CERVICAL CANCER SCREENING

ANNUAL REVIEW 2021

The cervical cancer screening programme in Finland has previously been based on the Pap test, which has worked well. In recent years, the Pap test has been increasingly replaced by a new test focusing on the detection of cancer-causing HPV viruses. The new test has led to a further increase in the number of cancers detected by screening, although it has become a challenge to distinguish progressive infections and precursors from transient ones.

SUMMARY

In 2019, 283 000 women were invited to the cervical cancer screening programme and 198 000 women (70%) were screened. Six out of ten participants were screened with the HPV test as the primary test. A total of 49 cervical cancers and 1 024 precancerous lesions were detected. The number of screening detections was higher than in previous years, and detections varied between different screening tests. As in previous years, participation in screening was lower for people not in employment than for the rest of the population, and among those whose mother tongue was other than the domestic languages. The expansion of HPV screening and the management of the problems posed by the coronavirus pandemic will require strengthened guidance on screening.

Finnish Cancer Registry

1. INTRODUCTION

The cervical cancer screening programme, which started in the early 1960s, has been very effective. Four out of five cases of cervical cancer that develop in our country have been prevented by screening based on the traditional Pap smear test. Both Finnish and international follow-up studies have shown that organised screening has reduced cervical cancer incidence and mortality by about 80%. Very few cases of cervical cancer have been reported in those who have participated in the screening programme (Figure 1) (IARC, 2005; Lönnberg et al. 2012 & 2013).

Since 2003, the HPV test has increasingly replaced the Pap test as the primary screening test in Finland. (Figure 2). In 2019, HPV tests already accounted for about 61% of all tests in the screening programme. The HPV test is more sensitive than the Pap test in detecting cervical cancer precursors (Leinonen et al. 2013; Anttila et al., eds. 2015). HPV screening therefore has the potential to improve the cancer prevention effect of screening (IARC, 2005; Anttila et al. 2015). On the other hand, more false positives, referrals for further examination and pre-treatments have been observed, than with the Pap tests, especially at the start of HPV screening. HPV screening also detects more non-prevalent precursors. For these reasons, it is highly important to monitor HPV screening detection rates. The increased referral and detection rates should also be weighed against the potential benefits of HPV screening, such as the additional effect of HPV screening in preventing cervical cancer.

The special theme of this annual review, which is based on the statistics of the Mass Screening Registry, is HPV screening. Different HPV testing methods are used in the laboratories, and the criteria for referral for further examination also differ. It is particularly important to take into account not only the five-yearly screening based on routine invitations, but also the findings of their follow-up tests (so-called risk group screening). It is therefore rather hard to get an overall picture of HPV screening from traditional screening statistics, and needs to be accompanied by longitudinal follow-up for the whole five-year screening round.

ANNUAL REVIEW

This annual review includes age-standardised cervical cancer screening results from 2018, nationwide and by region. Screening indicators, such as participation and detection rates percentages, are compared with previous years. Temporal comparisons are presented from 1991 onwards. The regional analysis is based on 21 hospital districts. Screening participation and other screening outcomes are also examined by population groups according to mother tongue, level of education and socio-economic status. Data on population groups are obtained from the Population Information System and Statistics Finland. For the first time, a longitudinal analysis of HPV and Pap screening is also presented in this annual review. Other annual screening statistics are available on the Finnish Cancer Registry website. In addition to the screening statistics, the review discusses current studies on cervical cancer screening and considers the key development needs in screening.

The coronavirus pandemic in Finland since 2019 has hampered cancer screening and reduced screening uptake (Cancer Society of Finland, 2020). It has also made it more difficult to conduct follow-up examinations and treatments. The results presented in this annual review will therefore also be relevant for future assessment of the impact of the coronavirus pandemic.

2. CERVICAL CANCER SCREENING IN FINLAND

THE SCREENING PROCESS

In accordance with the Government's Cervical Cancer Screening Decree, women aged 30–60 are invited to the cervical cancer screening programme every five years. In some municipalities, women aged 25 and/or 65 are also invited. The municipalities choose the screening provider, which can be the municipality itself or another provider. The screening test is taken at a health centre or screening laboratory and analysed in a pathology laboratory. The pathology laboratory also sends women a response to the test result and, if necessary, makes a referral for further examination.

Women with mild abnormalities (ASC-US, LSIL for women under 30 or a positive HPV test without referral for further examination) are recommended to be invited to the so-called risk group screening. Risk group screening is performed 12–24 months after the previous screening invitation. Those with more serious results are referred for cervical endoscopy, i.e. colposcopy and biopsy. A referral can also be made for a mild abnormality that has occurred 2–3 times. Follow-up examinations, necessary surgical procedures and treatment of precancerous and cancerous cervical lesions are carried out in specialised medical care.

MAIN FINDINGS 2019

In 2019, the screening programme sent out 283 000 invitations and 198 000 of the women invited took part in the screening (70% participation rate). Of the primary screening tests, 121 000 (61%) were HPV tests and the rest were conventional Pap tests (Table 1). About 93% of those screened received a normal test result and about 5.6% were recommended for risk group screening. A total of 2 800 women — about 1.4% of those screened — were referred for further examination (Table 2). Screening identified 1 024 histologically confirmed precancerous lesions (HSIL/AIS) and 49 cervical cancers — a total of about 5.4 cases per 1000 women screened.

COMPARISON WITH PREVIOUS YEARS

There have been no significant changes in national participation activity over the last few years and the coverage of invitations has long remained at about 100%, i.e. virtually the entire screening target population is invited for screening every five years in all municipalities (Figure 3). Participation rates have been strongly age group specific, with the 25-30 age group in particular being well below the other invitation groups (Figure 4).

The proportion of histologically confirmed precancerous lesions and cervical cancers has increased significantly over the last five years (Figure 5). In 2019, the detection rate of precancerous lesions was already more than 80% higher than five years earlier, and the number of cervical cancers detected at screening (49) was also exceptionally high. The increase in the number of serious detections suggests that the risk of cervical cancer has increased in Finland. The increase in detection rates is also partly explained by the increased use of HPV testing, which is more sensitive than Pap smears as a screening test, so that cancers and precursors may be diagnosed at an earlier stage.

3. CERVICAL CANCER SCREENING BY HOSPITAL DISTRICT

In 2019, the majority of primary screening tests were HPV tests in the hospital districts of Helsinki and Uusimaa, Kanta-Häme, Central Finland, Pirkanmaa, North Karelia, Päijät-Häme and Satakunta. In Southwest Finland, about a third of the primary screening tests were HPV tests and in the other hospital districts almost all screened with the Pap test.

There have been differences in participation rates between the hospital districts over the last five years. Age-standardised participation rates in 2015–2019 were highest in South Ostrobothnia (78%) and Åland (77%). The largest hospital district in terms of population, Helsinki and Uusimaa, had a lower age-standardised participation rate (67%) than several other hospital districts, and the lowest age-standardised participation rate was in North Savo, where it was 60% (Table 3, Figure 6). Participation rates may be influenced, among other things, by differences in the demographics of the hospital districts, but municipalities› invitation practices also play an important role. The time and place of the screening test should already be given in the invitation letter and non-participants should be reminded with follow-up invitations.

There are also regional differences in screening results, which are particularly affected by different diagnostic criteria in laboratories and the use of HPV testing. Age-standardised, the proportion of patients with a risk group recommendation varied between 2% and 13% by region (Figure 7) and the proportion of patients referred for further examination between 0.6% and 5% (Figure 8). The highest proportion of referrals was in Pirkanmaa, where the HPV test has been used the longest in the whole hospital district. The age-standardised proportion of histologically confirmed HSIL+ findings was also highest in Pirkanmaa, and clearly higher in Päijät-Häme (Figure 9).

