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Quantifying the public's view on social value judgments in vaccine decision-making

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Title: Quantifying the public's view on social value judgments in vaccine decision-making: a discrete choice experiment

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Abstract: Vaccination programs generate direct protection, herd protection and, occasionally, side effects, distributed over different age groups. This study elicits the general public's view on how to balance these outcomes in funding decisions for vaccines. We performed an optimal design discrete choice experiment with partial profiles in a representative sample (N=1499) of the public in the United Kingdom. Using a panel mixed logit model, we quantified, for four different types of infectious disease, the importance of a person's age during disease, how disease was prevented—via direct vaccine protection or herd protection—and whether the vaccine induced side effects. Our study shows clear patterns in how the public values vaccination programs. These diverge from the assumptions made in public health and cost-effectiveness models that inform decision-making. We found that side effects and infections in newborns and children were of primary importance to the perceived value of a vaccination program. Averting side effects was, in any age group, weighted three times as important as preventing an identical natural infection in a child whereas the latter was weighted six times as important as preventing the same infection in elderly aged 65-75 years. These findings were independent of the length or severity of the disease, and were robust across respondents' backgrounds. We summarize these patterns in a set of preference weights that can be incorporated into future models.

Reply to reviewers

We would like to thank both reviewers for their extensive and constructive feedback. This has substantially improved our paper. Below we respond point-by-point to their comments.

Reviewer #1: SSM-D-18-01397

Quantifying the public's view on social value judgements in vaccine decision making-a discrete choice experiment I've read with great interest the manuscript "Quantifying the public's view on social value judgements in vaccine decision making: a discrete choice experiment". The manuscript starts with describing that the usual framework of cost-effectiveness analysis does not consider alternatives regarding the public's view on value judgements in vaccine decision making. The authors have performed a discrete choice experiment in order to examine the importance of different age groups in the program's overall evaluation and the extent to which it matters whether these age groups are affected by either direct, herd or side effects. By quantifying these preferences and translating these into preference weights for health outcomes, they hope to incorporate these into a future economic evaluation framework. The choice experiment was conducted among a representative sample, recruited from a commercial panel, in the UK. Five attributes were chosen: direct effects of vaccination, targeted age of the vaccination programme, side effects related to vaccination, herd effects, the age group affected by the herd effects. It was an unlabelled design. The diseases were also unnamed but described based on the dimensions and level of the EQ-5D-3L. Four different disease profiles were presented: severe(lasting nine days), severe (lasting sixty days), mild (lasting nine days) and mild (lasting sixty days). The design was a D-optimal in a Bayesian framework. Results showed that vaccine induced side-effects and infections in young children were considered the most important when assessing a program's value. Averting side-effects of the vaccine was weighted three times that of preventing an identical natural infection in any age groups. Vaccination programs that prevent disease in children were weighted six times that of programmes preventing a disease in older adults.

As I've said before, I've read the manuscript with great interest and thought the manuscript was overall well written. However, I think the manuscript could benefit from a more in-depth and thorough explanation of not only the process of selecting the attributes/levels but also the discussion of the results.

Below you find my comments more in detail:

Introduction:

- The authors state that the CEA framework neglects key value judgements needed to evaluate vaccine programmes. Although they refer to a multiple of references, I would like to see a concrete example of which key values are missing and how this is taken into consideration within this discrete choice experiment.*

Reply: We agree that the development of the specific research question in the introduction was insufficiently clear and also insufficiently focused towards the concrete context of vaccines. It was also not entirely clear how our DCE provided answers to these problems. We have rewritten parts of the introduction to make it more focused and concrete, including examples and we have added a starting paragraph before the methods section to explain how our DCE can provide answers.

In the introduction:

“There is a growing literature about the limits of CEA in assessing the value of vaccination [9-15].

One important criticism is that CEA is limited in how it values the consequences of vaccination. Summary outcome measures [such as e.g. infections prevented or Quality-Adjusted Life Years (QALYs) gained] neglect the particular social context in which these outcomes occur. Nonetheless, such contextual features are important aspects to consider when evaluating a vaccination strategy [...] There are qualitative differences between these direct, herd and side effects. Creating herd protection can be of particular ethical value (e.g. to protect vulnerable groups who otherwise cannot protect themselves) and there is a profound psychological impact of vaccine-induced side effects. Moreover, the distribution of these three different effect types over different age groups is important. [...] Several notable examples illustrate that this broader social context of health outcomes needs to be considered in vaccine decision-making [18]. For instance, vaccines against rotavirus (Rotashield®) and pertussis (whole cell pertussis vaccine) were withdrawn from many countries because of a perceived risk of side effects, even though from a medical perspective the benefit from vaccination largely outweighed any potential risk [19-21]. Also, despite persuasive economic and public health benefits of childhood influenza vaccination, few countries have actually implemented such a preventive strategy, due in large part to concerns about the social acceptability and equity of targeting vaccination at children to protect the wider population [22]. And, in many countries introduction of an effective varicella vaccination program has been delayed because of concerns about the possible 'exogenous boosting effect' and its social repercussions, i.e. that reduced chickenpox transmission among children (due to varicella vaccination) might temporarily increase shingles incidence among older generations [23]. Misjudging ethical norms and social sensitivities in vaccination policy by over-relying on CEA can have important implications..."

In the methods:

"DCEs are a widely used survey method to quantify individuals' preferences [35, 36] (for a general review of applications, see [37]). Participants are presented with a series of choices, usually between two goods described by the same attributes but differing in their attribute levels. By observing respondents' preferred choices, researchers can infer how the value of the competing options is determined by the attributes of the product. In our case, we observe how people prioritize between vaccination programs based on the number of direct, herd and side effects generated by the program, and their distribution over different age groups. This allows us to estimate a utility function that describes how the public values vaccination programs, taking into account the different types of vaccine effect and their distribution."

Methods:

- *I miss a clear description of the selection of the attributes and the levels. Why were these specific 5 attributes chosen?*

Reply: This is an important point and it is in fact a substantial part of the work we did for this DCE. We agree that this aspect of the DCE should be more extensively described in the paper. We have now included more motivating discussion regarding the choice of attributes and levels.

"To develop the final attributes and levels of the vaccine programs included in the DCE, we followed a three stage iterative process. We performed a literature search of other vaccine-related DCEs to assess the choice context and which attributes and levels were considered. These attributes were disease incidence, case fatality risk, economic impact, duration of illness and duration of vaccine protection, severity of illness and severity of side effects, and various personal characteristics including age, gender and willingness/ability to get vaccinated. [40-44] From this list, we took the combination of attributes that was, in combination with the four disease profiles, best suited to answer our research question. We presented several versions to a convenience sample of lay persons, colleagues and collaborators at the market research company in a pilot questionnaire, which we revised in response to received comments. We re-iterated this process

until we found the right form for the DCE from which, with a relatively simple set of in total five core attributes (Table 1), we could robustly calculate preference weights.”

“After the design, we tested our survey among a pilot sample of the online panel (N=69) to confirm that respondents could fully understand and complete the survey. Based on the feedback from this pilot sample we judged that the experiment was understandable and that no further changes were needed.”

- *How realistic is it that the side effects were presented as identical to an episode of the disease a vaccine usually prevents? For me, it is not clear although the authors partly explain this in the discussion. However, the whole issue nowadays is that an increasing number of people think the benefit of a vaccine (i.e. preventing the disease) does not outweigh the "perceived" risks of the vaccine itself. This leads to a reduced uptake with potentially devastating consequences. My point is: how valid are the results of this study if the provided attributes do not provide the information that is necessary to make an informed choice regarding priority setting for a vaccine programme?*

Reply: The reviewer makes an excellent point. Indeed, the fact that respondents might ‘overestimate’ the importance of the side effects is in essence one of the subjects of this DCE. And indeed, we saw that there was a cluster of respondents who were more vaccine skeptical and gave higher weight to side effects. Evidence on the severity of side effects relative to the disease itself does vary, with most side effects typically less severe, however with exceptions. Several vaccines can have (although rarely) severe side effects, often more severe than the disease the vaccine is preventing - eg. Guillian-Barre syndrome, anaphylaxis, intussusception etc. But the risk of these severe events is much less than the risk reduction in getting the disease after getting vaccinated. We opted for equal severity between prevented disease and induced side effects because this simplification reduced the need for respondents to simultaneously trade-off two disease severity profiles as well as the number of cases, likely improving the reliability of our results. To mitigate this issue that the reviewer correctly highlights, our questionnaire included a difference in the size of the direct impact and side effects—including an at least 10-fold lower disease burden linked to side-effects compared to the prevented disease burden. Indeed, turning the overall effect of side effects by total burden in this manner allowed us to more simply compare the weight of side effects to direct or herd effects (without having to convert these health effects to e.g. QALYs). We have further clarified this point in the revised manuscript.

In the methods section:

“The side effects of vaccination were presented in the DCE as identical to an episode of the disease that the vaccine usually prevents, in order to enable a direct comparison between the three effect types. Not doing so would have meant using a second health profile within one choice option (one for the disease and one for the side effects) and this would also have made the experiment substantially more difficult for the participants.”

And in the study limitations:

“There are several limitations. We did not include any mortality effects, nor did we include a difference in severity between the three vaccine effects, even though this would be more realistic (as side effects of vaccines are usually milder than the disease being prevented). We chose not to include these aspects because we wanted to avoid increasing the complexity of the survey and reducing the validity of the respondents’ answers by adding a second disease profile. Also, keeping the disease outcome constant over age groups and effects enabled trade-offs that were wholly

reflective of the preference between age groups and effects instead of also reflecting additional considerations about disease severity.”

- *So, I would like to see a description of the qualitative process undertaken before the design of the DCE. For example: were qualitative interviews conducted with vaccination experts or people who are in favour or against vaccination? This would make it clear whether the selected attributes correspond with the missing information the public needs in order to make a valid judgement regarding priority setting for a vaccine programme. I could imagine that for example information about the long term effectiveness of a vaccine or protection duration could make a difference. For the attribute levels: the authors refer to expert opinion but again for me it is not clear what kind of experts were asked. The authors also refer to other DCE's although these were almost all disease-specific, referring to rotavirus or HPV vaccination. It is not clear how the levels from these choice experiments can easily translate to the ones used in this study.*

Reply: We agree that more info was needed on the process of selecting attributes and levels, see our response below. In fact, we think that constructing the list of 5 attributes for 4 different diseases was a merit of the design of this DCE. We used various inputs for this process and followed a trial and error approach towards finding the best possible form. We relied on our own judgment as researchers in this field and our assessment of the choice data that were needed to answer our research question, other DCEs in the literature but also on the feedback from colleagues and friends in earlier trial rounds and a pilot (N=69) in a later stage. Other DCEs were indeed context-specific but they gave us information on how various dimensions of health effect (e.g. mortality vs morbidity, competing dimensions of illness, side effects, etc.) were presented and traded-off, which personal attributes of vaccine recipients were included (age, gender, etc), etc. Some attributes with relevance in a wider assessment could be included indirectly, for example vaccine effectiveness could be modulated through the reduction in incidence of the disease. As with the nature of these questionnaires, a balance had to be struck between attribute inclusion and tractability for the respondent. We added the following in the methods section to provide more info on the process:

“To develop the final attributes and levels of the vaccine programs included in the DCE, we followed a three stage iterative process. We performed a literature search of other vaccine-related DCEs to assess the choice context and which attributes and levels were considered in other studies. These attributes were disease incidence, case fatality risk, economic impact, duration of illness and duration of vaccine protection, severity of illness and severity of side effects, and various personal characteristics including age, gender and willingness/ability to get vaccinated. [40-44] From this list, we took the combination of attributes that was, in combination with the four disease profiles, best suited to answer our research question. We presented several versions to a convenience sample of lay persons, colleagues and collaborators at the market research company in a pilot questionnaire, which we revised in response to received comments. We re-iterated this process until we found the right form for the DCE from which, with a relatively simple set of in total five core attributes (Table 1), we could robustly calculate preference weights.”

“After the design, we tested our survey among a pilot sample of the online panel (N=69) to confirm that respondents could fully understand and complete the survey. Based on the feedback from this pilot sample we judged that the experiment was understandable and that no further changes were needed.”

Results:

- *If I understand correctly, the cluster analysis revealed two group of respondents, one who attached no importance to the number of side-effects and another group who valued this*

highly. For cluster 1, it seems that the only predictor was no hesitancy on vaccination although the explained variance was low. However, I wonder if the authors also performed an analysis to examine what was the predictor for the highly valued side effects in cluster 2. Is it possible that these are people who are very hesitant for vaccination?

Reply: Thank you for this observation. Our previous phrasing was incomplete; the cluster 2 results were not mentioned whereas we in fact compared cluster 1 with cluster 2 in the analysis. We have changed this in the revised manuscript as follows:

“We used a logistic regression to determine predictors of cluster membership. Cluster 1, which attached almost no importance to the number of side effects, was characterized by high values on the VHS, indicating little hesitancy ($p < 0.0001$). On the other hand, cluster 2 who valued side effects more highly, was characterized by higher degrees of hesitancy on the VHS. However, the predictive power of this association for membership of the group was small (McFadden’s pseudo $R^2 = 0.6\%$), implying that there is much unexplained heterogeneity in the importance placed on side effects.”

Discussion:

- *the authors state that their study is the first one to quantify social value judgements in vaccine. Although this makes it difficult to compare their results with other studies, they indicate that one of their findings is in line with theoretical expectations about cognitive heuristics like loss aversion, act-omission bias and hyperbolic discounting. My question is: why and could the authors explain this more in detail? What is for example the link between their findings and hyperbolic discounting or act-omission bias?*

Reply: Thank you for this comment. We have expanded the text as follows, and hope this is clearer.

“The finding that individuals weighted one averted instance of a side effect equal to about three similarly severe natural infections in children can be explained with general theory on decision-making. For instance, well-documented psychological phenomena such as ‘loss aversion’ (58) (overvaluing risks and losses over opportunities and gains), the ‘act-omission bias’ (59) (judging the effects of an act—becoming vaccinated—differently from identical effects resulting from an omission—becoming infected), or ‘hyperbolic discounting’ (60) (overvaluing the present—in which side effects occur—over the future—in which disease prevention will occur) suggest that people put an extraordinary weight on side effects when evaluating a vaccination strategy.”

- *Then the authors state that it is important to study which aspects of health policy choices matter most to the public. They mention that in particular public trust, goodwill and participation are key to success and that one has to be aware of the sensitivities surrounding vaccination. My question is: explain more to what extent your results might help to take away the sensitivities surrounding vaccination? The problem nowadays is that public trust or goodwill are often related to perceptions of risks (and not the actual risk of vaccination), a misconception about the severity of the disease like thinking that measles is an innocent virus that has no severe consequences. How are the selected five attributes direct effects of vaccination, targeted age of the vaccination programme, side effects related to vaccination, herd effects, the age group affected by the herd effects related to these issues?*

Reply: We have expanded the text on how our results could be used in practice.

“Our findings provide empirical evidence on how to set vaccine priorities in line with public preferences. There is an important debate over the extent to which the public’s opinion should drive resource allocation in healthcare (see e.g. [67, 68]). But, many believe that the values of the public, who pays for healthcare, should at least somehow be acknowledged in the decision-making process. In the context of vaccination, where public support and participation is key to success, this concern becomes particularly crucial. Therefore, our results can be useful additions to vaccine appraisals. They can provide guidance in specific epidemiological cases where CEA does not provide the answers needed. For instance, our results would suggest that, despite their attractiveness in terms of cost-effectiveness, the public may not support a childhood influenza vaccination program that mainly benefits adults or elderly (), because preventing side effects in vaccinated children is preferred over preventing disease burden among adults and elderly. Furthermore, our study suggests that a childhood varicella-zoster vaccination program, in the case that it protects children against varicella disease at the expense of increased zoster in the elderly (the ‘exogenous boosting hypothesis’), might be justifiable. In contrast, previous analyses where QALY loss for children are weighted equally to those for the elderly find that the increased burden in the elderly offsets the QALY gains in children and determine the program not cost-effective (23 77).

Our results can also be directly incorporated into economic evaluations as sensitivity analyses to better align the underlying assumptions of CEA with the values of the population. Our estimated preference weights can be used in decision-analytic models as a parameter to weight QALYs or infections according to their ‘social value’. This would re-adjust the (equal) weight that QALYs receive in CEA according to how important people think that the age of the QALY-recipient is and whether the benefit was generated through direct protection, herd immunity or (avoiding) side-effects. There is an increased interest in such ‘extended’, ‘distributive’ or ‘equity-weighted’ economic evaluation (see e.g. 7 36 70-75), but, to our knowledge, such studies do not exist for the evaluation of vaccines. Our estimates are developed particularly for this context, and provide an opportunity to do so.”

Reviewer #2:

Thank you for the opportunity to review your interesting research. Overall this is a well written manuscript on an important topic.

- *Line 153 - did you pre-test your graphics to ensure comprehensibility and that it is measuring what you are expecting it to?*

Reply: Yes, we extensively tested the graphics and the wordings of the attributes and levels, first in groups of lay people and colleagues in our departments and among collaborators at the market research company and finally in a pilot of 69 online trial-participants. We have explained this piloting process more extensively in the revised manuscript.

“To develop the final attributes and levels of the vaccine programs included in the DCE, we followed a three stage iterative process. We performed a literature search of other vaccine-related DCEs to assess the choice context and which attributes and levels were considered in other studies. These attributes were disease incidence, case fatality risk, economic impact, duration of illness and duration of vaccine protection, severity of illness and severity of side effects, and various personal characteristics including age, gender and willingness/ability to get vaccinated. [40-44] From this list, we took the combination of attributes that was, in combination with the four disease profiles, best suited to answer our research question. We presented several versions to a convenience sample of lay persons, colleagues and collaborators at the market research company in a pilot questionnaire, which we revised in response to received comments. We re-iterated this process

until we found the right form for the DCE from which, with a relatively simple set of in total five core attributes (Table 1), we could robustly calculate preference weights..”

“After the design, we tested our survey among a pilot sample of the online panel (N=69) to confirm that respondents could fully understand and complete the survey. Based on the feedback from this pilot sample we judged that the experiment was understandable and that no further changes were needed.”

