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Social Science & Medicine 303 (2022) 114991

Contents lists available at ScienceDirect

Social Science & Medicine

journal homepage: www.elsevier.com/locate/socscimed

Social preferences for adopting new vaccines in the national immunization program: A discrete choice experiment

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ARTICLE INFO

Keywords:
Infectious diseases
Priority-setting
QALY
Preferences
Eradication
Equity
Uncertainty
Cost-effectiveness

ABSTRACT

Governments regularly have to decide whether new vaccines should be adopted in their national immunization program. These choices imply complex trade-offs of epidemiological, medical and socio-economic criteria. We investigated how the population in Flanders (Belgium) wants their government to set vaccine-funding priorities. In December 2019, we executed a discrete choice experiment in a sample of the Flemish population (N = 1636). In total, we analysed 16 360 choices between vaccines competing for funding, described in terms of eight characteristics. Using a panel mixed logit model, we quantified the relative importance of each characteristic and investigated differences in preferences across respondent groups. The observed vaccine priorities were different from those that would be identified through cost-effectiveness analysis. People valued the health impact from infectious diseases differently than their weight expressed in QALYs would suggest. Mortality and frequently occurring mild illness were valued higher, whereas lasting morbidity received lower weight. Contribution of the vaccine to disease eradication and uncertainty in vaccine effectiveness were both highly influential factors. Health equity impact was also important whereas the economic impact of the disease did not matter at all. Our results can be used to incorporate public values into vaccine decision-making.

1. Introduction

Governments regularly have to make decisions whether or not to adopt new vaccines in their national immunization program (WHO, 2014). They have to do this under various constraints. There is a finite, often earmarked budget for vaccination from which also the ongoing programs must be financed. There are capacity constraints to rolling out new vaccination programs. There is a concern not to overcrowd already crowded vaccine schedules. As a result, priority-setting decisions between competing vaccination programs are often inevitable. These are complex choices because they require simultaneous consideration of epidemiological characteristics of infectious diseases, morbidity and mortality risks, health system impact, cost, equity, as well as many other ways in which infectious diseases can impact our societies (Annemans et al., 2021; Barnighausen et al., 2014; Bloom et al., 2018; Luyten and Beutels, 2016). They are also value-driven decisions, as trade-offs are inevitably based on ethical judgment. It is important that decision-makers understand what the public, as a key stakeholder, considers a funding priority. This is true in healthcare in general (Florin and Dixon, 2004), but particularly in the context of vaccination policy where success is dependent on public goodwill and participation (Paterson and Larson, 2012).

In many countries, cost-effectiveness analyses (CEA) are used to assist policy-makers in making these complex evaluations. In these analyses, costs and health effects (usually expressed as Quality-Adjusted Life Years (QALYs)) are compared between vaccination and a counterfactual scenario, and summarized into an Incremental Cost-Effectiveness Ratio (ICER), a summary measure of the 'value-for-money' offered by the vaccine (Drummond et al., 2005). Although cost-effectiveness results are typically used as one out of many criteria instead of being the sole criterion, they are an influential element in vaccine priority setting (Ricciardi et al., 2015a, 2015b). Nonetheless, CEA is based on controversial assumptions and value judgments (Daniels and Sabin, 2008). It is therefore important that decision-makers understand which particular

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https://doi.org/10.1016/j.socscimed.2022.114991
Received 21 July 2021; Received in revised form 17 April 2022; Accepted 22 April 2022
Available online 28 April 2022

elements should be interpreted with caution and complemented with other forms of evidence.

In Belgium, the setting of this study, the federal government is responsible for treatment of disease, and reimbursement of medication (including vaccines) on a per-patient basis, whereas the regions (Flanders, Wallonia, Brussels) are responsible for disease prevention, including routine vaccination programs across the life span. Vaccine producers usually request federal health insurance reimbursement through the Commission for Reimbursement of Medicines. At the same time, considering recommendations from the European Medicines Agency, the national Superior Health Council, and Health Technology Assessments (HTA), mainly by the Federal Health care Knowledge Centre (KCE), the different regions may or may not choose to adopt a certain vaccine in the regional routine vaccination programme. In Flanders, the government does not adhere to a strict and formalized procedure and mostly makes vaccine funding decisions on a case-by-case basis, considering available evidence of effectiveness, cost-effectiveness, budget impact, program feasibility and various broader societal considerations (such as social acceptability or equity). When there are multiple vaccines available, the authorities will start a tendering procedure using explicitly weighted criteria such as price per dose, effectiveness against various disease outcomes, adverse events, delivery times and guarantees or supply chain requirements, which are chosen and weighted for each tender, considering the specific aspects of the available vaccines and disease characteristics. Vaccine funding is therefore based on flexible, *ad hoc* criteria and available budget space and the decision to adopt a new vaccine is not made through a formal priority-setting framework.

