

# Parents' attitude toward multiple vaccinations at a single visit with alternative delivery methods

Patricia Kaaijk\*, Deborah E Kleijne, Mirjam J Knol, Irene A Harmsen, Olga JAE Ophorst, and Nynke Y Rots

Netherlands Centre for Infectious Disease Control; National Institute for Public Health and the Environment (RIVM); Bilthoven, The Netherlands

**Keywords:** Parents' attitude, childhood routine vaccinations, alternative delivery methods, questionnaire, jet injector, patch, microneedle device, nasal spray device

**Abbreviations:** NIP, immunization program; M, mean; SD, standard deviation

Last decades, the number of routine childhood vaccinations has increased considerably, which consequently has led to multiple vaccine injections per consultation. Implementation of additional vaccines will probably lead to more than 2 vaccine injections per consult, which might be a barrier for parents to vaccinate their child. A decrease in vaccination coverage, however, increases the risk of disease outbreaks. Less stressful alternative methods for vaccine delivery might lead to an increased acceptance of multiple childhood vaccinations by parents. The present questionnaire study was set up to explore the maximum number of vaccine injections per visit that is acceptable for parents, as well as to gauge parents' attitude toward alternative needle-free methods for vaccine delivery. For this purpose, the parents' opinion toward a jet injector, a patch, a microneedle system, and nasal spray device as methods for vaccine delivery was assessed. The majority of the 1154 participating parents indicated that 3 vaccine injections per visit was perceived as too much. Most participants had a positive attitude with respect to the jet injector and the patch as alternative vaccine delivery method, whereas the microneedle device and an intranasal spray device were not perceived as better than the conventional syringe by the parents. Parents indicated that both the jet injector and the patch might increase their acceptance of giving their children more than 2 vaccinations at the same time. This should encourage vaccine developers and manufacturers to put efforts in developing these delivery methods for their vaccines.

## Introduction

Vaccination has greatly reduced the burden of infectious diseases. The impact of vaccination on global health has been enormous. With the exception of clean water, no other modality, not even antibiotics, has had such a major effect on mortality reduction and population growth.<sup>1</sup> While eradication is the ultimate goal for an immunization program, to date only smallpox has been fully eradicated, allowing discontinuation of routine smallpox immunization globally. Other infectious diseases, such as diphtheria, tetanus, yellow fever, Hemophilis influenzae type B, poliomyelitis, measles, rubella, typhoid, and rabies, are largely controlled by vaccination.<sup>1</sup> However, ongoing national immunization programs remain essential to prevent outbreaks and epidemics of these diseases. Over the past 2 decades, the number of vaccinations given within national immunization schedules has grown rapidly. Vaccination schedules have become complicated as many new vaccines have been developed and implemented. Especially the number of routine infant vaccinations has increased. For this reason, infants receive more than one injection at the same time, with various vaccines containing different vaccine components. Taking into account

the ongoing development and availability of new vaccines, and the fact that most vaccines require multiple doses for maximum effectiveness, more than 2 vaccinations per consult may become necessary in the future. Multiple vaccine injections at one consultation, however, can be a source of distress for (young) children. In the Netherlands, a maximum of 2 vaccine injections per consultation are given routinely (Table 1). In a previous pilot study, 75% of the 187 participating health care professionals giving vaccinations and 76% out of 218 participating parents stated to have objections against more than 2 vaccine injections per visit.<sup>2</sup> Nevertheless, in that study, the participants were also in favor of extending the vaccination program with new vaccines against other infectious diseases, although dependent on which vaccine it concerns. Implementation of new vaccines for infants within national immunization programs, however, will probably lead to more injections per consult. Alternative delivery methods for vaccines that are less stressful for young children and easy to administer, such as patches or other needle-free devices, might be a way to increase the acceptability by parents of giving their children multiple vaccinations at the same time.<sup>3,4</sup> Alternative devices administer the vaccine directly to relevant sites of the body in order to be able to activate the immune system via

\*Correspondence to: Patricia Kaaijk; Email: patricia.kaaijk@rivm.nl  
Submitted: 04/11/2014; Revised: 05/15/2014; Accepted: 05/26/2014  
<http://dx.doi.org/10.4161/hv.29361>

**Table 1.** Vaccination schedule of the national immunization program of the Netherlands (at the time of performing this questionnaire study)

Age	Injection 1	Injection 2
At birth (<48 h)	HBV <sup>a</sup>	
6–9 wk	DTaP-HBV-IPV/Hib	Pneumo
3 mo	DTaP-HBV-IPV/Hib	Pneumo
4 mo	DTaP-HBV-IPV/Hib	Pneumo
11 mo	DTaP-HBV-IPV/Hib	Pneumo
14 mo	MMR	MenC
4 y	DTaP-IPV	
9 y	DT-IPV	MMR
12 y	HPV <sup>b</sup>	

