Vaccine 36 (2018) 1467–1476

Contents lists available at ScienceDirect

Vaccine

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

The impact of vaccination and patient characteristics on influenza vaccination uptake of elderly people: A discrete choice experiment

Esther W. de Bekker-Grob [a,b,*], Jorien Veldwijk [a,c], Marcel Jonker [a], Bas Donkers [d], Jan Huisman [e], Sylvia Buis [f], Joffre Swait [g], Emily Lancsar [h], Cilia L.M. Witteman [i], Gouke Bonsel [j], Patrick Bindels [k]

[a] Section of Health Technology Assessment & Erasmus Choice Modelling Centre, Institute of Health Policy & Management, Erasmus University, Rotterdam, The Netherlands
[b] Section of Medical Decision Making & Erasmus Choice Modelling Centre, Department of Public Health, Erasmus MC – University Medical Centre, Rotterdam, The Netherlands
[c] Centre for Research Ethics & Bioethics, Uppsala University, Uppsala, Sweden
[d] Department of Business Economics & Erasmus Choice Modelling Centre, Erasmus School of Economics, Erasmus University, Rotterdam, The Netherlands
[e] General Practice, Het Doktershuis, Ridderkerk, The Netherlands
[f] General Practice, Gezondheidscentrum Ommoord, Rotterdam, The Netherlands
[g] Institute for Choice, University of South Australia, Sydney, Australia
[h] Centre for Health Economics, Monash University, Melbourne, Australia
[i] Behavioural Science Institute, Radboud University, Nijmegen, The Netherlands
[j] EuroQoL Foundation, Rotterdam, The Netherlands
[k] Department of General Practice, Erasmus MC – University Medical Centre, Rotterdam, The Netherlands

ARTICLE INFO

Article history:
Received 15 November 2017
Received in revised form 17 January 2018
Accepted 19 January 2018
Available online 6 February 2018

Keywords:
Influenza vaccination
Vaccination characteristics
Patient characteristics
Discrete choice experiment
Vaccination uptake

ABSTRACT

Objectives: To improve information for patients and to facilitate a vaccination coverage that is in line with the EU and World Health Organization goals, we aimed to quantify how vaccination and patient characteristics impact on influenza vaccination uptake of elderly people.
Methods: An online discrete choice experiment (DCE) was conducted among 1261 representatives of the Dutch general population aged 60 years or older. In the DCE, we used influenza vaccination scenarios based on five vaccination characteristics: effectiveness, risk of severe side effects, risk of mild side effects, protection duration, and absorption time. A heteroscedastic multinomial logit model was used, taking scale and preference heterogeneity (based on 19 patient characteristics) into account.
Results: Vaccination and patient characteristics both contributed to explain influenza vaccination uptake. Assuming a base case respondent and a realistic vaccination scenario, the predicted uptake was 58%. One-way changes in vaccination characteristics and patient characteristics changed this uptake from 46% up to 61% and from 37% up to 95%, respectively. The strongest impact on vaccination uptake was whether the patient had been vaccinated last year, whether s/he had experienced vaccination side effects, and the patient's general attitude towards vaccination.
Conclusions: Although vaccination characteristics proved to influence influenza vaccination uptake, certain patient characteristics had an even higher impact on influenza vaccination uptake. Policy makers and general practitioners can use these insights to improve their communication plans and information regarding influenza vaccination for individuals aged 60 years or older. For instance, physicians should focus more on patients who had experienced side effects due to vaccination in the past, and policy makers should tailor the standard information folder to patients who had been vaccinated last year and to patient who had not.

1. Introduction

Influenza is a major cause of illness and death [1]. Every year in the United States, influenza infections are associated with approximately 55,000 of deaths, the majority occurring from seasonal influenza among adults aged 65 years or older [2,3]. The same phenomenon is seen in Europe with a lower-bound estimated rate of excess deaths of 40,000 cases per season [4].

Influenza vaccination is promoted by many health authorities, as the single option of influenza prevention [5]. However, despite general consensus and recommendations that annual influenza vaccination should be given to all individuals with age 60 years

* Corresponding author at: Section of Health Technology Assessment & Erasmus Choice Modelling Centre, Erasmus School of Health Policy & Management, Erasmus University Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.
E-mail address: debekker-grob@eshpm.eur.nl (E.W. de Bekker-Grob).

https://doi.org/10.1016/j.vaccine.2018.01.054
0264-410X/

or older [5,6], many countries in Europe do not achieve high coverage in these groups [7]. In several countries, there is even a lowering trend of the influenza vaccination rate for elderly people [8,9]. To satisfy vaccination coverage recommendations in line with the EU and World Health Organization goals, more efforts are needed and more effective strategies have to be developed to increase influenza vaccination coverage [10].

A first important step towards better strategies is to obtain insights into how vaccination characteristics (the 'offer') and patient characteristics (the 'recipient') impact influenza vaccination uptake, assuming uptake is not random. These insights will be useful for i) general practitioners informing their patients (e.g., using more tailored type of invitation letter); and ii) policy makers to tailor their general brochures (e.g., focusing more on the facilitators or barriers regarding influenza vaccination uptake). However, there are no quantitative studies investigating how vaccination and patient characteristics impact on influenza vaccination uptake.

It is precisely this information that is needed to develop effective strategies to increase influenza vaccination uptake. Therefore, the aim of this study is to quantify how vaccination and patient characteristics impact on influenza vaccination uptake of elderly people. Towards this end we used a discrete choice experiment (DCE), a quantitative approach that is increasingly used in healthcare research to obtain quantitative information on the relative merits of complex outcomes. DCE combines an empirical task (respondents have to select one out of two stylized outcomes reflecting the decision at hand), with post hoc computations on the resulting data from a large set of respondents [11–13].

2. Methods

2.1. Discrete choice experiment

A DCE assumes that the overall preference for a multi-facetted medical intervention, such as an influenza vaccination, can be approached by first decomposing the intervention consequences into separate characteristics (technically called 'attributes'; e.g. vaccination effectiveness, risk of side effects, out-of-pocket costs) [14]. Those characteristics are further specified by variants of that characteristic (so-called attribute 'levels', such as for vaccination effectiveness 20%, 40%, 60%, 80% chance that the vaccinated person is protected against influenza symptoms).

The next step rests on the assumption that the individual's preference for a medical intervention (including rejection) is determined by the levels of those attributes [14]. The relative importance of attributes, and, within the attribute, the importance of the levels, can be empirically determined. In DCE, respondents are forced to make trade-offs by offering a series of choices between two (or more) medical intervention profiles [15] (see Fig. 1 for an example of such a so-called 'choice task'). Specific computational schemes enable the investigator to derive numbers for the relative preference for attribute levels [16].

