Pandemic influenza preparedness planning: lessons from Cambodia

Anthony C Huszar\textsuperscript{a}, Tom Drake\textsuperscript{a}, Teng Srey\textsuperscript{b}, Sok Touch\textsuperscript{b}, Richard J Coker\textsuperscript{a,c}

Introduction

Experts have estimated that a pandemic influenza outbreak could cost more than 60 million lives worldwide.\textsuperscript{1} When considered in combination with recent research demonstrating human-to-human transmission potential of the highly pathogenic strain of avian influenza A(H5N1),\textsuperscript{2} this highlights the growing need for public health officials to review their pandemic influenza preparedness strategy. This is especially true for South-East Asia which is predicted to be the likely epicentre of future pandemics.\textsuperscript{3}

Following the 2009 H1N1 swine flu pandemic, many governments drew upon guidance from the World Health Organization (WHO) pandemic influenza preparedness framework\textsuperscript{4} to revise their national pandemic influenza plans. Cambodia was no different and the government updated its National Comprehensive Avian and Human Influenza Plan by producing three further pandemic influenza strategies.\textsuperscript{5–7}

Interventions can be separated into pharmaceutical and non-pharmaceutical categories. Pharmaceutical options include antiviral stockpiling, the use of vaccines, which would take six months to produce, and there is now early evidence that certain immunemodulatory pharmaceuticals, including off-patent statins, may be effective in reducing influenza-related mortality.\textsuperscript{8} Non-pharmaceutical approaches are varied, but include investing in improved surveillance by way of sentinel sites and a network of approved laboratories, social distancing by risk communication, the closure of schools and workplaces, and the use of protective personal equipment (PPE).

One drawback of these guidance documents is that they hold a neutral perspective on which policy options might be the most beneficial, and furthermore do not give any indication on how best to allocate resources. It should be a priority to ensure that the US$ 2.7 billion that has been invested globally in the past seven years into pandemic preparedness\textsuperscript{9} is spent effectively.

As part of a wider project evaluating pandemic influenza mitigation investment options in Cambodia, we conducted semi-structured interviews with members of Cambodia’s pandemic influenza national coordinating committees to assess current beliefs. Informants were chosen from the...
National Pandemic Planning and Response Committee, National Committee for Disaster Management, National Pandemic Vaccine Committee, and the Joint Partners Interface Group. Of the 33 identified members, 14 (42%) responded and took part. Informants were first asked to score the 10 pandemic policy areas, as listed above, based on importance and their willingness to invest resources, on a scale of one to five (with five meaning 'very important'). Participants were permitted to use each number more than once in order to gain a more reflective estimate of how the different interventions compared with each other. They were then invited to comment on how they reached their decision for each area. Using basic statistical methods and Grounded Theory, two main themes emerged from the analysis of the transcripts, i.e. difficulties in prioritizing the different pandemic preparedness interventions, and a lack of consensus on certain interventions. We believe these problems are also likely to exist in other South-East Asian countries that share similar attributes.

## Difficulties in prioritization

Given that the ability to prioritize different policy areas or interventions is a key part of the health planning process, it was surprising that all but one of the policy areas scored between four and five, which we interpreted as 'important' to 'very important'. This highlighted an inability to differentiate adequately between policy areas. The single policy area that did not receive all-round acknowledgement of its importance was, unsurprisingly, generic immunemodulatory pharmaceuticals, due to the current paucity of evidence. The results are shown in Table 1.

### Contrasting concerns

Despite the overarching importance placed upon all of the WHO-backed interventions in the first instance, some informants raised concerns that were not held consistently across the group. This was observed with both pharmaceutical and non-pharmaceutical approaches.

#### Pharmaceutical interventions

Many informants spoke of the need to stockpile antivirals, with the majority of informants opening with a line similar to this participant:

“It is very critical to have a stockpile for Tamiflu.”

Yet in contrast to this stated need for Tamiflu, some informants raised concerns about the associated costs of antiviral stockpiling, including storage and distribution, as well as the assumptions made about the drug's efficacy. These concerns are illustrated by the following comments:

“[We] need to spend a lot of money and the duration of use is short thus stockpiling is not important... if we stock it, we waste money... It is not necessary for a developing country like us.”

“[We make an] assumption that antivirals are good...we assume that the virus is sensitive to antivirals... and that antivirals decrease mortality, and decrease the period of transmissibility.”

Vaccination strategies also appeared to invoke mixed concerns among the informants. All informants commented on at least one of the following issues: speed and capacity of vaccine manufacturing, unknown efficacy, and cost. Yet despite these legitimate concerns, investment for this policy option remained popular among respondents.
Non-pharmaceutical interventions

All 14 respondents agreed on the importance of governance, diagnostic capacity, and human resources, and that all medical staff must receive suitable PPE. Justifications included the International Health Regulations and healthworkers’ faith in the equipment. The general impression of PPE among informants was captured by this informant:

“without [PPE] we can’t do anything.”

In contrast, another stated:

“Our country is poor and the PPE is expensive and... if we wait for PPE we can’t do anything else.”

