World Health Organization

WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention

Use of human papillomavirus (HPV) DNA genotyping

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Abbreviations

cHPV	carcinogenic HPV
CIN	cervical intraepithelial neoplasia
DOI	declaration of interest
ERG	External Review Group
EtD	evidence-to-decision
GDG	Guideline Development Group
GRC	Guidelines Review Committee
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HPV	human papillomavirus
IARC	International Agency for Research on Cancer
LLETZ	large-loop excision of the transformation zone (also known as LEEP)
mRNA	messenger ribonucleic acid (referring to HPV E6/E7 messenger RNA)
NAT	nucleic acid test
PEPFAR	The United States President's Emergency Plan for AIDS Relief
UNFPA	United Nations Population Fund
USA	United States of America
USAID	United States Agency for International Development
VIA	visual inspection with acetic acid
WHO	World Health Organization

Executive summary

Background

In 2022, cervical cancer was the fourth most common cancer among women globally and the fourth leading cause of cancer death among women globally, accounting for around 662 000 new cases and around 349 000 deaths. It is the most common cancer in women in 25 countries, many of which are in sub-Saharan Africa *(1)*. Even while recognizing large differences in incidence rates, cervical cancer can be eliminated as a public health problem through the strengthening of the health systems and the implementation and scaling-up of evidence-based interventions included in the global cervical cancer elimination strategy, launched in 2020.

To support countries achieving the cervical cancer elimination target of screening 70% of women by the age of 35 and again by 45 years of age with high-performance tests, in 2021, the *WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition (2)* was released, recommending the use of human papillomavirus (HPV) DNA tests under screen-and-treat or screen, triage and treat simplified clinical algorithms. When using triage, a second test to identify HPV-positive women with high risk of having cervical pre-cancer or cancer, WHO suggested to use visual inspection with acetic acid (VIA), colposcopy or cytology. Two additional guidelines were published later in 2021 and in 2024, the first for the use of HPV mRNA tests also in primary screening *(3)* and the second for the use of dual-stain cytology to triage women after a positive HPV test *(4)*. The recommendations included in both guidelines are only applicable to the general population of women.

In the WHO target product profiles (TPPs) for HPV screening tests to detect cervical pre-cancer and cancer *(5)*, the 12 HPV types classified as “Group 1: carcinogenic to humans” in the 2007 IARC Monograph No. 90 *(6)*, were further stratified into four groups (1a, 1b, 1c and 1d) based on each HPV type cervical cancer attributable fraction. These 12 carcinogenic HPV (cHPV) types and four groups serve as the basis for recommendations presented in this document.

Over the last two decades, the number of HPV tests hitting the market has expanded rapidly. However, only around 20 HPV tests are recognized as clinically validated, either through international standard validation protocols or regulatory agencies.

Current HPV tests offer the possibility of identifying individually or grouped cHPV types. Depending on ability, tests may provide “no genotyping” (positive/negative result), limited genotyping (identifying groups 1a and 1b, and pooling other cHPV types), extended genotyping (identifying four groups 1a, 1b, 1c and 1d) or full genotyping (identifying individually all HPV types targeted).

HPV limited or extended genotyping offers a built-in molecular triage that allows for the simple stratification and prioritized management of HPV-positive women according to the risk of cervical pre-cancer and cancer granted by specific HPV types groups. However, the use of HPV DNA genotyping should be aligned with the country capacity to ensure retention of screened positives across the screening continuum including triage, treatment and follow-up.

In 2024–2025, WHO, in collaboration with a group of experts, compiled, analysed and modelled the available data on HPV genotyping that identify the 12 cHPV types. The results of this exercise have been used to produce the current guideline.

Objectives of this guideline

This guideline has two objectives:

- to provide evidence-based recommendations for the use of HPV DNA tests according to level of genotyping in a screening strategy;
- to support countries and national screening programmes in selecting screening and treatment strategies suitable to their context to prevent cervical cancer in the general population of women.

The term “women” is used to refer to all gender diverse people at risk for cervical cancer, recognizing that all individuals born with a female reproductive system require cervical cancer prevention services.

Target audience

This document is intended primarily for policy-makers, programme managers, programme officers and other professionals in the health sector who have responsibility for choosing evidence-based strategies for cervical cancer prevention.

Methods

This guideline has been developed according to the *WHO handbook for guideline development, second edition (7)*. A guideline development group (GDG) of programme managers, researchers, clinical experts and representatives from cervical cancer organizations including people living with cervical cancer was formed in 2022. A subgroup of this GDG, along with the systematic review teams, a modelling team and guideline methodologist, compiled and prepared the evidence and evidence-to-decision tables for review by the GDG. Evidence from a systematic review that pooled the cumulative risks of cervical intraepithelial neoplasia (CIN)2+, CIN3+ and cervical cancer associated with ranked series of HPV types and groups of types, and evidence from a mathematical disease model estimating critical outcomes of screening strategies by different genotyping informed the recommendations. The GDG met several times to review this evidence and make recommendations. The recommendations were reviewed by an external review group and approved by the WHO Guidelines Review Committee.

Considerations and summary of recommendations for the use of HPV DNA tests in the general population

This publication presents recommendations for the use of HPV DNA tests with no genotyping, limited genotyping or extended genotyping for cervical cancer screening.

These recommendations apply under the following considerations:

HPV testing in primary screening: For the general population of women, HPV DNA is the recommended primary screening test, but HPV mRNA detection may also be used rather than VIA or cytology *(2, 3)*. This recommendation has not changed.

HPV DNA genotyping output: Different levels of genotyping – including no genotyping, limited genotyping and extended genotyping – may be available in countries. This guideline provides recommendations on the preferred genotyping strategies based on country or programme follow-up capacity.

HPV DNA genotyping output:

i. No genotyping provides a positive/negative result with no individual identification of cHPV types.

ii. Limited genotyping separately identifies cHPV types HPV16/18±45 (groups 1a and 1b), and pools the non HPV16/18 cHPV types.

iii. Extended genotyping separately identifies cHPV types in groups 1a and 1b and identifies different combinations of cHPV types in groups 1c and 1d. Programmes using extended genotyping results should first assign the HPV result outputs to the cHPV groups (1a, 1b, 1c and 1d). If an output matches multiple groups, the output should be assigned to the highest relevant cHPV risk group. Matching outputs will help in selecting appropriate management. See section 1.4 for more details.

iv. While limited and extended genotyping tests provide results to differentiate cHPV types, the result can also be considered as a pooled positive/negative result, as in no genotyping.

Treatment type: Each suggested screening strategy includes ablative treatment for HPV-positive women or triaged positive women. Before treatment, each woman should be visually assessed to determine eligibility for ablative treatment. This can be performed with or without a colposcope after applying acetic acid to assess the size of the area of treatment and the type of transformation zone. Visually assessing eligibility for ablative treatment differs from using VIA to triage women who are HPV positive. HPV-positive women or triaged women who are not eligible for ablative treatment should receive excisional treatment.

Treatment capacity: Programmes should establish adequate treatment capacity before initiating a screening programme and/or implementing these recommendations on the use of HPV DNA tests in the general population.

Follow-up capacity: Decision-makers should assess whether a screening programme's readiness to complete subsequent steps in the care continuum (treatment, triage and follow-up) is high or low. High follow-up capacity is defined as more than 60% completion at ALL steps in the continuum (i.e. less than 40% of women lost to follow-up at ALL steps), while low follow-up capacity is defined as less than 60% completion (i.e. 40% or more lost to follow-up at any step). Failure to reach 60% at a single step is sufficient to consider it as low. This 60% threshold is not exact. Determining follow-up capacity is critical, as loss to follow-up among women with pre-cancerous lesions increases the risk of progression to cervical cancer if left untreated and reduces programme efficiency and cost-effectiveness. Further guidance for countries on assessing follow-up capacity is provided in Section 4.

Recommendations for the general population of women

Recommendations for settings with high follow-up capacity (60% or greater)

In settings with high follow-up capacity (60% or greater) and sufficient ablative treatment capacity, WHO suggests using HPV DNA testing with extended or limited genotyping OVER treating all HPV-positive women or triaging all HPV-positive women with additional tests.

In settings with high follow-up capacity (60% or greater) and sufficient ablative treatment capacity where HPV DNA extended genotyping is used, WHO suggests:

- treating all eligible women with ablative treatment who test positive for carcinogenic HPV (cHPV) types 16 (group 1a), 18 and 45 (group 1b) and 31, 33, 35, 52 and 58 (group 1c); AND triaging women who test positive for cHPV types 39, 51, 56 and 59 (group 1d);

  OVER

- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52, 58, 39, 51, 56 and 59 (groups 1c and 1d);

  OVER

- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52 and 58 (group 1c) AND returning women who test positive for cHPV types 39, 51, 56 and 59 (group 1d) to routine screening.

Remark: To determine the type of treatment, women should be visually evaluated for eligibility for ablative treatment. Women not eligible for ablative treatment should be treated using large-loop excision of the transformation zone (LLETZ) or referred for further management if cancer is suspected.

Conditional recommendation, low certainty in evidence of effects

Recommendations for settings with low follow-up capacity (less than 60%)

In settings with low follow-up capacity (less than 60%) and sufficient ablative treatment capacity, WHO suggests:

- treating all eligible women with ablative treatment who test positive for any carcinogenic HPV (cHPV) types 16 (group 1a), 18 and 45 (group 1b), 31, 33, 35, 52 and 58 (group 1c), 39, 51, 56 and 59 (group 1d), consistent with a no-genotyping approach;
- OR treating eligible women with ablative treatment who test positive for any cHPV types 16 (group 1a), 18 and 45 (group 1b) and 31, 33, 35, 52 and 58 (group 1c)[a]

  OVER
- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52, 58, 39, 51, 56 and 59 (groups 1c and 1d); or

  OVER
- triaging with additional tests all women who test positive for any cHPV types (1a, 1b, 1c and 1d).

Remark: As the number of visits increases, the risk of loss to follow-up also rises. Although the preferred strategies may result in some overtreatment, they reduce losses to follow-up among women with pre-cancerous lesions who are at high risk of progression to cervical cancer if left untreated.

Conditional recommendation, low certainty in evidence of effects

Regardless of follow-up capacity

If a programme provides triage with additional tests, WHO suggests using VIA or colposcopic impression (without histological confirmation) as the triage test rather than cytology or dual-stain cytology.

Remark: The choice of triage test will depend on availability, installed capacity, feasibility, training and programme quality assurance in countries. To determine treatment type, women should first undergo visual evaluation for eligibility for ablative treatment. Women who are not eligible for ablative treatment should be treated using large-loop excision of the transformation zone (LLETZ) or referred for further management if cancer is suspected.

Conditional recommendation, low certainty in evidence of effects

a This can be done when using an 8-cHPV type test (tests designed to detect the eight most cHPV types) as per WHO target product profiles for HPV screening tests, or when using extended genotyping HPV tests.

References

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L et al. Global Cancer Observatory: Cancer Today [website]. Lyon: International Agency for Research on Cancer; 2024 (https://gco.iarc.fr/today, accessed 8 March 2024).
2. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/342365).
3. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition: use of mRNA tests for human papillomavirus (HPV). Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/350652).
4. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention: use of dual-stain cytology to triage women after a positive test for human papillomavirus (HPV). Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/376492). Licence: CC BY-NC-SA 3.0 IGO.
5. Target product profiles for human papillomavirus screening tests to detect cervical pre-cancer and cancer. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/379099).
6. Human papillomaviruses. IARC monographs on the evaluation of carcinogenic risks to humans, Vol. 90. Lyon: International Agency for Research on Cancer; 2007 (https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Human-Papillomaviruses-2007).
7. WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/handle/10665/145714).

1. Introduction

1.1 Background

In 2022, cervical cancer was the fourth most common cancer among women globally and the fourth leading cause of cancer death among women, accounting for around 662 000 new cases and around 349 000 deaths. It is the most common cancer in women in 25 countries, many of which are in sub-Saharan Africa *(1)*. Even while recognizing varying incidence levels, cervical cancer can be eliminated as a public health problem, through the scale-up of the WHO Cervical Cancer Elimination Initiative.

In May 2018, Dr Tedros Adhanom Ghebreyesus, Director-General of the WHO, issued a call to action for the elimination of cervical cancer. The WHO *Global strategy to accelerate the elimination of cervical cancer as a public health problem* was presented and unanimously endorsed by the Seventy-third World Health Assembly in August 2020. Subsequently, WHO officially launched the Global Strategy to accelerate the elimination of cervical cancer on 17 November 2020 *(2)*.

By 2030, the Global Strategy aims to ensure that:

- **90% of girls are fully vaccinated with a human papillomavirus (HPV) vaccine by the age of 15;**
- **70% of women are screened with a high-performance test by the age of 35, and again by the age of 45;**
- **90% of women with cervical disease are treated (90% of women with pre-cancer are treated, and 90% of women with invasive cancer are managed)** *(2)*.

Following the Global Strategy, countries have updated their cervical cancer prevention and control plans, and are already implementing or scaling-up the target interventions.

Cervical disease (pre-cancer and invasive cancer) is typically caused by persistent infections with HPV, especially the high-risk HPV types such as types 16 and 18 (these two types cause more than 70% of cervical cancers) *(3, 4)*. Pre-cancer lesions or cervical intraepithelial neoplasia (CIN) lesions are categorized as CIN1 or CIN2/3 lesions. CIN1 lesions – also referred to as low-grade squamous intraepithelial lesions – are morphological correlates of HPV infections. CIN2/3 lesions – also referred to as high-grade squamous intraepithelial lesions – are correlates of cervical pre-cancers that, if left untreated, may progress to cervical cancer (for further details, refer to Chapter 1 of WHO's *Comprehensive cervical cancer control guidance [5]*). Women can be screened using various tests to identify those who have or are at risk of cervical pre-cancer including visual inspection with acetic acid (VIA), cytology and HPV nucleic acid tests (HPV NATs). HPV DNA is the recommended primary screening test for the general population of women, but HPV mRNA detection may also be used.

The landscape of commercially available HPV tests, as per a 2023 inventory, reported 264 HPV tests (and 511 tests variants), most of them (79%) lacking published evidence on analytical or clinical data that could provide insights on their performance and alignment with the internationally agreed validation criteria *(6)*. Despite the lack of evidence in their performance, several of these tests are being used by countries in their efforts to achieve the 70% screening elimination target, without clear understanding on the potential harmful consequences. In 2024, WHO published the target product profiles (TPPs) for HPV screening tests to detect cervical pre-cancer and cancer. The TPPs aim to guide manufacturers to develop tests with specific characteristics including performance, so as to release to the market HPV tests that are fit for purpose and are aligned with criteria useful for later validation.

To date, around 20 HPV tests *(7)* are recognized as clinically validated, either through international standard validation protocols or regulatory agencies *(8)*.

1.2 Previous and current WHO recommendations for cervical cancer screening and treatment and key definitions

In 2006, WHO published the *Comprehensive cervical cancer control: a guide to essential practice, second edition (C4GEP)*, which was updated in 2014 *(5)*, consolidating all the recommendations for screening and treatment to prevent and treat cervical cancer already released. The consolidated C4GEP included the WHO recommendations for HPV vaccination, treatment of cervical cancer and pre-cancer lesions, and palliative care, as well as the recommendations from the *WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention (9)* released in 2013. In 2019, WHO published guidance on the use of thermal ablation for treatment of cervical pre-cancer lesions *(10)* and in 2020, WHO published guidance to support the introduction and scale-up of screening and treatment interventions, specifically relating to HPV testing and relevant medical devices *(11)*.

In 2021 the second edition of the WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention was published. This guideline included 23 recommendations and seven good practice statements for the general population of women and for women living with HIV *(12)*. The main recommendations focused on the use of HPV DNA testing as the primary screening test. In addition, one recommendation addressed the types of triage tests that could be used after a positive primary screening test. In December 2021, WHO released the recommendation on the use of HPV mRNA testing as the primary screening test *(13)*. In June 2024, a new recommendation on the use of dual-stain cytology to triage women after a positive HPV test was released *(14)*. Table 1.1 provides a summary of current recommendations for the use of HPV DNA and mRNA detection for the general population of women.

Table 1.1 Summary recommendations

General population of women
» WHO recommends HPV NATs as the primary screening test.
» WHO suggests using HPV NATs either with triage or without triage in screening.
» In a screen-and-treat approach and using HPV NATs as the primary screening test, WHO suggests treating women positive for HPV. » In a screen, triage and treat approach using HPV NATs as the primary screening test, WHO suggests using limited genotyping (only when HPV DNA tests are used), colposcopy, VIA, cytology or dual-stain cytology to triage women after a positive HPV test.
» WHO suggests women who have screened HPV positive and then negative on triage test are retested with HPV NATs at 24 months and, if negative, move to the recommended regular screening interval.
» HPV DNA testing can be done on health-care provider or self-collected samples.
» Regular cervical cancer screening should start at age 30. Priority should be given to screen women aged 30–49 years. When tools are available to manage women aged 50–65 years, those in that age group who have never been screened should also be prioritized.
» Screening should be done every 5–10 years when using HPV DNA detection and every 5 years when using HPV mRNA detection.

