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# Human papillomavirus self-sampling for screening nonattenders: Opt-in pilot implementation with electronic communication platforms

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Cancer Epidemiology

**In organized cervical screening programs, typically 25% of the invited women do not attend. The Copenhagen Self-sampling Initiative (CSi) aimed to gain experiences on participation among screening nonattenders in the Capital Region of Denmark. Here, we report on the effectiveness of different communication platforms used in the pilot with suggestions for strategies prior to a full-implementation. Moreover, an innovative approach using self-sampling brushes with unique radio frequency**

**Key words:** HPV-based self-sampling, screening nonattenders, cervical cancer screening, pilot implementation study, electronic communication platforms

Additional Supporting Information may be found in the online version of this article.

## Conflicts of Interest

Janni Uyen Hoa Lam attended meetings with various HPV device manufacturers.

Matejka Rebolj attended meetings with various HPV device manufacturers. She and her former employer received fees for lectures on her behalf from Qiagen.

Ditte Møller Ejegod attended meetings with various HPV device manufacturers. She received honoraria from BD and Qiagen for lectures.

Helle Pedersen attended meetings with various HPV device manufacturers.

Carsten Rygaard participated in meetings with Roche with fee paid to the University of Copenhagen.

Elsebeth Lynge participated in meetings with Roche and Astra-Zeneca with fees paid to the University of Copenhagen, and was unpaid advisor to GenProbe and NorChip. Roche has provided test kits to Trial23.

Louise Thirstrup Thomsen declares no conflict of interest.

Susanne Krüger Kjaer has received lecture fees, scientific advisory board fees from Merck, Sanofi Pasteur MSD, BD, and unrestricted research grants through the affiliating institute from Merck.

Jesper Bonde attended meetings with various HPV device manufacturers. He used to serve as a paid advisor to Roche and Genomica, and has received honoraria from Hologic/Gen-Probe, Roche, Qiagen, Genomica and BD Diagnostics for lectures. He is principal investigator on studies funded by BD diagnostics.

Hvidovre Hospital holds a recompense agreement with Genomica on a KRAS/BRAF diagnostic system.

## Authors Contributions

Design of the study: Jesper Bonde (JB), Matejka Rebolj (MR), Carsten Rygaard, Elsebeth Lynge

Analysis of the data: Janni Uyen Hoa Lam, Ditte Møller Ejegod, JB, MR

Interpretation of the results: all authors Drafting of the manuscript: all authors

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identification chips allowed for unprecedented levels patient identification safety. Nonattenders from the capital region of Denmark were identified via the organized national invitation module. Screening history was obtained via the nationwide pathology registry. Twenty-four thousand women were invited, and as an alternative to the regular communication platforms (letter and phone), women could request a home test via a mobile-friendly webpage. Instruction material and video-animation in several languages were made available online. Chi-square test was used to test differences. Out of all invited, 31.7% requested a home test, and 20% returned it to the laboratory. In addition, 10% were screened at the physician after receiving the invitation. Stratified by screening history, long-term unscreened women were less likely to participate than intermittently screened women (28% *vs*. 16%, $p < 0.001$). Of all contacts received, 64% (63–65) came via letter, and 31% (95CI: 30–32%) via webpage/mobile-app. Self-sampling was well-accepted among nonattenders. Adopting modern technology-based platforms into the current organized screening program would serve as a convenient communication method between health authority and citizens, allowing easy access for the citizen and reducing the work load in administrating self-sampling approaches.

**What's new?**

Our implementation study is the first to evaluate opt-in self-sampling for 24,000 screening nonattenders, which can be basis for future routine implementation. Women could respond through a variety of communication channels (regular mail, phone and custom-made web/mobile-app). Our study utilized self-sampling brushes with a novel RFID-chip for secure patient-identification, eliminating inconveniences for the women to fill out forms on returning the brush and loss of brushes due to missing identification.



