CERVICAL CANCER SCREENING

UPDATED INSTRUCTIONS FOR BEST PRACTICES IN SCREENING FOR CERVICAL CANCER

Recommendations from an Expert Group set up by the National Steering Group for Cancer Screening (updated 14.12.2022)

These instructions include recommendations for the organisation of screening, the screening algorithms and HPV tests used in screening. The recommendations are based on the results from both randomised screening trials and retrospective screening studies, conducted in Finland and elsewhere in Europe[1-6].

HrHPV testing, able to detect human papillomavirus with high cancer risk, is recommended as the primary screening method for persons 30 years of age and older. Pap testing serves as the first follow-up test (i.e., as triage testing) after a positive hrHPV test. For ages 25–29, Pap testing is the sole primary screening method. Co-testing with Pap and hrHPV tests is not recommended[5-6].

Women testing positive for hrHPV in screening, for whom atypical squamous cells of LSIL degree or higher is confirmed through triage Pap testing, are sent to colposcopy for further examination by an urgency determined by the Pap test findings (see Current care guidelines -recommendation[7]).

Slightly abnormal findings (positive hrHPV and normal or ASC-US triage Pap test results) should be followed up for spontaneous remission after 18–24 months with control tests (i.e., screening of risk groups). If the risk group screening hrHPV test is recurringly positive, the screened woman is sent to colposcopy by an urgency determined by the triage Pap test findings (see Current care guidelines -recommendation[7]).

In screening of ages 25–29 through Pap testing, colposcopy is used for further examinations if the Pap test shows a degree of atypical squamous cells of at least ASC-H or any type of atypical glandular cells, or if LSIL- or ASC-US findings recur in the screening of risk groups (see Current care guidelines -recommendation[7]).

Because invitation to screening is central to the screening program coverage, best practices for invitation should be given special attention. Every invitation should state the time and place for the screening test, and the appointment should be easy to reschedule online or by phone.

A reminder letter should be sent to all women who did not participate in the first round, including women in risk group screening.