The full set of recommendations, along with relevant remarks, is provided in the guidelines published in 2021 and 2024, which focused on the use of HPV NATs *(12, 13, 14)*.

1.3 Objectives of this guideline

This guideline has two objectives:

- to provide evidence-based recommendations for the use of HPV DNA tests according to level of genotyping in a screening strategy;
- to support countries and national screening programmes in selecting screening and treatment strategies suitable to their context to prevent cervical cancer in the general population of women.

The term “women” is used to refer to “women and individuals with a cervix” as a population to whom cervical screening and treatment should be provided, including cisgender women and transgender men, non-binary and intersex individuals who have a cervix.

1.4 HPV tests, genotyping and result interpretation

Since the original HPV tests, the number of commercially available HPV tests has expanded rapidly, and current tests can identify individual HPV types or grouped sets of HPV types. In this guideline, limited genotyping or extended genotyping is used to refer to those tests that identify HPV16 or HPV18 genotypes and other HPV types as follows (see also Table 1.2):

- Limited genotyping: An HPV assay that separately identifies the most carcinogenic HPV (cHPV) types (HPV16, HPV18 and may include HPV45), and reports the remaining cHPV types as a combined group (typically the other 10 cHPV types and often one or two additional HPV types).
- Extended genotyping: An HPV assay that provides more detailed results than limited genotyping by separately identifying types HPV16, HPV18 and may include HPV45, and further pooling the other 10 cHPV types into two or three groups. Some assays may also individually identify other cHPV types than HPV16, HPV18 and HPV45 and one or two other HPV types.
- Full genotyping: An HPV assay that provides individual identification of all 12 cHPV types and may additionally individually identify other HPV types.

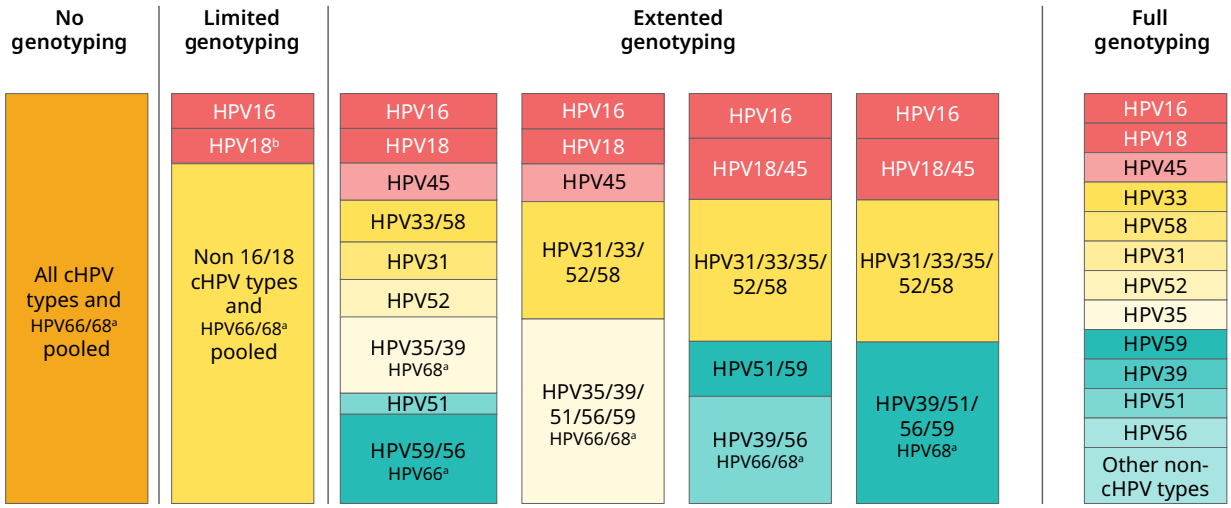
Table 1.2 HPV tests genotyping spectrum

Genotype spectrum

No genotyping	Limited genotyping	Extended genotyping	Full genotyping
» No individual HPV type results » Aggregated positive/ negative result for 12 cHPV types » Current tests also include HPV66 and HPV68	» Individual or combined results for HPV16 and HPV18; may include combined results with HPV45 » All other cHPV types combined » Current tests also include HPV66 and HPV68	» Individual or combined results for HPV16 and HPV18; may include combined results with HPV45; and results for the other 10 cHPV types usually pooled in 2–3 different groups » Current tests also include HPV66 and HPV68	» Individual results for each of the 12 cHPV types » Current tests include several additional HPV types, some of which are not carcinogenic and are unnecessary for screening purposes

Although current HPV tests that provide extended genotyping use different combinations of HPV types, most of them individually identify HPV16 and HPV18, and sometimes HPV45, while the other cHPV types are grouped in different combinations, some shown in Fig. 1.1.

Fig 1.1 Examples of current HPV tests: no genotyping (positive/negative results), limited genotyping, extended genotyping and full genotyping



a HPV68 (probably carcinogenic) and HPV66 (possibly carcinogenic) are not part of the carcinogenic HPV types included in the WHO-TPPs 1a, 1b, 1c and 1d, but they are still included in some current HPV tests.

b May or may not include HPV45.

Screening approaches using full genotyping results are not considered in this guideline, as management based on individual identification of HPV types is not necessary for screening purposes and adds complexity to screening programmes.

In the WHO TPPs for HPV screening tests to detect cervical pre-cancer and cancer *(15)*, the 12 HPV types classified as "Group 1: carcinogenic to humans" in the IARC Monograph No. 90, 2007, the IARC Handbook volume 18, 2022 and Wei et al. 2024 *(3, 16, 17)*, were further stratified into four groups (1a, 1b, 1c and 1d) based on each HPV type cervical cancer attributable fraction (see Table 1.3). While there is regional variability in the ranking of attributable fraction, especially for HPV35 in sub-Saharan Africa, this variability does not meaningfully change the group allocation.

Table 1.3 WHO TPPs groups 1a, 1b, 1c, 1d classification of the 12 cHPV types, based on their attributable fraction for cervical cancer

HPV types by subgroup[a]	% HPV type prevalence in people with invasive cervical cancer	% HPV type prevalence in people with normal cervical cytology	Odds ratio[b]	% Attributable fraction[c]
Group 1a				
HPV16	55.8	2.6	47.6	62.4
Group 1b				
HPV18	14.3	1.0	15.7	15.3
HPV45	4.8	0.6	8.3	4.8
Group 1c				
HPV33	4.0	0.6	7.1	3.9
HPV58	4.0	0.8	5.1	3.7
HPV31	3.5	1.0	3.7	2.9
HPV52	3.2	1.0	3.3	2.6
HPV35	1.6	0.4	3.9	1.4
Group 1d				
HPV59	1.2	0.4	2.9	0.9
HPV39	1.3	0.6	2.0	0.8
HPV51	1.0	0.9	1.2	0.2
HPV56	0.8	0.6	1.3	0.2

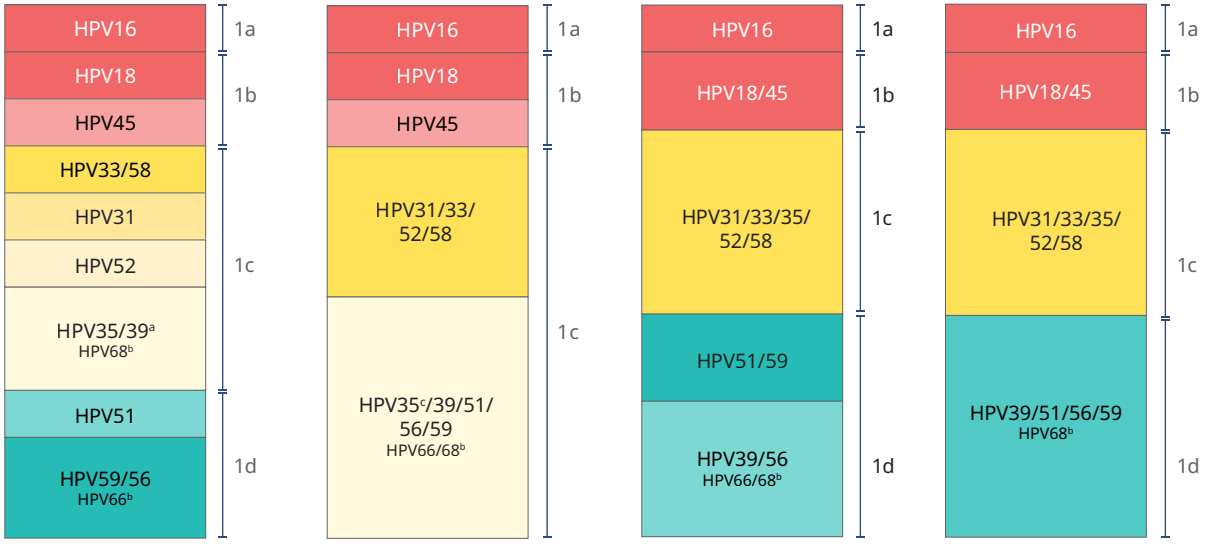
a The classification is based on their prevalence in cervical cancers.

b Odds ratios represent the odds of HPV type positivity in invasive cervical cancer compared with HPV positivity in cytologically normal controls.

c The attributable fraction is the percentage of cervical cancer caused by that HPV type. This table is sorted based on these values.

HPV limited or extended genotyping offers a built-in molecular triage that allows for the simple stratification and priority management of HPV-positive women according to the risk of cervical pre-cancer and cancer granted by specific HPV types groups. The WHO TPPs provide a standard classification of cHPV types into groups 1a, 1b, 1c and 1d, and will be used in future documents, including the recommendations in this guideline. Some HPV tests currently available do not align with this classification. In such cases, a test output should be assigned to the highest relevant cHPV risk group (see example in Fig. 1.2).

Fig 1.2 HPV genotype allocation to WHO TPP groups for some currently available HPV extended genotyping tests



a HPV39 belongs to WHO TPPs group 1d. However, in this specific HPV test, it is reported in a pooled result with HPV35, which is classified in group 1c. The pooled test output for HPV35/39/68 is allocated to group 1c.

b HPV68 (probably carcinogenic) and HPV66 (possibly carcinogenic) are not included in the cHPV types classified within WHO TPPs groups 1a, 1b, 1c and 1d; however, they are still included in some current HPV tests.

c Where HPV35 (group 1c) is reported in a pooled result with group 1d HPV types, the pooled output for HPV35/39/51/56/59/66/68 is allocated to group 1c. For these HPV tests, group 1d cannot be identified separately for specific management.

1.5 Target audience

This guideline is intended primarily for policy-makers, programme managers, programme officers and other professionals in the health sector who have responsibility for choosing evidence-based strategies for cervical cancer prevention, at country, regional and district levels. Health workers – such as doctors, nurses and community health workers providing reproductive health services, antenatal and postnatal care, family planning services and women's health services in clinics at the district and primary health care levels – may also consult this document to understand the basis of the recommendations and the critical importance of selecting and implementing evidence-based strategies for cervical cancer prevention.

This guideline can be used as a basis for developing an adapted publication for women and their families to support them in making decisions about cervical cancer screening and treatment.

2. Methods for developing recommendations

This guideline has been developed in accordance with the methods described in the *WHO handbook for guideline development, second edition (18)*.

2.1 Groups contributing to guideline development

Lists of all members of the Guideline Development Group (GDG), External Review Group (ERG), systematic review and statistical analysis team, modelling team and other contributors are provided in Annex 1, with details of their expertise and affiliations. The WHO Secretariat consisted of staff from various relevant WHO departments, and staff from the International Agency for Research on Cancer. The Steering Group of the WHO Secretariat led the coordination of the development of this guideline. Members of the Secretariat who were not part of the Steering Group were kept informed of the guideline development process and participated in the discussions, in particular during meetings of the various groups.

The GDG comprised 32 members (18 women and 14 men), from across all six WHO regions, including representatives from civil society organizations and women's groups, including women living with HIV. The members brought to the table their varied expertise on cervical screening and treatment. Two members acted as co-chairs and moderated the GDG meetings. Observers who attended the GDG meetings did not participate in the GDG discussions nor vote on recommendations. Once the GDG had agreed on the recommendations, the ERG reviewed the draft of the recommendations, the important considerations and the evidence and provided feedback. Its six members, none of whom was also a member of the GDG, had expertise in research, policy development, programme implementation and clinical care.

Multiple teams prepared evidence relevant to human papillomavirus (HPV) DNA tests (see details in Annex 2):

- One team conducted a systematic review of published and unpublished data.
- Another team adapted a pre-existing comprehensive natural history microsimulation model to simulate the use of HPV DNA tests in screening according to level of genotyping in the general population of women.

A guideline methodologist with experience of using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach *(19)* coordinated the presentation of evidence and decision-making processes that facilitated the development of the recommendations, as stipulated in the *WHO handbook for guideline development, second edition (18)*.

A subgroup prepared the evidence for discussion by the GDG. This group included members of the WHO Secretariat, the GDG, the systematic review and modelling team, the guideline methodologist and additional experts. The GDG members that took part in the subgroup ensured appropriate inclusion/exclusion criteria in reviews and other evidence needed for subgroup analyses, agreement on assumptions made in the model and inputs and clear presentation of results.

2.1.1 Declarations and management of conflicts of interest

Each invited GDG member completed a written declaration of interest (DOI) form (including those who had previously completed them prior to participation in the first phase of the guideline update). The DOIs were reviewed by two members of the WHO Secretariat. Silvina Arrossi, Neerja Bhatla, Kate Cuschieri, Teresa Darragh, Walaa Mahgoub, Nelly Mugo, Mario Poljak, Marion Saville, Julie Torode and Yin Ling Woo reported having received support for research activities from commercial entities or other organizations related to the topic. Kate Cuschieri and Nelly Mugo declared having received travel support to participate in meetings and Teresa Darragh, Walaa Mahgoub and Marion Saville having held positions representing interest related to the subject of work. After assessment, it was concluded that the reported conflicts related to the expertise of the GDG members on the topic and did not impede them in fully taking part in all proceedings of the GDG (see Annex 3). At the beginning of every GDG meeting, members were asked to declare any new conflicts of interest; none required any further assessment.

2.1.2 Confidentiality

Each GDG member signed a confidentiality agreement at the beginning of the guideline development process, and the WHO Secretariat restated at the start of each GDG meeting that all discussions and draft recommendations were to remain confidential until publication.

2.2 Question guiding the recommendation

In December 2022, the GDG identified the use of HPV DNA extended genotyping as a priority question in the general population and women living with HIV. However, the GDG agreed to develop recommendations for the general population first since evidence in women living with HIV was still accumulating. The question posed by the GDG was “Should WHO recommend the use of HPV DNA extended or limited genotyping over other HPV DNA testing to screen women in the general population to prevent cervical cancer?”

In the 2021 guideline *(12)*, HPV DNA was recommended as primary screening test in screen-and-treat or screen, triage and treat approaches. In this new guideline, these algorithms are nominated differently to facilitate understanding on the use of different HPV genotyping strategies, as shown in Table 2.1.

Table 2.1 New nomenclature for screen-and-treat and screen, triage and treat approaches

2021 guideline *(12)*	Present guideline	
Screening approach	**Screening strategy**	**Description**
Screen-and-treat	Treat all HPV-positive women	Treat women positive for any HPV types in groups 1a, 1b, 1c and 1d
Screen, triage and treat	Triage all HPV-positive women	Triage women positive for any HPV types in groups 1a, 1b, 1c and 1d with visual inspection with acetic acid (VIA), colposcopic impression or cytology/dual-stain cytology

Table 2.2 lists the screening strategies compared across levels of HPV DNA genotyping. The strategies include triaging with VIA, colposcopic impression and cytology among women testing positive for various cHPV groups based on the level of HPV DNA genotyping used.