<sup>a</sup>Only for children of whom the mother tested positive for HBsAg; <sup>b</sup>Only for girls; 3 doses at 0 d, 1 mo, and 6 mo. Abbreviations: HBV, Vaccine against hepatitis B virus; DTaP-HBV-IPV/Hib, Combination vaccine with diphtheria toxoid, tetanus toxoid, acellular pertussis, hepatitis B virus, inactivated poliomyelitis virus, and *Hemophilus influenzae* serotype b component; Pneumo, Pneumococcal vaccine; MMR, Measles, mumps, rubella vaccine; MenC, Vaccine against meningococcal serogroup C disease; DTaP-IPV, Combination vaccine with diphtheria toxoid, tetanus toxoid, acellular pertussis, and inactivated poliomyelitis virus; DT-IPV, Combination vaccine with diphtheria toxoid, tetanus toxoid, and inactivated poliomyelitis virus; HPV, Vaccine against human papillomavirus.

appropriate antigen-presenting cells. Furthermore, various delivery methods have the potential advantage of dose-sparing. In the present study, the parents' attitude toward the following needle-free alternative vaccine delivery methods, the jet injector,<sup>5,6</sup> the patch,<sup>7</sup> the microneedle system,<sup>8,9</sup> and intranasal spray device,<sup>10</sup> was explored. The vaccine delivery methods were selected based on the anticipated easiness for application and potentially close to the market, or already with marketing authorization (nasal spray device). Furthermore, the parents' attitude toward more than 2 injections per consultation was examined and the impact of the use of alternative delivery methods on the acceptance of more vaccinations at the same time.

## Results

### Response rate and demographic characteristics

The response rate was 21%; 1154 out of the 5600 approached parents completed the questionnaire. The demographic characteristics of the participants are presented in Table 2. In summary, 86% of the participants were female, and 82% of the parents were in the age category of 30–49 y. Half of the participants (50%) had 2 children, and 94% of the participants were born in the Netherlands. Most of the participants had an intermediate (42%) or higher education level (50%), and a modal family income (24%) (with a modal gross household income per year of €32500<sup>11</sup>) or above modal (41%).

### Vaccination status and factors that influenced vaccination behavior

Most parents (95%) reported that their children received all recommended vaccinations within the national immunization

program. Major reasons not to or incompletely vaccinate their child were: unclear what the vaccine does to the health of my child (15%), risk on occurrence of adverse events (15%), my child is receiving too many vaccinations (13%), my child is too young to be vaccinated (9.4%) or a presumed low risk of getting the disease prevented by vaccination (8.5%). A small proportion of the parents (4.5%) indicated that religious beliefs had influenced their opinion on vaccine uptake. In addition, users of homeopathy (3.4%) or naturopathy (2.9%), parents with anthroposophical lifestyle (2.1%) or another conviction (4.0%) indicated that their lifestyle or conviction influenced their vaccination behavior.

### Parents' intention to receive 3 vaccine injections per consultation for their child

The parents' attitude toward the current national immunization program (NIP) of the Netherlands or extension of the program was scored on a 7-point psychosocial Likert scale, with the end points labeled as 1 = totally disagree, and 7 = totally agree (4 = neutral). Parents indicated that they were in favor of extending the vaccination program with new vaccines against other infectious diseases (mean Likert scale score (M) of 5.47 (SD = 1.63); 77% with score >4). On the other hand, parents also indicate that the number of vaccinations in the current NIP is sufficient (M = 3.95, SD = 1.73, close to a neutral score; 37% with score >4). The majority of the parents (69% with score >4) indicated that 3 vaccine injections per visit is too much (M = 5.31, SD = 1.87). In addition, parents indicated to prefer an extra visit instead of more than 2 vaccine injection at the same time (M = 5.58, SD = 1.71; 77% with score >4). Nevertheless, when they were actually offered 3 vaccine injections per visit to their child, half of the parents indicated that they would probably still get these vaccinations (M = 4.31, SD = 2.04; 50% with score >4). Fathers were more likely to receive more than 2 vaccine injections per visit for their child than mothers were (fathers M = 4.69, SD = 2.01 (59% with score >4) vs. mothers M = 4.25, SD = 2.04 (49% with score >4);  $p_{\text{univariate}} = 0.011$ ). Furthermore, the intention to receive more than 2 vaccine injections per visit for their child appeared to be dependent on education. Higher educated parents were more likely to accept more than 2 vaccine injections per visit (high-education level M = 4.46, SD = 1.95 (54% with score >4), vs. M = 4.22, SD = 2.08 (48% with score >4), and M = 4.08, SD = 2.25 (44% with score >4) for parents with respectively intermediate- and low-education level;  $p_{\text{univariate}} = 0.025$ ). In addition, parents that indicated that their children received all recommended vaccinations within the national immunization program were also more likely to receive 2 vaccine injections or more per consultation for their child than parents not receiving all recommended vaccinations for all their children (respectively M = 4.38, SD = 2.01 (51% with score >4) vs. M = 3.11, SD = 2.13 (32% with score >4);  $p_{\text{univariate}} = 0.001$ ). Differences in intention to receive more than 2 vaccinations for above presented groups of parents were also significant in multivariate analysis ( $P < 0.05$ ).

