

# Determinants for Participation in Human Papillomavirus Self-Sampling among Nonattenders to Cervical Cancer Screening in Denmark

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## Abstract

**Background:** Offering human papillomavirus–based self-sampling to nonparticipants in routine cervical cancer screening can increase screening participation. However, little is known about characteristics of women who accept self-sampling. In this population-based study, we investigated determinants for participation in self-sampling among Danish nonattenders to routine cervical cancer screening.

**Methods:** During 2014 to 2015, a random sample of screening nonparticipants ages 27 to 65 years living in the Capital Region of Denmark were invited for self-sampling. Of 21,314 eligible women, 4,743 participated in self-sampling. Information on sociodemographic characteristics and mental and physical health of all the women was obtained from nationwide registries, and 3,707 women completed a questionnaire on lifestyle, sexual behavior, and reasons for nonparticipation in routine screening. We used logistic regression to estimate ORs for participation in self-sampling, crude, and adjusted for sociodemographic characteristics.

**Results:** Basic education [OR<sub>adjusted</sub> = 0.79; 95% confidence interval (CI), 0.72–0.88], low income (OR<sub>adjusted</sub> = 0.66; 95% CI, 0.59–0.73), origin from a nonwestern country (OR<sub>adjusted</sub> = 0.43; 95% CI, 0.38–0.48), and being unmarried (OR<sub>adjusted</sub> = 0.66; 95% CI, 0.61–0.72) were associated with lower self-sampling participation. Long-term unscreened women (OR<sub>adjusted</sub> = 0.49; 95% CI, 0.45–0.53), women with prior schizophrenia or other psychoses (OR<sub>adjusted</sub> = 0.62; 95% CI, 0.48–0.80), women with poor self-perceived health (OR<sub>adjusted</sub> = 0.42; 95% CI, 0.25–0.69), and women who perceived screening as unnecessary (OR<sub>adjusted</sub> = 0.54; 95% CI, 0.37–0.80) or irrelevant (OR<sub>adjusted</sub> = 0.81; 95% CI, 0.78–0.96) were less likely to self-sample.

**Conclusions:** Certain population groups, including women with low socioeconomic position or of nonwestern origin, were less likely to participate in self-sampling.

**Impact:** Targeted approaches may be needed to increase screening participation in these groups. *Cancer Epidemiol Biomarkers Prev*; 27(11); 1342–51. ©2018 AACR.

## Introduction

High coverage is essential for an effective cervical cancer screening program, but low participation remains a challenge in many countries (1). In the Danish national screening program, women ages 23 to 49 years are invited for screening every 3 years and those ages 50 to 65 every 5 years (2). Screening is

performed by liquid-based cytology in women ages 23 to 59 and by human papillomavirus (HPV) testing of clinician-taken samples in women ages 60 to 65 (2). Screening samples are obtained by general practitioners or gynecologists. In 2016, the coverage of the Danish screening program was 74%, which is below the national goal of >85% (3). Approximately 45% of Danish women diagnosed with cervical cancer have not been screened at the recommended intervals (4). Although screening visits and subsequent follow-up procedures are free of charge, previous Danish studies have found socioeconomic inequalities in screening participation (5, 6) and in the incidence of (7) and survival from (7, 8) cervical cancer.

Barriers to participation in cytology-based screening include organizational factors, e.g., limited clinic hours or difficulty in scheduling an appointment, and personal factors, e.g., discomfort or embarrassment associated with the gynecologic examination (9–11). Recently, self-sampling, in which women collect a sample in their home and send it to a laboratory for HPV testing, was proposed as a method to overcome these barriers. There is growing evidence that this method appeals to women who would not otherwise be screened (12–16). In the Copenhagen Self-sampling initiative (CSi), a large-scale implementation study

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in which self-sampling was offered to 23,632 nonparticipants in the Danish routine screening program, 20% of the invited women participated in self-sampling (16).

Despite the promising results of studies in which self-sampling was offered to nonparticipants in routine screening, we have limited knowledge about which population groups are reached by this screening method and about the characteristics of women who do not accept the offer. Previous studies have found that sociodemographic characteristics, including ethnicity and educational level (14, 17–19), and previous screening behavior (12, 16, 18–21) are associated with self-sampling participation. To increase our knowledge of participation in self-sampling among nonattenders at routine cervical cancer screening, we conducted a registry- and questionnaire-based study among women invited for the Danish CSi study. We collected detailed information on their sociodemographic characteristics, mental and physical health, lifestyle, sexual behavior, and reasons for nonparticipation in routine screening or self-sampling. Our aim was to identify determinants for participation in HPV self-sampling in a Danish population of nonattenders at routine screening.