The policy option for critical care equipment generated even more polarized results. Some informants firmly stated the importance of having life-saving critical care equipment, perhaps over-stating their efficacy, while others made comments about their being costly and potentially non-cost-effective. Social distancing raised similar mixed responses: four informants stated that it was a valid policy option, while five others raised concerns about efficacy and difficulties with implementation.

Why does this matter?

These interviews highlight the difficulties that policy-makers face when allocating resources to pandemic influenza preparedness in Cambodia, and may also reflect difficulties faced by their counterparts throughout South-East Asia. Our findings also show that drawing concrete conclusions from the current evidence base is challenging, possibly because the evidence has largely been generated in high-income settings. While high-income countries are able to allay the uncertainties by investing across the board, countries with limited resources may inadvertently invest in less cost-effective measures. This could in effect result in unnecessary loss of life in the event of a future pandemic.

What next?

In order to support the decision-making process in pandemic influenza policy, we suggest need for better research on two counts. First, there needs to be better evidence on the effectiveness of interventions, especially in low-income countries. Second, appropriate economic evaluation needs to complement these studies in order to guide decisions on implementation. While we recognize the inherent difficulties in pandemic influenza modelling due to its uncertain timing, and viral virulence and response to interventions, having a better grasp of the relative differences between the interventions described in the WHO pandemic influenza preparedness framework would allow for more intelligent decision-making by public health officials.

In order to facilitate this process of generating better evidence, we make two recommendations. First, pre-approved clinical trials, where ethical approval and funding would be confirmed ahead of the next pandemic, may be able to generate more reliable strain-specific data that could be used as events unfold. Second, improved communication could enable researchers to help policy-makers interpret their results in the context of pandemic uncertainty, and conversely, it is crucial that in such a challenging area of decision-making, policy-makers should liaise with researchers to help direct their work.

Acknowledgements

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Table 1: Fourteen key pandemic influenza informants in Cambodia were asked to score each pandemic influenza policy based on importance and their willingness to invest.

<table>
<thead>
<tr>
<th>Policy area</th>
<th>Key informant 1</th>
<th>Key informant 2</th>
<th>Key informant 3</th>
<th>Key informant 4</th>
<th>Key informant 5</th>
<th>Key informant 6</th>
<th>Key informant 7</th>
<th>Key informant 8</th>
<th>Key informant 9</th>
<th>Key informant 10</th>
<th>Key informant 11</th>
<th>Key informant 12</th>
<th>Key informant 13</th>
<th>Key informant 14</th>
<th>Mean score [95% CI]</th>
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</thead>
<tbody>
<tr>
<td>Health facility resources</td>
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<tr>
<td>Human resources (e.g. doctors, nurses, laboratory technicians)</td>
<td>5</td>
<td>5</td>
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<td>5</td>
<td>5</td>
<td>4.8 [3.8-5.0]</td>
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<td>Personal protective equipment (e.g. masks, gloves)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>2.5</td>
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<td>3.5</td>
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<td>No score</td>
<td>5</td>
<td>4</td>
<td>4.4 [3.4-4.9]</td>
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<td>Critical care equipment and training (e.g. ventilators)</td>
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<td>5</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>1.5</td>
<td>3</td>
<td>4.5</td>
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<td>3.5</td>
<td>4</td>
<td>5</td>
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<td>4.2 [3.2-4.7]</td>
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<td>Influenza diagnostic capacity</td>
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<td>4</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>No score</td>
<td>5</td>
<td>4.7 [3.7-5.0]</td>
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<tr>
<td>Stockpiling</td>
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<tr>
<td>Antiviral stockpiling</td>
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<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>4.5</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4.0 [3.0-4.5]</td>
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<tr>
<td>Personal protective equipment stockpiling (e.g. masks, gloves)</td>
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<td>5</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>3</td>
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<td>4</td>
<td>3</td>
<td>4</td>
<td>4.3 [3.3-4.7]</td>
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<td>Vaccination (assuming an effective vaccine can be produced approximately 6 months after the pandemic strain is identified)</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>4.5</td>
<td>2.5</td>
<td>5</td>
<td>4.5</td>
<td>5</td>
<td>3</td>
<td>No score</td>
<td>5</td>
<td></td>
<td>4.4 [3.4-4.9]</td>
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<td>Generic immune-modulators - developing a framework to support the use of statins or other immune-modulators</td>
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<td>No comment</td>
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<tr>
<td>Governance (including strategies for cooperation and legal frameworks)</td>
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<td>5</td>
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<td>4.5</td>
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<td>4.9 [3.9-5.0]</td>
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<td>Measures to temporarily reduce social contact (including school or work closure)</td>
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<td>5</td>
<td>4</td>
<td>3.5</td>
<td>4</td>
<td>3.75</td>
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<td>5</td>
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<td>4.5</td>
<td>No score</td>
<td>4</td>
<td>4.1 [3.1-4.9]</td>
</tr>
</tbody>
</table>

Scores were given from one to five (with five being the most important). ‘No comment’ was used when the informant had insufficient knowledge of the policy area to give a score. ‘No score’ was used when an opinion was expressed but no score was provided.
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References


