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

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 in November 2016. 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. Although the normative significance of these weights remains a matter open for debate, our study can, hopefully, contribute to the evaluation of vaccination programs beyond cost-effectiveness.

Keywords

United Kingdom; age; side effects, herd immunity, cost-effectiveness analysis, decision making; priority-setting, equity

1. Introduction

Economic evaluation methods such as cost-effectiveness analysis (CEA) are common components in public funding decisions for vaccines (Drummond, Sculpher, Torrance, O'Brien, & Stoddard, 2005; Walker, Hutubessy, & Beutels, 2010). They feature in the standard evidence considered by e.g. the Advisory Committee on Immunization Practices in the US, the Joint Committee on Vaccination and Immunization in England, the World Health Organization and non-governmental organizations such as the Bill & Melinda Gates Foundation (Ricciardi et al., 2015). At the same time, it is widely acknowledged that these evaluation frameworks have important shortcomings and that they alone offer insufficient basis for making fair and efficient vaccine funding decisions (Cookson, Drummond, & Weatherly, 2009; Dukhanin et al., 2018). There is a growing literature about the limits of CEA in assessing the value of vaccination (Barnighausen, Bloom, Cafiero-Fonseca, & O'Brien, 2014; Bloom, 2011; Bloom, Fan, & Sevilla, 2018; Luyten & Beutels, 2016).

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. Vaccination induces disease protection in those who become vaccinated, but it also creates *herd* protection (or indirect effects in third parties because of reduced pathogen transmission (Fine, Eames, & Heymann, 2011)) and, occasionally, adverse clinical *side* effects. 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. Side effects can be concentrated in one age group despite indirect protection from reduced transmission benefitting either the wider population, or in some cases a different age group entirely (Anderson & May, 1991). Examples include protecting the elderly through childhood influenza vaccination or future generations through a *polio* eradication program. Such broader, distributive aspects of vaccination are important but they remain neglected in standard cost-effectiveness or public health impact models.

Several notable examples illustrate that this broader social context of health outcomes needs to be considered in vaccine decision-making (Schwartz & Caplan, 2017). 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 (Blume & Zanders, 2006; Granstrom, 2011; Lynch et al., 2006). 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 (McGuire, Drummond, & Keeping, 2016). 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 (Luyten, Ogunjimi, & Beutels, 2014).

Misjudging ethical norms and social sensitivities in vaccination policy by over-relying on CEA can have important implications. It may affect the perceived equity of a program, its support by the public and its long-term sustainability (Charo, 2007; Feudtner & Marcuse, 2001; Salmon et al., 2006; Yaqub, Castle-Clarke, Sevdalis, & Chataway, 2014) (Hornsey, Harris, & Fielding, 2018; Tomeny, Vargo, & El-Toukhy, 2017). It can invoke public backlash to the vaccine, leading to reduced uptake, increased vaccine hesitancy and reduced overall effectiveness of the program (Bauch & Earn, 2004; Bhattacharyya, Bauch, & Breban, 2015; Ndeffo Mbah et al., 2012). Therefore, an empirical evidence-base is needed about the public's view on the key value judgments that need to be made in vaccine funding decisions (Bombard, Abelson, Simeonov, & Gauvin, 2011; Field & Caplan, 2012; Luyten, Dorgali, Hens, & Beutels, 2013; Makarovs & Achterberg, 2017; Poland & Marcuse, 2011). Such evidence can complement formalized appraisals like CEA, stimulate deliberation and discussion on how to prioritize vaccines within a budget constraint and, moreover, it can be explored whether such evidence can become quantitatively integrated into formal decision frameworks in some sort of 'extended' or 'weighted' CEA (Cookson et al., 2009; Fleurbaey, Luchini, Muller, & Schokkaert, 2013).

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

2. Methods

DCEs are a widely used survey method to quantify individuals' preferences (Louviere, Hensher, & Swait, 2000; Ryan, Gerard, & M, 2008) (for a general review of applications, see (de Bekker-Grob, Ryan, & Gerard, 2012)). 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.