Table 2.2 Screening strategies compared by level of HPV DNA genotyping

	HPV DNA genotyping level	Screening strategies using 12-cHPV type tests (tests that detect the 12 cHPV types)[a]	
1	No genotyping, pooled	1.1	Treat all HPV positives (groups 1a, 1b, 1c and 1d)[b]
		1.2	Triage all HPV positives with VIA
		1.3	Triage all HPV positives with colposcopic impression
		1.4	Triage all HPV positives with cytology/dual-stain cytology
2	Limited genotyping	2.1	Treat groups 1a and 1b; triage pooled groups 1c and 1d with VIA[b]
		2.2	Treat groups 1a and 1b; triage pooled groups 1c and 1d with colposcopic impression[b]
		2.3	Treat groups 1a and 1b; triage pooled groups 1c and 1d with cytology[b]

	HPV DNA genotyping level	Screening strategies using 12-cHPV type tests (tests that detect the 12 cHPV types)[a]	
3	Extended genotyping	3.1	Treat groups 1a, 1b and 1c; triage group 1d
		3.1.1	Treat groups 1a, 1b and 1c; triage group 1d with VIA
		3.1.2	Treat groups 1a, 1b and 1c; triage group 1d with colposcopic impression
		3.1.3	Treat groups 1a, 1b and 1c; triage group 1d with cytology
		3.2	Treat groups 1a, 1b and 1c; routine screen group 1d
		3.3	Treat groups 1a and 1b; triage group 1c; routine screen group 1d
		3.3.1	Treat groups 1a and 1b; triage group 1c with VIA; routine screen group 1d
		3.3.2	Treat groups 1a and 1b; triage group 1c with colposcopic impression; routine screen group 1d
		3.3.3	Treat groups 1a and 1b; triage group 1c with cytology; routine screen group 1d

a 1a: HPV16; 1b: HPV18, 45; 1c: HPV31, 33, 35, 52, 58; 1d: HPV39, 51, 56, 59.

b These strategies are also applicable when using 8-cHPV tests but do not include HPV types classified in group 1d.

2.3 Outcomes

The GDG agreed that the critical outcomes identified for the 2013 guideline *(9)* and for the 2021 guideline *(12)* continue to be the critical outcomes for the new recommendation question. These outcomes are listed below.

Critical outcomes for screening and treatment recommendations

- cervical cancer
- mortality
- high-grade cervical intraepithelial neoplasia (CIN2+, CIN3+)
- HPV infection
- preterm birth
- pre-cancer treatments

- adverse events (direct consequence of pre-cancer treatment):
  - major infections or bleeding
  - procedure-associated pain
  - cervical stenosis
  - infertility
  - spontaneous abortion
  - perinatal deaths
  - premature rupture of membrane
  - unnecessary interventions
  - increased viral shedding in women living with HIV
- costs
- equity
- acceptability
- feasibility

Adverse events were defined as outcomes that were a direct consequence of pre-cancer treatment and were grouped as one category, which was considered a critical outcome. For additional details and definitions, see the 2021 guideline *(12)*.

2.4 Syntheses of evidence

Evidence was synthesized according to the methods in the *WHO handbook for guideline development, second edition (18)*, and the *Cochrane handbook for systematic reviews of interventions (20)*. A systematic review and a dynamic model were conducted to inform the recommendations. The evidence was assessed using the GRADE approach and the certainty of the evidence presented as high, moderate, low or very low (see Table 2.3).

Table 2.3 Interpretation of the GRADE levels of certainty of evidence

High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	We have limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect

Schünemann et al., GRADEpro, 2013 *(19)*.

A systematic review up to October 2025 was conducted to identify studies that measured the critical outcomes when using screening strategies with different HPV genotyping. Because these studies were not found, data from cross-sectional and longitudinal studies were used to pool the cumulative risks of cervical intraepithelial neoplasia (CIN)2+, CIN3+ and cervical cancer associated with ranked series of HPV types and groups of types, by follow-up time. Further details of the methods and results are provided in Web Annex A.

The Policy1-Cervix platform is an extensively validated dynamic model of HPV transmission, vaccination, type-specific natural history, cancer survival, screening, diagnosis and treatment *(21–29)*. It was used to predict outcomes in the general population of women across all 78 low- and middle-income countries. It was reviewed and endorsed by the WHO Immunization and Vaccines-related Implementation Research Advisory Committee for the use in modelling elimination targets for WHO, and subsequently for global modelling of therapeutic HPV vaccination. Details of the model and analyses are provided in Web Annex A.

For the baseline analysis, it was assumed that 70% of women attend each routine screening visit, but that 10% would be never-screeners (so the 70% are selected from the 90% of ever-screeners). Three different levels of follow-up were modelled: 90% (very high), 60% (high) and 30% (low). Lower follow-up rates were applied to women referred to excisional treatment (due to being ineligible for ablative treatment), women referred for a separate triage visit within few weeks and women referred for a separate follow-up visit at 12 months. Lower follow-up rates were not applied when triage or treatment were offered at point-of-care. As per current guidelines, women from the general population who test negative on triage should attend a follow-up visit at 24 months and those receiving treatment should attend a post-treatment visit at 12 months; for the baseline analysis both visits were considered at 12 months.

The outcomes presented to the GDG for the three modelled levels of follow-up included the lifetime number of cervical cancer cases and deaths, as well as age-standardized incidence and mortality rates as measures of the benefit; the number of pre-cancer treatments needed to avert one cervical cancer death (number need to treat) as a measure of screening-related harms; and the cost per health-adjusted life year saved. When summarizing the evidence, results from these scenarios were consolidated into high follow-up capacity (60% or greater, based on the 60% level follow-up results of the model) and low follow-up capacity (less than 60%, based on the 30% level follow-up results of the model).

2.4.1 Values and preferences, feasibility, acceptability, resources and equity considerations

For the 2021 guideline *(12)*, systematic reviews and surveys were performed to inform values and preferences, feasibility, acceptability, resources and equity considerations. These assessed screening with cytology, VIA and HPV testing, but not extended genotyping. Given that the use of an HPV test, whether with extended or limited genotyping, would encompass concerns similar to the use of HPV tests with no genotyping, the GDG agreed that an updated review or survey was not necessary. During GDG meetings, the views of the members were also gathered to complement the information from the 2021 guideline.

2.5 Development of the recommendations

In September 2022, an in-person GDG meeting was held where draft recommendations were developed and the need for additional evidence was assessed. The GDG then met over a series of virtual meetings to review the evidence. A summary of the evidence (benefits and harms), relevant values and preferences information, and other issues, including use of resources and cost, feasibility, equity and acceptability were presented. Agreement on the recommendations was made by consensus during the GDG meetings, and the final written recommendations were then approved electronically. The GDG had agreed that, if consensus could not be reached, a majority vote of 51% would have been accepted to make recommendations – yet the group did reach a consensus on all the recommendations.

The GDG decided on a strong or conditional recommendation. **Strong recommendations** (worded as "WHO recommends") were made when all the desirable consequences of the intervention clearly outweighed the undesirable consequences in most settings. **Conditional recommendations** (worded as "WHO suggests") were made when the desirable consequences of the intervention **probably** outweighed the undesirable consequences in most settings. Table 2.4 describes how strong and conditional recommendations should be interpreted by different audiences.

Table 2.4 Interpretation of strong and conditional recommendations

Implications	Strong recommendation (WHO recommends...)	Conditional recommendation (WHO suggests...)
For individuals	Most individuals in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but some may not.
For health workers	Most individuals should receive the recommended course of action. Adherence to this recommendation (when it aligns with national guidelines) could be used as a quality criterion or performance indicator.	Clinicians should recognize that different choices may be appropriate for different individuals and that clinicians must help each individual arrive at a management decision consistent with the individual's values and preferences. Decision aids may be useful to help individuals make decisions consistent with their values and preferences.
For policy-makers	The recommendation can be adopted as policy in most situations.	Policy-making will require discussion and involvement of various stakeholders.

Source: Schünemann et al., GRADEpro, 2013 *(19)*.

2.6 Management of the external peer review

The draft guideline document was circulated to the ERG for comments. The WHO Secretariat then reviewed the comments, which were minor wording changes, without any implications for the substance of the recommendations themselves, and the guideline document was finalized.

3. Recommendations on the use of HPV DNA genotyping for cervical cancer screening

3.1 Considerations

This publication presents recommendations for the use of human papillomavirus (HPV) DNA tests with no genotyping, limited genotyping or extended genotyping for cervical cancer screening. These recommendations apply under the following considerations:

HPV testing in primary screening: For the general population of women, HPV DNA is the recommended primary screening test, but HPV mRNA detection may also be used, rather than visual inspection with acetic acid (VIA) or cytology *(12, 13)*. This recommendation has not changed.

HPV DNA genotyping output: Different levels of genotyping – including **no genotyping, limited genotyping or extended genotyping** – may be available in countries. This guideline provides recommendations on the preferred genotyping strategies based on country or programme follow-up capacity.

HPV DNA genotyping output:

i. No genotyping provides a positive/negative result with no individual identification of cHPV types.

ii. Limited genotyping separately identifies cHPV types HPV16/18±45 (groups 1a and 1b), and pools the non HPV16/18 cHPV types.

iii. Extended genotyping separately identifies cHPV types in groups 1a and 1b and identifies different combinations of cHPV types in groups 1c and 1d. Programmes using extended genotyping results should first assign the HPV result outputs to the cHPV groups (1a, 1b, 1c and 1d). If an output matches multiple groups, the output should be assigned to the highest relevant cHPV risk group. Matching outputs will help in selecting appropriate management. See section 1.4 for more details.

iv. While limited and extended genotyping tests provide results to differentiate carcinogenic HPV (cHPV) types, the result can also be considered as a pooled positive/negative result, as in no genotyping.

Treatment type: Each suggested screening strategy includes ablative treatment for HPV-positive women or triaged positive women. Before treatment, each woman should be visually assessed to determine eligibility for ablative treatment. This can be performed with or without a colposcope after applying acetic acid to assess the size of the area of treatment and the type of transformation zone. Visually assessing eligibility for ablative treatment differs from using VIA to triage women who are HPV positive. HPV-positive women or triaged women who are not eligible for ablative treatment should receive excisional treatment.

Treatment capacity: Programmes should establish adequate treatment capacity before initiating a screening programme and/or implementing these recommendations on the use of HPV DNA tests in the general population.

Follow-up capacity: Decision-makers should assess whether a screening programme's readiness to complete subsequent steps in the care continuum (treatment, triage and follow-up) is high or low. High follow-up capacity is defined as more than 60% completion at ALL steps in the continuum (i.e. less than 40% of women lost to follow-up at ALL steps), while low follow-up capacity is defined as less than 60% completion (i.e. 40% or more lost to follow-up at any step). Failure to reach 60% at a single step is sufficient to consider it as low. This 60% threshold is not exact. Determining follow-up capacity is critical, as loss to follow-up among women with pre-cancerous lesions increases the risk of progression to cervical cancer if left untreated and reduces programme efficiency and cost-effectiveness. Further guidance for countries on assessing follow-up capacity is provided in Section 4.

3.2 Recommendations for the general population of women

3.2.1 Recommendations for settings with high follow-up capacity (60% or greater)

In settings with high follow-up capacity (60% or greater) and sufficient ablative treatment capacity, WHO suggests using HPV DNA testing with extended or limited genotyping OVER treating all HPV-positive women or triaging all HPV-positive women with additional tests.

In settings with high follow-up capacity (60% or greater) and sufficient ablative treatment capacity where HPV DNA extended genotyping is used, WHO suggests:

- treating all eligible women with ablative treatment who test positive for carcinogenic HPV (cHPV) types 16 (group 1a), 18 and 45 (group 1b) and 31, 33, 35, 52 and 58 (group 1c); AND triaging women who test positive for cHPV types 39, 51, 56 and 59 (group 1d);

  OVER

- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b), AND triaging women who test positive for cHPV types 31, 33, 35, 52, 58, 39, 51, 56 and 59 (groups 1c and 1d);

  OVER

- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52 and 58 (group 1c) AND returning women who test positive for cHPV types 39, 51, 56 and 59 (group 1d) to routine screening.

Remark: To determine the type of treatment, women should be visually evaluated for eligibility for ablative treatment. Women not eligible for ablative treatment should be treated using large-loop excision of the transformation zone (LLETZ) or referred for further management if cancer is suspected.

Conditional recommendation, low certainty in evidence of effects

3.2.2 Recommendations for settings with low follow-up capacity (less than 60%)

In settings with low follow-up capacity (less than 60%) and sufficient ablative treatment capacity, WHO suggests:

- treating all eligible women with ablative treatment who test positive for any carcinogenic HPV (cHPV) types 16 (group 1a), 18 and 45 (group 1b), 31, 33, 35, 52 and 58 (group 1c), 39, 51, 56 and 59 (group 1d), consistent with a no-genotyping approach;
- OR treating eligible women with ablative treatment who test positive for any cHPV types 16 (group 1a), 18 and 45 (group 1b) and 31, 33, 35, 52 and 58 (group 1c)[a]

  OVER
- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52, 58, 39, 51, 56 and 59 (groups 1c and 1d); or

  OVER
- triaging with additional tests all women who test positive for any cHPV types (1a, 1b, 1c and 1d).

Remark: As the number of visits increases, the risk of loss to follow-up also rises. Although the preferred strategies may result in some overtreatment, they reduce losses to follow-up among women with pre-cancerous lesions who are at high risk of progression to cervical cancer if left untreated.

Conditional recommendation, low certainty in evidence of effects

a This can be done using an 8-cHPV type test (tests designed to detect the eight most cHPV types) as per WHO target product profiles for HPV screening tests, or when using extended genotyping HPV tests.

3.2.3 Regardless of follow-up capacity

If a programme provides triage with additional tests, WHO suggests using VIA or colposcopic impression (without histological confirmation) as the triage test rather than cytology or dual-stain cytology.

Remark: The choice of triage test will depend on availability, installed capacity, feasibility, training and programme quality assurance in countries. To determine treatment type, women should first undergo visual evaluation for eligibility for ablative treatment. Women who are not eligible for ablative treatment should be treated using large-loop excision of the transformation zone (LLETZ) or referred for further management if cancer is suspected.

Conditional recommendation, low certainty in evidence of effects

3.3 Recommendation for women living with HIV

No recommendation was made for using HPV DNA tests providing extended genotyping for women living with HIV because evidence on the outcomes applicable to this population have not yet been evaluated. Therefore, the following recommendation remains current for the use of triage tests for this population:

In a screen, triage and treat approach using HPV DNA detection as the primary screening test among women living with HIV, WHO suggests using limited genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test.

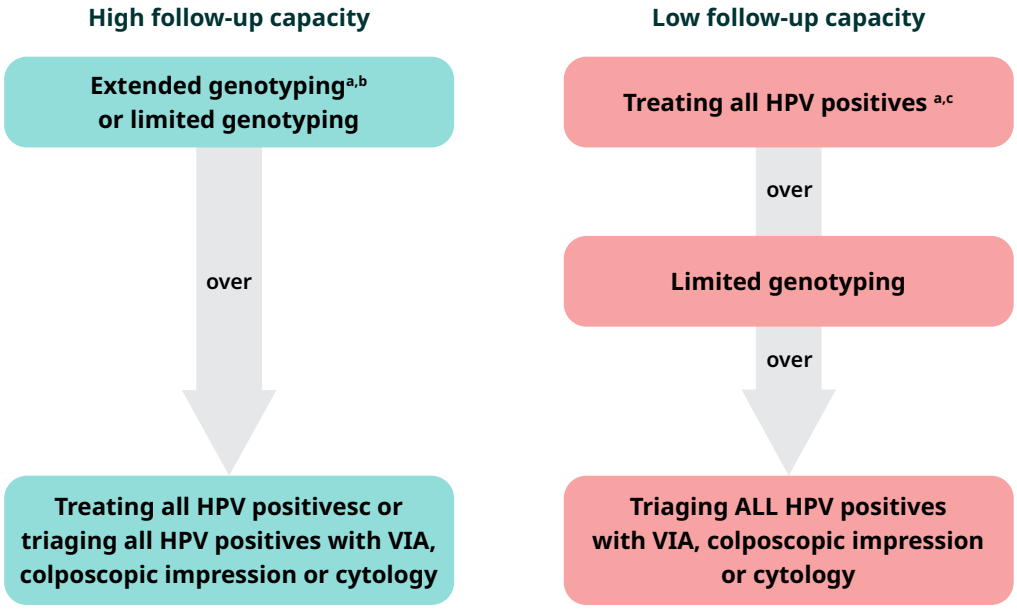
3.4 Recommendation flowcharts

Three flowcharts are provided to guide selection of HPV DNA genotyping levels according to WHO recommendations.

The first flowchart (Fig. 3.1) provides an overview of the recommendations for levels of HPV DNA genotyping for high follow-up capacity settings and low follow-up capacity settings.

The other flowcharts (Figs. 3.2, 3.3) illustrate the preferred HPV DNA genotyping strategies for settings with high and low follow-up capacity according to WHO recommendations. They also present the trade-offs between benefits (reduction in cancer deaths) and harms (overtreatment) and cost-effectiveness.

