Preventive Medicine 100 (2017) 41–49

Contents lists available at ScienceDirect

Preventive Medicine

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

Motivational and contextual determinants of HPV-vaccination uptake: A longitudinal study among mothers of girls invited for the HPV-vaccination

Mirjam Pot [a,b,*], Hilde M. van Keulen [b], Robert A.C. Ruiter [a], Iris Eekhout [b], Liesbeth Mollema [c], Theo W.G.M. Paulussen [b]

[a] Maastricht University, Department of Work & Social Psychology, P.O. Box 616, 6200 MD Maastricht, The Netherlands
[b] TNO Child Health, Netherlands Organization for Applied Scientific Research, P.O. Box 3005, 2316 ZL Leiden, The Netherlands
[c] National Institute for Public Health and the Environment (RIVM), Centre for Infectious Disease Control, P.O. Box 1, 3720 BA Bilthoven, The Netherlands

ARTICLE INFO

Article history:
Received 29 November 2016
Received in revised form 9 March 2017
Accepted 2 April 2017
Available online 4 April 2017

Keywords:
HPV
HPV-vaccination uptake
Cancer
Social-psychological determinants

ABSTRACT

Background. In the Netherlands, HPV-vaccination uptake among 12-year-old girls remains to be lower (61% in 2016) than expected. The present study is about 1) replicating the extent to which social-psychological determinants found in earlier cross-sectional studies explain HPV-vaccination intention, and 2) testing whether HPV-vaccination intention, as well as other social-psychological determinants, are good predictors of future HPV-vaccination uptake in a longitudinal design.

Methods. A random sample of mothers of girls invited for the vaccination in 2015 was drawn from the Dutch vaccination register (Praeventis) ($N = 36{,}000$) and from three online panels ($N = 2483$). Two months prior to the vaccination of girls, their mothers were requested to complete a web-based questionnaire by letter (Praeventis sample) or by e-mail (panel samples). HPV-vaccination uptake was derived from Praeventis. Backward linear and logistic regression analyses were conducted to examine most dominant predictors of HPV-vaccination intention and uptake, respectively. The total sample used for data analyses consisted of 8062 mothers. Response rates were 18% for the Praeventis sample and 47% for the panel samples.

Results. HPV-vaccination intention was best explained by attitude, beliefs, subjective norms, habit, and perceived relative effectiveness of the vaccination; they explained 83% of the variance in HPV-vaccination intention. Intention appeared to be the only stable predictor of HPV-vaccination uptake and explained 43% of the variance in HPV-vaccination uptake.

Conclusions. These results confirm what was found by earlier cross-sectional studies, and provide strong leads for selecting relevant targets in the planning of future communication strategies aiming to improve HPV-vaccination uptake.

1. Introduction

Worldwide, cervical cancer is the third most common cancer among women (Ferlay et al., 2010). Persistent infection by the human papillomavirus (HPV) appears the major cause of cervical cancer (Schiffman and Castle, 2003). In the Netherlands, yearly 600 new cases of cervical cancer are detected, of which 200 with fatal consequences (Gezondheidsraad, 2008), despite the national cervical cancer screening program for women aged 30–60 years (Braspenning et al., 2001). Therefore, since 2010, the HPV-vaccination of 12-year-old girls was included in the National Immunization Program (NIP). Beforehand, HPV-vaccination uptake was expected to be lower compared to the uptake rate usually found for other childhood d vaccinations in the Netherlands (around 95%), because the vaccine was new, targeting a sexual transmitted disease, and it was offered to a new age group and only to girls (Rondy et al., 2010). But, so far, HPV-vaccination uptake turned out to be even lower (61% in 2016) (van Lier et al., 2016) than was expected beforehand (70%). Earlier cross-sectional research (Van Keulen et al., 2013a; Van Keulen et al., 2013b) in the first two years after initial implementation of the HPV-vaccination showed mothers to be most important in the process of decision-making about their daughters' HPV-vaccination. Attitude, outcome beliefs, subjective norms, habit

* Corresponding author at: TNO Child Health, Netherlands Organization for Applied Scientific Research, P.O. Box 3005, 2316 ZL Leiden, The Netherlands.
E-mail address: mirjam.pot@tno.nl (M. Pot).

http://dx.doi.org/10.1016/j.ypmed.2017.04.005

strength, and decisional conflict were associated with significant proportions (82–94%) of the variance in the mothers' intention towards the HPV-vaccination of their daughter (Van Keulen et al., 2013b).

The aim of this study is to provide stronger leads for future education about the HPV-vaccination by 1) replicating the extent to which the social-psychological determinants found in earlier cross-sectional studies explain HPV-vaccination intention (Van Keulen et al., 2013a; Van Keulen et al., 2013b), and 2) longitudinally testing whether HPV-vaccination intention, as well as other social-psychological determinants, are good predictors of future HPV-vaccination uptake. We applied a briefer version of the questionnaire used by these former cross-sectional studies (Van Keulen et al., 2013a; Van Keulen et al., 2013b), to reduce the time burden for completing the questionnaire. We removed determinants that appeared non-significant in these former studies (e.g., opinions about alternative medicine) (Van Keulen et al., 2013a).

2. Methods

2.1. Participants and procedure

The study was approved by the METC, the ethical committee of the VU Medical Center in Amsterdam. The study was part of a planned evaluation of an innovative web-based intervention targeting mothers of girls-to-be-invited for the HPV-vaccination in 2015. Questionnaire data collected at baseline (January 2015, before the HPV-vaccination round) accounted for the social-psychological determinants and HPV-vaccination intentions. After completing that vaccination round, data about girls' actual HPV-vaccination uptake were derived from Praeventis. Because invited girls were given the opportunity to catch-up their missed HPV-vaccination, complete data on uptake came available 18 months after baseline (i.e., July 2016). We randomly recruited mothers from three internet panels (i.e., Veldkamp BV, Intromart GFK and NGO Flycatcher, $N = 2483$) in an attempt to guarantee a suitable subsample for the planned efficacy trial (Van Keulen et al., 2013a). These panels can be used for nationally representative surveys and surveys among subgroups. Panel members were recruited based on information about their characteristics, that is, being a mother of a 12-year-old girl. Panel members were pre-stratified by region for geographic diversity. In addition, we randomly recruited mothers of girls to-be-invited for the HPV-vaccination from Praeventis ($N = 36{,}000$). Praeventis is the Dutch electronic vaccination register which monitors the vaccination status for all children up to 18 years living in the Netherlands. Using this system, children are invited for receiving vaccinations to the NIP (van Lier et al., 2016). This subsample enabled us to anticipate the naturalistic condition for future implementation of the intervention, which provided the opportunity for testing the intervention's effectiveness. A flow diagram of the recruitment and response is shown in Fig. 1. In total, 537 participants were excluded, since they did not meet the inclusion criteria (i.e., female, aged 24–62 years, and having a daughter born in 2002). We also excluded participants that were found to be duplicates across the two samples ($n = 3$). The final response rate was 19% ($n = 6918$) in the Praeventis-sample and 47% ($n = 1144$) in the panel-sample. The final sample for data analyses consisted of 8062 mothers.

