assessing the study’s strengths and limitations.

Specifically, the authors should give greater attention to the limits of the analogy between chronic disease surveillance and syndromic surveillance. Most notably, syndromic surveillance typically operates on a daily time frame, if not more frequently in certain instances, while chronic disease surveillance typically operates on a much less urgent time frame. Given the need to run statistical aberration detection algorithms on a daily basis in syndromic surveillance, is it feasible to incorporate their findings regarding physician, patient, or billing-practice characteristics into syndrome classifications on such a rapid and frequent basis? For example, hospital emergency departments (ED) are common sources of information for syndromic surveillance. In the ED setting, where the physician staff rotates on-and-off duty in a daily cycle of shifts, can the necessary information about physician characteristics be obtained and incorporated into the daily cycle of syndrome classifications. Given that syndrome classifications for syndromic surveillance are often based on patients’ self-reported descriptions of their symptoms (i.e., their “chief complaints”), or that diagnoses recorded during ED visits and reported to syndromic surveillance systems might differ from “billing diagnoses” established later, how relevant to typical syndromic surveillance practice is the authors’ emphasis on “billing diagnoses?”

The stated objective of the study is to address the problem of “high false-positive rates,” presumably with respect to the frequency of statistical alerts indicating an increase in disease frequency relative to expected frequency. However, the authors do not sufficiently “connect the dots” between their observations regarding potential improvements in the predictive value of syndrome classifications and the resulting sensitivity, timeliness, or predictive value of statistical alerts based on observed disease trends. What is the relationship between the PPV of syndrome classifications and the statistical assessment of
disease trends using various syndrome classifications? Does this vary for different types of disease? For example, prior examinations of narrow or broad syndromic classifications used to monitor influenza-like illness demonstrate that aside from variations in the magnitude of resulting signals, the observed trends are generally parallel. The presentation of the results in terms of odds ratios per unit of incremental difference from the referent for a number of measures is not intuitively easy to grasp with respect to assessing whether the observed differences would likely make a difference in practice.

In sum, this is a very nice study of an important methodological question in syndromic surveillance practice, but the eventual importance of the findings to efforts to improve practice is unclear. If the authors cannot address this question, then the Introduction should be stated in more modest terms that describe how the study takes a step in that direction. A potential next step would be to apply these adjustments to syndrome classifications and test whether or not there are substantial differences in observed syndrome trends or, ideally, differences in the ability of syndromic surveillance to detect known events.

Minor essential revisions

Page 4, lines 4-5. The dependence on a single, 8-year old reference to justify the need for this study is disconcerting (reference #1), given the evolution of the field of syndromic surveillance practice and science since the Reingold article was published. It should be possible to describe more precisely the challenges associated with detecting trend aberrations and how this study addresses a specific dimension of that challenge.

Page 4, near bottom. I'd be careful in making a statement such as "no one has attempted" such an investigation. Recommend looking through ISDS or AMIA conference agendas and abstracts to be sure of that.

Page 11. The Results section should start with a more general description of the patient population.

Page 12. The first sentence under the header “Encounter characteristics” is unclear, including the reference to Table 3. Reference to seasonality in that same section is unclear. How is this driven by known trends in seasonal viral disease, either respiratory or gastrointestinal?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.

One of the coauthors of this paper (Dr. Buckeridge) is an officer of the International Society for Disease Surveillance (ISDS), and ISDS is currently receiving funding from the group I direct at the Centers for Disease Control and Prevention for a project related to syndromic surveillance--the topic of this manuscript. In addition, Dr. Buckeridge is also a contributor to other collaborations and projects related to syndromic surveillance that involve various members of the staff I direct.