Fig 3.1 Summary of the recommendations for the use of HPV DNA genotyping

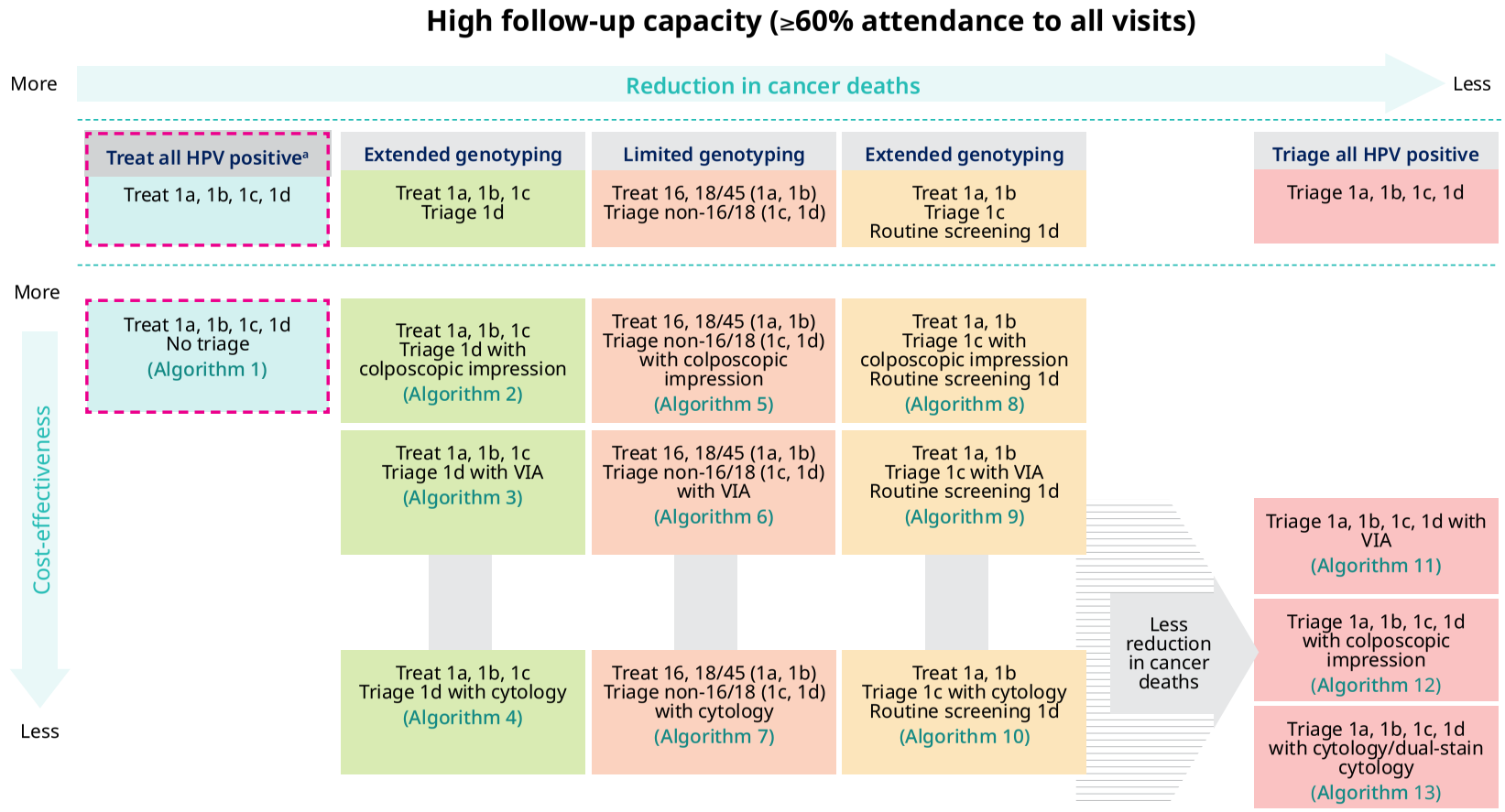


a See recommendations and algorithms for specific strategies that are recommended.

b Extended or limited genotyping was preferred over other strategies because it reduces the number of pre cancer treatments and overtreatment.

c Identifying all HPV positives can be done using no genotyping tests (positive/negative result), limited or extended genotyping tests (using a pooled-positive/negative result instead of the differentiated outputs). No genotyping and limited genotyping tests can target the 12 cHPV types or 8 cHPV types (groups 1a, 1b, 1c) when available.

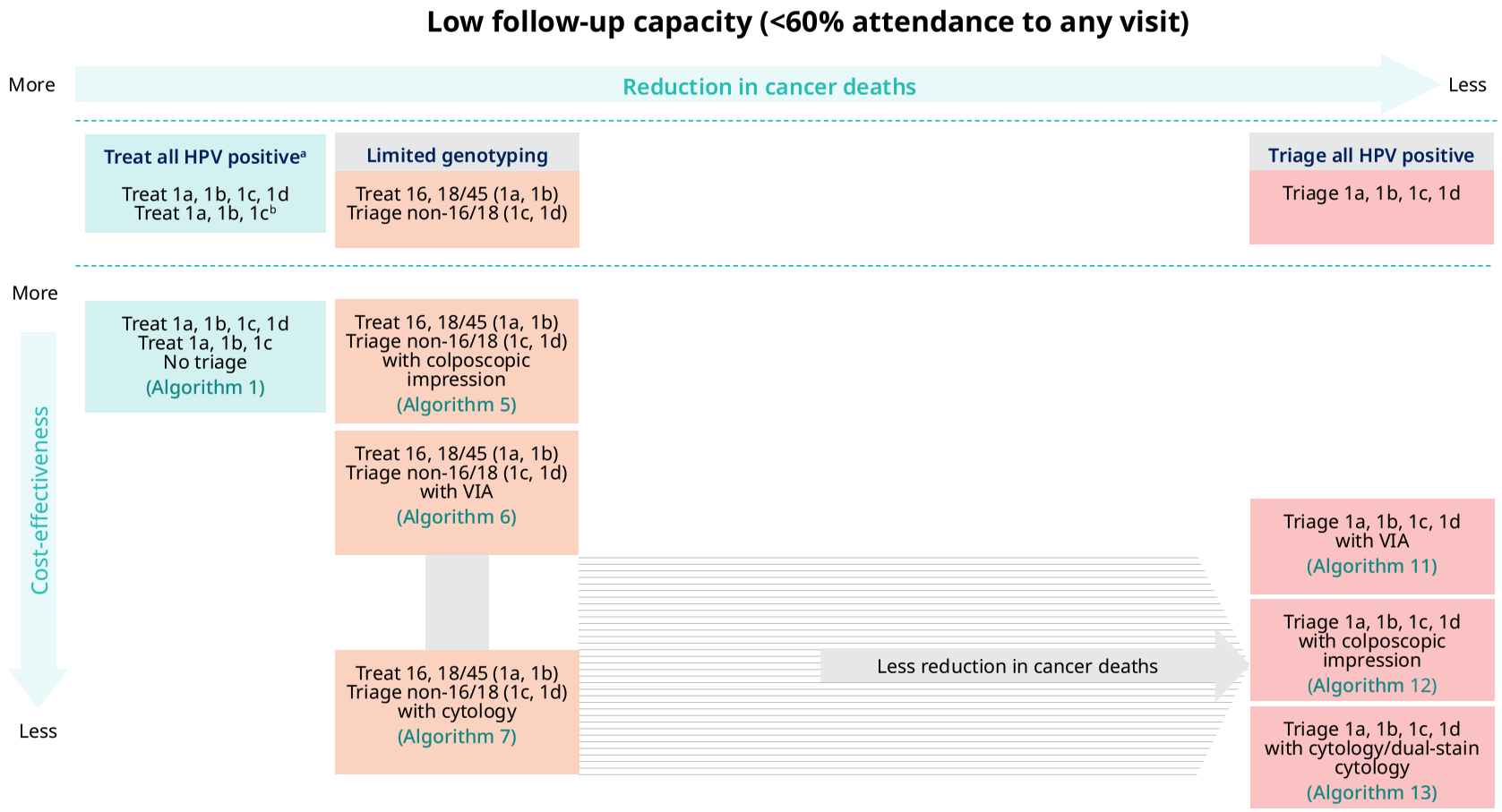
Fig 3.2 Preferred HPV DNA genotyping strategies for high follow-up capacity settings according to WHO recommendations



a Treating all HPV positive women is the most cost-effective strategy. However, despite being more cost-effective and reducing more cancer deaths than HPV extended or limited genotyping, this strategy leads to a larger number of pre-cancer treatments which in screening programmes with high follow-up capacity can be reduced as per recommendations.

Notes: In the figure, the most preferred strategies are on the left and the least preferred on the right; within each approach, the most cost-effective strategies are positioned at the top. Preferred strategies were identified based on a more favourable balance between benefits (reduction in cancer deaths) and cost-effectiveness.

Fig 3.3 Preferred HPV DNA genotyping strategies for low follow-up capacity settings according to WHO recommendations



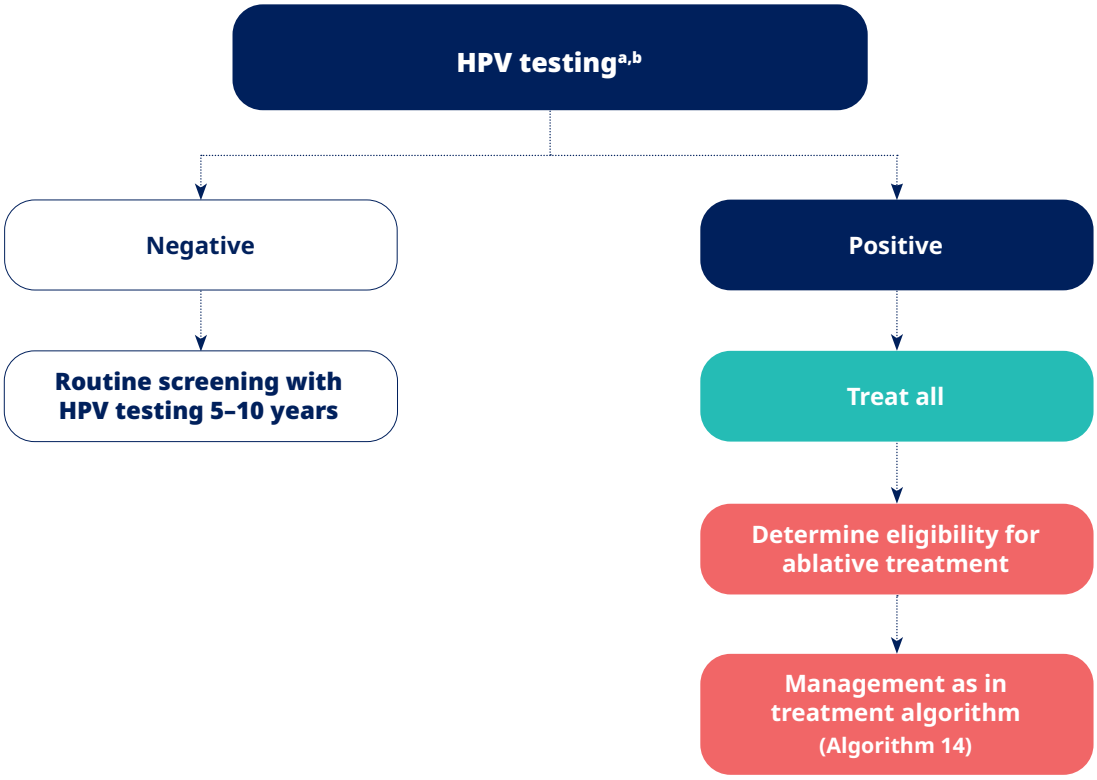
a Treating all HPV positive women is the most cost-effective strategy.

b When using HPV extended genotyping. treating women positive for any HPV type in groups 1a, 1b or 1c, and triaging those positive for any HPV type in group 1d is also very cost effective. Treating 1a, 1b, 1c would additionally be possible when 8 cHPV types tests become available.

Notes: In the figure, the most preferred strategies are on the left and the least preferred on the right; within each approach, the most cost-effective strategies are positioned at the top. Preferred strategies were identified based on a more favourable balance between benefits (reduction in cancer deaths) and harms (number of treatments) and cost-effectiveness.

3.5 Cervical cancer screening and treatment algorithms

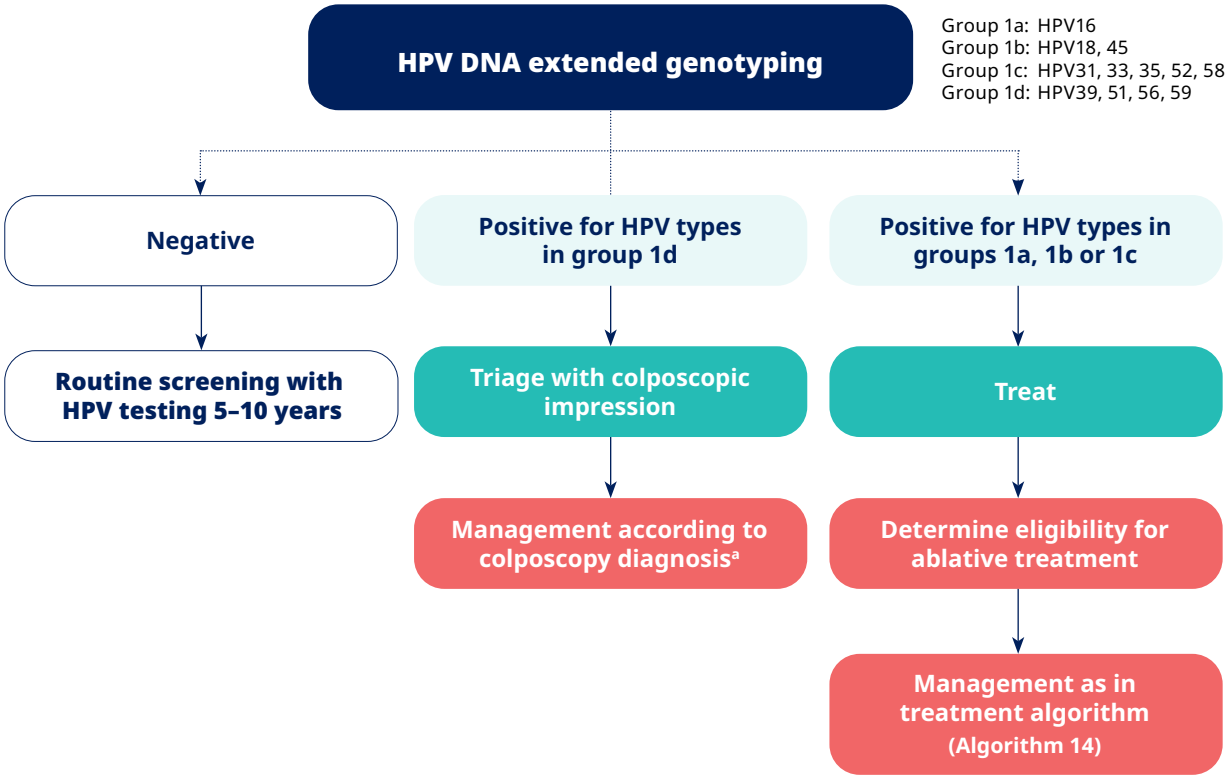
Algorithm 1. HPV with no genotyping, treating all women positive for HPV



a A positive/negative result can also be obtained by pooling differentiated outputs provided by limited or extended genotyping into a positive/negative result. No genotyping tests can target 8 cHPV types (HPV16, 18, 45, 31, 33, 35, 52, 58) when available.

