

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Public preferences for interventions to prevent emerging infectious disease threats: a discrete choice experiment
AUTHORS	Zhao, Xiahong; Cook, Alex; Chen, Mark I-Cheng; Finkelstein, Eric

VERSION 1 - REVIEW

REVIEWER	Eric Mayor Université de Neuchâtel, Switzerland
REVIEW RETURNED	26-Apr-2017

GENERAL COMMENTS	<p>I thank the authors for their very interesting and very clearly written manuscript. The authors do not test specific hypotheses, but are rather interested exploring broad research questions. Maybe the authors could find some worldwide infection estimate for each of the Emerging or Novel Infection Diseases the mention. Their list could be completed checking here https://wwwnc.cdc.gov/eid/ or here http://www.promedmail.org). I am quite surprised that the most obvious intervention: Vaccination is not part of the list of interventions among which the respondents could voice their opinion. The authors could comment on 'willingness to pay' as a standard criterion for such interventions. Should this be taken into account in policies ? My impression is that the consideration of the rights of individuals should be paramount (e.g., quarantine intervention). A questions relating interventions to the fundamental rights of individuals could be added in a new study.</p> <p>It would be great if the authors could include a graphic representation participants characteristics in relation to their responses (or a table). As random utility models go beyond my knowledge, I will let others comment on this aspect.</p> <p>Please clarify the following sentence in the abstract "On average, participants preferred more intense interventions and disfavoured death and tax." As currently phrased, it seems like 'death' and 'tax' are interventions ! The authors should clarify the content of the consent form.</p>
-------------------------	--

REVIEWER	Dr Emma Teasdale University of Southampton, UK
REVIEW RETURNED	12-Jun-2017

GENERAL COMMENTS	<p>I found this paper interesting and generally well written. It could be strengthened by addressing a few areas as outlined below.</p> <p>Introduction</p> <ul style="list-style-type: none"> • The authors state in the abstract that there is little known about public views of interventions to prevent emergent infection disease threats. This is not expanded upon in the introduction section. Consider moving the 1st paragraph of the discussion section to the introduction. • It would also be beneficial to provide the broader context for the study in the introduction. Consider adding a brief overview of previous research exploring public views and willingness to adopt particular mitigation strategies in different outbreak scenarios and highlighting the knowledge gaps before stating the rationale for the study. <p>Methods</p> <p>Fielding and Sample section</p> <ul style="list-style-type: none"> • The authors state that the study sample was obtained by contacting a list of households. It would be useful clarify how these potential participants were initially approached and by whom. • They also state that the survey was administered by trained interviewers. It would be useful to state whether this was done via the telephone or face to face and how the DCE tasks were presented to participants i.e. visually or described by interviewer. <p>Survey structure section</p> <ul style="list-style-type: none"> • Some of the language in this section seems quite technical and difficult to read. Further clarification in parts would increase relevance to a general readership. For example - 2nd paragraph, 3rd sentence describes the components of the DCE. It would be useful to define the term 'choice set' or to simplify the sentence as follows: 'Each participant was provided with a series of pairs of hypothetical alternatives, and asked to select one choice/option/scenario from each pair to indicate his/her preference' • The authors talk about 'choice sets' and 'tasks'. It would perhaps be better to use one or the other to be consistent. • The last sentence explains that participants were presented with 10 DCE tasks/choice sets in the survey. It would be useful to state this earlier in the section, perhaps in paragraph 2, when choice sets are first mentioned. • Paragraphs 3 and 5 seem to be a bit repetitive. Consider merging these paragraphs. <p>Discussion</p> <ul style="list-style-type: none"> • It would be useful to add some detail about how the findings of this study fit with previous research in this area and what the study findings add to current knowledge. • The discussion would benefit from a brief statement of the overall conclusions of the study.
-------------------------	--

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 (Dr Mayor)

Comment 2: I thank the authors for their very interesting and very clearly written manuscript. The authors do not test specific hypotheses, but are rather interested exploring broad research questions. Maybe the authors could find some worldwide infection estimate for each of the Emerging or Novel Infection Diseases the mention. Their list could be completed checking here <https://wwwnc.cdc.gov/eid/> or here <http://www.promedmail.org>).

Response: This is a good idea and we thank the reviewer for suggesting it. We have changed part of the introduction to read:

When faced with such threats—the impact of which is hard to predict in advance, as witnessed in the very different impact of recent outbreaks (e.g. a quarter of a million deaths for influenza A(H1N1pdm)11, over 10 000 deaths during the 2014/5 Ebola crisis¹², or around 600 deaths from MERS-CoV¹³)—policy makers worldwide have to decide which public health interventions to deploy should such an emerging infectious disease cause an outbreak in their territory.