## Materials and Methods

### The CSi study

The CSi is described in detail elsewhere (16). In brief, during May 2014 to April 2015, we invited a random sample of women ages 27 to 65 years living in the Capital Region of Denmark who had not been screened for at least 4 years (for those ages 27–49 years) or 6 years (for those ages 50–65 years) to participate in HPV self-sampling. A total of 23,632 women received an invitation letter at their home address. The invitation included information on HPV, cervical cancer and self-sampling; a reply form; and a prepaid return envelope. Women could opt in to the study by ordering a self-sampling kit on the study website, by phone, by e-mail, or by returning the reply form. Women who agreed to participate in self-sampling received a kit mailed to their home address with detailed instructions for taking the test and a prepaid return envelope. The invitation letter and mailed instructions for self-sampling were in Danish; however, information about HPV and cervical cancer and instructions for self-sampling were available on the study website in Arabic, English, French, and Turkish, and an animated instruction video was available on the website in Danish and English.

Returned self-samples were tested for HPV at the Department of Pathology, Copenhagen University Hospital, Hvidovre. HPV-positive women were recommended to see their general practitioner to have a cytology sample taken.

### Questionnaire study

In the CSi invitation letter, women were also invited to participate in a questionnaire study. The questionnaire was available online or could be ordered on paper. Woman who requested the paper version received it at their home address with a prepaid return envelope. Reminders were sent to women who did not respond within 3 weeks. Women who did not return their questionnaire within 3 weeks after the reminder were contacted by phone and offered the possibility of answering the questionnaire over the phone. The questionnaire contained questions on general health, lifestyle, sexual habits, and

sexually transmitted infections (STI). Women were asked why they had not participated in the previous round of routine screening, and those who did not order the self-sampling test were asked why they did not wish to take the test. The answer options to the latter question were: "It does not feel relevant to me," "I am unsure of the purpose," "I am not comfortable with performing self-sampling," "I am afraid of the result of the test," "I do not believe the test is useful," "Religious or cultural reasons," "I am too busy," and "Other." Multiple responses were allowed.

### Registry linkages

All Danish residents are assigned a unique personal identification number which is used as identification key in all national registers. From nationwide registers, we retrieved information on sociodemographic characteristics, mental health, and selected aspects of physical health of the study population. The variables were selected *a priori* on the basis of previous studies of determinants for participation in routine screening.

Information on sociodemographic characteristics (country of origin, marital status, highest attained educational level, and income) were obtained from Statistics Denmark (22). Country of origin was categorized as Denmark, western countries (European Union, Andorra, Iceland, Liechtenstein, Monaco, Norway, San Marino, Switzerland, the Vatican, Canada, the United States, Australia, and New Zealand), and nonwestern countries (all others). Educational level in the year of invitation was categorized as basic (mandatory school only, approximately  $\leq 9$  years), medium (high-school and vocational education, approximately 10–12 years), and high (short-, medium-, or long-term higher education,  $>12$  years). Income in the year of invitation was divided into quartiles on the basis of the income distribution in the CSi population.

Information on mental health was obtained from the Psychiatric Central Research Register, which contains information on psychiatric admissions since 1969 and psychiatric outpatient hospital contacts since 1995 (23). We included previous diagnoses of intoxicant abuse [International Classification of Diseases version 8 (ICD-8) 291, 294.30, 303–304; ICD-10 F10–19]; schizophrenia and other psychoses (ICD-8 295, 297, 298.39; ICD-10 F20–29); affective disorders (ICD-8 296, 298.09–19; ICD-10 F30–39); anxiety, adjustment and obsessive compulsive disorders (OCD; ICD-8 300; ICD-10 F40–43); and eating disorders (ICD-8 306.50–306.59; ICD-10 F50).

Information on HPV vaccination status at the time of invitation was obtained from the National Health Service Register (24), which contains information on free-of-charge HPV vaccination within the national program, and the Prescription Register (25), which holds information on HPV vaccines bought in pharmacies. Information on previous diagnoses of any cancer was obtained from the Cancer Register, which has recorded all cancer diagnoses in Denmark since 1943 (26). From the National Patient Register, we obtained information on all hospital admissions since 1977 and all outpatient hospital contacts since 1995 (27). We used this information to calculate the Charlson comorbidity index (28), a cumulative score for previous diagnoses of 19 conditions. Information on women's screening history was obtained from the Pathology Databank, which contains the dates and results of all cervical cytology and histology examinations in the country (29). We divided women into those who had been screened intermittently (last smear  $\leq 10$  years before CSi) and

those who were long-term unscreened (no previous smear or last smear >10 years before CSi). This variable was only defined for women aged  $\geq 34$  years who had been eligible for screening for >10 years.

#### Permissions and data handling

The questionnaire study and registry linkages were approved by the Danish Data Protection Agency (ref. no. 2014-41-2821). After the registry linkages, the women's personal identification numbers were removed from the dataset, and the data were subsequently stored and analyzed under a random study number.

