SHORT REPORT

Implementation of human papillomavirus testing in cervical screening without a concomitant decrease in participation rate

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Adding high-risk human papillomavirus (hrHPV) testing to screening increases the efficacy of cervical screening programmes. However, hrHPV testing may result in a lower participation rate because of the perceived association with sexually transmitted infections. We describe how testing for hrHPV was added to cervical screening in the POpulation-BAsed SCreening study AMsterdam (POBASCAM) trial. Participation rates of the screening programme before and after hrHPV implementation were evaluated in the region where the POBASCAM trial was carried out. The participation rate was 58.7% before and 61.4% after the addition of hrHPV testing to screening ($p<0.001$). An inventory of frequently asked questions is presented. Thus, hrHPV testing can be added to cervical screening by cytology without a decrease in participation rate.

An infection with high-risk human papillomavirus (hrHPV) is a necessary cause of cervical cancer.[1 2] Adding hrHPV testing to cytology will improve the efficiency of cervical screening.[3–5] However, hrHPV is a sexually transmitted agent and its perceived association with sexually transmitted diseases may hamper the introduction of hrHPV testing in cervical screening programmes.[6]

In The Netherlands, the POpulation-BAsed SCreening study AMsterdam (POBASCAM) trial evaluates the effectiveness of adding hrHPV testing to cervical screening by cytology within the confines of the regular population-based screening programme.[7] Here, we describe which measures were taken during implementation of the hrHPV test to prevent lower participation in cervical screening. We evaluated the effectiveness of these measures by comparing participation rates before and after the introduction of hrHPV testing, and tabulated frequently asked questions during the trial.

METHODS

The cervical screening programme in The Netherlands is a population registry-based programme, inviting women aged 30–60 years seven times at 5-year intervals.[8] The POBASCAM trial is a population-based randomised, controlled trial to evaluate the efficacy of screening using hrHPV testing. Participants were randomised either to a control group receiving repeat and referral recommendations based on cytology diagnosis only (ie, without receiving hrHPV test results), or to an intervention group receiving both cytology diagnosis and hrHPV test results. Baseline results have been described previously.[7]

Between 1999 and 2002, we included a total of 44 102 women invited for population-based cervical screening in the trial area. All general practitioners in the trial area were invited to contribute participants to the POBASCAM trial. Women received information on the trial and the nature of hrHPV infections, highlighting the lifetime prevalence and clearance rate of infections. Contributing general practitioners sampled cervical material for both a smear and hrHPV testing in screened women, and informed participants about the results of their test. Before and during the trial, contributing general practitioners were offered postgraduate courses on hrHPV and its relationship with cervical cancer. The information was aimed to be sufficient to answer any question of a participant in one consultation. If necessary, study coordinators (NWJB and SB) could be contacted by telephone by general practitioners and participants for further explanation. All questions were registered.

The Registry of the District Health Authority on participation rate was complete from 1997 onwards and for individual rates per general practitioner from 2000 onwards. Participation rates were defined as the ratio of the number of screening smears to the number of invitations. The participation rates in the periods before (1997–8, cytology only) and during the enrolment phase of POBASCAM (1999–2002, hrHPV and cytology combined) were compared for general practitioners in the study area who contributed to the POBASCAM trial and for non-contributing general practitioners. Ratios were compared using the χ^2 analysis and test for trend. p Values of $\leqslant 0.05$ were considered significant.

RESULTS

The participation rate of the cervical screening programme did not decrease after implementation of an hrHPV test in 1999 (table 1A).

The participation rate in the cervical screening programme was 58.7% (range 51.6–63.2%) in 1997–8 in the trial area and increased after the implementation of hrHPV testing in 1999–2002 to 61.4% (range 60.7–62.3%; p for trend = 0.267). Moreover, participation rate was higher for contributing GPs than for non-contributing general practitioners (66.8% *v* 52.7% respectively; $p<0.001$; table 1B).

We registered telephone consultations received throughout the intake phase of the trial; there were 51 calls of participants and 92 calls of contributing general practitioners on behalf of participants. Table 2 lists the most frequently asked questions and respective answers provided by the study coordinators. Mostly, questions were related to the viral nature and sexual transmission of hrHPV and seemed elicited on receiving a test result in the non-blinded arm of the trial with an advice requesting earlier repeat tests or more urgent referral advice for colposcopically directed biopsies.

