

Title:

**Women showed mixed intentions to uptake of HPV vaccinations for pre-adolescents; a questionnaire study.**

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## **ABSTRACT**

### **BACKGROUND**

General introduction of HPV vaccination as primary prevention of cervical cancer is subject of debate in the Netherlands.

### **METHODS**

We explored intentions towards HPV vaccinations for pre-adolescents in 1,367 women; screen invitees, women with abnormal smears, cervical cancer survivors, and a reference group.

### **RESULTS**

76% (screen invitees) to 81% (women with abnormal smears) said 'yes' to vaccinations, often motivated by 'prevention is better than cure'. Multivariate logistic regression showed that younger women were more positive than older women. Intentions were not related to education, job, marital status or having children. Both women who were pro and anti-HPV vaccinations expressed concerns about long-term effectiveness and side effects. Comments as 'cervical cancer runs in the family' demonstrated confused knowledge.

### **CONCLUSIONS**

Most respondents had a positive intention towards HPV vaccinations, but intention was lower than actual childhood vaccination uptake in the current National Immunisation Programme (95%). Uncertainties about long-term effectiveness and side effects were the major causes of doubt.

### **KEYWORDS**

- Cervix cancer;
- Human papilloma virus 16/18;
- Immunization program;
- Parental consent;
- Preventive measures.

## BACKGROUND

In Europe 60,000 women are diagnosed with cervical cancer annually.<sup>1</sup> In the Netherlands the risk of dying from cervical cancer is reduced with roughly 75% by fully participating in the cervical cancer screening program.<sup>2</sup> Women at higher risk of cervical cancer (e.g. from lower socio-economic groups) are over represented among non-attendees in screening programs.<sup>3</sup> Especially in these groups vaccinations against human papillomavirus (HPV) might improve protection against cervical cancer.

Persistent infection with high-risk HPV is a necessary cause of cervical cancer.<sup>4,5</sup> HPV is a very common sexually transmitted infection in Europe and the USA<sup>(6)</sup> with an estimated life-time risk of 75-80%.<sup>7-9</sup> Only a small percentage of HPV-infections persists and may develop into cervical intraepithelial neoplasia (CIN), the pre-stage of cervical cancer. A prophylactic vaccine against HPV types 16 and 18, that cause approximately 70% of cervical cancers,<sup>10</sup> is available in the European Union and a second vaccine is expected to be licensed soon.

Because the prevalence of HPV is highest in the first months of sexual activity,<sup>11-13</sup> and because protection is reduced after HPV infection, vaccination before sexual debut seems to be the best strategy. The optimal age for vaccination is thus 12 to 14 years, or younger. The Dutch government is currently considering the inclusion of HPV vaccinations in the National Immunisation Program (NIP).<sup>14</sup> Participation to the NIP is for free, no out-of-pocket contribution is required. Although the NIP is not obligatory, participation is currently considered self-evident by many, resulting in a current uptake of around 95%.<sup>15</sup> The effectiveness of the NIP depends on availability of high-quality vaccines and acceptance by the parents.<sup>16</sup> The last factor is extra important in the case of HPV-vaccinations considering the decision whether or not to introduce HPV-vaccination in the NIP as a female-only vaccination. If adherence among girls is estimated to be sufficiently high to achieve herd immunity, a female-only vaccination program is the most cost-effective strategy.<sup>17</sup> Expected uptake of HPV vaccinations is also important because a negative (parental) intention towards including HPV vaccinations in the NIP may endanger the acceptance of the entire NIP.

While awareness is a necessary condition for adherence to a vaccination program, recent studies in the UK and USA show that awareness of HPV, cervical cancer and HPV vaccinations is low among the general public, including parents of (pre)adolescents.<sup>18-21</sup> In the

context of an empirical quality of life study on the effects of cervical cancer screening, we assessed women's intentions towards HPV vaccinations and compared these with their attitudes towards other preventive activities.

## **METHODS**

### *Respondents*

Four groups were included: groups 1, 2, and 4 were recruited through the regional screening organisation in Maastricht (the Netherlands); group 3 was contacted via (former) gynaecologists.

