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Cancer Epidemiology, Biomarkers & Prevention

Research Article

Age-Specific Effectiveness of the Finnish Cervical Cancer Screening Programme

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Abstract

Background: There is currently some uncertainty about the effectiveness of screening outside the established core ages of 30 to 60. We audited the screening histories of cervical cancers and conducted a case–control evaluation of the effectiveness of organized screening in different ages.

Methods: Screening histories for 1,546 cervical cancer cases and 9,276 age-matched controls were derived by linkage to the screening register. ORs and 95% confidence intervals (CI) for the association of participation in a program screen and cervical cancer diagnosis in the following screening interval were estimated using conditional logistic regression and corrected for self-selection bias.

Results: Participation in a single screen was associated with a 47% decrease in cervical cancers, but this effect was age-dependent. Screening at 25 showed little or no impact on the risk of cervical cancer in the next interval, whereas screens at 40 to 65 showed protective effects of 51% to 66%.

Conclusions: Program screening at the age of 25 is not associated with a reduced risk of cervical cancer in the following screening interval. Additional analyses are needed that also take opportunistic screening of women during the first rounds of organized screening into consideration. In contrast, screening yields substantial risk reductions in older ages at least up to the age of 60. This study also provides moderate indication of a long-lasting risk reduction associated with screening at the age of 65.

Impact: Cervical cancer screening effectiveness is for the first time evaluated at different ages up to 65 with correction for self-selection bias of participation in organized screening. *Cancer Epidemiol Biomarkers Prev; 21(8); 1354–61. ©2012 AACR.*

Introduction

Screening is a complex process requiring a high level of organization and careful quality assurance procedures at each step to ensure an adequate balance between benefit and harm in the population. It is also important to evaluate the appropriateness of the screening interval and the age groups being targeted by screening and to do this repeatedly as the impact of risk and protective factors may change over time. One important evaluation tool is the audit of cancer cases with regard to their screening history, stage, and histology determinants (1). However, observational studies measuring the effectiveness of screening have been vulnerable to self-selection bias or the healthy screenee effect which, when present, will bias the effectiveness estimates in favor of screening (2). In settings with high invitational coverage and an established screening program the estimation of the self-selection bias can be challenging. Very few, if any, recent attempts have been made to take this bias into account in the effect estimation of cervical cancer screening. The current study evaluated the magnitude and duration of the protective effect of program screening tests in different age groups for all morphologic types of invasive cervical cancer of various stages at time of diagnosis. Particular attention was given to the marginal age groups 25 and 65, which are currently targeted by invitation only in some geographic areas. In addition, the impact of selection bias on screening effectiveness estimates was evaluated.

Materials and Methods

Setting

The cervical screening program in Finland was initiated in 1963 and roll out was completed by 1970. All women in the target age groups are invited with a personal letter regardless of preceding screening or health history, including hysterectomy. The recommended screening interval is 5 years for women between the ages of 30 and 60; some municipalities use target age groups extended to 25 or 65 or both. Borderline smears result in a risk-group invitation after 1 year instead of the routine 5. Low-grade

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squamous intraepithelial lesion or worse ($LSIL^+$) cytology leads to referral for colposcopy (3). Conventional cytology is the predominant screening test but a number of municipalities in Southern Finland participate in a randomized trial that compares primary human papillomavirus (HPV) DNA screening with cytology (4, 5). Program invitations and screening results for approximately 200,000 tests annually, along with possible colposcopy results, are centrally registered at the Mass Screening Registry. Opportunistic screening tests and diagnostic smears amount to another 300,000 smears per annum but information about these are still not routinely available at the screening register.