4. CERVICAL CANCER SCREENING BY POPULATION GROUP

Participation rates and screening results in 2019 were analysed by language, socio-economic status and education level for people aged 30–60. For mother tongue, a comparison was made between domestic or non-domestic language speakers. Finnish, Swedish and Sami were counted as domestic languages. Missing language data was not included in the comparison.

Data on socio-economic status and educational attainment was taken from the end of the previous year. Socio-economic status was examined in eight categories and individuals whose socio-economic group could not be determined were defined as unknown by socioeconomic status. Educational level was defined as primary, secondary or tertiary education, based on the highest level of education attained. Data on qualifications was only available from secondary level upwards, so primary education and missing education data were treated as the same group.

LANGUAGE

In 2019, domestic language speakers participated in screening clearly more actively than those of other languages. Non-domestic language speakers received slightly more recommendations for risk group screening than domestic language speakers, while the latter received more referrals for colposcopy than non-native speakers. There was no clear difference in the number of histologically confirmed precursors between the two language groups (Table 4).

SOCIOECONOMIC STATUS

In 2019, participation rates were highest for white-collar workers and slightly lower for self-employed and blue-collar workers. Participation rates were clearly lowest among pensioners and people whose socio-economic background was unknown (Table 5).

In age-standardised terms, those with unknown socio-economic background, the employed and the unemployed received the highest number of referrals for further examination. These groups were also found to have more age-standardised precursors than other groups. Students were the group with the lowest number of referrals

for further examination, with a low age-standardised proportion of precancerous lesions (Table 5).

LEVEL OF EDUCATION

Participation in screening in 2019 was more active the higher the level of education. The age-standardised participation rate for tertiary graduates was 5 percentage points higher than for those with no more than a secondary education and as much as 23 percentage points higher than for those with no more than a primary education (Table 6).

Those with higher education received fewer referrals for further examination in 2019 than those with lower education, and they also had fewer precancerous lesions than the latter (Table 6). Differences in screening results and detection rates may be due to more active participation in testing outside the screening programme by higher educated people.

5. HHPV SCREENING IN FINLAND

USE OF HPV MORE WIDESPREAD

HPV testing first started in Finland in 2003, when a randomised HPV screening roll-out study was launched as part of the cervical cancer screening programme (Anttila et al., 2006). Its aim was to investigate the feasibility, effectiveness and optimal screening practices of HPV testing (Leinonen, 2013). More than 236 000 women were invited for HPV or Pap smear screening. A total of nine municipalities in Uusimaa were included, of which Helsinki was completely excluded from the study after the first round of screening. The groups studied were screened for two rounds of HPV screening with HPV testing alone and a Pap test for those with a positive HPV result. Referral for colposcopy was done based on the Pap test result. If the HPV test was positive and the Pap smear was normal, two follow-up tests (risk group screening) were performed if necessary. A referral was also made if HPV positivity was still present at the second follow-up test. Pap smear screening was performed according to the standard practice at the time.

The HPV test has also been used in the screening programme in the so-called self-sampling study in 2011–2012. At that time, the HPV home test was offered to women who, even after a reminder, had not yet participated in the screening programme. The aim was to improve participation rates in screening (Virtanen, 2015).

Figure 10 shows HPV testing rates by municipality since 2003. Tampere was the first municipality to switch to HPV screening in 2012. Since then, HPV testing has gradually expanded to more and more municipalities, initially mainly in the regions of Pirkanmaa, Häme and Central Finland. In 2017, the city of Turku switched to HPV testing as the primary screening method, and in 2019 HPV screening was further expanded to, among others, the entire Hospital District of Helsinki and Uusimaa. At that time, the proportion of HPV-tested persons in the programme was already more than half of all tested persons, 61% (Figure 2). HPV screening is mainly provided for women aged 30 years or older, as the high number of harmless HPV infections in young women would lead to overdiagnosis (Anttila et al. eds., 2015).

NUMEROUS REFERRALS

The HPV test is more sensitive than the Pap test, so HPV screening has slightly more abnormal screening results than cytology screening. Table 7 shows the results of the 2015 age group screening (30 years and older) for Pap smear and HPV screening, and the subsequent risk group invitations and screenings from 2016 to 2019, for a full

five-year screening round. This allows for longitudinal comparisons between testing methods for both routine and risk group screening. Referral rates were particularly high in the risk group screenings following HPV screening. Over the five-year period, the combined referral rate for both age and risk group screening was 0.9% for Pap testing versus 4.4% for HPV testing (Table 7).

The high referral rate for HPV-tested patients is mostly due to the practice of referral for colposcopy already after the first repeat positive HPV test result. So if an HPV test is positive at routine screening and again at risk group screening after 1–2 years, a woman will be referred for further examination, even if the cytology is normal. The next section describes a new follow-up study based on a randomised HPV screening deployment trial, which aims to further investigate the specificities of the increasingly common HPV screening.

6. BENEFITS AND DRAWBACKS OF HPV BASED SCREENING

A long-term follow-up study aims to ascertain the benefits and drawbacks of HPV screening. The study investigates the impact of HPV screening on cancer burden compared to Pap smear screening and the extent of and factors influencing overdiagnosis of HPV screening. The aim is to create better screening practices that reduce overdiagnosis, including for follow-up tests. In addition to data from the mass screening and cancer registries and sample archives, the project will use data from Pap smears, colposcopies and precursors outside the screening programme. Preliminary results show that the total number of colposcopy referrals made in the screening programme, based on the above mentioned approach, was about 50% higher in the HPV group than in the Pap smear group for the first round of screening (Table 8). The difference between screening groups narrowed to about 30% when referrals made outside the programme were taken into account. This is due to the relatively high number of referrals made outside the screening programme, even between two screening visits.

7. COMPARISON OF NORDIC SCREENING PROGRAMMES

The Nordscreen project, led by the Finnish Cancer Registry, has developed an openly accessible web-based service (www.nordscreen. org), that allows us to compare cervical cancer screening programmes in the Nordic countries using a number of indicators. The project started in 2016 and aims to support the improvement of the quality of screening programmes by providing uniformly defined indicators. Where possible, the project will be extended to breast and colorectal cancer screening programmes in the coming years.

The tabulated indicators are based on individual-level screening data from national screening registries, which are of internationally comparable coverage and quality. The results show that Finland has a lower test coverage than the other Nordic countries. This is because the Finnish statutory screening registry currently only includes data from the invitation-based screening programme, whereas the registries in the other Nordic countries include data from all tests.

When comparing screening test results between countries, it was found that the proportion of positive test results in Finland is lower than in other Nordic countries (Partanen et al. 2021). The comparison between HPV testing and Pap tests also showed that the proportion of positive test results is higher for HPV testing, which

increases the proportion of women recommended for risk group screening. The project will continue to develop indicators by combining screening data with information on diagnostic follow-up, including follow-up tests, to better assess the effectiveness of different screening methods.

The comparison of Nordic screening programmes was complemented by a study to assess how well different Nordic countries follow international recommendations on organising screening (Partanen et al. 2020). All Nordic countries have legislation enabling a screening programme in line with the recommendations, but there are gaps in compliance with the recommendations in terms of both the administration and organisation of screening and the evaluation of the programme. None of the countries meet all the recommendations, but some of the countries do fulfil nearly all the recommendations.

For Finland, the main shortcomings in the organisation of the screening programme, apart from the decentralised organisational responsibility, are mainly related to data registration, as tests outside the screening programme are not routinely registered in the Cancer Registry. Furthermore, the screening history of cancer cases is not routinely checked, unlike in Denmark, Norway and Sweden.

