Author's response to reviews

Title: Post-exposure prophylaxis during pandemic outbreaks

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BMC Medicine

Dear Editor,

We would like to thank the reviewers for their insightful comments on our manuscript entitled:

“Post-exposure prophylaxis during pandemic influenza”

By S.M. Moghadas, C.S. Bowman, G. Röst, D.N. Fisman; J. Wu

We have taken these comments into full consideration and addressed them in the revised manuscript. Our responses are detailed below.

Response to Reviewer 1:

1. Emergence of drug resistance in the absence of drug pressure is an important point raised by the reviewer. We have included a brief discussion on this issue in the revised manuscript (Page 13) with the relevant citation, which provides evidence for the involvement of other factors in the emergence and spread of drug resistance:

On Page 13: “It is, however, important to note that the emergence and spread of resistance is also influenced by other factors, such as compensatory mutations that ameliorate the fitness costs associated with resistance evolution. For example, a dramatic rise in the emergence of drug resistance in seasonal influenza H1N1 viruses has been reported worldwide even in geographic areas where drugs have been infrequently used. Recent work suggests that the globally increasing frequency of resistance is more likely attributable to its interaction with fitness enhancing mutations rather than to direct drug selection pressure [33]. Thus, the use of drugs need not be the sole factor in the elevated population incidence of drug resistance.”

2. We have corrected Figure 1 for the description of “viral titers”.


Response to Reviewer 2:

1. We have now cited relevant studies that provide estimates of the risk of emergence of resistance during oseltamivir treatment in clinical trials (on page 6 of the revised manuscript), and described the relation between these rates and model parameters. As noted above, the discussion on emergence of resistance has also been expanded on page 13.

2. We have corrected the typo H1H1 (“H1N1”) on page 13.

We also would like to thank the Editor for the opportunity given to revise the manuscript for publication in BMC Medicine.

Sincerely,

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