Cases and controls

There were 1,548 cancer cases of the uterine cervix (C53) registered in the national Finnish Cancer Registry (FCR) with dates of incidence from January 2000 to December 2009. The ICD-O-3 morphologic code frequencies of all incident cervical cancer cases are presented in Supplementary Table S1. Two cases of squamous cell carcinoma (SCC) were excluded from the study because access to personal data in the population register for scientific purposes had been declined by the women. The case population derived from the FCR can be considered exhaustive in the light of a recent study that reported complete estimates of 99% for cervical cancer (6). The cases were categorized by morphology into SCCs, adenocarcinomas, and other or unspecified malignant neoplasms. The cases were also classified by clinical stage according to the International Federation of Gynecology and Obstetrics (FIGO) guidelines (7) into IA (microinvasive), IB-IIA (localized), or IIB^+ (advanced) using cancer notifications collected at the FCR. Missing clinical stage information was complemented with pathologic stage information (23% of cases).

For each of the 1,546 cases with data access, 6 controls were drawn from the population register, matched for birth year and month. Women were eligible as controls if they were alive and had not been diagnosed with cervical cancer at the time of diagnosis of the case.

Mode of detection and screening history

Linkage of study subjects by the unique personal identifier available for all residents in Finland to the screening register database enabled us to construct a history of program invitations and tests for each woman. The screening register electronic database is close to complete from 1990 onward so it was possible to derive a screening history of a minimum of 10 years retrospective follow-up, covering 2 complete screening rounds. Each case was assigned a mode of detection with respect to invitational screening as shown in Table 1. A case was classified as a nonattender if diagnosis occurred less than 5 years after nonresponse to a program invitation. Screen detection was defined as a date of diagnosis within 12 months of a screening test that resulted in referral (i.e., a positive screening test). Interval cases were diagnosed after a negative or borderline screening test or more than 12 months after a positive screening test, but before the next program invitation. The noninvited were divided into 3 categories: those diagnosed before first invitation and at an age under 30, those diagnosed 5 or more years after last invitation and at an age 64 or more, and those diagnosed within the recommended screening target age range of 30 to 64 but nevertheless lacking a registered invitation. The reasons for lacking an invitation within the target ages were immigration or relocation within the country (35% of this category), nonadherence to the screening age recommendations by the home municipality (24%), and missing invitational information from the home municipality (41%) in which case the real status of invitation was

Table 1. Numbers of invasive cervical cancer cases (Finland, 2000–2009), by mode of detection in relation to screening and stage

	FIGO stage				
	IA	IB-IIA	IIB^+	Unknown	Total
Mode of detection	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
All	332 (100.0)	552 (100.0)	482 (100.0)	180 (100.0)	1,546 (100.0)
Invited	252 (75.9)	337 (61.1)	211 (43.8)	91 (50.6)	891 (57.6)
Nonattender	101 (30.4)	136 (24.6)	141 (29.3)	49 (27.2)	427 (27.6)
Attender	151 (45.5)	201 (36.4)	70 (14.5)	42 (23.3)	464 (30.0)
Screen-detected[a]	82 (24.7)	64 (11.6)	10 (2.1)	11 (6.1)	167 (10.8)
Detected in interval	69 (20.8)	137 (24.8)	60 (12.4)	31 (17.2)	297 (19.2)
Not invited	80 (24.1)	215 (38.9)	271 (56.2)	89 (49.4)	655 (42.4)
Under screening age	33 (9.9)	23 (4.2)	7 (1.5)	5 (2.8)	68 (4.4)
Over screening age	25 (7.5)	140 (25.4)	248 (51.5)	78 (43.3)	491 (31.8)
Other reason	22 (6.6)	52 (9.4)	16 (3.3)	6 (3.3)	96 (6.2)

[a]Detected by invitational screen

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Table 2. Screening status of index round at time of cancer diagnosis (cases) or corresponding date (matched controls)