In Denmark, screening coverage is 75%,[1] but 45% of all cervical cancer cases are diagnosed among the 25% nonattending women, who have not been screened as recommended (nonattenders).[2] Therefore, an increased screening coverage through recruitment of nonattenders might decrease the incidence of cervical cancer. Cytology-based cervical screening samples are at present taken by healthcare professionals during a gynecological examination. In Denmark and many European countries, cervical screening is free of charge. The gynecological examinations associated with sampling, however, pose a barrier for some women due to discomfort, embarrassment, or lack of time.[3]

Human Papillomavirus (HPV)-based self-sampling is a new potentially useful screening method for nonattenders,[4,5] which, unlike cytology, allows women to take a screening sample in the privacy of their home, at a convenient time and without undergoing a gynecological examination. The self-taken sample can be returned for analysis directly to the laboratory using regular mail. In previous studies from screening programs with high screening coverage rates, such as the Netherlands and various Scandinavian countries, all nonattenders were mailed self-sampling kits ("opt-out" approach).[6–9] This strategy, where 6–34% of nonattenders returned their self-sampling kits for analysis,[6,10] leads to considerable waste of the distributed, but unused kits. An alternative approach is to have nonattenders actively "opt in," that is, order the self-sampling kits if interested after receiving an invitation from the screening program. Only few studies[11–16] have used the opt-in approach so far, with a reported return rate of 9–39%. A general concern is that by requiring additional effort from women to confirm their willingness to participate, this approach is vulnerable to low participation rates.[13,14]

The aim of the Copenhagen Self-Sampling Initiative (CSi) pilot implementation study was to offer opt-in self-sampling to nonattenders. Similar to the current screening program, self-sampling was a public health care offer and free of charge, yet by invitation only. To increase convenience and minimize the needed effort from the women, we combined classical mail-based correspondence with a custom-developed web platform that could also be used on mobile devices to order a self-sampling kit. In contrast to the current screening program, selected information and instruction material was available in several languages so as to avoid potential language barriers. The inclusion stage of the study is now completed and the women are currently undergoing clinical follow-up. To gain insight into the association between age, and screening history to the acceptance of self-sampling as an alternative to the current organized screening offer, we described the percentage of women responding to an invitation for a self-testing kit, and the percentage of kits returned, stratified by age and previous screening history.

## Material and Methods

### Study population

Danish women are invited for liquid-based cytology screening every three years at 23–49 and every 5 years at 50–59 years of age. Since 2012, women aged 60–65 years have been recommended to undergo HPV-based screening, after which they leave the target group if HPV-negative.[17] All screening and the subsequent follow-up are free of charge. CSi is being undertaken at Department of Pathology, Copenhagen University Hospital Hvidovre. This Department is responsible for and operates cervical cancer screening for the entire Capital Region including the administration of invitations, covering approximately one-third of the Danish population. Women

