

LETTERS

THE STORY OF ANTI-INFLUENZA DRUGS

Authors' reply to Dunning

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Dunning questions the relevance of our systematic review, suggesting that any research data—regardless of its quality—that tests the effect of neuraminidase inhibitors on non-pandemic influenza answers the wrong question.^{1 2} Because all randomised trial evidence is on non-pandemic influenza, he argues that we must look elsewhere and highlights non-randomised observational studies, which conclude that the drugs provide great benefit, contrary to the conclusions that can be drawn from randomised trials.

This line of argument has been made elsewhere,^{3 4} but there are several inherent problems.

Firstly, Dunning's description of 2009 H1N1 influenza as "severe influenza, illness caused by pandemic H1N1" assumes that so called pandemic H1N1 influenza is by definition severe and non-pandemic influenza is not. Seasons classed as "pandemic" receive more media attention than non-pandemics and the 1918 influenza was severe, but in all other so called pandemics (1957, 1968, and 2009) mortality was comparable with non-pandemic influenza.^{5 6} The randomised trial evidence does answer important questions.

Secondly, we are not convinced that we were wrong to exclude observational studies. We published our methodology in 2010, stating that we would focus on randomised trials. Since then, no experts or peer reviewers have questioned this approach.

Thirdly, funding matters. Dunning omits mentioning that the "systematic review" he cites as showing "significant reductions in mortality in adults" was funded by Roche, oseltamivir's manufacturer. Nor does he hypothesise how a drug that confers

modest benefit on what he considers mild seasonal influenza could produce such stunning benefits against severe influenza. If anything, the reverse would be true.

Lastly, context also matters. In 2003, Roche authored a paper claiming that randomised trial data showed that oseltamivir reduces complications and hospital admissions. Authorities trusted Roche's word and did not vet these data themselves. Had they done so, as we did in our review, they may have realised that the data did not support Roche's conclusions. Knowing this, authorities might have even supported properly assessing oseltamivir in a randomised trial during the so called pandemic of 2009. Clinical trials are ethical and the only way to answer the question Dunning says is important, unless you are seeking to defend a decision already made.

Competing interests: Our competing interests are the same as declared in the article (<http://dx.doi.org/10.1136/bmj.g2263>).

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Cite this as: *BMJ* 2014;348:g3018

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