2.1 Choice context

For all of their choices, respondents were randomly assigned one of four disease scenarios (see **Appendix A**). [insert link to appendix] These were introduced before the start of the DCE. After five choice sets this disease was presented again to the respondent as a reminder. The four disease profiles were described as (1) severe—lasting nine days, (2) mild—lasting nine days, (3) severe—lasting 160 days, and (4) mild—lasting 160 days. Influenza and pertussis were used as proxies for an acute severe and a longer lasting milder disease, respectively (van Hoek et al., 2014; van Hoek, Underwood, Jit, Miller, & Edmunds, 2011). To avoid participants' preconceived ideas, the diseases were unnamed and only described to participants by means of severity using the generic descriptors of the dimensions of a standard instrument to measure health-related quality of life, the EuroQoL EQ-5D-3L, based on average reported values for both influenza and pertussis (van Hoek et al., 2014; van Hoek et al., 2011). To exclude considerations about age differences in remaining life expectancy, we explicitly told the participants that the diseases were not fatal.

Before every choice set we told respondents the following: "*the government has to choose between two vaccination programs that will each be used in 100 000 people. Considering your conviction about vaccination policy, which program do you think the government should choose? Both options are equally costly, and identical in every way except for the following 5 differences.*"

2.2 Attributes and levels of vaccination programs

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 were typically 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. (de Bekker-Grob et al., 2010; Hofman et al., 2014; Lambooij et al., 2015; Sadique, Devlin, Edmunds, & Parkin, 2013; Veldwijk, Lambooij, Bruijning-Verhagen, Smit, & de Wit, 2014) From this list, we took the attributes that were, in combination with the four disease profiles, best suited to answer our research question. We presented several attribute combinations 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.

The first two attributes described the age group targeted for vaccination and magnitude of the direct effects among those vaccinated. The third attribute described the number of side effects occurring among those vaccinated. 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. The fourth and fifth attribute described the magnitude of the herd effects and the age group that received them. We decided to focus only on the morbidity aspects of illness because including mortality would require additional attributes for infected people in order to account for their differing life expectancy.

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

(insert **Table 1**)

We depicted both the age group and quantity of cases avoided or caused by vaccination using simple graphics (Ancker, Senathirajah, Kukafka, & Starren, 2006) (**Figure 1**). To explicitly investigate the assumption whether individuals ultimately look at the total impact of the program and to reduce the chance that respondents would adhere to a simple counting heuristic without reflection, we presented the net number of disease cases averted for each strategy separately (the sum of direct and herd effects minus side effects).

(insert **Figure 1)**

2.3 Experimental design of the choice sets

The design of a DCE refers to the number and composition of choice sets presented to each participant (Reed Johnson et al., 2013). A set of 45 choice sets was selected out of the 58,806 possible choice sets (see **Appendix B** for more info on the selection process [insert link to appendix]) and distributed over three survey versions, so to limit the number of choice sets to be completed per respondent to 15. Therefore, each of the four disease profiles was represented in three different surveys (see **Figure 2**).

(Insert **Figure 2)**

The choice alternatives (i.e. profiles) themselves were '*partial* profiles' (Kessels, Jones, & Goos, 2015). We varied and highlighted the levels of two to four of the five attributes in the choice sets and kept the remaining attribute(s) constant so that respondents did not have to simultaneously trade-off all five dimensions per choice (see **Appendix B [insert link to appendix]**). Limiting the cognitive burden for respondents in a DCE increases the validity and reliability of their answers (Dellaert, Donkers, & van Soest, 2012). The design we generated was 'D-optimal' in a Bayesian framework fitting with a multinomial logit (MNL) model for the attributes' main effects and six interactions between the two age attributes (direct and herd effects) and the three magnitude attributes we deemed to be important *a priori*. We chose a Bayesian framework to integrate prior information on the respondents' likely preferences (Kessels, Jones, Goos, & Vandebroek, 2011) (see **Appendix C [insert link to appendix]**). The Bayesian D-optimal design then results in the smallest possible standard errors for the utility estimates at the given sample size.

2.4 Sample

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.