The solicited disadvantages of receiving more than 2 vaccine injections at one visit with the highest mean scores were: 'detection of adverse events per vaccine is impossible', 'it is too much to process for my child's body' and 'the physical load is too high for my child' (Table 3).

**Table 2.** Demographic characteristics of the 1154 participants

Characteristic		% (n)			% (n)
<b>Gender</b>	<b>Female</b>	<b>86% (990)</b>			
	<b>Male</b>	<b>14% (164)</b>			
<b>Age</b>	Mean: 37.2 y, SD 7.5 y				
	<19 y	0.3 (3)			
	19–29 y	15 (171)			
	30–39 y	45 (518)			
	40–49 y	37 (428)			
	≥50 y	3 (34)			
<b>Number of children</b>	1	22% (250)			
	2	50% (578)			
	3	21% (245)			
	>4	7% (81)			
<b>Age of youngest child</b>	<1 y	35% (401)	<b>Age of oldest child</b>	<1 y	16% (179)
	1–3 y	10% (119)		1–3 y	9% (106)
	4–8 y	25% (285)		4–8 y	24% (277)
	9–11	20% (229)		9–11 y	20% (225)
	>12 y	10% (120)		>12 y	32% (367)
<b>Country of birth</b>	The Netherlands	94% (1087)			
	Suriname	1% (11)			
	The Netherlands Antilles and Aruba	0.6% (7)			
	Turkey	0.3% (3)			
	Morocco	0.3% (3)			
	Other	4% (43)			
<b>Country of birth (mother of participant)</b>	The Netherlands	92% (1062)			
	Other	8% (92)			
<b>Country of birth (father of participant)</b>	The Netherlands	91% (1050)			
	Other	9% (104)			
<b>Family income</b>	Below average	9% (102)			
	Average	24% (278)			
	Above average	41% (474)			
	Not answered	26% (300)			
<b>Highest education</b>	Lower level	7% (79)			
	Intermediate level	42% (477)			
	Higher level	50% (572)			
	Not answered	2% (26)			

Lower educational level was defined as the highest level of education being primary school, junior secondary technical school, or intermediate secondary education. Intermediate educational level was defined as the highest level of education being intermediate vocational education, higher secondary education, pre-university education. Higher educational level was defined as the highest level of education being higher vocational education and university.

**Table 3.** The solicited advantages or disadvantages for the intention to receive more than 2 vaccine injections per visit were listed in order of highest to lowest mean scores (n = 1154)

	Items	Mean (SD)
<b>Advantages</b>	Receiving 3 vaccine injections at one visit is more convenient, because it results in less stress than an extra visit	3.23 (2.00)
	Receiving 3 vaccine injections at one visit is more preferable, since there is only one moment for the risk of side effects	3.51 (2.00)
<b>Disadvantages</b>	Receiving more than 2 vaccine injections at one visit is not preferred, because detection of adverse events per vaccine is impossible	5.37 (1.51)
	Receiving more than 2 vaccine injections at one visit is not preferred, because it is too much to process for my child's body	4.90 (1.65)
	Receiving more than 2 vaccine injections at one visit is not preferred, because it the physical load is too high for my child	4.82 (1.75)
	Receiving more than 2 vaccine injections at one visit is not preferred, because the risk of more (serious) adverse events is too high	4.80 (1.68)
	Receiving more than 2 vaccine injections at one visit is not preferred, because it is too stressful for my child	4.54 (1.99)
	Receiving more than 2 vaccine injections at one visit is not preferred, because it is not good for my child's immune system	4.29 (1.69)

'Less stress than having an extra visit' and 'having the risk for side effects only once' were the determinants that were most related to the parent's intention willing to receive 3 vaccine injections for their child (partial correlation coefficient of respectively 0.21 and 0.19).

The intention to receive more than 2 vaccine injection per visit for their child depended on the age of the child (Table 4), and was lowest for children below 1 y of age, followed by children aged 4 y, 9-y-olds, and highest for 12-y-olds (all differences were statistically significant;  $P < 0.001$ ). When only the parents were considered that have or had children at the age of 4, 9, or 12 y, similar results were found although the scores were generally lower, indicating that these parents were slightly more critical (Table 4).