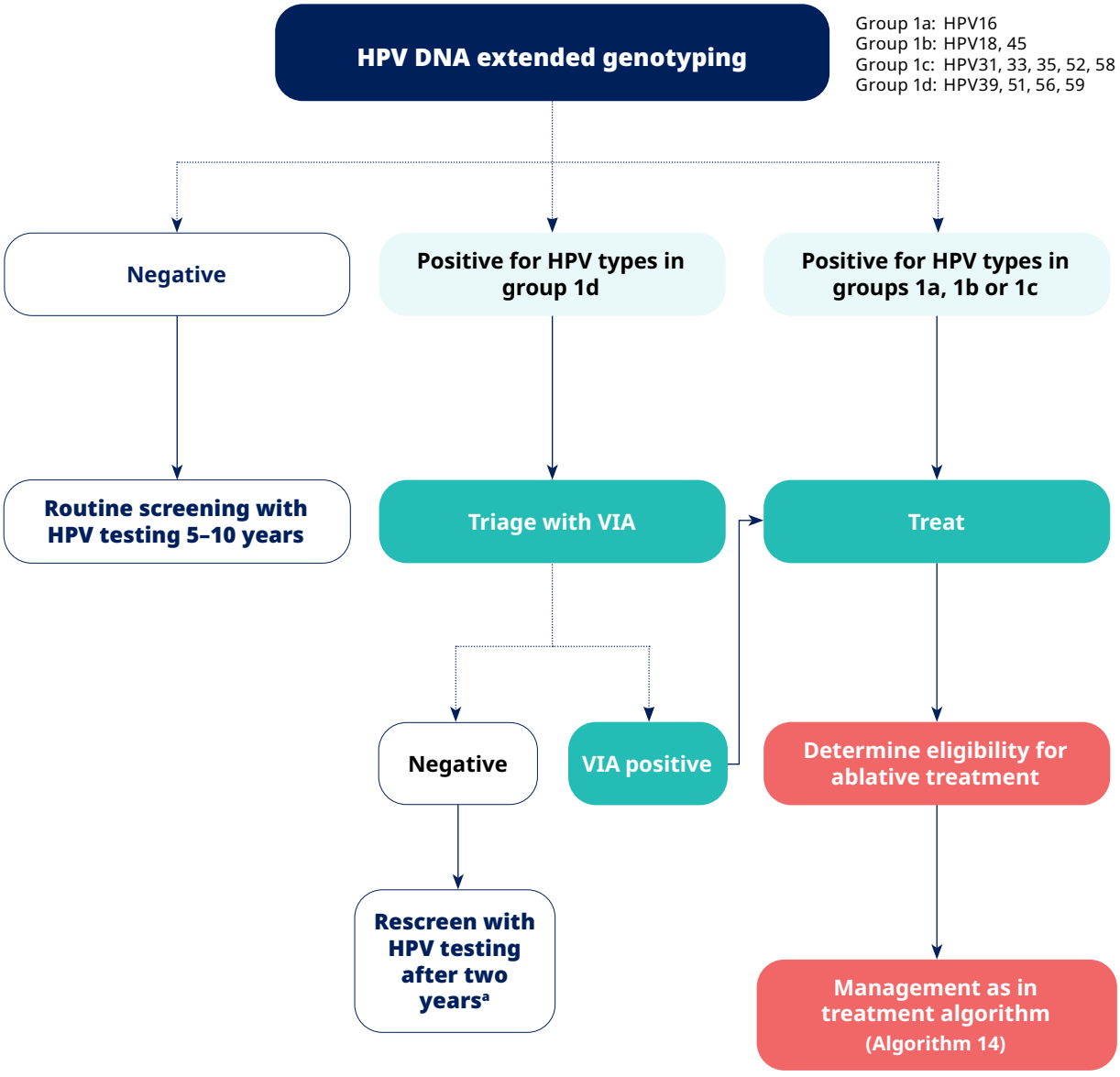
b Samples collected by health-care provider can be used with HPV DNA or mRNA tests. Self-collected samples can additionally be used with HPV DNA tests.

Algorithm 2. HPV DNA extended genotyping, treating groups 1a, 1b and 1c and triaging group 1d with colposcopic impression



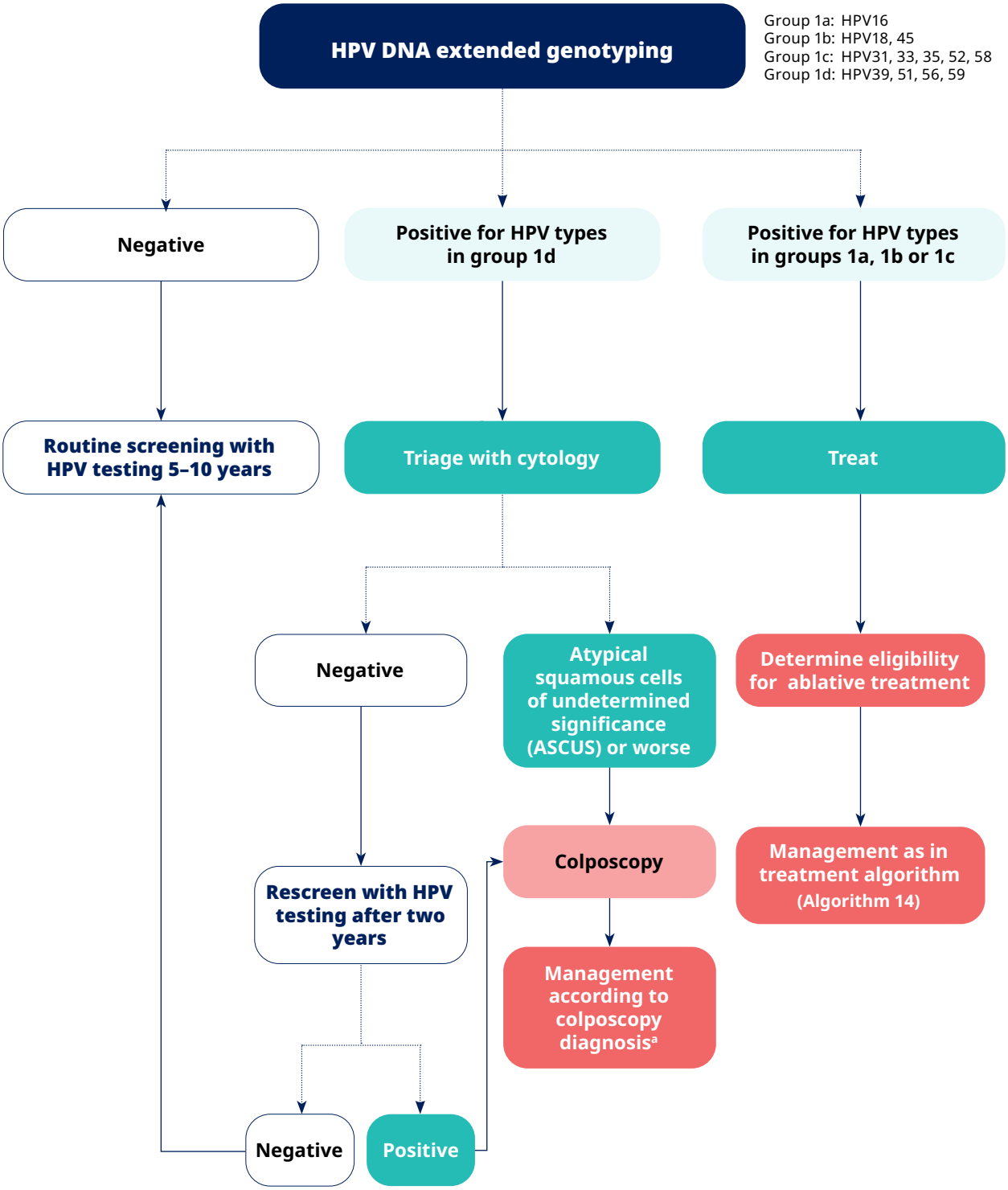
a Preferably without waiting for histology confirmation.

Algorithm 3. HPV DNA extended genotyping, treating groups 1a, 1b and 1c and triaging group 1d with VIA



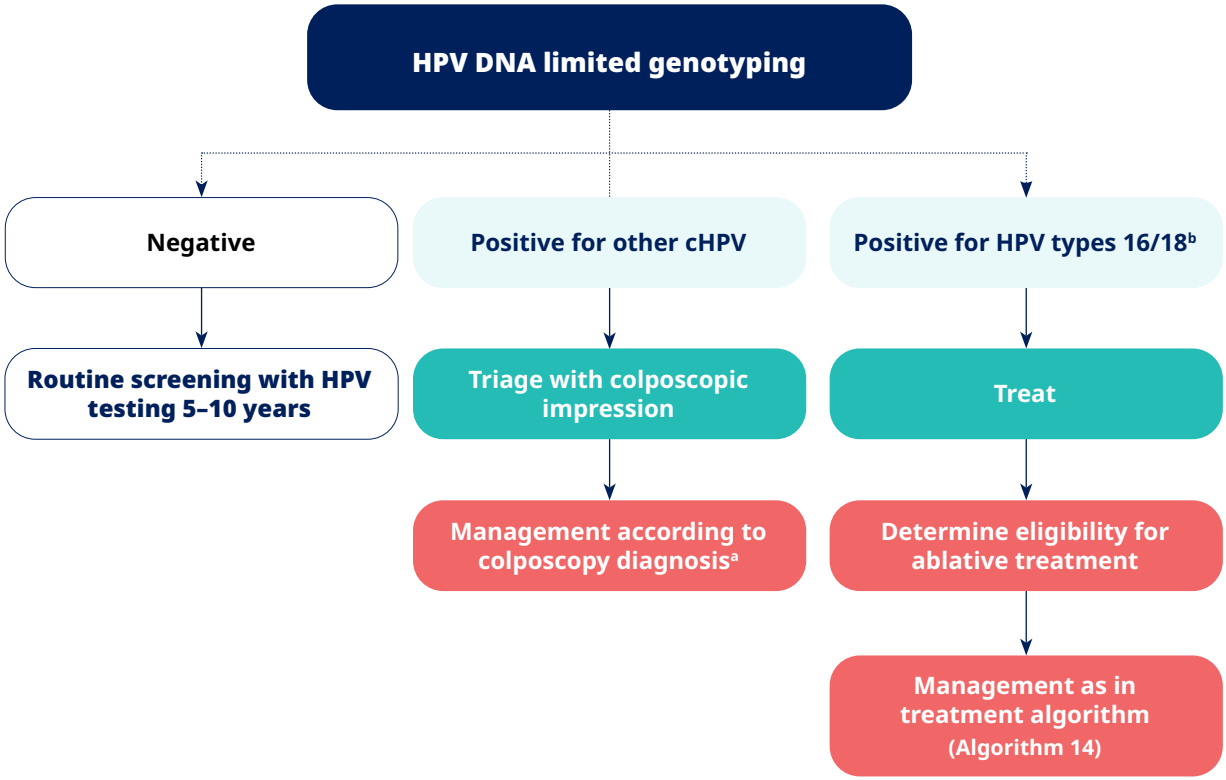
a If HPV negative, send to routine screening; if HPV positive, repeat algorithm.

Algorithm 4. HPV DNA extended genotyping, treating groups 1a, 1b and 1c and triaging group 1d with cytology



a Preferably without waiting for histology confirmation.

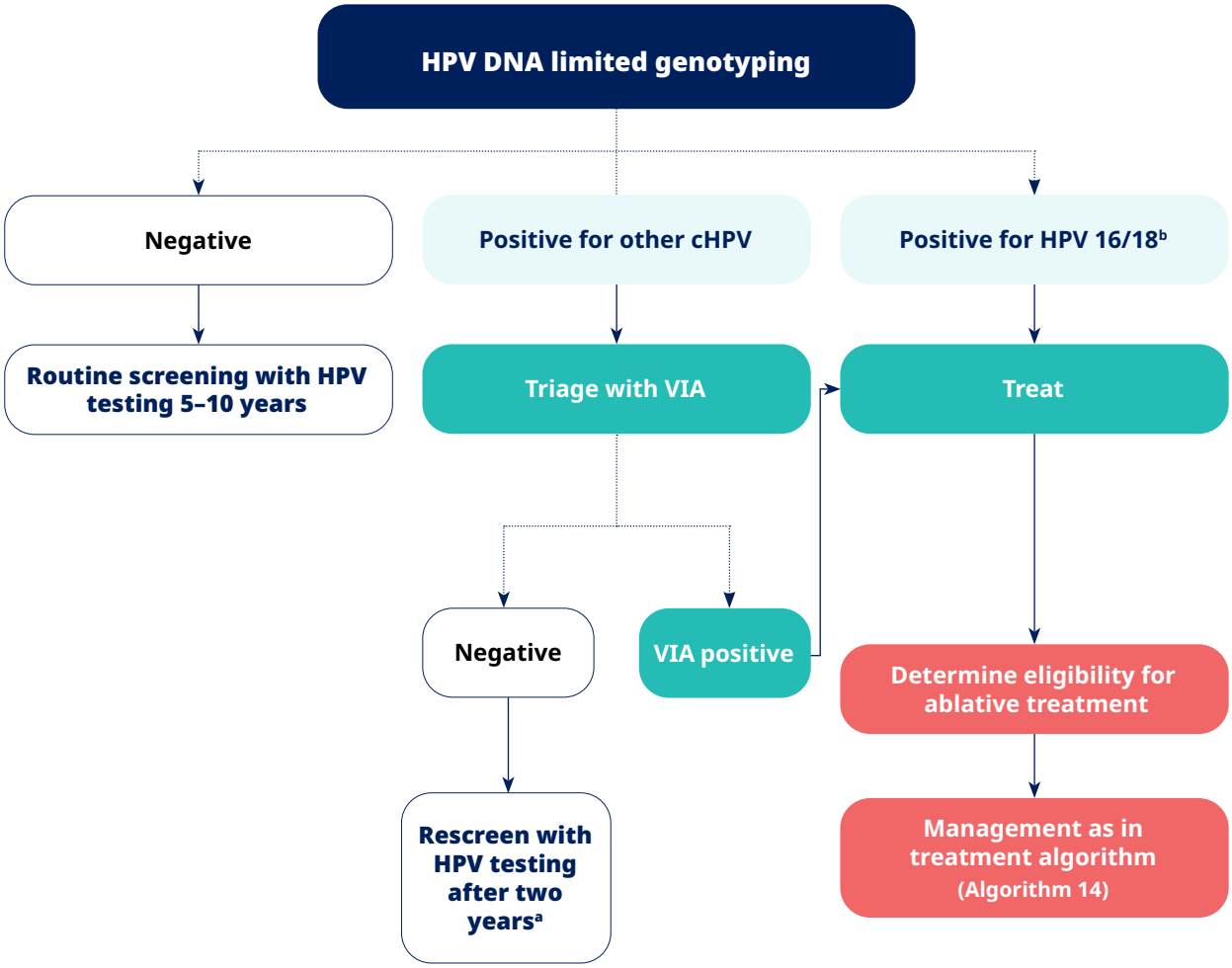
Algorithm 5. HPV DNA limited genotyping, treating women positive for HPV types 16/18 and triaging women positive for other carcinogenic HPV types (cHPV) with colposcopic impression



a Preferably without waiting for histology confirmation.

b May or may not be positive for HPV45.

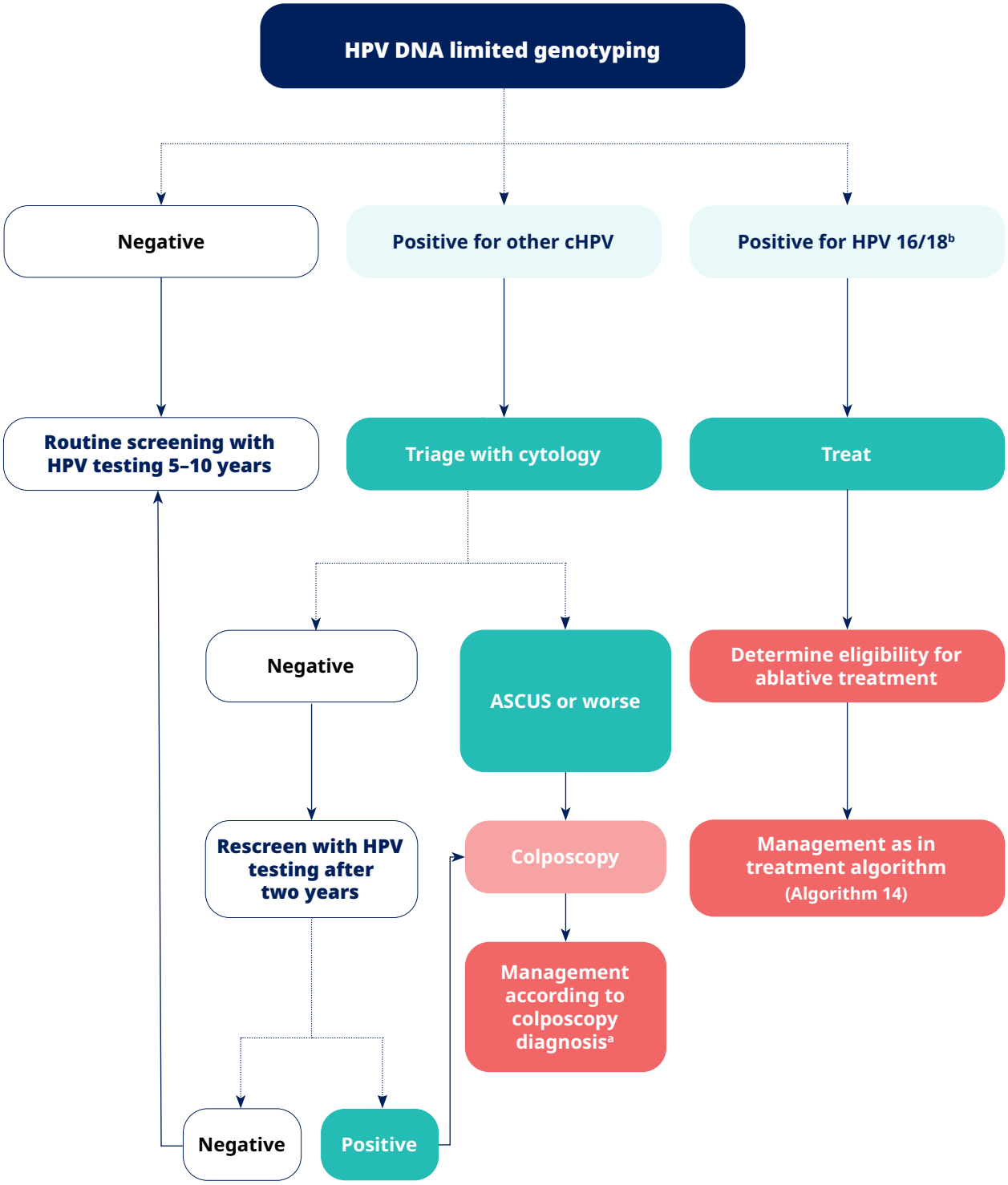
Algorithm 6. HPV DNA limited genotyping, treating women positive for HPV types 16/18 and triaging women positive for other cHPV with VIA



a If HPV negative, move to routine screening; if HPV positive, repeat algorithm.

b May or may not be positive for HPV45.