	Cases	Controls
Screening status	***N* (%)**	***N* (%)**
All	1,546 (100.0)	9,276 (100.0)
No invitation	686 (44.4)	3,994 (43.1)
Before first invitation	91 (5.9)	503 (5.4)
Over screening age[a]	487 (31.5)	2,920 (31.5)
Other reason	108 (7.0)	571 (6.2)
Nonattender	494 (32.0)	1,813 (19.5)
Never attended[b]	414 (26.8)	1,595 (17.2)
Lapsed attender	80 (5.2)	218 (2.4)
Screened	366 (23.7)	3,469 (37.4)
Negative cytology	254 (16.4)	3,190 (34.4)
Borderline cytology	94 (6.1)	164 (1.8)
Negative HPV test	4 (0.3)	96 (1.0)
Referral noncompliance	1 (0.1)	1 (0.0)
Negative histology for CIN	6 (0.4)	9 (0.1)
Positive histology for CIN	7 (0.5)	9 (0.1)

[a]Diagnosis 5 years or more after last program invitation.
[b]During period 1990–2009.

unknown. Each case and control was also classified with respect to the outcome of the preceding age-group invitation or index invitation (Table 2). The index invitation was defined by the last age-group program test within the 66-month period immediately preceding the diagnosis. This time period corresponds to one screening interval and a 6-month allowance for test date variation within the invitational year. Where no such test was found, the last age-group invitation within 72 months but excluding any invitations in the 6 months immediately preceding diagnosis, was used as index, to account for the delay between invitation and screening test. If the case was screen-detected, that screening event was disregarded and the previous invitational screening event determined the index screening status for the case and its matched controls. The majority, 97%, of all age-group invitations were targeted at women in ages divisible by 5.

Statistical methods

Conditional logistic regression analysis was used to estimate ORs of cervical cancer associated with participation among invited women, approximating the risk ratio of cervical cancer diagnosed in the interval between screening invitations up to and including any screen-detected diagnoses in the following screening event. Attendance in the index-screening event was regarded as the exposure. We estimated a correction factor to account for self-selection bias by calculating ORs for those not responding to invitation compared with those not having been invited. This was possible because some municipalities have invited women at the age of 25 (overall 32% national coverage by invitation over the study period), some at the age of 65 (14% invitational coverage), and the invitational coverage of age cohorts 30 and 60 have also been incomplete during the study period (81% and 83%). From the latter half of the 2000s, coverage by 5-yearly invitation of women aged 30 to 60 has been close to 100% (8). OR of cervical cancer in the following 5-year interval for those choosing not to attend screening after an invitation compared with those not invited was estimated at 1.29 [95% confidence interval (CI), 1.03–1.61]. The corrected ORs for screening effect were estimated by applying formula (5) from Duffy and colleagues (9), using the participation rate of 71% of the source population, that is, those invited to screening in 1990 to 2009 in the cervical cancer screening program. The association of cervical cancer with the age at last program screening test was examined using crude ORs of screened compared with not screened regardless of invitational status, as the purpose was internal comparison. STATA/MP 11.0 software (StataCorp LP) was used for all statistical calculations.

Results

Stage and morphology

The stage distribution of cancers of different morphology showed that microinvasive carcinomas (stage IA) constituted a clearly larger proportion of the SCCs (28%) than of the adenocarcinomas (12%). Conversely, a higher percentage of the adenocarcinomas were localized (44% compared with 33%) or advanced (33% compared with 29%). The group comprising other or unknown morphologies showed higher proportions of advanced (45%) and unknown (26%) stages than the 2 major types of cervical carcinoma.

The age distribution of case frequency for cervical cancer had 2 peaks (Fig. 1). Early stages of invasion dominated in the younger age groups whereas after the age of 65, the majority of cases were diagnosed in the advanced stages of disease. SCC was the most common morphologic type across the age groups. The proportion of SCCs decreased steadily until the age of 65 after which a new increase was observed.