2.2. Attributes and levels

We used a literature search [17–21], interviews with experts in the field of influenza vaccination (n = 4) and three focus groups with patients aged 60 years and older from general practices (n = 21; i.e., the target group) to develop and operationalize influenza vaccina-

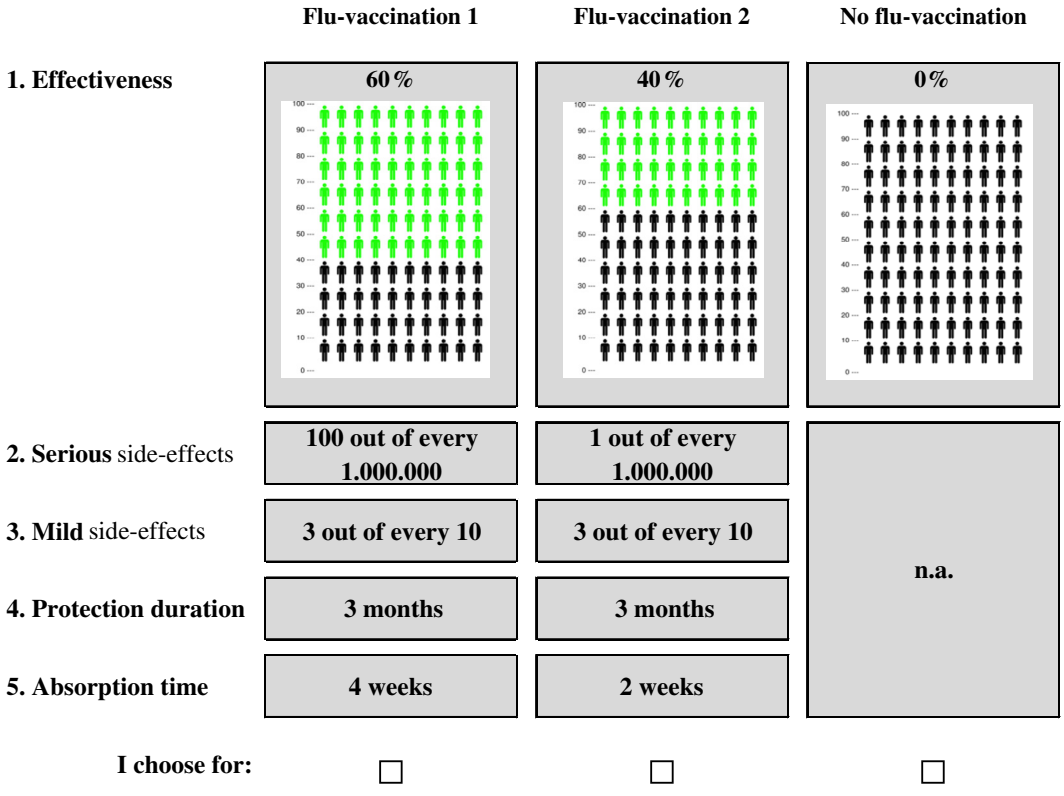


Fig. 1. Example choice set.

Table 1
Vaccination attributes and levels.

Vaccination attributes	Levels
Effectiveness (%)	20–40–60–80
Risk of severe side effects (× out of 1,000,000)	1–10–100
Risk of mild side effects (× out of 10)	1–3–5
Protection duration (months)	3–6–12
Vaccine will become active (× weeks after vaccination)	2–4

tion attributes with their levels. Noteworthy, in the Netherlands, recipients of 60 years and older (our target population) do not have to pay for influenza vaccination. After the qualitative work, the nominal group technique was applied, which allowed us to make a selection of influenza vaccination attributes [22]: vaccination effectiveness, risk of severe side effects, risk of mild side effects, protection duration, and absorption time (Table 1). The levels for each attribute incorporated the range of possible vaccination outcomes based on current literature and near future/plausible expectations (Table 1). To define vaccination effectiveness of –for example– 60% we used this description: "from all 100 persons who would normally get flu, due to vaccination 60 out of these 100 persons would not get flu anymore, while 40 persons would still get flu".

2.3. DCE design

The combination of, in our case, five attributes with two, three (three times) and four levels each results in 216 ($2^1 \times 3^3 \times 4^1$) potential influenza vaccination alternatives, and in 23,220 (216 $\times$ 215 $\times$ ½) different or unique comparisons of influenza vaccination scenarios (i.e., choice tasks). Choice tasks consisted of two influenza vaccination alternatives and a 'no vaccination' option was added to allow respondents to 'opt out' (Fig. 1). The 'opt out' alternative was necessary as influenza vaccination is a preventive intervention and, as in real life, respondents are not obliged to get vaccinated against influenza. Respondents were asked to consider all three alternatives in a choice task as realistic alternatives and to choose the alternative that appealed most to them.

Since it is not feasible to present a single individual with 23,220 choice tasks, selection procedures have been developed which create a much smaller subset of choice tasks with little loss of information or precision; these subsets are called 'designs'. So-called 'Bayesian efficient design algorithms' are designs which minimize the effort (respondent burden) to arrive at reliable parameters, i.e. the group's preference weights assigned to the attribute levels. Such algorithms maximise the D-efficiency criterion [23]; here we used Fortran programming language for computations. To maximize the D-efficiency of the DCE design while accommodating substantial respondent heterogeneity, a DCE design format commonly referred to as a heterogeneous DCE design [24] was used. That is, we used a heterogeneous DCE design consisting of 10 sub-designs. Each respondent was offered one sub-design containing 16 choice tasks. Together these sub-designs were optimal to estimate a so-called standard multinomial logit model, based on a main-effects utility function with several 2-way interactions (i.e., interaction between the attribute vaccination effectiveness and other attributes). The sub-designs deliberately restricted the number of different levels of attributes in each choice task to 3 (instead of 5), to avoid cognitive overload. The prior preference information (attribute weights) as required for the Bayesian efficient optimization approach was obtained from best guess priors, and updated after a pilot run of 300 respondents. As final result the developmental phase ended with 10 versions of questionnaires, each containing 16 different choice tasks, each choice task consisting of two different vaccination options and the no vaccination option. Pilot testing had provided the required prior preference information to run the computations after data collection.

2.4. Questionnaire

Apart from the 16 choice tasks described above, the questionnaire further contained questions on 19 patient characteristics. There were 8 background variables (age, gender, educational level, nationality, having any disease, GP visit last month, hospital visit last month, and heath condition); 8 influenza vaccination related variables (general attitude towards influenza vaccination, vaccinated last year, intention to opt for next influenza vaccination, experienced side effects, experienced flu although being vaccinated, experienced flu symptoms last year, religious or belief exemption for influenza vaccination, and impact of health condition on family); and 3 decision-making skills variables (decision style, health literacy, and numeracy). These 19 patient characteristics were of interest based on literature, expert opinions and focus groups (see Section 2.2), as they all are hypothesized to have an impact on vaccination uptake. The questionnaire also contained questions assessing experienced difficulty of the questionnaire (5-point scale) and the length of the questionnaire (3-point scale).

