QUALITY MANUAL FOR CERVICAL CANCER SCREENING

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1. SUMMARY

Cervical cancer screening aims to reduce the incidence of cancer and the number of deaths it causes. The wellbeing services counties and the City of Helsinki are responsible for organising the screening programme in their area. Screening must be offered every five years to women aged 30–65 years in line with the Government Decree on Screenings.

The primary screening test is the HPV test and the test used must be validated for screening purposes. The Pap test should only be used as a triage test after a positive HPV test and as the primary test if screening is also offered in the wellbeing services county to women aged 25 years. In 2023, about 80% of screening was already based on HPV testing.

In the case of a mild screening finding, it is sufficient to follow up with a new sample in 18-24 months in so-called risk group screening. This control test checks whether the screening finding recurs or whether the finding has regressed on its own. In the case of a serious screening finding or a recurrent mild finding, further examination and biopsy are needed to assess the need for treatment.

Slightly over 70% of those invited attend to screening and to improve participation, screening organisers need to put in place methods that have been shown to work, such as offering pre-booked appointment and sending reminders. In addition, it is recommended that self-sampling be offered as an alternative screening method for those who do not attend screening even after a reminder.

It is important to ensure the quality of the screening programme at all stages of the screening process. Quality assurance applies to screening sample taking and analysis as well as colposcopy and follow-up care. The different screening actors are each responsible for the implementation of quality assurance. The submission of data from all stages of the screening chain to the national register will support the evaluation of screening and allow comparison between operators.

The first HPV-vaccinated age group will reach the screening age of 30 years in 2028. The screening of the HPV-vaccinated age groups should be organised differently from the previous age groups due to the reduced risk. Legislative changes will have to be made to prepare for this. To improve the screening programme, all screening-related tests should also be centrally registered, which would allow a comprehensive assessment of the quality, effectiveness and costs of screening.

2. TERMINOLOGY AND ABBREVIATIONS

AGC-FN	atypical glandular cells, favor neoplasia
AGC-NOS	atypical glandular cells not otherwise specified
AIS	adenocarcinoma in situ
ASC-H	atypical squamous cells, cannot exclude HSIL
ASC-US	atypical squamous cells of undetermined significance
CIN	cervical intraepithelial neoplasia
	CIN 1 = mild dysplasia (dysplasia levis)
	CIN 2 = moderate dysplasia (dysplasia moderata)
	CIN 3 = severe dysplasia (dysplasia gravis, carcinoma in situ)
FINGOG	Finnish Gynaecological Oncology Group
FICAN	National Cancer Centre Finland
HPV	Human papilloma virus (HPV)
hrHPV	High-risk HPV genotype
HSIL	high-grade squamous intraepithelial lesion
IFCPC	International Federation of Cervical Pathology and Colposcopy
LSIL	low-grade squamous intraepithelial lesion
MDT meeting	Multidisciplinary team meeting
THL	National Institute for Health and Welfare

3. INTRODUCTION

This Quality Manual for Cervical Cancer Screening is intended to support decision-making and activity by those responsible for the organisation and practical implementation of screening. It provides recommendations, based on research evidence and practical experience, for implementing an effective and cost-effective organised cervical cancer screening programme. The treatment of precancerous lesions or cervical cancer is not specifically addressed in this manual. More detailed information on treatment recommendations can be found, for example, in the Current Care Guidelines and the FINGOG guidelines[1,2].

Scientific research concerning cervical cancer screening is active, so the quality manual will be regularly updated in light of the accumulating research evidence. Technological developments in screening methods offer promising options for improving the screening programme in the coming years. In addition, the HPV vaccination programme will reduce the incidence of cervical cancer, which will also require changes to the screening programme as vaccinated women reach screening age in the coming years. However, the impact of the vaccination programme on cervical cancer rates at the population level will only be seen in the 2030s, when the oldest vaccinated age groups will be between 30 and 40 years old, at which age cervical cancer will become prevalent.

4. BACKGROUND

The aim of this chapter is to give an overview of cervical cancer, its screening and HPV vaccination to provide a frame of reference for the following chapters.

4.1 EPIDEMIOLOGY OF CERVICAL CANCER

Cervical cancer is the fourth most common cancer in women worldwide. In 2020, an estimated 600 000 women were diagnosed, and 340 000 died from the disease[3]. Cervical cancer incidence and mortality in developing countries is many times higher than in Western countries[3].

Between 2017 and 2021, there were around 180 cases of cervical cancer diagnosed in Finland each year, or around six new cases per 100 000 person-years, and around 50 deaths due to cervical cancer4. Over a lifetime, cervical cancer in Finland affects around five women in every thousand4. After five years, around 73% of those diagnosed with cervical cancer are still alive. Finland's cancer rates are low in worldwide comparison and come from an unvaccinated population that has been screened for decades. In Finland the HPV vaccination programme started in 2013 for 11–15-year-old girls. The vaccinated cohorts are not yet, at the time of the publication of this Quality Manual, at the age where cervical cancer starts to appear.

4.2 HPV AND CANCER DEVELOPMENT

Human papillomavirus (HPV) infection is a key, but not by itself sufficient, aetiological factor in cervical cancer[5]. More than 180 types of HPV have been described, of which about 40 are capable of causing infection in the genital area. High-risk HPV (hrHPV) types, which are particularly at risk of developing into cancer in prolonged infections, include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59[6]. These viruses particularly affect the tissues of the cervical transformation zone and are usually transmitted sexually. However, the cancer risks of different types of hrHPV vary widely. HPV16 and HPV18 together account for almost 80% of HPV-positive cervical cancers, rising to 90-94% when HPV types protected by the 9-valent and 2-valent vaccines are included[7].

Although the majority of hrHPV infections heal spontaneously, persistent hrHPV infection can lead to the development of precancerous lesions of the

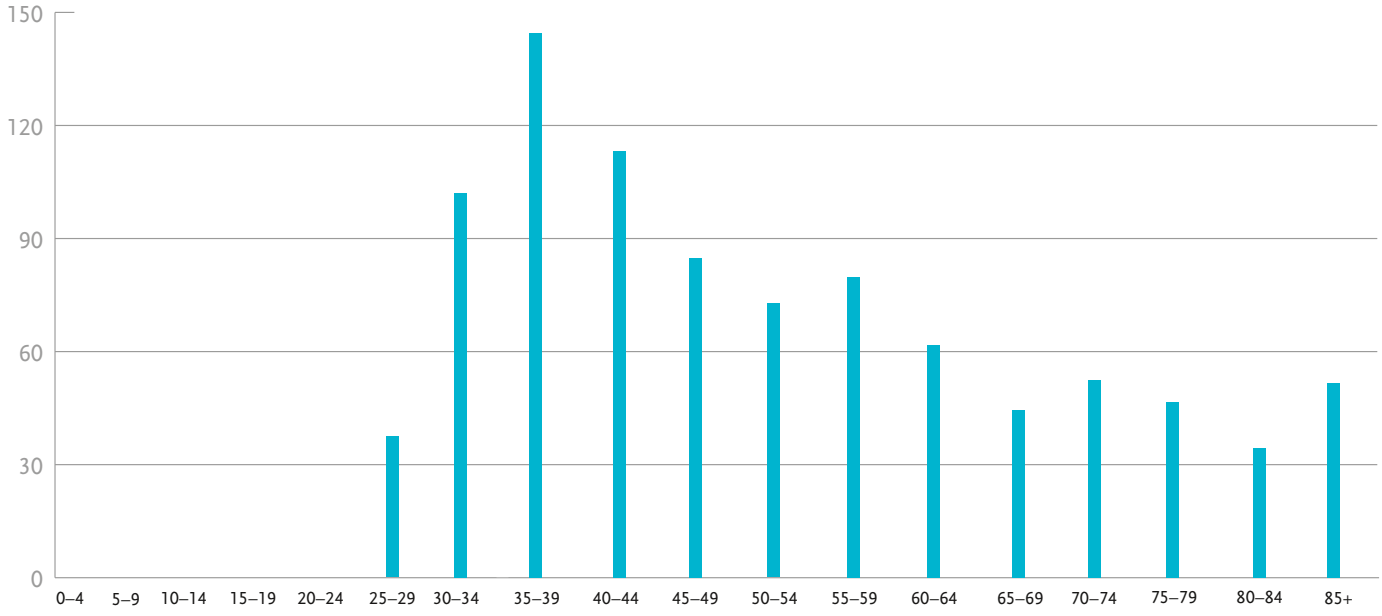

Figure 1 Average number of cervical cancer cases by age group 2017-2021

cervix. A large proportion of precancerous lesions also heal spontaneously, but some progress to cancer. As a rule, cancer progresses slowly from precancerous lesions, usually over years or even decades[8]. Several other inflammatory, chemical, hormonal, immunological and genetic factors contribute to the persistence of HPV infection and the development of cancer and its precursors[6].

HPV infection rates rise rapidly in young women after the onset of sexual activity. In Finland (and more generally in northern Europe), the prevalence of HPV infection is over 25% after the age of 20, after which it decreases with age, reaching around 5% in people aged 40–50. The prevalence peaks at around 30 years of age at the time of the start of screening (see below for more details on screening). Cancer incidence, on the other hand, has a bimodal pattern: the first incidence peak occurs shortly after the age of 30-35 years, and the second peak occurs after the end of screening in people over 65 years (Figure 1)

4.3 CERVICAL CANCER SCREENING

Cervical cancer screening aims to reduce the incidence and the mortality of cervical cancer. To achieve this goal, screening aims to detect and surgically remove precancerous lesions and early-stage cancers. The slow progression of precancerous lesions to cancer creates a long window of opportunity to detect and treat precancerous lesions, which is one of the key conditions for effective cancer control through population screening.

Traditionally, the cervical cancer screening programme in Finland has been carried out by inviting women to cervical screening, based on a cervical smear test, every five years from the age of 25 or 30. The starting age has varied from region to region. The last age-based screening invitation used to be sent to women aged 60, but from the beginning of 2022, screening has been extended to women aged 65. A single screening round includes an invitation and possible reminders, sampling and test analysis, and follow-up measures of a positive result (screening algorithm). In the case of a mild screening result, it is sufficient to follow up with a new sample in 18–24 months in a so-called risk group screening. This control test checks whether the screening finding recurs or whether the finding has regressed on its own. In the case of a serious screening finding, such as a recurrent mild finding, further follow-up examinations and biopsy are needed to assess the need for treatment. The importance of the screening algorithm for effective screening is important.

Most mild and moderate precancerous lesions, especially in young women, will regress spontaneously[9,10]. Finding a precancerous lesion that would regress spontaneously is called overdiagnosis. It leads to unnecessary treatment and monitoring and takes up healthcare resources. Optimally functioning cervical cancer screening would help identify progression-prone precancerous lesions while finding as few spontaneously regressing precancerous lesions and benign HPV-related lesions as possible. The aim of screening should therefore be not only contain costs, but also to minimise the health risks for women (e.g. repeated screening, loop treatments and possible resulting miscarriages/preterm births).

In Finland, it is estimated that screening has prevented more than 80% of cervical cancers and cancer deaths. However, the incidence of cervical cancer has increased since the late 1990s in women under 40 years of age, where the incidence is now at pre-screening levels[4]. In Finland, screening has been carried out not only within the screening programme but also outside it as so-called out-of-programme testing. More Pap tests are performed in Finland outside the programme (about 60%) than within the national screening programme[11,12]. The benefits of large-scale testing have been high screening coverage, taking into account both the screening programme and out-of-programme testing (overall, at least one screening test in five years for about 90% of the screening age group; participation in the screening programme for 30-year-olds of about 50%,

rising to 80% with age). A drawback of Finland's dual screening activity has been the poor management of the screening process overall, as out-of-programme screening tests have not been registered and there has been no systematic monitoring of the targeting or follow-up practices of these tests. This has led to both overdiagnosis and, in particular, higher screening costs.

It should be stressed that cervical cancer screening is not just a single test and a series of steps to deal with positive findings (the screening cycle and its algorithm), but a series of screening rounds that make up a screening process spanning decades. In controlling the screening process, the determination of the relevant target population and the screening intervals, the time between screening rounds, play an important role. The screening interval influences the balance of benefits and harms: a longer screening interval allows precancerous lesions to cure spontaneously, thus reducing overdiagnosis, but it may also give the cellular changes more time to progress to cancer, thus increasing the cancer burden. The effectiveness of screening tests and interventions is also linked to the optimal screening interval.

In past decades, the screening test was the Pap test, which looks for precancerous or cancerous changes in a cervical smear. Currently, the hrHPV test (primary test) is the preferred test, coupled with a Pap test (triage test) if necessary: the sample is first analysed for hrHPV status, and if the sample is positive for hrHPV, the Pap test is also performed. If the hrHPV test result is negative, the risk of developing cervical cancer in the near future is significantly lower than if the Pap test is negative, i.e. normal, because no oncogenic papillomavirus infection has been detected in the hrHPV-negative subject. This is very different from a negative Pap test alone, where a normal cell image does not exclude HPV infection. The sensitivity of Pap test-based screening to detect precancerous lesions is generally worse than that of hrHPV-based screening.13. On the other hand, the challenge of hrHPV testing is the choice of an appropriate algorithm for hrHPV-positive patients, as most HPV infections clear spontaneously and are thus not a criterion for a treatment. Recently, various triage tests and methods have been actively investigated to specifically identify precursors that develop into cancer among all detected precancerous lesions.

4.4 IMPACT OF THE HPV VACCINATION PROGRAMME ON SCREENING

A national vaccination programme against the most significant high-risk HPV types (including HPV genotypes 16 and 18) was launched in Finland in 2013 for girls and in 2020 for boys. With HPV vaccination, the cervical cancer prevention process starts earlier in life. The good protection offered by vaccines against the highest-risk HPV types is expected to greatly reduce the incidence of cervical cancer in those vaccinated. This has already led to the first scientific findings being published[14–16]. The indirect effects of vaccination also extend to those who are not vaccinated through a reduction in the circulation of the virus in the population. Indirect effects are particularly evident in the unvaccinated population of the vaccinated age groups since, in the young, infections are acquired from people of roughly the same age. Indirect effects are less significant in older age groups. With vaccination, the most oncogenic hrHPV infections and further HPV-related cancers will become less frequent in the vaccinated age groups in both vaccinated and unvaccinated individuals. Population-level herd immunity, where the HPV types the vaccine protects against are not able to spread into large-scale epidemics, will be achieved if vaccination coverage in both girls and boys reaches around 75%[17]. In recent years, around 80% of girls and 70% of boys in the age groups covered by the HPV vaccination programme have received the vaccine. It should be noted that with HPV vaccination, the distribution of HPV types in the population is changing, with the remaining HPV types having a much lower potential to progress from precancer to cancer.