- 1) Randomly selected women were sent a questionnaire attached to their invitation for the national screening program (Pap smear), the response was 44%. Data from the first 457 questionnaires that randomly became available after data input were included in this study.
- 2) 550 women with slightly abnormal smear results (Pap 2) in the previous 6-24 months were sent a questionnaire (response 49%).
- 3) 425 cervical cancer survivors were identified through the cancer registry in the south of the Netherlands. These women had been diagnosed in the years 1995-2003. Treatment guidelines as applies in this region have been described elsewhere.<sup>22</sup> Response to the questionnaire was 69%.
- 4) Randomly selected women who had not been invited for cervical cancer screening in the preceding 2 years, were sent a questionnaire. The response was 46%. Data from the first 349 questionnaires that randomly became available after data input were included in the current study.

### *Questionnaire*

The following item on HPV vaccinations was included:

'A vaccination against cervical cancer is currently being developed. To protect against cervical cancer it needs to be given at a young age. Imagine you have a 10-year-old (grand) daughter. Would you have her vaccinated? Please comment on your answer.'

Information on HPV being a sexually transmitted infection was not provided.

The respondents' attitude towards preventive health care was assessed by asking them which of a list of interventions they would recommend to the eligible groups. For instance, would you recommend a pregnant woman to take folic acid?

Information on age, marital status, education, profession, and country of birth was obtained from the respondents via the questionnaire.

### *Statistical analyses*

Differences between the 4 subgroups in background variables and in attitudes towards preventive health care activities were assessed using Kruskal-Wallis tests for continuous variables and Chi-square tests for categorical ones. We conducted logistic regression to analyse determinants of intentions towards vaccinations against cervical cancer. Women who skipped the item on HPV were included in the logistic regression since 59% of them did add a comment on the item. Women who skipped the item and women who said 'no' to vaccinations against cervical cancer were compared with women who said 'yes' to vaccinations. Subgroup, age (in categories), education, job status, marital status, having children, and country of birth were included in the analyses as covariates, since these variables differed statistically between subgroups (Table 1).

Statistical analyses were performed using SPSS for Windows, version 15. A  $p$ -value less than 0.05 (referring to two-sided statistical tests) was considered significant.

Comments of the respondents were classified into relevant themes, as selected by two of the authors (IK, MLEB).

## **RESULTS**

There was a significant difference in background variables between the 4 subgroups (Table 1). Women invited for screening and women with abnormal smears were aged 30-62 years, which is the age range of the cervical cancer-screening program in the Netherlands. The cervical cancer survivors were the oldest (average age 52.9 years) and had the highest percentage of single women, which included widows and divorced women.

In all groups a majority indicated a positive intention towards vaccination against cervical cancer (Table 2), ranging from 76% among women invited for screening to 81% among women with slightly abnormal smears. Multivariate logistic regression showed that education, marital and job status, having children or not, and country of birth, bore no significant influence on women's intention towards vaccination uptake. Only age was significantly associated with the intention towards vaccinations, with younger women having a more positive intention ( $p < 0.011$ ).

Comments regarding the choice on vaccinations against cervical cancer were classified into relevant themes (Tables 3 and 4). A pro-vaccination choice was often explained by the phrase 'prevention is better than cure'. Especially cervical cancer survivors expressed the wish that vaccinations might prevent infertility and unwanted childlessness. Concerns about potential side effects, lack of effectiveness or lack of (scientific) research were voiced by 228 respondents; 150 of them said 'yes' to vaccinations. Eighty-nine respondents indicated they needed more information to make a choice. Thirty-three women referred to the current cervical cancer-screening program, either to explain a positive intention towards HPV vaccinations ('the current screening program should include younger ages') or a negative intention ('the screening program provides us with sufficient protection'). A negative attitude towards vaccinating (against cervical cancer) was expressed by 29 women. Twenty-seven women made remarks about the age of 10 being very young or too young, e.g. a preference for vaccinating after menarche rather than before. Six women spontaneously addressed the infectious nature of HPV, either to explain a negative intention towards HPV vaccination (e.g. 'sexual views are too loose nowadays') or a positive intention ('it reassures me that my child will be safe the rest of her life since it is sexually transmitted').

Respondents' attitudes towards preventive health care were on average positive (Figure 1). They were least positive towards antenatal screening for chromosomal abnormalities; 36% (in women invited for screening) to 53% (in cervical cancer survivors) reported they would recommend it to pregnant women. Logistic regression analyses, correcting for age, showed statistical differences that attitudes differed between respondent groups only regarding antenatal screening. Women who said 'no' to vaccinations were significantly less positive considering all 7 preventive interventions than women who said 'yes' to vaccinations against

cervical cancer ( $p < 0.001$ ). For instance, of women who said 'yes' to vaccinations against cervical cancer, 97% said 'yes' to vaccinating babies against DtaP/IPV versus 87% of women who said 'no' to HPV vaccinations.