Participants received an invitational letter by mail (Praeventis-sample) or email (panel-sample), which included information about the study, a link to a secured website, and a unique code for entrance to the survey. On the website, participants were assured of their privacy, the confidentiality and security of handling their responses, and were informed that they could withdraw from participation at any time. Participants were then asked to provide informed consent and to give permission to have their daughters' HPV-vaccination status requested from Praeventis. A reminder was sent one week after the first invitation. The questionnaire was open for response January 17th–29th 2015.

2.2. The questionnaire

Mothers who consented to participate were asked to complete a web-based questionnaire. The empirical findings of Van Keulen et al. (Van Keulen et al., 2013a; Van Keulen et al., 2013b), the Theory of Planned Behaviour (Ajzen, 1991), Social Cognitive theory (Bandura, 1986) and the Health Belief Model (Becker, 1974) led to designing this questionnaire. The questionnaire was pre-tested and subsequently revised.

HPV-vaccination uptake was requested from Praeventis, which was registered as having received no, one or two injections. HPV-vaccination uptake was dichotomized into having received no HPV-injection (0 = not vaccinated) versus having received one or two HPV-injections (1 = vaccinated), as data-analyses indicated the largest differences on determinants between these two groups.

Social-psychological determinants accounted for were intention, attitude, risk perception, beliefs, anticipated regret, relative effectiveness of the HPV-vaccination compared to alternative methods, subjective norms, habit, and decisional conflict. Measurement details can be found in Table 1. Modifications that were made to the questionnaire used by the former study (Van Keulen et al., 2013a) concerned the assessments of intention, knowledge, subjective norms and self-efficacy, as described below.

HPV-vaccination intention was measured by two new items: 'are you planning on getting your daughter vaccinated against HPV?' and 'how big is the chance that you will get your daughter vaccinated?' (1 = definitely not/very low to 7 = definitely/very high). This was done because mothers in the former study had already made a decision about the HPV-vaccination, while in the present study, they had not.

The number of *subjective norms* items were reduced by only including the partner and daughter as social referents.

Self-efficacy was measured by two items from Van Keulen et al., (2013; 'having a good talk with my daughter about the HPV-vaccination' and 'having a good talk with my partner about the HPV-vaccination') (Van Keulen et al., 2013a), and three new items: 'guiding my daughter in the decision regarding the HPV-vaccination', 'motivating my daughter to have herself vaccinated' and 'getting the actual HPV-vaccination with my daughter'.

Knowledge was measured by eight items, of which two items from the former study ('HPV is a virus' and 'the HPV-vaccination in the Netherlands consists of three injections') were replaced by the items 'condoms fully protect against HPV' and 'my daughter does not need to get the HPV-vaccination if she is already sexually active' (−1 = incorrect, 0 = don't know, 1 = correct).

Socio-demographics were modeled as background variables: age, educational level, country of birth, and religion.

Level of education was measured by asking mothers about the highest completed level of education; it was classified as low (less than secondary or vocational education), intermediate (secondary through pre-university education) or high (professional or university education) (Van Keulen et al., 2013a).

Country of birth was dichotomized into 'Netherlands' versus 'other' because the percentage of participants in the latter category was too small (7%) for further subdivision.

Religion was measured by asking mothers about their religious convictions Religion was dichotomized into 'Protestant' (i.e., Protestant religion) versus 'not Protestant' (i.e., Roman Catholic, Muslim, Jewish, Buddhist, Hindu, other, or no religion), because data-analyses and earlier research showed that more people with a Protestant religion refrain from vaccination compared to the other groups (Van Keulen et al., 2013a).

2.3. Data analyses

Statistical Package for the Social Sciences (SPSS; version 22) was used for analyzing the data (IBM Corp., 2013). First, we examined the