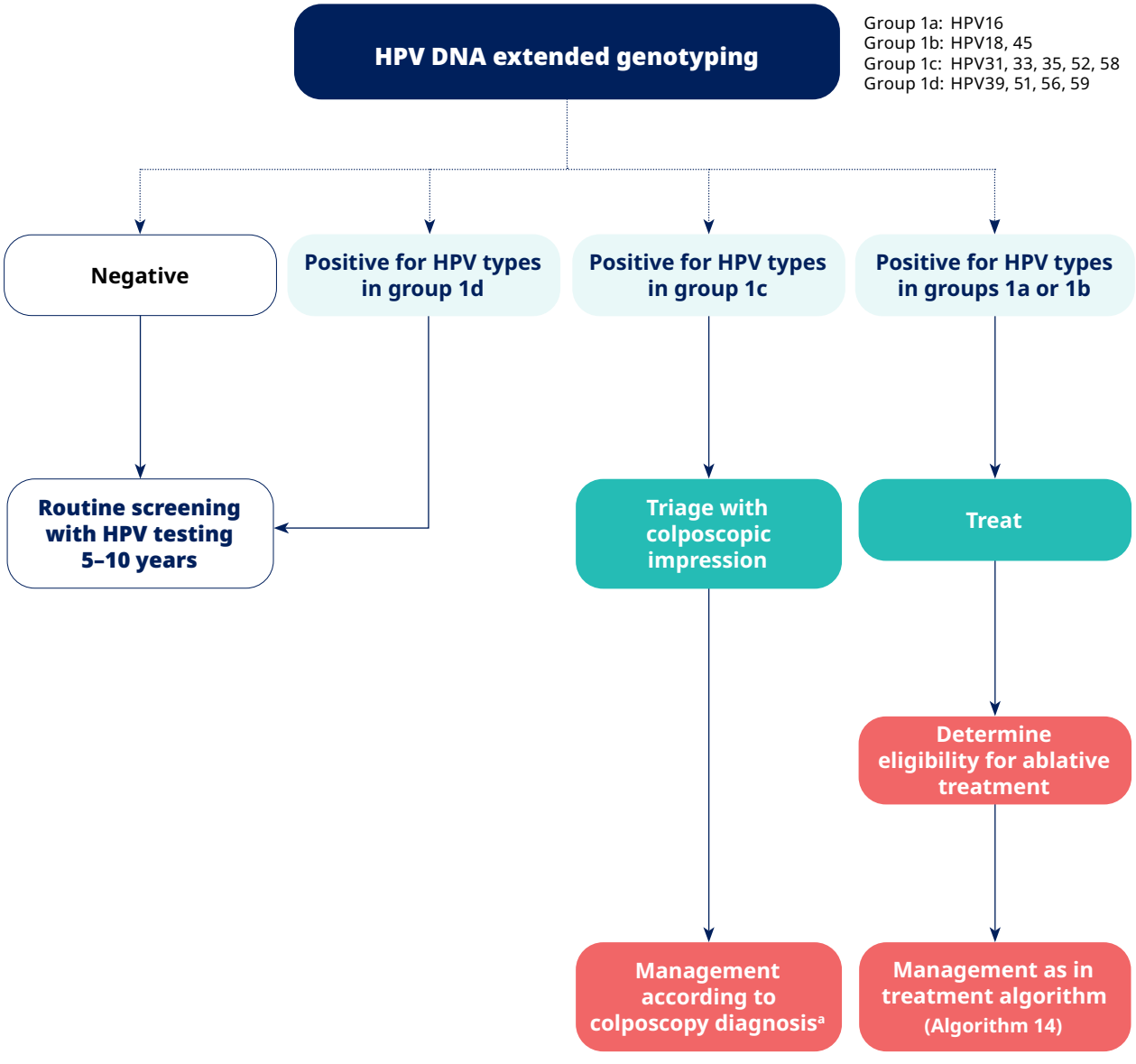
Algorithm 7. HPV DNA limited genotyping, treating women positive for HPV types 16/18 and triaging women positive for other HPV with cytology



a Preferably without waiting for histology confirmation.

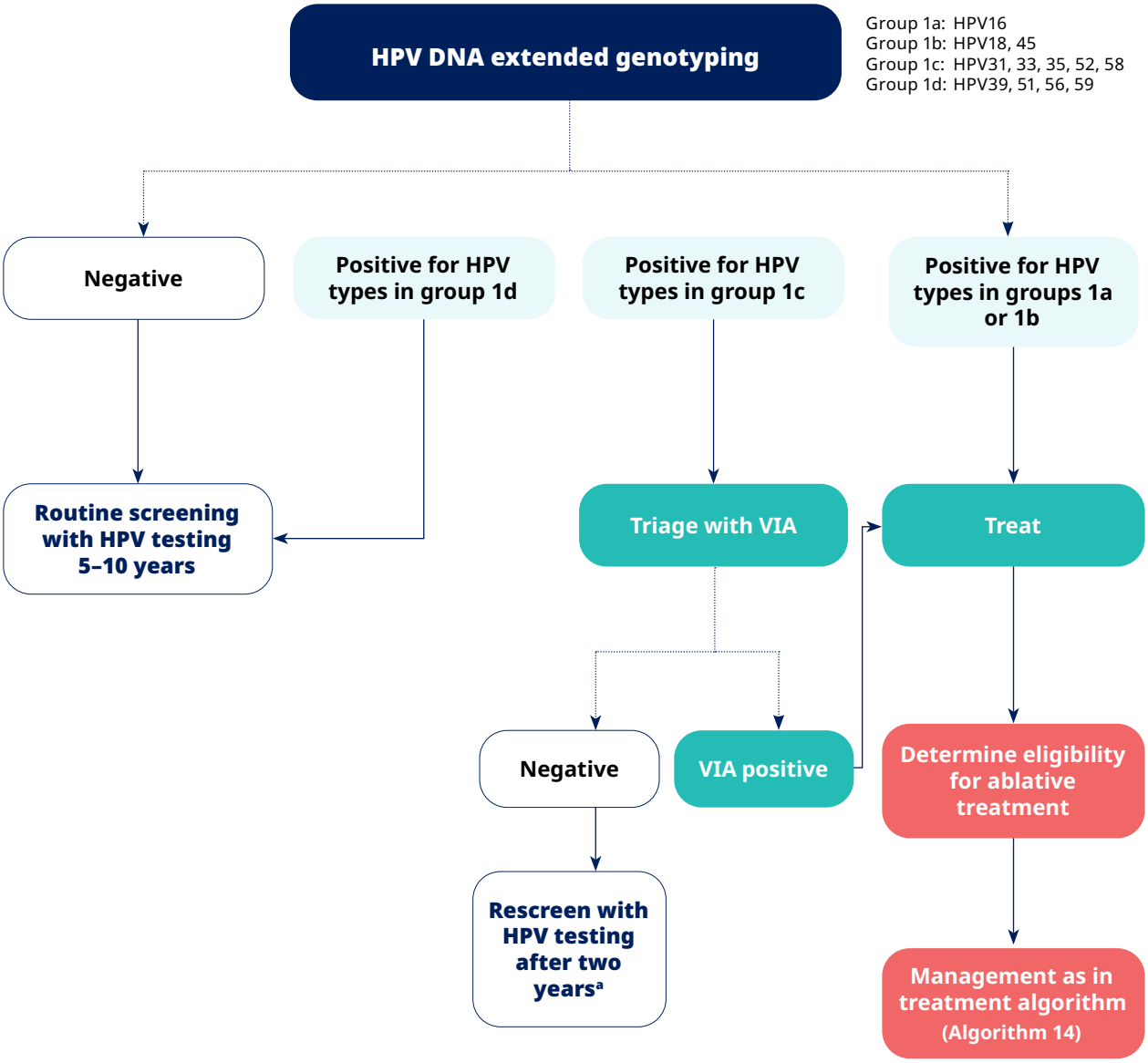
b May or may not be positive for HPV45.

Algorithm 8. HPV DNA extended genotyping, treating groups 1a and 1b, triaging group 1c with colposcopic impression and sending group 1d to routine screening



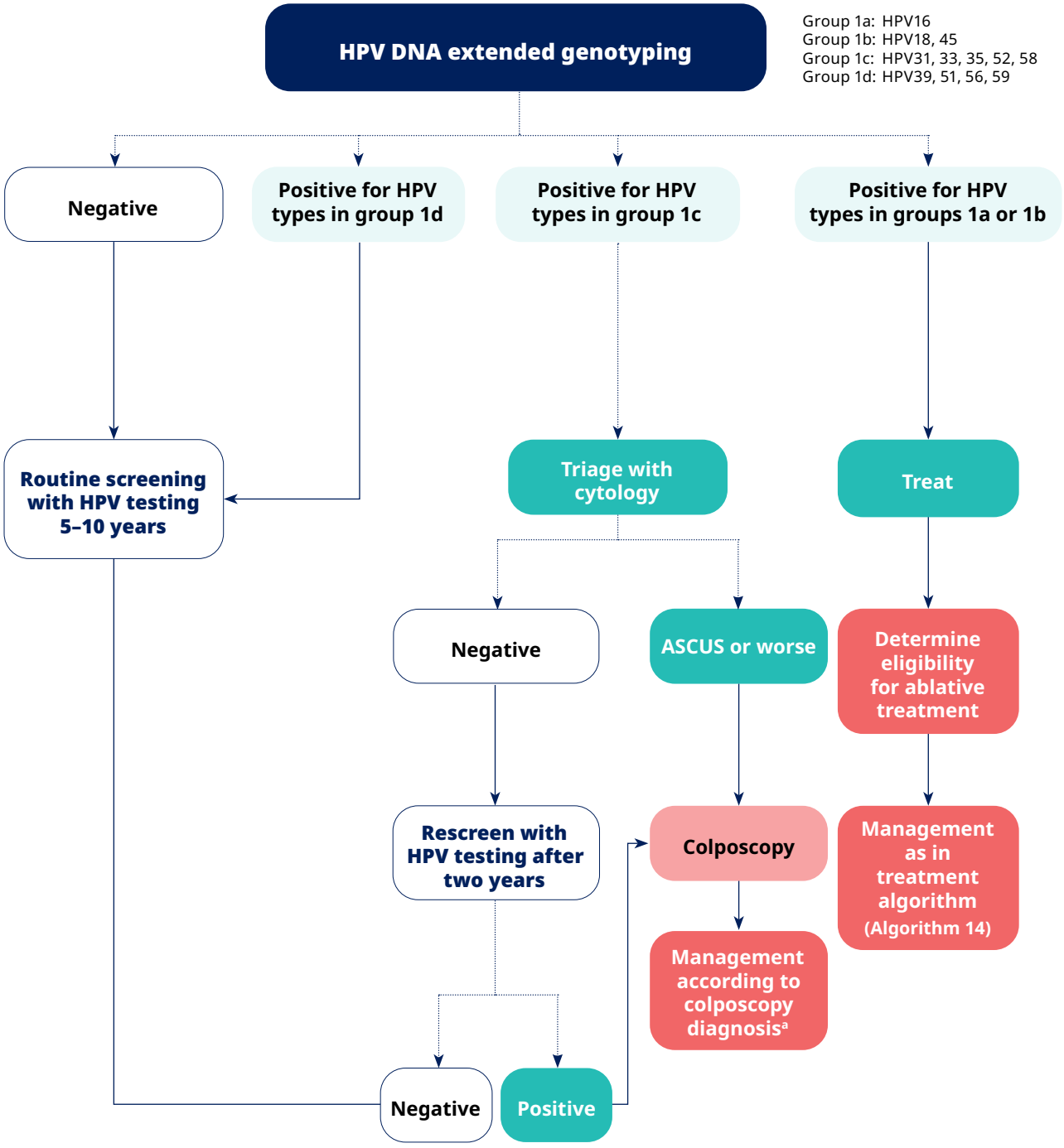
a Preferably without waiting for histology confirmation.

Algorithm 9. HPV DNA extended genotyping, treating groups 1a and 1b, triaging group 1c with VIA and sending group 1d to routine screening



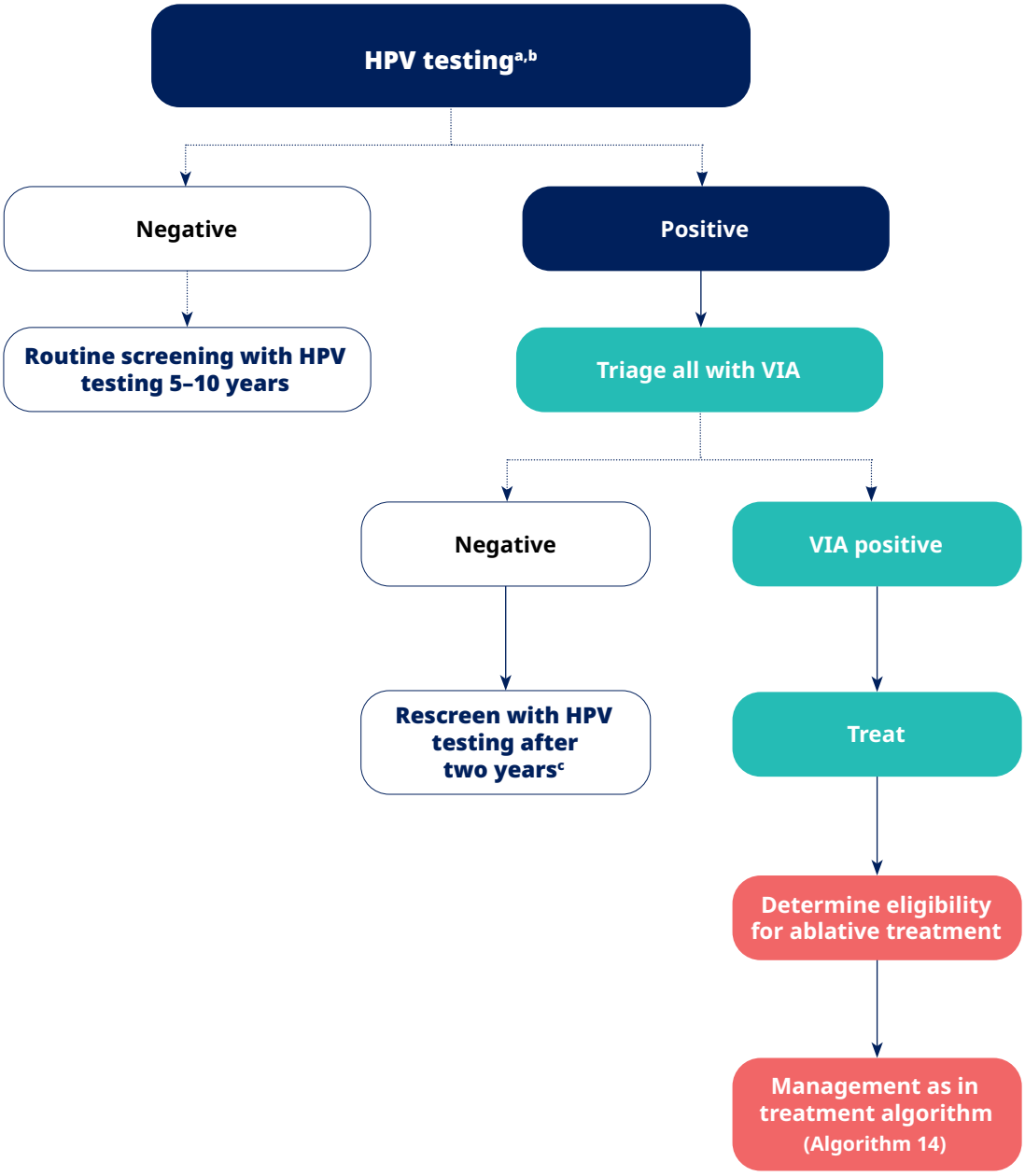
a If HPV negative, move to routine screening; if HPV positive, repeat algorithm.