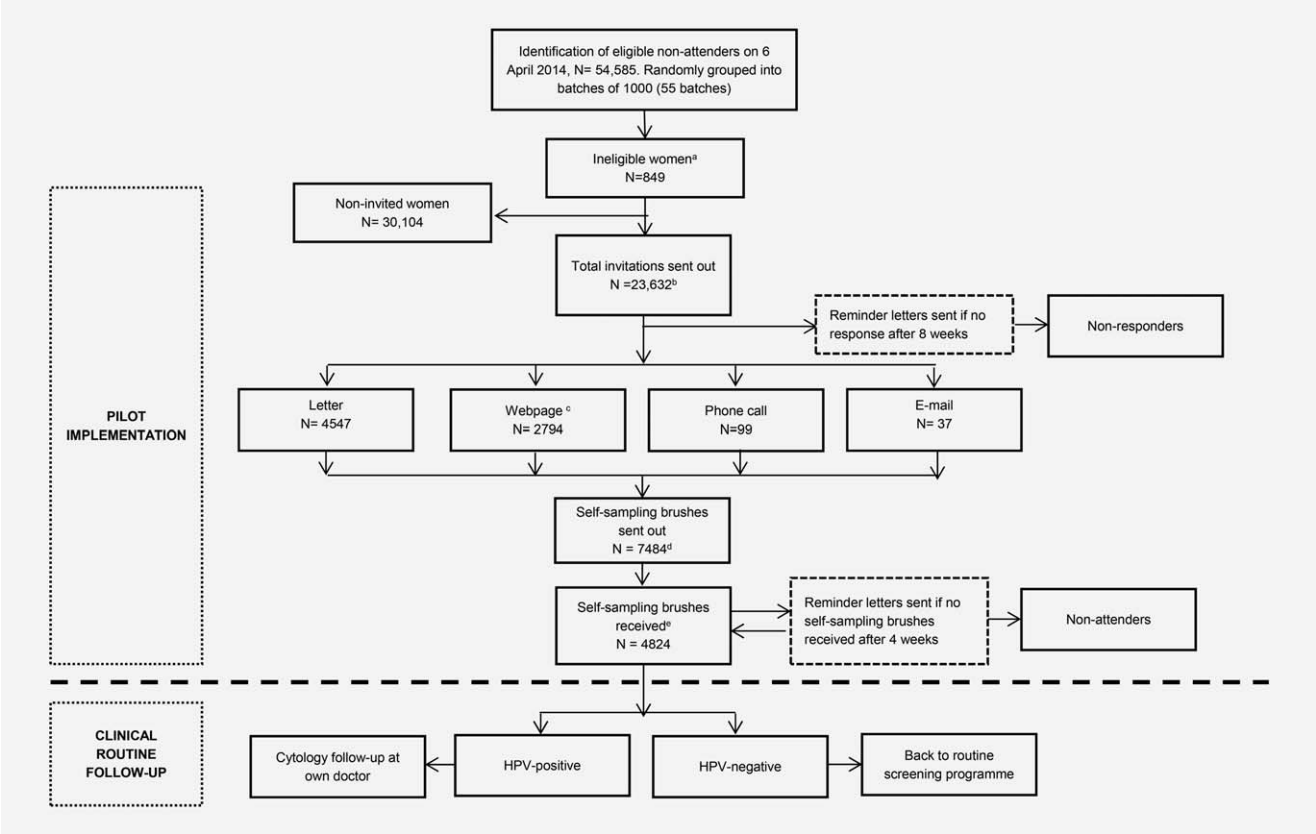


**Figure 1.** Flow chart of study design. (*a*) Women moved out of the region/country, got screened, opted out routine screening, or died before the address linkage. (*b*) Our initial target was to receive approximately 5,000 self-sampling brushes. This was achieved after 24 batches of invitations. (*c*) Webpage: access via desktop or mobile device. (*d*) 21 responses were received via a separate questionnaire study. Seven women requested the self-sampling brush, and six of these returned their self-sampling test. (*e*) HPV-testing was performed within 10 working days as according to routine practice. Women, who were high-risk HPV-positive, were recommended to go to their doctor, and have a cytology sample taken, whereas HPV-negative women were referred back to the routine screening programme.

are invited for screening in 3 or 5 years, depending on their age, after their last cervical sample registered in the Danish Pathology Database (Patobank).[18] The call-recall system is run by the CGI Institute (www.cgi.dk) and is based on the invitational module in the Patobank, combining the screening information from the Patobank's main pathology module with the residency status information from the Danish population register. Women are invited by a letter mailed to their home address, and receive reminders 3 and 6 months later.

CSi eligibility was determined on April 6, 2014, and the list of women was compiled by CGI at the Department's request. Women were eligible if they resided in, and received their last routine screening invitation, from the Capital Region. They had, despite reminders, no cervical sample taken in 12 months after the last invitation. Thus, eligible women were unscreened for at least 4 or 6 years, depending on their age. The youngest invited women were 27 and the oldest 65 years of age. In Denmark, the organized cervical screening program includes women 23–65 years of age. Even though the international consensus trends towards initiation of HPV screening from age 30 or 35, we chose in this first Danish initiative to offer a uniform service defined by nonattendance interval rather than by age stratification. Consequently, the youngest women offered self-sampling was 27 years of age. Women who actively opted out of the screening program, and/or were registered in the Patobank as ineligible for screening due to a hysterectomy (this registration is, though, highly incomplete) were not eligible. Using these criteria, 54,585 women were eligible and were randomly grouped into batches of 1,000 (Fig. 1). Unique random numbers doubling as study identification numbers were selected with R version 3.1.1 (R Development Core Team, Vienna, Austria). A gradual mailing of the batches allowed the department to plan the capacities and the logistics during this pilot period. For practical reasons, this list was linked to personal identification numbers, names and addresses on May 6, 2014. By then, 849 women became ineligible because they moved out of the Department's catchment area, underwent screening, opted out of routine screening, or died. Their addresses were unknown for study purposes.

The mailing of batches continued until, in line with financial considerations, the goal of approximately 5,000 returned brushes was reached. As the CSi invitations could not be entered into the Patobank's invitational module, some

women may have received new routinely scheduled screening invitations while CSi was ongoing. New linkages to determine which women were invited for routine screening were not possible in this pilot.