Comment 3: I am quite surprised that the most obvious intervention: Vaccination is not part of the list of interventions among which the respondents could voice their opinion.

Response: This is a very good question. It takes a considerable amount of time to develop a vaccine for an emerging infectious disease. Even for influenza, for which we produce new formulations quite frequently in response to antigenic changes in the circulating viruses, it takes ~6mo to get the vaccine out to market. This delay means that vaccination cannot be part of our pandemic response plans (unless we try vaccination with seasonal influenza vaccine in the hope that it stimulates a small amount of cross protection against a pandemic influenza vaccine). This is why we did not consider it as an option in our experiment. However, the reviewer is correct that it might be considered for regular epidemics, for instance, for seasonal influenza. Having said that, we would not typically implement the other interventions (such as school closure) for regular epidemics like seasonal influenza, so a quite different structure of experiment would be needed to assess willingness to pay for vaccine.

Action: We have clarified that vaccination was not considered and why in the methods section:

Five of the seven attributes consisted of measures the government could take to restrict the spread of an emerging infectious disease. We excluded vaccination as a control measure due to the long lead time required to get a vaccine to market, which is six months for a reformulated influenza vaccine³⁷ but can be much longer (for dengue, for instance, it has taken decades³⁸).

and the discussion:

We included interventions that would be considered for use in response to an emerging infectious disease, and so did not consider vaccination given the lead time needed to develop a vaccine. For many vaccine-preventable infections, however, decisions about whether to be vaccinated are made by the individual, rather than by the government, and so alternative study designs might be better suited to determining features that lead to vaccine uptake and support, such as standard cross-sectional surveys⁵⁸.

Comment 4: The authors could comment on 'willingness to pay' as a standard criterion for such interventions. Should this be taken into account in policies ? My impression is that the consideration

of the rights of individuals should be paramount (e.g., quarantine intervention). A questions relating interventions to the fundamental rights of individuals could be added in a new study.

Response: This is an excellent question. Fundamentally, public health decision making in the face of an epidemic involves deciding how to trade off rights of the individual and benefit to society as a whole. The purpose of our experiment was to assess how much people value their individual rights compared to preventing ill-health. The experiment directly provides estimates of utility (measured in utils on an arbitrary scale) which allows us to make statements like: respondents valued schools being closed X times as much as they valued 1000 infections being prevented.

Because this is relatively abstract, we convert utility to a scale that we are more familiar with from our daily lives, namely a monetary scale. This allows us convert a preference in terms of utils to a preference in dollar terms. Traditionally this is called a willingness to pay, because in most discrete choice experiments, participants are selecting between products with different features, whereas here, they express their preferences for policies, which are enacted by the government rather than they themselves.

Action: We have clarified why we call it 'willingness to pay' in the methods section:

The core of the survey was a discrete choice experiment (DCE), which is a method often used to identify preferences for, importance of, and willingness-to-pay (WTP) for specific features of products that are composed of multiple features. In this case, we used it to elicit preferences for specific policy responses to an infectious disease outbreak, and report WTP as an easy to understand scale of support.

We mention and reference the ethical aspects of restricting civil liberties during an outbreak in the discussion:

As in many countries, Singaporean law permits the government to curtail civil liberties in response to an infectious disease outbreak (in Singapore's case, under the Infectious Diseases Act), but the use of this power to isolate cases or quarantine potential cases requires careful weighting of the risk to others from not acting versus the loss of liberty of the individual being isolated or quarantined⁵³. Our survey found that most Singaporeans reported a high tolerance for interventions that curtail individual liberties, which may be related to their long-standing acceptance of a paternalistic streak in their government⁵⁴.

We have also mentioned the referee's suggestion that individual rights could be explored explicitly in future work, in the discussion:

Ethical issues regarding loss of liberty during an outbreak were not covered in our experiment, and should be explored in future studies, together with more contextual information on why policies were favoured or not⁵⁹.

Comment 5: It would be great if the authors could include a graphic representation participants characteristics in relation to their responses (or a table). As random utility models go beyond my knowledge, I will let others comment on this aspect.

Response: Yes, we agree that this would be interesting. We have created a chart describing the demographics of respondents in the two classes, as reproduced below.