- *Line 162 - what criteria did you use to choose your 45 choice sets?*

Reply: We have used the Bayesian D-optimal design criterion to generate the 45 choice sets of the DCE. This is also stated in the text at the end of Section 2.3, but for clarity, we added the following explanation:

“The Bayesian D-optimal design then results in the smallest possible standard errors for the utility estimates at the given sample size”.

- *Line 183 - This is a rather generic sentence that does not give information about your pilot testing - were there any major or minor changes that resulted from your pilot testing? I am curious especially in how participants understood the attributes with a risk component - which as you know, can be interpreted quite differently between individuals depending on how you frame your attribute and levels. Did participants suggest the graphics used for direct effects, side effects and indirect effects?*

Reply: We agree and have added more information in the revised manuscript on the process of pilot testing. We attempted to circumvent the problems related to risk by not including explicit risk-attributes, such as risk of disease, and instead include visual aids. As we did require some risk difference between attributes we chose to present the absolute number of prevented cases within the DCE, which is a combination of a risk of disease and a vaccine effectiveness. We helped the responders to differentiate between the numerical quantities by presenting graphical representations of the numbers in bars and blocks. We settled on the graphics within the iterative process of study design – a choice that highlights the order of magnitude difference between direct and side effects. Nevertheless, it might make a difference when we name the number of people without side effects rather than the complement with side effects (framing effects). However we think that our choice was defensible based on two considerations. First, we wanted to quantify the weight respondents placed on side effects and therefore we chose to frame side effects explicitly to ensure that people traded off vaccine-induced illness with natural infection, rather than neglect side effects and focus on the positive benefits. Second, our pilot testing showed that our framing made respondents reason in the way we anticipated: they clearly balanced good outcomes with negative ones. We agree that this point deserves more attention and we have therefore added the following to the Discussion section on study limitations in the revised manuscript.

“We also chose to present the number of side effects rather than its complement: the number of vaccinated people without side effects. This framing may have played a role in the observed weight for side effects and the other framing would have likely generated lower estimates. We however wanted people to explicitly trade-off side effects with protective benefits.”

- *Line 188 - 50 pence for a 12 minute survey seems very low to me? Is this the usual rate?*

Reply: This is indeed the usual rate that is applied by the market research company we recruited.

- *Line 232 - you mention 1546 started the questionnaire - how many survey links were sent out? i.e. the true response rate would be the number potentially eligible as your denominator.*

Reply: In total there were 1950 surveys sent out of which 1546 completed the full survey. We clarified this in the text as follows.

“A total of 1546 respondents out of 1950 (79%) who were sent the questionnaire completed it, of which 47 (3%) indicated that the questions were too difficult or their answers invalid, leaving 1499 questionnaires for analysis.”

- *Line 295 - you state your findings were robust across respondent characteristics - can you provide this information as supplemental information?*

Reply: Yes, we have now updated the manuscript accordingly and provide an extensive robustness check of the modelling results in Appendix D.

Discussion - I know your choice sets are not specific to any disease but use general descriptors for severity. However, doesn't the specific type of disease actually impact on preferences? e.g. I suspect people would view a cancer vaccine (e.g. HPV) quite differently from a vaccine for influenza, all things being equal as measured by your 5 attributes. There is something inherent in the disease itself that might be worth exploring for future studies. But in your manuscript, might be worth a few sentences to discuss this possibility.

Reply: Thank you for this suggestion. We have now raised this issue in the discussion with the study limitations.

“Also, we used generic disease profiles based on a description in EQ-5D terms to minimize respondents making personal associations to the disease and vaccine (e.g. ‘flu’ or ‘whooping cough’), but this may also have increased the level of abstraction and reduced the level of personal involvement. A suggestion for further research is to repeat our study with named diseases and to test whether our finding that the disease profile did not matter to people’s preferences is confirmed.”

- *Line 368 - how specifically can other researchers use your preference weights in their models? can you give a concrete example? do you mean these weights can be used change WTP thresholds?*

Reply: We think that our results could be used experimentally to ‘weight’ QALYs in a decision model for vaccines according to public preferences over the weight of QALYs. CEA counts QALYs and assumes that all QALYs are equally valuable but our results (in line with other more general studies) suggest that this is not the case. Our preference weights could be used to provide an additional layer of information to these QALYs, about their ‘social value’. A QALY gained in a child would therefore weigh more than one gained in an adult. This is of course contentious but it provides, in our opinion, useful information for vaccine decision making where health interests between generations sometimes need to be traded off. We have added some more sentences on this in the new manuscript and suggested some examples.

“For instance, our results would suggest that, despite their attractiveness in terms of cost-effectiveness, the public may not support a childhood influenza vaccination program that mainly benefits adults or elderly [69], because preventing side effects in vaccinated children is preferred over preventing disease burden among adults and elderly. Furthermore, our study suggests that a

childhood varicella-zoster vaccination program, in the case that it protects children against varicella disease at the expense of increased zoster in the elderly (the 'exogenous boosting hypothesis'), might be justifiable. In contrast, previous analyses where QALY loss for children are weighted equally to those for the elderly find that the increased burden in the elderly offsets the QALY gains in children and determine the program not cost-effective. Our findings can provide an empirical evidence base about how to set vaccine priorities in line with public preferences, because preventing side effects in vaccinated children is preferred highly over preventing disease burden among adults and elderly. [23, 70]"

And:

"Our results can also be directly incorporated into economic evaluations (e.g. as sensitivity analyses), to better align the underlying assumptions of CEA with the values of the population. The preference weights we illustrated in Figure 3 can be used in decision-analytic models as a parameter to weight QALYs or infections according to their 'social value'. This would re-adjust the (equal) weight that QALYs receive in CEA according to how important people think that the age of the QALY-recipient is and whether it was generated through direct protection, herd immunity or (avoiding) side-effects. There is an increased interest in such 'extended', 'distributive' or 'equity-weighted' economic evaluation (see e.g. [7, 34, 71-76]), but, to our knowledge, such studies are inexistent for the evaluation of vaccines. Our estimates are developed particularly for this context, and provide an opportunity to do so."

- *Table 1 - there is a big difference in the having children demographics between the study population and the UK population - any potential impact on your results?*

Reply: 42% is the percentage of UK families living with dependent children (<18 years old), which should be compared to 35% (both the 11% (0-4 yo) and 24% (5-20 yo) in the sample), so there is not a large difference in demographics between the sample and the UK population. Moreover, when we include parental status as a covariate in the model we see no significant effects of parental status (See supplementary material provided with this revision).

- *Table 1 - last row - 'participant affected by poor health' - seems like quite a significant proportion (27%) - how was poor health defined? - any potential impact on preferences?*

Reply: Poor health consisted of the following three answers: (1) neither I nor my close friends or family are affected by poor health, (2) I consider myself affected by poor health and (3) I am not affected but close friends or family are affected by poor health. The exact nature of "poor health" was left to the respondent rather than defined by us. However, this respondent characteristic had no impact on preferences, as indicated by a non-significant interaction effect with any of the attributes in the model. See supplementary material.

- *Table 2 - can you discuss the interpretation of your interaction results in your text in more detail?*

Reply: Thank you for this suggestion. We agree and we have added a new paragraph and a new figure to the revised manuscript. The interaction terms cannot easily be understood based on the estimates in the table but should be interpreted in terms of marginal utilities, consisting of the sum of the main effects of the two attributes involved and the interaction itself. We have added a new figure depicting the interaction between the two age groups and added the following to the results section:

“Figure 4 illustrates the interaction between the age of the vaccinated group and the age of the herd immunity recipients (see Table 3). This interaction should be understood as the additional utility that is given to (or taken away from) a vaccination program, purely depending on the particular combination of age groups that are involved, regardless of the magnitude of direct, indirect or side effects that are being generated. It presents the attractiveness of particular intergenerational vaccination strategies. Whereas a CEA perspective would consider all possible age combinations equally attractive (as long as they lead to the same number of infections prevented), our sample had clear intergenerational preferences over vaccination strategies. Any age group was deemed acceptable to vaccinate when there were herd immunity benefits for newborns. To generate herd immunity for adults, infants were the most attractive age group. To generate it to protect the elderly >80, adults were deemed most appropriate. The least attractive intergenerational combination was vaccinating elderly >80 while generating herd immunity in adults 30-50 years. The most attractive age combination was vaccinating children while generating herd immunity in newborns.”

- *Figure 3 - I am a bit confused with your utility weights for side effects - aren't these supposed to be negative? Or is the label supposed to be "prevention of side effects"?*

Reply: The QALYs for side effects are in principle negative but we presented them as a ‘weighting factor’ for QALYs that could be used in a decision model. In that case these QALYs are already being ‘lost’ and it’s our weighing factor that multiplies this loss. We added the following clarifications:

“Similarly, a vaccination strategy reduces its utility by causing side effects: reducing 34 side effects in children equals 100 prevented cases among the same age group.”

And also:

“The mean weight for side effects across all ages was -2.93, meaning that avoiding one vaccine-induced infection was weighted equally to avoiding around three natural infections among children.”

- *Appendix B - any internal tests of validity incorporated into your experimental design?*

Reply: There were no internal tests incorporated in our experimental design, apart from our explicit question whether participants understood the questionnaire. The ultimate test of the internal validity of the design lies with the quality and reliability of responses that we observed. The preciseness of the estimates we obtained justifies the priors we used for the Bayesian design construction (see appendix C), which were based upon extensive deliberation amongst the authors. We have extensively piloted the different choice sets amongst colleagues until the choice sets were balanced in the level of complexity and as such manageable to make meaningful trade-offs. Afterwards, only a small minority of respondents (N=47 or 3%) indicated that the choice sets were too difficult, and these respondents were excluded from the analysis. Moreover, the research company pledged to only include ‘serious’ responders based on previous experiences, time taken for the survey, etc.

MINOR CHANGES

- *Line 69 - please clarify your last phrase 'contestable perspective on them' - do you mean they only consider the healthcare perspective*

Reply: We agree that this statement was unclear and unnecessary and we have deleted this sentence from the introduction

- *A figure or table of all attributes with levels might be helpful.*

Reply: We have added a new table with all attributes and levels to the revised manuscript (Table 1).

Quantifying the public's view on social value judgments in vaccine decision-making: a discrete choice experiment

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1 **Quantifying the public’s view on social value judgments in**
2 **vaccine decision-making: a discrete choice experiment**

3
4

5 **Abstract**

6 Vaccination programs generate direct protection, herd protection and, occasionally,
7 side effects, distributed over different age groups. This study elicits the general
8 public’s view on how to balance these outcomes in funding decisions for vaccines.
9 We performed an optimal design discrete choice experiment with partial profiles in a
10 representative sample (N=1499) of the public in the United Kingdom. Using a panel
11 mixed logit model, we quantified, for four different types of infectious disease, the
12 importance of a person’s age during disease, how disease was prevented—via direct
13 vaccine protection or herd protection—and whether the vaccine induced side effects.
14 Our study shows clear patterns in how the public values vaccination programs.
15 These diverge from the assumptions made in public health and cost-effectiveness
16 models that inform decision-making. We found that side effects and infections in
17 newborns and children were of primary importance to the perceived value of a
18 vaccination program. Averting side effects was, in any age group, weighted three
19 times as important as preventing an identical natural infection in a child whereas the
20 latter was weighted six times as important as preventing the same infection in elderly
21 aged 65-75 years. These findings were independent of the length or severity of the
22 disease, and were robust across respondents’ backgrounds. We summarize these
23 patterns in a set of preference weights that can be incorporated into future models.

24
25

26 **Keywords**

27 Priority-setting; age; side effects, herd protection, cost-effectiveness analysis,
28 decision making; discrete choice experiment; preference weight, vaccination

29

30 1. Introduction

31 Economic evaluation methods such as cost-effectiveness analysis (CEA) are
32 common components in public funding decisions for vaccines [1, 2]. They feature in
33 the standard evidence considered by e.g. the Advisory Committee on Immunization
34 Practices in the US, the Joint Committee on Vaccination and Immunization in
35 England, the World Health Organization and non-governmental organizations such
36 as the Bill & Melinda Gates Foundation [3]. At the same time, it is widely
37 acknowledged that these evaluation frameworks have important shortcomings and
38 that they alone offer insufficient basis for making fair and efficient vaccine funding
39 decisions [4-8]. There is a growing literature about the limits of CEA in assessing the
40 value of vaccination [9-15].

41 One important criticism is that CEA is limited in how it values the consequences of
42 vaccination. Summary outcome measures [such as e.g. infections prevented or
43 Quality-Adjusted Life Years (QALYs) gained] neglect the particular social context in
44 which these outcomes occur. Nonetheless, such contextual features are important
45 aspects to consider when evaluating a vaccination strategy. Vaccination induces
46 disease protection in those who become vaccinated, but it also creates *herd*
47 protection (or indirect effects in third parties because of reduced pathogen
48 transmission [16]) and, occasionally, adverse clinical *side* effects. There are
49 qualitative differences between these direct, herd and side effects. Creating herd
50 protection can be of particular ethical value (e.g. to protect vulnerable groups who
51 otherwise cannot protect themselves) and there is a profound psychological impact
52 of vaccine-induced side effects. Moreover, the *distribution* of these three different
53 effect types over different age groups is important. Side effects can be concentrated
54 in one age group despite indirect protection from reduced transmission benefitting

55 either the wider population, or in some cases a different age group entirely [17].
56 Examples include protecting the elderly through childhood influenza vaccination or
57 future generations through a *polio* eradication program. Such broader, distributive
58 aspects of vaccination are important but they remain neglected in standard cost-
59 effectiveness or public health impact models.

60 Several notable examples illustrate that **this broader social context of health**
61 **outcomes needs to be considered in vaccine decision-making** [18]. For instance,
62 vaccines against rotavirus (Rotashield®) and pertussis (whole cell pertussis vaccine)
63 were withdrawn from many countries because of a perceived risk of side effects,
64 even though from a medical perspective the benefit from vaccination largely
65 outweighed any potential risk [19-21]. Also, despite persuasive economic and public
66 health benefits of childhood influenza vaccination, few countries have actually
67 implemented such a preventive strategy, due in large part to concerns about the
68 social acceptability and equity of targeting vaccination at children to protect the wider
69 population [22]. And, in many countries introduction of an effective varicella
70 vaccination program has been delayed because of concerns about the possible
71 'exogenous boosting effect' and its social repercussions, i.e. that reduced
72 chickenpox transmission among children (due to varicella vaccination) might
73 temporarily increase shingles incidence among older generations [23].

74 **Misjudging ethical norms and social sensitivities in vaccination policy by over-relying**
75 **on CEA can have important implications.** It may affect the perceived equity of a
76 program, its support by the public and its long-term sustainability [13, 24-26] [27, 28].
77 It can invoke public backlash to the vaccine, leading to reduced uptake, increased
78 vaccine hesitancy and reduced overall effectiveness of the program [29-31].
79 Therefore, an empirical evidence-base is needed about the public's view on the key

80 value judgments that need to be made in vaccine funding decisions [9, 10, 12, 32,
81 33]. Such evidence can complement formalized appraisals like CEA, stimulate
82 deliberation and discussion on how to prioritize vaccines within a budget constraint
83 and, moreover, it can be explored whether such evidence can become quantitatively
84 integrated into formal decision frameworks in some sort of 'extended' or 'weighted'
85 CEA [7, 34].

86 The objective of this study is to address this challenge by analyzing how the
87 population in the United Kingdom prioritizes vaccination programs and to investigate
88 whether its values diverge from the assumptions that are implicitly underlying CEA.
89 We use a discrete choice experiment (DCE) among a representative sample of the
90 population in the United Kingdom (UK) to investigate, for four different types of
91 infectious diseases, the role played by different age groups in a program's overall
92 evaluation and the extent to which it matters whether these age groups are affected
93 by either direct, herd or side effects. We summarize these findings into a set of social
94 preference weights for health outcomes (e.g. QALYs) that could be incorporated into
95 economic evaluation or public health impact models.

96

97 **2. Methods**

98 DCEs are a widely used survey method to quantify individuals' preferences [35, 36]
99 (for a general review of applications, see [37]). Participants are presented with a
100 series of choices, usually between two goods described by the same attributes but
101 differing in their attribute levels. By observing respondents' preferred choices,
102 researchers can infer how the value of the competing options is determined by the
103 attributes of the product. In our case, we observe how people prioritize between

104 vaccination programs based on the number of direct, herd and side effects
105 generated by the program, and their distribution over different age groups. This
106 allows us to estimate a utility function that describes how the public values
107 vaccination programs, taking into account the different types of vaccine effect and
108 their distribution.

109

110 **2.1 Choice context**

111 For all of their choices, respondents were randomly assigned one of four disease
112 scenarios (see **Appendix A**). These were introduced before the start of the DCE.
113 After five choice sets this disease was presented again to the respondent as a
114 reminder. The four disease profiles were described as (1) severe—lasting nine days,
115 (2) mild—lasting nine days, (3) severe—lasting 160 days, and (4) mild—lasting 160
116 days. Influenza and pertussis were used as proxies for an acute severe and a longer
117 lasting milder disease, respectively [38, 39]. To avoid participants' preconceived
118 ideas, the diseases were unnamed and only described to participants by means of
119 severity using the generic descriptors of the dimensions of a standard instrument to
120 measure health-related quality of life, the EuroQoL EQ-5D-3L, based on average
121 reported values for both influenza and pertussis [38, 39]. To exclude considerations
122 about age differences in remaining life expectancy, we explicitly told the participants
123 that the diseases were not fatal.

