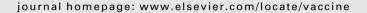


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## Vaccine





## Preferences for vaccines against children's diarrheal illness among mothers in Poland and Hungary



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### ARTICLE INFO

#### Article history: Received 30 October 2017 Received in revised form 27 July 2018 Accepted 1 August 2018 Available online 24 August 2018

Keywords: Vaccines Rotavirus Children Discrete-choice experiment Preference

#### ABSTRACT

Purpose: Although the World Health Organization recommends universal rotavirus immunization, uptake of the vaccine is low in Poland and Hungary, where it is not covered by the National Immunization Program. This study aimed to quantify mothers' preferences for vaccines preventing children's diarrheal illness and to examine whether willingness to vaccinate varies with working status. Methods: Mothers of children aged <3 years living in Poland and Hungary completed an online discrete-choice experiment survey. In each of 9 choice questions, respondents indicated whether they preferred no vaccination or one of two hypothetical vaccine profiles described in terms of 6 features. Vaccine preference parameters were estimated for working and non-working mothers using a random-parameter logit model and were used to calculate the relative importance of changes in vaccine features.

Results: 350 mothers in Poland and 350 mothers in Hungary were surveyed. Of the attributes evaluated, changes in vaccine cost were most important in both countries, followed by changes in severity of illness prevented, vaccine effectiveness, mode of administration, duration of illness prevented, and number of doses. Mothers in both countries had a strong preference for vaccination versus no vaccination, which was more pronounced among working mothers. In Poland, working mothers placed less weight on effectiveness, illness severity, and cost than non-working mothers and were more likely to rate disruptions in work, child care, and routines as important reasons to vaccinate. In Hungary, working mothers were statistically significantly less likely to opt out of vaccination than non-working mothers. Preference for vaccination itself, relative to improving vaccine effectiveness (from 50% to 90% effective), was 7 times greater among working than among non-working mothers in Poland but was not considerably different between working and non-working mothers in Hungary.

Conclusions: Polish and Hungarian working mothers are more likely to vaccinate children against diarrheal illness than non-working mothers.

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## 1. Introduction

An estimated 95% of the children who are unvaccinated for rotavirus are affected by rotavirus infection by the age of 5 years

[1]. Because of the high infection rate, the disease causes a considerable financial burden for society, with a high medical cost attributable to outpatient visits and hospitalizations and a high familial cost attributable to lost productivity of parents with affected children [2–4].

The World Health Organization recommends that all national immunization programs should include one of the two rotavirus vaccines that have been licensed for use and approved by the European Medicines Agency since 2006 [5,6]. Nevertheless, the status of rotavirus vaccination varies widely across European countries, both in terms of reimbursement coverage and uptake [7]. Most countries have accepted and registered the rotavirus vaccine, but

Abbreviations: DCE, discrete-choice experiment; RPL, random-parameter logit.

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for many the payment is not covered by the national health care system. This is the case of Poland and Hungary, requiring out-of-pocket expenditures for the vaccine [7]. Although the vaccination is strongly supported by clinical experts in both countries, uptake of the vaccine has been estimated to be low, between 10% and 20% [7,6].

Previous studies have estimated parents' preferences for rotavirus vaccines and vaccine outcomes [8–10]. However, little is known about mothers' specific motives for having their children vaccinated against rotavirus disease. Although out-of-pocket expenditures may be a barrier to vaccination, illness in children causes various types of disruptions in the lives of the adult caregiver, including health care appointments, health care expenditures, and caregiving. For working mothers, these disruptions may also include lost wages, work schedule disruptions, and the need to identify alternative child care arrangements. These elements may motivate mothers to seek vaccination of their children.

Our objectives were to explore the importance of the reasons mothers may choose to vaccinate their young children against a diarrheal disease such as rotavirus, to explore the impact of selected vaccine features on vaccine choices, and to examine whether these results vary depending on the working status of the mother. A discrete-choice experiment (DCE) survey was developed to address these objectives. The survey was administered to mothers of children younger than 3 years old in Poland and Hungary, where rotavirus vaccination is neither mandatory nor free.