#### Parents' attitude toward alternative vaccine delivery methods

In general, parents preferred to vaccinate their child with a jet injector ( $M = 6.03$ ,  $SD = 1.17$ ) or a patch ( $M = 5.40$ ,  $SD = 1.69$ ) compared with the conventional syringe (resp. 89% and 76% with score  $>4$ ; Table 5). However, the microneedle device ( $M = 4.03$ ,  $SD = 1.76$ ) or an intranasal spray device ( $M = 3.86$ ,  $SD = 2.06$ ) were not perceived as better than the conventional syringe by the parents (resp. 39% and 42% with score  $>4$ ). A preference for the jet injector and the patch above the microneedle and nasal spray device was observed among all age groups. All studied alternative vaccine devices were judged as more appropriate for the older aged children than for the younger children ( $P < 0.05$ ), with the exception of the opinion on the jet injector that did not differ significantly for the 9- vs. the 12-y olds (Table 5). There was a clear distinction in the parents' attitude dependent on the age of the child regarding the acceptance of intranasal vaccination; the acceptance was low for children aged 4 y or younger ( $M \leq 2.85$ ,  $SD = 1.9$ ), whereas the acceptance was considerably higher for children aged 9 y or older ( $M \geq 4.32$ ,  $SD = 2.0$ ). Approximately half of the parents responded positive that when one vaccine was given to their child with the jet injector or a patch, the number of

vaccinations per visit could increase from 2 to 3 (resp. 55% and 44% with score  $>4$ ;  $M = 4.60$ ,  $SD = 1.93$  and  $M = 4.06$ ,  $SD = 2.03$ ). Parents were less positive about replacement of the conventional syringe injection by an intranasal or a microneedle delivery method in order to allow more vaccinations per visit (resp. 33% and 23% with score  $>4$ , and  $M = 3.58$ ,  $SD = 2.02$  and  $M = 3.35$ ,  $SD = 1.78$ ).

## Discussion

In the present study, the majority of parents (69% with score  $>4$ ) indicated that 3 vaccine injections per visit is too much. On the other hand, parents indicated that they were in favor of extending the vaccination program with new vaccines against other infectious diseases (77% with score  $>4$ ). The finding that parents appeared to be open for adding new vaccines to the national immunization schedule is in agreement with a multinational survey among 7 countries, including Australia, Canada, and several European countries.<sup>12</sup> In that study a maximum of 2 vaccine injections (42% of the parents) was preferred over a restriction of 1 injection (15%) or a maximum of 3 vaccine injections (10%) per visit, which is also in accordance with our findings. Also in other studies, the majority of parents would not want their child to have more than 2 injections during a single visit.<sup>2,13-15</sup> However, 28% of the parents in the multinational survey indicated that they would probably have their child vaccinated whenever their doctor recommends this.<sup>12</sup> This finding was also observed in a study performed in a pediatric clinic in the US, where infants were routinely offered more than 2 injections at each visit. The 3, 4, or 5 injections that were offered by the physician in that study were accepted by the parents, in respectively 99% ( $n = 434$ ), 99% ( $n = 188$ ), and 89% ( $n = 27$ ) of the cases.<sup>16</sup> Therefore, the actual acceptance of more injections could be higher than estimated based on questionnaire studies.

In the present study, half of the parents indicated that when 3 vaccine injections were actually offered per visit to their child, they would probably get these vaccinations. In various studies, the child's pain and discomfort was the major concern that was reported by both parents and health care providers regarding the administration of more than 2 vaccinations during a single visit.<sup>2,12,13,17</sup> In a study, it was even shown that parents are willing to pay money to reduce or avoid the pain and emotional distress associated with childhood vaccine injections.<sup>18-21</sup> For this reason, alternative delivery methods for vaccines that are less stressful for young children might be a way to increase the acceptability of more than 2 vaccinations at the same time.