Algorithm 10. HPV DNA extended genotyping, treating groups 1a and 1b, triaging group 1c with cytology and sending group 1d to routine screening



a Preferably without waiting for histology confirmation.

Algorithm 11. HPV with no genotyping, triaging all women positive for HPV with VIA

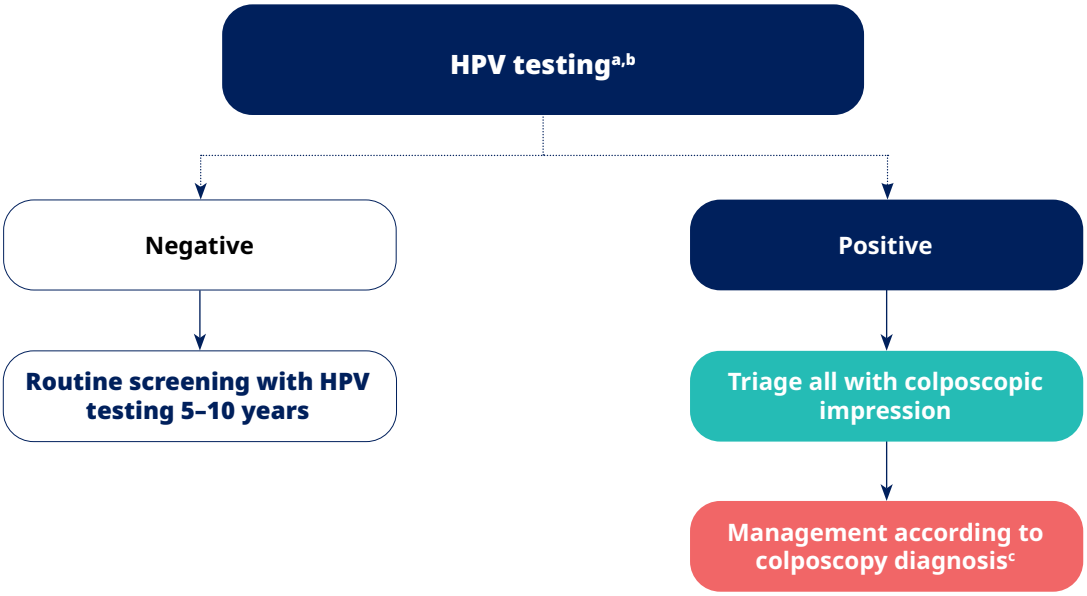


a A positive/negative result can also be obtained by pooling differentiated outputs provided by limited or extended genotyping into a positive/negative result. No genotyping tests can target 8 cHPV types (HPV16, 18, 45, 31, 33, 35, 52, 58) when available.

b Samples collected by health-care provider can be used with HPV DNA or mRNA tests. Self-collected samples can additionally be used with HPV DNA tests.

c If HPV negative, move to routine screening; if HPV positive, repeat algorithm.

Algorithm 12. HPV with no genotyping, triaging all women positive for HPV with colposcopic impression

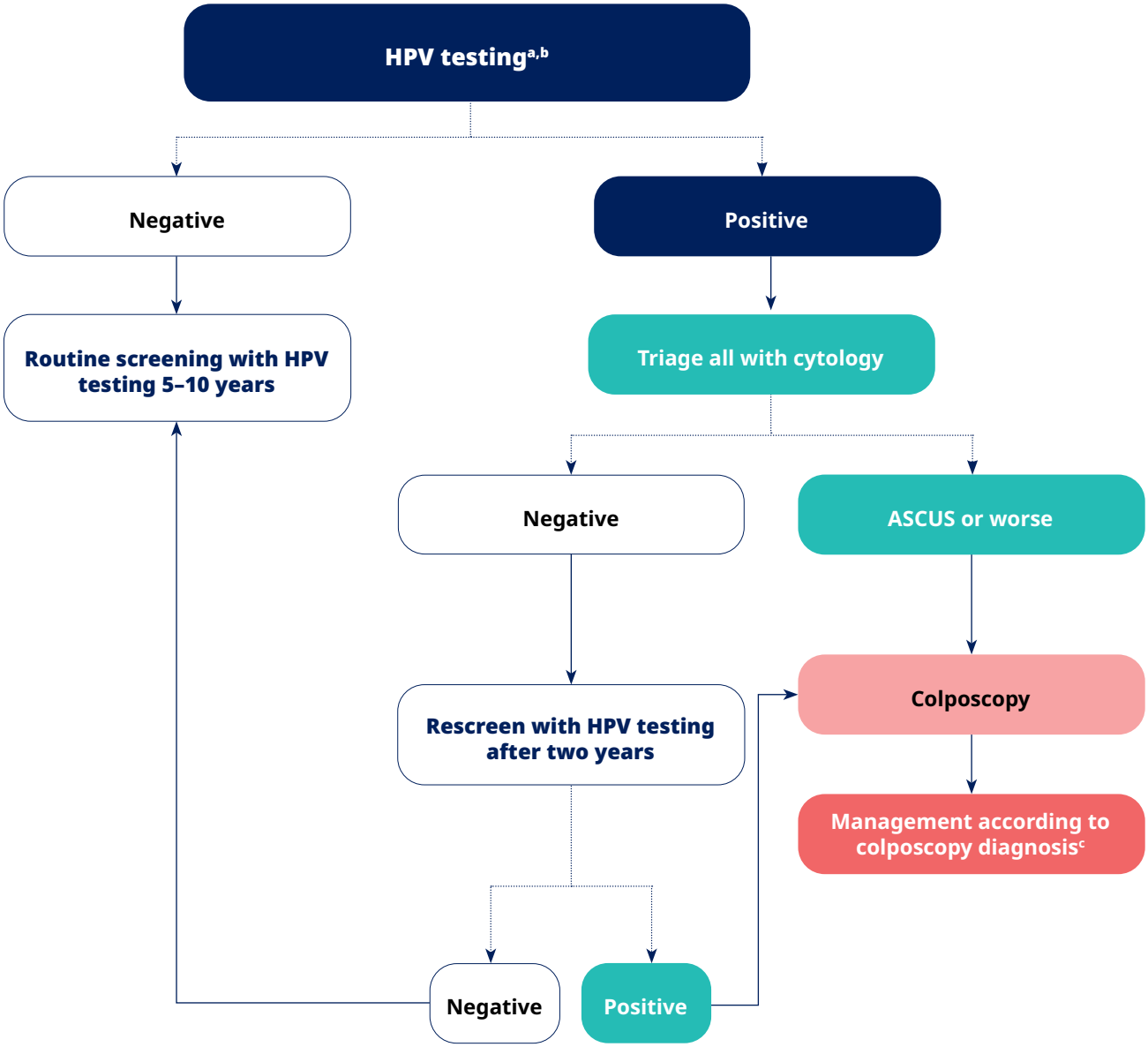


a A positive/negative result can also be obtained by pooling differentiated outputs provided by limited or extended genotyping into a positive/negative result. No genotyping tests can target 8 cHPV types (HPV16, 18, 45, 31, 33, 35, 52, 58) when available.

b Samples collected by health-care provider can be used with HPV DNA or mRNA tests. Self-collected samples can additionally be used with HPV DNA tests.

c Preferably without waiting for histology confirmation.

Algorithm 13. HPV with no genotyping, triaging all women positive for HPV with cytology

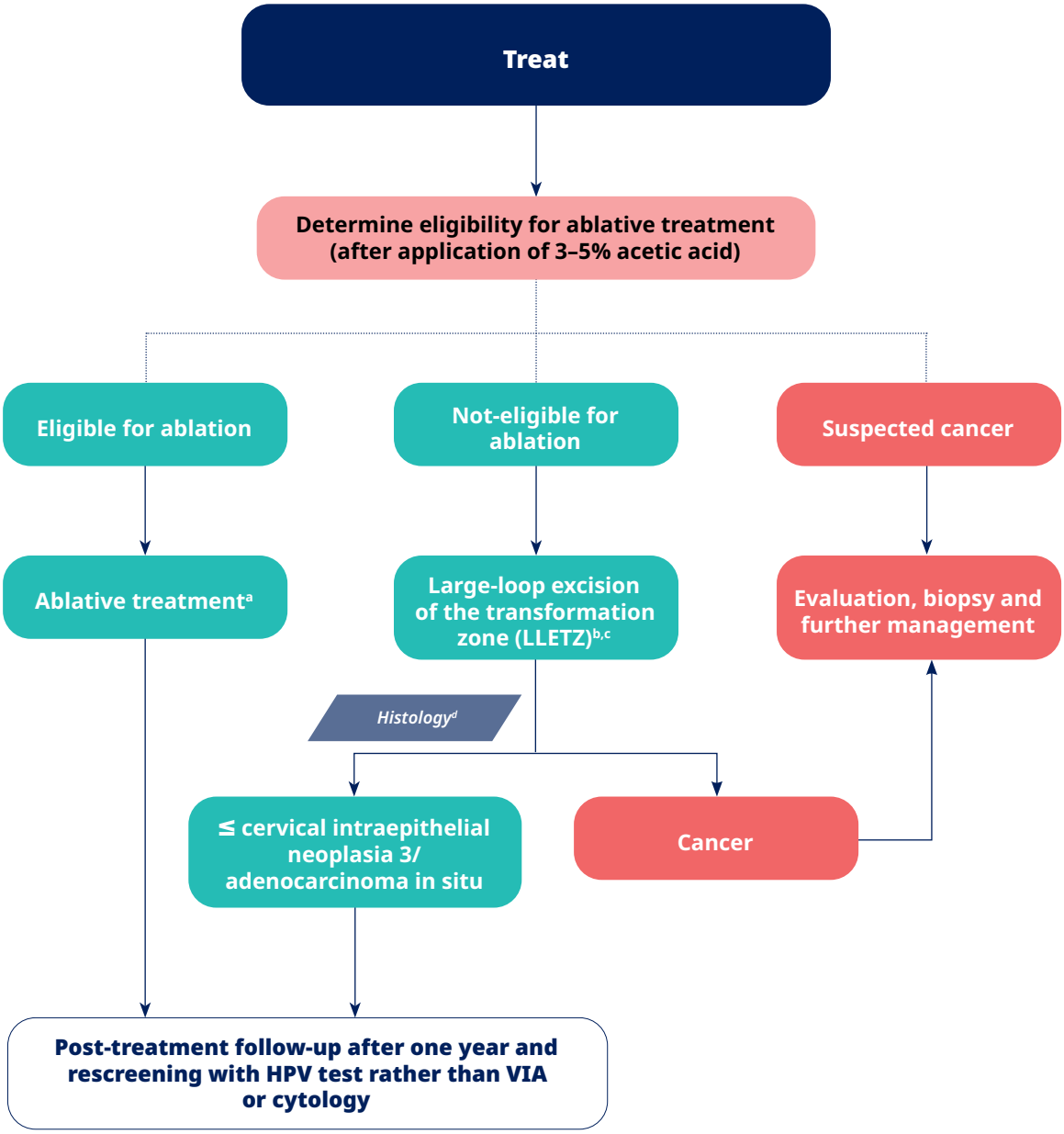


a A positive/negative result can also be obtained by pooling differentiated outputs provided by limited or extended genotyping into a positive/negative result. No genotyping tests can target 8 cHPV types (HPV16, 18, 45, 31, 33, 35, 52, 58) when available.

b Samples collected by health-care provider can be used with HPV DNA or mRNA tests. Self-collected samples can additionally be used with HPV DNA tests.

c Preferably without waiting for histology confirmation.

Algorithm 14. Treatment



a Ablative treatment includes cryotherapy and thermal ablation.

b Cold knife conization if LLETZ not available.

c LLETZ and loop electrosurgical excision procedure indicate the same procedure.

d Histology may not be available in certain settings; women should be advised to attend follow-up after 1 year or to report earlier, if they have any of the symptoms of cervical cancer.

4. Programme implementation considerations

Screening programmes should guarantee that each woman screened can receive treatment when required. The recommendations in this guideline are made under the overarching assumption that countries and programmes have treatment capacity in place before initiating screening. Treatment capacity assumes that ablative treatment (cryotherapy or thermal ablation) is available to treat eligible human papillomavirus (HPV)-positive women as per recommendations, and that large-loop excision of the transformation zone is available to treat HPV-positive women who are not eligible for ablative treatment. When there is not sufficient treatment capacity, countries should build this capacity ahead of initiating screening.

In this guideline, the recommendations are formulated for high and low follow-up capacity, using a 60% threshold that refers to the readiness of the screening programme to complete the next step in the care continuum (treatment, triage, follow-up). A screening programme with high follow-up capacity should have less than 40% lost to follow-up (60% or more attendance) at every step in the care continuum, while programmes with 40% or more lost to follow-up (less than 60% attendance) at any step in the care continuum should be considered as having low follow-up capacity. Countries can use a minimal set of indicators from the *Framework for Monitoring the Implementation of the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem (30)* to estimate follow-up capacity within screening programmes. This can be done by performing calculations using the following indicators:

- the percentage of screened positive women among all those tested that attended the next visit (triage or treatment);
- the percentage of women who tested negative at triage who attended the follow-up visit at two years;
- the percentage of women who were treated who attended the follow-up treatment visit at one year.

If all these percentages are above 60%, countries can assume having high follow-up capacity, and if any are below 60% or no data are available for any of the calculations, countries should consider having low follow-up capacity.

5. Justification

Overall, the certainty of the evidence for these recommendations is low and based on modelled outcomes, as data from longitudinal studies providing screening with extended genotyping and following outcomes of individuals is not yet available. The benefits, harms and cost-effectiveness of the strategies using extended, limited or no genotyping varies based on the follow-up capacity and treatment capacity in countries and regions. Although capacity is on a continuum in practice, the model is based on 90%, 60% and 30% capacity. The Guideline Development Group (GDG) identified that the effects at 60% and 30% capacity were similar and that capacity above 60% may be challenging for many programmes. Therefore a distinction was made between recommendations for settings with 60% and greater follow-up capacity versus less than 60% follow-up capacity. For each of these follow-up capacities, the GDG balanced the reduction in cervical cancer deaths and cervical cancer cases with the number of treatments (and overtreatment) and with cost-effectiveness to make the recommendations.

In settings with high follow-up capacity, extended genotyping, limited genotyping and no genotyping similarly reduced cervical cancer deaths (benefits) but extended and limited genotyping reduced overtreatment more than no genotyping, whether women were treated immediately or triaged. In settings with low follow-up capacity, extended genotyping resulted in a smaller reduction in cervical cancer deaths due to the need for more follow-up visits, except for strategies by which women positive to human papillomavirus (HPV) types in groups 1a, 1b or 1c were treated . Although no genotyping and limited genotyping resulted in more overtreatment, these strategies led to fewer cervical cancer deaths and were more cost-effective.

The GDG agreed that most strategies are probably acceptable and feasible, but it is necessary for programmes to assess their follow-up and treatment capacity. There were no concerns with the potential to create inequities with any strategies.

The evidence available on HPV genotyping in women living with HIV was sparce and therefore was not evaluated, and data from the general population of women might not be applicable to that population. Therefore, no recommendation was made for women living with HIV.

6. Summary of the evidence

The Guideline Development Group (GDG) considered evidence from cross-sectional and longitudinal studies, and from simulation modelling of long-term outcomes (refer to Web Annex A for the systematic review and results of the modelling, and Web Annex B for the evidence-to-decision framework).