These positive changes brought about by the vaccination programme pose a challenge to the effec-

tive implementation of the cervical cancer screening programme and highlight the role of controlling the screening process. Among the vaccinated age groups, HPV infection and pre-cancerous lesions are less likely to develop into cancer, so the current high level of screening and treatment of pre-cancerous lesions will continue to lead to increased overdiagnosis and a relative increase in the harms of screening[18]. To avoid this adverse development and to improve the cost-effectiveness of screening, all actors should in future follow screening recommendations much more closely and act together in a coordinated manner. In addition, to ensure effective coordination of the screening programme and to make changes where necessary, all Pap and HPV tests, follow-up examinations and treatments must be registered in a timely and comprehensive manner, irrespective of the actor.

5. ORGANISATION AND RESPONSIBILITIES OF THE SCREENING PROGRAMME

- The wellbeing services counties and the City of Helsinki are responsible for organising the screening programme.
- The implementation and development of screening are guided and monitored by the National Cancer Screening Steering Group, which is part of the National Cancer Centre Finland (FICAN), and the Expert Group on Cervical Cancer Screening, appointed by it.
- The Finnish Cancer Registry, in cooperation with other actors in the field, monitors and evaluates the ongoing screening programmes and the methods used in them.

5.1. LEGISLATION

According to Section 14 of the Health Care Act, a wellbeing services county must organise screenings in accordance with the national screening programme. The Government Decree on Screenings (339/2011) and its amendments (752/2021 and 1243/2022) stipulate in more detail that cervical cancer screening must be organised every five years for women aged 30–65. In addition, the screening decree (622/2023) provides that cervical cancer screening is also to be carried out for persons in the target group by sex at birth whose sex has been confirmed as male.

At the beginning of 2023, the responsibility for organising screenings was transferred from municipalities to 21 wellbeing services counties and the City of Helsinki. In addition, the Region of Åland is responsible for organising screening in its area. Screening is organised according to a programme decided in advance by the wellbeing services county, which must appoint a person responsible for each screening programme. The wellbeing services counties can either carry out the screening themselves or outsource the screening to a service provider of their choice. In either case, the programme must include an appropriate quality management and quality assurance procedure. The well-being region should monitor and evaluate the quality of the entire screening process and the reliability of the screening tests regularly and submit individual-level data on screening to the mass screening register maintained by the Finnish Cancer Registry, which will allow the quality and effectiveness of the screening to be assessed. The National Institute for Health and Welfare has commissioned the Finnish Cancer Registry to monitor and evaluate, in cooperation with other actors in the field, ongoing screening programmes and the methods used in them.

To organise screening that is not following the national screening programme (for example, when expanding the age groups for screening), the well-being services county must assess the requirements and impact of screening on the healthcare service system before starting screening.

5.2 SCREENING GUIDANCE AND OVERSIGHT

The National Cancer Screening Steering Group, part of Finnish Cancer Center (FICAN), provides guidance, monitoring and analysis of the initiation, implementation and development of cancer screening. The Steering Group consists of expert members from the FICAN and its five regional cancer centers, the Cancer Registry and a representative of the Ministry of Social Affairs and Health. The Steering Group has also appointed an expert group for each cancer screening programme to provide more detailed guidance on the implementation of screening.

A quality manual drawn up by the expert group gives more detailed guidance to the wellbeing services counties on how to implement the screening programme. The wellbeing services counties are responsible for implementing these guidelines.

The primary responsibility for monitoring the screening programme lies with the wellbeing services counties themselves. As with the rest of the

health system, the Regional State Administrative Agencies are also responsible for monitoring the screening organised by the wellbeing services counties. The Regional State Administrative Agencies also deal with complaints, except in cases of suspected malpractice resulting in the death or serious permanent disability of a patient.

5.3 TESTING OUTSIDE THE SCREENING PROGRAMME

Only about 40% of all screening-related testing is estimated to take place within the organized screening programme[11,12]. Testing outside the screening programme is currently not routinely registered centrally, leaving a gap in its utilization and quality assessment (see Chapter 6.3). Cervical screening tests should take place in the organized screening programme, as the target groups and screening intervals are based on research evidence and the risk of overdiagnosis is lower than with so-called opportunistic screening[19,20]. To improve the cost-effectiveness of screening, out-of-programme testing should also be integrated into the quality assessment of the screening programme and overlapping testing should be avoided.

Testing outside the screening programme is particularly focused on younger age groups[11,12]. For those younger than the screening age, testing takes place, particularly in the public health sector. For screening age groups, duplicate testing in and out of the programme is common, and out-of-programme testing is more often done in private health care 11. Out-of-programme testing has been shown to prevent cancer in the screening target population21–23. Testing outside the screening programme is most common among women employed in management, domestic language native speakers and those living in urban municipalities[12].

Testing outside the screening programme is only appropriate in certain cases, such as if a woman has not participated in the programme and it has been five years or more since her last screening test, or if she has symptoms (see Current Care Guidelines).

6. SCREENING TARGET POPULATION

- Cervical cancer screening for women aged 30–65 years every five years.
- The Expert Group recommends that wellbeing services counties should no longer extend cervical cancer screening to the age group of 25 years if screening has not previously been provided for this age group in a region.
- Legislative changes are needed to take HPV-vaccinated cohorts and those tested outside the screening programme into account in invitation practices.

6.1 AGE GROUPS TO BE SCREENED

The target group for cervical cancer screening is women aged 30–65 years every five years, according to the screening regulation. In addition, screening is organized according to sex at birth for target group members whose gender has been confirmed as male. Screening invitations are sent to the target group members on the years their age is divisible by five. The screening target age group, 30–65-year-olds, is based on research evidence on the screening effectiveness and the balance of benefits and harms of screening[19,24].

No separate invitations to screening are sent to persons who have confirmed their gender as male, as the invitations are based on the gender registration in the Digital and Population Data Services Agency. These persons are nevertheless eligible to participate in screening (see Chapter 8.1).

The Expert Group recommends that wellbeing services counties should no longer extend cervical cancer screening to the 25-year-old age group if the region has not previously provided screening for this age group. In some regions, the screening programme already starts at the age of 25. From 2023, this age cohort will be among those who have been offered the HPV vaccine during their school years. Vaccination coverage has fluctuated between 70% and 80% over the years. HPV vaccination is effective in preventing cervical pre-cancerous lesions and cancers, reducing the need for screening but highlighting the harms of screening. The results of screening in the vaccinated age groups will be evaluated and any changes to the screening programme will be based on the evidence from screening in these age groups (see Chapter 18 on the screening of HPV-vaccinated people for more details).

Cervical cancer screening has been shown to be effective until at least the age of 65 or even later[21,25,26]. On the other hand, women who have regularly attended screening and have only negative screening results after the age of 50 are at low risk of developing the disease later in life. However, the risk is increased if participation has been irregular or if abnormal results have been detected[27,28]. Risk group screening should be continued until age 69 in the screening programme, if necessary. Even after this, screening tests can be recommended in special cases (e.g. for HPV-related changes treated after menopause, in immunodeficient patients, etc.).

6.2 EXCLUSIONS TO SCREENED POPULATION

The Finnish screening programme has not made any further restrictions on the persons invited for screening and has, for example, invited people to be screened also after a hysterectomy. The expert group recommends that the wellbeing services counties continue to operate in this way.

In the other Nordic countries, all cervical screening tests, whether performed as a part of an organized screening programme or not, are registered nationally. Screening invitations are only sent to women who do not have a registered test during the screening period.

In Finland, the majority of cervical screening tests are performed outside the screening programme and a significant proportion of women have tests both within and outside the programme. Duplicate testing could also be reduced in Finland by inviting only people who have not been tested during the last five

years to screening. However, this requires that all laboratories analyzing screening tests report all tests performed in a comprehensive and timely manner to the Mass Screening Registry.

6.3 LEGISLATIVE CHANGES NEEDED

The first HPV-vaccinated age group will turn 30 in 2028, which will lead to changes in the screening programme, as the screening of these and subsequent age groups for cervical cancer will need to be organised differently from previous age groups due to the reduced risk (see section 4.4 on the impact of the HPV vaccine on screening). More detailed decisions on the modification of the screening programme for vaccinated persons will be taken at a later stage, but provision should be made for this by allowing the vaccinated population to be invited for screening in a different way from the unvaccinated birth cohorts.

Targeting screening according to HPV vaccination status can be achieved by using the existing Finnish National Vaccination Register (THL), which records HPV vaccinations administered under the national vaccination programme at the individual level. However, the use of vaccination registry data to limit the number of people invited for screening will require legislative changes, the preparation of which needs to start without delay.

Legislation also needs to be updated to oblige healthcare providers to report individual-level data on Pap and HPV tests and their results to the Mass Screening Registry of the Finnish Cancer Registry. This will allow for a comprehensive assessment of the quality, effectiveness and costs of all prevention interventions for HPV-associated diseases (HPV vaccination programme, organised screening and unorganised testing). The expert group recommends that all laboratories should be obliged to report comprehensive and timely individual-level data on all Pap smear and HPV tests performed to the Mass Screening Registry of the Finnish Cancer Registry. This could be followed by the consideration of moving to a practice whereby screening invitations are only sent to women who do not have a registered test during the screening interval.

7. SCREENING ALGORITHMS

- For women aged 30 or older, the primary screening method is the hrHPV test every five years and the Pap test is used as a follow-up or triage test to a positive hrHPV test.
- If screening is offered in the wellbeing services county for 25–29 year olds, the primary screening method is the Pap test alone.
- Certain immunodeficient patients are at increased risk of cervical cancer and its pre cursors, making more frequent screening as part of clinical surveillance recommended.

The hrHPV test, which identifies high-risk human papillomaviruses, has been found to be the best primary screening method for people aged 30 years and older[29] The Pap test is then used as the first follow-up or triage test to a positive hrHPV test. For 25–29 year olds, the Pap test alone is the primary screening method.

The screening algorithms used in the organized cervical cancer screening programme are presented in Figures 2 (for 30 year olds or older) and Figure 3 (for 25–29 year olds).

Co-testing with both hrHPV and Pap test as a primary test is not recommended.

SCREENING GUIDELINE CONCERNING SPECIAL GROUPS

Certain immunodeficient patients have an increased risk of developing pre-cancerous lesions and cervical cancer. A more frequent screening interval (3 years) is recommended for HIV patients, transplant patients, patients with inflammatory bowel disease on immunosuppressive medication, systemic lupus erythematosus (SLE) patients and rheumatoid arthritis patients on immunosuppressive medication. In practice, this could be done with one additional screening test in the middle of the 5-year screening interval as a part of clinical follow-up.1. For those not on immunosuppressive medication, follow-up according to the screening guidelines for the general population is recommended.

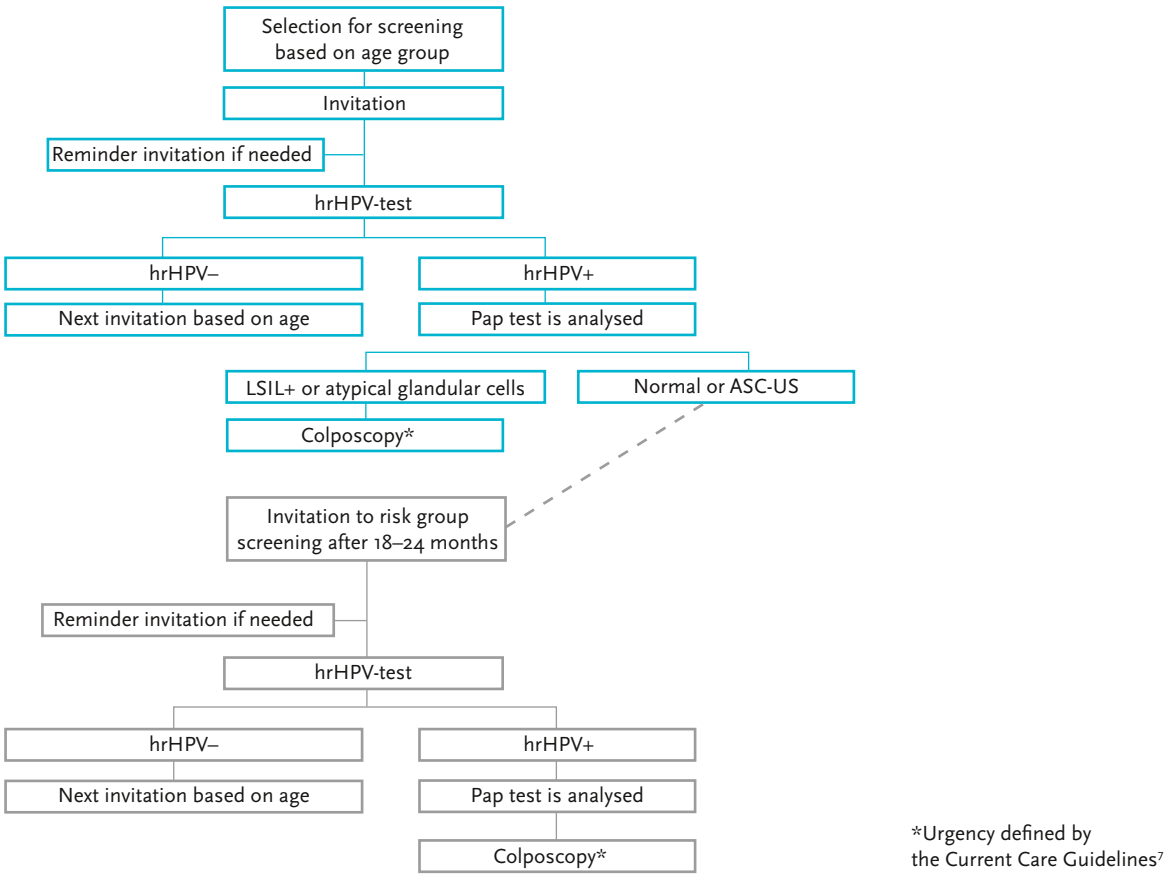

Figure 2 Screening algorithm, hrHPV test (women 30 years or older)