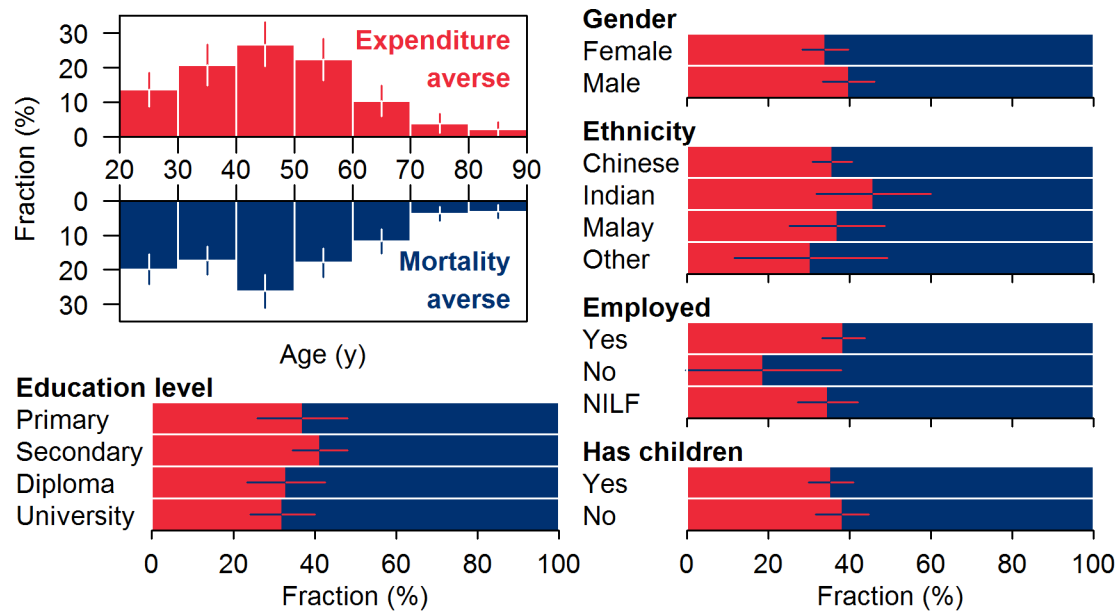


Figure 4: Demographics of participants classified as expenditure averse (imperial red) and mortality averse (navy blue). Whiskers indicate 95% confidence intervals. NILF = Not in the labor force.

We refer to this in the results section thus:

Those with post-secondary school education were more likely to belong to the mortality-averse group than to belong to the expenditure-averse group (adjusted odds ratio: 1.71, 95% CI: 1.12 – 2.61). Other demographic variables were not predictive of class membership (see Figure 4.).

We have also switched from presenting the OR to the adjusted odds ratio as on reflection this is a more sensible measure given the presence of potential confounders.

Comment 6: Please clarify the following sentence in the abstract "On average, participants preferred more intense interventions and disfavoured death and tax." As currently phrased, it seems like 'death' and 'tax' are interventions!

Response: Yes, this was not the best-phrased sentence we've written! We have rewritten it as

On average, participants preferred more intense interventions, and preferred scenarios with fewer deaths and lower tax.

Comment 7: The authors should clarify the content of the consent form.

Response: It was a standard participant information sheet and consent form, as required by our institutional review board. We have provided a copy in the resubmission and if the editor and reviewers think it necessary, this could be included in the supplementary information should the manuscript be accepted for publication.

Reviewer 2 (Dr Teasdale)

Comment 8: I found this paper interesting and generally well written. It could be strengthened by addressing a few areas as outlined below. Introduction: The authors state in the abstract that there is little known about public views of interventions to prevent emergent infection disease threats. This is not expanded upon in the introduction section. Consider moving the 1st paragraph of the discussion section to the introduction.

Response: We agree with this good suggestion. We have moved this paragraph as suggested, so that the end of the introduction now reads:

To this end, we conducted a 'conjoint' discrete choice experiment to explore the Singapore public's willingness to accept certain containment and mitigation strategies under various outbreak scenarios, spanning a range of infection and fatality rates. Specifically we assess three broad questions: (i) How informed are the public about infectious disease outbreaks and the effectiveness of different interventions? (ii) How much do the public support interventions—quarantine, isolation of contacts, school closure and mass screening—that restrict civil liberties in an outbreak? (iii) How consistent are overall preferences for intervention policies throughout the population? Are there subgroups whose preferences are in opposition to the majority? We hypothesised that the population would be broadly supportive of interventions that restricted their civil liberties, but that they might be averse to monetary impacts of those interventions. Our work was motivated by the past vulnerability of Singapore to a diversity of emerging infectious disease threats such as Nipah virus in the 1990s³¹, to SARS-CoV in 2003³², Chikungunya in 2008³³, pandemic influenza A(H1N1pdm09) in 2009³⁴ and the Zika epidemic in 2016³⁵, and its perceived vulnerability to future threats, given its location at the centre of South East Asia where various highly pathogenic strains of avian influenza continue to spread, its role as a transport hub, its highly urbanized environment and its tropical climate, which permits year round transmission of many viruses³⁶. These results are hence intended to allow policy makers to identify policies which will have high levels of public support and are hence expected to translate into high levels of compliance, while exemplifying a method that can be used to address the same questions in different settings.