8. CERVICAL CANCER SCREENING TESTING IN WOMEN PAST THE SCREENING AGE

The purpose of this Cancer Registry study was to examine cervical cancer test coverage in women who are past the screening age, and to investigate which socioeconomic factors influence participation at older ages (Keltto et al. 2021). According to international recommendations, screening should continue in high-risk groups beyond the general screening age for the whole female population. Such groups include irregular screening participants and women with a history of abnormal test results. Providing screening after the end of the general screening age is important because most cervical cancer deaths in Finland occur from cancers detected after the age at which the screening programme ends (Lönnberg et al., 2013).

The study data were based on women born between 1941 and 1951 who had received at least one screening invitation between the ages of 50 and 60. Mainly testing outside the screening programme after the screening age at 65–74 years was followed in these women until 2016.

About 30% of women had been tested at least once between the ages of 65 and 69, but the proportion tested between the ages of 70 and 74 was down to 15%. Testing at a later age was more common in the groups with previous abnormal test results and active screening participation. The high socio-economic status and high educational level of women also contributed to increased testing activity. Figure 11 shows testing coverage in women aged 65–69 or 70–74 years with abnormal results in the programme. In both age groups, the low socio-economic status and low educational level population had very low testing coverage, and significantly lower coverage than the other population groups (Figure 11).

The majority of women tested (75%) were not in the high-risk groups, meaning they had been screened regularly in the programme and had not shown abnormal results. The risk of cervical cancer in this section of the population after the programme is very low. It is also

not clear whether asymptomatic women benefit from post-programme testing. The results showed that the international recommendations for targeting testing in Finland are not being met. Out-of-screen testing favours populations that also participate well in the screening programme. On the other hand, continuing the screening programme in the entire female population at least until the age of 65 is an effective way to increase the coverage of cervical cancer testing (Pankakoski et al. 2019).

9. RECOMMENDATIONS AND CONCLUSIONS

The cervical cancer screening programme in Finland, which has been based on the traditional Pap test for decades, has been very effective. In recent years, the HPV test has increasingly replaced the Pap test in screening. In 2019, this newer method was already used for the majority of tests in the screening programme. The immediate benefit of HPV screening is an increase in the detection of the number of cervical cancer cases during screening in the so-called age-group screening. This suggests that HPV testing detects cervical cancers earlier than pap tests. A problem with the introduction of HPV testing has been the higher number of colposcopy samples and pre-cancerous lesions than with Pap smears, especially in follow-up tests.

The HPV test is very sensitive, so the challenge in its use is to distinguish HPV infections leading to progressive precancerous lesions and cancer from harmless and transient infections, that is to avoid overdiagnosis. Diagnosis and follow-up of these transient infections impose unnecessary costs on healthcare and burden on the individuals tested. On the other hand, it is precisely the sensitivity of HPV testing that allows for the capture of progressive precancers and cancers that would not be detected by Pap tests.

Detection and treatment of precancerous lesions in and outside the screening programme already prevents almost 1,000 cancer cases a year in Finland (Mass Screening Register, Annual Review 2018). There are currently some 175 cases of cervical cancer diagnosed in Finland each year. Of these, about a fifth, 30–40 cases, are detected in women who have participated in a screening programme during a five-year follow-up after the screening visit (Lönnberg et al., 2012). Methods that replace traditional screening tests can therefore only marginally improve cancer control. However, improving the participation rate of the screening programme and extending the target age group to an older one are very important aspects of improving effectiveness. Moreover, in the fight against cervical cancer in young women under 30 or 35 years of age, the HPV vaccination programme is currently a highly effective strategy (Lei et al., 2020).

Compared to the benefits of HPV screening, it seems obvious that there are too many referrals for further examinations. The prevalence of cancer-threatening HPV infections in our country is so high that a repeated positive HPV test is not a reasonable criterion for colposcopy referral in all age groups eligible for HPV screening. However, referral rates seem to vary depending on the criteria adopted. In the first round of HPV screening, referrals are made for up to about 4% of women screened in the five-year screening cycle if the referral is based on repeated HPV positivity. This is a significant number of referrals, also compared to referrals made outside the programme. The programme tests almost 200 000 women per year and HPV is repeatedly positive in a very high number of women screened.

EU-wide quality assurance guidelines should also allow for the application of a lower referral rate criterion in countries with high HPV prevalence (Anttila et al., eds. 2015). For example, in a situation of recurrent HPV positivity, a pap smear test with double reading could be used as a referral criterion. If the quality of the Pap test is not considered sufficient and a test method that identifies individual HPV types is available, referral could be considered in a situation of recurrent HPV positivity not only for cytology positives but also for specific HPV types with a high cancer risk (HPV 16, 18, 31, 33, 45, 52, 58; Hortlund et al., 2021). Such an approach would also meet current EU-level criteria, and could at the same time substantially improve the cost-benefit ratio compared to the current approach. In addition to these, there is a need to explore alternative testing and confirmatory screening approaches, such as immunostaining or methylation markers in addition to HPV typing (Anttila et al. eds., 2015).

There are significant differences in cervical cancer screening and cancer burden between population groups. New interventions need to be developed to reduce them. Systematic data on the benefits, drawbacks and cost-effectiveness of screening is still needed. Data is also needed on different target age selections, interventions to improve participation, and differences in screening characteristics between regions and population groups. For this purpose, data on out-of-programme services and on cancers of screened participants after screening visits is important in addition to screening statistics.

The outbreak of the coronavirus pandemic in early 2020 underlines the need for comprehensive registry data. Due to the pandemic, the 2020 screening year has had to be extended, so the time needed to evaluate the statistical year will be significantly longer than normal. The problem is also likely to be reflected in the screening invitations for 2021. Possibly lower participation rates in the pandemic year, or for example difficulties in accessing follow-up examinations and treatments, may also be reflected in the cancer burden in future years. A separate report on the impact of the pandemic is planned for the Mass Screening Registry at a later date.

There is a fairly pressing need for more detailed guidance on screening practices in Finland. A new national cancer screening steering group has been in place for some years now. One of the objectives of the steering group is to develop sufficiently reliable quality assurance for cancer screening programmes. The production of a quality manual for cervical cancer screening has not yet started due to lack of funding. This quality assurance work must be started without delay. At the same time, it must be ensured that good practices are applied consistently.

AUTHORS

AHTI ANTTILA, Research Director
MAIJU PANKAKOSKI, Researcher
AKU LEIVONEN, Statistician
SIRPA HEINÄVAARA, Senior Researcher
VELI-MATTI PARTANEN, Project Manager, Researcher
MAIJA VAHTERISTO, Researcher
NATALIE KELTTO, Researcher
TYTTI SARKEALA, Director of Mass Screening

Joukkotarkastusrekisteri, Suomen Syöpä-Mass Screening Registry, Finnish Cancer Registry, Helsinki

LINKS AND PUBLICATIONS

FINNISH CANCER REGISTRY

cancerregistry.fi

INTERACTIVE SCREENING STATISTICS 1991–2019

cancerregistry.fi/statistics/screening-statistics/

ANNUAL STATISTICS

cancerregistry.fi/statistics/screening-statistics/

KÄYPÄ HOITO 2019 – CURRENT CARE GUIDELINES 2019

Kohdunkaulan, emättimen ja ulkosynnytinten solumuutokset. Käypä hoito -suositus. Suomalaisen Lääkäriseuran Duodecimin ja Suomen Kolposkopiayhdistyksen asettama työryhmä. Helsinki: Suomalainen Lääkäriseura Duodecim, 2021 (referenced 7.6.2021). Online: www.kaypahoito.fi (In Finnish)

World Health Organization. (2005). IARC handbooks of cancer prevention. Volume 10: Cervix cancer screening.

Lönnberg, S., ym. (2012). Age-specific effectiveness of the Finnish cervical cancer screening programme. Cancer Epidemiology Biomarkers & Prevention 2012;21:1354–1361.