### Invitational procedure

When the study was launched, it received broad nationwide media coverage on approximately 20 media outlets, including radio, TV, online news and magazines and print newspapers. Each invited woman received an invitation package which included an information sheet, a reply form and a prestamped envelope. The information sheet included information on the association between HPV and cervical cancer, and stressed the importance of regular screening. Women could opt into the study by ordering a self-sampling kit by (1) returning the reply form, (2) phone, (3) e-mail or (4) signing up on a dedicated website (http://www.hpv-hjemmetest.dk). QR code was printed on invitations for easy web-redirection access. Instruction manuals were also available online in languages covering the major linguistic groups in the area (Danish, Arabic, French, Turkish and English). An animated instruction video was available in Danish and English. After receiving the opt-in response, the self-sampling kits were sent out after approximately two to three working days

In the invitation letter, women were informed that they could participate in a separate Danish Cancer Society questionnaire study investigating the reasons for screening nonattendance. Questionnaire participation did not affect eligibility for participation in CSi. Twenty-one women responded to their self-sampling invitation only via this substudy, of whom six (<1%) returned the self-sampling brush.

Reminders were sent 8 weeks after the initial invitation. A self-sampling kit with instruction material and a prestamped envelope were sent to all women who agreed to participate. If not returned for testing, women received a reminder letter 4 weeks later. Additional kits were sent to women who requested new ones.

### The self-sampling kit

We used the Evalyn Brush (The Rovers, Oss, The Netherlands), customized for CSi by embedment of a radio-frequency identification (RFID) chip. The chip ensured linkage between the woman's identity and the brush, securing correct patient identification without relying on paper documentation. After receiving the brush in the laboratory, HPV-testing was performed within 10 working days according to routine practice. The HPV-results were sent to participants by personal letter, in addition to the general practitioner if the woman agreed to this. Women, who were high-risk HPV-positive, were recommended to go to their doctor to have a cytology sample taken.

### Data sources

Women's screening history was determined through a linkage to the national Patobank from January 1, 2000 to December 1, 2015. All registered cytological samples were included in the analysis. Patobank's registration of cervical samples has been nearly complete since the mid-2000s (unpublished data).

### Statistical analysis

The analyses were based on the intention-to-treat principle. Response was defined among women who ordered the kit, whereas participation was defined among women who returned the brush to the laboratory. Both were determined by December 1, 2015, that is, within 7 months after the last batch of invitations was sent out.

We defined women with a cytology sample registered in $\leq$10 years before April 2014 as intermittently screened and other women as long-term unscreened. These analyses were limited to women aged $\geq$34 years, as they had been targeted for screening for >10 years.

The time for the women to return the brush was calculated as the number of days between the date the brush was sent out and the date it was received back in the laboratory.

Pearson's $\chi^2$- test was used to compare the differences in responses and participation by screening history and by response method. Analyses were performed using Stata SE 13.1 (StataCorp, TX) and Microsoft Excel 2010 (Microsoft, Redmond).

### Ethical approval

CSi was a time-limited pilot implementation offer, mandated by the Danish Health Authority and carried out by the regional screening authority of the Capital Region. Ethical approval was not required. Linkage of the study data with the Patobank was approved by Danish Data Protection Agency (AHH-2015–084, I-Suite number: 04139).

## Results

The first batch was sent on May 23, 2014 and the last, 24th batch on April 10, 2015. From these 24 pregrouped batches, 368 women became ineligible before address linkage and the remaining 23,632 (99%) women were invited for self-sampling (Fig. 1). The age distributions of the women with a successful address linkage who were not invited ($N = 30{,}104$) and those who were ($N = 23{,}632$) did not differ ($p = 0.90$).

Among the 23,632 invited women, 974 (4%; Table 1) women had a new screening sample registered in the Patobank before they received the invitation (but after the address linkages were made), either because they responded to a new routinely scheduled screening invitation or for some other reason unrelated to CSi. In total, 7,484 (32%) women responded by ordering the self-sampling brush, and 4,824 (20%) participated by returning it. These proportions slightly increased with age, although, owing to large numbers, the age-trends were statistically significant ($p < 0.001$). In addition, 2,288 (10%) women had a physician-taken cytology sample registered after their CSi invitation. This was higher at younger (13–16%; <50 years) than at older (3–4%, $\geq$50 years) age ($p < 0.001$). Combined, 34% of all invited women were screened by December 1, 2015, of which a majority