Comment 9: It would also be beneficial to provide the broader context for the study in the introduction. Consider adding a brief overview of previous research exploring public views and willingness to adopt particular mitigation strategies in different outbreak scenarios and highlighting the knowledge gaps before stating the rationale for the study.

Response: Unfortunately, there has been very little work done on assessing what the general population actually wants their governments to do in response to infectious disease outbreaks. We have alluded to this in this revised paragraph in the introduction:

Public health policy makers have several constituencies, but chief among these is the populace on whose behalf they make decisions. Yet, while tolerance and potential impact of interventions can (and should be) be assessed through surveys²⁹, when it comes to pandemic preparedness, it is remarkable how little is known about what interventions the general population actually wants their governments to undertake. This gap is especially noteworthy due to the considerable personal burden imposed by some interventions and the backlash against what some deemed excessive measures during the 2009 influenza pandemic^{25,30}.

Comment 10: Methods. Fielding and Sample section: The authors state that the study sample was obtained by contacting a list of households. It would be useful clarify how these potential participants were initially approached and by whom.

Response: The fielding of the survey was conducted by a market research company who were contracted to recruit 500 respondents using a formal sampling frame. They conducted the survey in

person at participants' doors. Interviewers were trained by the company, who regularly implement quality control (in fact, we outsourced it primarily because we expected the quality to be much higher than if we did it ourselves). These interviewers approached potential participants.

We have clarified these points in the methods:

This survey was fielded in Singapore between November 2012 and February 2013 by a market research company contracted by the authors. The sampling frame was based on a list of households obtained from the Singapore national database of dwellings and continued until 500 responses with written informed consent were obtained, which required 1,196 households to be contacted (yielding an unadjusted response rate of 41.8%). Respondent eligibility could not be determined in 41 households. The remaining households were found to have at least one eligible respondent (citizen or permanent resident aged 21 and over). For those with multiple eligible respondents, one was randomly selected to take the survey. Trained interviewers administered the paper survey face-to-face in English, Malay, Mandarin or Tamil. Participants were guided through the discrete choice experiment by the interviewer. The study was approved by the National University of Singapore Institutional Review Board. All methods were performed in accordance with relevant guidelines and regulations.

Comment 11: They also state that the survey was administered by trained interviewers. It would be useful to state whether this was done via the telephone or face to face and how the DCE tasks were presented to participants i.e. visually or described by interviewer.

Response: The survey was conducted face to face. We have clarified that in the methods. The DCE was shown to the participant visually and the participant guided through by the interviewer. This has also been clarified, as in the response to the previous comment.

Comment 12: Survey structure section. Some of the language in this section seems quite technical and difficult to read. Further clarification in parts would increase relevance to a general readership. For example - 2nd paragraph, 3rd sentence describes the components of the DCE. It would be useful to define the term 'choice set' or to simplify the sentence as follows: 'Each participant was provided with a series of pairs of hypothetical alternatives, and asked to select one choice/option/scenario from each pair to indicate his/her preference'

Response: Thanks for highlighting this. We have reworked this paragraph in particular to make it less technical and (we hope!) easier to read. The revised version reads:

The survey questioned respondents' travel habits, experience with two previous infectious disease outbreaks in Singapore (the 2009 influenza A(H1N1pdm09) pandemic and the 2003 SARS-CoV outbreaks), attitudes towards and knowledge of the effectiveness of interventions, and beliefs about the burden of infectious diseases in Singapore. Participants were also asked how frequently they attended various crowded public places and whether they would reduce such attendance in response to an outbreak. Socio-demographic questions were also included.

The core of the survey was a discrete choice experiment (DCE), which is a method often used to identify preferences for, importance of, and willingness-to-pay (WTP) for specific features of products that are composed of multiple features. In this case, we used it to elicit preferences for specific policy responses to an infectious disease outbreak, and report WTP as an easy to understand scale of support. Each policy scenario consists of a number of attributes (for example social distancing) and each attribute of a number of levels (for example, none, closure of schools, or closure of schools and cancellation of mass gatherings). Each participant was provided a series of ten pairs of hypothetical alternatives, and for each pair was asked to select one of the two options (with a combination of one level for each attribute) as being his or her preference. An example of a typical pair of options is

provided in Table 2. Each pair contains the same attributes but different levels of each attribute; the attributes and levels used are found in Table 1.