In this article, we summarize a study that investigates on which basis the Flemish population would want decision-makers to set vaccination priorities and we assess to what extent preferences are aligned with CEA. We did so by means of a Discrete Choice Experiment (DCE) in a sample of the Flemish population. Several studies have used DCEs to investigate which characteristics people value most in vaccines (for reviews see (Diks et al., 2021; Michaels-Igbokwe et al., 2017)). However, these studies focus on a distinct question: whether people want to become vaccinated or not, once a vaccine is introduced in order to predict vaccine uptake and coverage rates. Instead, we want to know how people value the broad range of benefits of vaccination and on which basis they think that funding priorities should be set, across many disease areas. This question has received less attention. Pooripussarakul et al. investigated which criteria decision-makers use to set priorities for vaccine introduction in Thailand (Pooripussarakul et al., 2016). This study used a different method (best-worst scaling), study population (decision--makers and experts) and context (vaccines for children less than five years old in Thailand) and did not compare results to CEA. Luyten et al. analysed to what extent side effects and herd immunity effects should be valued differently from a vaccine's direct protective effects in funding decisions (Luyten et al., 2019). However this study did not investigate priority-setting across the broader scope of potential benefits of vaccination.

2. Methods

A DCE is a survey method to study stated preferences (Louviere et al., 2000; Ryan et al., 2008). Participants are presented with a series of choice sets, usually consisting of two products or services that are described by a number of attributes with differing attribute levels. By observing a large number of choices, researchers can infer how underlying attributes and levels determine priority of competing options. We offered respondents a range of choice sets of competing vaccination profiles. Fig. 1 describes the different steps taken in the development of the DCE.

2.1. Attributes and levels used

In a separate study, we developed a 'longlist' of forty vaccine and disease characteristics with potential relevance to vaccine funding decisions and investigated their importance in a sample of the Flemish population (N = 1000) (Luyten et al, 2020a, b). These consisted of (more narrow) medical characteristics (e.g. disease mortality risk, symptom severity, duration, timing, infectiousness, eradicability of the pathogen, vaccine effectiveness, extent of scientific (un)certainty, risk of side effects) and (broader) social characteristics (e.g. public or private economic impact, social gradient in who gets infected, impact on educational outcomes or other non-health effects of illness, caregiver impact). Respondents were asked to indicate for each characteristic how relevant it was as an argument to justify public funding decisions for

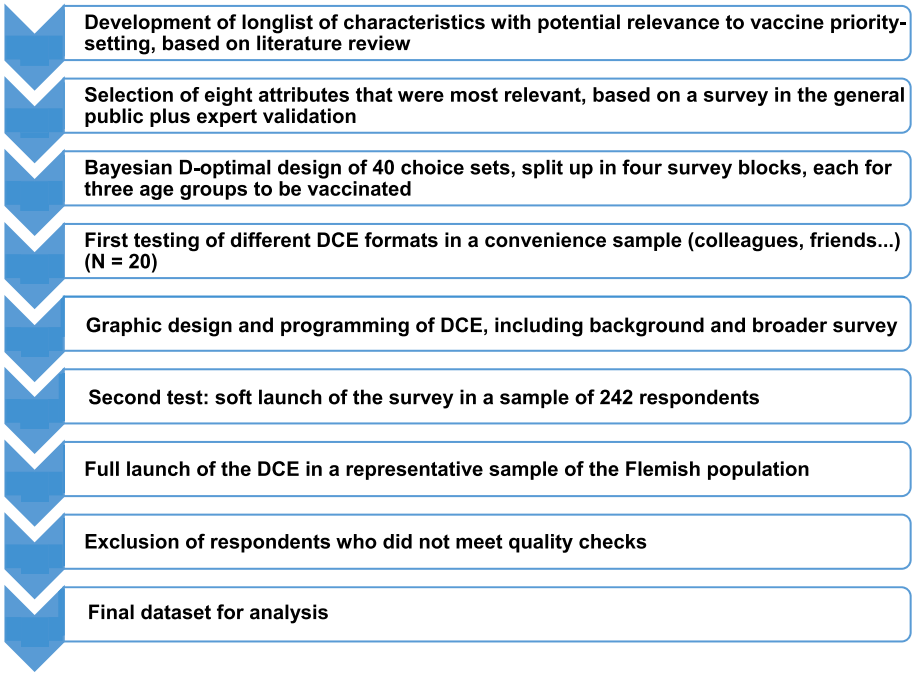


Fig. 1. Flowchart of the development of the DCE.

vaccines.

Based on the relevance scores of these forty characteristics, and a discussion of these results with vaccination experts at the Agency for Health and Care (AHC) of the Flemish Government (the body responsible for setting vaccination priorities in Flanders and the commissioner of the study), we constructed a 'shortlist' of vaccine characteristics with highest relevance to funding decisions: disease severity, duration of symptoms, incidence, vaccine effectiveness, risk of side effects, scientific (un)certainty, economic impact, age group of patients, potential to reduce social gradients and eradicability of the disease.