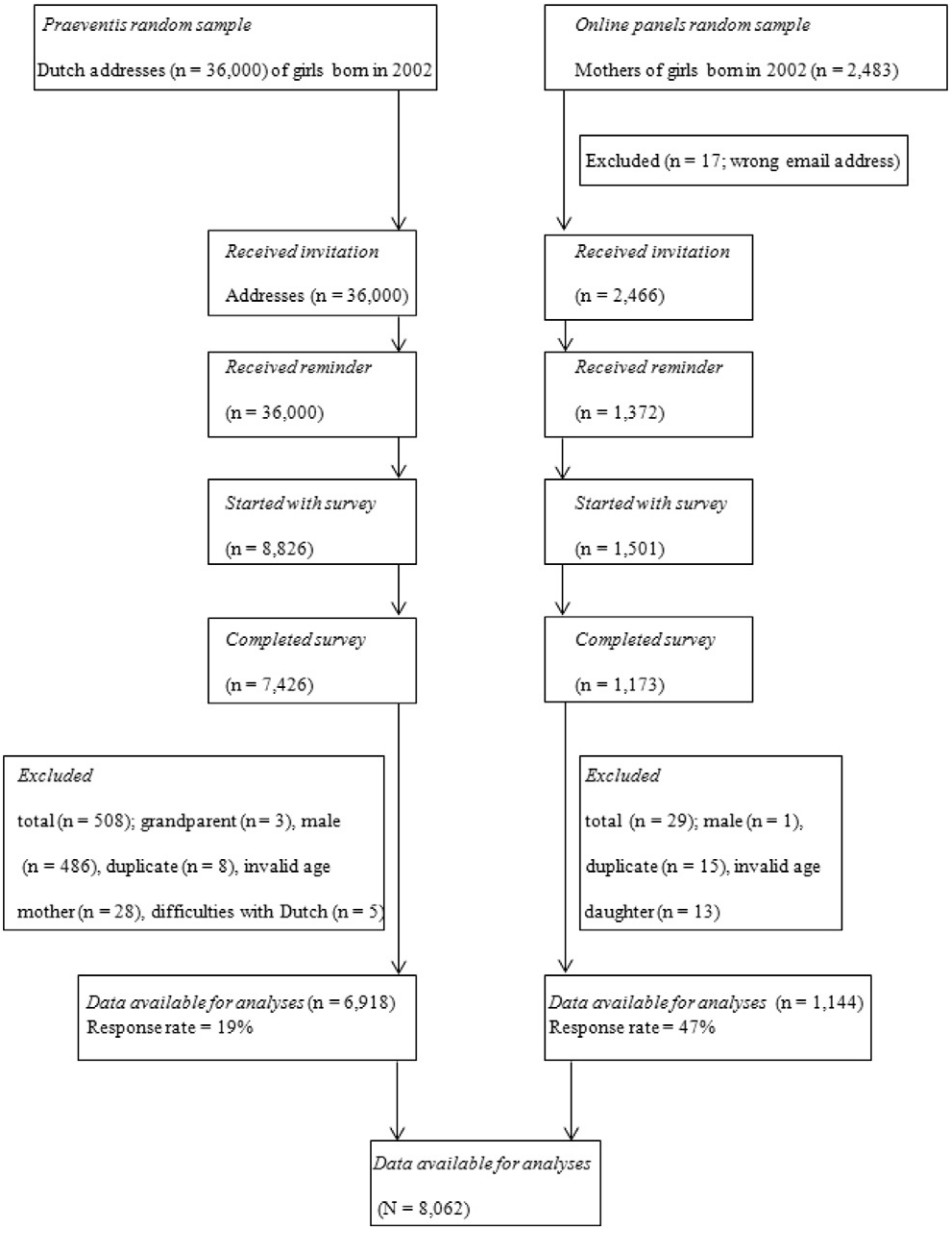

Fig. 1. Flow diagram of the recruitment and response of study participants. *Participants could be excluded based on multiple criteria (e.g., a male with an invalid age). Therefore, the total amount of Praeventis participants excluded differed from the sum of separate criteria for exclusion. This study has been conducted in the Netherlands, between January 2015–July 2016.

association between social-psychological determinants and HPV-vaccination intention by using univariate and multivariate regression analyses. Social-psychological determinants that appeared statistically significant in the univariate analyses ($p < 0.003$; Bonferroni corrected alpha = 0.05/17) were included in the multivariate linear regression analyses to assess the total amount of variance explained in HPV-vaccination intention, and to explore the unique proportion of variance explained by each step in the final regression model (1) social-psychological determinants; (2) socio-demographics; (3) sample background). Manual backward selection was used to exclude non-significant variables ($p > 0.003$; Bonferroni correction alpha = 0.05/17) except for socio-demographics and sample background because we wanted to forcefully adjust for these determinants in the final model. This provided us with the opportunity to address potential differences between mothers' with a different socio-demographic background and between the two different samples.

Social-psychological determinants that were significantly related to HPV-vaccination intention according to the multiple regression model ($p < 0.003$; Bonferroni correction alpha = 0.05/16) were entered in a logistic regression analysis, next to intention, with HPV-vaccination uptake as the outcome variable: (step 1) Intention; (2) social-psychological determinants; (3) socio-demographics; (4) sample background. Again, manual backward selection was used to exclude non-significant variables ($p < 0.005$; Bonferroni corrected alpha = 0.05/11), except for socio-demographics and sample background.

Both analyses using intention and uptake as the outcome variables, were performed on a random sample of 50% of the participants. The remaining 50% of participants were randomly split in: (1) one half (25% of the total sample) to check for stability (i.e., predictors from the final regression model of the first 50% sample were assumed stable when they remained significant in this 25% sample), and (2) the other half (the last 25% of the total sample) to check for generalizability. See Fig. 2 for a flowchart of the stepwise nature of the main analyses and the stability check. Model stability enables others to use the predictive model in different samples drawn from the same population (Palmer and O'Connell, 2009). The generalizability check was conducted in R (R Development

Table 1
Overview of social psychological measures[1TO].

Measure	Item	Answer options	Scale (minimum to maximum value)	Number of items	Cronbach's alpha (α) or Pearson's *r* (*r*) [2]	Reference
HPV-vaccination intention	Are you planning on getting your daughter vaccinated against HPV? How big is the chance that you will get your daughter vaccinated?	1 = definitely not to =7 = definitely yes 1 = very low to 7 = very high	1 = low intention to vaccinate to 7 = high intention to vaccinate	2	0.92 (*r*)	
Attitude towards the HPV-vaccination	Vaccinating my daughter against HPV is.	1 = very undesirable to 7 = very desirable; 1 = very bad to 7 = very good; 1 = very negative to 7 = very positive; 1 = very unimportant to 7 = very important.	1 = negative to 7 = positive attitude	4	0.98 (α)	(Paulussen et al., 2000)
Risk perception (having received no HPV-vaccination)	Imagine that your daughter was not vaccinated against HPV. The chance that my daughter will get cervical cancer is.	1 = very small to 7 = very large	1 = low to 7 = high risk perception (having received no HPV vaccination)	1	n/a	(Paulussen et al., 2000; Reiter et al., 2009)
Risk perception (having received the HPV-vaccination)	Imagine that your daughter was vaccinated against HPV. The chance that my daughter will get cervical cancer is.	1 = very small to 7 = very large	1 = low to 7 = high risk perception (having received the HPV vaccination)	1	n/a	(Paulussen et al., 2000; Reiter et al., 2009)
Anticipated regret about rejecting the HPV-vaccination	Imagine your daughter has not received the HPV-vaccination and she gets cervical cancer in the future. How much would you regret your decision to let her receive no vaccination?	1 = no regret and 5 = very much regret	n/a	1	n/a	(Van Keulen et al., 2013a)
Decisional conflict	As regards the HPV-vaccination	1 = completely	1 = high to 7 = low	3	0.94 (α)	(O'Connor, 1995)
About the HPV-Vaccination	– I felt sure what to choose; – The decision was relatively easy to make; – I was clear about the best choice for my daughter.	Disagree to 7= Completely agree	Decisional conflict			
Beliefs about the HPV-vaccination	– If the government offers the vaccination, I assume it will be safe; – Our government shows responsibility for the health of the Dutch population by introducing the HPV- vaccination; – The HPV-vaccination was only introduced because the pharmaceutical industry will earn a lot of money from it; – There is too little known about whether the HPV--vaccination effectively protects against cervical cancer; – There is too little known about the detrimental side effects of the HPV-vaccination; – My daughter is too young to receive the HPV-vaccination; – My daughter does not need the vaccination because she is not yet sexually active.	1 = completely disagree to 7 = completely agree	1 = negative to 7 = positive beliefs about the HPV vaccination	7	0.80 (α)	(Reiter et al., 2009; Gerend et al., 2009)
Subjective norms towards the HPV-vaccination[c]	*Normative beliefs* What is your expectation on the opinion of… about the HPV-vaccination of your daughter? Social referents: Partner, daughter *Motivation to comply* How motivated are you to comply with the opinion of…?	−2 = certainly not Vaccinating to 2 = certainly vaccinating, 3 = not applicable; Not applicable was recoded into '0' 1 = not at all to 5 = very much	−20 = negative to 20 = positive	2 2	0.64 (*r*)	(Paulussen et al., 2000)
Habit strength towards the HPV- vaccination	Letting my daughter receive the HPV- vaccination is something I do. – Automatically – Without thinking	1 = completely disagree to 7 = completely agree	1 = weak habit strength to 7 = strong habit strength	2	0.78 (*r*)	(Verplanken and Orbell, 2003)
Self-efficacy expectations towards the HPV- vaccination	– To what extend would you succeed in dealing with the following statements?	1 = I would certainly not succeed to 7 = I would	1 = low self-efficacy to 7 = high self-efficacy	4/5	0.82 (α)	