**Table 1.** Responders and participants, by age group

| Age group (years) | Invited (%)[1] | | Screened by self-sampling: Responders (%) | | Screened by self-sampling: Participants (%) | | Screened by physician: Before study invitation[2] (%) | | Screened by physician: After study invitation[2] (%) | | Total screened (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 27–29 | 2,291 | (100%) | 575 | (25%) | 383 | (17%) | 127 | (6%) | 303 | (13%) | 813 | (35%) |
| 30–39 | 5,711 | (100%) | 1,750 | (31%) | 1,080 | (19%) | 386 | (7%) | 898 | (16%) | 2,364 | (41%) |
| 40–49 | 5,633 | (100%) | 1,890 | (34%) | 1,200 | (21%) | 319 | (6%) | 730 | (13%) | 2,249 | (40%) |
| 50–59 | 5,888 | (100%) | 1,991 | (34%) | 1,265 | (21%) | 100 | (2%) | 250 | (4%) | 1,615 | (27%) |
| 60–65 | 4,109 | (100%) | 1,278 | (31%) | 896 | (22%) | 42 | (1%) | 107 | (3%) | 1,045 | (25%) |
| Total | 23,632 | (100%) | 7,484 | (32%) | 4,824 | (20%) | 974 | (4%) | 2,288 | (10%) | 8,086 | (34%) |
| *p* | | | *<0.001* | | *<0.001* | | *<0.001* | | *<0.001* | | *<0.001* | |

Responders= women who ordered a brush. Participants= women who returned their brush.
[1]Among all eligible women with a successful address linkage ($N = 53{,}736$), the age distribution did not differ between women who were invited ($N = 23{,}632$) and those who were not ($N = 30{,}104$) ($p = 0.90$).
[2]Women who did not also return a self-sampling kit.

**Table 2.** Responders and participants, by screening history

| Screening history[1] | Invited (%) | | Screened by self-sampling: Responders (%) | | Screened by self-sampling: Participants (%) | | Screened by physician: Before study invitation[2] (%) | | Screened by physician: After study invitation[2] (%) | | Total screened (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Long-term unscreened | 10,074 | (100%) | 2,598 | (26%) | 1,599 | (16%) | 187 | (2%) | 489 | (5%) | 2,275 | (23%) |
| Intermittently screened | 8,749 | (100%) | 3,611 | (41%) | 2,416 | (28%) | 500 | (6%) | 1,106 | (13%) | 4,022 | (46%) |
| Total | 18,823 | (100%) | 6,209 | (33%) | 4,015 | (21%) | 687 | (4%) | 1,595 | (8%) | 6,297 | (33%) |
| *p* | | | *<0.001* | | *<0.001* | | *<0.001* | | *<0.001* | | *<0.001* | |

Limited to women aged ≥34 years who had been eligible for screening for >10 years.
Responders= women who ordered a brush. Participants= women who returned their brush.
[1]Intermittently unscreened: cytology sample registered within the last 10 years (though not in the last screening round, see eligibility criteria). Long-term unscreened: no cytology sample registered in the last 10 years.
[2]Women who did not also return a self-sampling kit.

through self-sampling. With 25% of women being unscreened before this intervention,[1] this represents approximately 8.5% of the entire population targeted for screening, although it should be noted that these women were screened with a longer-than-recommended interval.

Among 8,749 intermittently screened women aged 34–65 years, 3,611 (41%) responded (Table 2). Among 10,074 long-term unscreened women, this was 2,598 (26%; $p < 0.001$). Also participation was higher among the intermittently screened ($N = 2{,}416$, 28%) than the long-term unscreened ($N = 1{,}599$, 16%) women ($p < 0.001$), as was screening by a physician subsequent to a self-sampling invitation (1,106 (13%) *versus* 489 (5%), $p < 0.001$). In total, 46% of intermittently screened and 23% of long-term unscreened women underwent some form of screening. If screening history was recategorized as never screened *versus* ever screened, we would have seen similar patterns for participation in each group: 14% for never-screened women and 26% for ever screened women (data not tabulated).

Most women responded by regular mail (4,574, 61%) or online (2,794, 37%; Table 3). Phone and email were seldom used (136, 2%). Women responding online were slightly younger than women using regular mail or phone.