#### Study population for analysis

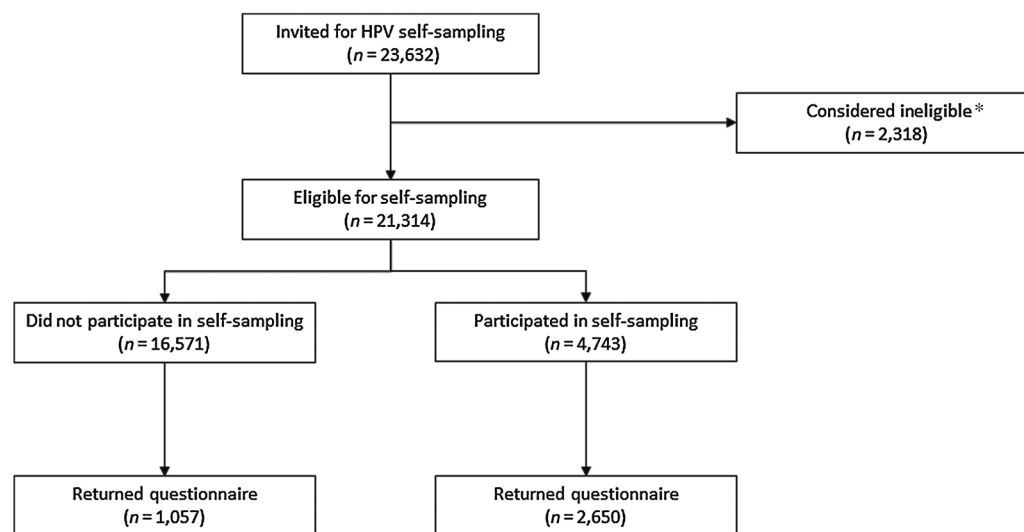
Of the 23,632 women invited for self-sampling, 1,344 were considered ineligible for the present study because they had emigrated ( $n = 138$ ), moved ( $n = 224$ ), or died ( $n = 38$ ) before receiving the invitation; were hysterectomized according to self-reporting or according to the National Patient Register ( $n = 771$ ); or reported that they were pregnant at the time of invitation ( $n = 173$ ). An additional 974 women were screened (i.e., a cytology was registered in the Pathology Databank) between the date of identification of the CSi population and the date of our contact. These women were excluded from the analysis, because they could not be considered screening nonattenders. Thus, 21,314 invited women were eligible for this study. Of these, 4,743 (22.3%) participated in HPV self-sampling, and, of these, 2,650 returned the questionnaire. Of the 16,571 women who did not participate in self-sampling, 1,057 returned the questionnaire (Fig. 1).

#### Statistical analyses

Initially, we investigated potential determinants of participation in self-sampling using registry data in the entire eligible study population ( $n = 21,314$ ). Analyses were performed by logistic

regression, with associations expressed as odds ratios (OR) with corresponding 95% confidence intervals (CI). Associations were reported unadjusted and adjusted for sociodemographic characteristics, because sociodemographic characteristics have been found associated with routine screening participation and could potentially be associated with mental and physical health. Women with missing information on specific variables (no information on education:  $n = 2,160$ ; no information on income:  $n = 1$ ; no information on country of origin:  $n = 1$ ) were excluded from analyses including those variables. When we repeated the analyses excluding women with missing information on sociodemographic characteristics from all models, our conclusions were unchanged.

Subsequently, we investigated potential determinants of participation in self-sampling based on questionnaire responses from women who returned the questionnaire ( $n = 3,707$ ). To assess the risk of nonresponse bias, we used registry data to compare the sociodemographic and health-related characteristics of women who did and did not return the questionnaire. Logistic regression models were used to estimate associations between questionnaire variables and participation in self-sampling. To take into account potential nonresponse bias, associations were adjusted for sociodemographic characteristics and mental and physical health as measured in registries. The potential determinants from questionnaires were general health [self-perceived health, body mass index (BMI), and self-perceived body size]; lifestyle (smoking and alcohol consumption); sexual health (ever having had sex, lifetime number of partners, age at sexual debut, number of new partners within the past 6 months, and history of genital warts, chlamydia, herpes, or gonorrhoea); and self-reported reasons for not participating in routine screening. BMI was categorized according to the World Health Organization's definitions, as



\* Women were considered ineligible if they died before our contact ( $n = 38$ ), emigrated before our contact ( $n = 138$ ), moved before our contact ( $n = 224$ ), were hysterectomized before our contact ( $n = 771$ ), were pregnant at the time of our contact ( $n = 173$ ), or were screened by general practitioner before our contact ( $n = 974$ ).

**Figure 1.**

Flowchart of the study population.

**Table 1.** Sociodemographic characteristics of nonattenders to cervical cancer screening in the Danish Capital Region invited for HPV self-sampling in the CSI Study, 2014–2015 (*n* = 21,314)

Sociodemographic characteristics	<i>N</i> (%)
Age at invitation (years)	
27–29	1,856 (8.7)
30–39	4,995 (23.4)
40–49	5,077 (23.8)
50–59	5,362 (25.2)
60–65	4,024 (18.9)
Country of origin <sup>a</sup>	
Denmark	15,211 (71.4)
Western countries	1,924 (9.0)
Nonwestern countries	4,178 (19.6)
Educational level (in the year of invitation) <sup>a</sup>	
Basic	5,020 (23.6)
Medium	7,006 (32.9)
High	7,128 (33.4)
Marital status (in the year of invitation)	
Married	9,075 (42.6)
Unmarried	7,904 (37.1)
Divorced or widowed	4,335 (20.3)

<sup>a</sup>Numbers do not add up to the total because of missing values.

underweight (BMI <18.5 kg/m<sup>2</sup>), normal weight (18.5–24.9), overweight (25.0–29.9), and obese (≥30.0). Alcohol consumption was measured as units per week and categorized according to the recommendation of the Danish National Board of Health (≤7 units/week recommended). Lifetime number of partners and age at sexual debut were categorized into ordinal variables based on quartiles (number of partners) or tertiles (age at debut) in the study population. Among women who did not return the self-sampling test but responded to the questionnaire, we described self-reported reasons for not participating in self-sampling. Statistical analyses were performed in R (version 3.4.2; ref. 30).