Table 1 (*continued*)

Measure	Item	Answer options	Scale (minimum to maximum value)	Number of items	Cronbach's alpha (α) or Pearson's *r* (*r*) [2]	Reference
	– Guiding my daughter in the decision regarding the HPV-vaccination – Having a good talk with my daughter about the HPV-vaccination – Having a good talk with my partner* about the HPV-vaccination – Motivating my daughter to have herself vaccinated – Getting the actual HPV- vaccination/two injections with my daughter	certainly succeed				
Knowledge about the HPV-vaccination[a]	– HPV is sexually transmittable; – Condoms fully protect against HPV; – My daughter is obliged to get the HPV-vaccination when she is invited; – You will always notice when you are infected by HPV; – Only women can get infected by HPV; – Women who received the HPV-vaccination are still advised to participate in the cervical cancer screening in the Netherlands; – r HPV-vaccination fully protects against cervical cancer; – My daughter does not need to get the HPV- vaccination if she is already sexually active.	−1 = incorrect 0 = don't know 1 = correct	−8 = incorrect 8 = correct	8	n/a	(Van Keulen et al., 2013a)
Relative effectiveness of the HPV vaccination[b]	How would you rate the effectiveness of the following methods of preventing cervical cancer: – Having safe sex – Having sex with only one person in a lifetime – Participating in the cervical cancer screening – Having a healthy lifestyle (e.g. not smoking) – The HPV vaccination – Participants rated the effectiveness of each method	1 = not at all effective to 10 = very effective	−9 = HPV vaccination least effective to 9 = HPV vaccination Most effective	5	n/a	(Van Keulen et al., 2013a)

Notes n/a = not applicable; 1 All scores on scaled items were averaged into a scale because they showed sufficient internal consistency (Cronbach's alpha ≥0.78 / Pearson's r > ≥0.64) 2 Cronbach's alpha was used for scales consisting of >2 items, whereas Pearson's *r* was used for scales consisting of 2 items; a) Knowledge is not a scale because the answer on one item does not predict the answer on other items; the items were summed up to present a sum score of knowledge; b) The difference between the rated effectiveness of the HPV vaccination and the most effective alternative represented the relative effectiveness score (−9 = HPV vaccination least effective to 9 = HPV vaccination most effective); c) The subjective norms score was first computed by multiplying normative beliefs and motivation to comply for each social referent, and then by summing up the multiplications of the social referents. *Only applicable if mother indicated that she had a partner. This study has been conducted in the Netherlands, between January 2015–July 2016.

Core Team, 2009) and examined the predictive value of the regression models for HPV-vaccination uptake in the general population. This was done to account for overestimation of the percentage of explained variance (Hastie et al., 2001). By keeping the estimated parameters (unstandardized regression coefficients) of the 50% sample model, we estimated the goodness-of-fit of the final regression model for the second 25% sample. We then compared the percentage of explained variance between the 50% and 25% samples, large differences indicated a large amount of overfitting (R Development Core Team, 2009).

3. Results

3.1. Sample description

The mean age of mothers was 44 years (SD = 4.25). Compared to the general Dutch population, the sample was overrepresented for women born in the Netherlands (76% versus 93%, respectively (CBS, 2016a)), for women with a high educational level (34% versus 43%, respectively) (CBS, 2016b)) and for HPV-vaccination uptake of girls (61% versus 73% (van Lier et al., 2016)). The sample was representative for religion (19% being Protestant compared to 16% in the Dutch population (CBS, 2015)). On average, mothers had a positive intention towards the HPV-vaccination of their daughter (M = 5.35, SD = 1.69). Mothers of whom the daughter received one or two HPV-injections reported a significantly higher HPV-vaccination intention than mothers of whom the daughter received no injection (M = 5.96, SD = 1.11, versus M = 3.70, SD = 1.89, respectively; $t(8046) = 65{,}81$. $p < 0.001$). Significant differences between the two different samples were found for all socio-demographics (i.e., age, country of birth, education, and religion).

3.2. Univariate and multivariate determinants of HPV-vaccination intention

All social-psychological measures were significantly ($p < 0.003$) associated with intention and were therefore included in the multiple linear regression analysis in the 50% sample ($n = 4015$; Table 2). These social-psychological determinants (step 1) accounted for 83% of the variance in intention ($p < 0.02$). Attitude, beliefs, decisional conflict, subjective norms, habit, anticipated regret and relative effectiveness were significantly associated with intention. Decisional conflict was removed from the final model (see Table 2), because the positive univariate association turned negative in the multivariate model, which might indicate a suppressor-effect. The proportion of unique variance in intention accounted for by the socio-demographic variables was small but significant (step 2; $\Delta R^2 = 0.001$, $p < 0.02$), whereas this was non-significant for sample background (step 3; $\Delta R^2 = 0.00$, $p > 0.02$).

The stability check ($n = 2015$) revealed that anticipated regret and risk perception no longer accounted for unique variance in intention (see Table 2). Again, decisional conflict was removed from the final model and further analyses because we were unable to interpret the