The first four attributes include interventions which were used in Singapore and other countries at various points of the 2009 influenza pandemic, 2003 SARS outbreak, and in response to other emerging outbreaks. The fifth assesses the tolerance to economic losses. The final two summarize the severity of the outbreak, in size (number of cases) and fatality rates.

Five of the seven attributes consisted of measures the government could take to restrict the spread of an emerging infectious disease. We excluded vaccination as a control measure due to the long lead time required to get a vaccine to market, which is six months for a reformulated influenza vaccine³⁷ but can be much longer (for dengue, for instance, it has taken decades³⁸). The Singapore government, during the 2009 influenza pandemic and 2003 SARS-CoV outbreaks, quarantined suspected cases and enforced the isolation of actual cases. Both of these measures were included as attributes with two levels for each: mandatory and voluntary. The cancellation of mass gatherings was also included as an attribute with levels ranging from no cancellations to the closure of schools and prohibition of other types of mass gatherings. Temperature screening using thermal scanners was used during both the two events in Singapore and was therefore also included with different levels indicating whether the screenings were to be conducted only at border checkpoints, at checkpoints and other sites within Singapore, or not at all. Finally, a monetary attribute was included which posited a hypothetical one-time tax to fund control efforts with the following values: S\$15, S\$20, S\$40 and S\$50 (in 2013 S\$1 ≈ US\$0.80). The two remaining attributes described the outcome of an infectious disease outbreak in terms of two metrics: the expected number of infections (five levels ranging from 200 to 1,000,000 cases) and the expected number of infection-related deaths (five levels; 0 – 180 deaths). Attributes and levels for the survey were determined through literature review, cognitive interviews, and piloting a draft instrument (n=50)³⁹ to span plausible ranges for emerging infectious disease outbreaks or pandemics.

Following standard practice in DCEs³⁹, respondents saw a fractional DCE design that is statistically efficient, minimizes level overlap (where levels do not vary across competing options) and ensures level balance (each level appears approximately the same number of times)⁴⁰. The design was produced using Sawtooth SSI Web v8.22 and included four versions, each version containing ten tasks.

Comment 13: The authors talk about ‘choice sets’ and ‘tasks’. It would perhaps be better to use one or the other to be consistent.

Response: We agree and have removed the phrase ‘choice set’ from the manuscript. Where needed we simply call these ‘sets.’

Comment 14: The last sentence explains that participants were presented with 10 DCE tasks/choice sets in the survey. It would be useful to state this earlier in the section, perhaps in paragraph 2, when choice sets are first mentioned.

Response: Agreed! This has now been done. Please see response to comment 12 for the amended text.

Comment 15: Paragraphs 3 and 5 seem to be a bit repetitive. Consider merging these paragraphs.

Response: They were very repetitive, sorry. We’ve merged these and reordered the paragraphs accordingly. Thank you for suggesting this. The amended section is provided in response to comment 12 above.

Comment 16: Discussion. It would be useful to add some detail about how the findings of this study fit with previous research in this area and what the study findings add to current knowledge.

Response: As mentioned in response to comment 9, there is very little known about what the general population wants from their government in response to an outbreak of an emerging infectious disease, and previous research has focused overwhelmingly on the policy, economic and epidemiologic elements of control measures. We have highlighted this in the new opening to the discussion:

Research on interventions to prevent or mitigate pandemics has assessed their effectiveness, using modelling^{45,46} or empirical evidence^{47,48}, on their indirect effects^{49,50}, their economic impacts^{51,52}, and the legal and ethical issues surrounding their use⁵³. This paper presents what we believe to be one of the first studies to measure the preferences of members of the public for control policies that form part of established pandemic preparedness plans.

Comment 17: The discussion would benefit from a brief statement of the overall conclusions of the study.

Response: We agree, and have added the following conclusion:

In conclusion, we report what we believe is the first discrete choice experiment to assess support for policies to control an emerging infectious disease outbreak, finding high levels of support among the Singaporean population for interventions that curtail individual liberties. Similar studies in other settings would be useful for public health decision makers.

VERSION 2 – REVIEW

REVIEWER	Eric Mayor Université de Neuchâtel Switzerland
REVIEW RETURNED	21-Jul-2017

GENERAL COMMENTS	The authors have addressed my comments.
-------------------------	---

REVIEWER	Dr Emma Teasdale University of Southampton, UK
REVIEW RETURNED	19-Jul-2017

GENERAL COMMENTS	I am happy with the revisions to this manuscript. I have no further comments.
-------------------------	---