Lönnberg, S., ym. (2013). Mortality audit of the Finnish cervical cancer screening programme. International Journal of Cancer 132:2134–2140.

Leinonen, M. (2013). Prevalence of HPV infection and use of HPV test in cervical cancer screening: Randomised evaluation within the organised cervical cancer screening programme in Finland. Dissertation, University of Helsinki.

Anttila, A., ym. (2015). Organization of cytology-based and HPV-based cervical cancer screening. S2. In: European guidelines for quality assurance in cervical cancer screening. Second edition, Supplements. Office for Official Publications of the European Union, Luxembourg, pp. 69–108.

Syöpäjärjestöt (2020). Kohdunkaulasyövän seulontaan osallistuminen laahaa selvästi viime vuotta perässä. Press release 19.11.2020 (Referenced 24.5.2021). Online: https://www.epressi.com/tiedotteet/terveys/kohdunkaulasyovan-seulontaan-osallistuminen-laahaa-selvasti-viime-vuotta-perassa.html

Anttila, A., ym. (2006). Alternative technologies in cervical cancer screening: a randomised evaluation trial. BMC Public Health, 6(1), 1–8.

Lei J, Ploner A, Elfström M, Wang J, Roth A, Fang F, Sundström K, Dillner J, Sparén P. HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med 2020;383:1340–8.

Virtanen, A., ym. (2015). Improving cervical cancer screening attendance in Finland. International Journal of Cancer, 136(6), E677–E684.

Partanen, V.M., ym. (2021). Comparison of cytology and human papillomavirus-based primary testing in cervical screening programs in the Nordic countries. Journal of Medical Screening, 09691413211992404.

Partanen, V. M., ym. (2020). Adherence to international recommendations in the governance and organisation of Nordic cervical cancer screening programmes. Acta Oncologica, 59(11), 1308–1315.

Keltto N, Leivonen A, Pankakoski M, Sarkeala T, Heinävaara S, Anttila A. Cervical testing beyond the screening target age – A register-based cohort study from Finland. Gynecol Oncol 2021; 162: 315–321.

Pankakoski, M., ym. (2019). Effectiveness of cervical cancer screening at age 65—A register-based cohort study. Plos one, 14(3), e0214486.

Cervical cancer screening programme. Annual review 2018. (Referenced 1.6.2021). Online: https://syoparekisteri.fi/assets/files/2019/01/Cervical-cancer-screening-programme-Annual-review-2018.pdf

Lei, J., ym. (2020). HPV vaccination and the risk of invasive cervical cancer. New England Journal of Medicine, 383(14), 1340–1348.

Hortlund, M., ym. (2021). Human papillomavirus load and genotype analysis improves the prediction of invasive cervical cancer. International Journal of Cancer.

TERMINOLOGY

BIOPSY Tissue removed from the living body

CANCER INCIDENCE The number of new cancer cases per population at risk, or per person-time of the population at risk, during a given period.

COLPOSCOPY Cervical endoscopy

CYTOLOGY SAMPLE Cell sample

HISTOLOGY SAMPLE Tissue sample

HPV Human Papilloma Virus

HPV TEST An HPV test approved for screening detects high-risk HPV virus types from a gynaecological loose cell sample. Sampling is done in the same way as in the Pap test. If the HPV test is positive, a Pap test is also performed on the same sample.

MORTALITY The number of deaths per population at risk, or per person-time of the population at risk, during a given period.

OPPORTUNISTIC TESTING The testing of symptomless persons outside the organised screening programme (in private or public health care). Symptom-related testing and patient follow-up are also performed outside the screening programme.

OVERDIAGNOSIS The detection of latent cancers or precancerous lesions that, if left untreated, would not have affect a person's health during their lifetime.

PAP TEST Examination of a cytology sample.

SCREENING COVERAGE Proportion of target population invited to screening (call coverage) or share of screened target population (test coverage). Test coverage can also be assessed using the same calculation rules in activities outside the screening programme.

SCREENING RESULTS

ASC-US Atypical squamous cells of undetermined significance.

AGC-NOS Atypical glandular cells not otherwise specified.

LSIL Low-grade squamous intraepithelial lesion.

HSIL High-grade squamous intraepithelial lesion.

AIS Adenocarcinoma in situ.

LSIL+ LSIL+ includes LSIL- and stronger changes (LSIL, HSIL, AIS, cancer)

HSIL+ HSIL + includes HSIL- and stronger changes (HSIL, AIS, cancer). Precursors of cervical cancer include histological HSIL and histological AIS.

LIST OF FIGURES AND TABLES

FIGURE 1: **Age-standardised incidence and mortality of cervical cancer in women in Finland 1953–2019.**