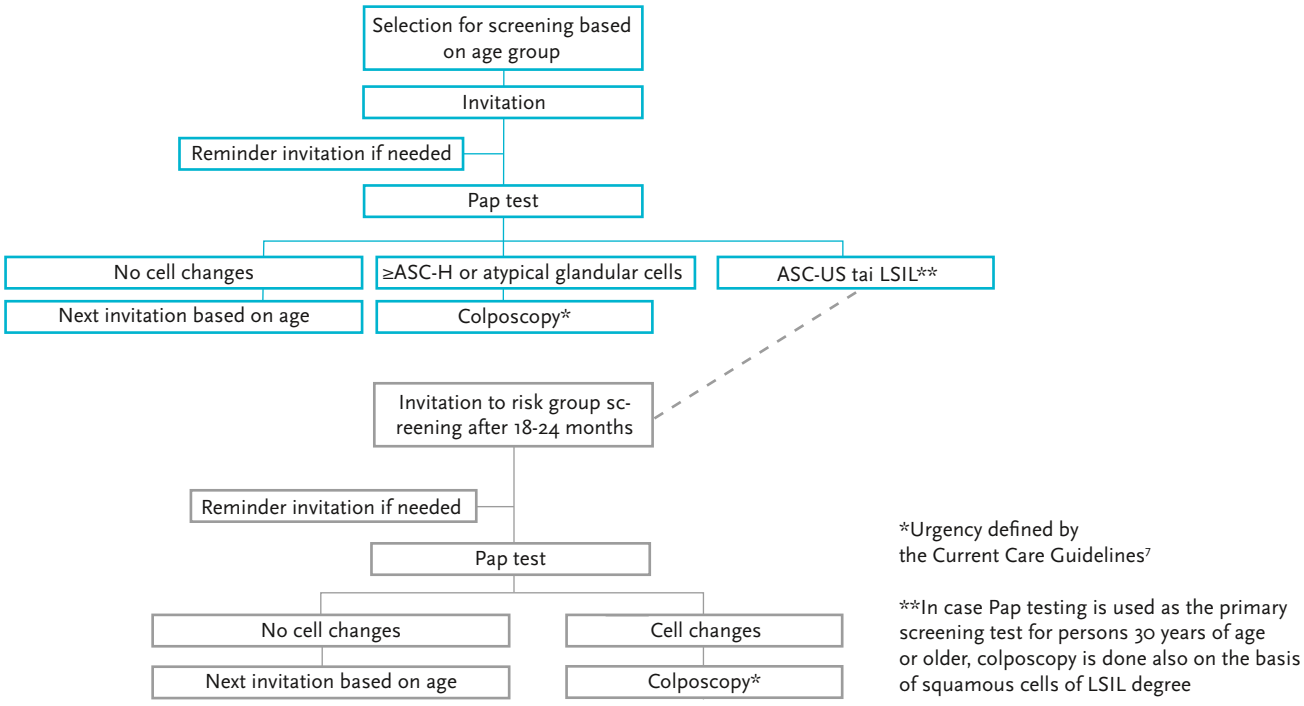

Figure 3 Screening algorithm, Pap test (women under 30 years)

8. INVITATION FOR SCREENING

- Persons invited for screening are extracted from the Digital and Population Data Services Agency (DVV) data system.
- Wellbeing services counties should ensure that people who are not included in this selection (such as persons subject to non-disclosure for personal safety reasons or those who have confirmed their gender as male) are also adequately informed and can easily book an appointment for screening.
- The invitation letter must be personally addresse to the person invited to the screening and must contain sufficient information about the screening and the pre-arranged time and place for the sample collection.
- A reminder will be sent to non-participants 4–8 weeks after the first invitation.
- Self-sampling tests are recommended to be introduced among the non-screened population if other means to improve participation are in place in the wellbeing services county.

8.1 SELECTION OF INVITEES AND SELECTION DATES

The persons invited for screening are selected from the Digital and Population Data Services Agency (DVV) based on their year of birth. At the beginning of each calendar year, the Cancer Registry sends a list of the personal identity codes of those to be invited for screening to the screening agents designated by the wellbeing services counties.

Persons subject to non-disclosure for personal safety reasons or those who have confirmed their gender as male, are not included in this sample. However, the wellbeing services county should also provide these groups with sufficient information about screening and easy access to book an appointment for screening. In addition, the screening provider must issue instructions on its website on how eligible persons can participate in the screening even if they have not received an invitation letter.

Information on the invitations sent is submitted to the Mass Screening Registry maintained by the Finnish Cancer Registry for quality assurance purposes.

In addition to those invited based on age group, persons whose previous screening test (age group screening) has shown mild cell changes (ASC-US or LSIL) or only hrHPV positivity and who have not been referred for further testing must be selected for screening. This risk group selection should be done in such a way that screening can be performed within 18–24 months of the previous test.

To make the organization of the screening process smoother, it is possible to use the paid invitation service provided by the Finnish Cancer Registry, where the screening organizer is provided not only with personal identification numbers but also with the address information for sending screening invitations. The contact details are extracted from the Population Information System. The selection of invitees for risk group screening is done either by the screening provider or by the Cancer Registry's invitation service.

Screening invitations should be sent in a manner that makes it possible for the age group screening to be performed during the screening year, or at the latest in the March of the following year.

8.2 CONTENT OF THE INVITATION

The invitation letter must be personally addressed to the person invited to screening. The invitation may also be sent electronically using the suomi.fi service or a similar channel that the person to be screened has chosen to use. The invitation letter should be either bilingual or in the recipient's own mother tongue if Finnish or Swedish is the mother tongue. If there are significant linguistic minorities in the wellbeing services county, consideration should be given to translating the invitation into other languages.

The invitation letter must contain the following information to support the decision to participate:

- The purpose of screening
- The screening test to be used and how the screening sample is taken and analyzed
- The importance of early detection of disease (cancer or pre-cancerous lesions)
- The benefits and harms of screening
- The possible follow-up examinations and their importance
- Pre-scheduled time and place for the screening test

The letter must also include:

- Information on how the participant will be informed of the screening test result
- Information on how quickly the screening test result will be delivered (target is less than four weeks and should not exceed eight weeks)
- Contact details for further information
- Indication of the address source (DVV Population Information System)

There are invitation letter templates (language versions in Finnish, Swedish, English, Northern Sami, and Russian) produced and maintained by the Cancer Registry, which can be used as a basis for or as an invitation letter. The invitation templates, as well as other screening materials of the Cancer Registry, can be found on the website of the Finnish Cancer Registry https://cancerregistry.fi/screening/organising-cancer-screening/

8.3 REMINDER INVITATION

If the person invited for screening does not attend the screening, the screening laboratory will send a reminder letter 4–8 weeks after the first invitation. A reminder letter template is available in Finnish, Swedish, and English on the Cancer Registry's website, along with other cervical cancer screening invitation and response letter templates.

8.4 OFFERING SELF-SAMPLING AS AN OPTION

A high proportion of cervical cancers are diagnosed in women who have not participated in screening adequately[25,30]. Self-sampling, where a screening sample is taken by the person to be screened, can be one way of increasing screening coverage[31]. The sample is usually taken from the vagina or first-void urine with a brush or sample stick and sent by post to a laboratory for analysis. The sample is analyzed for hrHPV, but the cytological analysis (Pap test) of the sample itself is not reliable, so those who test positive for hrHPV must be invited for a separate Pap test.

In the screening population, when analyzed with PCR-based HPV DNA tests, the self-taken sample was relatively as sensitive (0.99, 95% C.I. 0.97-1.02) but slightly less specific (0.98, 95% C.I. 0.97-0.99) in detecting HSIL-level precursors compared to a sample taken by healthcare professionals[32].

In studies conducted in Finland, self-sampling has been offered either in a 'mail-to-all' setting, where the self-sampling kit was sent by post to all women not participating in the screening, or in an 'opt-in' setting, where those not participating in the screening were offered the opportunity to order the sampling device at home. The average participation rate for self-sampling screening was 24% in the 'mail-to-all' setting and 15% in the 'opt-in' setting[33,34].

The Expert Group recommends that the use of self-sampling tests as the primary screening test should be limited to survey settings for the time being. Instead, it is recommended that self-sampling tests should be introduced as part of the screening programme in the non-participating population under the following conditions:

- The means to improve participation defined in th quality manual are already introduced in the well being services county, i.e. providing a reserved time and place and sending a reminder.
- Women will not have a registered sample outside the screening programme during the period of the screening interval.
- For self-sampling, the test will be provided to non-participants in the screening after a reminder invitation, either according to the mail-

to-all or the opt-in model. In the mail-to-all model, the kit for self-sampling is sent directly, while in the opt-in model, a letter is sent after the reminder invitation offering the possibility to order the self-sampling kit. The highest overall participation is likely to be achieved by offering the option of self-sampling according to the 'mail-to-all' model, only after a primary invitation and one reminder.

- The self-sampling test used must be validated for screening purposes (see list of approved tests in chapter 9.2).
- Follow-up examinations of people who test positive for hrHPV in a self-sampling test can be done either by inviting them back for a triage (Pap smear) at clinical sampling or by giving them a direct referral for a colposcopy. Referral to colpos copy and risk group screening is then made according to the normal screening algorithm. Women who do not undergo triage will also be referred to risk group screening according to the screening algorithm.
- Those who test hrHPV negative will be treated according to the normal screening algorithm.

The option of self-sampling in the screening programme should not make it more difficult for those who wish to be tested in the traditional way by a healthcare professional.

9. SCREENING TEST SAMPLING AND ANALYSIS

- Sampling activity must be accredited and the screening organisation is required to have a quality management programme for sample taking in place.
- Staff involved in sampling should receive adequate introduction training and later regular updating training to maintain their skills.
- The screening programme should only use tests that have been validated for screening purposes.
- The target time for a screening test response is less than 4 weeks in the optimal situation and should not exceed 8 weeks.
- A negative test result can be delivered by letter or SMS if the person being screened has given their consent and the telephone number is verified to be up-to-date and correct.
- In the case of a positive test result, the screening finding and its significance should be explained in a common language in the response letter and, in the case of suspected cancer, the screened person should be reached by telephone as a matter of urgency.

9.1 SAMPLING

In Finland screening samples are taken by licensed healthcare professionals, who are trained to the task. Sampling activities must be accredited and the screening organization is required to have a quality management programme for sample taking in place.

Sampling follows the instructions of the manufacturers of the screening test(s) in use. Staff involved in sampling shall receive adequate introduction training and subsequent regular updating training to maintain their competence. Laboratories have to monitor the sampling activity in terms of the percentage of insufficient samples and the prevalence of glandular cells per laboratory and per sampletaker and report this also to the wellbeing services county responsible for screening. The introduction of any new test methods and associated sampling will always require updating of guidelines and training of staff involved in sampling.

It should be noted that both the primary screening test and the triage test used will affect the sampling procedure. The stages of sampling must therefore be planned in such a way that both tests can be reliably performed on the collected sample material.

Menstrual bleeding is not a barrier to sampling if it is wiped away before sampling. Pregnancy is also not a barrier to cervical screening, although sampling after week 35 of pregnancy is not recommended. Screening providers should actively ensure, through training of the healthcare professionals taking the screening samples that pregnancy does not automatically delay or reduce participation in screening.

9.2 TEST ANALYSIS AND APPROVED TEST PLATFORMS

The microbiology laboratory carrying out the hrHPV testing of screening samples must be accredited and participate in a quality management programme. There must be guidelines concerning referrals, initiating, processing and response of samples.

The screening hrHPV testing process should follow the instructions of the test manufacturers. Adequate introduction training and updating training on these instructions should be provided for the staff. The introduction of any new test method always requires verification of the method, updating of instructions and re-training of staff separately for each laboratory.

The screening programme should only use tests that meet the internationally accepted criteria for screening tests and whose validation results have been published in a peer-reviewed journal.

The criteria for a validated HPV test for screening were developed in 2009 by an international expert group[35].

- The Hybrid Capture-2 and GP5+/6+ PCR-EIA tests, which have been shown to be more effective than cytological screening in randomized trials, will be used as comparators for the test under evaluation.
  - These tests target HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68 and the GP5+/6+ PCR test also targets the type 66.
- The sensitivity and accuracy of the new test to detect precancerous cervical lesions (histological HSIL, formerly CIN2/3) or cancer should be equivalent (non-inferior) to the comparator tests.
  - In addition, it is recommended that the samples used in the validation study are from a population-based screening target population of women aged 30–60 years or equivalent[36], taking into account the recommendations on the required sample sizes.
- Adequate intra-laboratory and inter-laboratory reproducibility of test results must also be demonstrated.

The list of validated hrHPV tests for screening of women aged 30 years and older is presented in Table 1.

Type of test	SCREENING TEST	VALIDATION STUDIES
hrHPV DNA test	Hybrid Capture-2 (Qiagen)	Ronco, 2014[37] Ronco, 2015[24]
	NeuMoDx HPV assay (Qiagen)	Heideman, 2022[38]
	PCR GP5+/6+ EIA	Ronco, 2014[37] Ronco, 2015[24]
	RealTime High Risk HPV assay (Abbott)	Carozzi, 2011[39] Poljak, 2011[40] Hesselink, 2013[41]
	Alinity (Abbott)	Arbyn, 2021[42]
	Cobas 4800 (Roche)	Heideman, 2011[43] Llovveras, 2013[44]
	Cobas 6800 (Roche)	Arbyn, 2021[42]
	PapilloCheck (Greiner Bio-one)	Hesselink, 2010[45] Arbyn, 2015[46] Heard, 2016[47]
	Onclarity HPV assay (BD)	Ejegod, 2014[48] Cuschieri, 2015[49] Ejegod, 2016[50]
	HPV-Risk assay (Self-Screen BV)	Hesselink, 2014[51] Polman, 2017[52]
	Anyplex II HPV HR (Seegene Inc)	Hesselink, 2016[53] Jung, 2016[54]
	Xpert HPV (Cepheid AB)	Cuschieri, 2016[55]
	Cervista (Hologic)	Boers, 2014[56]
hrHPV-RNA-test*	APTIMA assay* (Hologic)	Heideman, 2013[57]
Accepted self-sampling tests	FLOQSwab® + BD Onclarity™ HPV Assay	Martinelli, 2023[58]
	Evalyn + BD Onclarity™ HPV Assay	Latsuzbaia, 2022a[59]
	Qvintip + BD Onclarity™ HPV Assay	Latsuzbaia, 2022a[59]
	Evalyn Brush + Abbott RealTime High Risk HPV assay	Latsuzbaia, 2022b[60]
	Qvintip + Abbott RealTime High Risk HPV assay	Latsuzbaia, 2022b[60]
	Evalyn + Xpert HPV Assay	Latsuzbaia 2023[61]

Table 1. HrHPV tests validated for screening of women aged 30 or older

* The criteria for HPV tests validated for screening have been established for hrHPV DNA tests because the reference tests have shown a very low risk of high-grade precancerous lesions or cancer in long-term follow-up after a negative test result. The APTIMA assay (Holologic) is an RNA test but meets the criteria for a validated screening test in the light of cross-sectional studies. In addition, a 3-year longitudinal follow-up[62] and longer follow-up indirect longitudinal validation results have been published[63,64]. The majority opinion of the Expert Group is that the validity of Aptima as a screening test is therefore sufficiently established, even though the molecule to be tested is different from the reference tests (HC2 and G5/6).

9.3 CYTOLOGICAL TEST AS PRIMARY AND TRIAGE TEST

The cytology test is used in cervical cancer screening as the primary screening test for those under 30 years of age in the screening year and as a triage test for others. In addition to the traditional cytology test, the liquid-based cytology is increasingly used, as it allows primary and triage screening tests to be performed on the same cytology sample. In liquid-based cytology diagnostics, the sample is taken according to the manufacturer's instructions and it is possible to also utilize digitalization and artificial intelligence in the analysis.. The traditional cytology sample collection is described in the Annex 2.

For the interpretation of a cytological sample, a referral, which should contain the relevant anamnesis for the interpretation of the sample, is required. This includes information on factors affecting hormone levels (age, pregnancy/breastfeeding, menstrual status, hormonal medications), relevant information on previous cytology sample results and any histological findings and treatments, and any symptoms and abnormal findings of the patient at the time of sampling.