124 Before every choice set we told respondents the following: “*the government has to*
125 *choose between two vaccination programs that will each be used in 100 000 people.*
126 *Considering your conviction about vaccination policy, which program do you think*

127 *the government should choose? Both options are equally costly, and identical in*
128 *every way except for the following 5 differences.”*

129

130 **2.2 Attributes and levels of vaccination programs**

131 To develop the final attributes and levels of the vaccine programs included in the
132 DCE, we followed a three stage iterative process. We performed a literature search
133 of other vaccine-related DCEs to assess the choice context and which attributes
134 were typically considered. These attributes were disease incidence, case fatality risk,
135 economic impact, duration of illness and duration of vaccine protection, severity of
136 illness and severity of side effects, and various personal characteristics including
137 age, gender and willingness/ability to get vaccinated. [40-44] From this list, we took
138 the attributes that were, in combination with the four disease profiles, best suited to
139 answer our research question. We presented several attribute combinations to a
140 convenience sample of lay persons, colleagues and collaborators at the market
141 research company in a pilot questionnaire, which we revised in response to received
142 comments. We re-iterated this process until we found the right form for the DCE from
143 which, with a relatively simple set of in total five core attributes (**Table 1**), we could
144 robustly calculate preference weights.

145 The first two attributes described the age group targeted for vaccination and
146 magnitude of the direct effects among those vaccinated. The third attribute described
147 the number of side effects occurring among those vaccinated. The side effects of
148 vaccination were presented in the DCE as identical to an episode of the disease that
149 the vaccine usually prevents, in order to enable a direct comparison between the
150 three effect types. Not doing so would have meant using a second health profile

151 within one choice option (one for the disease and one for the side effects) and this
152 would also have made the experiment substantially more difficult for the participants.
153 The fourth and fifth attribute described the magnitude of the herd effects and the age
154 group that received them. We decided to focus only on the morbidity aspects of
155 illness because including mortality would require additional attributes for infected
156 people in order to account for their differing life expectancy.

157 For direct and herd protection we used 1000, 3000 or 5000 disease episodes
158 prevented per 100,000 people vaccinated (an attack rate of 1-5% for a vaccine with
159 a 100% efficacy), and for side effects 100, 300 or 500 disease episodes per 100,000
160 people vaccinated (an attack rate of 0.1-0.5%). For direct protection and side effects,
161 we considered the following three age groups: children aged between 3 months and
162 3 years of age, adults aged between 30 and 50 years, and elderly aged between 65
163 and 75 years. The age groups for herd protection represented groups that, in the
164 case of the first two, are often difficult to vaccinate for immunological reasons: young
165 children under 3 months, elderly above 80 years and unvaccinated adults between
166 30 and 50 years.

167

168 (insert **Table 1**)

169

170 We depicted both the age group and quantity of cases avoided or caused by
171 vaccination using simple graphics [45] (**Figure 1**). To explicitly investigate the
172 assumption whether individuals ultimately look at the total impact of the program and
173 to reduce the chance that respondents would adhere to a simple counting heuristic

174 without reflection, we presented the net number of disease cases averted for each
175 strategy separately (the sum of direct and herd effects minus side effects).

176

177 (insert **Figure 1**)

178

179 **2.3 Experimental design of the choice sets**

180 The design of a DCE refers to the number and composition of choice sets presented
181 to each participant [46]. A set of 45 choice sets was selected out of the 58,806
182 possible choice sets (see **Appendix B** for more info on the selection process) and
183 distributed over three survey versions, so to limit the number of choice sets to be
184 completed per respondent to 15. Therefore, each of the four disease profiles was
185 represented in three different surveys (see **Figure 2**).

186

187 (Insert **Figure 2**)

188

189 The choice alternatives (i.e. profiles) themselves were '*partial* profiles' [47, 54]. We
190 varied and highlighted the levels of two to four of the five attributes in the choice sets
191 and kept the remaining attribute(s) constant so that respondents did not have to
192 simultaneously trade-off all five dimensions per choice (see **Appendix B**). Limiting
193 the cognitive burden for respondents in a DCE increases the validity and reliability of
194 their answers [48]. The design we generated was 'D-optimal' in a Bayesian
195 framework fitting with a multinomial logit (MNL) model for the attributes' main effects
196 and six interactions between the two age attributes (direct and herd effects) and the

197 three magnitude attributes we deemed to be important *a priori*. We chose a Bayesian
198 framework to integrate prior information on the respondents' likely preferences [49]
199 (see **Appendix C**). The Bayesian D-optimal design then results in the smallest
200 possible standard errors for the utility estimates at the given sample size.

201

202 **2.4 Sample**

203 After the design, we tested our survey among a pilot sample of the online panel
204 (N=69) to confirm that respondents could fully understand and complete the survey.
205 Based on the feedback from this pilot sample we judged that the experiment was
206 understandable and that no further changes were needed.

207 From a consumer panel of 1 million UK members, 9613 random panelists were
208 approached to participate in “a scientific study on resource allocation in healthcare”.
209 Of these people, 4144 (43%) responded to the invitation. We recruited 1950 of them
210 to fulfill predetermined quotas to provide a representative sample of the UK
211 population in terms of gender, socio-economic strata (indicated by the occupation of
212 the head of the household), age groups (20-29, 30-39, 40-49, 50-59, 60+ years), and
213 urban vs. rural background.

214 The DCE was conducted in November 2016. An email containing a link to the survey
215 website was sent to participants and by clicking on the link respondents consented to
216 participate, although they were free to stop or close the survey at any point. All
217 respondents received a nominal incentive for study completion (£0.50 per 12-minute
218 questionnaire). Before completing the DCE, respondents were asked to administer a
219 survey tool to measure vaccine hesitancy [50], and were asked social-demographic
220 questions and whether they have or had children. After the DCE, we asked about

221 their experience with severe diseases, their interpretation of the validity of the
222 answers they provided and the overall difficulty of the DCE survey.

223 We obtained informed consent from all respondents and ethical approval of the study
224 from the Ethics Committee of the London School of Hygiene & Tropical Medicine
225 (Ref 10335). We conducted the research in accordance with the Code of Conduct of
226 the Market Research Society, which ensured that information is collected for
227 research purposes only, is kept confidential, and respondent anonymity is
228 guaranteed.

229

230 **2.5 Data analysis**

231 To quantify the weight of the five attributes and their levels in the utility attributed to a
232 vaccination strategy, a panel mixed logit model (fitted by the Hierarchical Bayes
233 method [51]) was used (see **Table 3**). The model involved seven main effects: four
234 related to the two three-level categorical attributes describing the utility impact of a
235 change in the targeted age group in direct and herd effects, and three related to the
236 continuous attributes describing the impact of a change in the absolute number of
237 disease cases via direct effects, side effects and herd effects. Besides these seven
238 main effects the model also includes attribute interaction effects, indicating the
239 additional change in utility because of a particular combination of attribute levels. We
240 computed the overall significance of the attributes using likelihood ratio (LR) tests
241 and measured the relative importance of the attributes by the logworth statistic (i.e. –
242 \log_{10} (p-value of the LR-test)). The coefficients of the logit model were obtained by
243 estimating the *a priori* model, i.e. the model with the utility function that seemed most
244 appropriate when planning the DCE, and subsequently dropping the non-significant

245 model terms until we obtained a *final* model in which all effects had significant
246 explanatory value at the 5% level. Models were fitted using the JMP 13 Pro Choice
247 platform (based on 10,000 iterations, with the last 5000 used for estimation)
248 assuming normally distributed parameters with no correlation between the attributes.
249 Combining the main and interaction effects, this model allows calculating the
250 additional utility of a vaccination program generated per additional health effect, i.e.
251 per type of effect per age group (see the nine variations in **Table 3**). The 95%
252 confidence intervals for the equity weights were estimated using the Delta method
253 [52].

254

255 We investigated heterogeneity in respondents' preferences in two ways. First, by
256 exploring the influence of the observed respondent characteristics on the average
257 preferences and, second, by studying the unobserved preference heterogeneity by
258 means of a hierarchical cluster analysis on the subject-specific estimates resulting
259 from the Hierarchical Bayes approach. We favoured this two-stage modelling method
260 as it performs equally well as one-stage modelling methods such as latent class
261 modelling [53] while enabling us to parsimoniously derive the preference weights and
262 their 95% confidence intervals.

263

264 **3. Results**

265

266 **3.1 Response**

267 A total of 1546 respondents out of 1950 (79%) who were sent the questionnaire
268 completed it, of which 47 (3%) indicated that the questions were too difficult or their
269 answers invalid, leaving 1499 questionnaires for analysis. Our final sample was
270 sufficiently representative of the UK population in terms of gender, family size, socio-
271 economic status and education level (**Table 2**).

272

273 (insert **Table 2**)

274

275 **3.2 Main effects and calculated weights**

276 Across all questionnaires, respondents made a total of 22,485 choices between
277 vaccination programs. There was no significant effect observed of which of the three
278 survey versions a participant received. Respondents did not systematically choose
279 the program with the highest overall public health impact, i.e. the total of all
280 prevented cases including direct, herd and side effects. In fact, only 99 respondents
281 (6.6%) consistently opted for the most effective program in all of their choice sets.
282 However, about half the respondents (738/1499) chose the most effective alternative
283 in at least 70% of their choices, indicating that the total effect on the disease burden
284 is important, but not the only factor in prioritizing vaccination programs.

285 **Table 3** presents an overview of the incremental utility of the main effects and
286 interactions. The vaccination program that was least preferred (i.e. yielding minimum
287 utility) was one that targeted the elderly (65-75y), generated the lowest number of
288 prevented cases, the highest number of side effects, and the lowest number of cases
289 prevented via herd protection in unvaccinated adults. The most preferred program
290 (i.e. yielding maximum utility) was one that targeted children, generated the highest

291 number of prevented cases, the lowest number of side effects, and the highest
292 number of cases prevented via herd protection in newborns.

293

294 (insert **Table 3**)

295

296 Using the same logit model, we then calculated preference weights for each effect
297 type per age group. These weights act as a multiplicative factor to transform identical
298 clinical symptoms into health effects with equal value in the public's view. We
299 compared the additional utility of a vaccination program that is generated through
300 preventing one specific disease case relative to the utility gained through directly
301 preventing a single disease case via vaccinating a child (**Figure 3**). These
302 preference weights reveal important patterns. First, preventing side effects of
303 vaccination was highly preferable to preventing natural infections, even though the
304 symptoms were equal in length and severity. The mean weight for side effects
305 across all ages was -2.93, meaning that avoiding one vaccine-induced infection was
306 weighted equally to avoiding around three natural infections among children. This
307 finding was consistent whether side effects occurred in children (-2.95 (95% CI: -
308 3.21; -2.69)), adults (-3.16 (95% CI: -3.51; -2.81)) or the elderly (-2.68 (95% CI: -
309 2.98; -2.37)). Second, respondents preferred vaccination programs that prevented
310 disease among newborns and children compared with those for adults and the
311 elderly, even though the prevented disease burden was similar. One episode
312 prevented in a newborn via herd protection was considered about twice as valuable
313 as directly protecting an adult via vaccination. Third, the extent to which respondents
314 preferred protecting adults and the elderly depends on the type of benefit conferred

315 by the program. Direct effects were the preferred mode of protection for adults
316 whereas herd effects were preferred for the elderly. Reducing disease burden by
317 directly vaccinating adults (aged 30-50 years) was weighted equally to reducing
318 disease burden in the elderly (aged 80+ years) via herd effects [0.75 (0.64; 0.85)
319 compared to 0.67 (0.58; 0.76), respectively]. In contrast, reducing disease burden in
320 adults (aged 30-50 years) by herd effects counted equally to reducing disease
321 burden in elderly (aged 65-75 years) directly via vaccination (0.12 (0.03; 0.20)
322 compared to 0.16 (0.06; 0.25), respectively).

323

324 (insert **Figure 3**)

325

326 From these results, we also calculated the number of infections needed to avert in
327 order to obtain equal utility as that from protecting 100 children directly via
328 vaccination (**Table 4**). Avoiding 100 infections in children via vaccination was
329 considered equivalent to protecting 632 elderly (65-75 years) or 134 adults. In turn,
330 these outcomes were equivalent to protecting 71 newborns, 865 adults or 150
331 elderly (>80y) via herd protection. Similarly, a vaccination strategy reduces its utility
332 by causing side effects. **Avoiding 34 side effects in children generates the same**
333 **utility as preventing 100 natural infections among the same age group.**

334

335 (insert **Table 4**)

336

337 **Figure 4** illustrates the significant interaction in our model between the age of the
338 vaccinated group and the age of the herd protection recipients (see **Table 3**). This
339 interaction must be understood as the additional utility that is given to (or taken away
340 from) a vaccination program depending on the particular combination of age groups
341 that are involved, regardless of the magnitude of direct, herd or side effects that are
342 being generated. It presents the attractiveness of particular intergenerational
343 vaccination strategies. Whereas a CEA perspective would consider all possible age
344 combinations equally attractive (as long as they lead to the same number of
345 infections prevented), our sample had clear intergenerational preferences over
346 vaccination strategies. Any age group was deemed acceptable to vaccinate when
347 there were herd protection benefits for newborns. To generate herd protection for
348 adults, children were the most attractive age group. To generate it to protect the
349 elderly >80, adults were deemed most appropriate. The least attractive
350 intergenerational combination was vaccinating elderly 65-75 years while generating
351 herd protection in adults 30-50 years. The most attractive age combination was
352 vaccinating children while generating herd protection in newborns.

353

354 (insert **Figure 4**)

355

356 **3.3 Preferences across disease types and respondents**

357 **As shown in Appendix D**, our results remained robust across all four different
358 disease types: the equity weights were statistically equivalent, regardless of whether
359 the condition was mild vs. severe or acute vs. chronic (indicated by a non-significant
360 interaction effect in our model between the attributes and the disease type). **Also, the**

361 appendix illustrates that our findings also remained robust across most respondent
362 characteristics: gender, age, occupation, level of education, urban-rural, socio-
363 economic background, experience with severe illness or parental status. Although
364 individuals with a low degree of vaccine hesitancy (indicated by high values on the
365 'vaccine hesitancy scale' (VHS) [50]) attributed less importance to side effects
366 ($p < 0.0001$), this effect was relatively small (a 10 unit increase in the VHS score (on a
367 scale from 10 to 50) led to a 10% decrease in absolute magnitude of the utility for
368 side effects (~ 0.03)).

369 The hierarchical cluster analysis of the individual preferences (see methods)
370 revealed two distinct groups of respondents: one group ($N=564$, *Cluster 1*) who
371 attached almost no importance to the number of side effects (with a mean weight of -
372 0.91 for side effects) and a larger group ($N=935$, *Cluster 2*) who valued this attribute
373 fairly highly (with a mean weight of -4.40) (**Table 3**). This clustering explains the
374 relatively high variation across respondents for the weight estimate for side effects
375 (the standard deviation to mean absolute value ratio of 0.043 for side effects is
376 almost twice the ratio for direct and herd effects). We used a logistic regression to
377 determine predictors of cluster membership. Cluster 1, who attached almost no
378 importance to the number of side effects, was characterized by high values on the
379 VHS, indicating little hesitancy ($p < 0.0001$). On the other hand, cluster 2, who valued
380 side effects more highly, was characterized by higher degrees of hesitancy on the
381 VHS. However, the predictive power of this association for membership of the group
382 was small (McFadden's pseudo $R^2=0.6\%$), implying that there is much unexplained
383 heterogeneity in the importance placed on side effects.

384

386 4. Discussion

387 In this study, we used a discrete choice experiment to analyse and quantify how the
388 public values the outcomes of vaccination programs. We observed several general
389 preference patterns, which were robust across different lengths and severities of
390 disease and respondent characteristics (socio-economic background, age, education
391 and parenthood). We observed that most respondents did not make choices purely
392 based on how to minimize the number of infections. In particular, individuals, on
393 average, weighted one averted instance of a side effect equal to about three similarly
394 severe natural infections in children and weighted one averted health outcome in
395 children up to six times more than preventing similarly severe health outcomes in the
396 elderly. Interestingly, our study has disentangled this latter phenomenon from the
397 type of effect as we observed a different weight given to protecting older people
398 depending on whether the benefits were directly vs. indirectly received. Our results
399 support a duty of care principle to provide herd protection for the elderly and an
400 aversion to protecting adults who are better able to protect themselves. The weight
401 given to side effects when evaluating a vaccination program was divisive, splitting
402 our sample into two clusters.

403 Our study, as far as we are aware, is the first of its kind to quantify the important
404 social value judgements that need to be made in vaccine funding decisions.
405 Although this limits comparability, our findings are in line with what can be learned
406 from other study domains. The finding that individuals weighted one averted instance
407 of a side effect equal to about three similarly severe natural infections in children can
408 be explained with general theory on decision-making. For instance, well-documented
409 psychological phenomena such as 'loss aversion' [55] (overvaluing risks and losses
410 over opportunities and gains), the 'act-omission bias' [56] [judging the effects of an

411 act (becoming vaccinated) differently from identical effects resulting from an
412 omission (becoming infected)], or ‘hyperbolic discounting’ [57] [overvaluing the
413 present (in which side effects occur) over the future (in which disease prevention will
414 occur)] suggest that people put an extraordinary weight on side effects when
415 evaluating a vaccination strategy. Moreover, also empirical studies that have
416 investigated people’s (stated) choices about whether or not they would personally
417 become vaccinated with a particular vaccine (e.g. [43, 58]) generated findings that
418 highlight the extraordinary weight of side effects. The preference given to health
419 benefits in younger people (newborns and children), up to six-fold, is also in line with
420 related studies on ‘ageism’ in other contexts of healthcare priority-setting (reviewed
421 in [59] and discussed elsewhere, e.g. [60, 61]).