Some invited women made several contacts with the laboratory, predominantly via phone and e-mail, and to request additional information before deciding on participation ($N = 308$; 4% of all invited women; data not tabulated).

Overall, 50% of all brushes were returned for testing within 15 days (Fig. 2). Almost no brushes were returned later than in 150 days. Little variation in how quickly the brushes were returned was observed by calendar month in which the invitations were sent (Supporting Information Fig. 1), except for a slight delay over the Christmas period.

Overall, 5,154 (22%) women responded after the first invitation, and an additional 2,330 (10%) after receiving a reminder (Fig. 3). Similarly, brush reminder letters increased the number of returned brushes (participation) from 3,258 (14%) to 4,824 (20%). The increases in the responses and returned brushes after sending out reminders did not seem to be age-dependent. The increase of the participation rate after sending out reminders was, however, slightly higher for

**Table 3.** Response and participation, by response method

| Response method | Median age of responders (years; IQR) | | Responders (%)[1] | | Participants (%) | | Screened by a physician[2] (%) | |
|---|---|---|---|---|---|---|---|---|
| Regular mail | 49 | (38–59) | 4,547 | (61%) | 2,886 | (60%) | 216 | (58%) |
| Phone call | 51 | (41–60) | 99 | (1%) | 58 | (1%) | 11 | (3%) |
| Webpage | 45 | (36–55) | 2,794 | (37%) | 1,853 | (38%) | 140 | (38%) |
| E-mail | 41 | (34–52) | 37 | (<1%) | 21 | (<1%) | 3 | (1%) |
| Total | 48 | (37–57) | 7,484 | (100%) | 4,824 | (100%) | 370 | (100%) |

Responders= women who ordered a brush. Participants= women who returned their brush. Webpage = access via desktop or mobile device.
Abbreviations: IQR: interquartile range. Note: Women may have made several contacts with the Department throughout the study period. The contact in which the women ordered the self-sampling kit is counted here.
[1]Twenty-one women responded to us via a separate questionnaire study. Seven women requested a self-sampling brush and six returned it.
[2]Screened by physician without returning their self-sampling test.

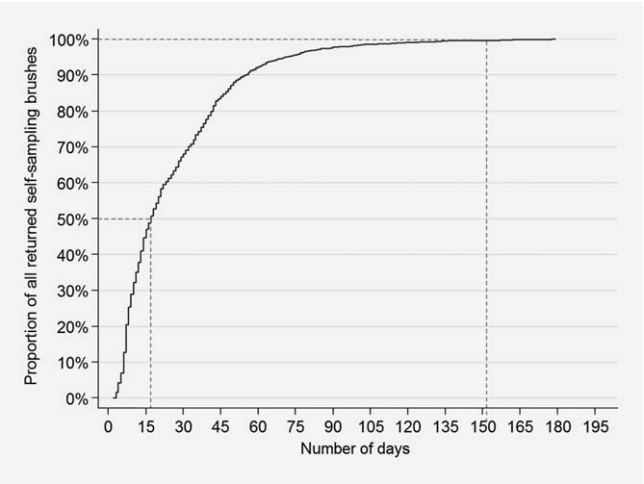


**Figure 2.** Response time[a]: Cumulative response time for all women participating in self-sampling. Response time defined as number of days between the self-sampling kit sent out to it being returned to the laboratory.

intermittently screened women than long-term unscreened (9% *vs.* 5%, respectively. Data not reported)

## Discussion

### Findings

In this first Danish pilot implementation of opt-in HPV-based self-sampling for screening nonattenders, women could respond to the invitation through various communication platforms with written information provided in several languages. In total, 20% of the nonattending women returned a self-sampling kit for testing. This was, despite the opt-in approach, substantially more than the proportion of women who sought screening of their own accord. The intervention was particularly acceptable for intermittently screened women, with the 28% participation in self-sampling contributing to the 46% overall coverage during the study period. For the long-term unscreened women, 16% participation was observed. Only 11% of the invited women requested a brush but did not return it, so loss of self-sampling kits was limited.

The choice of the Evalyn brush may have influenced the participation rates. We chose it based on the security consideration of not distributing medical liquids to private homes. Also, among Dutch women this brush was slightly more acceptable than a lavage device.[19] By our request, the manufacturer embedded a unique RFID chip into the each brush's handle. This allowed safe patient identification without women needing to return sample identification forms. Using the RFID, all returned brushes could be correctly identified.