We transformed these ten elements into eight concrete attributes for our DCE (see Table 1). To be able to distinguish between different disease severities we chose to use three general infection "archetypes": (1) a lethal infection (*type-I infection*), (2) an infection with severe, long-term quality-of-life impact (*type-II infection*) and (3) an infection with severe but short-lived illness (*type-III infection*). This is a simplified representation but it captures essential illness categories between which policy-makers need to make trade-offs in priority setting. In line with other studies (see e.g.(Gu et al., 2015; Luyten et al., 2019; Luyten et al., 2015), we used generic disease descriptions instead of specific disease names ('*polio*', '*influenza*', etc.) in order to prevent respondents from making diverging personal associations. Appendix A presents the graphical representation of each type on a QALY diagram, i.e. a graph plotting length of life against quality-of-life with the area-under-the-curve corresponding to the number of QALYs lived (for an introduction to QALYs, see (Weinstein et al., 2009)). Typically, type-III infections occur more frequently than type-II infections and the latter more frequently than type-I infections. We chose levels of yearly incidence for these three types of patients that were high enough but still reasonable for infectious disease epidemiology in Flanders (Sciensano, 2021a). Type-I infections were presented to occur 10, 50 or 100 times every year; type-II infections 100, 500 or 1000 times a year and type-III infections 1000, 5000 or 10 000 times a year. For comparison, by way of illustration, in a Flemish population of 6.6 million inhabitants, every year there are about 500 000 cases of influenza-like illness (a type-III infection), with about 5000 severe cases requiring hospitalization and 300 patients dying because of their infection (type-I and -II infections) (Sciensano, 2021b). In 2018, there were 66 invasive meningococcal infections (a very serious infection with a high mortality risk) relating to type-I infections here. We could also consider 1452 new hepatitis B infections (of which a substantial share will develop long-term, chronic liver disease) as examples of type-II infections and 1194 confirmed rotavirus cases (a usually benign and self-limiting infection) as examples of type-I infections (Sciensano, 2019). None of these or other illustrative examples were presented to respondents in our study.

Table 1
Attributes and levels used in the DCE.

Attribute	Levels
Expected number of deaths (per year)	10
	50
	100
Expected number of patients with lifelong morbidity (per year)	100
	500
	1000
Expected number of patients with short-term morbidity (per year)	1000
	5000
	10 000
Socio-economic background of those infected	Below poverty line
	Above poverty line
Economic impact of the disease	10 000€
	30 000€
Contribution of the program to disease eradication objectives	Yes
	No
Scientific certainty on vaccine effectiveness	100% certainty
	75% certainty

The cost attribute was expressed as an average cost per infection, taking into account direct healthcare costs (treatment, hospitalization) as well as productivity losses, for all patient types combined. We opted for relatively high cost levels of 10 000€ and 30 000€ per patient to ensure compatibility with the number of type-I and -II patients: a high number of type-I and -II patients (particularly in young age groups and in combination with a low level of number of type-III patients) would not have been compatible with a low cost level. Whereas the average cost of a type-III patient would rather be a few hundred euros, type-I and -II patients can cost several ten thousands of euros when lifetime productivity losses are included (Bilcke et al., 2014; Bilcke et al., 2012; Bilcke et al., 2013; Luyten and Beutels, 2009; Luyten et al., 2012; Thiry et al., 2009; Willem et al., 2018). We chose a factor of three difference between the levels to allow for sufficient variation to measure the weight of a cost attribute.

Age was included as an overarching criterion that differed across DCE surveys and not as a separate attribute in the choice sets. Including age would require that respondents not only had to compare different numbers of patients with different severity-of-illness, but they would also have to take into account differences in remaining life expectancy. We judged that this would be too complicated. We therefore set up three different surveys in which each time a different age group was considered: young children of 3 years old, adults of 35 years old and elderly people of 70 years old. Although vaccines are often given at other ages, these three age groups should be able to capture differences in preferences for vaccination across infants and children, adults and the elderly. The choice sets in these surveys used identical attributes and levels and only differed in the age group of the infected patients.

We considered adding a specific attribute about vaccine safety but decided not to do this. Side effects were judged as less relevant to the concrete prioritization problem of policy-makers and the actual trade-offs they need to make. This is because serious side effects are rare as approved vaccines all have an excellent safety profile, whereas vaccines do differ in terms of the other attributes that we used. A second reason for excluding side effects was that, in analogy to an age attribute, this would have required the introduction of at least one additional health description for respondents to trade-off, which would have made the exercise substantially more complicated. Therefore the prerequisite in every choice set was that all vaccines were equally safe.

The final list of attributes and levels was subsequently validated during a meeting with the study commissioners at AHC.

2.2. Statistical design of the choice sets

The complete design (see Appendix C) consisted of 40 choice sets (see Fig. 2), split into four blocks (for each of the three age groups, hence there were 12 different surveys). Every respondent answered one block of 10 choice sets that were presented in a random order and all blocks were distributed evenly over the respondents. To simplify the choice task for the respondents, the profiles in the choice sets were *partial profiles*: we kept three dimensions constant between the two vaccination profiles whereas four were varying (Kessels et al., 2011a; 2015). The varying attributes were highlighted in blue and the constant attributes were shown to the respondents to provide the overview and to be able to estimate interaction effects. The statistical design or the specific composition of the choice sets that we generated was 'D-optimal' within a Bayesian framework (Kessels et al., 2011b). Specifically, the design was constructed to precisely estimate the importance of the attributes as well as the two-way interactions between the number of type-I, -II, and -III patients on the one hand and socio-economic background of the patients, contribution to disease eradication and certainty around vaccine effectiveness on the other.