## Results

### Characteristics of the study population

Table 1 shows the sociodemographic characteristics of the study population. Most women were ages 30 to 59 years (72.4%), had medium (32.9%) or high (33.4%) education, and were of Danish origin (71.4%). Women of nonwestern origin were mainly from Turkey (*n* = 653, 16%), Pakistan (*n* = 556, 13%), and the Philippines (*n* = 349, 8%). Women of western origin were mainly from Poland (*n* = 378, 20%), Germany (*n* = 159, 8%), Sweden (*n* = 150, 8%), and Norway (*n* = 141, 7%).

### Registry-based analysis

Table 2 presents crude and adjusted associations between sociodemographic characteristics and participation in self-sampling. The crude odds for participation in self-sampling were slightly higher among women aged ≥30 years than among those ages 27 to 29 years. We found lower crude odds for self-sampling participation among women of non-Danish origin than among Danish women; among unmarried or divorced/widowed women than among married women; and among women with basic or medium education than among those with high education. The odds for participation in self-sampling decreased with decreasing income. After mutual adjustment for all sociodemographic characteristics, the odds for participation in self-sampling were no longer statistically significantly lower among women from western countries or women with medium education than among Danish women and women with high education, whereas the other associations were largely unchanged.

Table 3 shows the crude and adjusted ORs of participation in self-sampling according to mental and physical health as measured in the registries. The unadjusted analyses showed that women with a history of schizophrenia or other psychoses (OR<sub>crude</sub> = 0.49; 95% CI, 0.39–0.63) and anxiety, adjustment

**Table 2.** Associations between sociodemographic factors and participation in HPV self-sampling among nonattenders to routine cervical cancer screening invited for HPV self-sampling in the CSI study, 2014–2015 (*n* = 21,314)

Sociodemographic characteristics	<i>N</i>	(% self-sampling participants)	OR (95% CI)	OR <sup>a</sup> (95% CI)
Age at invitation (years)				
27–29	1,856	(19.0)	1	
30–39	4,995	(21.3)	1.16 (1.01–1.32)	
40–49	5,077	(23.4)	1.30 (1.14–1.48)	
50–59	5,362	(22.7)	1.25 (1.10–1.43)	
60–65	4,024	(22.8)	1.26 (1.10–1.45)	
Country of origin <sup>b</sup>				
Denmark	15,211	(25.2)	1	1
Western countries	1,924	(20.4)	0.76 (0.68–0.86)	0.89 (0.76–1.04)
Nonwestern countries	4,178	(12.5)	0.43 (0.39–0.47)	0.43 (0.38–0.48)
Marital status (in the year of invitation)				
Married	9,075	(25.2)	1	1
Unmarried	7,904	(19.7)	0.73 (0.68–0.78)	0.66 (0.61–0.72)
Divorced or widowed	4,335	(20.8)	0.78 (0.71–0.85)	0.77 (0.70–0.84)
Educational level (in the year of invitation) <sup>b</sup>				
Basic	5,020	(18.2)	0.63 (0.58–0.69)	0.79 (0.72–0.88)
Medium	7,006	(23.6)	0.88 (0.81–0.95)	0.96 (0.89–1.04)
High	7,128	(26.0)	1	1
Income (in the year of invitation) <sup>b</sup>				
Q1 (<€ 18,217)	5,187	(16.1)	0.47 (0.43–0.52)	0.66 (0.59–0.73)
Q2 (€ 18,217–26,213)	5,326	(19.0)	0.58 (0.53–0.63)	0.74 (0.67–0.82)
Q3 (€ 26,213–35,408)	5,418	(24.7)	0.81 (0.74–0.88)	0.90 (0.82–0.99)
Q4 (>€ 35,408)	5,382	(28.9)	1	1

<sup>a</sup>Adjusted for age, country of origin, marital status, educational level, and income.

<sup>b</sup>Numbers do add up to the total because of missing values.