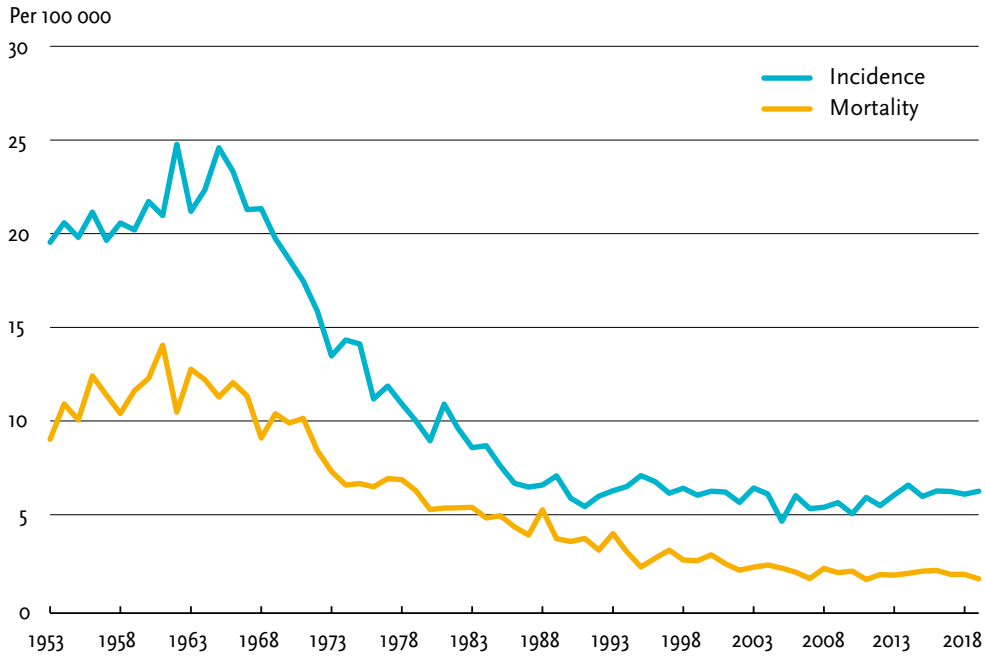


FIGURE 2: **Numbers of screening cytology and HPV tests 2003–2019.**

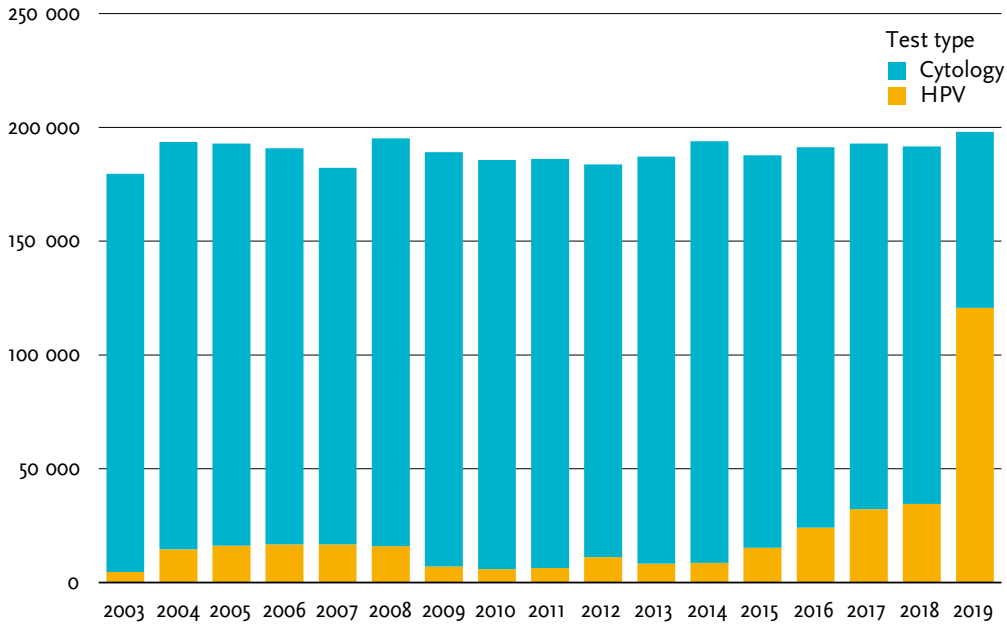


FIGURE 3: **Cervical cancer screening invitation coverage (%) and participation (%) in screening for 30–64 year olds 1991–2019, routine invitations**

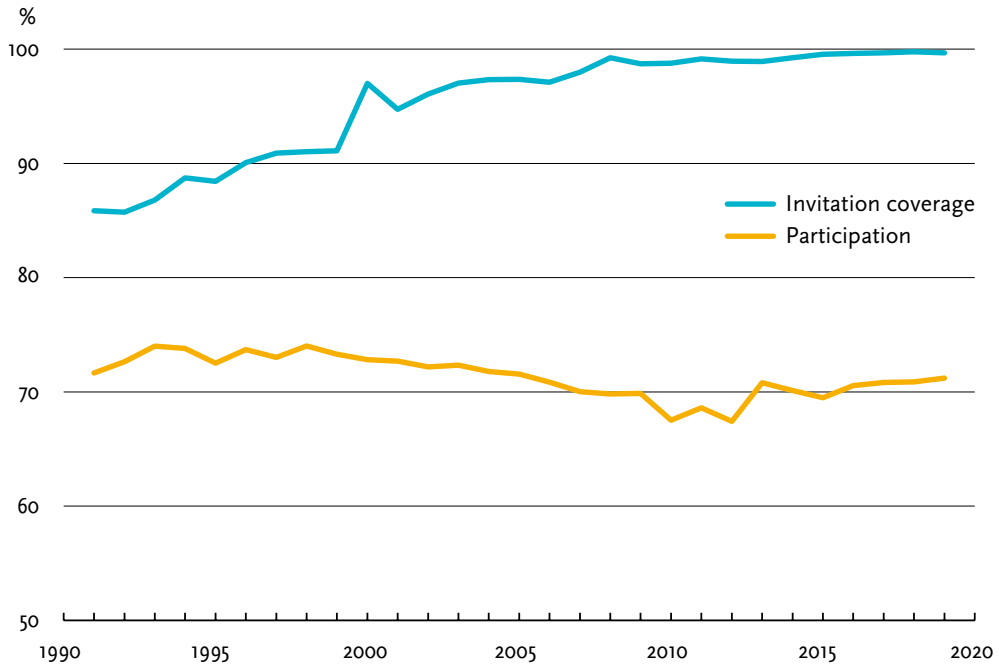


FIGURE 4: **Participation in cervical cancer screening (%) by age group 1991–2019, routine invitations.**

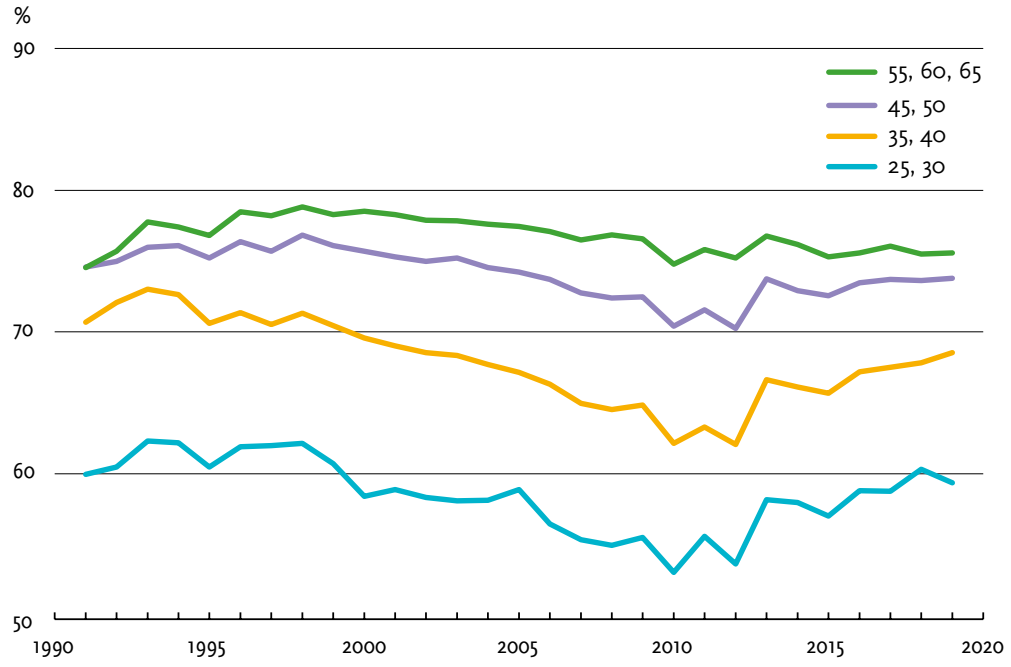


FIGURE 5: **Histologically confirmed HSIL prevalence or higher (%) in women aged 25–69 years 1991–2019**

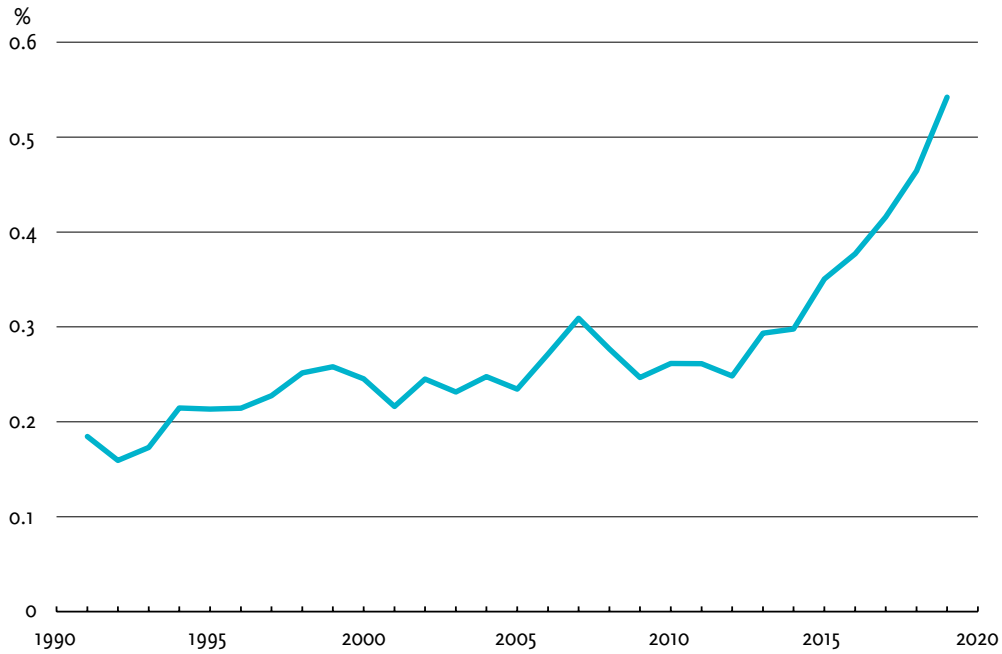


FIGURE 6: **Coverage of screening in women aged 30–60 years in 2015–2019 by hospital district, routine invitations (age-standardised, Finland 2014).**