Typical of a Bayesian design is that it requires the specification of 'priors', indicating the expected importance of the attributes and the direction of respondent preferences across levels as well as some degree of uncertainty around these expectations. We obtained the prior ranking

CHOICESET 1/10

Question: Diseases A and B both occur in adults aged 35 but can be avoided through vaccination. Both vaccines are identical unless otherwise described. Based on the information below, should the Flemish government first invest in a vaccination program for disease A or for disease B?

	DISEASE A	DISEASE B
How many type-I patients are expected to occur every year in Flanders? (Type I = deadly infection)	100	100
How many type-II patients are expected to occur every year in Flanders? (Type II = lifelong illness)	100	1 000
How many type-III patients are expected to occur every year in Flanders? (Type III = temporary illness)	10 000	1 000
How wealthy is the average patient?	Below poverty line	Above poverty line
What is the societal cost of one infected patient (average across all types, inclusive healthcare costs, unemployment benefits, etc)?	10 000€ per patient	30 000€ per patient
Does the vaccination program contribute to eradication of the disease in the long-term?	Yes	Yes
How certain are scientists about the effectiveness of the vaccine?	100% certain	100% certain
CHOICE	**I think that a vaccine for disease A should get priority** ○	**I think that a vaccine for disease B should get priority** ○

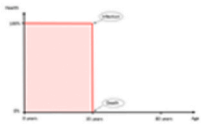
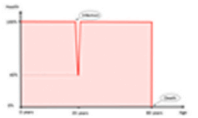
Type I patient	Type II patient	Type III patient
This type of patient dies within two weeks after an infection.	This type of patient will have a lifelong handicap because of the infection.	This type of patient will be severely ill for two weeks.
		

Fig. 2. Example choice set.

of the attributes from an enquiry among the four authors: each author individually indicated expected importance and direction of all attributes and levels after which consensus was formed through discussion. The priority ranking of the levels of an attribute had been mostly evident, especially when it comes to ordinal or continuous attributes (for example, it is better to have few rather than many deaths). By incorporating such knowledge in the design, the most informative choice sets could be selected. Our a-priori expectation of the respondent preferences related to the seven attributes used and their levels is shown in Appendix B. The same priors were taken for all age groups.

2.3. Graphic design, choice context and survey

Based on the 40 choice sets of the DCE design, we tested various visualisations among colleagues and volunteers (N = 20). The comments from these test subjects were implemented in a new format. To receive thoughtful responses, we added three 'exercise' choice sets before the ten 'real' ones. The first two of these choice sets consisted of a "dominant" vaccination profile that scored better on each dimension for which there was an unambiguous direction of preferences across the levels (i.e., the number of type-I, -II, and -III patients, certainty around vaccine effectiveness and cost), keeping the other attribute levels constant. A third warm-up choice set was identical to the tenth (and final) real choice set. A comparison of the resulting choices provided information about the choice consistency (but it is not necessarily a sign of poor quality if respondents chose differently in these identical choice sets).

The questionnaire (shown in Appendix G) started with an explanation of the purpose of the survey together with a short background to infectious disease control in Flanders and the need to set vaccine priorities. After asking for informed consent, a series of socio-demographic data about the respondent were enquired: gender, age, postcode, province, education level, number of children, job type, financial situation, opinion about vaccination (vaccine hesitancy scale (VHS) (Larson et al., 2015)) and vaccination status for a range of common diseases.

The different attributes of the DCE were then explained in detail one by one (see Appendix H). Each attribute was programmed on a separate page, and respondents could only click through to the next page after 10 seconds. The three possible disease outcomes were then presented graphically (see Appendix A) and textually. These diagrams were shown once more at the bottom of each choice set (see Fig. 2).

For each choice set, respondents were asked the following question (here for the age group of adults of 35 years old):

> "*Diseases A and B both occur in adults aged 35 but can be avoided through vaccination. Both vaccines are identical unless otherwise described. Based on the information below, should the Flemish government first invest in a vaccination program for disease A or for disease B?*"

At the end of the questionnaire, the respondents were asked to rate the difficulty of the entire study.

A starting or soft launch was held among the first 242 respondents. We checked whether the programming went smoothly and whether the data were recorded correctly. Of the 242 respondents, only 12 (5%) found the assignment "too difficult". On a 10-point scale for difficulty, where 1 means "not difficult at all" and 10 means "extremely difficult", the average score was 6.3 and the median 7. These findings were considered to be sufficiently positive for the full launch of the DCE.

2.4. Sample

We used the Belgian panel of the market research company Dynata, which is a permanently evaluated and updated panel of 5500 members drawn from 250 000 volunteers (2% of the Belgian population). This panel is recruited both online (e.g. social media advertisement) and offline (e.g. street recruitment) and resembles the Belgian population as good as possible according to various criteria (Statbel, 2020; Statistiek Vlaanderen, 2021). We used participants from the Flemish region only, fulfilling predetermined quota in line with the Flemish population for age, gender, level of education and province for each of the twelve (4*3) survey versions. The sample was recruited in December 2019.