## DISCUSSION

In spite of their concerns about (long-term) side effects, 76-81% of the women indicated a positive intention towards vaccinations against cervical cancer for their (hypothetical) 10-year-old (grand)daughters. Women who indicated ignorance towards HPV vaccinations, a need for more information or confused knowledge about the relationship between cervical cancer and HPV ( $n=101$ ), might well become positive towards HPV vaccinations if provided with information. On the other hand, women with a generally negative intention against any vaccinations ( $n=29$ ) (e.g. 'diseases are part of life') are less likely to change their opinion when provided with information about HPV and cervical cancer.

The intended uptake of vaccinations against cervical cancer as reported in this study is lower than the current childhood vaccination uptake of the NIP, which is 95%.<sup>15</sup> Many respondents may have been unfamiliar with HPV vaccinations. If HPV vaccinations would be included in the NIP – which is provided for free - the intention for uptake may increase, simply *because* the vaccinations are included in the NIP. The general population's trust in the NIP underlines that HPV vaccinations should only be included in the NIP if informed expectation of long term safety is sufficiently convincing.<sup>23</sup>

We compared the intention towards HPV vaccinations with the attitude towards other preventive interventions among 4 different respondent groups, a comparison that to our knowledge has not yet been reported. Beforehand we did not expect that personal experience seemed to affect decisions about preventive strategies so little. Intentions towards HPV vaccinations were more positive in all groups than the attitude towards the influenza vaccination for the elderly and antenatal screening for chromosomal abnormalities for pregnant women. We speculate that influenza was not considered a serious condition, while no real 'cure' can be expected from antenatal screening for chromosomal abnormalities. Breast cancer screening, heel prick, and DTaP/IPV participation are offered for free by the

Dutch government. Traditionally, uptake in the Netherlands is high and participation is considered almost self-evident.

In three earlier studies the intentions towards vaccination against HPV were assessed using a single item. In Manchester (UK) parents of 11-12-year-old children (n=317) were provided with facts about HPV and cervical cancer. Subsequently 38% said they certainly agreed to HPV vaccination for their child and 43% 'probably';<sup>21</sup> unfortunately, the response rate (22%) was rather low.

In Georgia (USA) data were collected from parents of 10-15-year-olds. Before a brief introduction into HPV and HPV vaccinations 55% indicated a positive intention towards vaccinating their child against HPV, and afterwards 75%.<sup>18</sup>

In Cuernavaca (Mexico) 880 female respondents were informed about the aetiology of cervical cancer and about the vaccine against HPV that was then (1998) in an experimental stage. Of the interviewed women, 84% said that they would allow their teenage daughter to receive this vaccine.<sup>24</sup>

The results as reported were in line with our study.

We found that only 6 respondents spontaneously addressed the issue of HPV being a sexually transmitted infection, illustrating the low level of awareness about HPV among the general public. In previous publications on HPV it is frequently argued that while some parents may welcome HPV vaccines, others may have doubts arising from the idea that such a vaccination may encourage sexual activity among adolescents.<sup>25, 26</sup> However, if awareness of HPV is low, as demonstrated previously,<sup>18-21</sup> it is unlikely that fear of HPV infection is discouraging many adolescents from being sexual active, and neither that vaccination against HPV will be a license for sexual activity. Some respondents in our study considered the fact that HPV vaccinations protect against a sexually transmittable infection reassuring as well.

In the present study, the intention towards vaccinations against cervical cancer was not influenced by education or job status, implying that the attitude towards HPV vaccinations may be similar in women with both low and high social economical status (SES). This confirms the finding of Davis and colleagues, who showed that education and ethnicity were not associated with vaccine acceptance,<sup>18</sup> which is important given the higher risk for cervical cancer in groups with lower SES.



