Cost–effectiveness analysis of pandemic influenza preparedness: what's missing?

Tom L Drake,[a] Zaid Chalabi[a] & Richard Coker[a]

Introduction

Highly pathogenic pandemic influenza viruses pose a real if poorly defined risk to public health and economies. In a study of potential mortality, Murray et al. estimated that 62 million excess deaths would have occurred globally had there been a pandemic event in 2004 with an excess mortality proportional to that observed in the 1918 Spanish influenza pandemic.[1] The United Nations System Influenza Coordination has outlined the impact of pandemic influenza not just on mortality, but also on health-care systems, animal health, agriculture, education, transport, tourism and the financial sector.[2] In short, a pandemic event threatens all aspects of the economic and social fabric.

In 2003, a highly pathogenic strain of avian influenza A (H5N1) virus re-emerged and continues to circulate. The risk of viral mutation facilitating transmission from human to human and the resulting likelihood of a pandemic event have been the subject of much concern, debate and research. In this context, the 2009 H1N1 swine flu pandemic catalysed action by public health decision-makers and international donors. Many countries have drawn up pandemic preparedness plans, invested in stockpiles of antivirals and equipped border points with thermal imaging technology. In 2010, the United Nations System Influenza Coordination reported that between 2003 and 2009 international donors had pledged over 4300 million United States dollars for pandemic influenza preparedness.[2] But how should such funds be used to maximize public health benefit? And in the context of existing resource constraints, especially in low- and middle-income countries, is pandemic preparedness a good use of funds compared with other public health investment options?

The total number of cost–effectiveness or economic evaluation studies of pandemic influenza preparedness options published to date is small but has risen sharply since 2009. In a recent systematic review, Pérez Velasco et al. identified 44 economic evaluations of pandemic preparedness strategies.[3] Although the first of these was published in 1999, the majority (75%) were published from 2009 onwards. Pérez Velasco et al. evaluated these 44 studies against a checklist of standard practices in the field of economic evaluation, but their stated aim was to summarize the literature and offer policy recommendations rather than to examine methodological approaches. In 2009, Lugnér & Postma conducted a review of 12 economic evaluations and recommended using dynamic rather than static transmission modelling in economic evaluations of pandemic influenza preparedness strategies.[4] Pandemic influenza transmission modelling studies are much more numerous than cost–effectiveness studies. We suggest Lugnér & Postma's recommendation might be turned around, that is, pandemic transmission modelling provides only a partial picture and should aim to incorporate the economic consequences of a pandemic.

The field of economic evaluation for epidemic or pandemic preparedness planning is at a nascent stage. However, as the control of communicable disease progresses, preparedness measures for epidemic events become increasingly important because the decreased burden of communicable disease increases the number of susceptible individuals and hence the risk outbreaks. The objective of this paper is to suggest improvements to the methods and scope of economic evaluations surrounding pandemic influenza and other epidemic or pandemic events. The paper has been produced as part of a wider study on investment options for pandemic influenza preparedness in Cambodia.

Critique of scope

Neglect of low-income countries

Pandemic influenza presents the greatest risk in low- and middle-income countries. Murray et al. found that, of the 62 million excess deaths estimated for a modelled pandemic in 2004, 96% would have occurred in countries not belonging to the Organisation for Economic Co-operation and Development. Their model also showed a strong negative correlation between per capita income and mortality associated with pandemic influenza; every 10% increase in income was accompanied by a 10% decrease in mortality.[1] Furthermore, the health impact of a pandemic in low-income countries and regions can be compounded by the lack of access to medical services, undernutrition, inadequate shelter, high population density, poor hygiene and a greater likelihood of co-infection with endemic disease.