#### 2. Material and methods

## 2.1. Survey instrument

We followed good research practices to develop a DCE survey instrument to elicit respondents' preferences for rotavirus vaccination options [11]. We initiated development of the survey instrument by first organizing a key informant discussion with a convenience sample of 15 working mothers who had at least one child aged 5 years or younger. The intent of the discussion was to elicit concepts from working mothers, with a focus on reasons mothers may opt to vaccinate their children against rotavirus, including some specific vaccine features, and the importance of each reason. This discussion took place in Wavre, Belgium (location

selected based on convenience). The key informants identified the following nine reasons to vaccinate a child: work disruptions, child care disruptions, unplanned expenses, disruptions to home and family routines, concerns about child's discomfort, concerns about child's health in the future, concerns about treatment, feelings of guilt, and concerns about spreading the disease.

The survey instrument was developed to elicit respondents' ratings of the importance of these nine reasons for vaccination and, via a DCE, respondents' preferences for six features of a hypothetical vaccine: effectiveness, severity and duration of the prevented disease, mode of administration, number of doses, and cost. Each attribute could take on one of two, three, or four different levels (Table 1). The attributes and the levels in the DCE were informed by the characteristics of existing vaccines against childhood diarrhea and by the findings from the key informants (Table 1). Survey respondents were told that all of the hypothetical vaccines in the survey would have the same low risk of mild side effects.

In the survey, the respondents were asked to rate the importance of each of the nine reasons when considering vaccination against mild, moderate, and severe diarrheal illness on a Likert-like scale of 1 ("not at all important") to 7 ("extremely important"). In addition, in each of a series of nine DCE questions, respondents had to choose between a pair of hypothetical vaccine profiles, each defined by vaccine features with varying levels, or to opt for no vaccine. Fig. 1 presents an example of a choice question. The vaccine profiles and the pairs were determined by an experimental design with known statistical properties.

The draft survey instrument was refined based on the findings of qualitative interviews with a convenience sample of 13 working mothers of children younger than 5 years in Belgium. The developed survey instrument was then translated into Polish and Hungarian and pretested in face-to-face semi-structured interviews with convenience samples of 15 mothers of children younger than 3 years, recruited in partnership with CEEOR [12]. The interviews tested the understandability of the survey instrument, the appropriateness of descriptive information, and the cognitive burden of the questions. The survey questionnaire was finalized based on these pretest findings.

In the final online survey, respondents were randomly assigned to a set of DCE questions with one of the two different vaccine cost ranges, one wider than the other, to allow an internal validity test

**Table 1** Attributes and attribute levels for choice questions.

Attribute	Attribute Level	Attribute Level			
Number of cases of diarrheal illness prevented in children under 5 years	10 cases of diarr	4 cases of diarrhea per 100 children, vaccine prevents 36 cases per 100 children 10 cases of diarrhea per 100 children, vaccine prevents 30 cases per 100 children 20 cases of diarrhea per 100 children, vaccine prevents 20 cases per 100 children			
Severity of illnesses prevented by vaccine	Mild Moderate Severe	Moderate			
Duration of illnesses prevented by vaccine	5 days for each il	3 days for each illness 5 days for each illness 9 days for each illness			
How vaccine is given		By injection in the thigh By mouth (liquid drops)			
Number of doses	2 doses 3 doses				
Personal cost of vaccine <sup>a</sup>	Poland	Poland		Hungary	
	Narrow	Wide	Narrow	Wide	
	No cost €28.75/125 zł €52.90/230 zł €92.00/400 zł	No cost €28.75/125 zł €92.00/400 zł €149.50/650 zł	No cost €29.76/9,300 Ft €55.04/17,200 Ft €96.00/30,000 Ft	No cost €29.76/9,300 Ft €96.00/30,000 Ft €176.00/55,000 Ft	

 $<sup>^{</sup>a}$  The personal cost attribute levels were presented to respondents in their local currency. The exchange rates used were  $\pm 0.23/1$  zł and  $\pm 0.0032/1$  Ft.

(*scope test*) of respondents' sensitivity to absolute cost differences [13] (see supplemental appendix).

Supplementary data associated with this article can be found, in the online version, at <a href="https://doi.org/10.1016/j.vaccine.2018.08">https://doi.org/10.1016/j.vaccine.2018.08</a>. 001.