422 It is important to study which aspects of health policy choices matter most to the
423 public. This is especially true in vaccination where public trust, goodwill and
424 participation are sensitive and key to success [62]. There is a growing concern that
425 public and political trust in scientific evidence is eroding, particularly in the context of
426 vaccination [63-65]. By being aware of the sensitivities around vaccination, decision
427 makers can understand and address some of the root causes of vaccine hesitancy,
428 adapt to concerns of the population and improve responses in communication
429 strategies.[66] Our findings provide empirical evidence on how to set vaccine
430 priorities in line with public preferences. There is an important debate over the extent
431 to which the public’s opinion should drive resource allocation in healthcare (see e.g.
432 [67, 68]). But, many believe that the values of the public, who pays for healthcare,
433 should at least somehow be acknowledged in the decision-making process. In the
434 context of vaccination, where public support and participation is key to success, this
435 concern becomes particularly crucial. Therefore, our results can be useful additions

436 to vaccine appraisals. They can provide guidance in specific epidemiological cases
437 where CEA does not provide the answers needed. For instance, our results would
438 suggest that, despite their attractiveness in terms of cost-effectiveness, the public
439 may not support a childhood influenza vaccination program that mainly benefits
440 adults or elderly [69], because preventing side effects in vaccinated children is
441 preferred over preventing disease burden among adults and elderly. Furthermore,
442 our study suggests that a childhood varicella-zoster vaccination program, in the case
443 that it protects children against varicella disease at the expense of increased zoster
444 in the elderly (the 'exogenous boosting hypothesis'), might be justifiable. In contrast,
445 previous analyses where QALY losses for children are weighted equally to those for
446 the elderly find that the increased burden in the elderly offsets the QALY gains in
447 children and determine the program not cost-effective [23, 70].

448 Our results can also be directly incorporated into economic evaluations as sensitivity
449 analyses to better align the underlying assumptions of CEA with the values of the
450 population. Our estimated preference weights can be used in decision-analytic
451 models as a parameter to weight QALYs or infections according to their 'social
452 value'. This would re-adjust the (equal) weight that QALYs receive in CEA according
453 to how important people think that the age of the QALY-recipient is and whether the
454 benefit was generated through direct protection, herd immunity or (avoiding) side
455 effects. There is an increased interest in such 'extended', 'distributive' or 'equity-
456 weighted' economic evaluation (see e.g. [7, 34, 71-76]), but, to our knowledge, such
457 studies do not exist for the evaluation of vaccines. Our estimates are developed
458 particularly for this context, and provide an opportunity to do so.

459 There are several limitations. We did not include any mortality effects, nor did we
460 include a difference in severity between the three vaccine effects, even though this

461 would be more realistic (as side effects of vaccines are usually milder than the
462 disease being prevented). We chose not to include these aspects because we
463 wanted to avoid increasing the complexity of the survey and reducing the validity of
464 the respondents' answers by adding a second disease profile. Also, keeping the
465 disease outcome constant over age groups and effects enabled trade-offs that were
466 wholly reflective of the preference between age groups and effects instead of also
467 reflecting additional considerations about disease severity. We also chose to present
468 the number of side effects rather than its complement the number of vaccinated
469 people *without* side effects. This framing may have played a role in the observed
470 weight for side effects. The alternative framing would probably have drawn less
471 attention to side effects and might have generated smaller weights. We however
472 wanted people to make explicit trade-offs between side effects with protective
473 benefits and chose for the more direct framing. Using the alternative is a suggestion
474 for further research. Also, we used generic disease profiles based on a description
475 in EQ-5D terms to minimize respondents making personal associations to the
476 disease and vaccine when we would have named the diseases (e.g. 'flu' or
477 'whooping cough'), but this may also have increased the level of abstraction and
478 reduced the level of personal involvement. A suggestion for further research is to
479 repeat our study with named diseases and to test whether our finding that the
480 disease profile did not matter to people's preferences is confirmed. Another limitation
481 is that, while our sample was broadly representative of the UK population, it was
482 recruited from an online panel where membership may be associated with
483 unobserved characteristics (e.g. interest in technology).

484 In conclusion, our study demonstrates clear and robust preference patterns in how
485 people value the impact of vaccination programs. A large majority of respondents

486 had a strong preference to minimize side effects and to prevent disease among
487 newborns and children. Our observations provide quantitative evidence about public
488 preferences around important and sensitive but neglected trade-offs in vaccine policy
489 decision-making, and can hopefully inspire further research and discussion.

490

491 **References**

- 492 1. Walker, D.G., R. Hutubessy, and P. Beutels, *WHO Guide for standardisation of economic*
493 *evaluations of immunization programmes*. Vaccine, 2010. **28**(11): p. 2356-2359.
- 494 2. Drummond, M., et al., *Methods for the economic evaluation of health care programmes*. Vol.
495 3. 2005, Oxford: Oxford University Press.
- 496 3. Ricciardi, G.W., et al., *Comparison of NITAG policies and working processes in selected*
497 *developed countries*. Vaccine, 2015. **33**(1): p. 3-11.
- 498 4. Daniels, N. and J. Sabin, *Setting limits fairly: learning to share resources for health*. 2008,
499 New York: Oxford University Press.
- 500 5. Hausman, D., *Valuing health: wellbeing, freedom and suffering*. 2015, Oxford: Oxford
501 University Press.
- 502 6. Powers, M. and R. Faden, *Social Justice. The Moral Foundations of Public Health and Health*
503 *Policy*. 2006, Oxford: Oxford University Press.
- 504 7. Cookson, R., M. Drummond, and H. Weatherly, *Explicit incorporation of equity*
505 *considerations into economic evaluation of public health interventions*. Health Econ Policy
506 Law, 2009. **4**(Pt 2): p. 231-45.
- 507 8. Dukhanin, V., et al., *Integrating social justice concerns into economic evaluation for*
508 *healthcare and public health: A systematic review*. Soc Sci Med, 2018. **198**: p. 27-35.
- 509 9. Poland, G.A. and E.K. Marcuse, *Developing vaccine policy: attributes of "just policy" and a*
510 *proposed template to guide decision and policy making*. Vaccine, 2011. **29**(44): p. 7577-8.
- 511 10. Field, R.I. and A.L. Caplan, *Evidence-based decision making for vaccines: the need for an*
512 *ethical foundation*. Vaccine, 2012. **30**(6): p. 1009-13.
- 513 11. Luyten, J. and P. Beutels, *The Social Value Of Vaccination Programs: Beyond Cost-*
514 *Effectiveness*. Health Aff (Millwood), 2016. **35**(2): p. 212-8.
- 515 12. Luyten, J., et al., *Public preferences over efficiency, equity and autonomy in vaccination*
516 *policy: an empirical study*. Soc Sci Med, 2013. **77**: p. 84-9.
- 517 13. Yaqub, O., et al., *Attitudes to vaccination: a critical review*. Soc Sci Med, 2014. **112**: p. 1-11.
- 518 14. Geelen, E., et al., *Taming the fear of voice: Dilemmas in maintaining a high vaccination rate*
519 *in the Netherlands*. Soc Sci Med, 2016. **153**: p. 12-9.
- 520 15. Sobo, E.J., *What is herd immunity, and how does it relate to pediatric vaccination uptake? US*
521 *parent perspectives*. Soc Sci Med, 2016. **165**: p. 187-195.
- 522 16. Fine, P., K. Eames, and D.L. Heymann, *"Herd immunity": a rough guide*. Clin Infect Dis, 2011.
523 **52**(7): p. 911-6.
- 524 17. Anderson, R. and R. May, *Infectious Diseases of Humans: Dynamics and Control*. 1991,
525 Oxford: Oxford University Press.
- 526 18. Schwartz, J.S. and A. Caplan, *vaccination ethics and policy*. 2017, Cambridge: MIT Press.
- 527 19. Lynch, M., et al., *Intussusception after administration of the rhesus tetravalent rotavirus*
528 *vaccine (Rotashield): The search for a pathogenic mechanism*. Pediatrics, 2006. **117**(5): p.
529 E827-E832.

- 530 20. Granstrom, M., *The History of Pertussis Vaccination: From Whole-Cell to Subunit Vaccines.*
531 History of Vaccine Development, 2011: p. 73-82.
- 532 21. Blume, S. and M. Zanders, *Vaccine independence, local competences and globalisation:
533 lessons from the history of pertussis vaccines.* Soc Sci Med, 2006. **63**(7): p. 1825-35.
- 534 22. McGuire, A., M. Drummond, and S. Keeping, *Childhood and adolescent influenza vaccination
535 in Europe: A review of current policies and recommendations for the future.* Expert Review of
536 Vaccines, 2016. **15**(5): p. 659-670.
- 537 23. Luyten, J., B. Ogunjimi, and P. Beutels, *Varicella-zoster virus vaccination under the exogenous
538 boosting hypothesis: two ethical perspectives.* Vaccine, 2014. **32**(52): p. 7175-8.
- 539 24. Feudtner, C. and E.K. Marcuse, *Ethics and immunization policy: promoting dialogue to
540 sustain consensus.* Pediatrics, 2001. **107**(5): p. 1158-64.
- 541 25. Charo, R.A., *Politics, parents, and prophylaxis--mandating HPV vaccination in the United
542 States.* N Engl J Med, 2007. **356**(19): p. 1905-8.
- 543 26. Salmon, D.A., et al., *Compulsory vaccination and conscientious or philosophical exemptions:
544 past, present, and future.* Lancet, 2006. **367**(9508): p. 436-42.
- 545 27. Hornsey, M.J., E.A. Harris, and K.S. Fielding, *The psychological roots of anti-vaccination
546 attitudes: A 24-nation investigation.* Health Psychol, 2018. **37**(4): p. 307-315.
- 547 28. Tomeny, T.S., C.J. Vargo, and S. El-Toukhy, *Geographic and demographic correlates of
548 autism-related anti-vaccine beliefs on Twitter, 2009-15.* Soc Sci Med, 2017. **191**: p. 168-175.
- 549 29. Bhattacharyya, S., C.T. Bauch, and R. Breban, *Role of word-of-mouth for programs of
550 voluntary vaccination: A game-theoretic approach.* Math Biosci, 2015. **269**: p. 130-4.
- 551 30. Bauch, C.T. and D.J. Earn, *Vaccination and the theory of games.* Proc Natl Acad Sci U S A,
552 2004. **101**(36): p. 13391-4.
- 553 31. Ndeffo Mbah, M.L., et al., *The impact of imitation on vaccination behavior in social contact
554 networks.* PLoS Comput Biol, 2012. **8**(4): p. e1002469.
- 555 32. Bombard, Y., et al., *Eliciting ethical and social values in health technology assessment: A
556 participatory approach.* Soc Sci Med, 2011. **73**(1): p. 135-44.
- 557 33. Makarovs, K. and P. Achterberg, *Contextualizing educational differences in "vaccination
558 uptake": A thirty nation survey.* Soc Sci Med, 2017. **188**: p. 1-10.
- 559 34. Fleurbaey, M., et al., *Equivalent income and fair evaluation of health care.* Health Econ,
560 2013. **22**(6): p. 711-29.
- 561 35. Ryan, M., K. Gerard, and A.-A. M., *Using Discrete Choice Experiments to Value Health and
562 Health Care.* 2008, Dordrecht: Springer.
- 563 36. Louviere, J., D. Hensher, and J. Swait, *Stated Choice Methods: Analysis and Applications.*
564 2000, Cambridge: Cambridge University Press.
- 565 37. de Bekker-Grob, E.W., M. Ryan, and K. Gerard, *Discrete choice experiments in health
566 economics: a review of the literature.* Health Econ, 2012. **21**(2): p. 145-72.
- 567 38. van Hoek, A.J., et al., *The impact of pandemic influenza H1N1 on health-related quality of
568 life: a prospective population-based study.* PLoS One, 2011. **6**(3): p. e17030.
- 569 39. van Hoek, A.J., et al., *The burden of disease and health care use among pertussis cases in
570 school aged children and adults in England and Wales; a patient survey.* PLoS One, 2014.
571 **9**(11): p. e111807.
- 572 40. Lambooi, M.S., et al., *Consistency between stated and revealed preferences: a discrete
573 choice experiment and a behavioural experiment on vaccination behaviour compared.* BMC
574 Med Res Methodol, 2015. **15**: p. 19.
- 575 41. Veldwijk, J., et al., *Parental preferences for rotavirus vaccination in young children: a discrete
576 choice experiment.* Vaccine, 2014. **32**(47): p. 6277-83.
- 577 42. Hofman, R., et al., *Have preferences of girls changed almost 3 years after the much debated
578 start of the HPV vaccination program in The Netherlands? A discrete choice experiment.* PLoS
579 One, 2014. **9**(8): p. e104772.

- 580 43. Sadique, M.Z., et al., *The effect of perceived risks on the demand for vaccination: results from*
581 *a discrete choice experiment*. PLoS One, 2013. **8**(2): p. e54149.
- 582 44. de Bekker-Grob, E.W., et al., *Girls' preferences for HPV vaccination: a discrete choice*
583 *experiment*. Vaccine, 2010. **28**(41): p. 6692-7.
- 584 45. Ancker, J.S., et al., *Design features of graphs in health risk communication: a systematic*
585 *review*. J Am Med Inform Assoc, 2006. **13**(6): p. 608-18.
- 586 46. Reed Johnson, F., et al., *Constructing experimental designs for discrete-choice experiments:*
587 *report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task*
588 *Force*. Value Health, 2013. **16**(1): p. 3-13.
- 589 47. Kessels, R., B. Jones, and P. Goos, *An improved two-stage variance balance approach for*
590 *constructing partial profile designs for discrete choice experiments*. Applied Stochastic
591 Models in Business and Industry, 2015. **31**(5): p. 626-648.
- 592 48. Dellaert, B.G.C., B. Donkers, and A. van Soest, *Complexity Effects in Choice Experiment-Based*
593 *Models*. Journal of Marketing Research, 2012. **49**(3): p. 424-434.
- 594 49. Kessels, R., et al., *The usefulness of Bayesian optimal designs for discrete choice experiments*.
595 Applied Stochastic Models in Business and Industry, 2011. **27**(3): p. 173-188.
- 596 50. Larson, H.J., et al., *Measuring vaccine hesitancy: The development of a survey tool*. Vaccine,
597 2015. **33**(34): p. 4165-75.
- 598 51. Train, K., *Discrete Choice Methods with Simulation*. 2nd Edition ed. 2009, Cambridge:
599 Cambridge University Press.
- 600 52. Bliemer, M.C.J. and J.M. Rose, *Confidence intervals of willingness-to-pay for random*
601 *coefficient logit models*. Transportation Research Part B-Methodological, 2013. **58**: p. 199-
602 214.
- 603 53. Crabbe, M., B. Jones, and M. Vandebroek, *Comparing Two-Stage Segmentation Methods for*
604 *Choice Data with a One-Stage Latent Class Choice Analysis*. Communications in Statistics-
605 Simulation and Computation, 2013. **42**(5): p. 1188-1212.
- 606 54. Kessels, R., B. Jones, and P. Goos, *Bayesian optimal designs for discrete choice experiments*
607 *with partial profiles*. Journal of Choice Modelling. 2011. **4**: p. 52-74.
- 608 55. Kahneman, D. and A. Tversky, *Prospect Theory - Analysis of Decision under Risk*.
609 Econometrica, 1979. **47**(2): p. 263-291.
- 610 56. Spranca, M., E. Minsk, and J. Baron, *Omission and Commission in Judgment and Choice*.
611 Journal of Experimental Social Psychology, 1991. **27**(1): p. 76-105.
- 612 57. Frederick, S., G. Loewenstein, and T. O'Donoghue, *Time discounting and time preference: A*
613 *critical review*. Journal of Economic Literature, 2002. **40**(2): p. 351-401.
- 614 58. Seanehia, J., et al., *Quantifying population preferences around vaccination against severe but*
615 *rare diseases: A conjoint analysis among French university students, 2016*. Vaccine, 2017.
- 616 59. Gu, Y., et al., *Attributes and weights in health care priority setting: A systematic review of*
617 *what counts and to what extent*. Soc Sci Med, 2015. **146**: p. 41-52.
- 618 60. Tsuchiya, A., *QALYs and ageism: philosophical theories and age weighting*. Health Econ,
619 2000. **9**(1): p. 57-68.
- 620 61. Bognar, G., *Fair Innings*. Bioethics, 2015. **29**(4): p. 251-261.
- 621 62. Cooper, L.Z., H.J. Larson, and S.L. Katz, *Protecting public trust in immunization*. Pediatrics,
622 2008. **122**(1): p. 149-53.
- 623 63. Larson, H.J., et al., *Addressing the vaccine confidence gap*. Lancet, 2011. **378**(9790): p. 526-
624 35.
- 625 64. Karafillakis, E., et al., *Vaccine hesitancy among healthcare workers in Europe: A qualitative*
626 *study*. Vaccine, 2016. **34**(41): p. 5013-5020.
- 627 65. Leask, J., H.W. Willaby, and J. Kaufman, *The big picture in addressing vaccine hesitancy*. Hum
628 Vaccin Immunother, 2014. **10**(9): p. 2600-2.
- 629 66. Diekema, D.S. and B. American Academy of Pediatrics Committee on, *Responding to parental*
630 *refusals of immunization of children*. Pediatrics, 2005. **115**(5): p. 1428-31.

- 631 67. Hausman, D.M., *Polling and public policy*. Kennedy Inst Ethics J, 2004. **14**(3): p. 241-7.
- 632 68. Hausman, D.M., *Valuing health: Well-Being, Freedom, and Suffering*. 2015, Oxford: Oxford
- 633 University Press.
- 634 69. Baguelin, M., et al., *Assessing optimal target populations for influenza vaccination*
- 635 *programmes: an evidence synthesis and modelling study*. PLoS Med, 2013. **10**(10): p.
- 636 e1001527.
- 637 70. Brisson, M., W.J. Edmunds, and N.J. Gay, *Varicella vaccination: impact of vaccine efficacy on*
- 638 *the epidemiology of VZV*. J Med Virol, 2003. **70 Suppl 1**: p. S31-7.
- 639 71. Nord, E., et al., *Incorporating societal concerns for fairness in numerical valuations of health*
- 640 *programmes*. Health Econ, 1999. **8**(1): p. 25-39.
- 641 72. Bleichrodt, H., *Health utility indices and equity considerations*. J Health Econ, 1997. **16**(1): p.
- 642 65-91.
- 643 73. Dolan, P., *The measurement of individual utility and social welfare*. J Health Econ, 1998.
- 644 **17**(1): p. 39-52.
- 645 74. Asaria, M., S. Griffin, and R. Cookson, *Distributional Cost-Effectiveness Analysis: A Tutorial*.
- 646 *Med Decis Making*, 2016. **36**(1): p. 8-19.
- 647 75. Round, J. and M. Paulden, *Incorporating equity in economic evaluations: a multi-attribute*
- 648 *equity state approach*. Eur J Health Econ, 2017.
- 649 76. Samson, A.L., et al., *Fairness in cost-benefit analysis: A methodology for health technology*
- 650 *assessment*. Health Econ, 2017.