The current study had some limitations. Response rates to the entire questionnaire ranged from 44-69% per subgroup. Respondents may have had a more positive attitude towards preventive health care activities than the general population. Furthermore, having one's (grand)daughter vaccinated or not was a hypothetical issue in the current study, because vaccines had not yet become available, and campaigns to promote them had not yet started. Finally, all respondents in this study were female, since the aspect of vaccinating against cervical cancer was assessed in the context of an empirical quality of life study on the effects of cervical cancer screening. However, fathers' opinions regarding vaccinating adolescent girls are also relevant for expected uptake rates. We recommend further study on attitudes towards HPV-vaccinations among fathers and mothers of (pre)adolescent girls. Strengths of our study are the respondents' wide variety of experiences with (screening on) cervical cancer. Furthermore, we included large samples and made a comparison between the intentions towards HPV vaccination versus attitudes towards other preventive interventions.

This study has shown that women with diverse socio-economic backgrounds and diverse experiences with cervical cancer and smear taking were positive about HPV vaccinations. However, should HPV vaccinations be introduced in the NIP educational interventions for parents, adolescents, and the medical profession should aim at addressing confused knowledge and anxiety for side effects.

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## **Conflict of interest statement**

One of the authors has one competing interest: M. van Ballegooijen is private investigator of a study on cost-effectiveness of HPV-vaccinations, financed by GSK (pharmaceutical company that produces HPV-vaccins). The other authors have no competing interests.

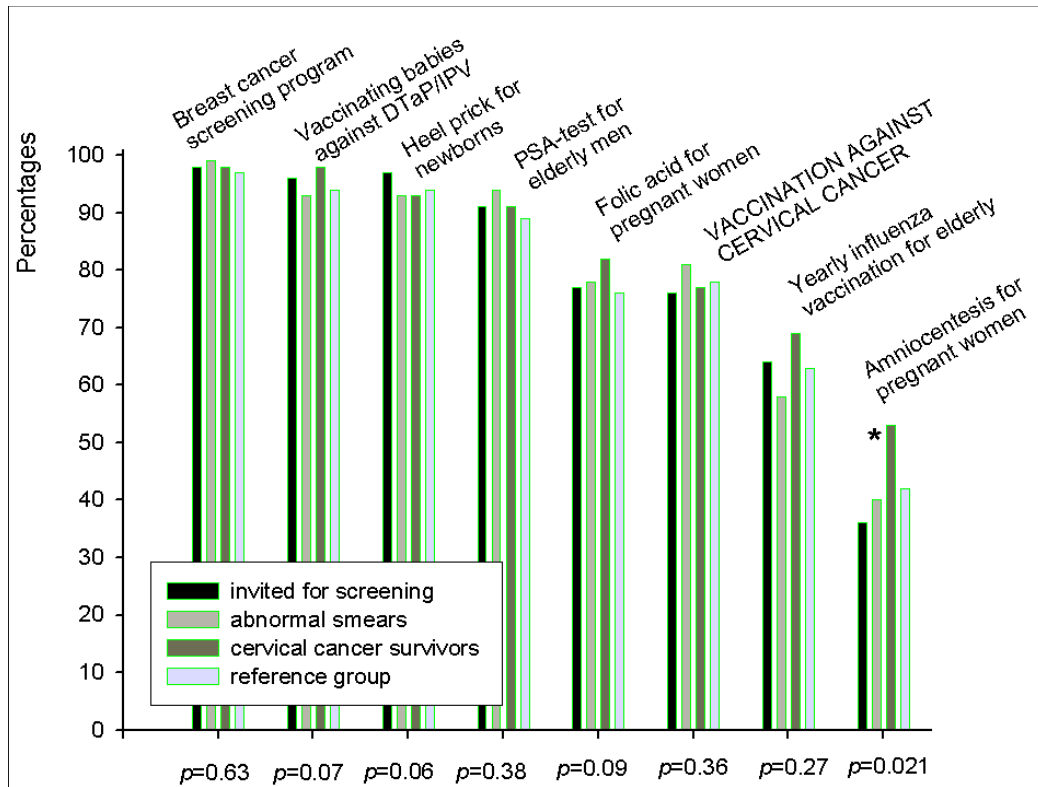
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**Figure 1.** The percentage of women that would recommend various preventive health care activities to eligible groups, per group and per activity. P-levels indicate the statistical differences between groups, assessed by logistic regression analyses, correcting for age.



DTaP/IPV: Diphtheria, tetanus, whooping cough, and poliomyelitis

PSA: Prostate-Specific Antigen

\*) Statistically significant differences between groups of respondents

**Table 1.** Background characteristics of the four groups of respondents in absolute numbers and percentages. P-values refer to the differences between the four groups.