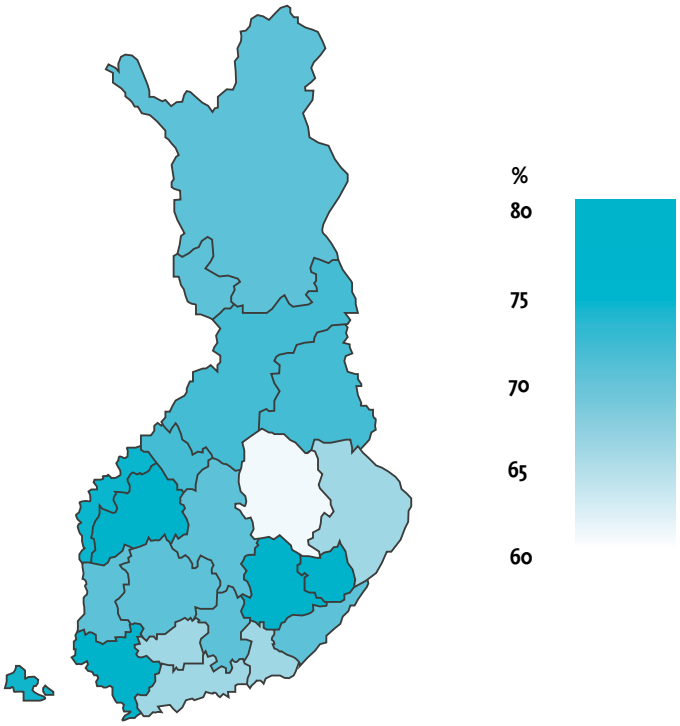


FIGURE 7: **Recommendation for risk group screening (%) for women aged 25–69 by hospital district 2015–2019 (age-standardised, Finland 2014).**

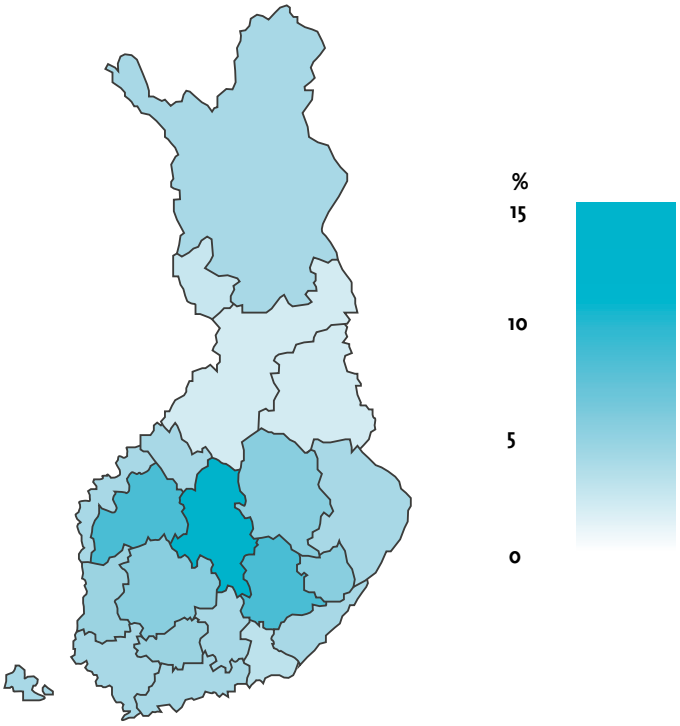


FIGURE 8: **Referral for follow-up examination (%) for women aged 25–69 by hospital district 2015–2019 (age-standardised, Finland 2014).**

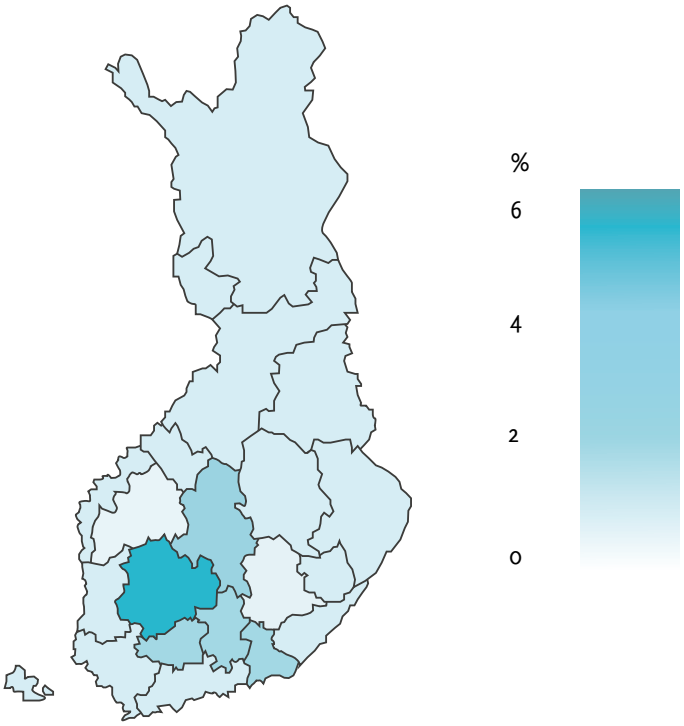


FIGURE 9: **Histological HSIL+ (%) in women aged 25–69 by hospital district 2015–2019 (age-standardised, Finland 2014).**

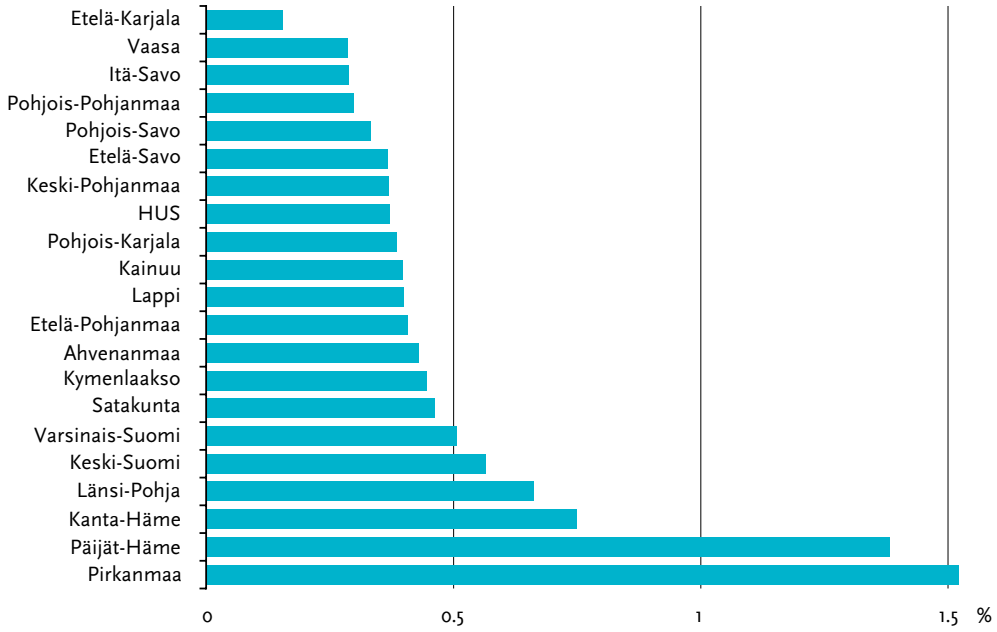


FIGURE 10: **Proportion of HPV-tested persons by municipality 2003–2019. Only municipalities/hospital districts with HPV-testing are included.**