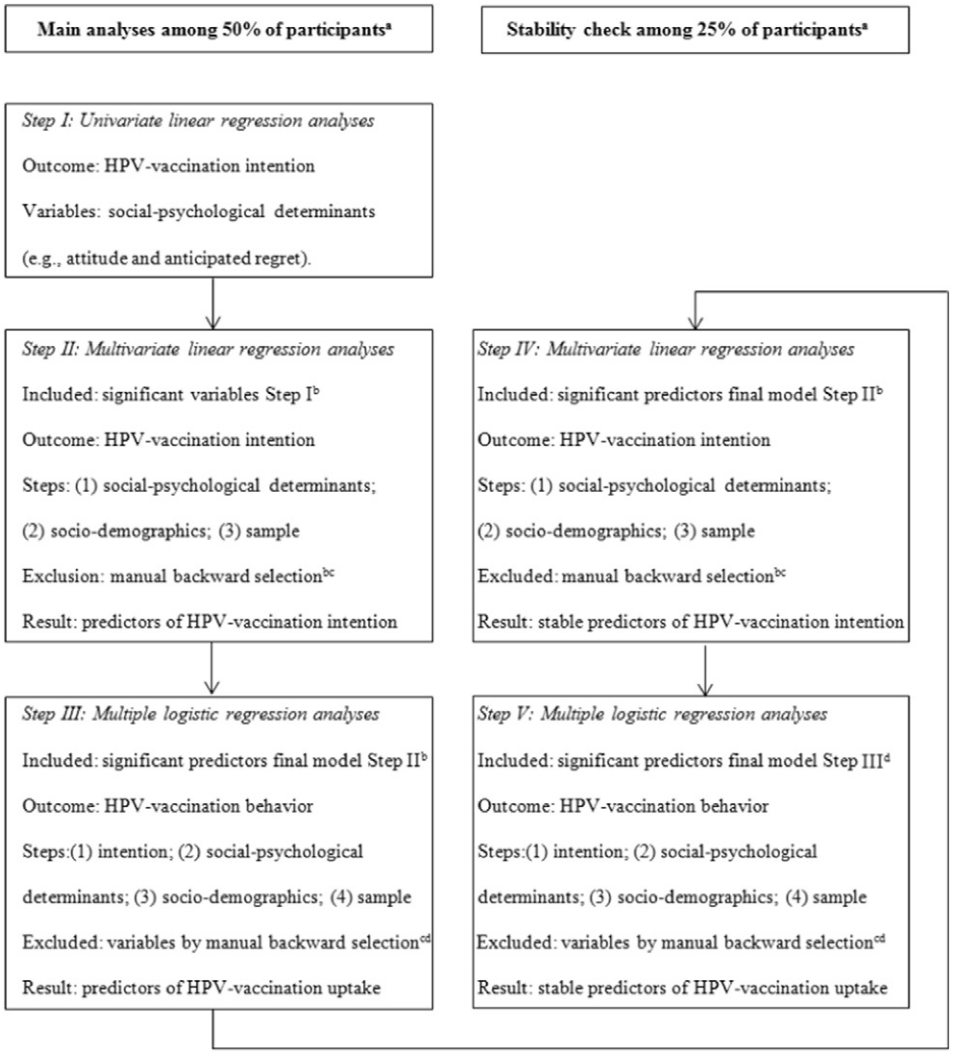

Fig. 2. Flowchart of the stepwise nature of the main analyses and the stability check.

switch to a negative association in the multivariate model. Attitude, beliefs, subjective norms, habit, and relative effectiveness were confirmed as stable determinants of intention and were therefore included in the analyses with HPV-vaccination uptake as the criterion. The generalizability check ($n = 2028$), confirmed the high proportion of explained variance found in the 50% sample ($R^2 = 83\%$ in both samples).

3.3. Multivariate prediction of HPV-vaccination uptake

Intention explained 43% of variance in HPV-vaccination uptake in the 50% sample (step 1; Nagelkerke $R^2 = 0.433$; Table 3). Both attitude and subjective norm added a small (Nagelkerke R^2 change $= 0.01$) unique proportion in uptake to what was explained by intention (step 2; $\chi 2$ $(2, N = 3994) = 40.18$, $p < 0.001$). Also, the socio-demographics added a small (Nagelkerke R^2 change $= 0.007$) but significant proportion to the explained variance in uptake (step 3; $\chi 2$ $(5, N = 3994) = 24.52$, $p < 0.01$). There was no significant additional impact of sample background (step 4; $\chi 2$ $(1, N = 3994) = 4.71$, $p = 0.03$; Nagelkerke R^2 change $= 0.001$). The stability check ($n = 2011$) revealed that intention and age were the only stable predictors of HPV-vaccination uptake in both the 50% and 25% sample. The generalizability check (sample 25% $n = 2028$) confirmed the high explained variance in the 50% sample (Nagelkerke $R^2 = 0.43\%$ in both samples).

3.4. Exploring the belief structure of the determinants of HPV-vaccination intention

Insight into the beliefs constituting the stable determinants of intention might be helpful for future communication about HPV-vaccination. Secondary simple linear regression analyses were therefore conducted for beliefs, subjective norms, and relative effectiveness to indicate the association between each item of the scale and HPV-vaccination intention. This did not account for attitude and habit since the items were too general to have relevance for future communication. All items of the constructs were moderately to strongly associated with intention (β's ranged from 0.40 to 0.74, $p < 0.001$; Table 4). Moderately to strong associations were found between HPV-vaccination intention and beliefs about (1) the responsibility of the government with regard to the HPV-vaccination, (2) the daughters' sexual behaviour and age in relation to the need for the HPV-vaccination, (3) the safety and effectiveness of the HPV-vaccination, and (4) the role of the pharmaceutical industry in the HPV-vaccination.

As for subjective norms, both the partner ($\beta = 0.74$, $p < 0.001$) and daughter ($\beta = 0.67$, $p < 0.001$) appeared influential. The relation between the HPV-vaccination intention and the relative effectiveness of each of the alternative methods to protect against cervical cancer compared to the HPV-vaccination appeared equally as strong (β's ranging from 0.48 to 0.53, $p < 0.001$). The HPV-vaccination was considered less

Table 2
Associates of the mothers' HPV-vaccination intention.

Variables (scale range)***	Univariate simple regression analysis among 50% of the mothers ($n = 4015$)			Multivariate backward regression analysis among 50% of the mothers ($n = 4002$)		Multivariate backward regression analysis among 25% of the mothers ($n = 2015$)	
	Mean (standard deviation) or percentage	Beta (standard error)	Standardized beta	Beta (standard error)	Standardized beta	Beta (standard error)	Standardized beta
*Social psychological variables****							
Attitude (1–7)	5.17 (1.48)	1.02 (0.01)	0.88*	0.56 (0.02)	0.48*	0.57 (0.02)	0.49*
Risk perception (having received no HPV vaccination) (1–7)	3.73 (0.98)	0.61 (0.03)	0.35*	n/a	n/a	n/a	n/a
Risk perception (having received the HPV vaccination) (1–7)	2.76 (1.07)	−0.29 (0.03)	−0.18*	n/a	n/a	n/a	n/a
Anticipated regret (1–7)	3.70 (1.26)	0.79 (0.02)	0.58*	0.08 (0.01)	0.06*	n/a	n/a
Decisional conflict (1–7)	4.36 (1.75)	0.32 (0.02)	0.32*	n/a	n/a	n/a	n/a
Beliefs (1–7)	4.21 (0.74)	1.65 (0.03)	0.71*	0.21 (0.02)	0.09*	0.22 (0.03)	0.10*
Subjective norm(−20−20)	5.95 (7.90)	0.17 (0.00)	0.78*	0.05 (0.00)	0.23*	0.06 (0.00)	0.27*
Habit (1–7)	4.29 (1.80)	0.69 (0.01)	0.73*	0.08 (0.01)	0.09*	0.07 (0.01)	0.08*
Self-efficacy (1–7)	6.27 (0.73)	0.68 (0.04)	0.29*	n/a	n/a	n/a	n/a
Knowledge (−8–8)	4.42 (2.17)	−0.04 (0.01)	−0.05*	n/a	n/a	n/a	n/a
Relative effectiveness (−9–9)	−2.01 (2.25)	0.51 (0.01)	0.67*	0.07 (0.01)	0.10*	0.08 (0.01)	0.10*
Socio-demographic variables							
Age	43.63 (4.25)	0.03 (0.01)	0.07*	0.01 (0.00)	0.02	0.01 (0.00)	0.02*
Highest completed level of education							
Low (reference)	14%						
Intermediate	43%	−0.07 (0.03)	−1.38	−0.02 (0.01)	−0.45	−0.02 (0.02)	−0.50
High	43%	0.07 (0.03)	1.38	−0.02 (0.01)	0.45	0.02 (0.02)	0.49
Country of birth							
The Netherlands (reference)	93%						
Other	7%	−0.33 (0.11)	−0.05*	0.11 (0.05)	0.02		
Protestant religion							
No (reference)	81%						
Yes	19%	−0.60 (0.07)	−0.14*	−0.07 (0.03)	−0.02	−0.02 (0.04)	−0.01
Sample							
Praeventis (reference)	85%						
Online panel	15%	−0.30 (0.08)	−0.06*	−0.07 (0.03)	−0.02	−0.07 (0.05)	−0.02
Model fit for multivariate models							
R2 of social-psychological variables					0.827		0.815
R2 change of social-psychological variables					0.827		0.815
F change of social-psychological variables					3172.28**		1773.41**
R2 of social-psychological variables + socio-demographic variables					. 828		0.817
R2 change of social-psychological variables + socio-demographic variables					0.001		0.002
F change of social-psychological variables + socio-demographic variables					5.00**		3.82**
R2 of social-psychological variables + socio-demographic variables + sample					0.828		0.817
R2 change of social-psychological variables + socio-demographic variables + sample					0.00		0.00
F change of social-psychological variables + socio-demographic variables + sample					4.78		2.54
Generalization check ($n = 2021$) R^2	0.83						