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Table 1. Attributes and levels used in the DCE

Attribute	Level
Age of vaccinated group (N=100 000)	Children (3 months - 3 years)
	Adults (30-50 years)
	Elderly (65-75 years)
Disease episodes prevented in vaccinated group	1000 cases
	3000 cases
	5000 cases
Number of vaccine-induced side-effects	100 cases
	300 cases
	500 cases
Disease episodes prevented via herd protection	1000 cases
	3000 cases
	5000 cases
Age of people receiving herd protection	Newborns (<3 months)
	Adults (30-50 years)
	Elderly (>80 years)

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657 **Table 2: Respondent characteristics.**

	Sample	UK population*
Total recruited	1546	
Excluded for analysis	47	
Included in the analysis	1499 (100%)	
<i>Gender</i>		
Male	703 (47%)	49%
Female	796 (53%)	51%
<i>Age (years)</i>		
20-29	296 (20%)	13%
30-39	285 (19%)	13%
40-49	288 (19%)	14%
50-59	308 (21%)	13%
60 and over	322 (21%)	23%
<i>Living in a city with more than 10,000 inhabitants</i>	1011 (67%)	83%
<i>Social grades based on the profession of the highest paid household member</i>		
A (upper middle class)	85 (6%)	4%
B (middle class)	297 (20%)	23%
C1 (lower middle class)	385 (26%)	27%
C2 (skilled working class)	330 (22%)	21%
D (working class)	72 (5%)	16%
E (non-working)	330 (22%)	9%
<i>Education level</i>		
No qualifications	48 (3%)	15%
Secondary education	322 (21%)	14.2%
Post-secondary education	288 (19%)	14.5%
Vocational qualification	254 (17%)	20.3%
Undergraduate degree, Post-graduate degree & Doctorate	427 (39%)	30%

	Not sure	2 (0.1%)	/
<i>Having children</i>			
	No children	585 (39%)	42%
	Children aged 0-4 years	168 (11%)	42%**
	Children aged 5-20 years	358 (24%)	/
	Children aged over 20 years	388 (26%)	15%
<i>Exposure to poor health</i>			
	Participant affected by poor health	407 (27%)	
	Close friends or family of the participant affected by poor health	470 (31%)	
	Neither participant nor close friends nor family affected by poor health	622 (41%)	

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659 *UK population data 2016: Office for National Statistics <https://www.gov.uk/government/publications>

660 **Percentage of UK families living with dependent children (<18 years old)

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676 **Table 3. Attributes that affected respondent choices, based on panel mixed logit model estimates (means and standard**
 677 **deviations) with p-values from likelihood ratio (LR) tests for significant attribute effects.**

Model term	Posterior mean	Posterior std dev	Subject std dev	P-value
Cases prevented in unvaccinated by herd effects (per 1000 cases)	0.715	0.018	0.101	<0.0001
Cases prevented in vaccinated by direct effects (per 1000 cases)	0.619	0.018	0.100	<0.0001
Cases of side effects in vaccinated (per 100 cases)	-0.285	0.012	0.110	<0.0001
Age of unvaccinated	[Newborns <3m]	0.614	0.048	<0.0001
	[Adults 30-50y]	-0.597	0.043	
	[Elderly >80y]	-0.017	NA	
Age of unvaccinated*Cases prevented in vaccinated by direct effects	[Newborns <3m]	-0.043	0.009	<0.0001
	[Adults 30-50y]	0.071	0.009	
	[Elderly >80y]	-0.028	NA	
Age of vaccinated	[Children 3m-3y]	0.305	0.040	<0.0001
	[Adults 30-50y]	0.142	0.048	
	[Elderly 65-75y]	-0.446	NA	
Age of unvaccinated*Age of vaccinated	[Newborns <3m]* [Children 3m- 3y]	-0.131	0.036	<0.0001
	[Newborns <3m]* [Adults 30- 50y]	-0.210	0.041	
	[Newborns <3m]* [Elderly 65- 75y]	0.341	NA	

	<i>75y]</i>				
	[Adults 30-50y]* [Children 3m-3y]	0.250	0.052	0.044	
	[Adults 30-50y]* [Adults 30-50y]	-0.079	0.049	0.045	
	<i>[Adults 30-50y]* [Elderly 65-75y]</i>	-0.171	NA	NA	
	<i>[Elderly >80y]* [Children 3m-3y]</i>	-0.119	NA	NA	
	<i>[Elderly >80y]* [Adults 30-50y]</i>	0.289	NA	NA	
	<i>[Elderly >80y]* [Elderly 65-75y]</i>	-0.170	NA	NA	
Age of vaccinated*Cases of side effects in vaccinated	[Children 3m-3y]	-0.032	0.008	0.040	<0.0001
	[Adults 30-50y]	-0.037	0.009	0.044	
	<i>[Elderly 65-75y]</i>	0.069	NA	NA	
Age of unvaccinated*Cases prevented in unvaccinated by herd effects	[Newborns <3m]	0.052	0.009	0.048	<0.0001
	[Adults 30-50y]	-0.005	0.008	0.043	
	<i>[Elderly >80y]</i>	-0.047	NA	NA	
Age of vaccinated*Cases prevented in vaccinated by direct effects	[Children 3m-3y]	0.051	0.010	0.044	<0.0001
	[Adults 30-50y]	-0.032	0.009	0.037	
	<i>[Elderly 65-75y]</i>	-0.019	NA	NA	

678 Note: Mean estimates corresponding to the last level of an attribute, either as a main effect or involved in an interaction, are italicized and calculated as minus
679 the sum of the estimates for the other levels of that attribute; NA means 'not assigned'.

680 **Table 4. Number of infections to prevent to gain equal utility, with 95%**
 681 **confidence intervals.**

Age group of vaccine effect	Direct effects	Herd effects	Side effects
Newborns (<3 months)	NA	71 [66; 76]	NA
Children (3 months – 3 years)	100 [index]	NA	-34 [-37; -31] Cluster 1: -221 [-340; -102] Cluster 2: -21 [-23; -20]
Adults (30–50 years)	134 [115; 153]	865 [242; 1487]	-32 [-35; -28] Cluster 1: -72 [-93; -51] Cluster 2: -23 [-25; -20]
Elderly (65–75 years)	632 [255; 1010]	NA	-37 [-42; -33] Cluster 1: -113 [-163; -64] Cluster 2: -25 [-27; -22]
Elderly (>80 years)	NA	150 [130; 169]	NA

682 Note: Cluster 1 and 2 have 564 and 935 respondents, respectively; NA refers to combinations of
 683 attribute levels not included in the choice profiles.

684

685 **Figure 1. Example of a choice set.**

686

687 **Figure 2. Schematic representation of the different arms of the questionnaire.**
688 **For each disease stratum, there was also an equal sampling over the socio-**
689 **economic groups (25% A+B; 25% C1; 25% C2; 25% E+D).**

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691 **Figure 3. Utility weights representing public preferences for identical health**
692 **outcomes with different attributes, with 95% confidence intervals.**

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694 **Figure 4. Intergenerational preferences: interaction effects between the age**
695 **group vaccinated and the age group receiving herd protection effects.**
696 **Marginal utility values consist of main effects of the attributes involved and**
697 **their interaction effect..**

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1 **Quantifying the public’s view on social value judgments in**
2 **vaccine decision-making: a discrete choice experiment**

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4

5 **Abstract**

6 Vaccination programs generate direct protection, herd protection and, occasionally,
7 side effects, distributed over different age groups. This study elicits the general
8 public’s view on how to balance these outcomes in funding decisions for vaccines.
9 We performed an optimal design discrete choice experiment with partial profiles in a
10 representative sample (N=1499) of the public in the United Kingdom. Using a panel
11 mixed logit model, we quantified, for four different types of infectious disease, the
12 importance of a person’s age during disease, how disease was prevented—via direct
13 vaccine protection or herd protection—and whether the vaccine induced side effects.
14 Our study shows clear patterns in how the public values vaccination programs.
15 These diverge from the assumptions made in public health and cost-effectiveness
16 models that inform decision-making. We found that side effects and infections in
17 newborns and children were of primary importance to the perceived value of a
18 vaccination program. Averting side effects was, in any age group, weighted three
19 times as important as preventing an identical natural infection in a child whereas the
20 latter was weighted six times as important as preventing the same infection in elderly
21 aged 65-75 years. These findings were independent of the length or severity of the
22 disease, and were robust across respondents’ backgrounds. We summarize these
23 patterns in a set of preference weights that can be incorporated into future models.

24
25

26 **Keywords**

27 Priority-setting; age; side effects, herd protection, cost-effectiveness analysis,
28 decision making; discrete choice experiment; preference weight, vaccination

29

30 **1. Introduction**

31 Economic evaluation methods such as cost-effectiveness analysis (CEA) are
32 common components in public funding decisions for vaccines [1, 2]. They feature in
33 the standard evidence considered by e.g. the Advisory Committee on Immunization
34 Practices in the US, the Joint Committee on Vaccination and Immunization in
35 England, the World Health Organization and non-governmental organizations such
36 as the Bill & Melinda Gates Foundation [3]. At the same time, it is widely
37 acknowledged that these evaluation frameworks have important shortcomings and
38 that they alone offer insufficient basis for making fair and efficient vaccine funding
39 decisions [4-8]. There is a growing literature about the limits of CEA in assessing the
40 value of vaccination [9-15].

41 One important criticism is that CEA is limited in how it values the consequences of
42 vaccination. Summary outcome measures [such as e.g. infections prevented or
43 Quality-Adjusted Life Years (QALYs) gained] neglect the particular social context in
44 which these outcomes occur. Nonetheless, such contextual features are important
45 aspects to consider when evaluating a vaccination strategy. Vaccination induces
46 disease protection in those who become vaccinated, but it also creates *herd*
47 protection (or indirect effects in third parties because of reduced pathogen
48 transmission [16]) and, occasionally, adverse clinical *side* effects. There are
49 qualitative differences between these direct, herd and side effects. Creating herd
50 protection can be of particular ethical value (e.g. to protect vulnerable groups who
51 otherwise cannot protect themselves) and there is a profound psychological impact
52 of vaccine-induced side effects. Moreover, the *distribution* of these three different
53 effect types over different age groups is important. Side effects can be concentrated
54 in one age group despite indirect protection from reduced transmission benefitting

55 either the wider population, or in some cases a different age group entirely [17].
56 Examples include protecting the elderly through childhood influenza vaccination or
57 future generations through a *polio* eradication program. Such broader, distributive
58 aspects of vaccination are important but they remain neglected in standard cost-
59 effectiveness or public health impact models.

60 Several notable examples illustrate that this broader social context of health
61 outcomes needs to be considered in vaccine decision-making [18]. For instance,
62 vaccines against rotavirus (Rotashield®) and pertussis (whole cell pertussis vaccine)
63 were withdrawn from many countries because of a perceived risk of side effects,
64 even though from a medical perspective the benefit from vaccination largely
65 outweighed any potential risk [19-21]. Also, despite persuasive economic and public
66 health benefits of childhood influenza vaccination, few countries have actually
67 implemented such a preventive strategy, due in large part to concerns about the
68 social acceptability and equity of targeting vaccination at children to protect the wider
69 population [22]. And, in many countries introduction of an effective varicella
70 vaccination program has been delayed because of concerns about the possible
71 'exogenous boosting effect' and its social repercussions, i.e. that reduced
72 chickenpox transmission among children (due to varicella vaccination) might
73 temporarily increase shingles incidence among older generations [23].

74 Misjudging ethical norms and social sensitivities in vaccination policy by over-relying
75 on CEA can have important implications. It may affect the perceived equity of a
76 program, its support by the public and its long-term sustainability [13, 24-26] [27, 28].
77 It can invoke public backlash to the vaccine, leading to reduced uptake, increased
78 vaccine hesitancy and reduced overall effectiveness of the program [29-31].
79 Therefore, an empirical evidence-base is needed about the public's view on the key

80 value judgments that need to be made in vaccine funding decisions [9, 10, 12, 32,
81 33]. Such evidence can complement formalized appraisals like CEA, stimulate
82 deliberation and discussion on how to prioritize vaccines within a budget constraint
83 and, moreover, it can be explored whether such evidence can become quantitatively
84 integrated into formal decision frameworks in some sort of ‘extended’ or ‘weighted’
85 CEA [7, 34].

86 The objective of this study is to address this challenge by analyzing how the
87 population in the United Kingdom prioritizes vaccination programs and to investigate
88 whether its values diverge from the assumptions that are implicitly underlying CEA.
89 We use a discrete choice experiment (DCE) among a representative sample of the
90 population in the United Kingdom (UK) to investigate, for four different types of
91 infectious diseases, the role played by different age groups in a program’s overall
92 evaluation and the extent to which it matters whether these age groups are affected
93 by either direct, herd or side effects. We summarize these findings into a set of social
94 preference weights for health outcomes (e.g. QALYs) that could be incorporated into
95 economic evaluation or public health impact models.

96

97 **2. Methods**

98 DCEs are a widely used survey method to quantify individuals’ preferences [35, 36]
99 (for a general review of applications, see [37]). Participants are presented with a
100 series of choices, usually between two goods described by the same attributes but
101 differing in their attribute levels. By observing respondents’ preferred choices,
102 researchers can infer how the value of the competing options is determined by the
103 attributes of the product. In our case, we observe how people prioritize between

104 vaccination programs based on the number of direct, herd and side effects
105 generated by the program, and their distribution over different age groups. This
106 allows us to estimate a utility function that describes how the public values
107 vaccination programs, taking into account the different types of vaccine effect and
108 their distribution.

109

110 **2.1 Choice context**

111 For all of their choices, respondents were randomly assigned one of four disease
112 scenarios (see **Appendix A**). These were introduced before the start of the DCE.
113 After five choice sets this disease was presented again to the respondent as a
114 reminder. The four disease profiles were described as (1) severe—lasting nine days,
115 (2) mild—lasting nine days, (3) severe—lasting 160 days, and (4) mild—lasting 160
116 days. Influenza and pertussis were used as proxies for an acute severe and a longer
117 lasting milder disease, respectively [38, 39]. To avoid participants' preconceived
118 ideas, the diseases were unnamed and only described to participants by means of
119 severity using the generic descriptors of the dimensions of a standard instrument to
120 measure health-related quality of life, the EuroQoL EQ-5D-3L, based on average
121 reported values for both influenza and pertussis [38, 39]. To exclude considerations
122 about age differences in remaining life expectancy, we explicitly told the participants
123 that the diseases were not fatal.

124 Before every choice set we told respondents the following: “*the government has to*
125 *choose between two vaccination programs that will each be used in 100 000 people.*
126 *Considering your conviction about vaccination policy, which program do you think*

127 *the government should choose? Both options are equally costly, and identical in*
128 *every way except for the following 5 differences.”*

129

130 **2.2 Attributes and levels of vaccination programs**

131 To develop the final attributes and levels of the vaccine programs included in the
132 DCE, we followed a three stage iterative process. We performed a literature search
133 of other vaccine-related DCEs to assess the choice context and which attributes
134 were typically considered. These attributes were disease incidence, case fatality risk,
135 economic impact, duration of illness and duration of vaccine protection, severity of
136 illness and severity of side effects, and various personal characteristics including
137 age, gender and willingness/ability to get vaccinated. [40-44] From this list, we took
138 the attributes that were, in combination with the four disease profiles, best suited to
139 answer our research question. We presented several attribute combinations to a
140 convenience sample of lay persons, colleagues and collaborators at the market
141 research company in a pilot questionnaire, which we revised in response to received
142 comments. We re-iterated this process until we found the right form for the DCE from
143 which, with a relatively simple set of in total five core attributes (**Table 1**), we could
144 robustly calculate preference weights.

145 The first two attributes described the age group targeted for vaccination and
146 magnitude of the direct effects among those vaccinated. The third attribute described
147 the number of side effects occurring among those vaccinated. The side effects of
148 vaccination were presented in the DCE as identical to an episode of the disease that
149 the vaccine usually prevents, in order to enable a direct comparison between the
150 three effect types. Not doing so would have meant using a second health profile

151 within one choice option (one for the disease and one for the side effects) and this
152 would also have made the experiment substantially more difficult for the participants.
153 The fourth and fifth attribute described the magnitude of the herd effects and the age
154 group that received them. We decided to focus only on the morbidity aspects of
155 illness because including mortality would require additional attributes for infected
156 people in order to account for their differing life expectancy.

157 For direct and herd protection we used 1000, 3000 or 5000 disease episodes
158 prevented per 100,000 people vaccinated (an attack rate of 1-5% for a vaccine with
159 a 100% efficacy), and for side effects 100, 300 or 500 disease episodes per 100,000
160 people vaccinated (an attack rate of 0.1-0.5%). For direct protection and side effects,
161 we considered the following three age groups: children aged between 3 months and
162 3 years of age, adults aged between 30 and 50 years, and elderly aged between 65
163 and 75 years. The age groups for herd protection represented groups that, in the
164 case of the first two, are often difficult to vaccinate for immunological reasons: young
165 children under 3 months, elderly above 80 years and unvaccinated adults between
166 30 and 50 years.

167

168 (insert **Table 1**)

169

170 We depicted both the age group and quantity of cases avoided or caused by
171 vaccination using simple graphics [45] (**Figure 1**). To explicitly investigate the
172 assumption whether individuals ultimately look at the total impact of the program and
173 to reduce the chance that respondents would adhere to a simple counting heuristic

174 without reflection, we presented the net number of disease cases averted for each
175 strategy separately (the sum of direct and herd effects minus side effects).

176

177 **(insert Figure 1)**

178

179 **2.3 Experimental design of the choice sets**

180 The design of a DCE refers to the number and composition of choice sets presented
181 to each participant [46]. A set of 45 choice sets was selected out of the 58,806
182 possible choice sets (see **Appendix B** for more info on the selection process) and
183 distributed over three survey versions, so to limit the number of choice sets to be
184 completed per respondent to 15. Therefore, each of the four disease profiles was
185 represented in three different surveys (see **Figure 2**).