Further information

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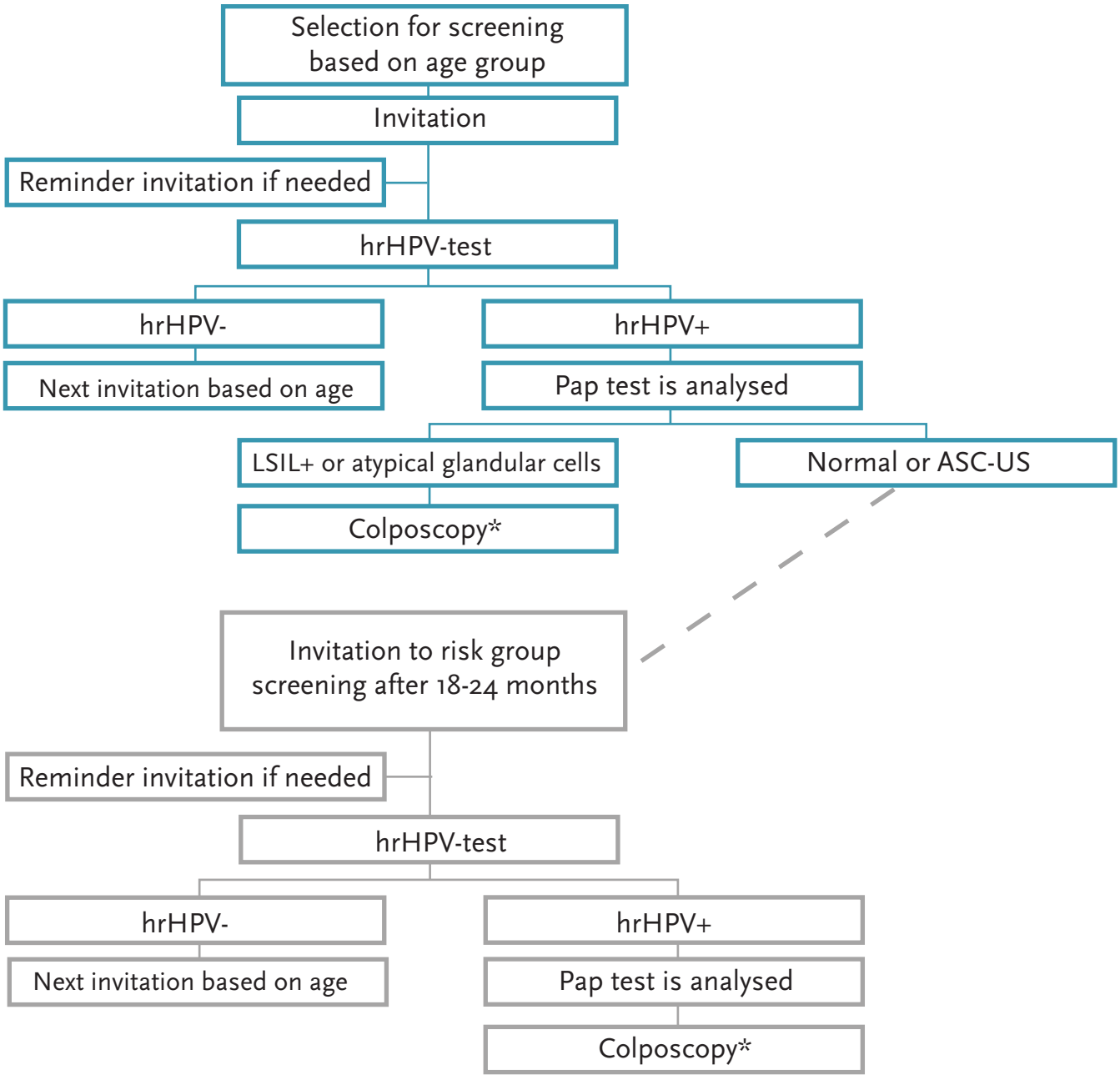
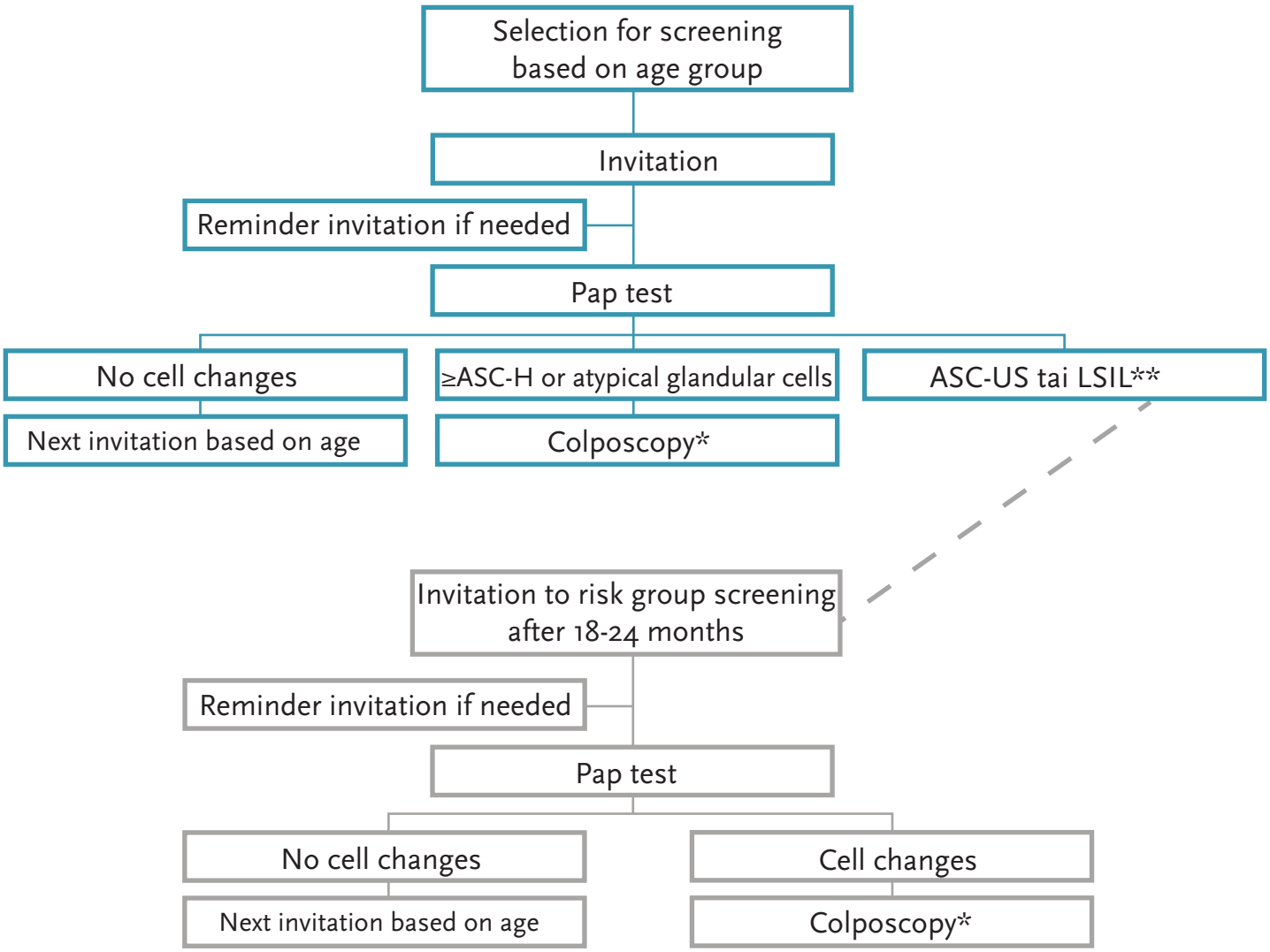
Screening algorithm, hrHPV test (women 30 years of age)