2.5. Data analysis

We estimated several panel mixed logit (PML) models using the Hierarchical Bayes (HB) technique in the JMP Pro 16 Choice platform (based on 10 000 iterations, the last 5000 of which have been used for the actual estimate; SAS Institute Inc, Cary, NC, USA). A PML model is a logit model in which it is assumed that the preference parameters differ from person to person. It is therefore a model that takes into account the heterogeneity of respondents. In the model estimation we assumed normally distributed preference parameters without correlation between attributes. In this way, these 'random' parameters capture the non-observed heterogeneity in the respondent preferences.

The average utility function in the PML model is the sum of the average values of the main and interaction utility effects of the attributes. We calculated the significance of the attributes using Likelihood Ratio (LR) or plausibility tests and the relative importance of the attributes using the logworth statistic (defined as $-\log_{10}$(p-value of the LR test)). We analysed the datasets by estimating an initial PML model that included all main effects as well as all dual (or two-way) interaction effects between the number of type-I, -II, and -III patients on the one hand and poverty status of the patients, contribution to disease eradication and certainty around vaccine effectiveness on the other. We then deleted the non-significant model terms to arrive at final models in which all effects had a significant explanatory value at the five percent level.

Based on the estimated model, we also investigated the presence of observed heterogeneity in the respondent preferences. We therefore included and estimated interactions between attributes and respondent characteristics one by one in the model. We then grouped the (individually significant) covariates to test them jointly in the model, and to retain only those that were significant.

The model results summarize how people make trade-offs between disease outcomes of mortality, lasting morbidity and self-limiting illness. The description of our type-I, -II and -III patients was done in EQ-5D terms, which enables translation to QALYs (see Table 2). As such, the modelled trade-offs (as observed in our sample) can be compared to the trade-offs that are implied in QALYs (based on time-trade-off experiments in the general population). Hence, these comparisons allow assessing the extent to which people prioritize patients in line with the algorithm underlying EQ-5D-based QALY estimation. To verify whether the design of the DCE can effectively estimate a PML model that is in line with the expected QALY relationships between the disease severities, we simulated a separate dataset of fictional choices for 1000 respondents with regard to the target group of 3-year olds. We ensured that choices were made purely in line with the objective to maximize QALYs gained, but we also added random noise to the QALY model because we assumed that choices were not fully deterministic.

2.6. Ethical approval

The Social and Societal Ethics Committee (SMEC) of KU Leuven decided that this study did not fall under the Belgian law on experiments as pseudonymized data collected by a third party were analysed. No ethics approval was deemed necessary.

3. Results

3.1. Included respondents

In total, 2724 Flemish panel members completed our survey (i.e. 87% of eligible panel members). However, for our base case analysis, we excluded 33% of respondents (N = 1088) because their answers were

Table 2
Three possible patient types per infectious disease.

Type	Description	Implied QALYs lost	Example
Type-I infection	Dead, two weeks after infection	In 3-year olds: 77 QALYs lost In 35-year olds: 44 QALYs lost In 70-year olds: 10 QALYs lost	*meningitis* due to a bacterial infection
Type-II infection	Severe, permanent morbidity. Lifelong reduction in QoL of 60%, state 43433 on EQ-5D-5L. [The patient will have serious problems in walking about, moderate problems washing or dressing him/herself, severe problems doing usual activities, moderate pain or discomfort and moderate anxiety or depression.]	In 3-year olds: 48 QALYs lost In 35-year olds: 28 QALYs lost In 70-year olds: 6 QALYs lost	*poliomyelitis* with the complication of paralysis
Type-III infection	Short-lived, severe infection, state 43433 on EQ-5D-5L lasting for two weeks.	0.024 QALYs lost for all age groups	*influenza* infection without further complications

judged as insufficiently reliable: 273 respondents were excluded because they completed the DCE unreliably fast (below one third of the median time to completion (10 min 38 s), which is a standard procedure of the market research company); 275 because they consistently gave the same answer to the ten choice sets ('straightliners'); and an additional 540 who gave a wrong answer to one of the two warm-up choice sets with a dominant profile. A final sample of 1636 respondents met all our quality criteria for analysis. In Appendix E we present the results of a separate analysis that included the 540 respondents failing the warm-up choice sets with a dominant profile (N = 2176).

Table 3 presents the demographic characteristics of the final sample (N = 1636). The distribution of the respondents was mostly similar across all survey versions. Appendix D compares the final sample to the Flemish population. Overall, it was judged as sufficiently representative in terms of age and province, but respondents with low educational attainment were underrepresented and there were relatively more women. We also checked how representative our sample was in terms of income and levels of vaccine hesitancy, as our analysis indicated that these variables predicted somewhat different preferences. Respondents had a higher net household income compared to the average household in Flanders. Based on the answers to the ten VHS statements we constructed a composite hesitancy score, ranging from 10 for minimal hesitancy to 40 for maximal hesitancy. Only a negligible part (<2.5%) of the sample had clear negative attitudes toward vaccination (score >25), and median and mean scores were both equal to 19, which is aligned with levels of vaccine hesitancy observed in another study in Flanders in 2020 (Kessels et al., 2021).

Of the 1636 final responses, 20% (N = 333) indicated that the assignment was "easy", 76% (N = 1229) that the assignment was "difficult but doable" and 5% (N = 74) found the assignment "too difficult". When asked to give a "difficulty score" out of 10, the average answer was 6.3, and the median and mode were both seven. Eighty percent of all respondents (N = 1307) indicated the same preference in the third warm-up choice set as in the tenth 'real' choice set.