Notes * $p < 0.003$ (Bonferroni: 0.05/17 factors); ** $p < 0.02$ (Bonferroni: 0.05/3 a steps); n/a = not applicable: these variables were excluded from the final model manually by backward regression analyses, *** Higher scores represent a more positive opinion about the HPV-vaccination, whereas, a higher score on decisional conflict represents more decisional conflict. This study has been conducted in the Netherlands, between January 2015–July 2016.

effective than having safe sex, participating in the cervical cancer screening and having a healthy lifestyle.

4. Discussion

This study was about a) replicating the extent to which the social-psychological determinants found in earlier cross sectional studies explain HPV-vaccination intention (Van Keulen et al., 2013a; Van Keulen et al., 2013b), and b) testing whether HPV-vaccination intention, as well as other social-psychological determinants are good predictors of future uptake of girls invited for the HPV-vaccination. To our knowledge, this is one of the first studies using a longitudinal study design to predict HPV-vaccination uptake (Hofman et al., 2014).

HPV-vaccination uptake was best explained by intention (43% explained variance), which was also found by Hofman and colleagues (Hofman et al., 2014). Moreover, intention was the single stable predictor of uptake, which provides support for the applicability of social cognitive models for predicting HPV-vaccination uptake (e.g., the Reasoned Action Approach (Fishbein and Ajzen, 1975)). In turn, attitude, beliefs, subjective norms, habit, and relative effectiveness explained significant unique proportions of variance in HPV-vaccination intention (83% explained variance). These findings confirm what was found in former cross-sectional studies (Van Keulen et al., 2013a; Van Keulen et al., 2013b), including the result that intention is predominantly attitude-driven, most importantly constituted in beliefs about (1) the responsibility of the government with regard to the HPV-vaccination, (2) the daughters' sexual behaviour and age in relation to the need for the

Table 3
Predictors of HPV-vaccination uptake.

	50% of the mothers ($n = 3994$) $N_{missing} = 15$		25% of the mothers ($n = 2011$) $N_{missing} = 8$	
	Odds ratio	95% C·I	Odds ratio	95% CI
Intention	1.78*	1.59–1.98	2.21*	1.97–2.48
Attitude	1.30*	1.14–1.47	n/a	n/a
Subjective norm	1.04*	1.02–1.06	n/a	n/a
Habit	n/a	n/a	1.25*	1.13–1.38
Beliefs	n/a	n/a	n/a	n/a
Relative effectiveness	n/a	n/a	n/a	n/a
Age	1.03	1.01–1.06	1.06*	1.03–1.10
Highest completed level of education				
Low (reference)				
Intermediate	0.93	0.84–1.02	0.84	0.73–0.97
High	1.08	0.98–1.19	1.19	1.04–1.37
Country of birth				
The Netherlands (reference)				
Other	0.74	0.50–1.08	0.84	0.50–1.40
Protestant religion				
No (reference)				
Yes	0.74	0.59–0.92	0.83	0.59–1.16
Sample	0.76	0.59–0.97	0.71	0.50–1.01
$\chi 2$ of intention (df)	1406.99 (1)**		717.87 (1)**	
Nagelkerke R2	0.43		0.44	
$\chi 2$ of social-psychological variables (df)	40.18 (2)**		15.10 (1)**	
Nagelkerke R2	0.44		0.45	
$\chi 2$ of social demographic (df)	24.52 (5)**		27.78 (5)**	
Nagelkerke R2	0.45		0.46	
$\chi 2$ of sample (df)	4.71 (1)		3.57 (1)	
Nagelkerke R2	0.45		0.46	
Generalizability check ($n = 2019$) Nagelkerke R2	0.43			

Notes *$p = 0.005$ (Bonferroni: 0.05/11 variables) **$p = .01$ (Bonferroni: 05/4 steps); a positive OR (OR > 1) represents a higher likelihood of HPV-vaccination uptake; the more positive the score, the higher the chance of the daughter being vaccinated. A negative OR (OR < 1) represents a lower likelihood of HPV-vaccination uptake; the more negative the score, the lower the chance of the daughter being vaccinated; n/a = backward regression analyses led to the exclusion of these determinants from the final model. This study has been conducted in the Netherlands, between January 2015 – July 2016.

HPV-vaccination, (3) the safety and effectiveness of the HPV-vaccination, and the (4) role of the pharmaceutical industry in the HPV-vaccination.

Mothers in the present study considered the HPV-vaccination as less effective in preventing cervical cancer than having a healthy lifestyle, which was also found in previous research (Van Keulen et al., 2013a; Van Keulen et al., 2013b). This is surprising, because the available research has shown us otherwise (International Agency for Research on Cancer, 2005). These misperceptions (e.g., underestimating the effectiveness of the HPV-vaccination while overestimating the effectiveness of having a healthy lifestyle) should be corrected in future communication. For instance, by referring to facts about the absolute versus relative effectiveness of protective methods as is indicated by various studies (Munoz et al., 2006; Schiffman et al., 2007).

The influence from both the mothers' partner and daughter (subjective norms) appeared important constituent for the mothers' HPV-vaccination intention. Therefore, future communication should also target the partner and daughter. In the case of the daughter, not only because she appeared an important referent for the mother, but as valuable target in its own right since Dutch girls are formally entitled to decide themselves about the HPV vaccination.