The questionnaire itself was structured as follows. First, the survey was briefly introduced, followed by the 8 background variable questions. Then the attributes and levels of influenza vaccination and the DCE choice tasks were explained. Subsequently, one warm-up question was included that carefully explained the layout and the required trade-offs of the DCE choice task questions. Then, the set of 16 pairwise choice tasks was shown. To promote respondent engagement with the DCE, halfway through the choice tasks (between tasks 8 and 9), 8 influenza vaccination-related variable questions were given. The pre-pilot study did not show signs of fatigue, and the break between choice sets 1–8 and 9–16 was positively debriefed. Finally, at the end of the survey, the respondents were asked validated Likert scale questions related to their decision style [25], health literacy [26,27], and numeracy [28,29], and questions about complexity and length of the questionnaire. We conducted a pre-pilot study with debriefing (n = 20; the patients used for this pre-pilot study were another 20 to the focus groups (i.e. no overlap)) to verify feasibility. On the one hand, it was a qualitative pre-pilot by using a think-aloud strategy to test whether patients understood the questionnaire and interpreted the attributes and levels in a way we wanted them to. On the other hand, it was also a quantitative pre-pilot as the DCE outcomes were used as prior information for the pilot DCE study design. The data of these patients were not included in the final analyses.

2.5. Study sample

An online sample of 1419 individuals aged 60 years and older from the Dutch general population, nationally representative in terms of age, gender, education, and geographic region was recruited via Survey Sampling International, a commercial survey sample provider. Calculation of optimal sample sizes for a DCE is complicated as it depends on the true values of the unknown parameters estimated in the discrete choice models [30]. However, based on our DCE design and pilot run, and using the sample size calculation of De Bekker-Grob et al. [31], a sample size of 1200 respondents was large enough to be able to find differences between attribute levels. Respondents were randomly assigned to 1 of the 10 questionnaire versions. Hence, each questionnaire agreed to 1 of the 10 DCE sub-designs created (noteworthy, each sub-design itself was given in a different order to the respondent, so that many different choice set versions were available). Respondents received a small financial compensation (€2,20) for completing the survey. Approval for the study was obtained from the Medical Ethics Committee, Erasmus MC (MEC-2016-095).

2.6. Statistical analyses

Several models exist to analyse discrete choice data [12,32,33]. Each choice model has its set of features, which should fit best to the intentions of the research. The aim of our study was to quantify how vaccination and patient characteristics impact on influenza vaccination uptake so that information for patients and uptake can be improved. Therefore, we were especially interested in relaxing the preference homogeneity and/or IID assumption. That is, observed differences in estimated preference parameters in discrete choice models can be due to preference and/or choice inconsistency. Considering choice consistency (i.e. scale effects or scale heterogeneity) may account for a significant amount of the observed variation in the results of the DCE when comparing preferences across subgroups (e.g. persons aged 60–69 years old might have a higher choice consistency than persons aged 70 years and older (scale heterogeneity), while their preferences might be similar (preference homogeneity)). Given our interest in accounting for systematic preference heterogeneity (i.e., to determine whether vaccination uptake depends on specific patient characteristics), while also taking scale effects and our sample size into account, led to the decision to employ a random intercept MNL model with error term heteroscedasticity (or scale variation) to analyse the choice observations. A (random) treatment preference (in DCE language also called a random alternative specific constant (i.e., random intercept)) is the difference in the mean of the preference (utility) for the no flu vaccination alternative compared to the flu vaccination alternative, if all attributes are set to zero. Using Pythonbiogeme Software and taking the best model fit into account based on the Bayesian Information Criterium (BIC), the observations were analysed by a heteroscedastic model in error component. We used a four-step approach to determine the optimal utility function. First, we tested a number of different specifications for the utility function (i.e. categorical or numerical attribute levels, two-way interactions between attributes, several attribute transformations) (model 1; MNL model). Second, we added and tested a number of different scale components to the utility function (model 2; HMNL model). Third, we allowed for several covariates (19 patient characteristics) to enter as interactions into the utility function (model 3; HMNL model plus systematic preference heterogeneity). Finally, a random intercept was added to the utility function to define the best utility function (model 4; same model as model 3, but taking the IIA assumption into account as well by using a random intercept). The random intercept takes into account whether respondents systematically viewed the flu vaccination(s) differently from the no flu vaccination alternative. The random intercept model is a simple form of mixed logit model, in which only the ASC is assumed to be distributed across the population. This specification essentially creates two nests (one for the vaccination alternative(s), another for the no-flu alternative), thus mimicking a nested logit specification.

For the coefficients, the statistical significance (p-value ≤ 0.05) indicates that respondents considered the attribute important in making their choices in the DCE. The sign of the coefficient reflects whether the attribute has a positive or negative effect on utility. In terms of the scale parameters, statistically significant parameter estimates indicate that the associated covariate captures more (positive parameter) or less (negative parameter) consistent choices.

2.7. Expected uptake of flu vaccination

Choice probabilities (mean uptakes) were calculated to provide a way to convey DCE results to general practitioners and policy makers that are more easily understood. We calculated the choice probability for a base case vaccination and a base case patient by taking the exponent of the total utility for vaccination divided by the exponent of utility of both vaccination and no vaccination. Noteworthy, in the calculation of the mean uptake we took all heterogeneity into account as the mean uptake is not just equal to the uptake of someone with average coefficient values. The base-case vaccination program was chosen to resemble a common practice situation, and included the following attribute levels: vaccine effectiveness of 60%, 1 out of 1,000,000 risk of severe side effects, 30% risk of mild side effects, protection duration of 6 months, and absorption time of 2 weeks. As there was no clear rationale to choose a specific base case patient, we decided to opt for a base case patient that had all dummy-coded '1' characteristics: male, good numeracy, good health literacy, aged >65 years, no flu symptoms last year, no GP visit last month, not having a disease, positive vaccination attitude, deliberative decision style, higher educated, no impact health condition family, good health, no flu vaccination last year, no vaccination side effects, and no flu after being vaccinated. To investigate the impact of changing a vaccination characteristic or a patient characteristic on vaccination uptake, univariate estimates (i.e. one-way impact) for predicted probability of vaccination uptake were calculated.

3. Results

3.1. Respondents

From the total of 1419 panel members aged 60 years and older who started the survey, 1261 (88.9%) completed the questionnaire, resulting in 158 dropouts (11.1%) (Table 2). Less than 3% of respondents that completed the survey had difficulty filling in the questionnaire, and 1043 respondents (82.7%) judged the length of the questionnaire as fine. Respondents had a mean age of 66.1 years (SD = 5.1), 712 respondents (56.6%) were male, and one third had a lower educational level (Table 3). About 75% of the respondents reported that they were in good health, 336 respondents (26.6%) had experienced influenza (symptoms) last year, and 387 respondents (30.7%) mentioned that they had never been vaccinated against influenza (Table 2). Sixty-four percent (64%) of the respondents stated that they would opt for flu vaccination if they would receive an invitation this year.

Table 2
Descriptives.

	N	%
Responsiveness		
Completes	1261	
Dropouts	158	11.1
Time between starting and ending DCE part of the questionnaire		
Median (sec)	641	
3–5 min	50	4.0
5–10 min	482	38.2
10–15 min	465	36.9
15–20 min	153	12.1
20–25 min	57	4.5
>25 min	54	4.3
Difficulty filling the questionnaire (yes)		
Very easy	270	21.4
Easy	638	50.6
Neutral	318	25.2
Difficult	32	2.5
Very difficult	3	0.2
Length of the questionnaire (good)		
Too long	218	17.3
Not too long, not too short	1043	82.7
Too short	0	0

Table 3
Respondents' characteristics.