*Urgency defined by the Current Care Guidelines[7]

Screening algorithm, Pap test (women under 30 years of age*)



*Urgency defined by the Current Care Guidelines[7]
**In case Pap testing is used as the primary screening test for persons 30 years of age or older, colposcopy is done also on the basis of squamous cells of LSIL degree

HPV TESTS USED IN SCREENING FOR CERVICAL CANCER

The Expert Group recommends that only such tests that comply with internationally accepted criteria for a validated screening test and the validation research results of which have been published in a peer-reviewed publication, should be used in the screening program.

The criteria for screening validated HPV tests was drafted in 2009 by an international group of experts (Meijer 2009.)

- The comparison tests for the test under evaluation are Hybrid Capture-2 and GP5+/6+ PCR-EIA tests whose efficacy, in comparison to the cytological Pap test-based screening, has been proven in randomised trials.
    - These tests target the HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68 and GP5+/6+ PCR testing also 66.
- The sensitivity and specificity of the compared test to detect histological HSIL lesions (formerly CIN2/3) or cancer, must be non-inferior to the comparison tests.
    - In addition, it is recommended that the samples used for validation are taken from a population-based screening cohort of women aged 30-60 years or comparable data (Arbyn 2016), taking guidelines for required sample amounts into account.
- Sufficient intra- and interlaboratory reproducibility of the test results must also be proven.

With these criteria, the hrHPV tests listed in the table have been validated for cancer screening of women 30 years of age and older.

Test type	Screening test	Validation studies
hrHPV-DNA-test	Hybrid Capture-2 (Qiagen)	Ronco, 2014 Ronco, 2015
	PCR GP5+/6+ EIA	Ronco, 2014 Ronco, 2015
	RealTime High Risk HPV assay (Abbot)	Carozzi, 2011 Poljak, 2011 Hesselink, 2013
	Alinity (Abbott)	Arbyn, 2021 review
	Cobas 4800 (Roche)	Heideman, 2011 Llovveras, 2013
	Cobas 6800 (Roche)	Arbyn, 2021 review
	PapilloCheck (Greiner Bio-one)	Hesselink, 2010 Arbyn, 2015 review Heard, 2016
	Onclarity HPV assay (BD)	Ejegod, 2014 Cuchieri, 2015 Ejegod, 2016
	HPV-Risk assay (Self-Screen BV)	Hesselink, 2014 Polman, 2017
	Anyplex II HPV HR (Seegene Inc)	Hesselink, 2016 Jung, 2016
	Xpert HPV (Cepheid AB)	Cuchieri, 2016
hrHPV-RNA-test*	Cervista (Hologic) APTIMA assay* (Hologic)	Boers, 2014 Heideman, 2013

* The criteria for the screening validated HPV tests have been drafted for hrHPV-DNA tests because the comparison tests for which, through long-term follow-up after a negative test result, a very low risk of severe precursors or cancer has been proven, are DNA tests. APTIMA assay (Hololgic) is an RNA test but, in the light of cross-sectional studies, complies with the criteria for screening validated tests. Furthermore, indirect validation results of a 3-year longitudinal study (Reid 2015) and studies with longer follow-up have been published, (Forslund 2019, Iftner 2019). Thus, a majority of the Expert Group considers the validity of Aptima for screening to have been sufficiently proven, even though the molecule to be tested is different than in the reference tests (HC2 ja G5/6).

The table was updated 14.12.2022. If needed, the Expert Group updates the table with available information.

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