3.2. Relevance of attributes and levels

A first observation was that the cost attribute turned out to be insignificant in predicting choices whereas all other six attributes of Table 1 had explanatory power. In line with our expectations, the highest priority was given to a vaccine that had the most desirable levels in all six attributes. The lowest priority program was the reverse profile. Also the directions of preferences on each of the attribute levels were as expected. In terms of relative importance (see Fig. 3), certainty about vaccine effectiveness and disease eradication were most important. Least important was the equity attribute about poverty status of infected patients. The attribute about patients with lifelong morbidity was about as important as the attribute about mortality but this is related to the different scale of the former vs. the latter type of patients; one type-I

Table 3
Final sample characteristics.

Characteristic		Sample	
		N = 1636	100%
Gender	Male	755	46%
	Female	881	54%
Age	18–24	182	11%
	25–34	272	17%
	35–44	293	18%
	45–54	328	20%
	55–64	292	18%
	65–80	269	16%
Province	Antwerp	498	30%
	Limburg	210	13%
	East-Flanders	384	23%
	Flemish-Brabant	258	16%
	West-Flanders	286	18%
Education	None	2	0%
	Primary school	56	3%
	First degree secondary school	110	7%
	Second degree secondary school	104	6%
	Third degree secondary school	592	36%
	Higher, non-university	517	32%
	University or post-university	246	15%
	PhD	9	1%
Number of children	0	589	36%
	1	312	19%
	2	505	31%
	3	144	9%
	>3	86	5%
Profession	Working	912	56%
	Homemaker	73	4%
	Student	129	8%
	Unemployed	43	3%
	Disabled	112	7%
	Retired	367	22%
Household income	0-1000€	69	4%
	1000-2000€	418	26%
	2000-3000€	498	31%
	3000-4000€	399	24%
	4000-5000€	181	11%
	5000-6000€	50	3%
	>6000€	21	1%
Difficulties with monthly expenses	Never	564	34%
	Once a year	514	31%
	Once every three months	368	23%
	Every month	190	12%
Vaccine hesitancy	Mean = Median	19	
	Std Dev	4.14	
	Min; Max	10; 37	

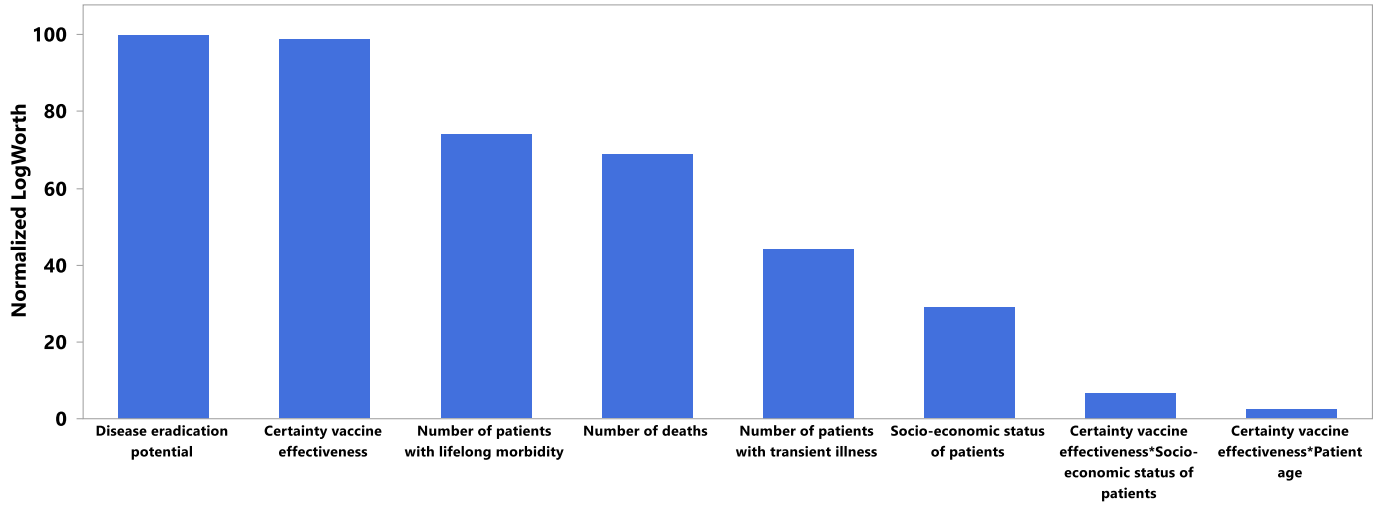


Fig. 3. Importance of all significant (p-value < 0.05) attribute effects in the DCE relative to the most important attribute, i.e. contribution to disease eradication.

patient was still more important than one type-II patient (see section 3.3). Interactions among the six significant attributes were investigated, and two were significant. First, the importance of poverty status of patients increased when the vaccine's effectiveness was more certain. This demonstrates that respondents were more inclined to attribute an equity 'bonus' to a vaccine when its effects are more certain. Second, the importance of certainty around vaccine effectiveness was greater when predominantly older age groups became vaccinated. Possible explanations for the latter effect could be that people want to spare older ages from the burden of becoming vaccinated with a more uncertain vaccine or that respondents think that vaccine funding for younger age groups does not require the same effectiveness standards.