	Respondents	
	N = 1261	(%)
Male	712	56.5
Age (mean; sd)	66.1	5.1
Aged 60–65 years	583	46.2
Aged 65 years or older	678	53.8
Education		
Low	424	33.6
Medium	434	34.4
High	399	31.6
Nationality Dutch	1241	98.4
Health		
Good	945	74.9
Moderate	277	22.0
Bad	39	3.1
Visited GP last month (yes)	409	32.4
Visited Hospital last month (yes)	294	23.3
Suffering from the following disease:		
Lung	199	15.8
Heart	163	12.9
Diabetes	194	15.4
Kidney	24	1.9
Low resistance	28	2.2
None	789	62.6
Influenza (symptoms) last year (yes)	336	26.6
Impact of certain conviction on flu vaccination (yes)	49	3.9
Vaccinated against influenza		
Yes, last year	643	51.0
Yes, 2 years or longer ago	228	18.1
No	387	30.7
Vaccination experience effectiveness (good)	646	51.2
Vaccination experience side effects		
None	670	53.1
Mild	157	12.5
Severe	47	3.7
Family impacts influenza decision (yes)	70	5.6
Say that s/he will opt for vaccination (fixed choice; yes)	807	64.0
General attitude vaccination		
In favour	549	43.5
Neutral	394	31.2
Against	318	25.2
Health literacy		
Average (mean; sd)	2.9	0.5
Good health literacy (scored 3 or higher)	563	44.6
Numeracy		
SNS average (mean; sd)	4.1	1.1
Objective scores correct (yes)	852	67.6
Good numeracy (i.e. 4 or higher SNS + obj scores correct (yes))	628	49.8
Decision style		
Decision style average (mean; sd)	2.8	0.5
Rather deliberative (3<)	219	17.4
Neutral (3)	303	24.0
Rather intuitive (<3)	739	58.6

3.2. DCE results

The heteroscedastic multinomial logit model, that included patient characteristics as well as a random intercept, resulted in the best model fit (see column HMNL++, Tables 4 and 5). As a validity check, the predicted vaccination uptake of 62.3% (CI 59.6%–65.0%) at an aggregate level was in line with the observed vaccination uptake of 64% (i.e., what respondents stated they will do; see previous paragraph) (Table 5). That is, the observed flu vaccination uptake on the group level was correctly predicted by our DCE (see Table 4, column HMNL++, which we used as our final analysis). As a check for response fatigue, the consistency in responses to choice set 9–16 did not differ significantly from the consistency in responses to choice set 1–8 ($p = 0.24$).

Table 5 presents the DCE results in detail. In general, all attributes proved to be important ($p < .01$), except for absorption time ($p = .25$). The attribute levels had the expected sign and order (Table 5) and showed, therefore, theoretical validity. In other words, there was a higher probability to opt for vaccination, if the vaccine was more effective, had a smaller risk of serious and mild side effects, and had a longer protection duration.

The estimated standard deviation of the alternative specific constant (i.e. random intercept) was strongly significant ($p < .001$), which indicated preference heterogeneity among respondents for the option 'no vaccination' (Table 5). The significant two-way interaction between the attribute 'vaccination effectiveness' and attribute level 'a 10 out of 1,000,000 risk of serious side effects' showed that the total positive value of 'vaccination effectiveness' was tempered if there was 'a 10 out of 1,000,000 risk of serious side effects' compared to 'a 1 out of 1,000,000 risk of serious side effects'.

Our findings detected scale heterogeneity. That is, the consistency of the choices depended on the numeracy skills and gender of respondents, and whether respondents had experienced flu symptoms last year: the choices to opt-in or opt-out for flu vaccination were more consistent if the respondent had good numeracy skills, was female, and/or did not experience flu symptoms last year (Table 5).

Preference heterogeneity among respondents from systematic sources was found to be substantial. Fifteen out of 19 patient characteristics had an impact on one or more attribute levels, and hence directly on the predicted vaccination uptake (see next paragraph).

3.3. Expected uptake of flu vaccination

Assuming a common practice influenza vaccination (i.e., vaccine effectiveness of 60%, 1 out of 1,000,000 risk of severe side effects, 30% risk of mild side effects, protection duration of 6 months, and absorption time of 2 weeks) and a base case patient, the utilities were 8.8 and 7.2 for the vaccination and 'no vaccination' option respectively. That is, the predicted influenza vaccination uptake was 58% (Figs. 2a and 2b). One-way changes in vaccination characteristics changed this uptake from 46% to 61% (Fig. 2a). Note especially that the vaccination uptake decreases substantially (from 58% to 46% and from 58% to 51%, respectively) if the vaccination effectiveness decreases from 60% to 20%, or if the risk of severe side effects increases from 1 out of 1,000,000 to 100 out of 1,000,000.

Table 4
DCE model fit results based on 1261 respondents.

	MNL	HMNL	HMNL+	HMNL++
Predicted vaccination uptake: mean (95% CI)	62.3% (59.6–65.0%)	60.4% (57.7–63.1%)	63.3% (60.6–65.9%)	62.3% (59.6–65.0%)
LogLikelihood	−17,228	−17,177	−13,539	−11,506
Degrees of freedom	12	20	76	77
AIC	1.709	1.705	1.350	1.148
BIC	1.712	1.710	1.369	1.168
Respondents (n)	1261			
Observed vaccination uptake	64.0%			

Note: MNL = multinomial model; HMNL = heteroscedastic model; HMNL+ = heteroscedastic model plus systematic preference heterogeneity; HMNL++ = Heteroscedastic model plus systematic preference heterogeneity plus random intercept; AIC = Akaike Information Criterion; BIC = Baysian Information Criterion.

Table 5
DCE results.