Mode of detection

Nearly one third of both SCCs and adenocarcinomas were diagnosed more than 5 years after the age of last invitation. Close to 30% of cases of both morphologies were diagnosed in nonattenders (Fig. 2). However, there was a clear difference between these 2 cancer morphologies with respect to the proportion of interval cancers, constituting 17% of the SCCs and 25% of the adenocarcinomas. Also, a slightly larger proportion of the SCCs were screen-detected (12%) than the adenocarcinomas (10%). Of stage IA cancers, 24% were detected as a result of a program screening test, compared with 12% of stage IB-IIA cancers and only 2% of advanced cancers (Table 1). The proportion of cases diagnosed in nonattenders was

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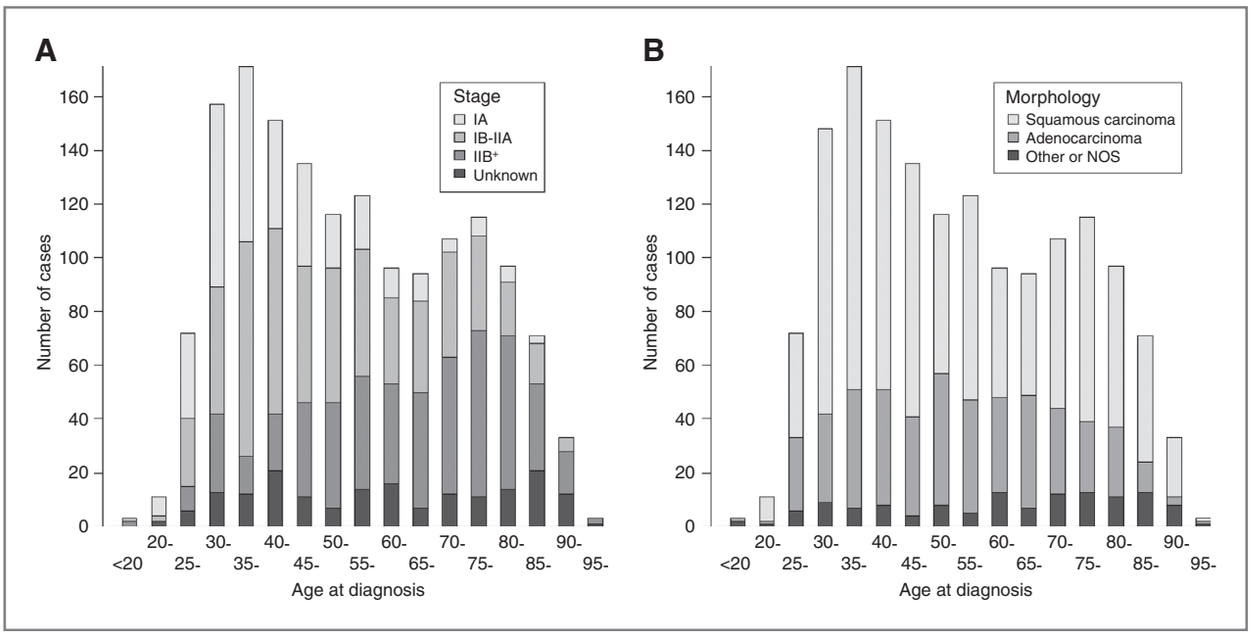

Figure 1. The stage (A) and morphology (B) distributions of invasive cervical cancers diagnosed in Finland in 2000 to 2009, by 5-year age groups at diagnosis.

fairly constant across stage whereas the proportions of cases diagnosed in noninvited women was clearly larger in the advanced (56%) than in the microinvasive (24%) stages of cancer at time of diagnosis.

Effect of screening

Clear differences were found in the screening status distribution of cases and controls (Table 2). One third of the cases were nonattenders compared with 20% of the controls. Also, only 24% of the cases attended screening in the index round compared with 37% of the controls, and of those case women that did attend, a higher proportion had borderline or positive screening results compared with the controls.