In addition to the rating and DCE questions, the survey instrument collected data on experience with children's diarrheal disease, demographic characteristics, and vaccine-experience characteristics. The survey instructed each respondent to think of their child younger than 3 years when answering the questions. If the respondent had more than one child younger than 3 years, she was instructed to think of the youngest one.

## 2.2. Study population

The online DCE survey was administered to mothers of children younger than 3 years living in Poland and Hungary.

The study sought to recruit both working and non-working mothers, but no specific quotas were targeted. Respondents' employment status was determined by whether they were working outside the home for pay at the time of the survey and whether or not they were on temporary leave from work to take care of a child (or children).

Respondents were recruited by All Global/Lightspeed, a health care panel research firm [14]. In Poland, web panelists who were likely to be eligible for the survey were selected for invitation to participate based on known characteristics. In Hungary, invitations were sent to web panelists via e-mail, but they were not targeted because the characteristics of the web panelists were unknown. All study respondents provided informed consent before accessing the survey. The study was approved by the Office of Research Protection and Ethics at RTI International and complied with the standards of Declaration of Helsinki guidelines.

Vaccine Feature	Vaccine A	Vaccine B	Neither Vaccine
Number of cases of diarrheal illness prevented in children under 5 years	4 cases of diarrhea per 100 children Vaccine prevents 36 cases per 100 children	10 cases of diarrhea per 100 children Vaccine prevents 30 cases per 100 children	
Severity of illnesses prevented by vaccine	Mild	Severe	
Duration of illnesses prevented by vaccine	5 days for each illness	3 days for each illness	
How vaccine is given	By mouth	By injection	
Number of doses	3 doses	2 doses	
Personal cost of the vaccine	No Cost	9,300 Hungarian forint <sup>a</sup>	
Which would you choose?			

Fig. 1. Example choice question. <sup>a</sup>All costs were shown in local currency (Hungarian forint or Polish złoty). This example choice question uses Hungarian currency to describe the personal cost of the vaccine.

#### 2.3. Statistical methods

The percentage of respondents in each sample who rated each reason to vaccinate against children's diarrheal disease as the "most important" (i.e., the reason that received the highest importance rating, given illness severity) was calculated by disease severity level.

The statistical analysis of the respondents' choices in the DCE questions comprised preference modeling and subgroup analysis of working versus non-working respondents. Monetary equivalents (a proxy for willingness to pay) were also calculated (see supplemental appendix) [15]. The vaccine choice data from the DCE were analyzed using a random-parameter logit (RPL) model, which relates vaccine choices from each respondent to attributes of the vaccine alternatives in the questions. RPL models control for potential bias in the estimation of the mean preference due to unobserved preference heterogeneity [16–18]. Mean parameter estimates from RPL models are known as *preference weights* corresponding to the attribute levels. Preference weights can be interpreted to indicate the relative strength of preference for an attribute level. More preferred outcomes have higher weights.

The RPL model included all the attribute levels for the choice questions presented in Table 1 and an alternative-specific constant for "Neither Vaccine". Model-specification and scope tests were conducted (see supplemental appendix). The alternative-specific constant was 1 if "Neither Vaccine" was chosen and 0 if not. The levels for all attributes for the choice questions other than cost were coded using effect-coded variables. The cost term was modeled using a linear term, and the cost attribute levels were interacted with the log of the gross annual household income (in local currency) to control for the effect of income on cost preferences.

Subgroup analysis was conducted to explore whether working and non-working respondents had statistically significantly different vaccine preferences. We created a dummy variable equal to 1 if the respondent was employed at the time of the survey and not on a temporary leave from work to take care of a child (or children) and 0 otherwise. The dummy variable was interacted with all of the independent variables in the DCE model, and the model was re-estimated with the additional interactions. A chi-squared test of the joint significance of the interaction terms indicates whether preferences between the groups were statistically significantly different. The RPL parameter estimates for the interaction terms can be interpreted as preference-weight adjustments that apply only to respondents in the corresponding subgroup. Although the scale of the preference weights is arbitrary and not directly interpretable, the vertical distance between preference weights represents the relative importance of moving from one level to the other of the same attribute. The preference weights were used to

calculate preferences for vaccination relative to no vaccination, independent of vaccine features, and the preferences for specific improvements in vaccine effectiveness. The preference for vaccination relative to no vaccination was measured by the difference between the estimated preference weights on the alternative-specific constants for vaccination and no vaccination. These results were calculated for each country and for employment subgroups.