	MNL model			HMNL model			HMNL model + systematic preference heterogeneity			HMNL model + systematic preference heterogeneity + random intercept		
Utility function		95% CI			95% CI			95% CI			95% CI	
	coeff	Lower	Upper	coeff	Lower	Upper	coeff	Lower	Upper	coeff	Lower	Upper
Alternative-specific constant												
No vaccination	2.50	2.30	2.70	2.58	2.17	2.99	2.09	1.40	2.78	6.65	4.36	8.94
		95% CI			95% CI			95% CI			95% CI	
	OR	Lower	Upper	OR	Lower	Upper	OR	Lower	Upper	OR	Lower	Upper
Attributes (main effects)												
Effectiveness (log)	1.93	1.83	2.03	1.92	1.73	2.13	0.99	0.83	1.18	1.29	1.05	1.59
Serious side effects												
1/1.000.000 (ref)	1.65			1.71			1.29			1.24		
10/1.000.000	1.80	1.49	2.18	1.78	1.46	2.16	1.68	1.33	2.12	1.60	1.26	2.04
100/1.000.000	0.34	0.27	0.42	0.33	0.25	0.43	0.46	0.35	0.60	0.50	0.38	0.66
Mild side effects (per 10%)	0.94	0.93	0.95	0.58	0.57	0.58	0.90	0.88	0.92	0.86	0.84	0.89
Protection duration												
3 mo (ref)	0.60			0.63			0.72			0.65		
6 mo	1.31	1.08	1.58	1.29	1.08	1.55	1.16	0.93	1.45	1.11	0.88	1.40
12 mo	1.28	1.05	1.57	1.23	1.01	1.49	1.20	0.94	1.54	1.39	1.08	1.79
Waiting time												
2 wks (ref)	0.98			0.98			0.99			1.03		
4 wks	1.02	1.00	1.04	1.02	1.00	1.04	1.02	0.97	1.06	0.97	0.93	1.02
Two-way interactions												
Log_eff x serious10	0.86	0.82	0.91	0.87	0.82	0.91	0.88	0.83	0.93	0.90	0.84	0.95
Log_eff x serious100	1.16	1.10	1.23	1.18	1.12	1.24	1.04	0.98	1.12	0.96	0.89	1.02
Log_eff x dur6	0.95	0.90	1.00	0.95	0.90	1.00	0.97	0.92	1.03	0.99	0.93	1.05
Log_eff x dur12	1.01	0.96	1.07	1.01	0.96	1.08	1.02	0.96	1.08	1.01	0.95	1.08
	coeff	95% CI		coeff	95% CI		coeff	95% CI		coeff	95% CI	
		Lower	Upper		Lower	Upper		Lower	Upper		Lower	Upper
Scale heterogeneity												
Good nummeracy	–	–	–	0.42	0.31	0.54	0.20	0.13	0.27	0.29	0.15	0.43
Deliberative DM style	–	–	–	0.22	0.10	0.34	−0.26	−0.35	−0.17	0.01	−0.14	0.15
good health literacy	–	–	–	−0.10	−0.20	0.01	−0.02	−0.08	0.05	−0.03	−0.13	0.07
Age >65 years	–	–	–	−0.11	−0.22	0.00	−0.09	−0.15	−0.02	−0.03	−0.12	0.06
Flu symptoms last year	–	–	–	−0.16	−0.29	−0.03	−0.13	−0.20	−0.06	−0.15	−0.25	−0.05
gp visit last month	–	–	–	−0.12	−0.24	0.01	−0.05	−0.11	0.02	−0.06	−0.15	0.04
Male	–	–	–	−0.28	−0.39	−0.17	−0.03	−0.09	0.04	−0.15	−0.24	−0.05
No disease	–	–	–	0.15	0.02	0.27	−0.03	−0.10	0.03	−0.04	−0.14	0.06
		95% CI			95% CI			95% CI			95% CI	
	OR	Lower	Upper	OR	Lower	Upper	OR	Lower	Upper	OR	Lower	Upper
Systematic preference heterogeneity												
Age >65 yr × eff	–	–	–	–	–	–	0.92	0.89	0.96	0.86	0.79	0.92
Age >65 yr × dur6	–	–	–	–	–	–	1.00	0.93	1.07	0.99	0.87	1.12
Age >65 yr × dur12	–	–	–	–	–	–	0.93	0.87	1.00	1.31	1.22	1.40
Attitude for × eff	–	–	–	–	–	–	2.08	1.92	2.25	2.02	1.69	2.41
Attitude for × serious10	–	–	–	–	–	–	1.03	0.95	1.12	1.03	0.95	1.12
Attitude for × serious100	–	–	–	–	–	–	0.84	0.76	0.94	0.91	0.81	1.02
Attitude for × dur6	–	–	–	–	–	–	0.98	0.90	1.07	0.98	0.90	1.07
Attitude for × dur12	–	–	–	–	–	–	1.36	1.24	1.50	1.31	1.18	1.45
Attitude for × wait4	–	–	–	–	–	–	0.94	0.88	1.00	0.95	0.89	1.01
No disease × constant 'no vacc'	–	–	–	–	–	–	0.59	0.50	0.70	0.57	0.14	2.39
No disease × serious10	–	–	–	–	–	–	1.00	0.93	1.07	0.99	0.92	1.06
No disease × serious100	–	–	–	–	–	–	0.89	0.82	0.98	0.88	0.80	0.97
Deliberative DM style × constant 'no vacc'	–	–	–	–	–	–	24.53	9.43	63.85	5.10	0.78	33.57
Deliberative DM style × eff	–	–	–	–	–	–	2.37	1.87	3.00	1.89	1.46	2.44
Deliberative DM style × serious10	–	–	–	–	–	–	1.04	0.94	1.16	1.02	0.93	1.11
Deliberative DM style × serious100	–	–	–	–	–	–	0.79	0.68	0.91	0.89	0.77	1.03
Deliberative DM style × wait4	–	–	–	–	–	–	1.11	1.02	1.19	1.06	0.99	1.13
High education × constant 'no vacc'	–	–	–	–	–	–	2.25	1.30	3.90	2.16	0.48	9.78
High education × eff	–	–	–	–	–	–	1.31	1.14	1.50	1.33	1.14	1.54
High education × serious10	–	–	–	–	–	–	1.04	0.96	1.12	1.03	0.96	1.11
High education × serious100	–	–	–	–	–	–	0.88	0.80	0.96	0.89	0.81	0.99
Impact family × eff	–	–	–	–	–	–	1.14	1.05	1.22	1.49	1.15	1.94
Impact family × wait4	–	–	–	–	–	–	0.88	0.79	0.97	0.87	0.78	0.97
Flu symptoms last year × constant 'no vacc'	–	–	–	–	–	–	2.01	1.12	3.60	0.93	0.19	4.46
Flu symptoms last year × eff	–	–	–	–	–	–	1.19	1.03	1.37	1.23	1.03	1.47
Last month GP visit × dur6	–	–	–	–	–	–	1.03	0.95	1.11	1.02	0.94	1.10
Last month GP visit × dur12	–	–	–	–	–	–	1.09	1.00	1.18	1.10	1.01	1.19
Good health × ascn	–	–	–	–	–	–	4.39	2.49	7.76	26.58	4.50	156.92

Table 5 (*continued*)