To the best of our knowledge, this is the first study that investigates the parents' attitude toward alternative vaccine delivery methods. In this study, parents appeared to prefer to vaccinate their child with a jet injector ( $M = 6.03$ ,  $SD = 1.17$ ) or a patch ( $M = 5.40$ ,  $SD = 1.69$ ) compared with the conventional syringe (resp. 89% and 76% with score >4). However, no distinction could be made between the opinion of the parent with respect to a microneedle device ( $M = 4.03$ ,  $SD = 1.76$ ) or an intranasal spray device ( $M = 3.86$ ,  $SD = 2.06$ ) compared with a syringe (resp. 39% and 42% with score >4). The parents' opinion regarding the suitability of the various vaccine delivery methods to vaccinate their child appeared to be dependent on the age of the child. This was also observed for the acceptability of 3 vaccine injections per visit. The acceptability was highest in older children (12 y of age), followed by children aged 9 y, 4-y-olds and infants (<1 y). Strikingly, there was a clear distinction in the parents' attitude dependent on the age of the child regarding the acceptance of intranasal vaccination; the acceptance was low for children aged 4 y or younger, whereas the acceptance was considerably higher for children aged 9 y or older. It is important to note that the only intranasal vaccine that is currently licensed in the US and Europe, a live influenza vaccine, is indicated for persons above 2 y of age.<sup>22</sup> Clinical studies with this intranasal vaccine showed an increased risk of hospitalizations in recipients aged 6–11 mo compared with the placebo control group. Considering these safety aspects, it might be that intranasal vaccination for children <1 y will not be approved for the market by competent authorities.

Based on these results, alternative delivery methods for vaccines that are less stressful, especially jet injectors and patches might increase the acceptability by parents of giving their children more than 2 vaccinations at the same time. However, the results should be interpreted with some caution, because the various vaccine delivery methods were exemplified by showing a video visible within the online questionnaire. Although the videos were carefully selected to ensure that it had no promotional character, it cannot be ruled out that the type of video may have caused a certain degree of subjectivity in the parents' attitude. Another limitation of the study was that the participants appeared to have a higher average household income and were higher educated than average. However, this seems difficult to avoid and inherent to this type of questionnaire studies where highly educated people seem more likely to participate.<sup>23</sup> The intention to receive more than 2 vaccine injections per visit for their child appeared

**Table 4.** Mean scores of parents for the intention to receive more than 2 vaccine injections per consultation, per age group of the child

If 3 vaccine injections were offered, then I would get them all if my child were:	All parents	Only parents that <u>do</u> or <u>do not</u> have/ had children at the age of 4, 9, or 12 y	
	Mean (SD)	do not Mean (SD)	do Mean (SD)
<1 y	3.60 (2.13)	n.a.*	n.a.*
4 y	4.01 (2.06)	4.57 (1.93)	3.83 (2.06)
9 y	4.47 (2.08)	4.73 (2.00)	4.22 (2.12)
12 y	4.71 (2.09)	4.83 (2.03)	4.44 (2.19)

The intention to receive more than 2 vaccine injections per visit among all parents was lowest for children below 1 y of age, followed by children aged 4, 9, and 12 y-olds resp. (all differences were statistically significant;  $P < 0.001$ ); Scores for parents that have or had children in the age of 4, 9, or 12 y were significantly lower than parents that had only younger children ( $p$ -value were resp.  $P < 0.001$ ;  $P < 0.001$ ,  $P = 0.003$ ); \*All parents have or had children aged <1 y, i.e., inclusion criterium.

to be dependent on education; higher educated parents were more likely to accept more than 2 vaccine injections per visit. This is in agreement with findings from other studies and presented in a systematic review of factors underlying parental vaccination decisions, where in comparison with vaccine-acceptors, vaccine-decliners had lower incomes and levels of educational attainment.<sup>23,24</sup> For this reason, it might be that the parents in our study had a more positive attitude regarding multiple vaccinations per visit than the population norm. On the other hand, there was also an overrepresentation of females (86%), but male parents were more likely to accept more than 2 vaccine injections per visit for their child than females. This would again lead to a more critical attitude regarding multiple vaccinations per visit than the population norm, and this might perhaps abolish the effect of overrepresentation of higher educated and wealthier parents. Nevertheless, the percentage of parents (95%) that reported that their children received all recommended vaccinations within the national immunization program, is in agreement with the vaccination coverage of approximately 95% in the Netherlands.<sup>25</sup> This suggests that this questionnaire gives a good reflection with respect to vaccination behavior of the Dutch population.

In the Netherlands, the NIP is a voluntary program offering routine vaccination for children free of charge. Recent vaccination campaigns in the Netherlands, such as the HPV vaccination campaign and the H1N1 pandemic influenza vaccination in 2009, suggest that parents have become more critical with respect to vaccination.<sup>26,27</sup> Suboptimal vaccination coverage may result in disease outbreaks. The success of national immunization programs largely depend on the public's willingness to be vaccinated. Therefore, less stressful alternative methods of vaccine delivery that might increase the acceptance of childhood vaccinations by parents deserves more attention. The present questionnaire study shows that parents have a positive attitude with respect to the jet injector and the patch as alternative vaccine delivery method for the conventional syringe. This should encourage vaccine developers and vaccine companies to put efforts in developing these delivery methods for their vaccines.