186

187 **(Insert Figure 2)**

188

189 The choice alternatives (i.e. profiles) themselves were '*partial* profiles' [47, 54]. We
190 varied and highlighted the levels of two to four of the five attributes in the choice sets
191 and kept the remaining attribute(s) constant so that respondents did not have to
192 simultaneously trade-off all five dimensions per choice (see **Appendix B**). Limiting
193 the cognitive burden for respondents in a DCE increases the validity and reliability of
194 their answers [48]. The design we generated was 'D-optimal' in a Bayesian
195 framework fitting with a multinomial logit (MNL) model for the attributes' main effects
196 and six interactions between the two age attributes (direct and herd effects) and the

197 three magnitude attributes we deemed to be important *a priori*. We chose a Bayesian
198 framework to integrate prior information on the respondents' likely preferences [49]
199 (see **Appendix C**). The Bayesian D-optimal design then results in the smallest
200 possible standard errors for the utility estimates at the given sample size.

201

202 **2.4 Sample**

203 After the design, we tested our survey among a pilot sample of the online panel
204 (N=69) to confirm that respondents could fully understand and complete the survey.
205 Based on the feedback from this pilot sample we judged that the experiment was
206 understandable and that no further changes were needed.

207 From a consumer panel of 1 million UK members, 9613 random panelists were
208 approached to participate in “a scientific study on resource allocation in healthcare”.
209 Of these people, 4144 (43%) responded to the invitation. We recruited 1950 of them
210 to fulfill predetermined quotas to provide a representative sample of the UK
211 population in terms of gender, socio-economic strata (indicated by the occupation of
212 the head of the household), age groups (20-29, 30-39, 40-49, 50-59, 60+ years), and
213 urban vs. rural background.

214 The DCE was conducted in November 2016. An email containing a link to the survey
215 website was sent to participants and by clicking on the link respondents consented to
216 participate, although they were free to stop or close the survey at any point. All
217 respondents received a nominal incentive for study completion (£0.50 per 12-minute
218 questionnaire). Before completing the DCE, respondents were asked to administer a
219 survey tool to measure vaccine hesitancy [50], and were asked social-demographic
220 questions and whether they have or had children. After the DCE, we asked about

221 their experience with severe diseases, their interpretation of the validity of the
222 answers they provided and the overall difficulty of the DCE survey.

223 We obtained informed consent from all respondents and ethical approval of the study
224 from the Ethics Committee of the London School of Hygiene & Tropical Medicine
225 (Ref 10335). We conducted the research in accordance with the Code of Conduct of
226 the Market Research Society, which ensured that information is collected for
227 research purposes only, is kept confidential, and respondent anonymity is
228 guaranteed.

229

230 **2.5 Data analysis**

231 To quantify the weight of the five attributes and their levels in the utility attributed to a
232 vaccination strategy, a panel mixed logit model (fitted by the Hierarchical Bayes
233 method [51]) was used (see **Table 3**). The model involved seven main effects: four
234 related to the two three-level categorical attributes describing the utility impact of a
235 change in the targeted age group in direct and herd effects, and three related to the
236 continuous attributes describing the impact of a change in the absolute number of
237 disease cases via direct effects, side effects and herd effects. Besides these seven
238 main effects the model also includes attribute interaction effects, indicating the
239 additional change in utility because of a particular combination of attribute levels. We
240 computed the overall significance of the attributes using likelihood ratio (LR) tests
241 and measured the relative importance of the attributes by the logworth statistic (i.e. –
242 \log_{10} (p-value of the LR-test)). The coefficients of the logit model were obtained by
243 estimating the *a priori* model, i.e. the model with the utility function that seemed most
244 appropriate when planning the DCE, and subsequently dropping the non-significant

245 model terms until we obtained a *final* model in which all effects had significant
246 explanatory value at the 5% level. Models were fitted using the JMP 13 Pro Choice
247 platform (based on 10,000 iterations, with the last 5000 used for estimation)
248 assuming normally distributed parameters with no correlation between the attributes.
249 Combining the main and interaction effects, this model allows calculating the
250 additional utility of a vaccination program generated per additional health effect, i.e.
251 per type of effect per age group (see the nine variations in **Table 3**). The 95%
252 confidence intervals for the equity weights were estimated using the Delta method
253 [52].

254

255 We investigated heterogeneity in respondents' preferences in two ways. First, by
256 exploring the influence of the observed respondent characteristics on the average
257 preferences and, second, by studying the unobserved preference heterogeneity by
258 means of a hierarchical cluster analysis on the subject-specific estimates resulting
259 from the Hierarchical Bayes approach. We favoured this two-stage modelling method
260 as it performs equally well as one-stage modelling methods such as latent class
261 modelling [53] while enabling us to parsimoniously derive the preference weights and
262 their 95% confidence intervals.

263

264 **3. Results**

265

266 **3.1 Response**

267 A total of 1546 respondents out of 1950 (79%) who were sent the questionnaire
268 completed it, of which 47 (3%) indicated that the questions were too difficult or their
269 answers invalid, leaving 1499 questionnaires for analysis. Our final sample was
270 sufficiently representative of the UK population in terms of gender, family size, socio-
271 economic status and education level (**Table 2**).

272

273 (insert **Table 2**)

274

275 **3.2 Main effects and calculated weights**

276 Across all questionnaires, respondents made a total of 22,485 choices between
277 vaccination programs. There was no significant effect observed of which of the three
278 survey versions a participant received. Respondents did not systematically choose
279 the program with the highest overall public health impact, i.e. the total of all
280 prevented cases including direct, herd and side effects. In fact, only 99 respondents
281 (6.6%) consistently opted for the most effective program in all of their choice sets.
282 However, about half the respondents (738/1499) chose the most effective alternative
283 in at least 70% of their choices, indicating that the total effect on the disease burden
284 is important, but not the only factor in prioritizing vaccination programs.

285 **Table 3** presents an overview of the incremental utility of the main effects and
286 interactions. The vaccination program that was least preferred (i.e. yielding minimum
287 utility) was one that targeted the elderly (65-75y), generated the lowest number of
288 prevented cases, the highest number of side effects, and the lowest number of cases
289 prevented via herd protection in unvaccinated adults. The most preferred program
290 (i.e. yielding maximum utility) was one that targeted children, generated the highest

291 number of prevented cases, the lowest number of side effects, and the highest
292 number of cases prevented via herd protection in newborns.

293

294 (insert **Table 3**)

295

296 Using the same logit model, we then calculated preference weights for each effect
297 type per age group. These weights act as a multiplicative factor to transform identical
298 clinical symptoms into health effects with equal value in the public's view. We
299 compared the additional utility of a vaccination program that is generated through
300 preventing one specific disease case relative to the utility gained through directly
301 preventing a single disease case via vaccinating a child (**Figure 3**). These
302 preference weights reveal important patterns. First, preventing side effects of
303 vaccination was highly preferable to preventing natural infections, even though the
304 symptoms were equal in length and severity. The mean weight for side effects
305 across all ages was -2.93, meaning that avoiding one vaccine-induced infection was
306 weighted equally to avoiding around three natural infections among children. This
307 finding was consistent whether side effects occurred in children (-2.95 (95% CI: -
308 3.21; -2.69)), adults (-3.16 (95% CI: -3.51; -2.81)) or the elderly (-2.68 (95% CI: -
309 2.98; -2.37)). Second, respondents preferred vaccination programs that prevented
310 disease among newborns and children compared with those for adults and the
311 elderly, even though the prevented disease burden was similar. One episode
312 prevented in a newborn via herd protection was considered about twice as valuable
313 as directly protecting an adult via vaccination. Third, the extent to which respondents
314 preferred protecting adults and the elderly depends on the type of benefit conferred

315 by the program. Direct effects were the preferred mode of protection for adults
316 whereas herd effects were preferred for the elderly. Reducing disease burden by
317 directly vaccinating adults (aged 30-50 years) was weighted equally to reducing
318 disease burden in the elderly (aged 80+ years) via herd effects [0.75 (0.64; 0.85)
319 compared to 0.67 (0.58; 0.76), respectively]. In contrast, reducing disease burden in
320 adults (aged 30-50 years) by herd effects counted equally to reducing disease
321 burden in elderly (aged 65-75 years) directly via vaccination (0.12 (0.03; 0.20)
322 compared to 0.16 (0.06; 0.25), respectively).

323

324 (insert **Figure 3**)

325

326 From these results, we also calculated the number of infections needed to avert in
327 order to obtain equal utility as that from protecting 100 children directly via
328 vaccination (**Table 4**). Avoiding 100 infections in children via vaccination was
329 considered equivalent to protecting 632 elderly (65-75 years) or 134 adults. In turn,
330 these outcomes were equivalent to protecting 71 newborns, 865 adults or 150
331 elderly (>80y) via herd protection. Similarly, a vaccination strategy reduces its utility
332 by causing side effects. Avoiding 34 side effects in children generates the same
333 utility as preventing 100 natural infections among the same age group.

334

335 (insert **Table 4**)

336

337 **Figure 4** illustrates the significant interaction in our model between the age of the
338 vaccinated group and the age of the herd protection recipients (see **Table 3**). This
339 interaction must be understood as the additional utility that is given to (or taken away
340 from) a vaccination program depending on the particular combination of age groups
341 that are involved, regardless of the magnitude of direct, herd or side effects that are
342 being generated. It presents the attractiveness of particular intergenerational
343 vaccination strategies. Whereas a CEA perspective would consider all possible age
344 combinations equally attractive (as long as they lead to the same number of
345 infections prevented), our sample had clear intergenerational preferences over
346 vaccination strategies. Any age group was deemed acceptable to vaccinate when
347 there were herd protection benefits for newborns. To generate herd protection for
348 adults, children were the most attractive age group. To generate it to protect the
349 elderly >80, adults were deemed most appropriate. The least attractive
350 intergenerational combination was vaccinating elderly 65-75 years while generating
351 herd protection in adults 30-50 years. The most attractive age combination was
352 vaccinating children while generating herd protection in newborns.

353

354 (insert **Figure 4**)

355

356 **3.3 Preferences across disease types and respondents**

357 As shown in **Appendix D**, our results remained robust across all four different
358 disease types: the equity weights were statistically equivalent, regardless of whether
359 the condition was mild vs. severe or acute vs. chronic (indicated by a non-significant
360 interaction effect in our model between the attributes and the disease type). Also, the

361 appendix illustrates that our findings also remained robust across most respondent
362 characteristics: gender, age, occupation, level of education, urban-rural, socio-
363 economic background, experience with severe illness or parental status. Although
364 individuals with a low degree of vaccine hesitancy (indicated by high values on the
365 'vaccine hesitancy scale' (VHS) [50]) attributed less importance to side effects
366 ($p < 0.0001$), this effect was relatively small (a 10 unit increase in the VHS score (on a
367 scale from 10 to 50) led to a 10% decrease in absolute magnitude of the utility for
368 side effects (~ 0.03)).

369 The hierarchical cluster analysis of the individual preferences (see methods)
370 revealed two distinct groups of respondents: one group ($N=564$, *Cluster 1*) who
371 attached almost no importance to the number of side effects (with a mean weight of -
372 0.91 for side effects) and a larger group ($N=935$, *Cluster 2*) who valued this attribute
373 fairly highly (with a mean weight of -4.40) (**Table 3**). This clustering explains the
374 relatively high variation across respondents for the weight estimate for side effects
375 (the standard deviation to mean absolute value ratio of 0.043 for side effects is
376 almost twice the ratio for direct and herd effects). We used a logistic regression to
377 determine predictors of cluster membership. Cluster 1, who attached almost no
378 importance to the number of side effects, was characterized by high values on the
379 VHS, indicating little hesitancy ($p < 0.0001$). On the other hand, cluster 2, who valued
380 side effects more highly, was characterized by higher degrees of hesitancy on the
381 VHS. However, the predictive power of this association for membership of the group
382 was small (McFadden's pseudo $R^2=0.6\%$), implying that there is much unexplained
383 heterogeneity in the importance placed on side effects.

384

386 **4. Discussion**

387 In this study, we used a discrete choice experiment to analyse and quantify how the
388 public values the outcomes of vaccination programs. We observed several general
389 preference patterns, which were robust across different lengths and severities of
390 disease and respondent characteristics (socio-economic background, age, education
391 and parenthood). We observed that most respondents did not make choices purely
392 based on how to minimize the number of infections. In particular, individuals, on
393 average, weighted one averted instance of a side effect equal to about three similarly
394 severe natural infections in children and weighted one averted health outcome in
395 children up to six times more than preventing similarly severe health outcomes in the
396 elderly. Interestingly, our study has disentangled this latter phenomenon from the
397 type of effect as we observed a different weight given to protecting older people
398 depending on whether the benefits were directly vs. indirectly received. Our results
399 support a duty of care principle to provide herd protection for the elderly and an
400 aversion to protecting adults who are better able to protect themselves. The weight
401 given to side effects when evaluating a vaccination program was divisive, splitting
402 our sample into two clusters.

403 Our study, as far as we are aware, is the first of its kind to quantify the important
404 social value judgements that need to be made in vaccine funding decisions.
405 Although this limits comparability, our findings are in line with what can be learned
406 from other study domains. The finding that individuals weighted one averted instance
407 of a side effect equal to about three similarly severe natural infections in children can
408 be explained with general theory on decision-making. For instance, well-documented
409 psychological phenomena such as 'loss aversion' [55] (overvaluing risks and losses
410 over opportunities and gains), the 'act-omission bias' [56] [judging the effects of an

411 act (becoming vaccinated) differently from identical effects resulting from an
412 omission (becoming infected)], or ‘hyperbolic discounting’ [57] [overvaluing the
413 present (in which side effects occur) over the future (in which disease prevention will
414 occur)] suggest that people put an extraordinary weight on side effects when
415 evaluating a vaccination strategy. Moreover, also empirical studies that have
416 investigated people’s (stated) choices about whether or not they would personally
417 become vaccinated with a particular vaccine (e.g. [43, 58]) generated findings that
418 highlight the extraordinary weight of side effects. The preference given to health
419 benefits in younger people (newborns and children), up to six-fold, is also in line with
420 related studies on ‘ageism’ in other contexts of healthcare priority-setting (reviewed
421 in [59] and discussed elsewhere, e.g. [60, 61]).

422 It is important to study which aspects of health policy choices matter most to the
423 public. This is especially true in vaccination where public trust, goodwill and
424 participation are sensitive and key to success [62]. There is a growing concern that
425 public and political trust in scientific evidence is eroding, particularly in the context of
426 vaccination [63-65]. By being aware of the sensitivities around vaccination, decision
427 makers can understand and address some of the root causes of vaccine hesitancy,
428 adapt to concerns of the population and improve responses in communication
429 strategies.[66] Our findings provide empirical evidence on how to set vaccine
430 priorities in line with public preferences. There is an important debate over the extent
431 to which the public’s opinion should drive resource allocation in healthcare (see e.g.
432 [67, 68]). But, many believe that the values of the public, who pays for healthcare,
433 should at least somehow be acknowledged in the decision-making process. In the
434 context of vaccination, where public support and participation is key to success, this
435 concern becomes particularly crucial. Therefore, our results can be useful additions

436 to vaccine appraisals. They can provide guidance in specific epidemiological cases
437 where CEA does not provide the answers needed. For instance, our results would
438 suggest that, despite their attractiveness in terms of cost-effectiveness, the public
439 may not support a childhood influenza vaccination program that mainly benefits
440 adults or elderly [69], because preventing side effects in vaccinated children is
441 preferred over preventing disease burden among adults and elderly. Furthermore,
442 our study suggests that a childhood varicella-zoster vaccination program, in the case
443 that it protects children against varicella disease at the expense of increased zoster
444 in the elderly (the 'exogenous boosting hypothesis'), might be justifiable. In contrast,
445 previous analyses where QALY losses for children are weighted equally to those for
446 the elderly find that the increased burden in the elderly offsets the QALY gains in
447 children and determine the program not cost-effective [23, 70].

448 Our results can also be directly incorporated into economic evaluations as sensitivity
449 analyses to better align the underlying assumptions of CEA with the values of the
450 population. Our estimated preference weights can be used in decision-analytic
451 models as a parameter to weight QALYs or infections according to their 'social
452 value'. This would re-adjust the (equal) weight that QALYs receive in CEA according
453 to how important people think that the age of the QALY-recipient is and whether the
454 benefit was generated through direct protection, herd immunity or (avoiding) side
455 effects. There is an increased interest in such 'extended', 'distributive' or 'equity-
456 weighted' economic evaluation (see e.g. [7, 34, 71-76]), but, to our knowledge, such
457 studies do not exist for the evaluation of vaccines. Our estimates are developed
458 particularly for this context, and provide an opportunity to do so.

459 There are several limitations. We did not include any mortality effects, nor did we
460 include a difference in severity between the three vaccine effects, even though this

461 would be more realistic (as side effects of vaccines are usually milder than the
462 disease being prevented). We chose not to include these aspects because we
463 wanted to avoid increasing the complexity of the survey and reducing the validity of
464 the respondents' answers by adding a second disease profile. Also, keeping the
465 disease outcome constant over age groups and effects enabled trade-offs that were
466 wholly reflective of the preference between age groups and effects instead of also
467 reflecting additional considerations about disease severity. We also chose to present
468 the number of side effects rather than its complement the number of vaccinated
469 people *without* side effects. This framing may have played a role in the observed
470 weight for side effects. The alternative framing would probably have drawn less
471 attention to side effects and might have generated smaller weights. We however
472 wanted people to make explicit trade-offs between side effects with protective
473 benefits and chose for the more direct framing. Using the alternative is a suggestion
474 for further research. Also, we used generic disease profiles based on a description
475 in EQ-5D terms to minimize respondents making personal associations to the
476 disease and vaccine when we would have named the diseases (e.g. 'flu' or
477 'whooping cough'), but this may also have increased the level of abstraction and
478 reduced the level of personal involvement. A suggestion for further research is to
479 repeat our study with named diseases and to test whether our finding that the
480 disease profile did not matter to people's preferences is confirmed. Another limitation
481 is that, while our sample was broadly representative of the UK population, it was
482 recruited from an online panel where membership may be associated with
483 unobserved characteristics (e.g. interest in technology).