**Table 3.** Associations between mental and physical health and participation in HPV self-sampling among nonattenders to routine cervical cancer screening invited for HPV self-sampling in the CSI study, 2014–2015 ( $n = 21,314$ )

Mental and physical health <sup>a</sup>	N	(% self-sampling participants)	OR (95% CI)	OR <sup>b</sup> (95% CI)
Mental health				
Intoxicant abuse				
Never	20,629	(22.3)	1	1
Ever	685	(20.0)	0.87 (0.72–1.05)	0.99 (0.81–1.20)
Schizophrenia and other psychoses				
Never	20,732	(22.5)	1	1
Ever	582	(12.5)	0.49 (0.39–0.63)	0.62 (0.48–0.80)
Affective disorders				
Never	20,059	(22.4)	1	1
Ever	1,255	(20.3)	0.86 (0.77–1.02)	0.97 (0.83–1.12)
Anxiety, adjustment disorders, and OCD				
Never	19,353	(22.3)	1	1
Ever	1,961	(19.9)	0.86 (0.76–0.96)	0.93 (0.82–1.05)
Eating disorders				
Never	21,095	(22.2)	1	1
Ever	219	(25.1)	1.17 (0.86–1.60)	1.15 (0.84–1.57)
Physical health				
HPV vaccination status				
Never	20,307	(21.1)	1	1
Ever	1,007	(24.4)	1.14 (0.98–1.32)	1.55 (1.24–1.94)
Previous cancer diagnosis (any cancer)				
Never	20,418	(22.1)	1	1
Ever	896	(26.5)	1.27 (1.09–1.48)	1.17 (1.00–1.37)
Charlson comorbidity index				
0	17,098	(22.4)	1	1
1	2,375	(21.7)	0.96 (0.87–1.07)	1.00 (0.90–1.11)
≥2	1,841	(21.8)	0.97 (0.86–1.09)	1.06 (0.94–1.20)

<sup>a</sup>All variables are based on registry data and are measured as never/ever at the time of study start.

<sup>b</sup>Adjusted for age, country of origin, marital status, educational level, and income.

disorders, or OCD ( $OR_{crude} = 0.86$ ; 95% CI, 0.76–0.96) had lower odds for participation in self-sampling than women without such a history. After adjustment for sociodemographic characteristics, women with schizophrenia or other psychoses still had lower odds for participation in self-sampling ( $OR_{adj} = 0.62$ ; 95% CI, 0.48–0.80), whereas the association with anxiety, adjustment disorders, and OCD was attenuated and became statistically nonsignificant. Women who had been vaccinated against HPV ( $OR_{crude} = 1.14$ ; 95% CI, 0.98–1.32) or had a previous diagnosis of any cancer ( $OR_{crude} = 1.27$ ; 95% CI, 1.09–1.48) had marginally increased odds for participation in self-sampling in the crude analysis. After adjustment for sociodemographic characteristics, the association between HPV vaccination and self-sampling became more pronounced ( $OR_{adj} = 1.55$ ; 95% CI, 1.24–1.94), whereas the association with previous cancer became statistically nonsignificant ( $OR_{adj} = 1.17$ ; 95% CI, 1.00–1.37). We found no association between Charlson comorbidity index and participation in self-sampling, in either the crude or the adjusted analysis.

In the subset of the study population aged  $\geq 34$  years at the time of invitation ( $n = 17,348$ ), women who were long-term unscreened were less likely to participate in self-sampling than those who were screened intermittently ( $OR_{crude} = 0.47$ ; 95% CI, 0.44–0.51). This association remained after adjustment for sociodemographic characteristics ( $OR_{adj} = 0.49$ ; 95% CI, 0.45–0.53; Supplementary Table S1).

#### Questionnaire-based analysis

Of the 3,707 women who responded to the questionnaire, 1,748 (47%) responded on paper, 1,591 (43%) on the Internet, and 368 (10%) by phone. Supplementary Table S2 pre-

sents sociodemographic and health-related characteristics of women who did and did not return the questionnaire. Those who did not return the questionnaire were slightly younger, more likely to have low education and income, and more likely to be of nonwestern origin than women who returned the questionnaire.

Table 4 shows the crude and adjusted ORs of participation in self-sampling, according to general health, lifestyle, and sexual behavior as reported in the questionnaire. Women with poor self-perceived health were less likely to participate in self-sampling ( $OR_{crude} = 0.41$ ; 95% CI, 0.25–0.67), and the association was virtually unchanged after adjustment for sociodemographic variables. BMI and self-perceived body size were not significantly associated with participation. Former smokers were more likely to participate in self-sampling than never smokers, both in the crude ( $OR_{crude} = 1.28$ ; 95% CI, 1.07–1.53) and adjusted ( $OR_{adjusted} = 1.24$ ; 95% CI, 1.02–1.49) models. However, current smoking and alcohol consumption were not associated with self-sampling participation. Women who had never had sex were less likely to accept self-sampling than those who had had their sexual debut, both in the unadjusted ( $OR_{crude} = 0.59$ ; 95% CI, 0.38–0.91) and in the adjusted ( $OR_{adjusted} = 0.60$ ; 95% CI, 0.37–0.96) models. Among those who had had sex, lifetime number of sexual partners, age at sexual debut, and number of recent, new sexual partners were not associated with participation in self-sampling. Furthermore, we found no association with history of STIs. When the estimates in Table 4 were further adjusted for registry-based measures of mental health and physical health, all associations were virtually unchanged (Supplementary Table S3).