ORs corrected for self-selection, of the association of cervical cancer and participation in screening, suggest that there was little or no effect of screening at the age of 25 to 29 (Table 3). A screening test at the age of 30 to 34 and 35 to 39 lowered the risk of cervical cancer in the next interval by 21% to 27% according to the point estimates but the CIs of the ORs include 1. For the age groups of 40 to 64, significant risk reductions of more than 50% were observed. For screening at the age of 65 to 69 a nonsignificant effect of 51% was observed. Overall risk reduction effected by a single age-group test in the screening program was estimated at 47%.

The main results were calculated with cervical cancer diagnosis of any stage or morphology as outcome. As

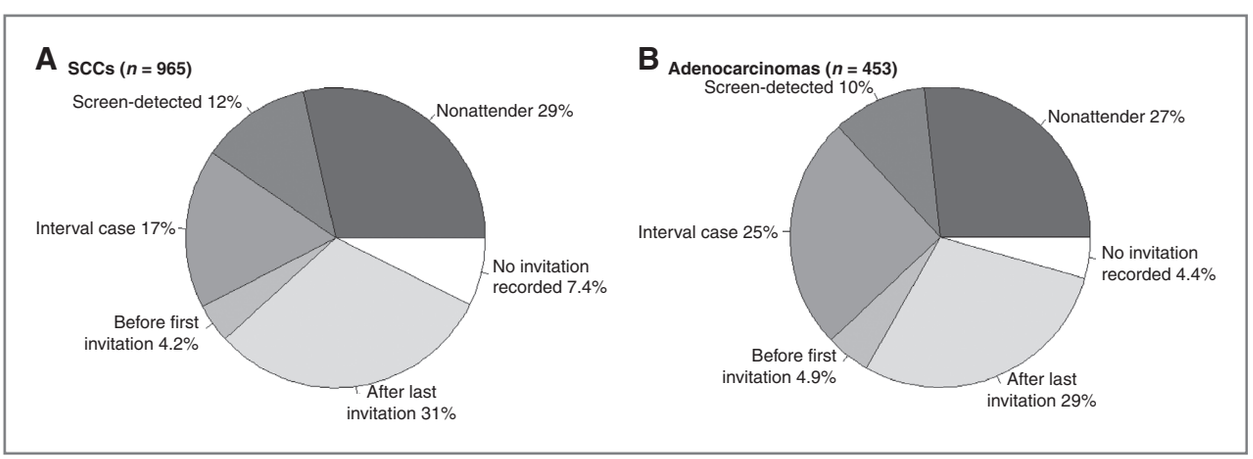

Figure 2. Invasive cervical cancers (Finland, 2000–2009), by morphology and mode of detection in relation to screening.

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Table 3. ORs of the association between cervical cancer and screening participation

Age at invitation	Cases screened Y/N[a]	Controls screened Y/N[a]	Crude OR[b]	Corrected OR (95% CI)[c]
Overall	366/494	3,469/1,813	0.37	0.53 (0.46–0.62)
25–29	11/18	77/77	0.65	0.95 (0.36–2.49)
30–34	50/75	422/351	0.54	0.79 (0.53–1.16)
35–39	61/80	529/377	0.50	0.73 (0.50–1.06)
40–44	44/87	527/296	0.26	0.38 (0.26–0.58)
45–49	50/66	514/216	0.28	0.41 (0.27–0.62)
50–54	53/57	486/183	0.30	0.44 (0.29–0.68)
55–59	49/63	497/165	0.23	0.34 (0.22–0.52)
60–64	40/39	350/128	0.33	0.49 (0.28–0.84)
65–69	8/9	67/20	0.33	0.49 (0.10–2.41)

[a]Number of cases and controls with invitation and exposed to screening yes/no.

[b]Estimated using conditional logistic regression.