	Women invited for screening (n=457)	Slightly abnormal smear (n=270)	Cervical cancer survivors n=291	Reference group n=349	p-value	All respondents n=1,367
<b>Age (years)</b>					<b>&lt;0.001</b>	
Average (SD)	46.0 (9.4)	43.0 (7.9)	52.9 (13.8)	50.5 (10.8)		48.0 (11.2)
Range	29-60	30-62	31-88	27-70		27-88
<b>Education</b>					<b>&lt;0.001</b>	
Low education	105 24%	39 16%	115 44%	103 32%		362 29%
Medium	217 50%	132 56%	118 45%	159 49%		626 50%
High	111 26%	67 28%	29 11%	60 19%		267 21%
<b>Job status</b>					<b>&lt;0.001</b>	
Paid job	272 65%	168 74%	96 41%	183 58%		719 60%
Housewife/unpaid job/student	99 23%	34 15%	86 37%	84 27%		303 25%
No job	42 10%	26 11%	28 12%	20 6%		116 10%
Retired	9 2%	-	22 10%	29 9%		60 5%
<b>Marital status</b>					<b>&lt;0.001</b>	
Married/cohabiting	360 83%	188 74%	186 66%	273 78%		1,007 76%
Partner, but living alone	21 5%	24 10%	16 6%	8 2%		69 5%
No partner	55 13%	41 16%	78 28%	68 20%		242 18%
<b>Children</b>					<b>0.009</b>	
No	77 18%	69 27%	61 21%	48 15%		255 20%
Yes	353 82%	187 73%	224 79%	279 85%		1,043 80%
Average no., range	2, 0-7	2, 0-8	2, 0-11	2, 0-7		
<b>Country of birth</b>					<b>&lt;0.001</b>	
the Netherlands	413 99%	237 93%	261 92%	327 99%		1,238 97%
<b>Country of birth of parents</b>						
Father born in Netherlands	398 98%	227 89%	253 92%	316 99%	<b>&lt;0.001</b>	1,194 95%
Mother born in Netherlands	394 98%	233 91%	248 90%	311 99%	<b>&lt;0.001</b>	1,186 95%
Both parents non-Dutch birth	8 2%	18 7%	20 7%	2 1%	<b>&lt;0.001</b>	1,233 96%

The p-values indicate the differences between the 4 groups.

**Table 2.** Frequency (%) and multivariate odds ratios of women who said 'yes' to vaccinations against cervical cancer for their hypothetical 10-year-old (grand)daughter.

		<b>Multivariate</b>		
	<b>'Yes'</b>	<b>Odds Ratio (95% C.I.)</b>		<b>p-value</b>
<b>Subgroup</b>				0.20
Invited for screening	76%	0.8	(0.55 - 1.28)	
Slightly abnormal smear	81%	1.4	(0.81 - 2.30)	
Cervical cancer survivors	77%	1.2	(0.72 - 2.00)	
Reference group	78%	1.0		
<b>Age group</b>				0.01
<40 years	83%	6.3	(2.30 - 17.13)	
40-50 years	81%	5.4	(2.05 - 14.24)	
50-60 years	75%	5.1	(1.94 - 13.31)	
60-70 years	73%	3.8	(1.48 - 9.60)	
≥70 years	55%	1.0		
<b>Education</b>				0.09
Low	79%	1.2	(0.76 - 1.99)	
Medium	82%	1.6	(1.03 - 2.32)	
High	75%	1.0		
<b>Job status</b>				0.69
Paid job	80%	1.0		
Unpaid job/housewife/student	76%	1.1	(0.69 - 1.82)	
No job	85%	1.3	(0.68 - 2.32)	
Retired	75%	1.7	(0.66 - 4.08)	
<b>Marital status</b>				0.88
Partner	80%	1.04	(0.66 - 1.63)	
No partner	74%	1.0		
<b>Children</b>				0.54
Children	79%	1.1	(0.75 - 1.73)	
No children	79%	1.0		
<b>Country of birth</b>				0.87
The Netherlands	79%	1.1	(0.39 - 3.04)	
Elsewhere	77%	1.0		

C.I. = Confidence Interval

**Table 3.** Main themes as reported by respondents who commented on their choice regarding vaccinating 10-year-olds against cervical cancer (percentages per group of women, percentages do not add up to 100%).