**Table 5.** Mean scores of parents' perception of suitability of the various vaccine delivery methods to vaccinate their child at specific age

		Mean scores (SD)			
		Jet injector	Patch	Microneedles	Intranasal spray
<b>Preference compared with conventional syringe injection</b>		6.03 (1.17)	5.40 (1.69)	4.03 (1.76)	3.86 (2.06)
Age group	<1 y	5.10 (1.64)	3.66 (2.07)	3.55 (1.76)	2.65 (1.88)
	4 y	5.40 (1.47)	3.90 (2.00)	3.88 (1.72)	2.85 (1.85)
	9 y	5.57 (1.42)	4.92 (1.80)	4.35 (1.72)	4.32 (2.05)
	12 y	5.59 (1.44)	5.22 (1.71)	4.46 (1.73)	4.73 (2.02)

All comparisons among age groups are statistically significant with the exception of the opinion on the jet injector for 9 vs. 12-y-olds

## Respondents and Methods

### Study design

Between September 2012 and May 2013, this cross-sectional study was performed among Dutch parents with children aged between 0–12 y. A total of 5600 parents from both rural and urban areas across all 12 counties of the Netherlands were randomly selected from the national database for vaccination registration (Praeventis). Parents were approached with a letter send by e-mail, which contained an Internet link. The internet link gave, after completing a login code as indicated in the e-mail, direct access to the questionnaire. In the invitation letter and at the start of the questionnaire, participants were assured of their privacy and confidentiality of their responses. Participants who completed the questionnaire received a voucher of 10 euros as a tribute. Review by the Ethical Committee Board of this non-intervention questionnaire study was not required according to the 'Medical Research Involving Human Subjects Act' of the Netherlands (WMO). The study was performed in accordance with the Helsinki Declaration of 1975, and the obtained data were processed according to EU GCP guidelines.

### Questionnaire

The questionnaire consisted of 78 questions and completion of the survey was estimated to take 15 min. In addition, the online questionnaire contained 4 videos, demonstrating the 4 different alternative vaccine delivery methods (jet injector, patch, microneedles, intranasal spray device). In the videos the delivery methods were briefly described as listed below. The jet injector with a mechanical spring-based system and using a disposable needle-free syringe, penetrates the liquid vaccine through the skin at high speed, i.e., less than 1/3 of a second.<sup>5,6</sup> The patch is applied on the skin and needs to be left there for a few hours. Prior to the application of the patch, the skin is lightly roughened in order to partly remove the stratum corneum. The vaccine antigens are subsequently entered by passive diffusion through the pre-treated skin into the viable epidermis.<sup>7</sup> For the microneedle system, disposable microneedles are loaded on an injector. The injector with a mechanical spring-based system delivers vaccine in less than a second through the skin via the microneedles.<sup>8,9</sup> The nasal spray device creates a fine spray that primarily deposits the vaccine in the nose and nasopharynx. A half dose is administered per nostril.<sup>10</sup>

Demographic data of the participants, i.e., age, gender, country of origin, education, household income, number of children, as well as vaccination status of children, and philosophy of life that

influenced choice of vaccination were scored separately from the psychosocial measures with respect to parents' attitude toward number of vaccinations and alternative methods of vaccine delivery. The psychosocial measures were scored on a 7-point Likert scale labeled as 1 = totally disagree, 2 = disagree, 3 = somewhat disagree, 4 = neutral, 5 = somewhat agree, 6 = agree, and 7 = totally agree. Questions regarding the parents' vision toward childhood vaccinations, i.e., maximum number of vaccinations and attitude toward alternative vaccine delivery methods, were subdivided in questions concerning different age groups of the children (<1 y; 4 y; 9 y; >12 y), i.e., the same question was asked 4 times, each time with regard to a different age group. The age groups were based on the vaccination moments within the Dutch immunization program.

### Statistics

#### Only fully completed surveys were included in the statistical analysis

Characteristics of the study population were described with mean (M) and standard deviation (SD) in case of continuous variables and with percentages in case of categorical variables. Mean and SD, as well as the percentage with score >4 were calculated to describe parents' attitude toward (the extension of) the NIP, to describe their opinion on the solicited objections against more than 3 vaccine injections per visit, and to describe their vision with respect to various alternative vaccine delivery methods. To indicate whether the characteristics of the participants were related to parents' intention to receive 3 vaccine injections per consultation for their child, univariable and multivariable linear regression analysis was performed. To analyze whether the intention to receive 3 vaccine injections per visit was different for various ages of the child (<1 y vs 4 y vs 9 y vs 12 y of age), the scores for the 4 questions were compared with a repeated measures ANOVA. To assess which arguments were most important in determining the parents' intention to receive 3 vaccine injections per consultation for their child, we performed a multivariable linear regression and ranked the arguments according to the absolute value of their partial correlation coefficient. To analyze whether the opinion of the parents with regard to the suitability of the alternative vaccine delivery methods to vaccinate their child was different for various ages of the child (<1 y vs 4 y vs 9 y vs 12 y of age), the means for the 4 questions regarding age were compared with a repeated measures ANOVA. An analysis on clustering of responses was not performed, since the objective of the study was merely comparing the intention of vaccination (with different delivery methods) among parents.