[c]Corrected using self-selection bias factor 1.29 and attendance rate 0.71.

other authors have sometimes chosen to limit the analysis to specific subgroups, relevant subgroup analyses were also conducted to facilitate comparison. Here, three 5-yearly age group invitations were combined for more robust estimates. The ORs for SCC remained similar to those for all invasive cervical cancer, even though a suggestion of greater effect in the older age groups was observed (Table 4). For adenocarcinoma, smaller but significant effects were observed, except for screening at 55 or later. The effect on microinvasive cancers appears more uncertain than on the higher stage cancers. Considering only frankly invasive SCCs, the differences between age groups become more marked so that the effect on these cancers by a single screen in the ages 55 to 69 reached more than 80%, whereas in those under the age of 40 the OR was equal to 1 (Table 4).

We also investigated the effect of participating in the preceding round for those with no screening test in the index round to gain some insight into the duration of the protective effect. In this analysis, there was a significant OR of 0.35 (0.20–0.62) after correction for self-selection bias for a smear in the age groups 55 to 69, similar to the short-term effect described in the main analysis. No remaining protective effect could be shown in the younger age groups with point estimates 1.14 for participation at ages 25 to 39 and 0.84 at 40 to 54.

There was a similar association between cervical cancer in the advanced ages 66 to 80 (second peak of incidence) and a last program screening test at either 55 (OR, 0.54; 95% CI, 0.26–1.14), 60 (OR, 0.49; CI, 0.33–0.73), or 65 (OR, 0.41; CI, 0.23–0.74) compared with no screening test in this age range. However, the point estimates were slightly lower and significant only for ages 60 and 65. By narrowing the age interval for diagnosis to 71 to 80 the difference was more evidently in favor of screening in the later ages (ORs: 0.77, 0.47, and 0.23). We also estimated the OR associated with cervical cancer at any age 65 or more and screening participation among those invited at the age of 65. We found a crude OR of 0.45 and after correcting for self-selection, the estimate was 0.66 (0.29–1.50). The median time between invitation to screen and diagnosis in this analysis was 8 years with a range of 1 to 19.

Discussion

This study estimated the protective effect of a single age-group invitational program screening test in the following 5-year interval up to and including any screen-detected cancers in the next screening round. The overall effect of screening participation in the ages covered by the screening program was a 47% reduction in the risk of cervical cancer of any morphologic type or stage. The effect was strongly dependent on the age at invitation so that a program screening test at the age of 25 to 29 appeared to have little or no impact. A single screen at the ages of 30 to 34 and 35 to 39 had a moderate, nonsignificant effect. Clear effects of more than 50% were observed for each of the 5-yearly invitational age groups from 40 to 64 and a nonsignificant 51% for the single age group at 65 to 69 with relatively few cases among invited women available.

Effectiveness appears to decrease toward the younger age groups. A Swedish audit study (10) did not find any differences in screening effectiveness across age intervals, with effects of screening in excess of 50% for diagnosis in the ages of 21 to 29. Selection of cases and their controls may not have been suitable for evaluating protective effects (11). However, in a rapid response, the authors showed that the effect persisted for women in the ages of 27 to 29 even when restricting the analysis to stage IB$^+$ cancers, whereas this was not the case for women in the ages of 23 to 26 (12). Other studies have found diminishing effects toward lower ages. In particular, a large study

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Table 4. Self-selection–corrected ORs showing association of cervical cancer and screening participation by morphology and stage