484 In conclusion, our study demonstrates clear and robust preference patterns in how
485 people value the impact of vaccination programs. A large majority of respondents

486 had a strong preference to minimize side effects and to prevent disease among
487 newborns and children. Our observations provide quantitative evidence about public
488 preferences around important and sensitive but neglected trade-offs in vaccine policy
489 decision-making, and can hopefully inspire further research and discussion.

490

491 **References**

- 492 1. Walker, D.G., R. Hutubessy, and P. Beutels, *WHO Guide for standardisation of economic*
493 *evaluations of immunization programmes*. Vaccine, 2010. **28**(11): p. 2356-2359.
- 494 2. Drummond, M., et al., *Methods for the economic evaluation of health care programmes*. Vol.
495 3. 2005, Oxford: Oxford University Press.
- 496 3. Ricciardi, G.W., et al., *Comparison of NITAG policies and working processes in selected*
497 *developed countries*. Vaccine, 2015. **33**(1): p. 3-11.
- 498 4. Daniels, N. and J. Sabin, *Setting limits fairly: learning to share resources for health*. 2008,
499 New York: Oxford University Press.
- 500 5. Hausman, D., *Valuing health: wellbeing, freedom and suffering*. 2015, Oxford: Oxford
501 University Press.
- 502 6. Powers, M. and R. Faden, *Social Justice. The Moral Foundations of Public Health and Health*
503 *Policy*. 2006, Oxford: Oxford University Press.
- 504 7. Cookson, R., M. Drummond, and H. Weatherly, *Explicit incorporation of equity*
505 *considerations into economic evaluation of public health interventions*. Health Econ Policy
506 Law, 2009. **4**(Pt 2): p. 231-45.
- 507 8. Dukhanin, V., et al., *Integrating social justice concerns into economic evaluation for*
508 *healthcare and public health: A systematic review*. Soc Sci Med, 2018. **198**: p. 27-35.
- 509 9. Poland, G.A. and E.K. Marcuse, *Developing vaccine policy: attributes of "just policy" and a*
510 *proposed template to guide decision and policy making*. Vaccine, 2011. **29**(44): p. 7577-8.
- 511 10. Field, R.I. and A.L. Caplan, *Evidence-based decision making for vaccines: the need for an*
512 *ethical foundation*. Vaccine, 2012. **30**(6): p. 1009-13.
- 513 11. Luyten, J. and P. Beutels, *The Social Value Of Vaccination Programs: Beyond Cost-*
514 *Effectiveness*. Health Aff (Millwood), 2016. **35**(2): p. 212-8.
- 515 12. Luyten, J., et al., *Public preferences over efficiency, equity and autonomy in vaccination*
516 *policy: an empirical study*. Soc Sci Med, 2013. **77**: p. 84-9.
- 517 13. Yaqub, O., et al., *Attitudes to vaccination: a critical review*. Soc Sci Med, 2014. **112**: p. 1-11.
- 518 14. Geelen, E., et al., *Taming the fear of voice: Dilemmas in maintaining a high vaccination rate*
519 *in the Netherlands*. Soc Sci Med, 2016. **153**: p. 12-9.
- 520 15. Sobo, E.J., *What is herd immunity, and how does it relate to pediatric vaccination uptake? US*
521 *parent perspectives*. Soc Sci Med, 2016. **165**: p. 187-195.
- 522 16. Fine, P., K. Eames, and D.L. Heymann, *"Herd immunity": a rough guide*. Clin Infect Dis, 2011.
523 **52**(7): p. 911-6.
- 524 17. Anderson, R. and R. May, *Infectious Diseases of Humans: Dynamics and Control*. 1991,
525 Oxford: Oxford University Press.
- 526 18. Schwartz, J.S. and A. Caplan, *vaccination ethics and policy*. 2017, Cambridge: MIT Press.
- 527 19. Lynch, M., et al., *Intussusception after administration of the rhesus tetravalent rotavirus*
528 *vaccine (Rotashield): The search for a pathogenic mechanism*. Pediatrics, 2006. **117**(5): p.
529 E827-E832.

- 530 20. Granstrom, M., *The History of Pertussis Vaccination: From Whole-Cell to Subunit Vaccines.*
531 History of Vaccine Development, 2011: p. 73-82.
- 532 21. Blume, S. and M. Zanders, *Vaccine independence, local competences and globalisation:*
533 *lessons from the history of pertussis vaccines.* Soc Sci Med, 2006. **63**(7): p. 1825-35.
- 534 22. McGuire, A., M. Drummond, and S. Keeping, *Childhood and adolescent influenza vaccination*
535 *in Europe: A review of current policies and recommendations for the future.* Expert Review of
536 Vaccines, 2016. **15**(5): p. 659-670.
- 537 23. Luyten, J., B. Ogunjimi, and P. Beutels, *Varicella-zoster virus vaccination under the exogenous*
538 *boosting hypothesis: two ethical perspectives.* Vaccine, 2014. **32**(52): p. 7175-8.
- 539 24. Feudtner, C. and E.K. Marcuse, *Ethics and immunization policy: promoting dialogue to*
540 *sustain consensus.* Pediatrics, 2001. **107**(5): p. 1158-64.
- 541 25. Charo, R.A., *Politics, parents, and prophylaxis--mandating HPV vaccination in the United*
542 *States.* N Engl J Med, 2007. **356**(19): p. 1905-8.
- 543 26. Salmon, D.A., et al., *Compulsory vaccination and conscientious or philosophical exemptions:*
544 *past, present, and future.* Lancet, 2006. **367**(9508): p. 436-42.
- 545 27. Hornsey, M.J., E.A. Harris, and K.S. Fielding, *The psychological roots of anti-vaccination*
546 *attitudes: A 24-nation investigation.* Health Psychol, 2018. **37**(4): p. 307-315.
- 547 28. Tomeny, T.S., C.J. Vargo, and S. El-Toukhy, *Geographic and demographic correlates of*
548 *autism-related anti-vaccine beliefs on Twitter, 2009-15.* Soc Sci Med, 2017. **191**: p. 168-175.
- 549 29. Bhattacharyya, S., C.T. Bauch, and R. Breban, *Role of word-of-mouth for programs of*
550 *voluntary vaccination: A game-theoretic approach.* Math Biosci, 2015. **269**: p. 130-4.
- 551 30. Bauch, C.T. and D.J. Earn, *Vaccination and the theory of games.* Proc Natl Acad Sci U S A,
552 2004. **101**(36): p. 13391-4.
- 553 31. Ndeffo Mbah, M.L., et al., *The impact of imitation on vaccination behavior in social contact*
554 *networks.* PLoS Comput Biol, 2012. **8**(4): p. e1002469.
- 555 32. Bombard, Y., et al., *Eliciting ethical and social values in health technology assessment: A*
556 *participatory approach.* Soc Sci Med, 2011. **73**(1): p. 135-44.
- 557 33. Makarovs, K. and P. Achterberg, *Contextualizing educational differences in "vaccination*
558 *uptake": A thirty nation survey.* Soc Sci Med, 2017. **188**: p. 1-10.
- 559 34. Fleurbaey, M., et al., *Equivalent income and fair evaluation of health care.* Health Econ,
560 2013. **22**(6): p. 711-29.
- 561 35. Ryan, M., K. Gerard, and A.-A. M., *Using Discrete Choice Experiments to Value Health and*
562 *Health Care.* 2008, Dordrecht: Springer.
- 563 36. Louviere, J., D. Hensher, and J. Swait, *Stated Choice Methods: Analysis and Applications.*
564 2000, Cambridge: Cambridge University Press.
- 565 37. de Bekker-Grob, E.W., M. Ryan, and K. Gerard, *Discrete choice experiments in health*
566 *economics: a review of the literature.* Health Econ, 2012. **21**(2): p. 145-72.
- 567 38. van Hoek, A.J., et al., *The impact of pandemic influenza H1N1 on health-related quality of*
568 *life: a prospective population-based study.* PLoS One, 2011. **6**(3): p. e17030.
- 569 39. van Hoek, A.J., et al., *The burden of disease and health care use among pertussis cases in*
570 *school aged children and adults in England and Wales; a patient survey.* PLoS One, 2014.
571 **9**(11): p. e111807.
- 572 40. Lambooi, M.S., et al., *Consistency between stated and revealed preferences: a discrete*
573 *choice experiment and a behavioural experiment on vaccination behaviour compared.* BMC
574 Med Res Methodol, 2015. **15**: p. 19.
- 575 41. Veldwijk, J., et al., *Parental preferences for rotavirus vaccination in young children: a discrete*
576 *choice experiment.* Vaccine, 2014. **32**(47): p. 6277-83.
- 577 42. Hofman, R., et al., *Have preferences of girls changed almost 3 years after the much debated*
578 *start of the HPV vaccination program in The Netherlands? A discrete choice experiment.* PLoS
579 One, 2014. **9**(8): p. e104772.

- 580 43. Sadique, M.Z., et al., *The effect of perceived risks on the demand for vaccination: results from*
581 *a discrete choice experiment*. PLoS One, 2013. **8**(2): p. e54149.
- 582 44. de Bekker-Grob, E.W., et al., *Girls' preferences for HPV vaccination: a discrete choice*
583 *experiment*. Vaccine, 2010. **28**(41): p. 6692-7.
- 584 45. Ancker, J.S., et al., *Design features of graphs in health risk communication: a systematic*
585 *review*. J Am Med Inform Assoc, 2006. **13**(6): p. 608-18.
- 586 46. Reed Johnson, F., et al., *Constructing experimental designs for discrete-choice experiments:*
587 *report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task*
588 *Force*. Value Health, 2013. **16**(1): p. 3-13.
- 589 47. Kessels, R., B. Jones, and P. Goos, *An improved two-stage variance balance approach for*
590 *constructing partial profile designs for discrete choice experiments*. Applied Stochastic
591 Models in Business and Industry, 2015. **31**(5): p. 626-648.
- 592 48. Dellaert, B.G.C., B. Donkers, and A. van Soest, *Complexity Effects in Choice Experiment-Based*
593 *Models*. Journal of Marketing Research, 2012. **49**(3): p. 424-434.
- 594 49. Kessels, R., et al., *The usefulness of Bayesian optimal designs for discrete choice experiments*.
595 Applied Stochastic Models in Business and Industry, 2011. **27**(3): p. 173-188.
- 596 50. Larson, H.J., et al., *Measuring vaccine hesitancy: The development of a survey tool*. Vaccine,
597 2015. **33**(34): p. 4165-75.
- 598 51. Train, K., *Discrete Choice Methods with Simulation*. 2nd Edition ed. 2009, Cambridge:
599 Cambridge University Press.
- 600 52. Bliemer, M.C.J. and J.M. Rose, *Confidence intervals of willingness-to-pay for random*
601 *coefficient logit models*. Transportation Research Part B-Methodological, 2013. **58**: p. 199-
602 214.
- 603 53. Crabbe, M., B. Jones, and M. Vandebroek, *Comparing Two-Stage Segmentation Methods for*
604 *Choice Data with a One-Stage Latent Class Choice Analysis*. Communications in Statistics-
605 Simulation and Computation, 2013. **42**(5): p. 1188-1212.
- 606 54. Kessels, R., B. Jones, and P. Goos, *Bayesian optimal designs for discrete choice experiments*
607 *with partial profiles*. Journal of Choice Modelling. 2011. **4**: p. 52-74.
- 608 55. Kahneman, D. and A. Tversky, *Prospect Theory - Analysis of Decision under Risk*.
609 Econometrica, 1979. **47**(2): p. 263-291.
- 610 56. Spranca, M., E. Minsk, and J. Baron, *Omission and Commission in Judgment and Choice*.
611 Journal of Experimental Social Psychology, 1991. **27**(1): p. 76-105.
- 612 57. Frederick, S., G. Loewenstein, and T. O'Donoghue, *Time discounting and time preference: A*
613 *critical review*. Journal of Economic Literature, 2002. **40**(2): p. 351-401.
- 614 58. Seanehia, J., et al., *Quantifying population preferences around vaccination against severe but*
615 *rare diseases: A conjoint analysis among French university students, 2016*. Vaccine, 2017.
- 616 59. Gu, Y., et al., *Attributes and weights in health care priority setting: A systematic review of*
617 *what counts and to what extent*. Soc Sci Med, 2015. **146**: p. 41-52.
- 618 60. Tsuchiya, A., *QALYs and ageism: philosophical theories and age weighting*. Health Econ,
619 2000. **9**(1): p. 57-68.
- 620 61. Bognar, G., *Fair Innings*. Bioethics, 2015. **29**(4): p. 251-261.
- 621 62. Cooper, L.Z., H.J. Larson, and S.L. Katz, *Protecting public trust in immunization*. Pediatrics,
622 2008. **122**(1): p. 149-53.
- 623 63. Larson, H.J., et al., *Addressing the vaccine confidence gap*. Lancet, 2011. **378**(9790): p. 526-
624 35.
- 625 64. Karafillakis, E., et al., *Vaccine hesitancy among healthcare workers in Europe: A qualitative*
626 *study*. Vaccine, 2016. **34**(41): p. 5013-5020.
- 627 65. Leask, J., H.W. Willaby, and J. Kaufman, *The big picture in addressing vaccine hesitancy*. Hum
628 Vaccin Immunother, 2014. **10**(9): p. 2600-2.
- 629 66. Diekema, D.S. and B. American Academy of Pediatrics Committee on, *Responding to parental*
630 *refusals of immunization of children*. Pediatrics, 2005. **115**(5): p. 1428-31.

- 631 67. Hausman, D.M., *Polling and public policy*. Kennedy Inst Ethics J, 2004. **14**(3): p. 241-7.
- 632 68. Hausman, D.M., *Valuing health: Well-Being, Freedom, and Suffering*. 2015, Oxford: Oxford
- 633 University Press.
- 634 69. Baguelin, M., et al., *Assessing optimal target populations for influenza vaccination*
- 635 *programmes: an evidence synthesis and modelling study*. PLoS Med, 2013. **10**(10): p.
- 636 e1001527.
- 637 70. Brisson, M., W.J. Edmunds, and N.J. Gay, *Varicella vaccination: impact of vaccine efficacy on*
- 638 *the epidemiology of VZV*. J Med Virol, 2003. **70 Suppl 1**: p. S31-7.
- 639 71. Nord, E., et al., *Incorporating societal concerns for fairness in numerical valuations of health*
- 640 *programmes*. Health Econ, 1999. **8**(1): p. 25-39.
- 641 72. Bleichrodt, H., *Health utility indices and equity considerations*. J Health Econ, 1997. **16**(1): p.
- 642 65-91.
- 643 73. Dolan, P., *The measurement of individual utility and social welfare*. J Health Econ, 1998.
- 644 **17**(1): p. 39-52.
- 645 74. Asaria, M., S. Griffin, and R. Cookson, *Distributional Cost-Effectiveness Analysis: A Tutorial*.
- 646 *Med Decis Making*, 2016. **36**(1): p. 8-19.
- 647 75. Round, J. and M. Paulden, *Incorporating equity in economic evaluations: a multi-attribute*
- 648 *equity state approach*. Eur J Health Econ, 2017.
- 649 76. Samson, A.L., et al., *Fairness in cost-benefit analysis: A methodology for health technology*
- 650 *assessment*. Health Econ, 2017.

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653 **Table 1. Attributes and levels used in the DCE**

Attribute	Level
Age of vaccinated group (N=100 000)	Children (3 months - 3 years)
	Adults (30-50 years)
	Elderly (65-75 years)
Disease episodes prevented in vaccinated group	1000 cases
	3000 cases
	5000 cases
Number of vaccine-induced side-effects	100 cases
	300 cases
	500 cases
Disease episodes prevented via herd protection	1000 cases
	3000 cases
	5000 cases
Age of people receiving herd protection	Newborns (<3 months)
	Adults (30-50 years)
	Elderly (>80 years)

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657 **Table 2: Respondent characteristics.**

	Sample	UK population*
Total recruited	1546	
Excluded for analysis	47	
Included in the analysis	1499 (100%)	
<i>Gender</i>		
Male	703 (47%)	49%
Female	796 (53%)	51%
<i>Age (years)</i>		
20-29	296 (20%)	13%
30-39	285 (19%)	13%
40-49	288 (19%)	14%
50-59	308 (21%)	13%
60 and over	322 (21%)	23%
<i>Living in a city with more than 10,000 inhabitants</i>	1011 (67%)	83%
<i>Social grades based on the profession of the highest paid household member</i>		
A (upper middle class)	85 (6%)	4%
B (middle class)	297 (20%)	23%
C1 (lower middle class)	385 (26%)	27%
C2 (skilled working class)	330 (22%)	21%
D (working class)	72 (5%)	16%
E (non-working)	330 (22%)	9%
<i>Education level</i>		
No qualifications	48 (3%)	15%
Secondary education	322 (21%)	14.2%
Post-secondary education	288 (19%)	14.5%
Vocational qualification	254 (17%)	20.3%
Undergraduate degree, Post-graduate degree & Doctorate	427 (39%)	30%

	Not sure	2 (0.1%)	/
<i>Having children</i>			
	No children	585 (39%)	42%
	Children aged 0-4 years	168 (11%)	42%**
	Children aged 5-20 years	358 (24%)	/
	Children aged over 20 years	388 (26%)	15%
<i>Exposure to poor health</i>			
	Participant affected by poor health	407 (27%)	
	Close friends or family of the participant affected by poor health	470 (31%)	
	Neither participant nor close friends nor family affected by poor health	622 (41%)	

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659 *UK population data 2016: Office for National Statistics <https://www.gov.uk/government/publications>

660 **Percentage of UK families living with dependent children (<18 years old)

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676 **Table 3. Attributes that affected respondent choices, based on panel mixed logit model estimates (means and standard**
 677 **deviations) with p-values from likelihood ratio (LR) tests for significant attribute effects.**

