Reviewer's report

Title: Quarantine for pandemic influenza control at borders in small island nations

Version: 1 Date: 11 September 2008

Reviewer: Ying-Hen Hsieh

Reviewer's report:

Major Compulsory Revisions

Traditionally, optimal length of quarantine was determined based on incubation time. The authors proposed to incorporate the release of asymptomatic infectives which intuitively would lead to longer quarantine period. However, due to absence of detailed data, as the authors had mentioned, and additional (at time unrealistic) assumptions, further uncertainties regard the reliability of the results is unavoidable. Below are some remarks:

1. The authors assumed (p. 7) a combined reproduction number of 3 (2+1) as “the average numbers of symptomatic and asymptomatic secondary transmissions caused by single primary case” and cited references [24] and [25]. I don’t see where this number is used in this work. Moreover, this number is larger than the range of reproduction number used in reference [24]. Reference [25] did give ranges of ranges 1.2–3.0 and 2.1–7.5 for community-based and confined settings, respectively. Is it due to the authors’ hypothetical setting of a small island nation? The authors should clarify how their assumption is made and how it is used in their work.

2. The authors used arrival time as the latest time of possible infection but admitted that, “in reality, earlier acquisition of infection would increase the probability of non-infection after quarantine and therefore increase the effectiveness” (p. 8). This affects the result significantly, as time since infection upon arrival is important information but is not considered, leading to perhaps considerable overestimate in optimal quarantine time.

3. Another factor that was not considered is that the measure of effectiveness only considers the risk of introducing infectives to the community. However, during SARS outbreak, even though there was no evidence of asymptomatic infection for SARS, one study (Hsieh et al. 2005) have shown that an indirect benefit of quarantined is that the previous quarantined infectives were detected significantly faster than those who were not, thereby limiting their opportunities to infect other after onset. That is, the mean time from onset of symptoms to diagnosis for the previously quarantined infective (1.20 days) was much shorter than that of those who were not (2.89 days).

4. The authors claimed (P. 9) that by assuming that the length of generation time among asymptomatic individuals is identical to that among symptomatic cases yields a conservative effectiveness estimate. It seems to me that whether the
estimate is conservative or not would depend on whether the generation time length among asymptomatic individuals is longer or shorter than that of symptomatic cases, which is uncertain since the matter depends on two factors: per contact transmission probability (where asymptomatic transmission might be less due to less virus shedding) and contact frequency (where an asymptomatic infect might have more contact). Hence we are only sure of more uncertainty this assumption brings.

5. During the 2003 SARS outbreak, many affected areas instituted exit border screening at airport also, which would lower the number of symptomatic infected travelers and subsequently lessen the effectiveness of quarantine since the prevalence of incoming travelers, p, would be smaller (see Equation 6 on p. 12). Another related issue is the authors assume one source country. In the case of multiple affected areas, as in the case of SARS, multiple values of p need to be considered in the expression for PPV and NPV, but which should not be difficult to derive but perhaps harder for simulation purposes.

Minor Essential Revisions
1. The authors assumed (p. 7, line 124) a flu symptomatic ratio of 66.7% and cited, among several references, reference [12] which, as far as I can see, gave no such estimate.

2. I am not sure what the authors mean by “At least, we selected this dataset…” (p. 8, line 150).

3. P. 17, line 381, the first two commas are unnecessary.

Discretionary Revisions
1. As the authors had noted, perfect quarantine was assumed (p. 6), e.g., perfect quarantine, detection of symptoms, and isolation. Recent studies (e.g., Hsieh et al. 2005) on quarantine for 2003 SARS outbreak have shown the above assumption might be too idealistic, if not unrealistic. Perhaps such results could be useful to quantitatively study the uncertainty due to imperfect quarantine, lack of detection, etc.

Level of interest: An article of importance in its field

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