The pathology laboratory examining the cytology samples must be accredited. The laboratory must have a quality management programme and staff must be involved in internal and external quality assurance. There must be careful instructions for referring, processing and reporting samples. The pathology specialists responsible for the interpretation of samples and the pathology specialists working under their supervision must be licensed in Finland and familiar with gynaecological cytology.

Samples are evaluated according to the current Bethesda classification, a response in table form is recommended in addition to the report.

Specimen type	Conventional smear Liquid based preparation
Specimen adequacy	Satisfactory Adequate, endocervical cells absent Interpretation uncertain (reason) Not interpretable (reason)
General categorization	Negative for intraepithelial lesion or malignancy Epithelial cell abnormality Other change, see Report
Abnormal microbes	Bacterial vaginosis, clue-cells Mixed bacterial flora Fungal organisms Actinomyces Trichomonas vaginalis Herpes
Reactive cellular changes	Inflammation Regeneration Radiation Change caused by intrauterine contraceptive device (IUD)
Other non-neoplastic changes	Endometrial cells in a woman over 50 years of age Glandular cells post-hysterectomy Atrophy Cytolysis
Squamous cell abnormalities	ASC-US (atypical squamous cells of undetermined significance) ASC-H (atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion) LSIL (low-grade squamous intraepithelial dysplasia) HSIL (high-grade squamous intraepithelial lesion) Squamous cell carcinoma
Glandular cell abnormalities	AGC-NOS in endocervical cells (atypical glandular cell-not otherwise specified) AGC-FN in endocervical cells (atypical glandular cell favor neoplasia) In endometrial cells, significance unclear In endometrial cells, suspicion of neoplasia Origin not determinable, meaning unclear Origin not determinable, suspicion of neoplasm Adenocarcinoma in situ Adenocarcinoma
Hormonal effects	Maturity index Matches age and anamnesis Does not match age and anamnesis (reason) Cannot be interpreted (reason)

Table 2. Bethesda 2014 classification for the analysis of cytology samples

9.4 INFORMING THE PERSON SCREENED OF THE SCREENING TEST RESULT

The target time for a screening test response is less than 4 weeks in the optimal situation and should not exceed 8 weeks. A negative test result can be delivered by letter or SMS. When using SMS, the laboratory must ensure that the subject agrees to the use of SMS and that the telephone number is up-to-date and correct during the relevant screening round. For data protection reasons, the SMS should not contain any personal information.

In the case of a positive test result, the screening result and its significance should be explained in a non-specialist language in the response letter. The Cancer Registry provides answer templates that screening providers can use. In the case of a suspected cancer, the person screened should be reached urgently by telephone.

10. HPV-POSITIVE TRIAGE TESTING

- In the case of a positive HPV test, a triage cytology test is performed on the same sample.
- The use of other triage methods, such as genotyping, methylation, and biochemical markers, will be limited to scientific research settings.

10.1 CYTOLOGY AS A TRIAGE TEST

If the HPV test used as the primary test is positive, cytological analysis of the same sample is performed as a triage test (see previous chapter).

10.2 TRIAGE METHODS UNDER RESEARCH

Genotyping

There is a paucity of data on genotyping as a triage method for primary HPV screening under routine conditions. In the Finnish data, HPV types 16 and 18 were associated with more severe cytological and histological changes than other hrHPV genotypes, but the majority of hrHPV-positive individuals are genotyped with hrHPV types other than HPV16 or 18 (non16/18 types) and are also significantly associated with precancerous lesions[65].

As there is only preliminary scientific evidence of the potential benefits of genotyping in screening, the use of genotyping as a triage test is limited for the time being to scientific research settings.

Methylation

Research data on the use of methylation as a triage or primary screening method has started to accumulate from a few European countries and is being followed up. So far, methylation tests have not replaced existing screening tests in any country.

As the potential benefits of methylation tests in screening have not yet been scientifically proven, the expert working group recommends that the use of methylation tests as a triage test be limited to scientific research settings for the time being.

Biochemical markers p16/Ki-67

There are a few studies and meta-analyses on the use of biochemical markers such as p16 and Ki-67 in cervical cancer screening, but their use has mainly been investigated as a triage test after Pap test compared to hrHPV triage.

Compared to the HPV test, p16/Ki-67 has been found to be more specific, but with similar sensitivity. The method requires a cytological sample and the p16/Ki67 method has moderate agreement[66].

There is insufficient research evidence on the use of biomarkers as a triage test for HPV-based screening, and the Expert Group recommends that the use of biochemical markers as a triage test be limited to research settings.

11. GUIDANCE ON RISK GROUP SCREENING AND FOLLOW-UP EXAMINATIONS

- In mildly abnormal screening findings (hrHPV test positive once and triage Pap test normal or ASC-US), spontaneous recovery of hrHPV infection should be followed up in the screening programme with a repeat test after 18–24 months (so-called risk group screening).
- If the hrHPV test remains positive at risk group screening, the woman is sent for colposcopy with the urgency set by the triage Pap test.
- hrHPV-positive women with a triage Pap test showing a squamous cell atypia of LSIL level or higher, or any glandular cell abnormality, are referred for further colposcopy with the urgency determined by the Pap test.
- In patients under 30 years of age, a cytological result of ASC-US or LSIL leads to risk group screening and no separate HPV test is performed and a referral for colposcopy is made if the pap smear shows at least ASC-H level squamous cell atypia or any glandular cell type, or if the LSIL or ASC-US result is repeated in risk group screening.

11.1 RECOMMENDATION TO RISK GROUP SCREENING

In mildly abnormal screening findings (hrHPV single positive and triage Pap test normal or ASC-US), spontaneous cure of hrHPV infection should be followed up in the screening programme with a repeat test after 18–24 months (so-called risk group screening). If the hrHPV test is still positive at risk group screening, the woman is sent for colposcopy with the urgency determined by the triage Pap test.

In patients under 30 years of age, a cytological result of ASC-US or LSIL leads to risk group screening and no separate HPV test is performed.

11.2 REFERRAL TO FOLLOW-UP EXAMINATIONS

At screening, hrHPV-positive women with a triage Pap test showing LSIL or stronger atypical squamous cells or any glandular cell type are referred for further colposcopy with the urgency determined by the Pap test findings. Referral to follow-up examination is also made in a mild abnormal finding persists in risk group screening. During pregnancy and childbirth, colposcopy should be performed according to the chart in Current Care guidelines (Figure 4)

In Pap smear screening for 25–29-year-olds, a colposcopy is performed as a follow-up if the Pap smear shows at least ASC-H level squamous cell atypia or any glandular cell abnormality or if the LSIL or ASC-US finding is repeated in risk group screening.

Urgency of colposcopy according to the Current Care Recommendation[1].

HRHPV POSITIVE TEST RESULT AND TRIAGE TEST (CYTOLOGY)

Suspicion of cancer	immediately
HSIL: colposcopy	within one month
ASC-H: colposcopy	within one month
LSIL: colposcopy	within 6 months
repeat ASC-US: colposcopy	within 6 months of the last test
AGC-FN, suspicion of glandular epithelial neoplasia: colposcopy	within one month
AGC-NOS, glandular epithelial atypia of unknown significance: colposcopy	within 2 months
repeat hrHPV-positive: colposcopy	within 6 months, even if the Pap test result is normal

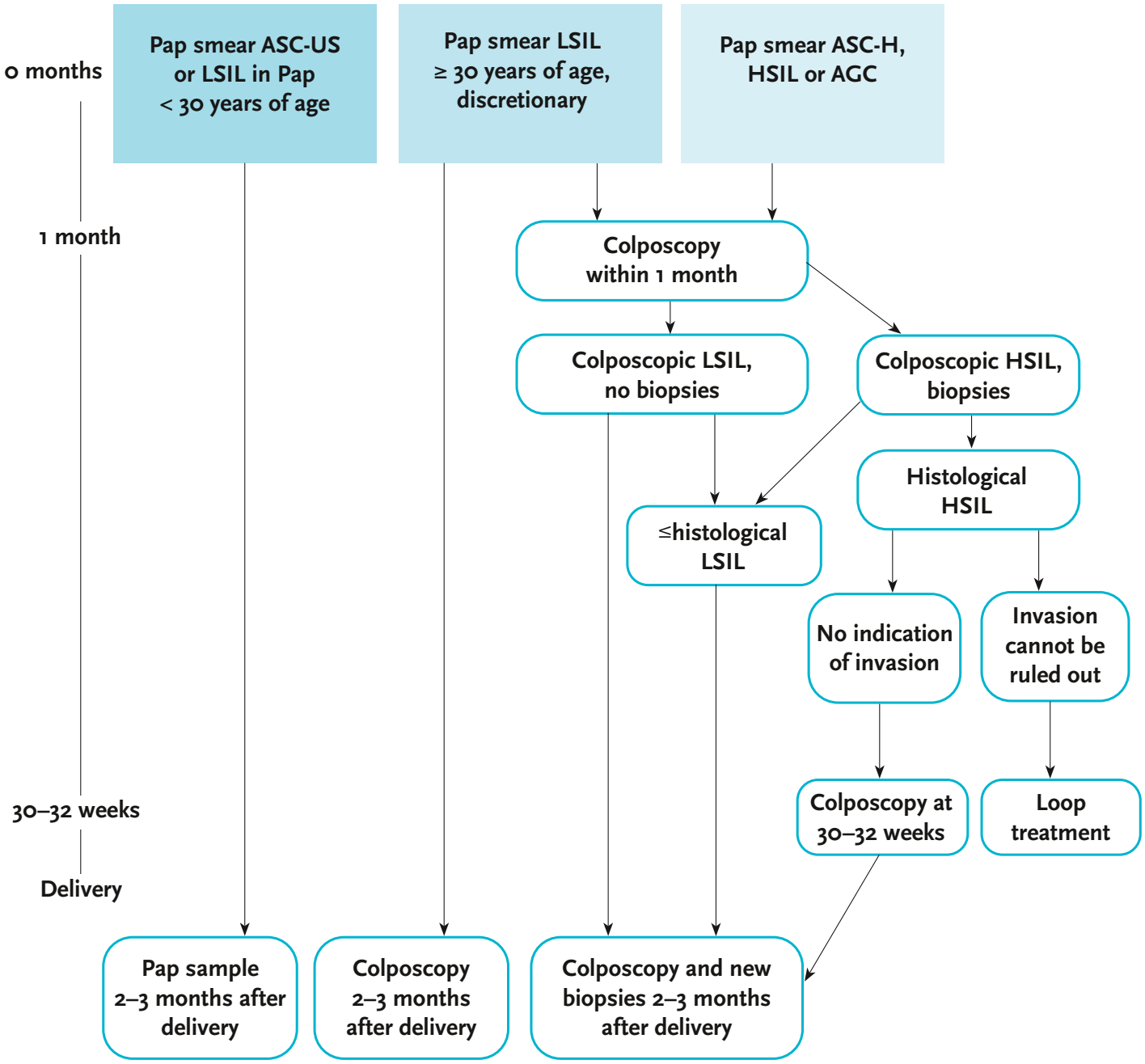

Figure 4 Monitoring and treatment of cellular changes during pregnancy and postpartum

12. FOLLOW-UP EXAMINATIONS (COLPOSCOPY)

- The colposcopist must be properly trained and preferably certified.
- The room used for colposcopy examinations must be sufficiently large and peaceful.
- The colposcopist must use defined terminology in the description of findings and record certain specified things about the examination in the medical record.
- The unit performing the colposcopy should report to the screening provider on the colposcopies. performed on the basis of screening referrals and this information should also be defined as data to be submitted to the Mass Screening Registry.
- Treatment and follow-up of precancerous lesions and cancer are carried out in accordance with the recommendations of Current Care Guidelines and FINGOG Guidelines.

12.1 COLPOSCOPY

A colposcopy is an examination of the cervix, vagina and vulva using a magnifying optical device. It is the most common follow-up examination following an abnormal finding in the cervical cancer screening and allows a diagnosis to be made of the suspected change. Possible treatment is also carried out with colposcopy.

The colposcopist, the physician who performs the colposcopy, is usually the first health professional a screened woman will see after screening. Therefore, the colposcopist plays an important role in informing the woman after an abnormal screening finding and in planning the whole treatment process together with the patient. The Finnish Current Care Guidelines for Cervical, Vaginal and Perineal Cell Tumours and the corresponding EU treatment recommendations provide guidance and support for the development of a treatment plan, but they obviously cannot answer all questions because of the wide range of variables involved in screening and treatment. Many factors will influence the treatment decision such as the preferences of a well-informed and counselled patient, age, previous screening history and other possible medical conditions, as well as the HPV status/type, Pap test response, PAD response of biopsies, colposcopist experience and patient readiness for follow-up. The colposcopist should therefore be appropriately trained and preferably certified (see below).

12.2 COLPOSCOPY TRAINING

The colposcopy training programme was launched by the Finnish Colposcopy Society (SKY) in 2016 to contribute to the Finnish cervical cancer prevention programme and its quality maintenance (see Annex 1). For good patient care, colposcopists must be technically and diagnostically competent and have good interpersonal skills. Finland has been one of the pioneering countries in colposcopy training.

The training programme aims to provide trainees with the core knowledge and skills necessary to perform colposcopy examinations independently and to help them develop the personal and professional qualities needed to become competent colposcopists. As a mark of competence, the trainee will be awarded a SKY colposcopy certificate upon successful completion of the training. The colposcopy certificate must be updated every four years.

12.3 COLPOSCOPY UNIT AND EXAMINATION ROOM QUALITY REQUIREMENTS

The reception room used for colposcopy examinations must be sufficiently large and peaceful. The colposcope must be of good quality (good optics and sufficient magnification) and be equipped with imaging facilities for recording digital images in the patient's medical record. In addition, the patient must be able to follow the examination via a camera connected to the colposcope and an image monitor.

The colposcopy unit must have a doctor in charge who is trained and certified as a colposcopist. The unit must also have a nurse in charge who is familiar

with the subject and has the necessary skills to take cytological samples and advise patients.

12.4 PERFORMING AND RECORDING COLPOSCOPY

The colposcopist should use IFCPC (International Federation of Cervical Pathology and Colposcopy) terminology to describe the findings and the patient's report should include the examination in accordance with the Current Care Recommendation:

- reason for the test, hrHPV test result (HPV type if possible) and degree of cytological change
- previous relevant screening history
- type of transformation zone (TZ1, TZ2 or TZ3)
- description of colposcopy findings according to IFCPC classification
- scoring of the findings using the Swedescore scoring system
- colposcopic diagnosis, which is also recorded on any PAD referral (e.g. SNOMED CT), including vaginal and vulvar diagnoses
- preferably a (digital) image of the lesion
- description of the biopsy sites (using clock face notation 1–12)

12.5 QUALITY CONTROL OF COLPOSCOPY

Quality monitoring and control of the whole screening chain is of great importance for the effectiveness and development of screening. As colposcopy is an essential part of the screening chain, the requirement for quality control also applies to it.