As regards to habit, the results showed that mothers had higher intentions to let their daughters receive the HPV-vaccination if they perceived this as something they did automatically, without thorough examining the pros and cons. It might be tempting to leave this situation as it is, since this relatively large group of mothers is more likely to comply to the invitation to get their daughter vaccinated. However, a less informed decision is constituted in rather instable beliefs which are susceptible to counterarguments. Nowadays, many counterarguments can be found on the internet and online social media, posted by, for instance, worried parents, anti-vaccination groups, and the alternative medical community (Kata, 2012). Therefore, future education should initiate active processing of verifiable information about the risks and effectiveness of the HPV-vaccination in order to inoculate these mothers with arguments that become accessible in case they are confronted with (new) information that might challenge their initial positive intentions (McGuire, 1964; Paulussen et al., 2006).

The present study suggests that attitude, beliefs, subjective norms, habit, and relative effectiveness are priority targets for future education about the HPV-vaccination, because these appeared stable determinants of the mothers' HPV-vaccination intention. But because univariate regression analyses showed that anticipated regret, risk perception, self-efficacy, and knowledge were also associated with HPV-vaccination intention, these remain relevant targets for future education as well.

The present study had some limitations. First, the total study sample did not fully represent the Dutch population. The sample was overrepresented for mothers born in the Netherlands, those having high levels of education, and those having daughters being vaccinated against HPV. A possible source of selection bias could be that access to the Internet was required for participation. However, the percentage of internet availability and usage in the Netherlands is high; 86% of individuals are daily users and 97% of households has access to the Internet (Eurostat, 2017). Therefore, we do not consider this to be a source of selection bias. Furthermore, participants from the panels could differ from a more 'naturalistic' setting as they actively chose both to be part of a panel and to participate in this study and, therefore, are self-selected. In addition, participants from the panels received a reward for their participation, whereas participants from Praeventis did not. However, although this will limit generalization of the presented mean-scores and percentages, it will hardly have obscured the tested associations, as these are less sensitive for sample selection.

Besides, the present study also had important strengths. The first is the longitudinal design, which allows us to verify the extent to which HPV-vaccination intentions predict actual uptake. Also, there was a strong fit between our empirical results and theoretical assumptions in social cognitive models predicting vaccination uptake; there was a strong relationship between intention and uptake, and between intention and the social-psychological determinants. Another strength was the quality of the renewed questionnaire; it had high predictive validity ($R^2 = 0.83$) and all scales showed sufficient reliability (Cronbach's $\alpha \geq 0.80$ and Pearson's $r \geq 0.64$). Also, the use of registered instead of self-reported uptake had added value.

In conclusion, this study provides a stable and generalizable model for predicting HPV-vaccination uptake. HPV-vaccination intention was best explained by attitude, beliefs, subjective norms, habit, and relative effectiveness of the HPV-vaccination; 83% of the variance of intention was explained by these factors. In turn, intention appeared to be the only stable predictor of HPV-vaccination uptake and explained 43% of the variance in uptake. This confirms earlier cross-sectional studies, and provides strong leads for selecting relevant targets in the planning of future communication strategies aiming to improve HPV-vaccination uptake: Future education should (1) focus on the most relevant determinants in decision-making about the HPV-vaccination (i.e., attitude, beliefs, subjective norms, habit, and relative effectiveness) and (2) target the partner and daughter because they appeared to be important social referents for the mother and because girls have their own right to know.

Conflict of interest statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

Table 4
Relationship of items of stable social-psychological determinants with the mothers' HPV-vaccination intention.

Variabels/items	Univariate simple regression analyses ($n = 4009$)		
	Mean (SD)	Beta (standard error)	Standardized beta
Beliefs about the HPV-vaccination (1–7)[a]			
– If the government offers the vaccination, I assume it will be safe;	4.87 (1.63)	0.69 (0.01)	0.65*
– Our government shows responsibility for the health of the Dutch population by introducing the HPV-vaccination;	5.01 (1.24)	0.80 (0.02)	0.58*
– My daughter does not need the vaccination because she is not yet sexually active.	2.62 (1.49)	−0.59 (0.02)	−0.51*
– There is too little known about the detrimental side effects of the HPV-vaccination;	5.24 (1.26)	−0.65 (0.02)	−0.48*
– The HPV-vaccination was only introduced because the pharmaceutical industry will earn a lot of money from it;	3.17 (1.50)	−0.56 (0.02)	−0.49*
– My daughter is too young to receive the HPV-vaccination;	3.11 (1.47)	−0.53 (0.02)	−0.46*
– There is too little known about whether the HPV-vaccination effectively protects against cervical cancer;	4.62 (1.38)	−0.50 (0.02)	−0.40*
Subjective norms towards the HPV-vaccination (−10; −10)[b]			
– Partner	3.67 (4.74)	0.27 (0.00)	0.74*
– Daughter	2.28 (3.98)	0.29 (0.01)	0.67*
Relative effectiveness of the HPV-vaccination (−9; −9)[c]			
– Participating in the cervical cancer screening	−0.1.31 (2.59)	0.35 (0.01)	0.53*
– Having a healthy lifestyle (e.g. not smoking)	−0.23 (3.02)	0.30 (0.01)	0.52*
– Having sex with only one person in a lifetime	2.04 (3.57)	0.24 (0.01)	0.51*
– Having safe sex	−0.20 (3.35)	0.25 (0.01)	0.48*

Notes * $p < 0.001$; [a] Higher scores represent a more positive opinion about HPV vaccination; [b] Higher scores represent a more positive subjective norm; [c] The relationship between relative effectiveness and intention was measured for each method by the association between intention and the difference between rated effectiveness of the HPV-vaccination and the alternative method; higher scores indicate the HPV-vaccination was rated as more effective in preventing cervical cancer than the alternative method. This study has been conducted in the Netherlands, between January 2015–July 2016.

Acknowledgements

We would like to thank Petra Oomen (National Institute for Public Health and the Environment) for her help with data collection.