#### 3. Results

#### 3.1. Sample characteristics

In Poland, 911 individuals were invited to be screened to participate in the survey. The survey was made accessible to these individuals when they logged into their personal All Global webaccount. Of those who were invited, 416 individuals were eligible and consented to participate, and 350 individuals (84% of those who were eligible and consented) completed the survey. In Hungary, 16,663 individuals were invited to be screened to participate in the survey. Of those invited, 2,103 responded to the invitation and accessed the survey. Of those who responded, 441 (21.0%) were eligible and consented to participate, and 350 individuals (79.4% of those who were eligible and consented) completed the survey. More individuals were invited to be screened in Hungary than in Poland because more information was available on the web panelists in Poland and invitations could be targeted to those likely to be eligible.

Table 2 summarizes the respondents' demographic characteristics and their children's experiences with diarrheal illness. In Poland, 95 respondents (27.1%) were working at the time of the survey and 162 respondents (46.3%) were on temporary leave from work. In Hungary, only 77 respondents (22.0%) were working and 222 (63.4%) were on temporary leave from work.

### 3.2. Importance ratings

Fig. 2 presents the percentage of respondents from the Polish and Hungarian samples of working and non-working respondents who rated each of the potential reasons as the most important reason to vaccinate a child against mild, moderate, or severe diarrheal illness. Working respondents in Poland rated work and child care disruptions more highly than non-working respondents, whereas working respondents in Hungary did not.

## 3.3. Random-parameter logit model results

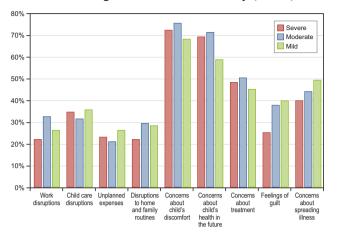
Fig. 3 summarizes the estimates of the mean parameters from the RPL models estimated with data for the employment

**Table 2** Respondents' demographic characteristics.

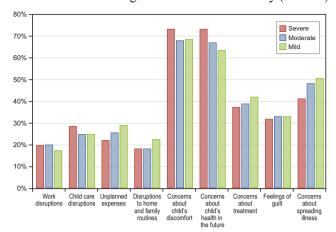
Characteristic	Poland (N = 350) n (%)	Hungary (N = 350) n (%)
Mean (SD) age, years	27.7 (4.9)	32.1 (7.8)
Married/living as married/civil partnership	302 (86.3%)	307 (87.7%)
Working at the time of the survey (this was defined as working outside the home for pay	95 (27.1%)	77 (22.0%)
at the time of the survey and not being on temporary leave from work to take care of a child or children)		
Not working at the time of the survey (this was defined as not working outside of the home for pay at the time of the survey or being on temporary leave from work to take care of a child or children)	255 (72.9%)	273 (78.0%)
On temporary leave from work, planning to return to work in the future	162 (46.3%)	222 (63.4%)
Receiving financial aid from the government while on temporary leave	77 (22.0%)	175 (50.0%)
Typical type of child care: full-time care by mother or father	251 (71.7%)	226 (64.6%)
Youngest child has had diarrhea	192 (54.9%)	233 (66.8%)
Child hospitalized/taken to ER due to diarrhea	110 (31.4%)	66 (18.9%)
Youngest child has received vaccine injection	235 (67.1%)	215 (61.4%)
Paid for vaccine for child in the past	216 (61.7%)	211 (60.3%)

## A. Polish Respondents

## Mothers Working at the Time of the Survey (n = 95)

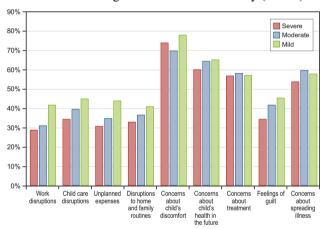


## Mothers Not Working at the Time of the Survey (n = 255)



## B. Hungarian Respondents

## Mothers Working at the Time of the Survey (n = 77)



## Mothers Not Working at the Time of the Survey (n = 273)

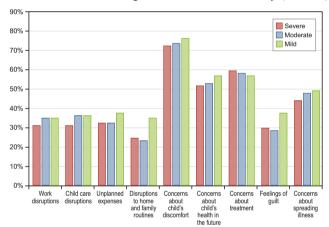


Fig. 2. Percentage of respondents within each sample rating each reason as most important.