The Expert Group recommends that the unit performing the colposcopy should report the following information to the screening provider on the colposcopy performed on the basis of the screening referrals:

- whether and if so, when a colposcopy was done
- colposcopic diagnosis: cancer / strong change/ mild change / within normal limits / non-diagnostic colposcopy
- transformation zone type: TZ1/TZ2/TZ3
- Swede Score overall points

A similar practice currently exists in the colorectal cancer screening programme for reporting colonoscopies. Similarly, the quality of colposcopy can be monitored nationally by submitting this information to the Mass Screening Registry.

12.6 TREATMENT AND SURVEILLANCE OF PRECANCEROUS LESIONS AND CANCER

The Current Care Guidelines provide guidelines and flow charts for the treatment and surveillance of detected precancerous lesions1. The treatment of cancer cases is in line with the FINGOG Good Care Guidelines[2].

Treatment of cervical precursors is always performed under colposcopy by or under the supervision of a certified colposcopist. As a rule, the treatment is carried out under local anaesthesia by loop electrosurgical excision procedure (LEEP/LLETZ). The treatment involves a repeat colposcopic diagnosis and a description of the findings as described above. The instrumentation and imaging must also meet these criteria.

Treatment is planned according to the transformation zone. According to the European Federation for Colposcopy's quality recommendations, more than 85% of those treated must have a CIN 2+ lesion from cone biopsy or earlier biopsy.

Follow-up of treated precancerous lesion is done six months after treatment with hrHPV and Pap tests. If both tests are negative, the next follow-up biopsy will be taken 24 months after treatment. If the hrHPV and Pap tests are still negative at this time, the patient's clinical surveillance will be discontinued, but they will continue to receive an invitation for screening according to their age group. If, on the other hand, the follow-up hrHPV test is positive or a significant epithelial cell abnormality is detected in the Pap smear, the patient will undergo a new colposcopy to detect possible recurrent or residual disease.

13. HISTOLOGICAL DIAGNOSIS

- The pathology laboratory examining the biopsy specimens must be accredited and participate in internal and external quality assurance.
- The pathology specialists responsible for interpreting the biopsy and the pathology specialists working under their supervision must be licensed in Finland and familiar with gynaecological pathology.
- Optimum target time from sampling to response is less than 2 weeks, maximum target time is 4 weeks.

The referral letter accompanying the histological specimen should include a summary of the patient's previous findings, the change now detected, and where and how the tissue biopsies now sent for examination were taken.

The pathology laboratory examining the specimens must be accredited. The laboratory must have a quality management programme and participate in internal and external quality assurance. There must be guidelines for referral, initiating, processing and responses concerning biopsies. The pathology specialists responsible for the interpretation of a biopsy and the pathology specialists working under their supervision must be licensed in Finland and familiar with gynaecological pathology. Continuous training should be provided to update and maintain the skills of pathologists.

The laboratory must also have the facilities for immunohistochemistry (for example p16) for diagnostics. The response time must support the diagnostic and treatment chain. The optimal target time from sample to response is less than 2 weeks, the maximum target time is 4 weeks.

The responses to biopsy samples are given according to the latest WHO classification[67] and a tabular response is recommended in addition to the report. Diagnoses are given according to the latest WHO tumour classification and the SNOMED CT diagnostic list. For patients aged 30 years or less, it is recommended that the cervical tissue sample responses also provide an estimate of the HSIL finding according to the CIN classification, as sometimes the healing of a CIN2-level change may be missed where CIN3-level lesions are treated.

Challenging cases should be able to be dealt with in a multidisciplinary MDT meeting involving both gynaecologists/colposcopists and pathologists.

14. DATA TRANSMISSION AND REPORTING

- The task of the screening operator is to collect data from all stages of the screening chain for reporting to the Finnish Cancer Registry and to send the collected data to the Mass Screening Registry of the Finnish Cancer Registry according to the defined data model and parameters.
- In order to improve the quality monitoring of colposcopies, parameters related to the quality of colposcopy should be added to the parameters of the Cancer Registry to assess the quality of the operation.

It is the responsibility of the screening provider, i.e. the wellbeing services county or its outsourced provider, to collect data from all stages of the screening chain for reporting to the Cancer Registry. It is also essential that data collection maintains the link between the different steps in the process (e.g. referral, biopsy and analysis, follow-up examinations) so that the data can be analyzed as a coherent screening chain.

The controller of the patient data generated in connection with the screening is the wellbeing services county or the City of Helsinki, even if it procures the service from an external service provider. The screening data are patient records and confidential. However, the screening provider has a legal right to process all screening data, including data from follow-up procedures and specialist care. Likewise, follow-up and specialist care units have a statutory right to provide this information to the screening provider for reporting to the Cancer Registry.

The cancer screening provider must ensure that individual-level data on the different stages of screening are submitted to the Mass Screening Registry of the Finnish Cancer Registry. The quality and effectiveness of the screening will be assessed on the basis of the data submitted to the Cancer Registry. It is advisable that data submission is an automated periodical routine, but the data should be submitted latest by the end of August of the year following the screening year.

According to the THL administrative decision (https://thl.fi/aiheet/tiedonhallinta-sosiaali-ja-terveysalalla/maaraykset-ja-maarittelyt/hallintopaatokset), individual-level screening invitation and screening data and data on the first treatment offered must be submitted in accordance with the data model and parameters defined by the Finnish Cancer Registry. More detailed instructions and descriptions of the data model and parameter set are available on the Cancer Registry website.

In order to improve the quality monitoring of colposcopies, the Expert Group also recommends that the parameters described in the chapter on colposcopy be added to the Cancer Registry parameters:

- whether a colposcopy has been done
- the date of the colposcopy
- colposcopic diagnosis: cancer / severe change/ moderate change / within normal limits/non-diagnostic colposcopy
- transformation zone type: TZ1/TZ2/TZ3
- Swede Score – overall points

The Act on the Processing of Client Data in Healthcare and Social Welfare (703/2023) obliges the archiving of patient data in the patient data archive of the national Kanta services. Laboratory results from screening tests must be stored in Kanta by 1 October 2026 at the latest.

15. SCREENING MONITORING AND PROGRAMME QUALITY ASSURANCE

- Wellbeing services counties, screening laboratories and specialized healthcare units are each responsible for implementing quality assurance.
- The Finnish Cancer Registry publishes annual statistics and a broader statistical report on the implementation of the screening programme.

The Finnish Cancer Registry publishes annual statistics on the implementation of cervical cancer screening on behalf of the National Institute for Health and Welfare. In addition, it publishes a more comprehensive statistical report on the activities of the screening programme every year. The Cancer Registry and other actors, such as university hospitals, also carry out follow-up research on the effectiveness of screening by combining data on cervical cancer and cancer deaths from the Cancer Registry with screening data.

Wellbeing services counties, screening laboratories and specialized health care units are each responsible for implementing quality assurance. The Cancer Registry should support this quality assurance by reporting the screening result data for each wellbeing services county and screening laboratory, compiled from the data submitted to it. This reporting will allow comparison between screening providers and support quality improvement measures in screening.
Target levels for indicators such as screening coverage:

- Coverage of the invitations (>99%)
- Participation rates by age group and demographic group (EU recommendation: at least over 70%, target over 85%)
- Delays in communicating screening and follow-up examination results to the person being screened (target of 90% within the deadline)
- Delays in completion of follow-up examinations (target 90% on time)

In addition, large variations between wellbeing services countys/laboratories in different indicators (e.g. proportion of people invited to the risk group, referral rate, positive predictive value, participation in follow-up) require further investigation by the wellbeing services county or laboratory.

Since the effectiveness of cervical cancer screening is largely based on the treatment of benign precancerous lesions, there must be a regular assessment of the effectiveness of cervical cancer screening in relation to harms.

16. HARMS OF CERVICAL CANCER SCREENING

- The inconvenience to the person being screened is usually minor.
- The loop electrosurgical excision procedure may increase the risk of preterm birth in later pregnancies.
- To minimise the resources required for overdiag nosis, overtreatment and screening, all screening-related testing should take place within a national screening programme.
- The harms of screening, as well as the benefits, should be clearly communicated to the person being screened at the invitation stage.

Screening targets a healthy population, so there are inevitable harms involved. The harms directly affecting the person being screened are both physical and psychological. They may also be felt at the societal level, such as the additional costs of overdiagnosis.

In cancer screening, overdiagnosis is generally defined as the detection of a cancer that would not have harmed a person during their lifetime if it had not been diagnosed. In cervical cancer screening, the detection of precancerous lesions that heal spontaneously or never progress to cancer is also classified as overdiagnosis. Such findings constitute a significant proportion of overdiagnosis in cervical cancer screening.

In developing a national screening programme, the benefits and harms of the programme must be weighed up at the population level, and an acceptable balance must be struck. The harms of screening, as well as the benefits, should also be clearly communicated to the person to be screened at the invitation stage.

16.1 SCREENING HARMS FOR THE INDIVIDUAL

In most cases, the harm to the person being screened is minimal. However, there may be both physical and psychological harms associated from screening tests, such as pain, discomfort, fear, embarrassment, or anxiety[68]. Even mild abnormal screening results require frequent follow-up. Although HPV infection or mild cellular changes only very rarely lead to cancer, the knowledge of an abnormal screening result can cause considerable psychological distress, such as anxiety and stress, for the screened individual[69,70]. Waiting for test results and possible follow-up tests or further examinations is an essential part of the screening process. However, it can be difficult for the person being screened when the fear of cancer is real. Good communication can reduce fears (see Chapter 17).

Colposcopy is an essential part of the screening chain, as any precancerous lesions are identified and treated in a colposcopy. Naturally, psychological fear, anxiety and fear of cancer are associated with colposcopy and waiting for it, even in situations where it would not be appropriate. This is why the colposcopist needs to understand the situation of the individual being screened and, through good information and counselling, reduce the psychological distress as much as possible. The same applies, of course, to other medical staff, such as colposcopists and telephone counsellors.

A well-prepared colposcopy is usually not a procedure that causes significant pain for a well-advised patient. The biopsy associated with the procedure may cause momentary pain, so it is advisable to discuss the need for local anesthesia with the patient.

If necessary, a loop electrosurgical excision procedure, where the abnormal area of the mucous membrane is removed under local anesthesia, is performed to treat a detected cervical precancerous lesion. The perception of pain caused by a loop electrosurgical excision is usually in the range of 0–4 on a 10-point Visual Analogue Scale (VAS) . After treatment, the patient will have a bloody brownish discharge for about three weeks, during which sexual intercourse, bathing, tampon, and period cup use are prohibited due an increased risk of infection. Everything else is allowed and no sick leave

is required. Loop electrosurgical treatment may increase the risk of preterm delivery in subsequent pregnancies (risk ratio 1.3-2.3)[71,72]. The magnitude of the risk depends on the extent of the loop electrosurgical excision. Fertility is not affected by HPV infection, cervical cell changes or loop electrosurgical excision.

A small proportion of women continue to be infected with hrHPV for years and some may have recurrent precancerous lesions requiring treatment in the cervix, vagina, vulva, or anus – or in more than one site. In such cases, centralized monitoring by specialized healthcare and confirmation of treatment plans at MDT meetings will reduce unnecessary follow-up visits, examinations and treatment and thus reduce the burden on the patient.

16.2 THE SOCIETAL HARMS OF SCREENING

False positive screening results, i.e. findings that lead to further follow-up visits and examinations without changes needing treatment are harmful to the person being screened and also consume healthcare resources. Given the transient nature of HPV infection, the hrHPV test and the Pap test, which identifies cellular changes associated with HPV infection, are most likely to detect acute infections or precursors that heal spontaneously. Especially in young women, HPV infections and precancerous lesions often heal spontaneously [9,73]. Too frequent screening increases the number and proportion of false positive test results, which in turn leads to unnecessary follow-up examinations and colposcopies, and further potentially futile treatments.

HPV screening has a higher rate of test positives than cytology screening, on average around 7-8% of those invited for screening. In this case, the number of control biopsy recommendations and colposcopy referrals is generally higher than in cytology screening[74], resulting in a significant increase in the number of risk group screening tests and colposcopy tests for high-risk groups. Especially in the first round of screening, the number of colposcopy referrals is high, up to 3–4 times higher than in cytology screening. The number of referrals among the already HPV screened decreases in subsequent rounds[75], which is probably explained by the fact that for some, HPV screening leads to earlier detection and treatment of precancerous lesions. However, HPV screening also detects precancerous lesions that cytology screening would not detect. It is possible that some of the new precancerous lesions detected by HPV screening are self-healing or non-progressive in nature.

Overtreatment means treating precancerous lesions that would not have progressed to cancer during the lifetime of the person being screened. Cervical cancer screening can result in overtreatment due to false positive screening results, misdiagnosis and overly conservative histological classification. To minimize overdiagnosis, overtreatment and the resources required for screening, all screening testing should take place within the national screening programme, and testing elsewhere in the health care system should be well justified, of high quality and controlled (see section 5.3 and the Current Care Guidelines).

17. COMMUNICATION AND INFORMATION

- Communication on screening is primarily the responsibility of the wellbeing services counties.
- Communication should provide a good understanding of the purpose of screening, the screening process and the benefits and harms of screening.
- Communication should also aim to reach people who have not participated in the screening programme.

17.1 THE AIM OF COMMUNICATION

Screening has significantly reduced the incidence and mortality of cervical cancer. The benefits of screening have also been estimated to far outweigh the harms. To ensure that screening continues to be effective, the communication on screening programme should aim to achieve the highest possible screening coverage in the target population.

Communication should provide a good understanding of the purpose of screening, the screening process, and the benefits and harms of screening. It should also increase a sense of safety at different stages of the screening chain. Good communication and information can minimize the potential psychological harm caused by screening.

Communication on screening is primarily the responsibility of the wellbeing services counties. The wellbeing services county must ensure that its residents have access to sufficient information about the objectives and effectiveness of screening, the potential risks associated with screening, and the organization of screening.

17.2 COMMUNICATION CONTENT

Good information is needed at all stages of the screening chain: the screening invitation, sampling, screening response, and possible follow-up.
Clear and accurate written information must be available to the person invited for screening at all times.

Both summarized basic information and more detailed information on the different stages of screening should be available. Screening invitations and materials should contain the same information throughout the country to ensure regional parity. The Cancer Registry provides and updates materials materials (e.g. leaflets, invitation letters, response letters) freely for use by screening providers. Materials are available in different languages.

Particular attention should be paid to informing those with abnormal results. For example, for an hrHPV-positive patient with a normal or ASC-US cytology test result, the 18–24 month wait for a risk group screening can cause significant stress. This can be reduced by accurate and timely communication. The screening response should emphasize that such a finding is associated with a very low risk of cancer in absolute terms, and that the viral infection very often clears spontaneously within a few follow-up tests. The colposcopist also has an important role to play in communication for women undergoing further examinations (see Chapter 12 Colposcopy)

17.3 COMMUNICATING ABOUT CHANGES TO THE SCREENING PROGRAMME

It is necessary to inform those who are invited for screening about the switch to HPV screening. On the other hand, it should be stressed that the HPV test is taken similarly as a Pap smear. The increasing number of different test results in HPV screening (HPV+ and different Pap smear responses) has been taken into account in the model responses produced by the Cancer Registry.