The analysis that included the respondents who failed the dominance check (N = 2176, see Appendix E) generated largely similar results. What was different was that the certainty attribute had become slightly more important whereas the two interaction effects had become less significant.

3.3. Preference heterogeneity

By adding respondent characteristics to the model, we investigated to what extent different respondents made different choices (see Appendix F). We observed several statistically significant interaction effects, although these remained small in magnitude. The most important covariate was age. Older respondents attached higher value to certainty around vaccine effectiveness and poverty background than younger respondents. Another important covariate was income: respondents with higher income considered poverty status of infected patients less important than respondents with lower income. Also, higher educated respondents attached higher weight to the number of type-I and -II patients, and men considered certainty around vaccine effectiveness more important than women. Finally, the more vaccine hesitant respondents were, the more value they attached to the number of type-II patients and the disease eradication potential. Because our final sample was not fully representative in terms of age, gender, education and income, and because these characteristics led to somewhat different preferences, the weight given to the attributes certainty and poverty status in Table 3 and Fig. 3 may have been (slightly) underestimated, whereas the weight of number of type-I and -II patients may have been (slightly) overestimated.

3.4. Trade-offs

Because the cost attribute was not significant, we cannot calculate willingness-to-pay estimates for improvements in the levels. We did explore for all attributes the change required to contribute the same level of utility to the vaccination program as preventing one death (one type-I patient). These trade-offs were similar for all age groups, which indicates that respondents took little account of the remaining life expectancy of patients. A death or lifelong illness was almost equally bad regardless of the age group that was affected. More specifically, amongst 3-year olds, the prevention of one death corresponded to the prevention of approximately 12 lifelong illnesses and approximately 113 short-term illnesses. Amongst 35-year olds, one death weighed as much in the evaluation of a program as 10 lifelong illnesses and 116 temporary illnesses. Amongst 70-year olds, one death corresponded to 10 lifelong illnesses and 110 short-term illnesses. When a vaccine would target a disease with an outspoken social gradient, that fact in itself was equally valuable as preventing about 20 deaths, regardless of the age group. Contributing to disease eradication objectives or having certainty in terms of the effectiveness of the program was equally valuable as preventing about 45 deaths.

As our three patient types can also be expressed in terms of QALYs lost (see Table 2), the trade-offs between infections that we observed can be compared to those assumed in cost-utility analyses. For instance, one type-I patient in a 3-year old would amount to a loss of approximately 77 QALYs, one 3-year-old type-II patient would lose 48 QALYs, and any type-III patient would lose 0.024 QALYs. As shown in Table 5, where our model results are compared to the trade-offs in terms of QALYs, the difference in importance between a death and a life-long severe illness was considered more important by our sample than is assumed in the QALY calculation algorithm. However, also temporary illness was given a greater weight in our sample than its weight expressed in QALYs. As explained in the methods section, we simulated choices in accordance with QALY maximization (Coast, 2009), and subsequently estimated a new PML model. The obtained coefficients from our model were indeed in line with the values that we would expect when respondents follow a QALY maximization approach throughout the DCE.

Of course, the DCE trade-offs we observed were made more indirectly and are based on different context and information than those observed in studies underlying QALYs.

4. Discussion

In this study, we elicited a population perspective on how to set vaccine priorities based on eight characteristics of vaccines. Criteria such as contribution to eradication objectives and effectiveness uncertainty were considered highly important. Cost considerations did not matter to our respondents while social gradients did. Health benefits were valued differently from how they would be in QALYs. Prevention of a death was more important relative to a severe lifelong illness than when these two patient profiles would be expressed in QALYs, and more frequent, short-term illness was given a greater weight as compared to the weight such a patient would receive in QALYs. These findings provide some insights into how the public intuitively values vaccines, and to what extent there is a divergence from a valuation through CEA.

In principle, our results (the model summarized in Table 4) allow producing an explicit ranking of vaccines, when their performance is expressed in the levels of the attributes we used. Doing so would enable policy-makers to judge whether the priorities set would match those of the public (at least in Flanders and as measured in this study). We have developed an Excel-spreadsheet (available upon request) in which priority rankings can be calculated. This is an oversimplified approach to vaccine evaluation but it illustrates the potential of developing formal priority-setting algorithms. These enable a consistent and transparent way of priority setting and can be a complement to more deliberative or *ad hoc* vaccine evaluations. More extensive examples of such algorithmic approaches to priority setting are the '*Vaccines for the* 21st *century*' (Stratton et al., 2000) and the '*Smart Vaccines*' (Knobler et al., 2017; Phelps et al., 2014) models of the National Academy of Sciences (NAS) of the United States.

Table 4
Panel mixed logit model estimates (means and standard deviations (SD)) and likelihood ratio (LR) chi-square statistics of the significant attribute effects.