	Age at invitation	Cases screened Y/N[a]	Controls screened Y/N[a]	OR (95% CI)[b]
All cervical cancers	25–69	366/494	3,469/1,813	0.53 (0.46–0.62)
	25–39	122/173	1,028/805	0.81 (0.63–1.05)
	40–54	147/210	1,527/695	0.44 (0.35–0.56)
	55–69	97/111	914/313	0.37 (0.27–0.52)
Squamous carcinoma	25–69	205/327	2,134/1,200	0.50 (0.41–0.61)
	25–39	88/116	703/583	0.91 (0.67–1.24)
	40–54	79/138	931/444	0.40 (0.29–0.54)
	55–69	38/73	500/173	0.23 (0.14–0.37)
Adenocarcinoma	25–69	142/135	1,129/532	0.69 (0.53–0.91)
	25–39	28/51	270/194	0.59 (0.36–0.98)
	40–54	62/59	511/223	0.61 (0.41–0.91)
	55–69	52/25	339/115	0.88 (0.50–1.54)
Stage IA	25–69	95/132	850/562	0.62 (0.46–0.84)
	25–39	44/70	403/339	0.69 (0.45–1.07)
	40–54	34/54	346/179	0.43 (0.27–0.70)
	55–69	17/8	101/44	1.12 (0.41–3.06)
Stage IB+	25–69	234/309	2,269/1,069	0.50 (0.41–0.61)
	25–39	68/86	546/399	0.93 (0.65–1.32)
	40–54	102/132	1,026/445	0.47 (0.35–0.63)
	55–69	64/91	697/225	0.27 (0.18–0.40)
Stage IB+ squamous carcinoma	25–69	114/187	1,275/634	0.44 (0.35–0.56)
	25–39	44/48	329/255	1.04 (0.68–1.58)
	40–54	48/81	573/259	0.39 (0.27–0.56)
	55–69	22/58	373/120	0.19 (0.11–0.32)

[a]Number of cases and controls with invitation and exposed to screening yes/no.
[b]Estimated using conditional logistic regression and corrected for self-selection.

from the United Kingdom reported little or no impact of screening in women aged 20 to 24 on rates of invasive cancers up to the age of 30, whereas screening in ages 30 and above were associated with reductions in cervical cancer rates in the range of 40% to 80% (11). Lower impact of screening in younger ages was also shown in an earlier U.K. study (13) and an Italian study describing the Florentine screening programme (14). None of these studies corrected for self-selection bias.

More research is needed yet to determine why the effectiveness of program screens seems to be low in the younger age groups especially below 30. A possible explanation is more intensive opportunistic screening of the younger women, which may dilute the effect of program screens and for which there is some indication from Finland. In a recent report, all smears taken in the capital area, opportunistic and organized, were reported by age using individual linkage of records (15). Approximately half of all those participating in organized screening, were also opportunistically screened within a 5-year period. This proportion was fairly constant over the target ages. The proportion with only opportunistic screening tests decreased from 40% in the youngest target age groups to 10% in the oldest. While young women are subject to considerable opportunistic screening activity, extensive use of opportunistic services has also occurred in older age groups, where program screening nevertheless was associated with a significant impact in preventing cervical cancers in the current study. Program screens have been associated with a larger reduction in cervical cancer risk in an earlier case–control study (16). Suggested explanations include better quality control of the organized screening service and selection of women at low risk to undergo opportunistic screening. Another reason for lower effectiveness of screening in younger ages could be age-dependent rates of regression and progression of cervical cancer precursors. The evidence for this is currently weak and the hypothesis requires further study (17, 18).

On the other hand, effect seems to persist better toward the upper age margin. The 51% effect estimate of an invitation at the age of 65 to 69 is not statistically significant but the CIs are wide due to small numbers and it appears likely that screening has some effect also at this age. With a follow-up of up to 19 years after invitation at the age of 65, a nonsignificant protective effect of 34% was still observed for participation. ORs for association of

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cervical cancer in ages 66 to 80 or 71 to 80 with last screen at 65 compared with no screen at the ages of 55, 60, or 65 were significant and similar or lower than with a last screen at 60. These estimates were not corrected for self-selection bias because they describe the screened women compared with those not screened irrespective of invitational status and so should not be interpreted as absolute effect estimates. However, the comparison with last screen at 60 is valid and is compatible with an additional impact of screening at 65 on cervical cancer incidence at higher ages. We could argue for extension of invitations to the age of 65 particularly as a major part of the remaining cervical cancer burden occurs in the ages beyond the current screening program. To our knowledge, no other studies have addressed specifically the impact of screening at the age of 65. We had only limited statistical power to study impact of screening at this age, because only rather few regions had invited 65-year-old women.