The Expert Group recommends that, under certain conditions, wellbeing services counties should offer HPV self-sampling to women who have not attended screening since the reminder. In such cases, the possibility of self-sampling should be communicated in a new invitation letter, either by sending

the self-sampling option to non-participants directly (mail-to-all) or by offering the possibility to subscribe to the self-sampling option free of charge (opt-in).

The HPV vaccine reduces the future need for screening, but for the time being, all screening age groups are recommended to participate in screening despite the possibility of HPV vaccination. Communication therefore applies to both the unvaccinated and vaccinated population.

17.4 IMPROVING PARTICIPATION

Communication should also aim to reach people who have not participated in the screening programme. Reminders are key to improving participation and should be used routinely throughout the country[33]. In regions where screening participation is lower than average, regional communication activities and campaigns can be implemented as appropriate.

Communication must emphasize the need for screening in a way that does not compromise the right to self-determination and the possibility of opting out. The high uptake of tests outside the screening programme among young women is likely to reduce screening uptake among younger age groups. Elsewhere in healthcare, women should be encouraged to participate in a screening programme that is monitored and developed, with lower overall costs and lower risk of overdiagnosis.

17.5 SPECIAL GROUPS

A major challenge in communicating about the screening programme is the variety of recipients of the information. Information material may need to be tailored to suit different audiences. For example, socioeconomic, linguistic and cultural differences need to be taken into account. Information should be available through different channels and in different languages, and, where appropriate, cooperation can be established, for example, with different ethnic communities[76].

We also need to ensure that trans men whose uterus has not been removed know that they are entitled to free screening, even if the invitation does not come after the change of personal identity code. Information can be provided, for example, by the services that coordinate gender reassignment treatments.

The right to screening for other special groups, such as people with physical disabilities, visual disabilities, deaf people and people with intellectual disabilities, must also be ensured through appropriate and accessible communication. For those who move during the screening year, a contact channel should be provided to ensure participation in screening.

17.6 INFORMATION AND COMMUNICATION CHANNELS

The screening invitation letter is an important first contact with the person to be screened. It should be concise and clear, preferably with a pre-booked time and place for the screening, and instructions on how to change these online and by phone. The invitation should also indicate where more detailed information is available (see section 8.2).

Comprehensive and up-to-date but general information is available on the internet, for example on the following websites

Health Village Women's House:
https://www.terveyskyla.fi/naistalo/gynekologinen-terveys/kohdunsuun-irtosolumuutokset-papa

Cancer Society of Finland:
https://www.freefromcancer.fi/check-your-body/cervical-cancer-screening/

Background material for health professionals includes. Current treatment recommendation:
https://www.kaypahoito.fi/hoi50049

Healthcare professionals taking the screening samples are in direct contact with the people being screened, so they should be trained in communication skills. This will allow them to answer questions from the screened individuals or tell them where more information is available, thus increasing trust

in the screening programme. Written materials, such as screening leaflets, should also be available at screening visits.

A person with an abnormal screening result should be able to contact a healthcare professional in person for further information if they wish. Contact details for this purpose can be included, for example, in the letter informing of the screening results. The health professional should stress that an abnormal screening result does not indicate cancer or even a precursor of cancer and does not require, for example, immediate further examinations. Psychological support is available, for example, from the Cancer Society's counselling service.

Wellbeing services counties should inform about any changes to the screening programme, for example a possible switch to HPV testing. This could be done through a press release, for example.

17.7 KEY MESSAGES OF THE SCREENING PROGRAMME

Below are key messages based on research evidence to support the communication on the screening programme.

- Screening has reduced cervical cancer incidence and mortality by up to 80%.
- Screening has benefits as well as harms, such as an increased risk of preterm birth after a precancer treatment.
- The age groups and screening intervals of the screening programme are based on scientific evidence.
- Testing outside the screening programme is only necessary in special cases.
- HPV infection is very common, almost everyone gets it in their lifetime.
- The HPV test identifies HPV infections. Both HPV and Pap smears can be tested on the same sample.
- The Pap test looks for cellular changes suggestive of precancerous lesions/cancer. Pap smears are only tested in people aged 30 and over who are found to have an HPV infection.
- An abnormal screening result does not mean cancer. Cell changes usually heal of their spontaneously.
- Smoking increases the risk of cervical cancer.

18. IMPACT OF THE HPV VACCINATION PROGRAMME ON THE SCREENING PROGRAMME

- The first HPV vaccinated cohort turns 30 and enters the cervical cancer screening programme in 2028.
- The modelling suggests that very light screening should be sufficient for vaccinated women, but that a considerable amount of screening is needed for unvaccinated women before the emergence of herd immunity, even though the prevalence of HPV infections is decreasing also among them.
- In the later vaccinated age groups, the HPV genotypes that the vaccine protects against have been virtually eliminated in unvaccinated women, thanks to herd immunity. In these age groups, there is no longer any difference in screening between vaccinated and unvaccinated women, so that screening can be equally light for all women.

18.1 NATIONAL HPV VACCINATION PROGRAMME

HPV vaccination for girls was introduced in the national vaccination programme in autumn 2013 and for boys in autumn 2020. THL recommends that the HPV vaccination series should start in the fifth grade of primary school. The vaccine used in the vaccination programme is put out to tender every few years. Up until 2023, a bivalent vaccine (Cervarix) has been used.

THL monitors the coverage of HPV vaccination through a national vaccination register. When HPV vaccination for girls was launched, those born in 1998 were the oldest birth cohort eligible for HPV vaccination as part of the vaccination programme. This birth cohort will turn 30, the statutory age for cervical cancer screening in 2028. Boys born in 2005 were the oldest birth cohort eligible for HPV vaccination. By autumn 2022, nearly 73% of girls and 63% of boys in the 6th grade cohort born in 2010 had received the HPV vaccine. Among boys born in 2009 who started secondary school, vaccination coverage was about 70% and 79% for girls in autumn 2022.

There are regional differences in HPV vaccination coverage. In autumn 2022, HPV vaccination coverage for those born in 2009 varied as follows. The vaccination coverage for girls was 88% in the North Savo Hospital District and 70% in Central Ostrobothnia. For boys, vaccination coverage was over 80% in East-Savo, Southwest Finland and Åland. In contrast, coverage in Päijät-Häme, North Ostrobothnia and South Ostrobothnia was 63%.

Information on vaccination given is transferred and stored in the THL national vaccination register if the information on vaccination given is recorded in accordance with uniform national classifications and the patient information system is linked to the Avohilmo data transfer. Due to problems in recording and transferring vaccination data, actual vaccination coverage may be higher than the figures in the vaccination register. Vaccination coverage can be viewed using the interactive map published by THL[77]. This reports the regional coverage by year of birth and sex of those who have received at least one HPV vaccination.

Even before the vaccination programme started, around 20 000 girls or women and 3 000 boys or men were in HPV vaccination trials, the first of which were carried out in the early 2000s. In addition, HPV vaccines have been administered in small quantities before the vaccination programme, with the introduction of the 4-valent Gardasil vaccine in 2006 and the 2-valent Cervarix vaccine in 2007.

18.2 FUTURE OUTLOOK: HPV INFECTIONS IN DIFFERENT AGE GROUPS

HPV vaccination divides women into different groups in terms of HPV infection in two ways. First, vaccination divides women into vaccinated and unvaccinated groups. For HPV-vaccinated women, vaccines are expected to radically reduce the number of potentially oncogenic HPV infections, which nat-

urally reduces the need for screening in vaccinated women. Secondly, the HPV vaccination programme divides age groups into three categories: unvaccinated age groups, early vaccinated age groups and later vaccinated age groups. Within these different age groups, unvaccinated women benefit from the indirect protection offered by vaccination in different ways. The vaccination programme for girls and boys is expected to reach a critical level of herd immunity for the HPV types for which vaccines provide protection, effectively eliminating these types from the population[17,78]. Even partial vaccine protection is sufficient to reach the critical level at the population level for many HPV types.

In the unvaccinated age groups (Figure 5, 2015 age group clearly diagonal to the left), where all are unvaccinated, vaccination affects the incidence of HPV infection only a few decades after vaccination. This is because HPV is largely transmitted through sexual contacts, which are concentrated close to the age of the individual (the age range is narrow in the young and increases gradually with age), so infections are also concentrated close to the age of the individual, and vaccination of younger age groups does little to reduce potential sources of infection from older ones. In terms of screening, this means that screening in the unvaccinated age groups will have to continue as at present - although as screening methods improve, screening in these age groups will improve.

In the early vaccinated age groups (Figure 5, close to the 2015 age group), the infection pressure from own and slightly younger age groups is already reduced, but there is still significant infection pressure from unvaccinated slightly older age groups. Therefore, unvaccinated women in the early vaccinated age

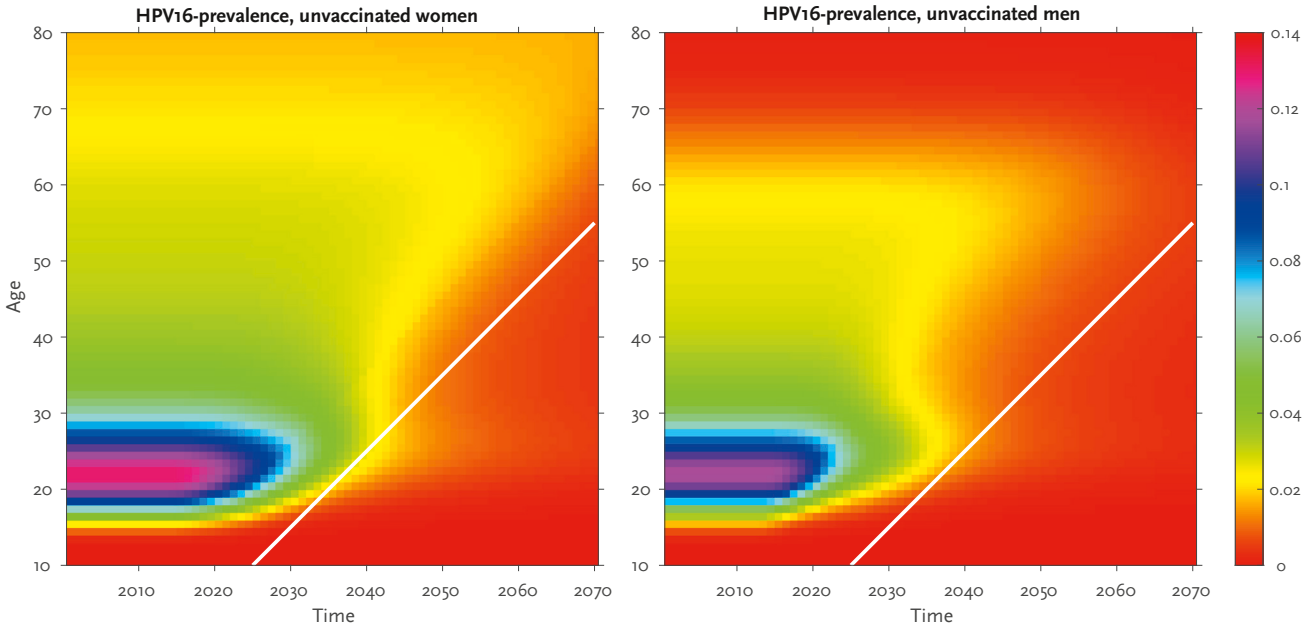

Figure 5 Estimates of HPV-16 prevalence in unvaccinated women (left) and men (right) over time and age using the Finnish vaccination programme coverage up to and beyond the 2009 age groups, using 80% and 65% vaccination coverage for girls and boys, respectively. The white diagonal line represents the 2015 age cohort. Calculation: Vänskä 2013[79]

groups still face infections, but at a reduced rate compared to the earlier age groups. These are probably the most difficult age groups to screen. For vaccinated women, very light screening should be sufficient, but unvaccinated women will still need significant screening, even though HPV infections are already declining in them. For these age groups, either it must be possible to organize screening differently for vaccinated and unvaccinated women, or the screening process must be adaptive so that it automatically targets women at higher risk. The organization of such screening of under-vaccinated populations is currently under investigation. However, if vaccination progresses favorably among both girls and boys, there will not be many such age groups (10–20). On the other hand, if there were widespread problems with vaccination and herd immunity were not achieved, the situation would remain stable.

In the late vaccinated age groups (Figure 5, some years after the 2015 age group), the HPV types that are protected by the vaccine have been virtually eliminated from unvaccinated women thanks to herd protection. In these age groups, there is no longer a screening difference between vaccinated and unvaccinated women, as the HPV types that are protected by the vaccine are absent in both. In this case, screening can be equally light for all women (see section 18.3).

National herd protection will not help the unvaccinated if they (or their partner) are infected abroad in areas where oncogenic HPV types are still prevalent. In such cases, some form of a targeted approach may be necessary in the future. However, an infection acquired abroad will not become an epidemic because of herd immunity in the home country of the infected individual.

Figure 5 is an indicative estimate modelled to help plan the alignment of screening and vaccination programmes, and the 2015 age group, in particular, may not represent such a clear division in unvaccinated women. There may also be differences between HPV types. The prevalence of HPV types in the population needs to be monitored and screening activities adjusted accordingly.

18.3 FUTURE PROSPECTS: SCREENING IN A HERD IMMUNITY ENVIRONMENT

The interplay between vaccination and screening is illustrated in Figure 6, which shows the population-level disease burden (30,000 female + 30,000 male age groups) under different vaccination and screening scenarios in a new post-vaccination equilibrium. The scenarios are calculated using THL's HPV models[79–81]. For comparison, the figure also includes a "no vaccination" vaccination scenario. The burden of disease is represented by the loss of health (x-axis), in terms of quality-adjusted life years (QALYs), and the costs (y-axis) of treating and monitoring cervical cancer and screening findings, as well as the screening itself. The graph does not include the costs of vaccination, as the focus is on screening. The different vaccination scenarios are separated by colours and the screening scenarios by symbols. The circle is for the screening scenario 'not screened' and the cross is for screening before vaccination, including both programme and non-programme screening. Other screening scenarios (dots) are not further specified here, but typically scenarios more to the right indicate lighter screening. The lightest screening scenarios in the graph consist of only one screening round.

Pre-vaccination screening (black cross) was associated with high health benefits compared to no screening (black circle). However, screening that did take place may not have been fully optimal, especially in terms of cost (other scenarios, black dots). On the other hand, vaccination as a stand-alone prevention measure is very effective in substantially reducing the loss of health from cervical cancer (coloured circles vs black circle). However, vaccination alone may not be sufficient to achieve the level of health loss achieved by pre-vaccination screening, especially if only a vaccination programme for girls is in place (reddish circles)

and/or the product used is not sufficiently effective against the different oncogenic HPV types.