The returned self-sampling brushes were likely not the only effect of the CSi invitations. We observed that 10% of all invited women had a physician-taken cytology sample registered in the Patobank after receiving the CSi invitation. It is unknown whether the CSi invitation was the main motivation for having a routine cytology sample taken, or whether it acted in concert with other considerations. This effect, however, differed markedly by age. Whereas about 15% of younger women (27–49 years) underwent such sampling, this was only 3–4% in older women (50–65 years). From this, it could be speculated that older nonattenders specifically avoid screening for not wanting to have the gynecology examination required for a physician-taken sample or because they think that screening may no longer be needed. The questionnaire study by the Danish Cancer Society is underway to study this.

### Strength and limitations of the study

Women eligible for the study were randomly selected for CSi, and were representative of all eligible nonattenders in the Danish Capital Region. Their screening statuses were determined from national administrative registration, avoiding subjective recall. As we could not use the updated information on the women's screening activities within the study period, 4% of the invited women actually underwent cytology-based screening prior to receiving a self-sampling invitation. In a routine setup, the invitation module would be updated on a daily basis allowing the invitations being targeted at true nonattenders. The initial national media coverage of the CSi may have resulted in a somewhat higher

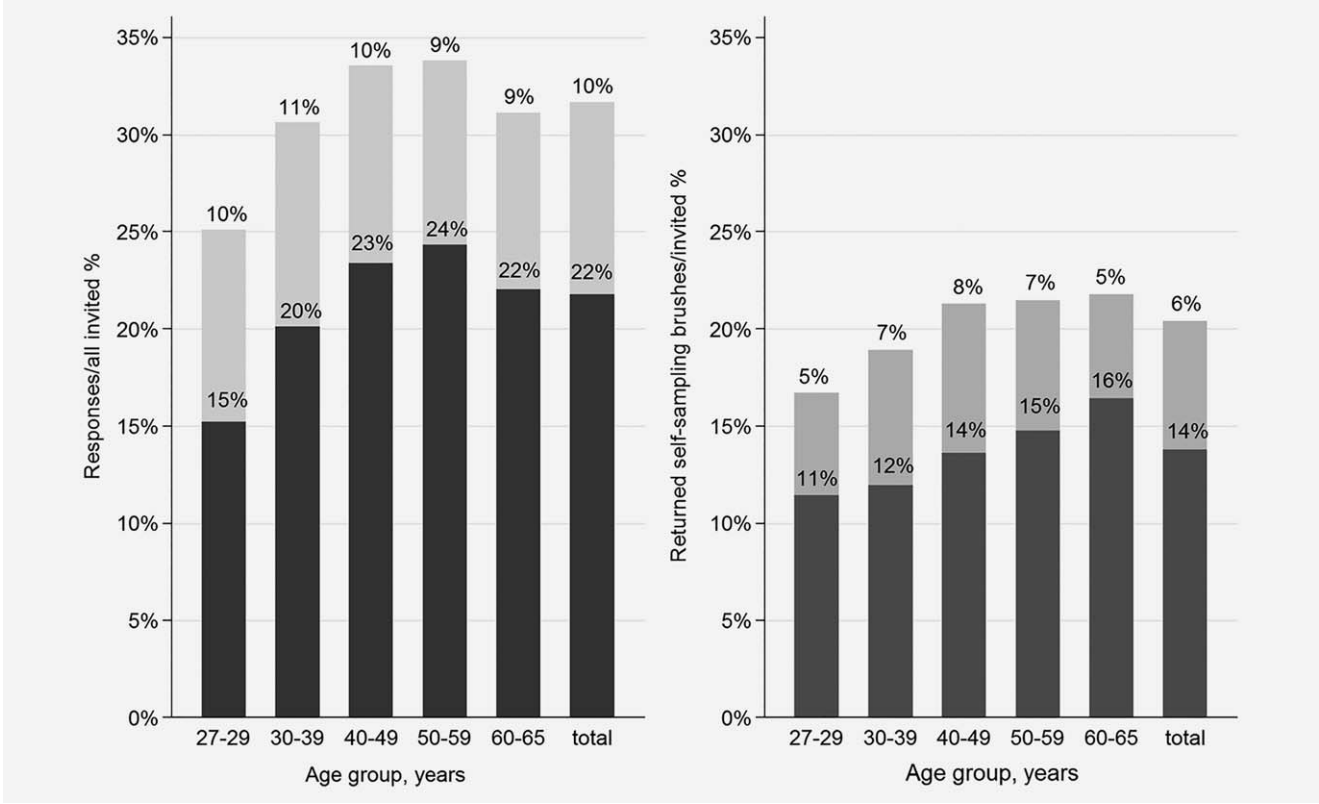


**Figure 3.** Response and participation before and after reminder letters sent out, by age group[a]. (*a*) Left-hand side: Darker shade= proportion of responses out of all invited women after first invitation sent out. Lighter shade= Proportion of responses out of all invited women after invitation reminders sent out. Right-hand side: Darker shade =Proportion of returned self-sampling tests out of all invited women. Lighter shade= Proportion of returned self-sampling tests out of all invited women after self-sample reminders sent out.

recruitment than can be expected in a steady state. Nevertheless, the effect was relatively small and time-limited, even if statistically significant (27% participation after the first batch *versus* 20% after the remaining 23 batches combined, $p < 0.001$).

### Comparison with other studies

The response to opt-in strategies tends to be lower compared to opt-out strategies.[20] Our choice for an opt-in strategy was mainly based on considerations of cost of purchase and mailing of self-sampling kits including the administration of reminders. Two Swedish opt-in studies by Sanner *et al.*[12] and Stenvall *et al.*[11] targeted women unscreened for 6 years. Their screening history was determined from a cytology register, suggesting that these women had been screened before. The achieved participation rates, using the Qvintip device, were 39%[12] and 31%.[11] In the latter study, therefore, a similar participation rate was achieved as in our intermittently screened Group (28%). Both studies also observed the very long time for self-sampling devices to be returned for testing. In another Swedish opt-in study, Broberg *et al.