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

The DCE was conducted in November 2016. An email containing a link to the survey website was sent to participants and by clicking on the link respondents consented to participate, although they were free to stop or close the survey at any point. All respondents received a nominal incentive for study completion (£0.50 per 12-minute questionnaire). Before completing the DCE, respondents were asked to administer a survey tool to measure vaccine hesitancy (Larson et al., 2015), and were asked social-demographic questions and whether they have or had children. After the DCE, we asked about their experience with severe diseases, their interpretation of the validity of the answers they provided and the overall difficulty of the DCE survey.

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.

2.5 Data analysis

To quantify the weight of the five attributes and their levels in the utility attributed to a vaccination strategy, a panel mixed logit model (fitted by the Hierarchical Bayes method (Train, 2009)) was used (see **Table 3**). The model involved seven main effects: four related to the two three-level categorical attributes describing the utility impact of a change in the targeted age group in direct and herd effects, and three related to the continuous attributes describing the impact of a change in the absolute number of disease cases via direct effects, side effects and herd effects. Besides these seven main effects the model also includes attribute interaction effects, indicating the additional change in utility because of a particular combination of attribute levels. We computed the overall significance of the attributes using likelihood ratio (LR) tests and measured the relative importance of the attributes by the logworth statistic (i.e. $-\log_{10}$ (p-value of the LR-test)). The coefficients of the logit model were obtained by estimating the *a priori* model, i.e. the model with the utility function that seemed most appropriate when planning the DCE, and subsequently dropping the non-significant model terms until we obtained a *final* model in which all effects had significant explanatory value at the 5% level. Models were fitted using the JMP 13 Pro Choice platform (based on 10,000 iterations, with the last 5000 used for estimation) assuming normally distributed parameters with no correlation between the attributes. Combining the main and interaction effects, this model allows calculating the additional utility of a vaccination program generated per additional health effect, i.e. per type of effect per age group (see the nine variations in **Table 3**). The 95% confidence intervals for the equity weights were estimated using the Delta method (Bliemer & Rose, 2013).

We investigated heterogeneity in respondents' preferences in two ways. First, by exploring the influence of the observed respondent characteristics on the average preferences and, second, by studying the unobserved preference heterogeneity by means of a hierarchical cluster analysis on the subject-specific estimates resulting from the Hierarchical Bayes approach. We favoured this two-stage modelling method as it performs equally well as one-stage modelling methods such as latent class modelling (Crabbe, Jones, & Vandebroek, 2013; Kessels, Jones, & Goos) while enabling us to parsimoniously derive the preference weights and their 95% confidence intervals.

3. Results

3.1 Response

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. Our final sample was sufficiently representative of the UK population in terms of gender, family size, socio-economic status and education level (**Table 2**).

(insert **Table 2**)

3.2 Main effects and calculated weights

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

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

(insert **Table 3**)

Using the same logit model, we then calculated preference weights for each effect type per age group. These weights act as a multiplicative factor to transform identical clinical symptoms into health effects with equal value in the public's view. We compared the additional utility of a vaccination program that is generated through preventing one specific disease case relative to the utility gained through directly preventing a single disease case via vaccinating a child (**Figure 3**). These preference weights reveal important patterns. First, preventing side effects of vaccination was highly preferable to preventing natural infections, even though the symptoms were equal in length and severity. 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. This finding was consistent whether side effects occurred in children (-2.95 (95% CI: -3.21; -2.69)), adults (-3.16 (95% CI: -3.51; -2.81)) or the elderly (-2.68 (95% CI: -2.98; -2.37)). Second, respondents preferred vaccination programs that prevented disease among newborns and children compared with those for adults and the elderly, even though the prevented disease burden was similar. One episode prevented in a newborn via herd protection was considered about twice as valuable as directly protecting an adult via vaccination. Third, the extent to which respondents preferred protecting adults and the elderly depends on the type of benefit conferred by the program. Direct effects were the preferred mode of protection for adults whereas herd effects were preferred for the elderly. Reducing disease burden by directly vaccinating adults (aged 30-50 years) was weighted equally to reducing disease burden in the elderly (aged 80+ years) via herd effects [0.75 (0.64; 0.85) compared to 0.67 (0.58; 0.76), respectively]. In contrast, reducing disease burden in adults (aged 30-50 years) by herd effects counted equally to reducing disease burden in elderly (aged 65-75 years) directly via vaccination (0.12 (0.03; 0.20) compared to 0.16 (0.06; 0.25), respectively).