Typically, even a small amount of screening combined with vaccination is enough to bring health loss to pre-vaccination levels, and much lower. On the other hand, after a certain level, it is difficult to achieve significant health benefits by increasing screening and it is not at all rational to allocate health resources to screening beyond the borderline. Such a threshold depends on the vaccination scenario.

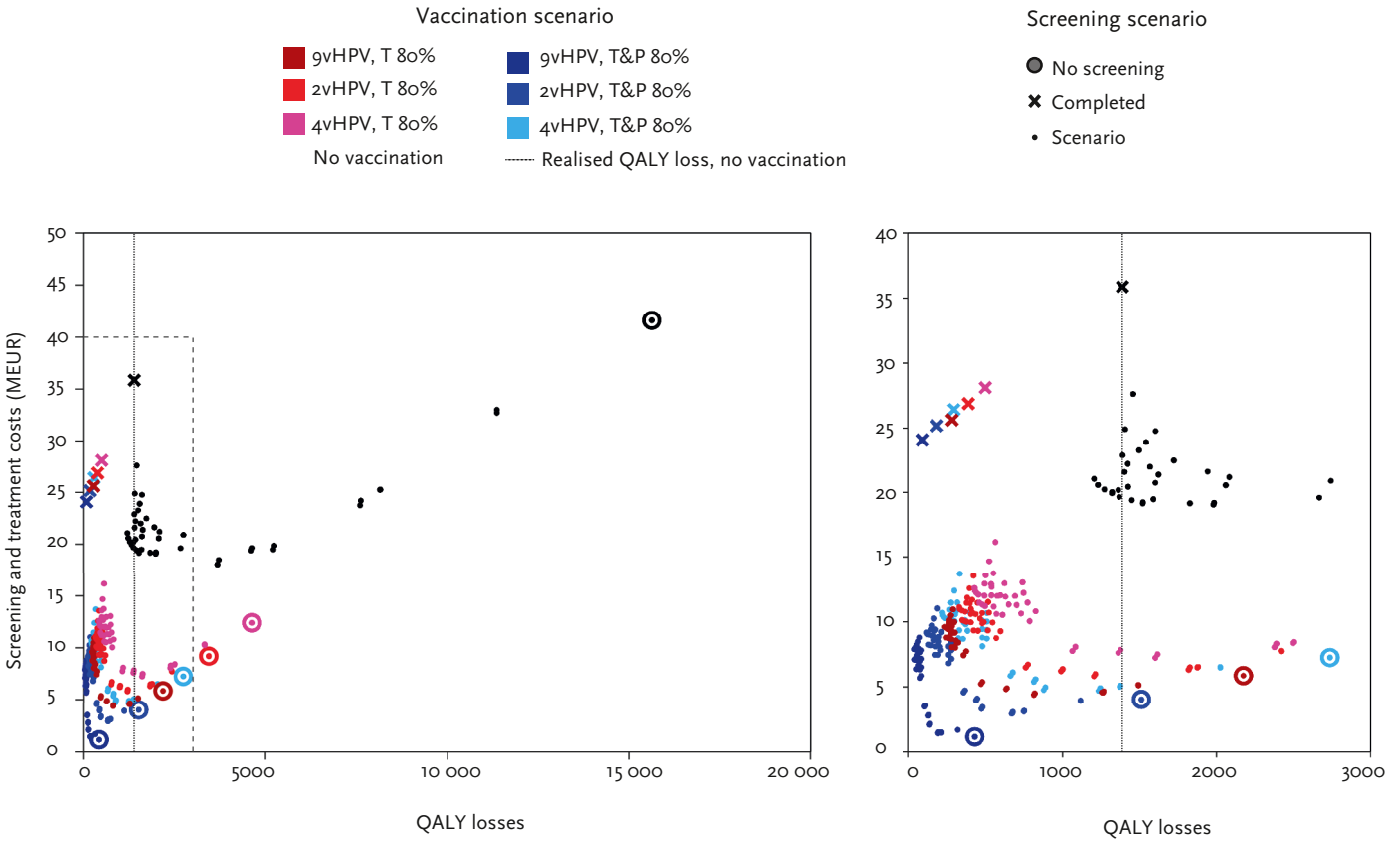

Figure 6 Annual burden of disease associated with cervical cancer and its screening (QALY loss, x-axis; screening and treatment costs, y-axis) for different screening and vaccination scenarios in a population of 30,000 + 30,000 birth cohorts. The dashed portion of A is shown enlarged in B. Each marker represents one scenario. Vaccination scenarios are 80% coverage programs using 9-valent, 2-valent or 4-valent vaccine (reddish: girls only; blueish: girls and boys; black: no vaccination). Screening scenarios are represented by labels: circle - no screening, cross - completed screening programme, dots – various unspecified scenarios. The vertical dotted line represents the actual level of QALY losses before the vaccination programme started. Calculation by Vänskä 2013[79]; Vänskä 2019[80]; THL working group[81]

19. REFERENCES

1. Working group set up by the Finnish Medical Society Duodecim and the Finnish Cardiac Society. Kohdunkaulan, emättimen ja ulkosynnytinten solumuutokset. Käypä hoito -suositus. Published online 2023. www.kaypahoito.fi

2. Suomen Gynekologisen Onkologian Erikois-lääkärit (FIN-GOG). Gynekologisten syöpien hoito-ohjeisto. Published online 2022. https://gynekologiyhdistys.fi/wp-content/uploads/2022/08/fingogkelpohoito2022.pdf

3. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA A Cancer J Clinicians.* 2021;71(3):209-249. doi:10.3322/caac.21660

4. Suomen Syöpärekisteri. Syöpätilastot. https://tilastot.syoparekisteri.fi/syovatilastot. syoparekisteri.fi/syovat

5.Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol.* 1999;189(1):12-19. doi:10.1002/(SICI)1096-9896(199909)189:1<12::AID-PATH431>3.0.CO;2-F

6. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Biological agents. *IARC Monogr Eval Carcinog Risks Hum.* 2012;100 (Pt B):1-441.

7. Vänskä S, Luostarinen T, Lagheden C, et al. Differing Age-Specific Cervical Cancer Incidence Between Different Types of Human Papillomavirus: Implications for Predicting the Impact of Elimination Programs. *American Journal of Epidemiology.* 2021;190(4):506-514. doi:10.1093/aje/kwaa121

8. Vink MA, Bogaards JA, van Kemenade FJ, de Melker HE, Meijer CJLM, Berkhof J. Clinical Progression of High-Grade Cervical Intraepithelial Neoplasia: Estimating the Time to Preclinical Cervical Cancer From Doubly Censored National Registry Data. *American Journal of Epidemiology.* 2013;178(7):1161-1169. doi:10.1093/aje/kwt077

9. Tainio K, Athanasiou A, Tikkinen KAO, et al. Clinical course of untreated cervical intraepithelial neoplasia grade 2 under active surveillance: systematic review and meta-analysis. *BMJ.* Published online February 27, 2018:k499. doi:10.1136/bmj.k499

10. Loopik DL, Bentley HA, Eijgenraam MN, IntHout J, Bekkers RLM, Bentley JR. The Natural History of Cervical Intraepithelial Neoplasia Grades 1, 2, and 3: A Systematic Review and Meta-analysis. *J Low Genit Tract Dis.* 2021;25(3):221-231. doi:10.1097/LGT.0000000000000604

11. Salo H, Nieminen P, Kilpi T, et al. Divergent coverage, frequency and costs of organised and opportunistic Pap testing in Finland. *International Journal of Cancer.* 2014;135(1):204-213. doi:10.1002/ijc.28646

12. Pankakoski M, Heinävaara S, Anttila A, Sarkeala T. Differences in cervical test coverage by age, socioeconomic status, ethnic origin and municipality type - A nationwide register-based study. *Prev Med.* 2020;139:106219. doi:10.1016/j.ypmed.2020.106219

13. Leinonen M, Nieminen P, Kotaniemi-Talonen L, et al. Age-Specific Evaluation of Primary Human Papillomavirus Screening vs Conventional Cytology in a Randomized Setting. *JNCI J Natl Cancer Inst.* 2009;101(23):1612-1623. doi:10.1093/jnci/djp367

14. Falcaro M, Castañon A, Ndlela B, et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. *The Lancet.*

2021;398(10316):2084-2092. doi:10.1016/S0140-6736(21)02178-4

15. Lei J, Ploner A, Elfström KM, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. *N Engl J Med*. 2020;383(14):1340-1348. doi:10.1056/NEJMoa1917338

16. Lehtinen M, Lagheden C, Luostarinen T, et al. Human papillomavirus vaccine efficacy against invasive, HPV-positive cancers: population-based follow-up of a cluster-randomised trial. *BMJ Open*. 2021;11(12):e050669. doi:10.1136/bmjopen-2021-050669

17. Vänskä S, Luostarinen T, Bausssano I, et al. Vaccination with moderate coverage eradicates oncogenic human papillomaviruses if a gender -neutral strategy is applied. *J Infect Dis*. Published online March 11, 2020. doi:10.1093/infdis/jiaa099

18. Salo, Heini, Nieminen, Pekka, Kilpi, Terhi, et al. Papa-koekäytäntö ei vastaa suosituksia. *Suom Lääk-L*. 2014;69(39).

19. Arbyn M, European Union, European Commission, Health and Consumer Protection Directorate-General. *European Guidelines for Quality Assurance in Cervical Cancer Screening*. Office for Official Publications of the European Communities; 2008.

20. Anttila A, von Karsa L, Arbyn M, et al. European guidelines for quality assurance in cervical cancer screening. Summary of the supplements on HPV screening and vaccination. *Papillomavirus research*. 2015;1:22-31.

21. Pankakoski M, Sarkeala T, Anttila A, Heinävaara S. Effectiveness of Cervical Testing in and outside a Screening Program-A Case-Control Study. *Cancers (Basel)*. 2022;14(21):5193. doi:10.3390/cancers14215193

22. Arbyn M, Raifu AO, Weiderpass E, Bray F, Anttila A. Trends of cervical cancer mortality in the member states of the European Union. *European Journal of Cancer*. 2009;45(15):2640-2648. doi:10.1016/j.ejca.2009.07.018

23. Nieminen P, Kallio M, Anttila A, Hakama M. Organised vs. spontaneous pap-smear screening for cervical cancer: A case-control study. *Int J Cancer*. 1999;83(1):55-58. doi:10.1002(SICI)1097-0215(19990924)83:1<55::AID-IJC11>3.0.CO;2-U

24. European Commission. Directorate General for Health and Food Safety. *European Guidelines for Quality Assurance in Cervical Cancer Screening : Second Edition : Supplements*. Publications Office; 2015. Accessed November 21, 2023. https://data.europa.eu/doi/10.2875/93363

25. Lönnberg S, Anttila A, Luostarinen T, Nieminen P. Age-Specific Effectiveness of the Finnish Cervical Cancer Screening Programme. *Cancer Epidemiology, Biomarkers & Prevention*. 2012;21(8):1354-1361. doi:10.1158/1055-9965.EPI-12-0162

26. Kamineni A, Weinmann S, Shy KK, Glass AG, Weiss NS. Efficacy of screening in preventing cervical cancer among older women. *Cancer Causes Control*. 2013;24(9):1653-1660. doi:10.1007/s10552-013-0239-4

27. Wang J, Andrae B, Sundström K, et al. Effectiveness of cervical screening after age 60 years according to screening history: Nationwide cohort study in Sweden. Zheng W, ed. *PLoS Med*. 2017;14(10):e1002414. doi:10.1371/journal.pmed.1002414

28. Castañón A, Landy R, Cuzick J, Sasieni P. Cervical Screening at Age 50–64 Years and the Risk of Cervical Cancer at Age 65 Years and Older: Population-Based Case Control Study. Franco EL, ed. *PLoS Med*. 2014;11(1):e1001585. doi:10.1371/journal.pmed.1001585

29. World Health Organization. *WHO Guideline for Screening and Treatment of Cervical Pre-Cancer Lesions for Cervical Cancer Prevention: Use of mRNA Tests for Human Papillomavirus (HPV)*. Second edition. World Health Organization; 2021.

30. IARC. *IARC Handbooks of Cancer Prevention. Cervix Cancer Screening*. Vol 10. IARC; 2005.

31. Costa S, Verberckmoes B, Castle PE, Arbyn M. Offering HPV self-sampling kits: an updated meta-analysis of the effectiveness of strategies to increase participation in cervical cancer screening. *Br J Cancer*. 2023;128(5):805-813. doi:10.1038/s41416-022-02094-w

32. Arbyn M, Smith SB, Temin S, Sultana F, Castle P. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. *BMJ*. Published online December 5, 2018:k4823. doi:10.1136/bmj.k4823

33. Virtanen A, Anttila A, Luostarinen T, Malila N, Nieminen P. Improving cervical cancer screening attendance in Finland. *Int J Cancer*. 2015;136(6):E677-684. doi:10.1002/ijc.29176

34. Auvinen E, Nieminen P, Pellinen J, Dillner J, Tarkkanen J, Virtanen A. Human papillomavirus self-sampling with mRN testing benefits routine screening. *Intl Journal of Cancer*. 2022;151(11):1989-1996. doi:10.1002/ijc.34170

35. Meijer CJLM, Berkhof J, Castle PE, et al. Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women 30 years and older. *Intl Journal of Cancer*. 2009;124(3):516-520. doi:10.1002/ijc.24010

36. Arbyn M, Depuydt C, Benoy I, et al. VALGENT: A protocol for clinical validation of human papillomavirus assays. *Journal of Clinical Virology*. 2016;76:S14-S21. doi:10.1016/j.jcv.2015.09.014

37. Ronco G, Dillner J, Elfström KM, et al. Efficacy of HPV-Based Screening for Prevention of Invasive Cervical Cancer: Follow-up of Four European Randomized Controlled Trials. *Obstetrical & Gynecological Survey*. 2014;69(8):472-473. doi:10.1097/01.ogx.0000453824.69728.co

38. Heideman DAM, Oštrbenk Valencak A, Doorn S, et al. Clinical Validation of the Fully Automated NeuMoDx HPV Assay for Cervical Cancer Screening. *Viruses*. 2022;14(5):893. doi:10.3390/v14050893

39. Carozzi FM, Burroni E, Bisanzi S, et al. Comparison of Clinical Performance of Abbott RealTime High Risk HPV Test with That of Hybrid Capture 2 Assay in a Screening Setting. *J Clin Microbiol*. 2011;49(4):1446-1451. doi:10.1128/JCM.02311-10

40. Poljak M, Oštrbenk A, Seme K, et al. Comparison of Clinical and Analytical Performance of the Abbott RealTime High Risk HPV Test to the Performance of Hybrid Capture 2 in Population-Based Cervical Cancer Screening. *J Clin Microbiol*. 2011;49(5):1721-1729. doi:10.1128/JCM.00012-11

