

Time to review New Zealand's antiviral stockpile for pandemic preparedness?

New Zealand (NZ) seems to have done a reasonably good job of influenza pandemic planning, as we concluded in a previous review published just before the 2009 pandemic.¹ This planning may even have contributed to some of the favourable features of the NZ health sector response to that pandemic (albeit a relatively mild pandemic compared to previous ones).²

Part of the NZ Ministry of Health's current planning includes stockpiling of antivirals, reported to comprise more than one million doses of oseltamivir (*Tamiflu*) and 300,000 of zanamivir (*Relenza*), costing \$32 million.

However a recent Cochrane systematic review has raised questions around the effectiveness of these antivirals.³ This review benefited from the inclusion of many previously unpublished reports from the pharmaceutical industry and also the European Medicines Agency. It found fairly modest benefits from the treatment of adults e.g., "oseltamivir reduced the time to first alleviation of symptoms by 16.8 hours". But in terms of hospitalisations, the treatment of adults with oseltamivir had no significant effect on hospitalisations and zanamivir hospitalisation data were unreported. Furthermore, the Cochrane reviewers also noted that there were many limitations with the trials they reviewed (e.g., selection bias, attrition bias, "non-identical presentation of the placebo" and even that some of the placebo interventions "may have contained active substances").

Debate about the findings of this Cochrane review and other evidence for and against antivirals being worthwhile have featured in recent issues of the *British Medical Journal* (especially the 12 April and 3 May issues of 2014).

So given such debate, the large cost of the antiviral stockpile to the NZ taxpayer, and the need for the public and health workers to have confidence in any antiviral stockpile, it is probably desirable that NZ health authorities conduct a thorough and transparent review of this topic. This review could address the following issues:

- What information besides the new Cochrane review needs to be considered (e.g., one systematic review of observational studies suggested a benefit from antivirals;⁴ and another indicated a mortality reduction benefit for hospitalised patients⁵).
- What is the evidence around the practicalities of using antivirals during a pandemic for prophylaxis and also for treatment? For example, one article on the UK experience in 2009 has suggested that antivirals were of no practical benefit for prophylaxis in the community.⁶
- What is the evidence around likely cost-effectiveness such as the cost-per-illness prevented (e.g., in an emergency worker during a pandemic) and cost-per-hospitalised patient prevented from dying? New economic modelling work might be required to answer such questions since former modelling that

included consideration of the cost-effectiveness of NZ doing stockpiling might now be outdated.⁷

- How do any of the above cost-effectiveness estimates compare with other ways to reduce spread of an influenza pandemic (e.g., mass media campaigns around improving hygiene and promoting staying at home when sick)? Or how might it compare with enhancing hospital surge capacity? Our own work based on the 2009 pandemic does suggest that hospital care was likely to be a relatively cost-effective means of preventing death from pandemic influenza.⁸
- If antivirals are ultimately thought to have a worthwhile role in pandemic control and reducing burden on the health system – then what is the best approach to obtaining them? Is it to continue to have a national stockpile (with the associated waste when expired product gets discarded), or is it more cost-effective to have a contract and annual fee payment to manufacturers for guaranteed immediate supply as per “manufacturer reserve programmes”? The issues are quite complex, as described in the economic modelling literature.⁹

Finally, such a review process might also be an opportunity to consider further upgrades to pandemic planning. In particular, it would be good to see modelling work that assessed the scope for imposing temporary restrictions at national borders and internal borders (e.g., between the North and South Islands and offshore islands).

NZ's border screening used in the 2009 influenza pandemic appeared to have been relatively ineffective,¹⁰ so improving these processes should be a key priority. Such control could buy time to prepare better or reduce peak effects during a pandemic (with reduced risks of health services being overwhelmed). Such planning could also inform responses to other potential pandemic agents—including future genetically-engineered bioweapons.

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