In a case–control evaluation of screening, it is important to ascertain that there is equal opportunity of exposure for cases and controls. It has been proposed that the preclinical invasive phase before diagnosis can be excluded from the exposure window (19). However, it is difficult to estimate the preclinical phase either collectively or individually and the exclusion of a period may bring other biases. For instance, cases have more prediagnostic borderline smears within 12 to 24 months of a diagnosis, as these lead to intensified follow-up where detection rates are higher. The exclusion of these tests would inflate the effectiveness estimate.

Choosing to participate in screening may reflect a generally healthier lifestyle. Those that do not participate may have more exposure to cervical cancer risk factors including smoking, early sexual debut, higher number of sexual partners, and less overall use of health care services. The baseline risk for cervical cancer in this material was 29% higher (OR, 1.29) in those choosing not to respond to an invitation for screening compared with those not invited. Assuming unity risk in the invited population compared with time before invitation, the above point estimate, and a 71% screening participation, it follows that the risk of those choosing to participate was 0.88 ($100\% \times 1.00 = 29\% \times 1.29 + 71\% \times 0.88$). Without correction for self-selection bias, the observed effect of participation would be 32% ($1 - 0.88/1.29$) in the absence of any real effect of screening.

There may be some misclassification in the invitational status of those without invitations in the recommended screening target ages of 30 to 64. Among the cases, 41% of this category was assumed to be noninvited only because the home municipality did not report them as invited. This corresponds to 17% of the noninvited case women in total in the ages of 25 to 69.

There are no randomized trials available that could provide comparisons of the relative risk of nonattenders compared with a noninvited control group but a few early cohort studies exist that provide equivalent estimates. A Canadian study describing the screening program in British Columbia found a relative risk of 1.08 for unscreened women (20), a study from the first decade of cervical screening in Finland compared those unscreened in the program with expectations drawn from time before screening and observed a relative risk of 1.6 (21), and a Norwegian study observed relative risks for incidence of 1.61 in invited but unscreened women compared with neighboring regions without screening (22). With a correction factor of 1.6 the ORs for the association of cervical cancer and screening participation in the current study would be more than 1 for screening at 25, 30, and 35 and 0.5 to 0.7 for screening at ages 40 to 65. At the lower end, a correction factor of 1.1 as observed in the study from British Columbia would yield ORs close to the crude estimates in Table 4. These correction factors are strongly dependent on the proportion of women participating in screening and the distribution of risk factors in the population under study and may not be applicable to other study populations. This may have contributed to the fact that few or no case–control studies for the evaluation of cervical cancer screening have attempted the correction. However, it seems that it is important to account for self-selection when absolute effectiveness estimates are sought. In the evaluation of breast cancer screening, such corrections are more easily available and also more commonly used (23–25).

To conclude, we have shown that a single screening test taken within the Finnish cervical cancer screening program reduces the risk for cervical cancer in the following 5-year interval by half but that this impact is age-dependent. An association between program screening at 25 and cervical cancer in risk in the next 5-year interval was not observed in a population with also opportunistic screening activity. On the basis of these results, we hesitate to recommend program screening at the age of 25 at present, before additional analyses that also take opportunistic screening of women during the first rounds of organized screening into consideration. Further analyses on mortality outcome are also required. Screening at 65 is supported, as there is moderate indication of a long-lasting impact on cancer risks in the older ages and also as 32% of cervical cancers diagnosed in Finland occur in women above the currently recommended target ages for screening.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: S. Lönnberg, T. Luostarinen, A. Anttila, P. Nieminen
Development of methodology: S. Lönnberg, A. Anttila, P. Nieminen
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): A. Anttila, P. Nieminen
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): S. Lönnberg, T. Luostarinen, A. Anttila, P. Nieminen
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