41. Hesselink AT, Meijer CJLM, Poljak M, et al. Clinical Validation of the Abbott RealTime High Risk HPV Assay According to the Guidelines for Human Papillomavirus DNA Test Requirements for Cervical Screening. *J Clin Microbiol*. 2013;51(7):2409-2410. doi:10.1128/JCM.00633-13

42. Arbyn M, Simon M, Peeters E, et al. 2020 list of human papillomavirus assays suitable for primary cervical cancer screening. *Clinical Microbiology and Infection*. 2021;27(8):1083-1095. doi:10.1016/j.cmi.2021.04.031

43. Heideman DAM, Hesselink AT, Berkhof J, et al. Clinical Validation of the cobas 4800 HPV Test for Cervical Screening Purposes. *J Clin Microbiol*. 2011;49(11):3983-3985. doi:10.1128/JCM.05552-11

44. Lloveras B, Gomez S, Alameda F, et al. HPV Testing by cobas HPV Test in a Population from Catalonia. Scheurer M, ed. *PLoS ONE*. 2013;8(3):e58153. doi:10.1371/journal.pone.0058153

45. Hesselink AT, Heideman DAM, Berkhof J, et al. Comparison of the Clinical Performance of PapilloCheck Human Papillomavirus Detection with That of the GP5+/6+-PCR-Enzyme Immunoassay in Population-Based Cervical Screening. *J Clin Microbiol*. 2010;48(3):797-801. doi:10.1128/JCM.01743-09

46. Arbyn M, Snijders PJF, Meijer CJLM, et al. Which high-risk HPV assays fulfil criteria for use in primary cervical cancer screening? *Clinical Microbiology and Infection*. 2015;21(9):817-826. doi:10.1016/j.cmi.2015.04.015

47. Heard I, Cuschieri K, Geraets DT, Quint W, Arbyn M. Clinical and analytical performance of the PapilloCheck HPV-Screening assay using the VALGENT framework. *Journal of Clinical Virology*. 2016;81:6-11. doi:10.1016/j.jcv.2016.05.004

48. Ejegod DM. Clinical Validation of the BD Onclarity? HPV Assay Using a Non-Inferiority Test. *J Med Microb Diagn*. 2015;s3. doi:10.4172/2161-0703.S3-003

49. Cuschieri K, Geraets DT, Moore C, Quint W, Duvall E, Arbyn M. Clinical and Analytical Performance of the Onclarity HPV Assay Using the VALGENT Framework. Tang YW, ed. *J Clin Microbiol*. 2015;53(10):3272-3279. doi:10.1128/JCM.01366-15

50. Ejegod D, Bottari F, Pedersen H, Sandri MT, Bonde J. The BD Onclarity HPV Assay on Samples Collected in SurePath Medium Meets the International Guidelines for Human Papillomavirus Test Requirements for Cervical Screening. Tang YW, ed. *J Clin Microbiol*. 2016;54(9):2267-2272. doi:10.1128/JCM.00508-16

51. Hesselink AT, Berkhof J, Van Der Salm ML, et al. Clinical Validation of the HPV-Risk Assay, a Novel Real-Time PCR Assay for Detection of High-Risk Human Papillomavirus DNA by Targeting the E7 Region. Caliendo AM, ed. *J Clin Microbiol*. 2014;52(3):890-896. doi:10.1128/JCM.03195-13

52. Polman NJ, Oštrbenk A, Xu L, et al. Evaluation of the Clinical Performance of the HPV-Risk Assay Using the VALGENT-3 Panel. Tang YW, ed. *J Clin Microbiol*. 2017;55(12):3544-3551. doi:10.1128/JCM.01282-17

53. Hesselink AT, Sahli R, Berkhof J, et al. Clinical validation of Anyplex™ II HPV HR Detection according to the guidelines for HPV test requirements for cervical cancer screening. *Journal of Clinical Virology*. 2016;76:36-39. doi:10.1016/j.jcv.2016.01.009

54. Jung S, Lee B, Lee KN, Kim Y, Oh EJ. Clinical Validation of Anyplex II HPV HR Detection Test for Cervical Cancer Screening in Korea. *Archives of Pathology & Laboratory Medicine*. 2016;140(3):276-280. doi:10.5858/arpa.2015-0117-OA

55. Cuschieri K, Geraets D, Cuzick J, et al. Performance of a Cartridge-Based Assay for Detection of Clinically Significant Human Papillomavirus (HPV) Infection: Lessons from VALGENT (Validation of HPV Genotyping Tests). Loeffelholz MJ, ed. *J Clin Microbiol*. 2016;54(9):2337-2342. doi:10.1128/JCM.00897-16

56. Boers A, Wang R, Slagter-Menkema L, et al. Clinical Validation of the Cervista HPV HR Test According to the International Guidelines for Human Papillomavirus Test Requirements for Cervical Cancer Screening. Tang YW, ed. *J Clin Microbiol*. 2014;52(12):4391-4393. doi:10.1128/JCM.02716-14

57. Heideman DAM, Hesselink AT, Van Kemenade FJ, et al. The Aptima HPV Assay Fulfills the Cross-Sectional Clinical and Reproducibility Criteria of International Guidelines for Human Papillomavirus Test Requirements for Cervical Screening. *J Clin Microbiol.* 2013;51(11):3653-3657. doi:10.1128/JCM.01517-13

58. Martinelli M, Latsuzbaia A, Bonde J, et al. *Performance of BD Onclarity HPV Assay on FLOQSwabs Vaginal Self-Samples.* Public and Global Health; 2023. doi:10.1101/2023.07.08.23292408

59. Latsuzbaia A, Vanden Broeck D, Van Keer S, et al. Validation of BD Onclarity HPV Assay on Vaginal Self-Samples versus Cervical Samples Using the VALHUDES Protocol. *Cancer Epidemiology, Biomarkers & Prevention*. 2022;31(12):2177-2184. doi:10.1158/1055-9965.EPI-22-0757

60. Latsuzbaia A, Vanden Broeck D, Van Keer S, et al. Clinical Performance of the RealTim e High Risk HPV Assay on Self-Collected Vaginal Samples within the VALHUDES Framework. Lainhart W, ed. *Microbiol Spectr.* 2022;10(5):e01631-22. doi:10.1128/spectrum.01631-22

61. Latsuzbaia A, Vanden Broeck D, Van Keer S, et al. Comparison of the Clinical Accuracy of Xpert HPV Assay on Vaginal Self-Samples and Cervical Clinician-Taken Samples within the VALHUDES Framework. *The Journal of Molecular Diagnostics*. 2023;25(9):702-708. doi:10.1016/j.jmoldx.2023.06.004

62. Reid JL, Wright TC, Stoler MH, et al. Human Papillomavirus Oncogenic mRNA Testing for Cervical Cancer Screening. *American Journal of Clinical Pathology*. 2015;144(3):473-483. doi:10.1309/AJCPHVD7MIP3FYVV

63. Forslund O, Miriam Elfström K, Lamin H, Dillner J. HPV-mRNA and HPV-DNA detection in samples taken up to seven years before severe dysplasia of cervix uteri. *Intl Journal of Cancer.* 2019;144(5):1073-1081. doi:10.1002/ijc.31819

64. Iftner T, Neis KJ, Castanon A, et al. Longitudinal Clinical Performance of the RNA-Based Aptima Human Papillomavirus (AHPV) Assay in Comparison to the DNA-Based Hybrid Capture 2 HPV Test in Two Consecutive Screening Rounds with a 6-Year Interval in Germany. Tang YW, ed. *J Clin Microbiol*. 2019;57(1):e01177-18. doi:10.1128/JCM.01177-18

65. Kares S, Veijalainen O, Kholová I, et al. HIGH-RISK HPV testing as the primary screening method in an organized regional screening program for cervical cancer: the value of HPV16 and HPV18 genotyping? *APMIS.* 2019;127(11):710-716. doi:10.1111/apm.12990

66. Benevolo M, Allia E, Gustinucci D, et al. Interobserver reproducibility of cytologic p16 ^{INK4a}/Ki-67 dual immunostaining in human papillomavirus-positive women. *Cancer Cytopathology.* 2017;125(3):212-220. doi:10.1002/cncy.21800

67. WHO. WHO Classification of Tumours Online. Published online 2023. https://tumourclassification.iarc.who.int/welcome/

68. Bloomfield HE, Olson A, Greer N, et al. Screening Pelvic Examinations in Asymptomatic, Average-Risk Adult Women: An Evidence Report for a Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med*. 2014;161(1):46. doi:10.7326/M13-2881

69. Korfage IJ, van Ballegooijen M, Huveneers H, Essink-Bot ML. Anxiety and borderline PAP smear results. *European Journal of Cancer.* 2010;46(1):134-141. doi:10.1016/j.ejca.2009.07.003

70. Ideström M, Milsom I, Andersson-Ellström A. Women's experience of coping with a positive Pap smear: a register-based study of women with two

consecutive Pap smears reported as CIN 1. *Acta Obstet Gynecol Scand.* 2003;82(8):756-761. doi:10.1080/j.1600-0412.2003.00165.x

71. Athanasiou A, Veroniki AA, Efthimiou O, et al. Comparative effectiveness and risk of preterm birth of local treatments for cervical intraepithelial neoplasia and stage IA1 cervical cancer: a systematic review and network meta-analysis. *The Lancet Oncology*. 2022;23(8):1097-1108. doi:10.1016/S1470-2045(22)00334-5

72. Kyrgiou M, Athanasiou A, Paraskevaidi M, et al. Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis. *BMJ.* Published online July 28, 2016:i3633. doi:10.1136/bmj.i3633

73. Ronco G, Giorgi-Rossi P, Carozzi F, et al. Results at Recruitment From a Randomized Controlled Trial Comparing Human Papillomavirus Testing Alone With Conventional Cytology as the Primary Cervical Cancer Screening Test. *JNCI Journal of the National Cancer Institute.* 2008;100(7):492-501. doi:10.1093/jnci/djn065

74. Leinonen MK, Nieminen P, Lönnberg S, et al. Detection rates of precancerous and cancerous cervical lesions within one screening round of primary human papillomavirus DNA testing: prospective randomised trial in Finland. *The BMJ.* 2012;345. doi:10.1136/bmj.e7789

75. Veijalainen O, Kares S, Kotaniemi-Talonen L, et al. Primary HPV screening for cervical cancer: Results after two screening rounds in a regional screening program in Finland. *Acta Obstet Gynecol Scand.* 2021;100(3):403-409. doi:10.1111/aogs.14021

76. Sarkeala, Tytti, Lamminmäki, Maarit. Miten houkuttelen syöpäseulontoihin? *Duodecim.* 2022;138(16). Accessed November 21, 2023. https://www.duodecimlehti.fi/duo16976

77. Rokotuskattavuus. https://www.thl.fi/roko/vaccreg/atlas/public/atlas.html?show=hpv

78. Lehtinen M, Baussano I, Paavonen J, Vänskä S, Dillner J. Eradication of human papillomavirus and elimination of HPV-related diseases – scientific basis for global public health policies. *Expert Review of Vaccines*. 2019;18(2):153-160. doi:10.1080/14760584.2019.1568876

79. Vänskä S, Auranen K, Leino T, et al. Impact of Vaccination on 14 High-Risk HPV Type Infections: A Mathematical Modelling Approach. Wu JT, ed. *PLoS ONE*. 2013;8(8):e72088. doi:10.1371/journal.pone.0072088

80. Vänskä S, Bogaards JA, Auranen K, Lehtinen M, Berkhof J. Fast approximate computation of cervical cancer screening outcomes by a deterministic multiple-type HPV progression model. *Mathematical Biosciences*. 2019;309:92-106. doi:10.1016/j.mbs.2019.01.006

81. Terveyden ja hyvinvoinnin laitoksen asettaman papilloomavirustautien torjuntatyöryhmän selvitys 30.4.2011. Published online 2011. https://www.julkari.fi/bitstream/handle/10024/80336/94d6f45d-22e1-4b53-b615-2eea48d90e1c.pdf?sequence=1&isAllowed=y

20. ANNEXES

APPENDIX 1. THE CONTENT OF THE TRAINING PROGRAMME OF THE FINNISH COLPOSCOPY ASSOCIATION

Link to SKY's website: https://www.kolposkopiayhdistys.fi/)

The training includes the following topics:

- Clinical competence, general competence, commitment to continuous updating of medical knowledge and skills, core professional values.
- The trainee must be a specialist in gynaecology and obstetrics or a specialist in the field. All trainees must be familiar with the latest Current Care Guidelines and complete the associated online exam and course, before starting the clinical part of the course. The Basic Colposcopy Course organised by the European Federation for Colposcopy (EFC) complements this and is also recommended.
- It is recommended that clinical training is carried out over a 12-month period. The trainee must see/manage 50 patients (of which 20 must be first visits) in supervised practice and 50 patients (of which 30 first visits) in indirect practice. Treatment interventions may be included in these figures. Good communication skills and mastery of the patient encounter are key skills for a colposcopist. The trainee must attend at least six meetings with pathologists (Multidisciplinary Team Meeting).
- The logbook documents the trainee's progress on the theoretical and clinical side. The trainer should regularly review the logbook and identify any problems with the trainee. The logbook also reflects the accumulation of clinical experience.

ANNEX 2. TAKING A TRADITIONAL CYTOLOGICAL SAMPLE

The traditional cytological sample is taken in three stages:

1. The vaginal sample is scraped with the round/ flatter end of the spatula around the base of the cervix and smeared on the glass slide as a thin film on the furthest edge of the glass slide as viewed from the frosted end.

2. The sample from the entrance to the uterus is taken by placing the longer tip of the notched end of the spatula into the cervical canal with the notched edge resting on the uterine lining and, to collect the cell sample, rotating the spatula in this position around the outside of the cervical canal for 1–2 turns to collect cells from the so-called transformation zone of the cervix. The portion of the sample is smeared onto the central part of the glass slide as a thin film.

3. An endocervical sample is collected with a cervical brush, which is inserted into the cervical canal with the bristles hidden and rotated 360 degrees (1 turn) along the mucosal surface of the cervical canal. If the first sample is very slimy, the actual sample should be taken using a new cell brush. The endocervical sample is transferred from the cervical brush to the glass slide by rotating the brush on the slide. The endocervical sample is placed on the slide nearest to the frosted end adjacent to the sample portion.

The specimen is fixed with fixative spray immediately after the endocervical specimen is loaded onto the slide. If a fixative spray is used, 3–4 sprays are applied to the slide from a distance of 20–30 cm so that the entire glass is covered. The specimen slide is then allowed to dry before packing in the transport container. The sample can also be fixed by immersion of the sample glass slide immediately after sampling, preferably in 90 % ethanol for 10–15 minutes. It is then air-dried before being transported. An unfixed sample is of no use at all.

The liquid-based cytology sample is taken with a sampling device according to the manufacturer's instructions from the cervical canal transformation zone (cf. sample from the entrance to the uterus). The collected cell material is then transferred to the transport fluid according to the instructions.