For all statistical analysis, P values < 0.05 were considered statistically significant. Data were analyzed with IBM SPSS Statistics version 19.0.

## Disclosure of Potential Conflicts of Interest

The authors have no (financial or personal) conflicts of interest to declare.

## References

- Plotkin SL, Plotkin SA. A short history of vaccination: 1-16. In: Plotkin S, Orenstein W, Offit PA. Vaccines, 5th edition, Philadelphia: Saunders (Elsevier Inc.), 2008.
- Kaaijk P, Kleijne DE, Rots NY. Extending the number of vaccinations per visit: vision of parents and professionals [in Dutch] Uitbreiding aantal prikken per vaccinatieconsult: mening van ouders en professionals. Infectieziekten Bulletin 2012; Jaargang 23 (8). Themanummer Vaccinaties:265-7. <http://www.rivm.nl/dsresource?objectid=rivmp:187542&type=org&disposition=inline>
- Amorij JP, Kersten GF, Saluja V, Tonnis WF, Hinrichs WL, Slütter B, Bal SM, Bouwstra JA, Huckriede A, Jiskoot W. Towards tailored vaccine delivery: needs, challenges and perspectives. J Control Release 2012; 161:363-76; PMID:22245687; <http://dx.doi.org/10.1016/j.jconrel.2011.12.039>
- Matsuo K, Hirobe S, Okada N, Nakagawa S. Frontiers of transcutaneous vaccination systems: novel technologies and devices for vaccine delivery. Vaccine 2013; 31:2403-15; PMID:23523401; <http://dx.doi.org/10.1016/j.vaccine.2013.03.022>
- Soonawala D, Verdijk P, Wijmenga-Monsuur AJ, Boog CJ, Koedam P, Visser LG, Rots NY. Intradermal fractional booster dose of inactivated poliomyelitis vaccine with a jet injector in healthy adults. Vaccine 2013; 31:3688-94; PMID:23770332; <http://dx.doi.org/10.1016/j.vaccine.2013.05.104>
- Simon JK, Carter M, Pasetti MF, Sztein MB, Kotloff KL, Weniger BG, Campbell JD, Levine MM. Safety, tolerability, and immunogenicity of inactivated trivalent seasonal influenza vaccine administered with a needle-free disposable-syringe jet injector. Vaccine 2011; 29:9544-50; PMID:21986218; <http://dx.doi.org/10.1016/j.vaccine.2011.09.097>
- Seid RC Jr., Look JL, Ruiz C, Frolov V, Flyer D, Schafer J, Ellingsworth L. Transcutaneous immunization with Intercell's vaccine delivery system. Vaccine 2012; 30:4349-54; PMID:22682290; <http://dx.doi.org/10.1016/j.vaccine.2011.09.113>
- Kang SM, Song JM, Kim YC. Microneedle and mucosal delivery of influenza vaccines. Expert Rev Vaccines 2012; 11:547-60; PMID:22697052; <http://dx.doi.org/10.1586/erv.12.25>
- Van Damme P, Oosterhuis-Kafeja F, Van der Wielen M, Almagor Y, Sharon O, Levin Y. Safety and efficacy of a novel microneedle device for dose sparing intradermal influenza vaccination in healthy adults. Vaccine 2009; 27:454-9; PMID:1902318; <http://dx.doi.org/10.1016/j.vaccine.2008.10.077>
- Rose MA, Zielen S, Baumann U. Mucosal immunity and nasal influenza vaccination. Expert Rev Vaccines 2012; 11:595-607; PMID:22827245; <http://dx.doi.org/10.1586/erv.12.31>
- CBS statistics Netherlands: Inkomensverdeling [in Dutch]. <http://www.cbs.nl/nl-NL/menu/themes/inkomen-bestedingen/cijfers/extra/inkomensverdeling.htm>.
- Bakhache P, Rodrigo C, Davie S, Ahuja A, Sudovar B, Crudup T, Rose M. Health care providers' and parents' attitudes toward administration of new infant vaccines--a multinational survey. Eur J Pediatr 2013; 172:485-92; PMID:23271490; <http://dx.doi.org/10.1007/s00431-012-1904-4>
- Bedford H, Lansley M. More vaccines for children? Parents' views. Vaccine 2007; 25:7818-23; PMID:17920170; <http://dx.doi.org/10.1016/j.vaccine.2007.08.057>