**Table 4.** Associations between general health, lifestyle and sexual behavior, and participation in HPV self-sampling among nonattenders to routine cervical cancer screening invited for HPV self-sampling in the CSI study, 2014–2015 ( $n = 3,707$ )

Self-reported variables	N <sup>a</sup>	(% self-sampling participants)	OR (95% CI)	OR <sup>b</sup> (95% CI)
<b>General health</b>				
Self-perceived health				
Very good	1,827	(72.2)	1.01 (0.87-1.18)	1.01 (0.86-1.19)
Good	1,388	(72.0)	1	1
Not good	391	(68.5)	0.85 (0.66-1.08)	0.81 (0.63-1.05)
Poor	70	(51.4)	0.41 (0.25-0.67)	0.42 (0.25-0.69)
<b>BMI</b>				
<18.5	119	(67.2)	0.76 (0.51-1.13)	0.73 (0.48-1.10)
18.5-24.9	1,866	(72.9)	1	1
25-29.9	957	(70.1)	0.87 (0.74-1.04)	0.85 (0.71-1.01)
30+	711	(71.0)	0.91 (0.75-1.11)	0.90 (0.74-1.10)
Self-perceived body size				
Too thin	141	(69.5)	0.94 (0.64-1.37)	0.88 (0.59-1.30)
Satisfied	1,160	(70.9)	1	1
A little too big	1,664	(72.5)	1.09 (0.92-1.28)	1.05 (0.89-1.25)
Very big	729	(70.5)	0.98 (0.80-1.21)	0.95 (0.77-1.18)
<b>Lifestyle</b>				
Smoking				
Never smoked	1,405	(70.0)	1	1
Previous smoker	1,075	(74.9)	1.28 (1.07-1.53)	1.24 (1.02-1.49)
Current smoker	1,212	(70.2)	1.01 (0.85-1.19)	0.98 (0.82-1.18)
Alcohol consumption				
Never drinks alcohol <sup>c</sup>	617	(70.7)	1.02 (0.84-1.25)	1.04 (0.84-1.30)
<1-7 units per week	2,062	(70.2)	1	1
8-14 units per week	444	(73.9)	1.20 (0.95-1.52)	1.16 (0.91-1.47)
>14 units per week	271	(74.2)	1.22 (0.92-1.63)	1.12 (0.83-1.51)
<b>Sexual habits</b>				
Has had sex				
Never	85	(60.0)	0.59 (0.38-0.91)	0.60 (0.37-0.96)
Ever	3,572	(71.9)	1	1
Lifetime number of sexual partners <sup>d</sup>				
1-3	811	(71.6)	1	1
4-7	952	(69.9)	0.92 (0.75-1.13)	0.89 (0.71-1.11)
8-14	815	(73.4)	1.09 (0.88-1.36)	1.08 (0.85-1.37)
≥15	835	(72.3)	1.04 (0.84-1.28)	1.07 (0.85-1.36)
Age at sexual debut <sup>d</sup>				
≤15 years	977	(72.4)	0.94 (0.78-1.14)	0.97 (0.80-1.17)
16-17 years	1,293	(73.4)	1	1
≥18 years	1,258	(70.0)	0.84 (0.70-1.00)	0.84 (0.70-1.01)
Number of recent new partners <sup>d,e</sup>				
0	3,171	(71.7)	1	1
≥1	366	(74.3)	1.14 (0.89-1.46)	1.23 (0.94-1.60)
<b>STIs<sup>d</sup></b>				
Genital warts				
Never	3,227	(72.2)	1	1
Ever	344	(68.6)	0.84 (0.66-1.07)	0.84 (0.65-1.07)
Chlamydia, herpes, or gonorrhea				
Never	2,752	(71.9)	1	1
Ever	787	(71.4)	0.98 (0.82-1.17)	1.00 (0.83-1.19)

<sup>a</sup>Numbers do not add up to the total because of missing values.

<sup>b</sup>Adjusted for age, country of origin, marital status, educational level, and income as measured in registries.

<sup>c</sup>Includes never and former drinkers.

<sup>d</sup>Among women who had ever had sex.

<sup>e</sup>New sexual partners within the past 6 months.

Table 5 presents associations between women's self-reported reasons for nonparticipation in routine screening and the odds of participation in self-sampling. Women who reported that they did not like gynecologic examinations were more likely to participate in self-sampling than women who did not give this reason. A similar trend, although not statistically significant, was seen for women who found gynecologic examinations embarrassing or who could not schedule a suitable appointment with their doctor. In contrast, women who

found screening irrelevant or who did not think they needed screening were less likely to participate in self-sampling than women who did not give those reasons. The associations were largely unchanged after adjustment for sociodemographic characteristics.