Since poverty is widely associated with endemic disease, one might expect poor countries to suffer a greater burden of pandemic disease. However, of the 44 economic evaluations of pandemic influenza preparedness options performed to date, none has focused specifically on low-income or lower-middle-income countries. One study by Carrasco et al. evaluated the cost–effectiveness of antiviral stockpiling in 10 countries, including three lower-middle-income and one low-income country.[5] The authors concluded that for two thirds of the world's population, antiviral stockpiling is not cost–effective and that "under perfect allocation higher resourced countries should aim to store antiviral stockpiles".[5] This conclusion is problematic, however, because it does not necessarily follow from the study results that antivirals are less effective or that stockpiling them is more costly in poorer countries; it is simply that such countries are less able to afford the drugs. Using the perspec-

[a] London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, England.
Correspondence to Tom L Drake (e-mail: thomas.drake@lshtm.ac.uk).
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tive of a transnational payer such as the Gates Foundation or any national aid programme (i.e. valuing health gains in all countries as being equal) would more accurately reflect how cost–effectiveness varies among countries and would allow affordability comparisons.

Selection bias favouring pharmaceutical interventions

Pharmaceutical interventions, principally vaccine and antiviral stockpiling, feature heavily in the literature on the economics of pandemic preparedness options. Of the 44 studies identified by Pérez Velasco et al., 34 (77%) focus exclusively on pharmaceutical interventions. Only four studies (9%) focus solely on non-pharmaceutical interventions, namely school closures, air travel restrictions, sick leave authorizations and the use of face masks. Pérez Velasco et al. note the general disregard for interventions based on public hygiene and disinfection. Thus, there seems to be an intervention selection bias within the literature with the potential to influence policy decisions and affect the course of further research. This bias in favour of pharmaceutical interventions may be driven by the fact that antiviral stockpiling and vaccination programmes are expensive and therefore have important financial implications for funders. All of this further underscores the point made earlier, that research to date has neglected the question of how scarce resources in poor countries might be effectively used to save lives, and has centred instead on determining how to allocate with greater efficiency the more substantial funds available in high-income countries. It is perhaps also fair to venture that economic evaluations of antiviral stockpiling make for a simpler research question that researchers might be inclined to favour over complex economic analyses of non-pharmaceutical interventions.

Critique of methods

Disregard for health system capacity

The ability of the health system as a whole to cope with a sudden increase in service demand is fundamental to minimizing pandemic influenza mortality and morbidity. Health system capacity has so far been excluded from all economic evaluations of pandemic influenza preparedness. Recent work by Rudge et al. highlights health system resource gaps for pandemic influenza scenarios in six countries in south-eastern Asia and, not surprisingly, the greatest gaps between service demand and health system capacity were frequently found in the poorest areas.[6] Ignoring health system capacity implicitly assumes that capacity is unlimited, an assumption that is even less justifiable in a low- or lower-middle-income context than in that of a high-income. The question of whether health system strengthening in poor countries is the most effective investment in pandemic preparedness is still to be answered.

Neglect of pandemic uncertainty

Uncertainty is a characteristic feature of pandemic events; the year in which a pandemic will occur, the incidence rate, the associated burden of morbidity and the case-fatality proportion are never known in advance. Evaluations of the cost–effectiveness of endemic disease control strategies are performed on the implicit assumption that the public health burden remains consistent over time so that the results have relevance for future policy-making. This is a reasonable assumption for endemic but not for pandemic disease, which is marked by uncertainties in disease burden and event timing. However, in many economic evaluations of pandemic preparedness options, a fixed pandemic scenario is assumed to simplify analysis. For instance, the pandemic event could be assumed to have the same characteristics as the 1957 pandemic. Some studies test these assumptions with fixed-point univariate sensitivity analyses, but few take a probabilistic approach and simulate multiple pandemic scenarios. Robust approaches to incorporating and presenting pandemic event uncertainty are needed to improve the methods applied in performing economic evaluations of pandemic preparedness options.

Conclusion

The evidence base for the cost–effectiveness of pandemic influenza preparedness policy options is small but growing rapidly. Modelling methods vary considerably between studies and the literature is limited in scope. To contribute to improving quality and consistency in this emerging study area, we recommend: (i) greater focus on low-resource settings; (ii) inclusion of non-pharmaceutical interventions; (iii) incorporation of health system capacity; and (iv) more robust analysis and presentation of pandemic event uncertainty. So, what's missing from pandemic influenza preparedness cost–effectiveness analysis? Answer: poor countries, non-pharmaceutical interventions, health system capacity and pandemic uncertainty. ■

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