subgroups from Poland and from Hungary. The estimated preference weights for all attributes except duration of illnesses prevented by the vaccine were consistent with the natural ordering of the levels—that is, better outcomes or features were preferred to worse outcomes or features. For example, on average, respondents in both samples preferred vaccines that were more effective in preventing children's diarrheal illness to vaccines that were less effective and lower-cost than higher-cost vaccines.

In both countries, the preference weights corresponding to the levels of the duration of illness prevented were not consistent with the natural order of the levels. Although respondents preferred a vaccine that prevented a shorter illness to a vaccine that prevented a longer illness, the preference weights corresponding to different levels of this attribute were not statistically significantly different from one another in either sample, indicating that respondents likely did not distinguish between levels of duration of illness prevented when they made vaccine choices in the survey.

The results indicated that the most important vaccine attributes were the same in both countries. Vaccine cost was most important, followed by severity of illness prevented, effectiveness of the vaccine, mode of administration, duration of illness prevented, and number of doses (in order of decreasing importance).

In both the Polish sample and the Hungarian sample, preferences were statistically significantly different between working and non-working respondents (P = 0.03 and P < 0.01, respectively) (Fig. 3). Polish working respondents placed less weight on some changes in cost, vaccine effectiveness, and severity of prevented cases than non-working respondents. In both the Polish sample and the Hungarian sample, working respondents were also less likely to opt out of vaccination than non-working respondents, but this difference was not statistically significant for the Polish sample.

# 3.4. Preferences for vaccination against children's diarrheal illness independent of vaccine features

In the Polish sample, "no vaccination" was chosen in 16.6% of choice questions (523 of 3149 answered questions) among the pooled sample, in 13.1% of choice questions (112 of 855 answered questions) among working respondents, and in 17.9% of choice questions (411 of 2294 answered questions) among non-working respondents. In the Hungarian sample, "no vaccination" was chosen in 18.6% of choice questions (586 of 3148 answered questions) among the pooled sample, in 22.3% of choice questions (154 of 692

answered questions) among working respondents, and in 17.6% of choice questions (432 of 2456 answered questions) among non-working respondents.

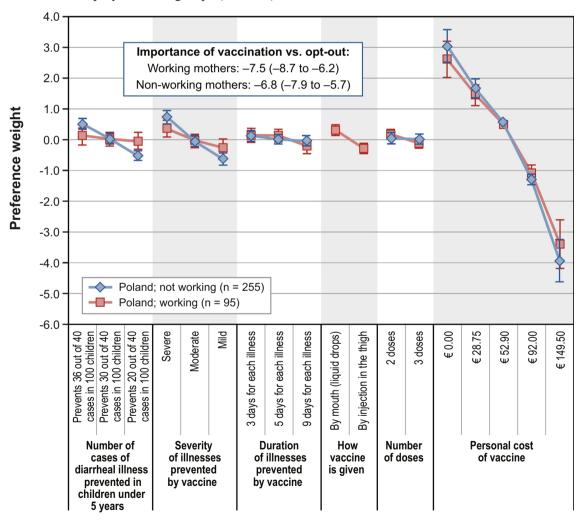
On average, respondents in both Poland and Hungary preferred vaccination to no vaccination, independent of the specific features of the vaccine. In addition, respondents' preferences for vaccination itself were greater than those for improving vaccine effectiveness in both countries and about the same as preferences for lower-cost vaccines. However, the preference for vaccination itself was greater among working respondents than non-working respondents (Table 3). For example, preferences for vaccination itself relative to those for an improvement in vaccine effectiveness from 50% to 90% were 7.1 (= 50/7) times greater among working respondents than among non-working respondents in Poland. Similarly, the preferences for vaccination itself relative to those for improving the vaccine by preventing more severe diarrhea were  $2.4 \, (= 12/5)$  times greater among working respondents than among non-working respondents in Poland. In contrast, preferences for

vaccination itself relative to those for improvements in vaccine features were similar among working and non-working respondents in Hungary.