References

Ajzen, I., 1991. The theory of planned behaviour. Organ. Behav. Hum. Decis. Process. 50, 179–211.
Bandura, A., 1986. Social Foundations of Thought and Action: A Social Cognitive Theory. Prentice Hall, New York.
Becker, M.H., 1974. The health belief model and personal health behaviour. Health Educ. Monogr. 30, 324–508.
Braspenning, J., Tacken, M., Penders, A., Van den Hoogen, H., De Bakker, D., 2001. Opkomst bevolkingsonderzoek baarmoederhalskanker, 1997–1999. TSG 6, 341–345.
CBS, 2015. Religieuze betrokkenheid van bevolkingsgroepen, 2010–2014. Centraal Bureau voor de Statistiek. https://www.cbs.nl/-/media/imported/documents/2015/20/2015bt11-religieuze-betrokkenheid-van-bevolkingsgroepen-20102014.pdf [accessed 16.09.2016].
CBS, 2016a. Bevolking per maand; 20 tot 65 jarigen; vrouwen; herkomst; alle generaties. Centraal Bureau voor de Statistiek. http://statline.cbs.nl/Statweb/publication/?DM=SLNL&PA=71090ned&D1=0&D2=l&D3=0,121&D4=0-1&D5=0&D6=4-6,52-54,112-114,124-126&HDR=T,G3&STB=G2,G4,G5,G1&VW=T [accessed 16.09.2016].
CBS, 2016b. Bevolking; hoogst behaald onderwijsniveau; vrouwen; 25 tot 65 jaar. Centraal Bureau voor de Statistiek. http://statline.cbs.nl/Statweb/publication/?DM=SLNL&PA=82275ned&D1=0&D2=l&D3=3-6&D4=0-1,4-5&D5=0,4-5,8,12-13&D6=60-66&HDR=T,G1,G3,G5&STB=G2,G4&VW=T [accessed 16.09.2016].
Eurostat, 2017. Internet Access and Use Statistics - Households and Individuals. http://ec.europa.eu/eurostat/statistics-explained/index.php/Internet_access_and_use_statistics_-_households_and_individuals [accessed 03.03.2017].
Ferlay, J., Shin, H.R., Bray, F., Forman, D., Mathers, C., Parkin, D.M., 2010. Estimates of worldwide burden of cancer in 2008. Int. J. Cancer 127 (12):2893–2917. http://dx.doi.org/10.1002/ijc.25516.
Fishbein, M., Ajzen, I., 1975. Beliefs, Attitude, Intention and Behaviour: An Introduction to Theory and Research. Addison-Wesley, Reading, MA.
Gerend, M.A., Weibley, E.B.S., Bland, H.M.D., 2009. Parental response to human papillomavirus vaccine availability: uptake and intentions. J. Adolesc. Health 45 (5):528–531. http://dx.doi.org/10.1016/j.jadohealth.2009.02.006.
Gezondheidsraad, 2008. Vaccinatie tegen baarmoederhalskanker. Den Haag: Gezondheidsraad 154.
Hastie, T., Tibshirani, R., Friedman, J., 2001. The Elements of Statistical Learning: Data Mining, Inference, and Prediction. Springer, New York.
Hofman, R., van Empelen, P., Richardus, J.H., de Kok, I.M.C.M., de Koning, H.J., van Ballegooijen, M., et al., 2014. Predictors of HPV vaccination uptake: a longitudinal study among parents. Health Educ. Res. 29 (1):83–96. http://dx.doi.org/10.1093/her/cyt092.
IBM Corp, 2013. IBM SPSS Statistics for Windows, Version 22.0. IBM Corp, Armonk, NY.
International Agency for Research on Cancer, 2005. Cervix Cancer Screening. 10. IARC Press, Lyon.
Kata, A., 2012. Anti-vaccine activists, web 2.0, and the postmodern paradigm–an overview of tactics and tropes used online by the anti-vaccination movement. Vaccine 30 (25):3778–3789. http://dx.doi.org/10.1016/j.vaccine.2011.11.112.
McGuire, W.J., 1964. In: Berkowitz, L. (Ed.), Advances in experimental social psychology. Vol. I. Academic Press, New York, pp. 191–229.
Munoz, N., Castellsague, X., de Gonzalez, A.B., Gissmann, L., 2006. Chapter 1: HPV in the etiology of human cancer. Vaccine 24 (Suppl. 3):S1–S10. http://dx.doi.org/10.1016/j.vaccine.2006.05.115.
O'Connor, A.M., 1995. Validation of a decisional conflict scale. Med. Decis. Mak. 15 (1): 25–30. http://dx.doi.org/10.1177/0272989X9501500105.
Palmer, P.B., O'Connell, D.G., 2009. Regression analysis for prediction: understanding the process. Cardiopulm Phys. Ther. J. 20 (3), 23–26.
Paulussen, T.G., Hoekstra, F., Lanting, C.I., Buijs, G.B., Hirasing, R.A., 2006. Determinants of Dutch parents' decisions to vaccinate their child. Vaccine 24 (5):644–651. http://dx.doi.org/10.1016/j.vaccine.2005.08.053.
Paulussen, T.G.W., Lanting, C.I., Buijs, G.B., Hirasing, R.A., 2000. Ouders over het Rijksvaccinatieprogramma: Tevredenheid en Vaccinatiebereidheid van Ouders van Jonge Kinderen in Nederland [Parents about the Governments Immunization Program: Satisfaction and Vaccine Intention of Dutch Parents of Toddlers]. TNO, Leiden.
R Development Core Team, 2009. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna.
Reiter, P.L., Brewer, N.T., Gottlieb, S.L., McRee, A.L., Smith, J.S., 2009. Parents' health beliefs and HPV vaccination of their adolescent daughters. Soc. Sci. Med. 69 (3):475–480. http://dx.doi.org/10.1016/j.socscimed.2009.05.024.
Rondy, M., van Lier, A., van de Kassteele, J., Rust, L., de Melker, H., 2010. Determinants for HPV vaccine uptake in the Netherlands: a multilevel study. Vaccine 28 (9): 2070–2075. http://dx.doi.org/10.1016/j.vaccine.2009.12.042.
Schiffman, M., Castle, P.E., 2003. Human papillomavirus: epidemiology and public health. Arch. Pathol. Lab. Med. 127 (8):930–934. http://dx.doi.org/10.1043/1543-2165(2003)127<930:HPEAPH>2.0.CO;2.
Schiffman, M., Castle, P.E., Jeronimo, J., Rodriguez, A.C., Wacholder, S., 2007. Human papillomavirus and cervical cancer. Lancet 370 (9590):890–907. http://dx.doi.org/10.1016/S0140-6736(07)61416-0.
Van Keulen, H.M., Otten, W., Ruiter, R.A.C., Fekkes, M., Van Steenbergen, J., Dusseldorp, E., Paulussen, T.W.G.M., 2013a. Determinants of HPV vaccination intentions among Dutch girls and their mothers: A cross-sectional study. BMC Public Health 13:111. http://dx.doi.org/10.1186/1471-2458-13-111.
Van Keulen, H.M., Otten, W., Ruiter, R.A.C., Van Steenbergen, J., Fekkes, M., Paulussen, T.W.G.M., 2013b. Redenen om zich te laten vaccineren tegen HPV. Ned Tijdschr Geneeskd 157, A5523.
van Lier, E.A., Oomen, P.J., Giesbers, H., van Vliet, J.A., Drijfhout, I.H., Zonnenberg-Hoff, I.F., de Melker, H.E., 2016. Vaccinatiegraad Rijksvaccinatieprogramma Nederland: verslagjaar. http://www.rivm.nl/Documenten_en_publicaties/Wetenschappelijk/Rapporten/2016/juni/Vaccinatiegraad_Rijksvaccinatieprogramma_Nederland_Verslagjaar_2016 [accessed 04.07.2016].
Verplanken, B., Orbell, S., 2003. Reflections on past behavior: a self-report index of habit strength. J. Appl. Soc. Psychol. 33:1313–1330. http://dx.doi.org/10.1111/j.1559-1816.2003.tb01951.x.