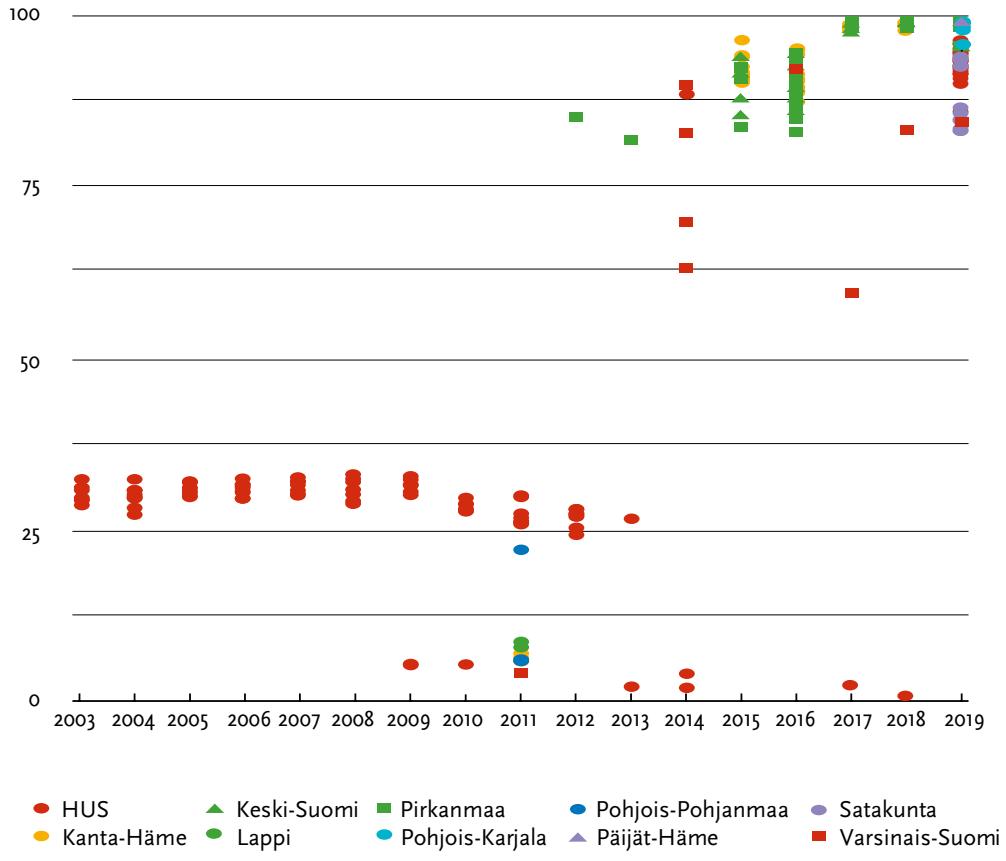
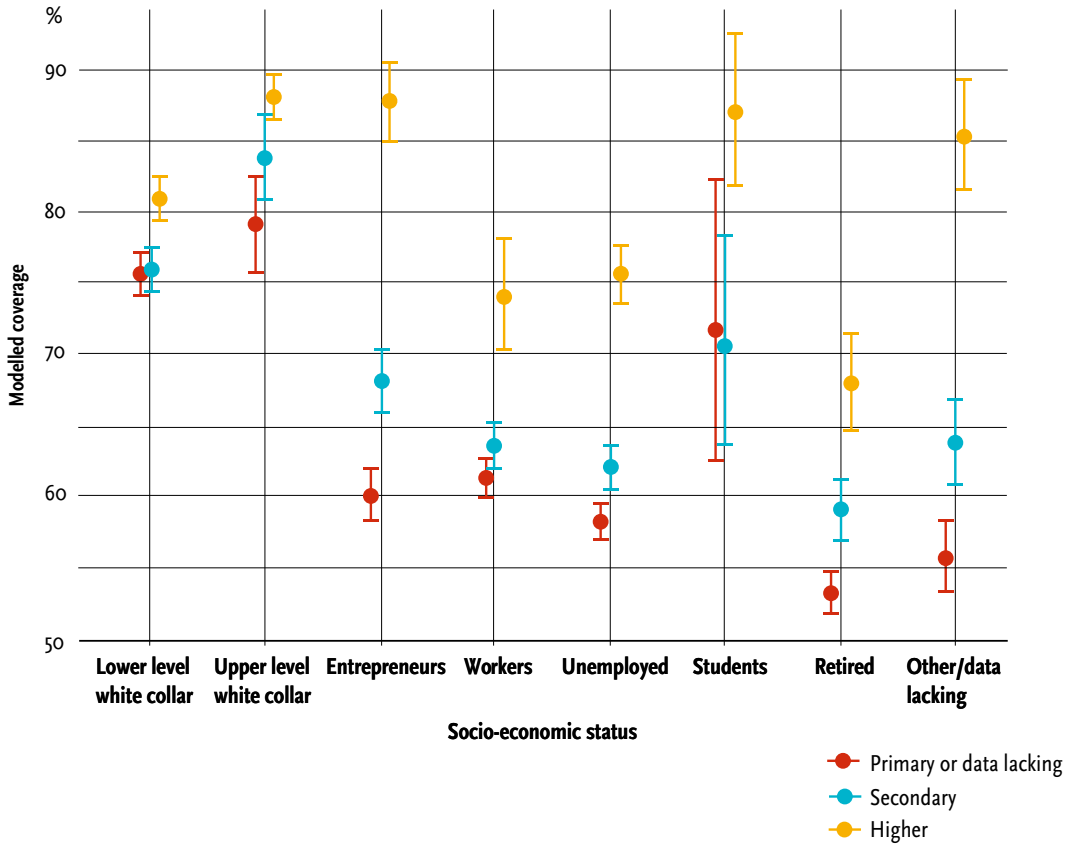
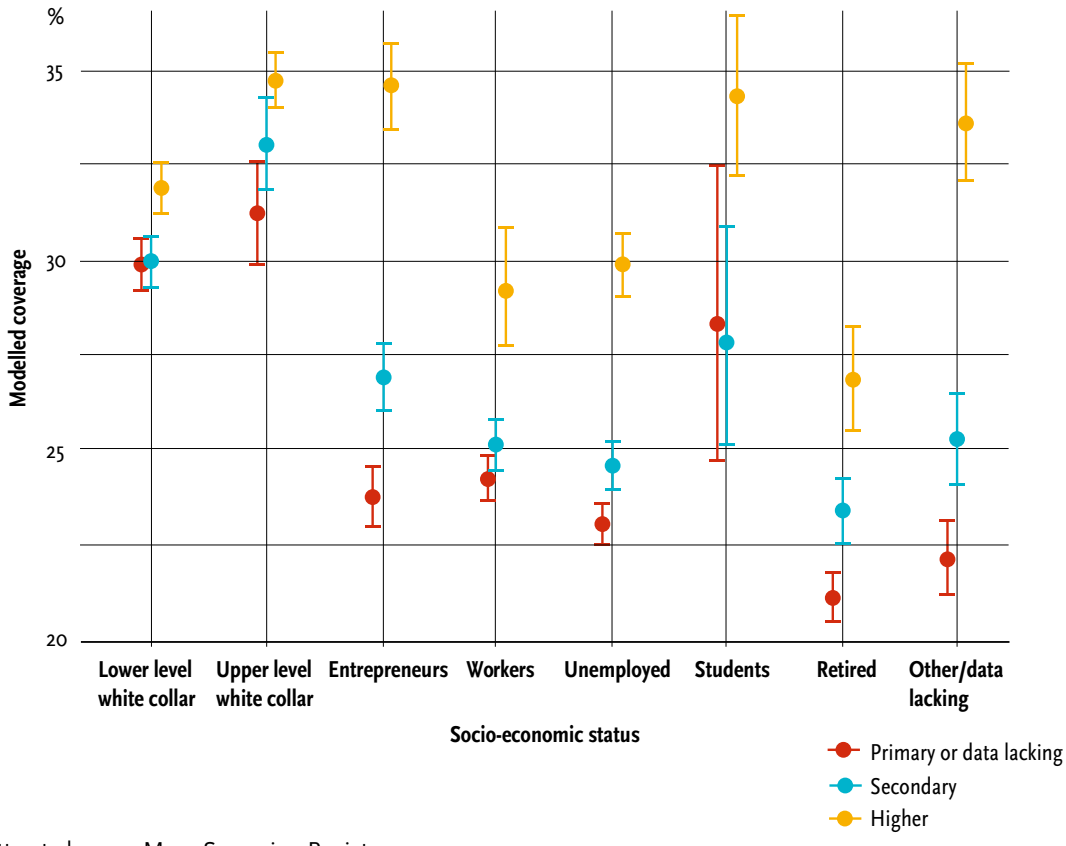