SUBGROUPS	Effectiveness, safety, and			Cervical cancer	
	Prevention is good	research is important	More information needed for a proper choice	screening worse/better than vaccinations	Against vaccinations
Invited for screening	27%	19%	13%	1%	3%
Slightly abnormal smear	41%	21%	5%	4%	3%
Cervical cancer survivors	40%	9%	2%	3%	1%
Reference group	32%	17%	6%	2%	2%



**Table 4.** Examples of comments according to main theme.

**Prevention is good**

- 'To prevent (cervical cancer) is better than to cure.'
- 'Prevention is always good.'
- 'To prevent regret.'
- 'If one can prevent cervical cancer, why not.'

**Effectiveness, safety and research is important**

- 'Yes, if no adverse effects are to be expected.'
- 'Yes, if effectiveness is proven.'
- 'Only in case of 100% protection.'
- 'Yes, if scientific research into the results has been conducted.'
- 'No, because what are the adverse effects.'

**More information is needed to make a proper choice**

- 'More information is needed.'
- 'I have never heard of this new development.'

**Cervical cancer screening program is better/worse than vaccinations**

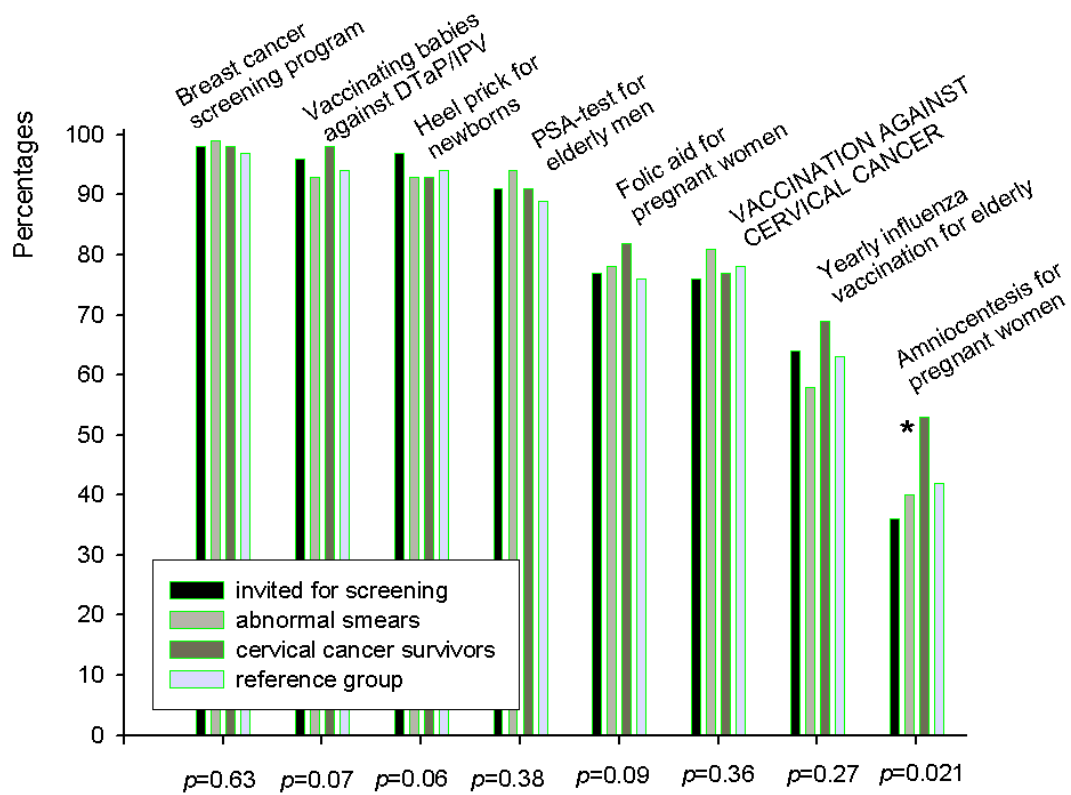
- 'It's better to be vaccinated than to have a smear taken.'
- 'Why vaccinate if you can have your smear taken?'

**Anti-vaccinations**

- 'Diseases are part of life.'
- 'One cannot vaccinate against all diseases.'

**Incorrect knowledge**

- 'Cervical cancer runs in the family.'
- 'I only want my daughter to be vaccinated if she is at risk.'
- 'Cervical cancer is not infectious.'



DTaP/IPV: Diphtheria, tetanus, whooping cough, and poliomyelitis  
 PSA: Prostate-Specific Antigen  
 \*) Statistically significant differences between groups of respondents