Utility function	MNL model			HMNL model			HMNL model + systematic preference heterogeneity			HMNL model + systematic preference heterogeneity + random intercept		
		95% CI			95% CI			95% CI			95% CI	
	coeff	Lower	Upper	coeff	Lower	Upper	coeff	Lower	Upper	coeff	Lower	Upper
Good health × eff	–	–	–	–	–	–	1.28	1.11	1.47	1.31	1.12	1.52
Good health literacy × Constant 'no vacc'	–	–	–	–	–	–	0.48	0.29	0.79	0.36	0.09	1.39
Good health literacy × eff	–	–	–	–	–	–	0.83	0.73	0.94	0.84	0.73	0.96
Good health literacy × mild	–	–	–	–	–	–	1.04	1.01	1.07	1.04	1.01	1.07
Good health literacy × serious10	–	–	–	–	–	–	1.02	0.95	1.09	1.02	0.95	1.09
Good health literacy × serious100	–	–	–	–	–	–	1.11	1.01	1.21	1.09	0.99	1.21
Good nummeracy × constant 'no vacc'	–	–	–	–	–	–	5.47	3.02	9.93	7.24	1.51	34.68
Good nummeracy × eff	–	–	–	–	–	–	1.47	1.36	1.58	1.47	1.20	1.81
Good nummeracy × serious10	–	–	–	–	–	–	0.99	0.86	1.14	1.00	0.93	1.07
Good nummeracy × serious100	–	–	–	–	–	–	0.90	0.84	0.96	0.93	0.81	1.07
Good numeracy × dur6	–	–	–	–	–	–	1.05	0.98	1.13	1.05	0.98	1.13
Good nummeracy × dur12	–	–	–	–	–	–	0.86	0.77	0.95	0.82	0.75	0.90
Male × constant 'no vacc'	–	–	–	–	–	–	0.61	0.52	0.71	0.19	0.05	0.71
Male × serious10	–	–	–	–	–	–	0.98	0.91	1.05	0.97	0.91	1.04
Male × serious100	–	–	–	–	–	–	1.21	1.11	1.32	0.86	0.78	0.94
Vacc last year × constant 'no vacc'	–	–	–	–	–	–	0.12	0.07	0.20	<0.01	<0.01	<0.01
Vacc last year × eff	–	–	–	–	–	–	1.02	0.89	1.16	0.95	0.81	1.13
Vacc last year × serious10	–	–	–	–	–	–	1.05	0.96	1.14	1.04	0.95	1.14
Vacc last year × serious100	–	–	–	–	–	–	0.83	0.74	0.94	0.96	0.84	1.09
Vacc last year × mild	–	–	–	–	–	–	0.97	0.94	1.00	1.00	0.97	1.04
Vacc last year × dur6	–	–	–	–	–	–	1.02	0.93	1.10	1.00	0.91	1.09
Vacc last year × dur12	–	–	–	–	–	–	1.30	1.18	1.43	1.24	1.12	1.38
Vacc last year × wait4	–	–	–	–	–	–	0.92	0.86	0.98	0.93	0.87	1.00
Flu although being vacc × eff	–	–	–	–	–	–	0.92	0.87	0.97	0.87	0.73	1.03
No side effects × constant 'no vacc'	–	–	–	–	–	–	0.35	0.29	0.41	0.02	<0.01	0.08
No side effects × serious10	–	–	–	–	–	–	0.97	0.90	1.05	0.97	0.89	1.05
No side effects × serious100	–	–	–	–	–	–	1.11	1.01	1.23	1.13	1.02	1.26
No side effects × wait4	–	–	–	–	–	–	1.06	1.00	1.12	1.07	1.00	1.13
		95% CI			95% CI			95% CI			95% CI	
	SD	Lower	Upper	SD	Lower	Upper	SD	Lower	Upper	SD	Lower	Upper
Random intercept	–	–	–	–	–	–	–	–	–	7.69	6.20	9.18
Goodness−of−fit												
LL	−17,228			−17,177			−13,539			−11,506		
Number Free Param.	12			20			76			77		
AIC	1.709			1.705			1.350			1.148		
BIC	1.712			1.710			1.369			1.168		
Respondents	1261			1261			1261			1261		

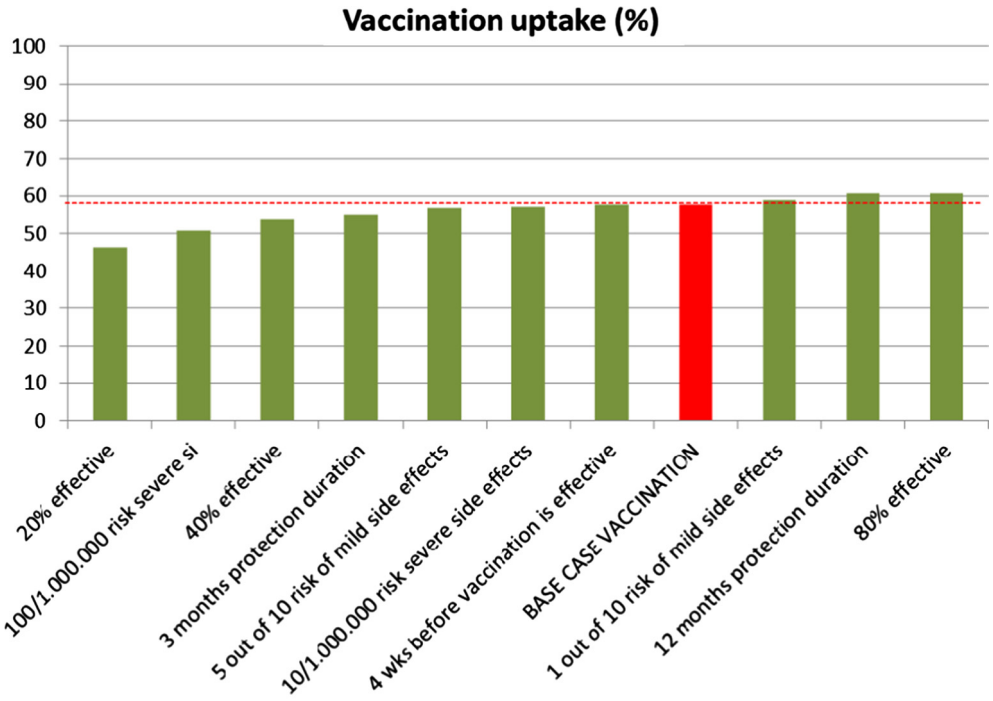
One-way changes in patient characteristics have an even larger impact on the predicted vaccination uptake. Assuming a common practice influenza vaccination and the base case respondent mentioned above (that led to a predicted vaccination uptake of 58%), one-way changes of patient characteristics changed this uptake substantially from 37% to 95% (Fig. 2b). The strongest impact on vaccination uptake was due to whether the patient had been vaccinated last year, whether s/he had experienced vaccination side effects, and the patient's general attitude towards vaccination, respectively.

4. Discussion

This study showed that vaccination and patient characteristics both significantly influence influenza vaccination uptake. Assuming a base case respondent and a common practice vaccination scenario, the predicted influenza vaccination uptake was 58%. One-way changes in vaccination characteristics changed this uptake from 46% to 61%, whereas one-way changes of patient characteristics changed this uptake from 37% to 95%. The strongest impact on vaccination uptake was whether the patient had been vaccinated last year, whether s/he had experienced vaccination side effects, and the patient's general attitude towards vaccination, respectively.

There are no previous DCE studies investigating how vaccination and patient characteristics impact on influenza vaccination uptake. However, DCE studies that investigated individuals' preferences for HPV vaccination or rotavirus vaccination found that vaccination effectiveness, protection duration, and/or risk of side-effects influence individuals' preferences for vaccination [34,35], which is in line with our findings. Our finding that the experienced vaccination side effects had an important influence on vaccination uptake was also found by a DCE study who focused on the effect of perceived risks on the demand for vaccination [18]. Our finding that if a patient was not in good health, or had a family member with such a condition, s/he had a higher probability to opt for influenza vaccination is an encouraging one. This is exactly the category of patients that benefits most of influenza vaccination.