Of the women who did not return the self-sampling test but responded to the questionnaire ( $n = 1,057$ ), 290 reported why they did not participate in self-sampling. The most common reasons were "I am too busy" ( $n = 70$ , 24%), "It does not feel relevant

**Table 5.** Associations between self-reported reasons for nonparticipation in routine screening and participation in HPV self-sampling among women invited for self-sampling in the CSI study, 2014–2015 ( $n = 3,523$ )<sup>a</sup>

Self-reported reasons for nonparticipation in routine screening	N	(% self-sampling participants)	OR for participation in self-sampling	
			Crude OR (95% CI)	Adjusted OR <sup>b</sup> (95% CI)
It did not feel relevant to me				
No	2,664	(72.1)	1	1
Yes	859	(68.5)	0.84 (0.71–0.99)	0.81 (0.68–0.96)
I do not need screening, because I can feel whether I am sick				
No	3,406	(71.6)	1	1
Yes	117	(59.0)	0.57 (0.39–0.83)	0.54 (0.37–0.80)
Religious or cultural reasons				
No	3,495	(71.3)	1	1
Yes	28	(64.3)	0.73 (0.33–1.58)	0.73 (0.33–1.61)
I do not believe in the result of the examination				
No	3,503	(71.3)	1	1
Yes	20	(55.0)	0.49 (0.20–1.19)	0.51 (0.21–1.23)
I am afraid of the result of the examination				
No	3,183	(71.3)	1	1
Yes	340	(70.9)	0.98 (0.77–1.26)	0.99 (0.78–1.29)
I do not like gynecologic examinations				
No	2,203	(68.9)	1	1
Yes	1,320	(75.2)	1.37 (1.17–1.60)	1.39 (1.18–1.62)
I find gynecologic examinations embarrassing				
No	3,156	(70.8)	1	1
Yes	367	(74.9)	1.23 (0.96–1.58)	1.26 (0.98–1.63)
I could not schedule a suitable appointment with my doctor				
No	3,302	(70.9)	1	1
Yes	221	(76.5)	1.34 (0.97–1.84)	1.37 (0.98–1.91)
I was too busy				
No	2,691	(71.9)	1	1
Yes	832	(69.1)	0.88 (0.74–1.04)	0.91 (0.76–1.09)
I forgot				
No	2,402	(71.2)	1	1
Yes	1,121	(71.2)	1.00 (0.85–1.17)	1.00 (0.85–1.17)
Other reasons				
No	2,709	(72.5)	1	1
Yes	814	(66.8)	0.76 (0.65–0.90)	0.75 (0.63–0.89)

<sup>a</sup>Of the 3,707 women who responded to the questionnaire, 184 did not reply to the question on reasons for nonparticipation in routine screening.

<sup>b</sup>Adjusted for age, country of origin, marital status, educational level, and income as measured in registries.

to me" ( $n = 62$ , 21%), "I do not like to perform self-sampling" ( $n = 44$ , 15%), and "Other reasons" ( $n = 145$ , 50%).

## Discussion

In this large registry- and questionnaire-based study of nonparticipants in the Danish routine cervical cancer screening program who were offered HPV self-sampling, we identified sociodemographic inequalities in women's participation in self-sampling. Women with basic education or low income were less likely to participate in self-sampling than those with high education or income; women of nonwestern origin were less likely to participate than Danish women; and unmarried women were less likely to participate than married women. Furthermore, we identified aspects of mental and physical health, lifestyle, and sexual behavior that were significantly associated with lower participation in self-sampling, including a history of schizophrenia or other psychoses, no screening for >10 years, poor self-perceived health, and never having had sex. Finally, women who reported that they considered cervical cancer screening to be irrelevant or unnecessary were less likely to participate in self-sampling than those who gave other reasons for nonattendance at routine screening.

## Comparison with studies of determinants for participation in HPV self-sampling

In line with our findings, previous studies of HPV self-sampling also found sociodemographic inequalities in the response rate to self-sampling (14, 17–19, 31). In a Finnish study, low educational level was associated with reduced odds for accepting self-sampling (14), and in a study from the United States, women who rejected self-sampling were less likely to have completed college than those who accepted the offer (17). Likewise, in a British study, self-sampling participation was highest among women living in the most socially affluent areas (31). Also in accordance with our findings, several studies found that immigrants (14, 18, 19) and racial or ethnic minorities (17) were less likely to accept self-sampling than the majority population.

Our finding of low self-sampling participation among long-term routine screening nonattenders was previously reported for the CSI study (16) and is in line with other studies of self-sampling from Denmark (12), Finland (19), United Kingdom (20), Sweden (21), and the Netherlands (18). Adding to the previous findings, our analysis showed that the association between screening history and self-sampling participation remained after adjustment for sociodemographic characteristics. Our finding of higher self-sampling participation among intermittently screened women than among long-term nonattenders indicates the importance

of targeting intermittent nonattenders with self-sampling initiatives before they become long-term unscreened.

#### Comparison with studies of determinants for participation in routine screening

The risk factors for nonparticipation in self-sampling identified in the present study are similar to those reported for nonparticipation in routine screening. Registry-based studies in Denmark and other countries with organized screening programs found that women with basic education or low income and immigrants were less likely to participate in routine screening (5, 6, 14, 32–34). These studies also found that women who were unmarried or lived alone were less likely to participate in routine screening than married women (5, 6, 32–34). Furthermore, a Danish register study (5) and British and Canadian studies based on medical records (35, 36) found that women with schizophrenia were less likely to participate in routine screening than women without this condition. Some (37, 38), but not all (39, 40), survey studies found that women with poor self-perceived health were less likely to participate in routine screening than those with excellent or good self-perceived health. These findings underline that when self-sampling is implemented as a general population-based offer to nonattenders at routine screening, certain groups may be reached disproportionately by both the routine screening offer and the offer of self-sampling.