Model term	Mean (SD; subject SD)	LR Chi-square
Number of type-I patients (expected mortality)	0.794 (0.026; 1.032)	562.816
Number of type-II patients (expected lifelong morbidity)	0.067 (0.002; 0.096)	606.226
Number of type-III patients (expected short-term morbidity)	0.007 (0.000; 0.014)	359.953
Socio-economic status of those infected		234.201
Below poverty line	14.760 (0.690; 26.981)	
Above poverty line	−14.760	
Disease eradication potential		820.857
Yes	29.006 (0.879; 40.018)	
No	−29.006	
Scientific certainty around vaccine effectiveness		811.203
100%	29.552 (0.781; 31.195)	
75%	−29.552	
Scientific certainty around vaccine effectiveness * Socio-economic status of those infected		51.374
100% * Below poverty line	10.829 (0.749; 22.708)	
100% * Above poverty line	−10.829	
75% * Below poverty line	−10.829	
75% * Above poverty line	10.829	
Scientific certainty around vaccine effectiveness * Patient age		19.898
100% * 3 years	−2.900 (0.427; 0.171)	
100% * 35 years	−0.603 (0.692; 0.775)	
100% * 70 years	3.503 (0.472; 0.322)	
75% * 3 years	2.900	
75% * 35 years	0.603	
75% * 70 years	−3.503	

Note: All model terms are significant at $p < 0.001$.

Table 5
Equivalence table (Type-I = base, only vertical equivalence).

	DCE model	QALY losses in 3-year-old patients	QALY losses in 35-year-old patients	QALY losses in 70-year-old patients
Type-I patients	1	1	1	1
Type-II patients	11.8	1.6	1.6	1.6
Type-III patients	113.4	3208	1875	416

One type-I patient was equivalent to 11.8 type-II and 113.4 type-III patients in the DCE. Expressed in QALYs a type-I patient in a 3-year old was equivalent to 1.6 type-II patients and 3208 type-III patients.

There were several methodological limitations to our study. First, we evaluated vaccines on eight criteria but excluded many others. One was the risk of side effects. Although we believe that there are more important trade-offs to be made for vaccines with excellent safety profiles, a DCE with a side effects attribute included would likely have found this attribute to be influential. In a similar DCE about vaccine funding, Luyten et al. compared the weight of vaccine-induced side effects to their protective effects and found that the same health effect weighted three times heavier when it was induced through side effects instead of through 'natural' infection (Luyten et al., 2019). Second, a difficulty that we encountered was to disentangle the effect of the per-person severity of an infection from its frequency of occurring (which proved to be important). We chose to combine both in one attribute (e.g. number of type-I patients occurring 10/50/100 times) that simultaneously captures scale and severity. The consequence of this choice is that it becomes impossible to assess whether some of the results (i.e. the calculated weights per patient type) now only reflect the differences in disease severity or also the differences in scale. Although the scales are realistic, our results that one death is about hundred times as bad as a temporary illness may be an artefact of the constructed orders of magnitude of the levels. To test whether the severity of the type is influenced by the scale on which it occurs, one could repeat the DCE with equal scale sizes between the types. However, this would have the disadvantage that the DCE choice sets would be less realistic in terms of the real policy trade-offs. Moreover, we can ask ourselves whether scale should not be an integral part of these choices. After all, the dilemma is often how to choose between many mild illnesses and some serious ones. Third, the specific levels that we chose for other attributes may also have played a role. For instance, our cost attribute did not include a very low cost level, which would have allowed for more variation as both 10 000€ and 30 000€ are still substantial costs. Potentially this could have made the cost attribute more significant. Also, the specific age groups we considered (3, 35 and 70 years) are not the typical ages at which vaccination occurs and this may have made the priority setting dilemmas less realistic. Fourth, we used an online panel where membership may be associated with unobserved characteristics (e.g., Internet access). In case these characteristics would translate into different preferences, our results would reflect these. Fifth, although we started with a panel representative of Flanders in terms of age, gender, province and educational attainment, after our quality checks the included respondents were not fully representative anymore in terms of several characteristics. Some of these were shown to lead to slightly different choices and this may have somewhat distorted our estimates. Sixth, our results summarize preferences in Flanders and different results may have been found in other countries. Other DCEs about vaccination that were executed simultaneously in several countries (but that also investigated different subjects) have however found mostly similar results across populations (Duch et al., 2021; Verelst et al., 2021).

5. Conclusion

Vaccine funding priorities observed in a sample of the Flemish population were substantially different from those that would emerge through CEA. The weight given to different attributes and levels can be used to stimulate debate and involve public values in vaccine decision-making.

Credit author statement

JL: conceptualization, methodology, investigation, writing – original draft, visualization, supervision, project administration, funding acquisition. **PB:** conceptualization, writing – review and editing, funding acquisition. **CV:** conceptualization, writing – review and editing, funding acquisition. **RK:** conceptualization, methodology, software, investigation, formal analysis, writing –review and editing, visualization, funding acquisition.

Funding sources that supported the work

Financial support for this study was provided entirely by the Flemish Government, Agency of Health and Care. The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report.

Declaration of competing interest

No conflicts of interest to declare.

Acknowledgments

We thank the members of the infectious disease unit of the Agency of Health and Care (Flemish Government) for their financial support to conduct this study and for their constructive feedback and input in the research process. Dr. Kessels acknowledges the JMP division of SAS Institute for financial support.

Appendices A-H. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2022.114991.

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