## 4. Discussion

This study aimed to characterize mothers' reasons for vaccinating children against diarrheal illness in Poland and Hungary; to quantify preferences for features of vaccines that prevent such illness, given that out-of-pocket expenditures are required for rotavirus vaccination in both countries; and to examine how vaccine preferences differ between working and non-working mothers. Among both the Polish and Hungarian respondents surveyed, vaccine cost, severity of illness prevented, and vaccine effectiveness were key drivers of preferences for vaccines against children's diarrheal illness. Respondents' preferences in both samples indicated strong preference for vaccination rather than no vaccination, independent of the specific features of the vaccine, with

## A. Polish Employment Subgroups (N = 350)



**Fig. 3.** Preference model results: subgroups defined by whether mothers were working at the time of the survey. *Notes*: The vertical bars surrounding each mean preference weight denote the 95% confidence interval (CI) about the point estimate. If the CIs do not overlap for pairs of levels in a particular attribute, the mean estimates are statistically significantly different from each other at the 5% level of significance. Red squares represent the working respondents and blue diamonds represent the not working respondents. In case of similar scores, the red squares overlap with blue diamonds (i.e. for Polish sample, mode of administration, for Hungarian sample, number of doses). For the Polish sample, the estimated preference weights for the alternative-specific constant for vaccination over no vaccination, independent of vaccine features, were -7.5 (95% CI, -8.7 to -6.2) for working mothers and -6.8 (95% CI, -7.9 to -5.7) for non-working mothers. For the Hungarian sample, the estimated preference weights for the alternative-specific constant for vaccination over no vaccination, independent of vaccine features, were -8.4 (95% CI, -10.1 to -6.8) for working mothers and -6.0 (-7.1 to -4.9) for non-working mothers. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

## B. Hungarian Employment Subgroups (N = 350)

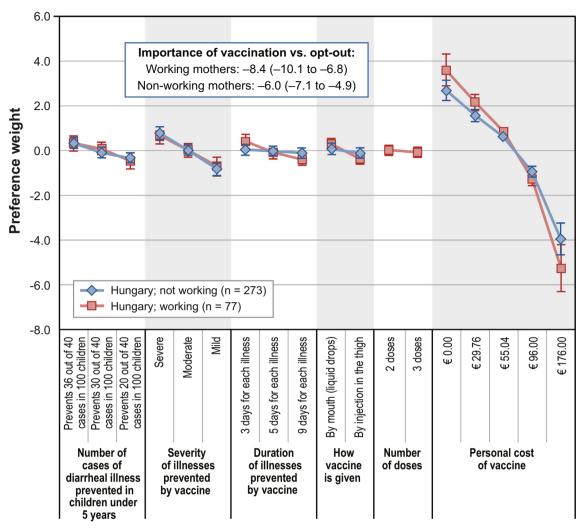


Fig. 3 (continued)

 Table 3

 Mothers' preferences for vaccination itself relative to preferences for specific improvements in vaccine features.

Preference for Vaccination Relative to Preferences for	Poland (N = 350)	Polish Working (n = 95)	Polish Non- working (n = 255)	Hungary (N = 350)	Hungarian Working (n = 77)	Hungarian Non- working (n = 273)
Improvement in vaccine effectiveness from 50% to 90% (preventing 20/40 cases to preventing 36/40 cases)	9	50	7	11	11	9
Improvement from preventing mild to preventing severe illness	6	12	5	5	6	4

Each value presented is a ratio of the preference for vaccination (relative to no vaccination, independent of vaccine features) to the preference for a specific improvement in vaccine effectiveness for the given sample or subgroup. The preference for vaccination relative to no vaccination was measured by the difference between the estimated preference weights on the alternative-specific constants for vaccination and no vaccination. The preference for a specific improvement in vaccine effectiveness was measured by the difference between the estimated preference weights associated with the corresponding vaccine feature levels.

vaccination being about as important as vaccine cost (the most important vaccine feature). This implies that, on average, respondents prefer to vaccinate their children against diarrheal illness (regardless of vaccine features) than to not vaccinate.