(insert **Figure 3**)

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

(insert **Table 4**)

Figure 4 illustrates the significant interaction in our model between the age of the vaccinated group and the age of the herd protection recipients (see **Table 3**). This interaction must be understood as the additional utility that is given to (or taken away from) a vaccination program depending on the particular combination of age groups that are involved, regardless of the magnitude of direct, herd 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 protection benefits for newborns. To generate herd protection for adults, children 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 65-75 years while generating herd protection in adults 30-50 years. The most attractive age combination was vaccinating children while generating herd protection in newborns.

(insert **Figure 4**)

3.3 Preferences across disease types and respondents

As shown in **Appendix D ([insert link to appendix]**, our results remained robust across all four different disease types: the equity weights were statistically equivalent, regardless of whether the condition was mild vs. severe or acute vs. chronic (indicated by a non-significant interaction effect in our model between the attributes and the disease type). Also, the appendix [insert link to appendix] illustrates that our findings also remained robust across most respondent characteristics: gender, age, occupation, level of education, urban-rural, socio-economic background, experience with severe illness or parental status. Although individuals with a low degree of vaccine hesitancy (indicated by high values on the 'vaccine hesitancy scale' (VHS) (Larson et al., 2015)) attributed less importance to side effects ($p<0.0001$), this effect was relatively small (a 10 unit increase in the VHS score (on a scale from 10 to 50) led to a 10% decrease in absolute magnitude of the utility for side effects (~0.03)).

The hierarchical cluster analysis of the individual preferences (see methods) revealed two distinct groups of respondents: one group (N=564, *Cluster 1*) who attached almost no importance to the number of side effects (with a mean weight of -0.91 for side effects) and a larger group (N=935, *Cluster 2*) who valued this attribute fairly highly (with a mean weight of -4.40) (**Table 3**). This clustering explains the relatively high variation across respondents for the weight estimate for side effects (the standard deviation to mean absolute value ratio of 0.043 for side effects is almost twice the ratio for direct and herd effects). We used a logistic regression to determine predictors of cluster membership. Cluster 1, who 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.

4. Discussion

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

Our study, as far as we are aware, is the first of its kind to quantify the important social value judgements that need to be made in vaccine funding decisions. Although this limits comparability, our findings are in line with what can be learned from other study domains. 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' (Kahneman & Tversky, 1979) (overvaluing risks and losses over opportunities and gains), the 'act-omission bias' (Spranca, Minsk, & Baron, 1991) [judging the effects of an act (becoming vaccinated) differently from identical effects resulting from an omission (becoming infected)], or ‘hyperbolic discounting’ (Frederick, Loewenstein, & O'Donoghue, 2002) [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. Moreover, also empirical studies that have investigated people’s (stated) choices about whether or not they would personally become vaccinated with a particular vaccine (e.g. (Sadique et al., 2013; Seanehia et al., 2017)) generated findings that highlight the extraordinary weight of side effects. The preference given to health benefits in younger people (newborns and children), up to six-fold, is also in line with related studies on ‘ageism’ in other contexts of healthcare priority-setting (reviewed in (Gu, Lancsar, Ghijben, Butler, & Donaldson, 2015) and discussed elsewhere, e.g. (Bognar, 2015; Tsuchiya, 2000)).

It is important to study which aspects of health policy choices matter most to the public. This is especially true in vaccination where public trust, goodwill and participation are sensitive and key to success (Cooper, Larson, & Katz, 2008). There is a growing concern that public and political trust in scientific evidence is eroding, particularly in the context of vaccination (Karafillakis et al., 2016; Larson, Cooper, Eskola, Katz, & Ratzan, 2011; Leask, Willaby, & Kaufman, 2014). By being aware of the sensitivities around vaccination, decision makers can understand and address some of the root causes of vaccine hesitancy, adapt to concerns of the population and improve responses in communication strategies.(Diekema & American Academy of Pediatrics Committee on, 2005) 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. (Hausman, 2004, 2015)). 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 (Baguelin et al., 2013), 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 losses 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 (Brisson, Edmunds, & Gay, 2003; Luyten et al., 2014).

