We would like to add to the debate on neuraminidase inhibitor (NI) data recently initiated by the BMJ, by highlighting what lower efficacy may mean from a population-wide perspective. If NI agents are less effective than those given in published data, future influenza pandemic responses which rely on such efficacy data may be significantly compromised. Even following the 2009 influenza pandemic, such NI-based interventions remain an untested strategy.

We have used the limited published data on NI efficacy in a series of modelling studies based on a population of ~30,000 in Western Australia (1). These studies aimed to determine the population-level effectiveness of a range of NI-based intervention strategies, on their own and coupled with various social distancing interventions (2).

Recently, we conducted sensitivity analyses on the NI efficacy parameters, both for treatment and prophylaxis. This has allowed us to examine how the potential mitigating effect of NI-based interventions (in terms of illness attack rate (AR) reduction) might be impacted if their efficacy was lower than that suggested in the literature (3, 4, 5). The results indicate that if NI efficacy is lower than claimed, interventions involving NI use show a significant variation in outcome, see Table.

Data in the Table indicate how reduction in NI efficacy from a baseline of 66% for treatment and 85% for prophylaxis alters the AR of an influenza pandemic having a basic reproduction number of 1.8 and an unmitigated AR of 32%. These were the most recent efficacy estimates which we could find, relying on an analysis (3) of two oseltamivir trial studies (4, 5). The left hand column in the Table indicates assumed NI efficacy, as % reduction in infectiousness when used for treatment, and % reduction in susceptibility when used for prophylaxis; the latter being bracketed. We have examined the five NI-based intervention strategies described in the Table under a range of efficacy estimates lower than the baseline. Two examples are given; one having 11% treatment efficacy (and 14% for prophylaxis) and the other with 33% treatment efficacy (and 42% prophylaxis efficacy).

Depending on the strategy applied, lessening NI efficacy from the baseline alters the population-wide effectiveness of interventions differently, depending on whether social distancing interventions are combined with the NI-based interventions or not.

If combined with rigorous and sustained social distancing (continuous school closure and reduced workplace and community contact; right hand column) lower NI efficacy does not alter the AR reduction
achieved (from 32% to 6%); the significant reduction is due to the rigorous social distancing applied. However, weaker social distancing involving only 2 weeks of school closure when combined with NI interventions (3rd column from right) gives a strategy much more reliant on the mitigating effect of the NI antivirals, resulting in ARs of 20% and 23% with the two efficacy reductions, compared to the high efficacy baseline of a 15% AR. All other intervention strategies presented in the Table also become less effective due to reduced NI efficacy, as illustrated by proportionate increases in their AR.

Experience of NI-based interventions used during the 2009 pandemic give little guidance as to their effectiveness. If the NI efficacy is lower than claimed, detailed modelling studies such as (1, 2) may be used to give guidance on how this negatively impacts on pandemic preparedness plans which are partially reliant on NI-based strategies. If a future influenza pandemic has higher morbidity and mortality rates than occurred with the “mild” H1N1 2009 pandemic, investment in creating and maintaining NI stockpiles may be viewed as costly and ineffective.


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