- Theeten H, Hens N, Aerts M, Vandermeulen C, Roelants M, Hoppenbrouwers K, Van Damme P, Beutels P. Common attitudes about concomitant vaccine injections for infants and adolescents in Flanders, Belgium. Vaccine 2009; 27:1964-9; PMID:19368778; <http://dx.doi.org/10.1016/j.vaccine.2009.01.096>
- Mollema L, Wijers N, Hahné SJ, van der Klis FR, Boshuizen HC, de Melker HE. Participation in and attitude towards the national immunization program in the Netherlands: data from population-based questionnaires. BMC Public Health 2012; 12:57; PMID:22264347; <http://dx.doi.org/10.1186/1471-2458-12-57>
- Melman ST, Nguyen TT, Ehrlich E, Schorr M, Anbar RD. Parental compliance with multiple immunization injections. Arch Pediatr Adolesc Med 1999; 153:1289-91; PMID:10591308; <http://dx.doi.org/10.1001/archpedi.153.12.1289>
- Mills E, Jadad AR, Ross C, Wilson K. Systematic review of qualitative studies exploring parental beliefs and attitudes toward childhood vaccination identifies common barriers to vaccination. J Clin Epidemiol 2005; 58:1081-8; PMID:16223649; <http://dx.doi.org/10.1016/j.jclinepi.2005.09.002>
- Meyerhoff AS, Weniger BG, Jacobs RJ. Economic value to parents of reducing the pain and emotional distress of childhood vaccine injections. Pediatr Infect Dis J 2001; 20(Suppl):S57-62; PMID:11704725; <http://dx.doi.org/10.1097/00006454-200111001-00009>
- Theeten H, Hens N, Aerts M, Vandermeulen C, Roelants M, Hoppenbrouwers K, Van Damme P, Beutels P. Caregivers' willingness to pay to reduce the number of vaccine injections in infants. Pediatr Infect Dis J 2009; 28:61-3; PMID:19034063; <http://dx.doi.org/10.1097/INF.0b013e318184ee43>
- Lieu TA, Black SB, Ray GT, Martin KE, Shinefield HR, Weniger BG. The hidden costs of infant vaccination. Vaccine 2000; 19:33-41; PMID:10924784; [http://dx.doi.org/10.1016/S0264-410X\(00\)00154-7](http://dx.doi.org/10.1016/S0264-410X(00)00154-7)
- Gidengil C, Lieu TA, Payne K, Rusinak D, Messonnier M, Prosser LA. Parental and societal values for the risks and benefits of childhood combination vaccines. Vaccine 2012; 30:3445-52; PMID:22449423; <http://dx.doi.org/10.1016/j.vaccine.2012.03.022>
- Kaaijk P, Luytjes W, Rots NY. Vaccination against RSV: is maternal vaccination a good alternative to other approaches? Hum Vaccin Immunother 2013; 9:1263-7; PMID:23442726; <http://dx.doi.org/10.4161/hv.24096>
- Brown KF, Kroll JS, Hudson MJ, Ramsay M, Green J, Long SJ, Vincent CA, Fraser G, Sevdalis N. Factors underlying parental decisions about combination childhood vaccinations including MMR: a systematic review. Vaccine 2010; 28:4235-48; PMID:20438879; <http://dx.doi.org/10.1016/j.vaccine.2010.04.052>
- Hak E, Schönbeck Y, De Melker H, Van Essen GA, Sanders EA. Negative attitude of highly educated parents and health care workers towards future vaccinations in the Dutch childhood vaccination program. Vaccine 2005; 23:3103-7; PMID:15837208; <http://dx.doi.org/10.1016/j.vaccine.2005.01.074>
- van Lier E, Oomen PJ, Mulder M, Conyn-van Spaendonck MA, Drijfhout IH, de Hoogh PAAM, et al. RIVM Rapport 150202001/2013 Immunisation coverage National Immunisation Programme in the Netherlands; 2013. <http://www.rivm.nl/dsresource?objectid=rivmp:209251&type=org&disposition=inline>
- Rondy M, van Lier A, van de Kasstele J, Rust L, de Melker H. Determinants for HPV vaccine uptake in the Netherlands: A multilevel study. Vaccine 2010; 28:2070-5; PMID:20045095; <http://dx.doi.org/10.1016/j.vaccine.2009.12.042>
- Bults M, Beaujean DJ, Richardus JH, van Steenberghe JE, Voeten HA. Pandemic influenza A (H1N1) vaccination in The Netherlands: parental reasoning underlying child vaccination choices. Vaccine 2011; 29:6226-35; PMID:21736915; <http://dx.doi.org/10.1016/j.vaccine.2011.06.075>