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. (Asaria, Griffin, & Cookson, 2016; Bleichrodt, 1997;

Cookson et al., 2009; Dolan, 1998; Fleurbaey et al., 2013; Nord, Pinto, Richardson, Menzel, & Ubel, 1999; Round & Paulden, 2017; Samson et al., 2017)), 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.

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. 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. The alternative framing would probably have drawn less attention to side effects and might have generated smaller weights. We however wanted people to make explicit trade-offs between side effects with protective benefits and chose for the more direct framing. Using the alternative is a suggestion for further research. 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 when we would have named the diseases (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. Another limitation is that, while our sample was broadly representative of the UK population, it was recruited from an online panel where membership may be associated with unobserved characteristics (e.g. interest in technology).

In conclusion, our study demonstrates clear and robust preference patterns in how people value the impact of vaccination programs. A large majority of respondents had a strong preference to minimize side effects and to prevent disease among newborns and children. Our observations provide quantitative evidence about public preferences around important and sensitive but neglected trade-offs in vaccine policy decision-making, and can hopefully inspire further research and discussion.

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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)

Table 2: Respondent characteristics.

	Sample	UK population*
Total recruited	1546	
Excluded for analysis	47	
Included in the analysis	1499 (100%)	
Gender		
Male	703 (47%)	49%
Female	796 (53%)	51%
Age (years)		
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%
Living in a city with more than 10,000 inhabitants	1011 (67%)	83%
Social grades based on the profession of the highest paid household member		
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%
Education level		
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%)	/
Having children		
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%
Exposure to poor health		
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%)	

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

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

Table 3. Attributes that affected respondent choices, based on panel mixed logit model estimates (means and standard 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	0.090	<0.0001
	[Adults 30-50y]	-0.597	0.043	0.105	
	[Elderly >80y]	*-0.017*	NA	NA	
Age of unvaccinated*Cases prevented in vaccinated by direct effects	[Newborns <3m]	-0.043	0.009	0.054	<0.0001
	[Adults 30-50y]	0.071	0.009	0.041	
	[Elderly >80y]	*-0.028*	NA	NA	
Age of vaccinated	[Children 3m-3y]	0.305	0.040	0.063	<0.0001
	[Adults 30-50y]	0.142	0.048	0.062	

	[Elderly 65-75y]	*-0.446*	NA	NA	
Age of unvaccinated*Age of vaccinated	[Newborns <3m]* [Children 3m-3y]	-0.131	0.036	0.053	<0.0001
	[Newborns <3m]* [Adults 30-50y]	-0.210	0.041	0.065	
	[Newborns <3m] [Elderly 65-75y]*	*0.341*	NA	NA	
	[Adults 30-50y]* [Children 3m-3y]	0.250	0.052	0.044	
	[Adults 30-50y]* [Adults 30-50y]	-0.079	0.049	0.045	
	[Adults 30-50y] [Elderly 65-75y]*	*-0.171*	NA	NA	
	[Elderly >80y] [Children 3m-3y]*	*-0.119*	NA	NA	
	[Elderly >80y] [Adults 30-50y]*	*0.289*	NA	NA	
	[Elderly >80y] [Elderly 65-75y]*	*-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	
	[Elderly 65-75y]	*0.069*	NA	NA	
	[Newborns <3m]	0.052	0.009	0.048	<0.0001

Age of unvaccinated*Cases prevented in unvaccinated by herd effects	[Adults 30-50y]	-0.005	0.008	0.043	
	[Elderly >80y]	*-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	
	[Elderly 65-75y]	*-0.019*	NA	NA	

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 the sum of the estimates for the other levels of that attribute; NA means ‘not assigned’.

Table 4. Number of infections to prevent to gain equal utility, with 95% 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

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

Figure 1. Example of a choice set.

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

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

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