FIGURE 11: Cervical testing in women aged 65–69 and 70–74 with a previously abnormal result in the mass screening programme.

65–69-year olds:



70–74-year olds:



Keltto et al, 2021; Mass Screening Registry, 2021

TABLE 1: Target population of cervical cancer screening and invited, screened and HPV-tested women in 2019

	Target population	Invited	Invited of population (coverage)	Screened	Screened of invited	HPV test
Routine screening: ages 25–65	313 327	268 891	86	189 366	70	114 543
Routine screening: ages 30–60	241 861	240 682	100	171 370	71	105 377
Routine and risk group screening: 25–69	313 327	283 463	91	197 956	70	120 689

TABLE 2: Screening results 2019

	Screened	Negative or normal		Recommendation for risk group screening		Referral for follow-up examination		Histological HSIL+		Not interpretable or data missing
	N	N	%	N	%	N	%	N	%	N
Routine screening: ages 25–65	189 366	177 257	94	10 373	5.5	1 723	0.9	821	0.4	13
Routine screening: ages 30–60	171 370	160 329	94	9 401	5.5	1 628	0.9	776	0.5	12
Routine and risk group screening: 25–69	197 957	184 179	93	10 993	5.6	2 772	1.4	1 073	0.5	13
HPV screening (routine screening: 30–65)	114 543	105 940	92	7 536	6.6	1 061	0.9	497	0.4	6
HPV screening (routine and risk group screening: 30–69)	120 689	110 819	92	7 907	6.6	1 957	1.6	703	0.6	6

TABLE 3: Screening coverage in women aged 30–60 years in 2015–2019 by hospital district, routine invitations

Hospital District	Invited	Screened	
	N	N	%*
Ahvenanmaa	6 619	5 105	77
Etelä-Karjala	27 187	19 662	71
Etelä-Pohjanmaa	39 883	31 105	78
Etelä-Savo	20 918	16 002	76
HUS	395 663	271 813	67
Itä-Savo	6 538	5 031	76
Kainuu	15 201	11 219	73
Kanta-Häme	37 339	25 627	68
Keski-Pohjanmaa	15 865	11 450	72
Keski-Suomi	52 553	37 374	71
Kymenlaakso	35 417	24 504	68

Hospital District	Invited	Screened	
	N	N	%*
Lappi	25 067	18 132	72
Länsi-Pohja	12 624	9 028	71
Pirkanmaa	115 472	81 313	71
Pohjois-Karjala	34 357	23 195	67
Pohjois-Pohjanmaa	84 458	60 725	72
Pohjois-Savo	52 124	31 668	60
Päijät-Häme	44 940	31 908	70
Satakunta	45 837	32 845	71
Vaasa	34 404	25 836	75
Varsinais-Suomi	104 804	78 652	75

* age-standardised (Finland 2014)

TABLE 4: Invitations and screenings and main findings by language in 2019

Language	Invited	Screened		Recommendation for risk group screening		Referral for follow-up examination		Histological HSIL+	
		N	%*	N	%*	N	%*	N	%*
Domestic	256 512	182 801	71	10 047	5.6	2 576	1.4	983	0.5
Other	25 755	14 495	57	912	6.0	191	1.0	87	0.5

* age-standardised (Finland 2014)

TABLE 5: Invitations and screenings and main findings by socio-economic status in 2019

Socio-economic status	Invited	Screened		Recommendation for risk group screening		Referral for follow-up examination		Histological HSIL+	
		N	%*	N	%*	N	%*	N	%*
Entrepreneurs	16 721	11 929	70	656	5.9	167	1.3	56	0.5
Lower level white collar	109 373	80 499	73	4 613	5.9	1 158	1.3	469	0.5
Upper level white collar	56 019	41 937	74	2 093	5.1	474	1.1	151	0.4
Workers	37 404	25 675	69	1 568	6.1	455	1.7	210	0.8
Students	10 329	6 001	63	386	5.6	93	1.0	39	0.4
Retired	22 645	14 574	53	581	4.6	131	1.3	41	0.4
Unemployed	19 532	11 780	60	722	6.5	183	1.5	68	0.6
Other/data lacking	11 440	5 561	50	374	6.2	111	1.8	39	0.6

* age-standardised (Finland 2014)

TABLE 6: Invitations and screenings and main findings by level of education in 2019

Educational level	Invited	Screened		Recommendation for risk group screening		Referral for follow-up examination		Histological HSIL+	
		N	%*	N	%*	N	%*	N	%*
Primary or data lacking	31 593	16 436	51	934	5.7	253	1.5	110	0.7
Secondary	114 228	78 472	69	4 639	5.9	1 281	1.6	559	0.7
Higher	137 642	103 048	74	5 420	5.3	1 238	1.2	404	0.4

* age-standardised (Finland 2014)

TABLE 7: **Results of routine screening (30 years and older) in 2015 for pap smears and HPV, with subsequent risk group invitations and screening in 2016–2019.**

		Risk group invitation 2016–2019	Risk group screening 2016–2019	Referral for follow-up examination at the risk group screening 2016–2019
	N	%	%	%
Cytology				
Negative of normal	146 116 (95.3)	5 258 (3.4)	3 146 (2.1)	24 (0)
Recommendation for risk group screening	6 019 (3.9)	5 577 (3.6)	4 033 (2.6)	225 (0.1)
Referral for follow-up examination	1 238 (0.8)	83 (0.1)	19 (0)	3 (0)
Not interpretable or data lacking	25 (0)	0 (0)	0 (0)	0 (0)
Total	153 398 (100)	10 918 (7.1)	7 198 (4.7)	252 (0.2)
HPV				
Negative or normal	13 488 (91.8)	3 (0)	0 (0)	0 (0)
Recommendation for risk group screening	950 (6.5)	892 (6.1)	690 (4.7)	396 (2.7)
Referral for follow-up examination	246 (1.7)	8 (0.1)	4 (0)	2 (0)
Not interpretable or data lacking	2 (0)	0 (0)	0 (0)	0 (0)
Total	14 686 (100)	903 (6.1)	694 (4.7)	398 (2.7)

TABLE 8: **HPV and Pap smear screening invitees and participants, and colposcopy referrals during the first round of screening after randomisation. Referrals in the programme and treatment registry are tabulated by age group screening attendees during the five-year screening cycle. In the Care Register for Healthcare, the number of referrals is estimated on the basis of the person's first colposcopy episode.**

	Participants in the routine screening	Women referred by the screening programme		Referred women in the Care Register for Health Care	
		N	%	N	%
HPV-group	77 279	1 665	2.15	2 618	3.39
Pap smear group	76 785	1 122	1.46	2 048	2.67