*[16] observed a 17% participation rate among women who had not responded to at least four screening invitations, which was similar to 16% in our long-term unscreened group. An additional 9% chose to undergo physician-taken sampling after the self-sampling invitation. Intermittently screened women were more likely to participate than long-term unscreened women. Giorgi-Rossi *et al.* invited Italian women for opt-in self-sampling if they had not responded to a routine invitation for 3–5 months.[13,14] Here, 20% women participated when offered to have the kit sent to home and 9–11% when they could pick it up from a local pharmacy. In Denmark, this is the period in which women still receive screening reminders; these reminders almost double the participation rate.[1] Women selected for CSi were those who were harder to reach and did not respond to the two reminders. Hence, the two Italian studies showed a much lower participation rate than CSi.

### Implications for operationalization of self-sampling for nonattenders

In a routine screening program, the numbers of screening samples are affected by the opening hours of general practitioners and by public holidays. In our Department, this leads to an up to 50% seasonal variation in the number of received samples, with lowest numbers during the summer holidays. We sent out CSi invitations throughout an entire calendar year and observed no seasonal variation, with the exception of a small delay over the Christmas period (Supporting Information Fig. 1). This enables laboratories to plan operational capacity more evenly over the course of a business year.

Reminders led to a 9–11% increase in response, and to an increase of 5–8% in returned brushes (Fig. 3). An "invitation-reminder" strategy thus seems preferable if planning a full routine roll-out, even though formal cost-effectiveness calculations to support this are still needed.

The option of multiple electronic platforms is a new feature. Nowadays, 93% of Danes have a smartphone or cell phone, and 81% of these use it online.[21] We developed a dedicated webpage. This convenient and easy-to-use platform was used by one-third of all responders and it was well accepted by all age groups. Nevertheless, online communication methods were used slightly more frequently by younger women—suggesting that, with an influx of ever younger birth cohorts into the screening programme, online methods may, over time, become increasingly important to reach nonattenders.

This study used approximately 1,600 kg of paper to communicate with women (Supporting Information Table 1), equaling to 51 sheets of paper and/or envelopes (plus the accompanying postage) per returned brush. Adding to this was the logistics of the mailing (invitations, reminders and brushes) and administration of the responses and additional questions from women, which were all handled by the laboratory staff. These all need to be taken into account when planning the capacities for a full roll-out.

## Conclusions and policy implications

The combination of self-sampling with HPV testing has the potential to improve screening participation among women who participate infrequently or not at all. Our opt-in strategy generated a reasonable response and brush return rate, and the electronic communication platforms showed promising uptake rates. However, long-term nonattenders remain a challenging group to motivate for cervical screening.



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