Our study showed that if the patient had in general a negative attitude towards vaccination and/or if the patient had not opted for an influenza vaccination last year, both had a significant negative impact on the vaccination uptake. The use of this information by GPs (in The Netherlands, the GP invites the patients for influenza vaccination) and policy makers can increase uptake; for example by taking the opportunity to inform such patients aged 60 years and older directly regarding influenza vaccination, when s/he visits the GP several weeks before the seasonal influenza vaccination. That is, to clarify that



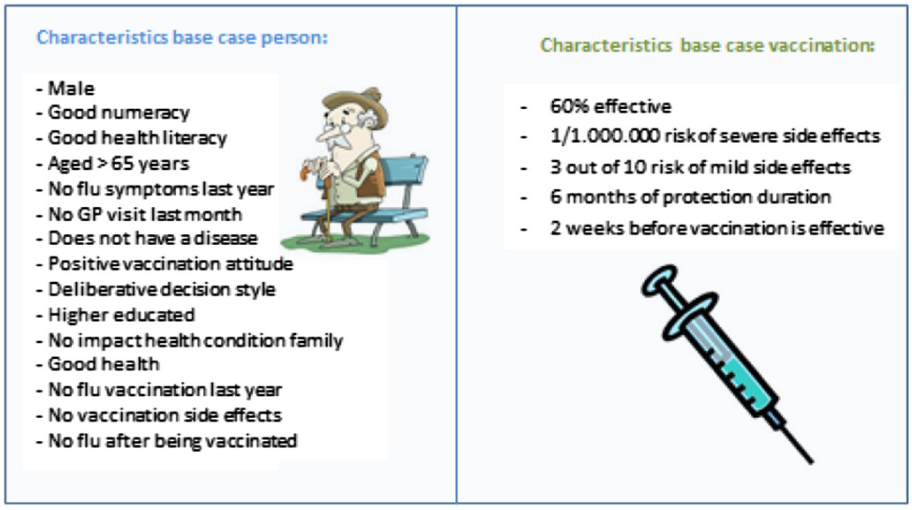


Fig. 2a. One-way impact vaccination characteristics on vaccination uptake for base case.

a patient will not get influenza because of the vaccination as it contains a dead virus, or to explain that several symptoms reported after influenza vaccination are not always the result of the vaccination. Further research is warranted to ascertain whether the GP's or other healthcare professionals' beliefs about influenza vaccination will moderate the positive impact of such a strategy on influenza vaccination uptake. Another strategy that begs further research is to investigate whether sending a more tailored letter to non-attenders of influenza vaccination last year might have a positive impact on vaccination uptake.

The current study has several strengths. First, we used qualitative techniques (interviews, focus groups, and nominal group techniques) to obtain insights into influenza vaccination attributes to inform the design of the DCE. Using qualitative methods to inform a DCE is important to ascertain that relevant attributes are included in the choice task [13]. Second, a state-of-the-art heterogeneous DCE design was used. Such a DCE design, which included several sub-designs, accommodated substantial respondent heterogeneity in an efficient way [24], while keeping the burden of a respondent to a manageable level. Third, our sample size of 1261 respondents was relative large compared to other health related DCE studies [36]. Such a relative large sample size is beneficial for reasons other than statistical precision (e.g. to facilitate in-depth analysis) [31].

A potential weakness of the present study is that numbers and rates were included in our DCE. This might have caused problems with understanding the choice task. However, 97% of the respondents reported that they did not find the DCE questions difficult. We therefore believe that interpretation problems in our DCE did not influence the results to a large extent. Second, the reported diseases were based on respondent self-reports. This might deviate from what a GP or formal medical registry would have reported,

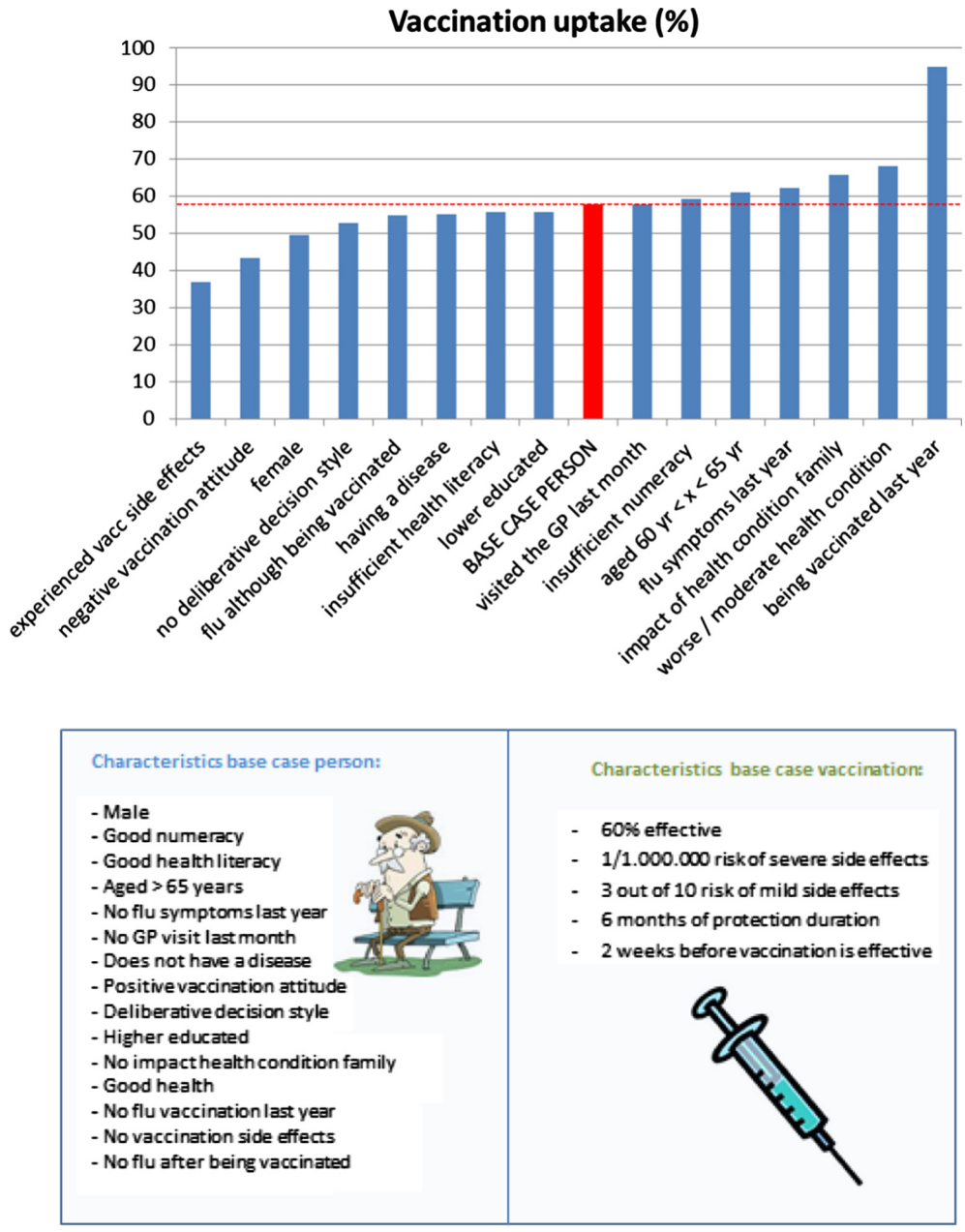


Fig. 2b. One-way impact patient characteristics on uptake base case vaccination.

and hence might have had an influence on the results. Third, although, the percentage of respondents (64%) who stated they would opt for flu vaccination was in line with current Dutch practice (58%; CI 51%-65%), we cannot exclude that selection bias may exist in our sample. Finally, the current results could gain credibility if it were possible to compare the stated preferences of elderly people with their actual behaviour in influenza vaccination.