Model term	Posterior mean	Posterior std dev	Subject std dev	P-value	
Cases prevented in unvaccinated by herd effects (per 1000 cases)	0.715	0.018	0.101	<0.0001	
Cases prevented in vaccinated by direct effects (per 1000 cases)	0.619	0.018	0.100	<0.0001	
Cases of side effects in vaccinated (per 100 cases)	-0.285	0.012	0.110	<0.0001	
Age of unvaccinated	[Newborns <3m] [Adults 30-50y] [Elderly >80y]	0.614 -0.597 -0.017	0.048 0.043 NA	0.090 0.105 NA	<0.0001
Age of unvaccinated*Cases prevented in vaccinated by direct effects	[Newborns <3m] [Adults 30-50y] [Elderly >80y]	-0.043 0.071 -0.028	0.009 0.009 NA	0.054 0.041 NA	<0.0001
Age of vaccinated	[Children 3m-3y] [Adults 30-50y] [Elderly 65-75y]	0.305 0.142 -0.446	0.040 0.048 NA	0.063 0.062 NA	<0.0001
Age of unvaccinated*Age of vaccinated	[Newborns <3m]* [Children 3m- 3y] [Newborns <3m]* [Adults 30- 50y] [Newborns <3m]* [Elderly 65-	-0.131 -0.210 0.341	0.036 0.041 NA	0.053 0.065 NA	<0.0001

	<i>75y]</i>				
	[Adults 30-50y]* [Children 3m-3y]	0.250	0.052	0.044	
	[Adults 30-50y]* [Adults 30-50y]	-0.079	0.049	0.045	
	<i>[Adults 30-50y]* [Elderly 65-75y]</i>	-0.171	NA	NA	
	<i>[Elderly >80y]* [Children 3m-3y]</i>	-0.119	NA	NA	
	<i>[Elderly >80y]* [Adults 30-50y]</i>	0.289	NA	NA	
	<i>[Elderly >80y]* [Elderly 65-75y]</i>	-0.170	NA	NA	
Age of vaccinated*Cases of side effects in vaccinated	[Children 3m-3y]	-0.032	0.008	0.040	<0.0001
	[Adults 30-50y]	-0.037	0.009	0.044	
	<i>[Elderly 65-75y]</i>	0.069	NA	NA	
Age of unvaccinated*Cases prevented in unvaccinated by herd effects	[Newborns <3m]	0.052	0.009	0.048	<0.0001
	[Adults 30-50y]	-0.005	0.008	0.043	
	<i>[Elderly >80y]</i>	-0.047	NA	NA	
Age of vaccinated*Cases prevented in vaccinated by direct effects	[Children 3m-3y]	0.051	0.010	0.044	<0.0001
	[Adults 30-50y]	-0.032	0.009	0.037	
	<i>[Elderly 65-75y]</i>	-0.019	NA	NA	

678 Note: Mean estimates corresponding to the last level of an attribute, either as a main effect or involved in an interaction, are italicized and calculated as minus
679 the sum of the estimates for the other levels of that attribute; NA means 'not assigned'.

680 **Table 4. Number of infections to prevent to gain equal utility, with 95%**
 681 **confidence intervals.**

Age group of vaccine effect	Direct effects	Herd effects	Side effects
Newborns (<3 months)	NA	71 [66; 76]	NA
Children (3 months – 3 years)	100 [index]	NA	-34 [-37; -31] Cluster 1: -221 [-340; -102] Cluster 2: -21 [-23; -20]
Adults (30–50 years)	134 [115; 153]	865 [242; 1487]	-32 [-35; -28] Cluster 1: -72 [-93; -51] Cluster 2: -23 [-25; -20]
Elderly (65–75 years)	632 [255; 1010]	NA	-37 [-42; -33] Cluster 1: -113 [-163; -64] Cluster 2: -25 [-27; -22]
Elderly (>80 years)	NA	150 [130; 169]	NA

682 Note: Cluster 1 and 2 have 564 and 935 respondents, respectively; NA refers to combinations of
 683 attribute levels not included in the choice profiles.

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685 **Figure 1. Example of a choice set.**

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687 **Figure 2. Schematic representation of the different arms of the questionnaire.**
688 **For each disease stratum, there was also an equal sampling over the socio-**
689 **economic groups (25% A+B; 25% C1; 25% C2; 25% E+D).**

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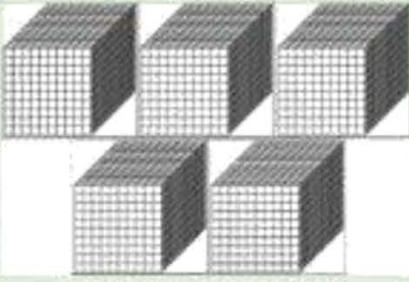




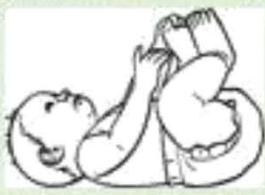
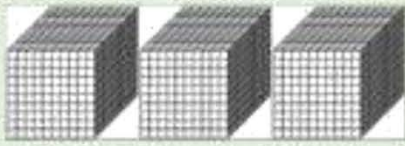
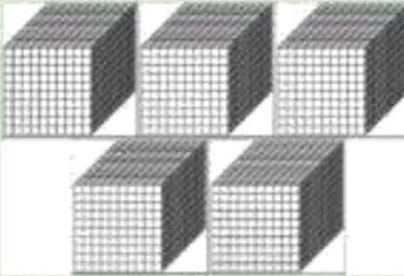
691 **Figure 3. Utility weights representing public preferences for identical health**
692 **outcomes with different attributes, with 95% confidence intervals.**

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694 **Figure 4. Intergenerational preferences: interaction effects between the age**
695 **group vaccinated and the age group receiving herd protection effects.**
696 **Marginal utility values consist of main effects of the attributes involved and**
697 **their interaction effect..**

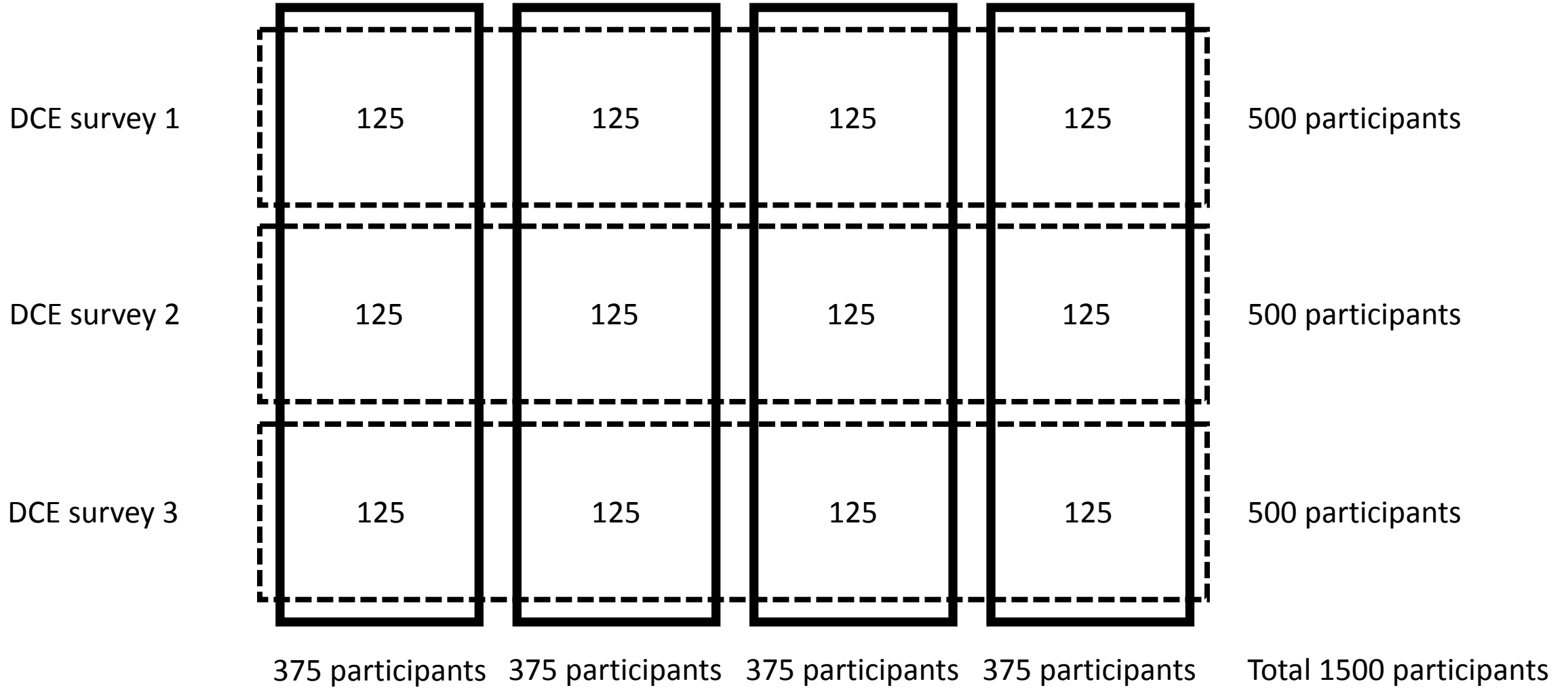
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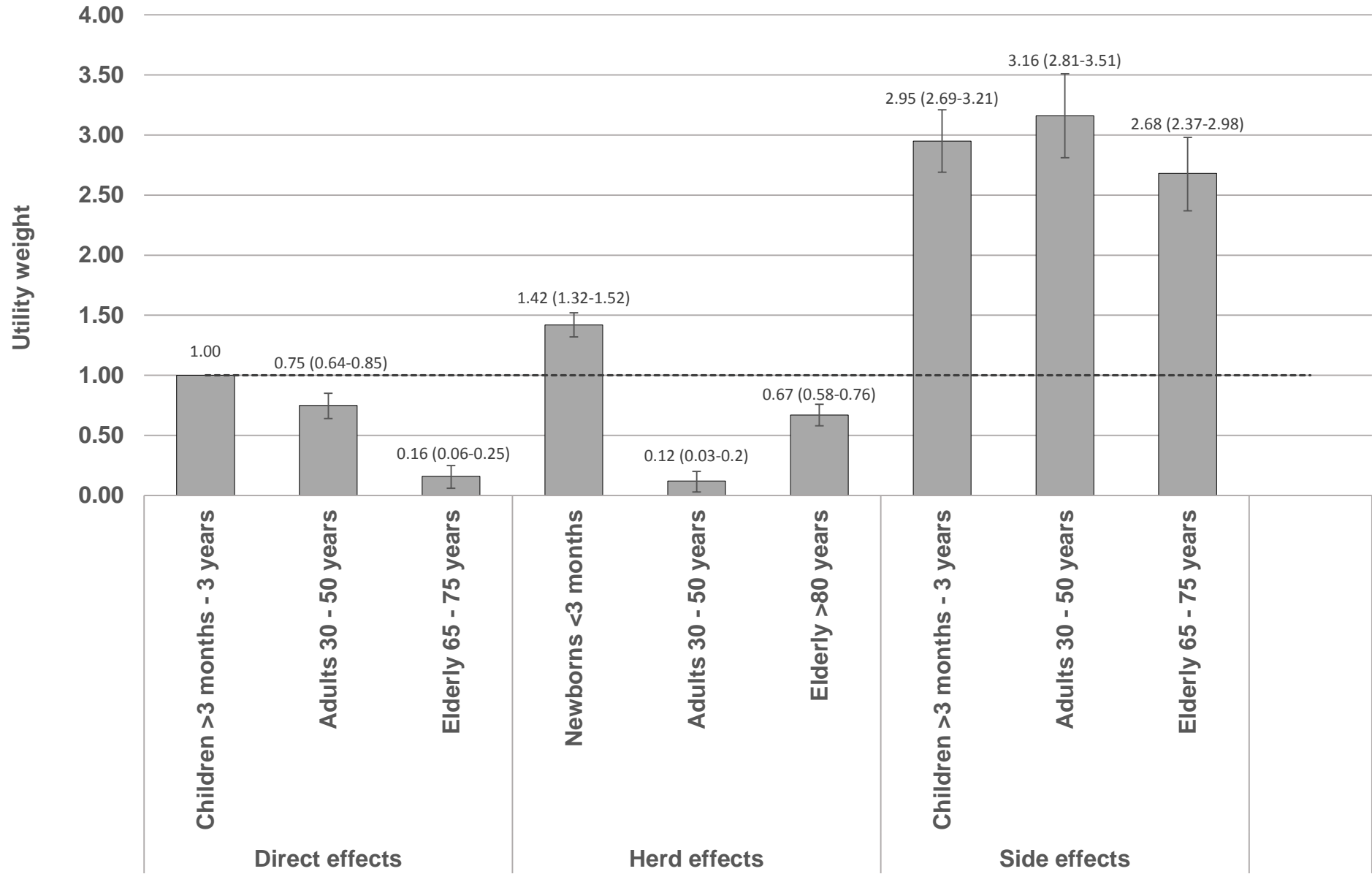
	PROGRAM A	PROGRAM B
TOTAL NUMBER OF PREVENTED CASES (per 100,000)	7500	7700
Direct effects <i>How old are the 100,000 people who will become vaccinated?</i>	Adults (30-50 years) 	Adults (30-50 years) 
<i>How many cases of disease will be prevented in the 100,000 who become vaccinated?</i>	5000 cases prevented 	3000 cases prevented 
Side-effects <i>How many of the 100,000 vaccinated persons will get the disease through side effects of vaccination?</i>	500 cases occurring 	300 cases occurring 
Indirect effects <i>How old are those who will benefit from the indirect protection but are not vaccinated themselves?</i>	Infants (Under 3 months) 	Infants (Under 3 months) 
<i>How many cases of disease will be prevented via indirect protection in those who will not be vaccinated?</i>	3000 cases prevented 	5000 cases prevented 

Disease description

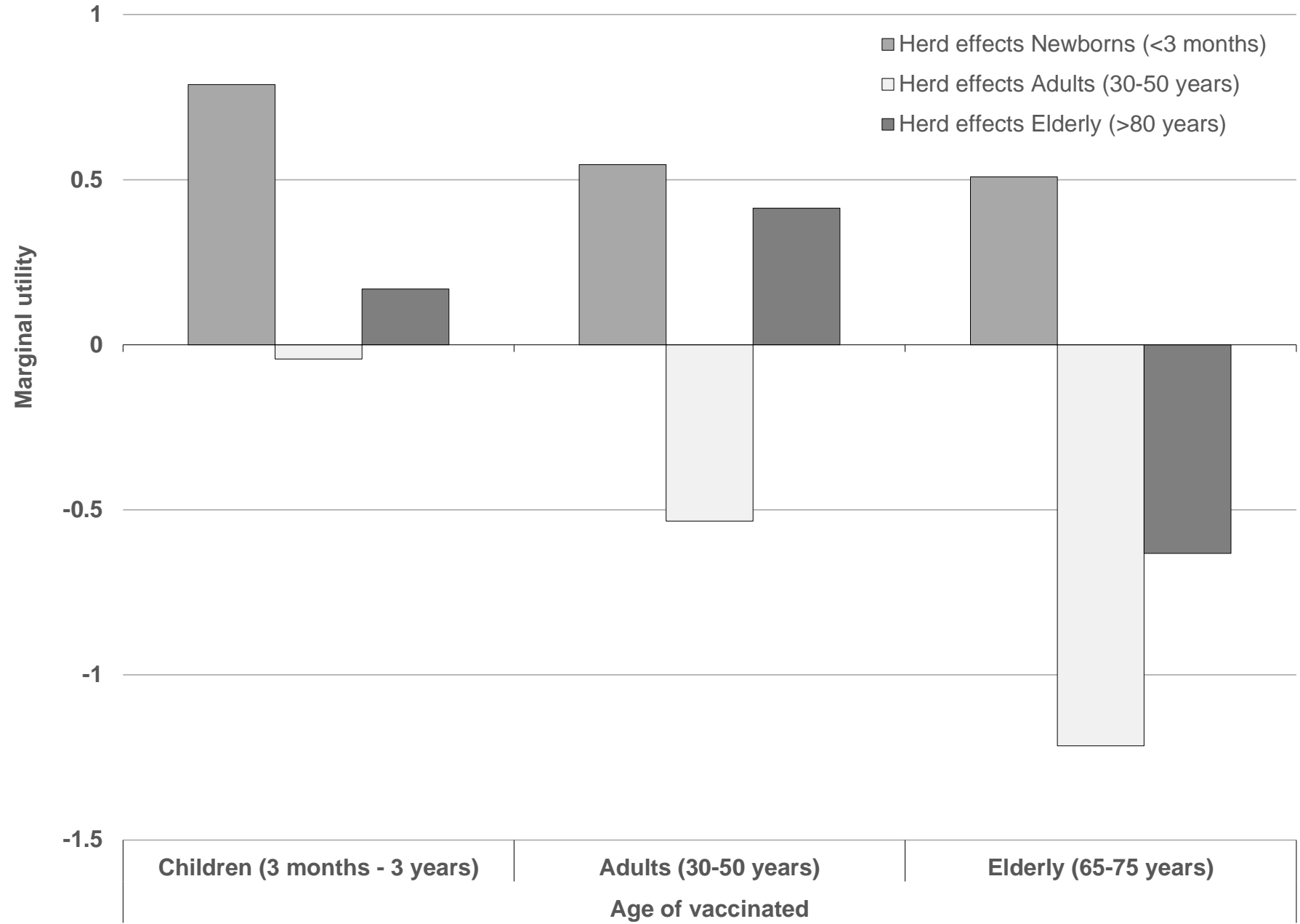
Mild / 9 days Mild / 160 days Severe / 9 days Severe / 160 days



Figures (NO AUTHOR DETAILS)



Figures (NO AUTHOR DETAILS)



Electronic Supplementary Material (online publication only - NO AUTHOR DETAILS)

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Ethical approval

We obtained informed consent from all respondents and ethical approval of the study from the Ethics Committee of the London School of Hygiene & Tropical Medicine (Ref 10335). We conducted the research in accordance with the Code of Conduct of the Market Research Society, which ensured that information is collected for research purposes only, is kept confidential, and respondent anonymity is guaranteed.

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