We found that respondents who were working at the time of the survey had different preferences than respondents who were not working. The working respondents in both Poland and Hungary were more likely to opt for vaccination. In Poland, they placed less weight on some of the changes in effectiveness and severity, as well as on vaccine cost, than non-working respondents. Hungarian working respondents placed greater weight on mode of administration and on cost. Working respondents in Poland were more likely than non-working respondents to rate work disruptions (including loss of income, missed work time [e.g., missed a shift, missed a day, missed meetings], and/or having to make up work during evenings or leisure times due to absence) and child care disruptions (e.g., having to make different child care arrangements that caused inconvenience and/or added expense) as the most important impact. In contrast, Hungarian respondents who were working did not rate work disruptions as a more important impact.

Previous studies of preferences for rotavirus vaccination have indicated that parents prefer reducing the severity and the duration of rotavirus illness [10] and that health literacy affects parents' preferences for rotavirus vaccination [8]. A recent study by Veldwijk and colleagues [9] of preferences of parents in the Netherlands found that efficacy, rotavirus severity, and out-of-pocket cost were key attributes influencing parents' preferences for rotavirus vaccines. Although the vaccine preferences identified in DCEs and other stated-preference studies may differ from revealed and actual preferences, research to quantify preferences for vaccines may help to characterize what drives vaccine demand and decisions to vaccinate, particularly in the absence of coverage for a particular vaccine by a national health care system.

This study is subject to several limitations that must be considered when the results are interpreted. The survey was administered online from an Internet panel, and respondent characteristics were self-reported. Panelists' self-selection bias may influence generalizability of the study findings. In addition, the study data are based on responses to hypothetical scenarios and lack the clinical, financial, or emotional consequences of actual real-world decisions. Differences may occur between stated preferences and actual choices. However, the study has a number of strengths. A key strength of the study is its rigorous methodology. We followed best practices, as described in Bridges et al. [11], to develop the survey instrument, which was informed by key informant qualitative interviews and in-depth pretest interviews in Poland and Hungary. An experimental design was used to determine the vaccine profiles, profile pairs, and series of DCE questions presented to each respondent. The RPL model used to analyze the DCE data avoids estimation bias from unobserved heterogeneity.

## 5. Conclusions

Vaccine cost, severity of illness, and vaccine effectiveness were key drivers of preferences for vaccines against children's diarrheal illness among respondents in Poland and Hungary, and there was a strong preference for vaccination over no vaccination. Vaccine preferences varied with working status: working respondents in both countries placed greater weight on vaccination, independent of vaccine features. Polish working respondents placed less weight on vaccine cost and some of the changes in effectiveness and severity than non-working respondents. They rated avoiding work and child care disruptions as more important.

## **Funding**

GlaxoSmithKline Biologicals S.A. funded this study (GSK Study identifier: HO-13-14114) and all costs related to the development of this publication.

## **Authors' contributions**

Christine Poulos and Brett Hauber contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, and revised the article critically for important intellectual content. Baudouin Standaert and Brigitte Sloesen contributed to the conception and design of the study, analysis and interpretation of data, and revised the article critically for important intellectual content. Izabella Stryjewska and Anna Janitsary contributed to the conception and design of the study and revised the article critically for important intellectual content. All authors provided final approval of the version to be submitted.

#### **Conflict of interest**

Christine Poulos and A. Brett Hauber are employees of RTI Health Solutions, which received research funding from the GSK group of companies during the conduct of this study. Baudouin Standaert, Izabella Stryjewska, and Anna Janitsary are employees of the GSK group of companies. Baudouin Standaert holds shares in the GSK group of companies. Brigitte Sloesen was an employee of the GSK group of companies when this study was conducted and is currently an employee of Novartis Pharma AG.

## Acknowledgments

The authors acknowledge the contributions of Joshua Posner, Angelyn Fairchild, and Amy Pugh throughout the study, Ales Tichopád for insights and field support during survey development and pretests, Agnieszka Skowronek-Madej for support during survey development, and Kimberly Moon for project management support. Kate Lothman provided medical writing services, which were funded by GSK Vaccines. The authors thank Business & Decision Life Sciences platform for editorial assistance and manuscript coordination, on behalf of GSK. Amandine Radziejwoski coordinated manuscript development and editorial support.

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