In summary, although vaccination characteristics proved to influence influenza vaccination uptake, certain patient characteristics (i.e., whether the patient had been vaccinated last year, whether s/he had experienced vaccination side effects, and the patient's general attitude towards vaccination) had an even higher impact on influenza vaccination uptake. Policy makers and general practitioners can use these insights to improve their plans and information regarding influenza vaccination for individuals aged 60 years or older. For instance, physicians should focus more on patients who had experienced side effects due to vaccination in the past, and policy makers should tailor the standard information folder to patients who had been vaccinated last year and to patient who had not.

Acknowledgement

Grant support was from The Netherlands Organisation for Scientific Research (NWO-Talent-Scheme-Veni-Grant No. 451-15-039). The funders had no role in the study design, in the collection, analysis and interpretation of data, in the writing of the report and in the decision to submit the article for publication.

Conflict of interest statement

None of the authors have competing interests.

References

[1] Nichol KL et al. Effectiveness of influenza vaccine in the community-dwelling elderly. N Engl J Med 2007;357(14):1373–81.
[2] Thompson WW et al. Estimating influenza-associated deaths in the United States. Am J Public Health 2009;99(Suppl 2):S225–30.
[3] Simonsen L et al. Impact of influenza vaccination on seasonal mortality in the US elderly population. Arch Intern Med 2005;165(3):265–72.
[4] Blank PR, Schwenkglenks M, Szucs TD. Vaccination coverage rates in eleven European countries during two consecutive influenza seasons. J Infect 2009;58 (6):446–58.
[5] Thomas RE, Russell M, Lorenzetti D. Interventions to increase influenza vaccination rates of those 60 years and older in the community. Cochrane Database Syst Rev 2010;8(9):CD005188.
[6] Jung N, Lehmann C, Fätkenheuer G. The "Choosing Wisely": initiative in infectious diseases. Infection 2016;44(3):283–90.
[7] Mereckiene J, et al. Differences in national influenza vaccination policies across the European Union, Norway and Iceland 2008-2009. Euro Surveill, 2010;15 (44).
[8] Tacken MA et al. Dutch influenza vaccination rate drops for fifth consecutive year. Vaccine 2015;33(38):4886–91.
[9] Jimenez-Garcia R et al. Negative trends from 2008/9 to 2011/12 seasons in influenza vaccination coverages among high risk subjects and health care workers in Spain. Vaccine 2014;32(3):350–4.
[10] Dube E et al. Seasonal influenza vaccination uptake in Quebec, Canada, 2 years after the influenza A(H1N1) pandemic. Am J Infect Control 2014;42(5):e55–9.
[11] Ryan M, Gerard K. Using discrete choice experiments to value health care programmes: current practice and future research reflections. Appl Health Econ Health Policy 2003;2(1):55–64.
[12] de Bekker-Grob EW, Ryan M, Gerard K. Discrete choice experiments in health economics: a review of the literature. Health Econ 2012;21(2):145–72.
[13] Clark MD et al. Discrete choice experiments in health economics: a review of the literature. Pharmacoeconomics 2014;32(9):883–902.
[14] Ryan M. Discrete choice experiments in health care. BMJ 2004;328 (7436):360–1.
[15] Hensher DA, Rose JM, Greene WH. Applied choice analysis: a primer. Cambridge: Cambridge University Press; 2005.
[16] Mangham LJ, Hanson K, McPake B. How to do (or not to do) Designing a discrete choice experiment for application in a low-income country. Health Policy Plan 2009;24(2):151–8.
[17] Determann D et al. Acceptance of vaccinations in pandemic outbreaks: a discrete choice experiment. PLoS One 2014;9(7):e102505.
[18] Sadique MZ et al. The effect of perceived risks on the demand for vaccination: results from a discrete choice experiment. PLoS One 2013;8(2):e54149.
[19] Shonoa A, Kondob M. Parents' preferences for seasonal influenza vaccine for their childrenin Japan. Vaccine 2014;32:5071–6.
[20] Goodwin K, Viboud C, Simonsen L. Antibody response to influenza vaccination in the elderly: a quantitative review. Vaccine 2006;24(8):1159–69.
[21] Burns VE, Ring C, Carroll D. Factors influencing influenza vaccination uptake in an elderly, community-based sample. Vaccine 2005;23(27):3604–8.
[22] Hiligsmann M et al. Nominal group technique to select attributes for discrete choice experiments: an example for drug treatment choice in osteoporosis. Patient Prefer Adherence 2013;7:133–9.
[23] Reed Johnson F et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR conjoint analysis experimental design good research practices task force. Value Health 2013;16(1):3–13.
[24] Sàndor Z, Wedel M. Heterogeneous conjoint choice designs. J Marketing Res 2005;42:210–8.
[25] Pachur T, Spaar M. Domain-specific preferences for intuition and delibration is decision making. J Appl Res Memory Cognition 2015;4:303–11.
[26] Ishikawa H. Takeuchi T, and Y. E., *Measuring functional, communicative, and critical health literacy among diabetic patients*. Diabetes Care 2008;31:874–9.
[27] van der Vaart R et al. Validation of the Dutch functional, communicative and critical health literacy scales. Patient Educ Couns 2012;89:82–8.
[28] Fagerlin A et al. Measuring numeracy without a math test: development of the subjective numeracy scale. Med Decis Making 2007;27(5):672–80.
[29] Zikmund-Fisher BJ et al. Validation of the subjective numeracy scale: effects of low numeracy on comprehension of risk communications and utility elicitations. Med Decis Making 2007;27(5):663–71.
[30] Lancsar E, Louviere J. Conducting discrete choice experiments to inform healthcare decision making: a user's guide. Pharmacoeconomics 2008;26 (8):661–77.
[31] de Bekker-Grob EW et al. Sample size requirements for discrete-choice experiments in healthcare: a practical guide. Patient 2015;8(5):373–84.
[32] Hauber AB et al. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR conjoint analysis good research practices task force. Value Health 2016;19(4):300–15.
[33] Lancsar E, Fiebig DG, Hole AR. Discrete choice experiments: a guide to model specification estimation and software. Pharmacoeconomics 2017;35 (7):697–716.
[34] de Bekker-Grob EW et al. Girls' preferences for HPV vaccination: a discrete choice experiment. Vaccine 2010;28(41):6692–7.
[35] Veldwijk J et al. Parental preferences for rotavirus vaccination in young children: a discrete choice experiment. Vaccine 2014;32(47):6277–83.
[36] Marshall D et al. Conjoint analysis applications in health - how are studies being designed and reported?: an update on current practice in the published literature between 2005 and 2008. Patient 2010;3(4):249–56.