Abbreviations: hrHPV, high-risk human papillomavirus; POBASCAM, POpulation-BAsed SCreening study AMsterdam

Table 1 Participation rates in cervical screening

A. Before and after introduction of hrHPV testing

	Overall		
Year	Invitations	Smears	Participation rate
1997	31 534	16 263	51.6
1998	32 555	20 566	63.2
1999	33 489	20 334	60.7
2000	32 298	20 111	62.3
2001	34 204	21 316	62.3
2002	32 986	19 879	60.3

B. Non-contributing and contributing gerenal practitioners in hrHPV testing

	Cytology only*			Cytology and hrHPV†		
Year	Invitations	Smears	Participation rate	Invitations	Smears	Participation rate
2000	10 573	5622	53.2	21 725	14 489	66.7
2001	13 153	6971	53.0	21 051	14 345	68.1
2002	12 923	6733	52.1	20 063	13 146	65.5

hrHPV, high-risk human papillomavirus.
*Non-contributing general practitioners; †contributing general practitioners.

DISCUSSION

Before initiating the POBASCAM trial, a survey conducted among 1551 Dutch women indicated that hrHPV testing would not interfere with participating in cervical screening.[9] Indeed, the overall participation did not decrease after starting the trial. More remarkably, the participation rate was increased in contributing general practitioners compared with non-contributing general practitioners. Several explanations can be offered for this increase in participation rates. Firstly, contributing general practitioners were more motivated to achieve good participation rates. Unfortunately, the District Health Authority did not register participation rates stratified per general practitioner before 2000. Secondly, women participating in the POBASCAM trial were more motivated because of the possibility of more extensive testing.

All invited women received information by the health authorities about the trial, together with the invitation. In our study, a few participants contacted the study coordinators to obtain more information than was supplied routinely. FAQs dealt mainly with the viral nature of hrHPV, the mode of transmission especially for women faced with a positive test result and the clinical course of the infection. Various studies indicate that hrHPV testing might upset women as hrHPV is sexually transmitted and may cause cancer.[10–13] However, high lifetime prevalence, high spontaneous clearance and the rarity of cervical cancer complicating an hrHPV infection minimise the potential negative effect of a positive test.[12 14] Therefore, it is essential that information about hrHPV is consistent to minimise any deleterious effects to maintain the present participation rate achieved by testing with cytology only.

We have shown that adding hrHPV testing to cervical screening in the POBASCAM trial did not decrease participation rates. Given our experience, we expect the implementation of hrHPV testing to the regular screening programme to be well accepted, without a decrease in participation rate if attention is paid to the nature of information regarding hrHPV given to screened women.

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Table 2 Frequently asked questions in the POBASCAM trial regarding infections with hrHPV

Question:	What are the consequences of having an hrHPV infection in a normal smear?
Answer:	Most women will have cleared the virus within 1½ years. Only the small number of women who still have an hrHPV infection after this time have an increased risk to develop cervical abnormalities, which, if left untreated, could eventually lead to cervical cancer. Therefore, annual follow-up is needed until both smear and hrHPV test are negative. Referral for colposcopically directed biopsies is necessary in case of an abnormal smear or when a persistent hrHPV infection is diagnosed after 18 months.
Question:	Is hrHPV a very common virus and how do you become infected with hrHPV?
Answer:	Yes, hrHPV is a very common virus. Up to 85% of all women will at some point in their life have experienced an hrHPV infection. hrHPV is sexually transmitted. We cannot, however, totally exclude other ways of transmission.
Question:	Will an hrHPV infection be cleared at the next test?
Answer:	Usually, the virus will be undetectable in 80% of all women after 1½ to 2 years.
Question:	How can I have an hrHPV infection after 25 years of monogamous relationship, knowing that hrHPV is sexually transmitted?
Answer:	hrHPV may be present in very low quantities under the level of detection, and harmless for your body. Now, many years later, the virus may be activated, possibly due to a weakened immune system. The virus may replicate and increase in quantity, and subsequently cause cervical lesions. So, you cannot deduct from a positive hrHPV test that hrHPV is acquired from recent extramarital contact.
Question:	How can an infection with hrHPV be treated?
Answer:	Currently, there is no treatment for an hrHPV infection. Most hrHPV infections (80%) are cleared by the immune system itself. Should you have the virus and eventually have developed cervical abnormalities, the latter can be treated by your gynaecologist. Usually, after treatment of cervical lesions hrHPV can also no longer be detected. At the moment, prophylactic vaccines are being developed.

Take-home messages

- Overall participation in the screening programme did not decrease after the introduction of hrHPV testing.
- With the introduction of hrHPV testing in a screening programme, most questions by participants concerned the viral nature and sexual transmission of hrHPV.
- Attention has to be paid to give clear and consistent information about hrHPV to screened women and to general practitioners.

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