In the present study, women who had never had sex were less likely to participate in self-sampling, but we found no associations with the number of sexual partners, age at sexual debut, or history of STIs. Similarly, most studies of routine cervical cancer screening have found no clear correlations between participation in screening and the number of partners or age at sexual debut (41–43). From a preventive perspective, it is reassuring that women at high risk for cervical cancer due to their sexual history, e.g., many lifetime partners, appear to be as likely to accept self-sampling as those at lower risk.

We found no differences in self-sampling participation according to self-perceived body size or BMI, whereas previous studies have found lower participation in cytology-based screening among overweight or obese women (5, 44). This may potentially suggest that the privacy of self-sampling can overcome weight-related barriers for clinician-taken cervical samples, such as embarrassment or fear of lectures on weight loss (44).

#### Potential reasons for nonparticipation in self-sampling

Our register- and questionnaire-based study does not fully elucidate why certain population groups were less likely to participate in self-sampling. A previous study based on the "health belief model" (45) found that women's willingness to participate in HPV self-sampling was influenced by their perceived self-efficacy to take the sample correctly; their understanding of the link between HPV and cervical cancer; and their perception of the benefits of and barriers to self-sampling (46). Thus, our observation that women with low education were less likely to self-sample might be due to lower self-efficacy to perform self-sampling or lower awareness of the benefits of cancer screening (47, 48). Moreover, socioeconomically disadvantaged groups and women with severe mental illness may experience a challenging everyday life, which could potentially result in decreased capacity to participate in preventive care,

even when offered a free-of-charge and convenient screening method such as self-sampling.

All the women of non-Danish origin in our study were lawful residents of Denmark and were thus legally entitled to the same free-of-charge health care as Danish women. Although in our study information on self-sampling was available online in several languages, the invitation letter was only in Danish, and this may have prevented the participation of some non-Danish women. Furthermore, cultural and religious beliefs and social norms in different ethnic groups may influence perceptions of the benefits of and barriers to self-sampling (49). Some immigrants may choose not to self-sample because they prefer seeking health care in their country of origin (50, 51). Finally, the migration process itself may be a stressor limiting the time and mental resources to participate in preventive care (52).

#### Strengths and limitations

The strengths of this study include the large sample (>21,000 eligible women) and the population-based design. We were able to collect information on several variables for all the eligible women from high-quality nationwide Danish registries, thus eliminating the risk of selection bias in the registry-based analysis. Moreover, to our knowledge, this is the first study in which comprehensive questionnaire data were collected on the lifestyle and sexual behavior of women invited for self-sampling.

The study also has some limitations. First, not all invited women responded to the questionnaire, and the sociodemographic characteristics of responders and nonresponders differed somewhat. We took potential nonresponse bias into account by adjusting the analysis of self-reported determinants for registry-based variables measured among all women. Although these adjustments did not change our results, we cannot exclude the possibility that women who did not respond to the questionnaire differed from responders in terms of lifestyle and sexual behavior. Therefore, the nonresponses may have affected our estimates of associations between self-reported variables and participation in self-sampling. In addition, some misclassification may have occurred in the women's responses to the questionnaire because of social desirability bias or inexact recollection of variables such as number of sexual partners. Such misclassification would most likely be nondifferential, meaning that the observed associations with participation in self-sampling would be underestimated.

#### Conclusions and implications

In conclusion, we found lower self-sampling participation in women with basic education or low income, women from nonwestern countries, women with a history of severe mental disease, and women who had not been screened for  $\geq 10$  years. These findings are most likely generalizable to other countries with organized screening programs where self-sampling is implemented as a population-based offer to nonattenders at routine screening. Our results imply that although population-based self-sampling initiatives are likely to increase general screening coverage (12–21), certain groups of vulnerable women will still not be screened. Smaller, directly targeted interventions may be needed to increase screening uptake in these groups, such as home visits where self-sampling is offered by community health workers (53, 54). Targeted interventions



should include educational materials tailored to specific groups; should be based on theoretical models of behavior change; and should be designed to empower women by increasing their knowledge and building self-efficacy for self-sampling (55). Telephone consultations to assess barriers and provide support for participation may also improve uptake (56). Further research is needed to determine how targeted interventions could be integrated into routine screening programs in order to reduce socioeconomic inequalities in cervical cancer incidence and mortality.

### Disclosure of Potential Conflicts of Interest

J. Bonde is Cervical Screening Commission member on behalf of the Capital Region of Denmark at the Danish National Health Authority, and reports receiving commercial research funding and speakers bureau honoraria from BD Diagnostics. S.K. Kjaer reports receiving commercial research funding and speakers bureau honoraria from, and is a consultant/advisory board member for, Merck. No potential conflicts of interest were disclosed by the other authors.

### Authors' Contributions

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