Data from six published and unpublished cross-sectional and longitudinal (up to 10 years' follow-up) studies were used to calculate the risk of cervical intraepithelial neoplasia (CIN)3+ lesions over time. Genotyping information of approximately 72 000 women with a carcinogenic human papillomavirus (cHPV)-positive result at HPV-based cervical cancer screening across four continents was pooled in a meta-analysis. The results showed that HPV16 (WHO target product profile group 1a) is associated with a very high immediate absolute risk of CIN3+ (around 18%), exceeding the risks associated with other HPV type groups. In contrast, HPV types belonging to group 1d are associated with a quite limited immediate absolute risk (around 1%) of CIN3+. The HPV type groups 1b and 1c with an intermediate carcinogenic potential show average absolute risks of 7% and 5% respectively. The average absolute risk of CIN3+ after 9 years of follow-up were 24%, 10%, 8% and 2% for groups 1a, 1b, 1c, 1d respectively.

No longitudinal studies were available that measured the effects of identifying specific HPV types through screening, treating affected women and following them over time for important outcomes. Instead, evidence from the dynamic model simulating important outcomes was used. The reduction in cervical cancer deaths and cervical cancer cases, the number of treatments (and overtreatment), and the cost-effectiveness of the strategies were presented, considered and balanced when making the recommendations. Illustrations of the balance of these factors are provided in Fig. 3.2 for high follow-up capacity and in Fig. 3.3 for low follow-up capacity.

Therefore, relying on model evidence alone represents low-certainty evidence. The model predicts that varying intervals from five-yearly to 10-yearly can substantially impact cervical cancer deaths when follow-up rates are very high (90%, in line with 90-70-90 targets), with an expected decreasing trend in the reduction of cancer deaths with longer screening intervals (fewer screens over a lifetime). A similar trend is observed when follow-up rates are high (60%) or low (less than 60%), although with overall fewer reductions and significant variability by choice of approach.

Overall, treating all HPV-positive women or treating those positive for groups 1a, 1b and 1c and triaging group 1d, in particular with colposcopy, resulted in the largest reduction in cancer deaths compared to triaging all HPV-positive women, particularly with cytology.

The results suggest that for five-yearly HPV screening in a setting with very high follow-up capacity (90%) treating all women, using extended genotyping or limited genotyping led to more cervical cancer reductions than triaging all HPV-positive women. For less frequent screening (10-yearly or twice in lifetime), the largest reduction in cancer deaths was achieved when using extended genotyping with treatment of groups 1a, 1b and 1c and triaging of group 1d with colposcopy. Similar results were observed for scenarios with lower follow-up capacity (high if follow-up rates were 60% or more, low if follow-up rates were less than 60%), although triaging all HPV-positive women with cytology resulted consistently in the lowest reductions in cancer deaths.

In terms of pre-cancer treatment, modelling evidence indicates that treating all women who test positive for HPV results in a higher number of pre-cancer treatments than when using extended or limited genotyping (at five-yearly intervals, with similar findings at 10-yearly intervals). The lowest numbers for pre-cancer treatments occurred when:

i. women positive for group 1a or 1b were treated and those positive for group 1c were triaged (and treated if positive on triage), and those positive for group 1d were not treated;

ii. women positive for group 1a or 1b were treated and those positive for other cHPV types were triaged (and treated if positive on triage);

iii. all women who tested positive for HPV were triaged with colposcopy.

Cost-effectiveness was also modelled and varied by follow-up capacity. In high follow-up settings, all primary HPV testing algorithms appeared clustered near the cost-effectiveness frontier. In settings with follow-up rates of 60%, strategies involving treatment of women positive to any cHPV types in groups 1a, 1b and 1c remained close to the frontier, while strategies involving triage of all HPV-positive women (particularly cytology triage) were positioned further from the frontier. When considering 30% follow-up, strategies triaging all HPV-positive women were positioned even further from the frontier and were substantially less cost-effective than strategies involving treatment of all HPV-positive women or those positive for any cHPV types in groups 1a, 1b and 1c.

Based on these results, the GDG agreed that in high follow-up settings, the most cost-effective strategies included extended genotyping where most women were treated (groups 1a, 1b and 1c) and women in group 1d were triaged, while in low follow-up settings, the GDG agreed that the most cost-effective strategy was to treat all cHPV-positive women (independently of genotyping).

Overall, in high follow-up settings, the best balance of reductions in cervical cancer cases and deaths with little overtreatment and best cost-effectiveness will be achieved with the use of extended and limited genotyping. In low follow-up settings, the best balance of reductions in cervical cancer cases and deaths with the least risk of loss to follow-up of HPV-positive women – who could have pre-cancerous lesions progressing to cervical cancer – and best cost-effectiveness will be achieved when all women positive for cHPV are treated.

The findings of the surveys and systematic reviews for values and preferences, acceptability, feasibility and equity were considered when formulating recommendations. No research evidence was found for equity considerations. However, the GDG agreed that providing HPV DNA testing may lead to greater access to screening, but extended genotyping may be limited in some settings. Systematic review of reviews of provider perspectives *(12)* found a lack of understanding about HPV tests and types, and the meaning of a positive result; but in low- and middle-income countries, there is the perception that implementing HPV would increase uptake, lead to more treatment (if same day) and be more sensitive to detect pre-cancerous lesions. The GDG also indicated that programmes may need guidance about how to interpret and assess follow-up and treatment capacity.

7. Dissemination and updating of the guideline

7.1 Guideline dissemination and impact

This guideline will be disseminated using WHO's worldwide and three-level network to make sure that it reaches decision-makers, health workers and programme managers so that the most recent evidence is integrated and accessible for clinical decision-making to prevent cervical cancer. The full dissemination strategy was approved for the second edition and includes dissemination on the official Cervical Cancer Elimination Initiative (CCEI) website and in the next edition of the CCEI newsletter. The recommendations will also be disseminated using the GRADEpro software tool *(31)*, which allows a user-friendly experience of the guidelines and will include all the GRADE evidence profiles and evidence-to-decision (EtD) tables. The EtD tables can facilitate adaptation of the recommendations by national programmes.

WHO headquarters will work with WHO regional offices and country offices to ensure that countries will be supported in the adoption, implementation and monitoring of the guideline. For this purpose, regional workshops and webinars in different languages will be organized to present, discuss and plan guideline adaptation and implementation, as well as to update current national guidelines.

7.2 Guideline update

Evidence on the impact of these tests on important outcomes is accumulating, and syntheses of this evidence are needed. These syntheses will be used in a continual process to develop new recommendations *(32)*.

The Guideline Development Group (GDG) will continue to work with the WHO Secretariat on an ad hoc basis to address the research gaps identified during the process. The GDG anticipates that as data and experience with new screening tests and modalities advance, new recommendations will be needed. During preliminary discussions with the GDG, it was suggested that the recommendations developed for human papillomavirus extended genotyping may require updating in 1–3 years. A subgroup of the GDG has already been identified and will be consulted to inform a timeline for updating as appropriate.

References

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L et al. Global Cancer Observatory: Cancer Today [website]. Lyon: International Agency for Research on Cancer; 2024 (https://gco.iarc.fr/today, accessed 8 March 2024).
2. Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/336583).
3. Human papillomaviruses. IARC monographs on the evaluation of carcinogenic risks to humans, Vol. 90. Lyon: International Agency for Research on Cancer; 2007 (https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Human-Papilloses-2007).
4. de Martel C, Plummer M, Vignat J, Franceschi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. Int J Cancer. 2017;141(4):664–70. (https://doi.org/10.1002/ijc.30716).
5. Comprehensive cervical cancer control: a guide to essential practice, second edition. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/handle/10665/144785).
6. Poljak M, Oštrbenk Valenčak A, Cuschieri K, Bohinc KB, Arbyn M. 2023 global inventory of commercial molecular tests for human papillomaviruses (HPV). J Clin Virol. 2024;172:105671. (https://doi.org/10.1016/j.jcv.2024.105671).
7. WHO list of prequalified in vitro diagnostic products. Geneva: World Health Organization (https://extranet.who.int/prequal/vitro-diagnostics/prequalified/in-vitro-diagnostics).
8. Arbyn M, et al. Validated HPV tests usable in cervical cancer screening on clinician-collected cervical specimens. HPV World [website]. 2024;(270) (https://www.hpvworld.com/articles/validated-hpv-screening-tests:-the-importance-of-validation/).
9. WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. Geneva: World Health Organization; 2013 (https://apps.who.int/iris/handle/10665/94830).
10. WHO guidelines for the use of thermal ablation for cervical pre-cancer lesions. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/329299).
11. Introducing and scaling up testing for human papillomavirus as part of a comprehensive programme for prevention and control of cervical cancer: a step-by-step guide. Geneva: World Health Organization: 2020 (https://apps.who.int/iris/handle/10665/336668).
12. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/342365).
13. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition: use of mRNA tests for human papillomavirus (HPV). Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/350652).
14. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention: use of dual-stain cytology to triage women after a positive test for human papillomavirus (HPV). Geneva: World Health Organization; 2024. (https://iris.who.int/handle/10665/376492). Licence: CC BY-NC-SA 3.0 IGO.
15. Target product profiles for human papillomavirus screening tests to detect cervical pre-cancer and cancer. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/379099).
16. International Agency for Research on Cancer. IARC handbooks of cancer prevention: cervical cancer screening, Vol. 18. Lyon: IARC Press; 2022 (https://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Cervical-Cancer-Screening-2022).
17. Wei F, Georges D, Man I, Baussano I, Clifford GM. Causal attribution of human papillomavirus genotypes to invasive cervical cancer worldwide: a systematic analysis of the global literature. Lancet. 2024;404(10451):435–44. (https://doi.org/10.1016/S0140-6736(24)01097-3).
18. WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/handle/10665/145714).
19. Schünemann H, Brożek J, Guyatt G, Oxman A. GRADE handbook: handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach [website]. GRADEpro; updated October 2013 (https://gdt.gradepro.org/app/handbook/handbook.html).

20. Higgins, J, Thomas J, Chandler J, Cumpston M, Li T, Page M et al., editors. Cochrane handbook for systematic reviews of interventions, version 6.5 (updated 2024). Cochrane; 2024 (https://www.cochrane.org/authors/handbooks-and-manuals/handbook)

21. Brisson M, Kim JJ, Canfell K, Drolet M, Gingras G, Burger EA et al. Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. Lancet. 2020;395(10224):575–90. (https://doi.org/10.1016/S0140-6736(20)30068-4).

22. Burger EA, Smith MA, Killen J, Sy S, Simms KT, Canfell K, Kim JJ. Projected time to elimination of cervical cancer in the USA: a comparative modelling study. Lancet Public Health. 2020. 5(4):e213–e222. (https://doi.org/10.1016/S2468-2667(20)30006-2).

23. Canfell K, Kim JJ, Brisson M, Keane A, Simms KT, Caruana M et al. Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. Lancet. 2020;395(10224):591–603. (https://doi.org/10.1016/S0140-6736(20)30157-4).

24. Hall MT, Simms KT, Lew JB, Smith MA, Brotherton JML, Saville M et al. The projected timeframe until cervical cancer elimination in Australia: a modelling study. Lancet Public Health. 2019;4(1):e19–e27. (https://doi.org/10.1016/S2468-2667(18)30183-X).

25. Kitchener HC, Canfell K, Gilham C, Sargent A, Roberts C, Desai M, Peto J. The clinical effectiveness and cost-effectiveness of primary human papillomavirus cervical screening in England: extended follow-up of the ARTISTIC randomised trial cohort through three screening rounds. Health Technol Assess. 2014;18(23):1–196. (https://doi.org/10.3310/hta18230).

26. Lew J-B, Simms K, Smith M, Lewis H, Neal H, Canfell K. Effectiveness modelling and economic evaluation of primary HPV screening for cervical cancer prevention in New Zealand. PLoS ONE. 2016;11(5):e0151619. (https://doi.org/10.1371/journal.pone.0151619).

27. Lew J-B, Simms KT, Smith MA, Hall M, Kang YJ, Xu XM et al. Primary HPV testing versus cytology-based cervical screening in women in Australia vaccinated for HPV and unvaccinated: effectiveness and economic assessment for the National Cervical Screening Program. Lancet Public Health. 2017;2(2):e96–e107. (https://doi.org/10.1016/S2468-2667(17)30007-5).

28. Shi JF, Canfell K, Lew JB, Zhao F-H, Legood R, Ning Y et al. Evaluation of primary HPV-DNA testing in relation to visual inspection methods for cervical cancer screening in rural China: an epidemiologic and cost-effectiveness modelling study. BMC Cancer. 2011;11:239. (https://doi.org/10.1186/1471-2407-11-239).

29. Simms KT, Steinberg J, Caruana M, Smith MA, Lew J-B, Soerjomataram I et al. Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020–99: a modelling study. Lancet Oncol. 2019;20:394–407. (https://doi.org/10.1016/S1470-2045(18)30836-2).

30. Framework for Monitoring the Implementation of the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem. Geneva: World Health Organization; 2023 (https://www.who.int/publications/m/item/framework-for-monitoring-the-implementation-of-the-who-global-strategy-to-accelerate-the-elimination-of-cervical-cancer-as-a-public-health-problem, accessed on 20 January 2026).

31. GRADEpro. GRADEpro online software platform. (https://www.gradepro.org/).

32. Vogel J, Dowswell T, Lewin S, Bonet M, Hampson L, Kellie F et al. Developing and applying a “living guidelines” approach to WHO recommendations on maternal and perinatal health. BMJ Glob Health. 2019;4(4):e001683. (https://doi.org/10.1136/bmjgh-2019-001683).

Annexes

Annex 1. Guideline groups

Guideline Development Group members

WHO region	Last name	First name	Institution	Country
Africa	Awori	Ruth	Uganda Network of Young People living with HIV	Uganda
Africa	Bitilinyu	Joseph	Government of Malawi	Malawi
Africa	Botha	Hennie	University of Stellenbosch	South Africa
Africa	Bothwell	Guzha	University of Zimbabwe's College of Health Sciences	Zimbabwe
Africa	Chime	Christopher	Institute of Human Virology	Nigeria
Africa	Chirenje	Z. Mike	University of Zimbabwe	Zimbabwe
Africa	Diop	Mamadou	Joliot Curie Cancer Institute	Senegal
Africa	Kamfwa	Paul	Cancer Diseases Hospital; Ministry of Health	Zambia
Africa	Mugo	Nelly	Kenya Medical Research Institute	Kenya
Africa	Muzingwani	Laura	I-TECH Namibia	Namibia
Africa	Nakawala	Karen	Representative from survivors community, Teal Sisters Foundation Zambia	Zambia
Africa	Yuma	Safina	Ministry of Health Tanzania	United Republic of Tanzania
The Americas	Arrossi	Silvina	Centro de Estudios de Estado y Sociedad	Argentina
The Americas	Bento Claro	Itamar	National Cancer Institute José Alencar Gomes da Silva	Brazil
The Americas	Chavez	Karla	Representative from survivors community, Cervivor	Honduras

WHO region	Last name	First name	Institution	Country
The Americas	Darragh	Teresa	University of California San Francisco	USA
The Americas	Matos	Andrea	Ministry of Health	Peru
The Americas	Murillo	Raul	Hospital Universitario San Ignacio	Colombia
The Americas	Ross Quiroga	Gracia Violetta	Bolivian Network of People Living with HIV/ AIDS	Bolivia (Plurinational State of)
Eastern Mediterranean	Walaa	Mahgoub	Focal person, Eastern Mediterranean Regional Office , Federal Ministry of Health	Sudan
Eastern Mediterranean	Ghanbari-Motlagh	Ali	Ministry of Health	Iran (Islamic Republic of)
Eastern Mediterranean	Zafar	Noreen	Doctors Hospital and Medical Centre	Pakistan
Europe	Cuschieri	Kate	University of Edinburgh, Scotland	United Kingdom of Great Britain and Northern Ireland
Europe	Petignat	Patrick	Hôpitaux Universitaires de Genève	Switzerland
Europe	Poljak	Mario	University of Ljubljana	Slovenia
Europe	Torode	Julie	King's College London	United Kingdom of Great Britain and Northern Ireland
South-East Asia	Bhatla	Neerja	All India Institute of Medical Sciences	India
South-East Asia	Lumbiganon	Pisake	Khon Kaen University	Thailand
Western Pacific	Nguyen	Vu Quoc Huy	Hue University of Medicine and Pharmacy	Vietnam
Western Pacific	Saville	Marion	Australian Centre for the Prevention of Cervical Cancer	Australia
Western Pacific	Woo	Yin Ling	International Papillomavirus Society	Malaysia
Western Pacific	Zhao	Fanghui	National Cancer Centre and Cancer Hospital, Chinese Academy of Medical Sciences	China

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Grading of Recommendations Assessment, Development and Evaluation methodologist supporting guideline development

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Modelling team

The modelling team supported the development of these guidelines for women in the general population. The modelling work was performed by the team led by Karen Canfell at Cancer Elimination Collaboration, Sydney School of Public Health, The University of Sydney, Sydney, Australia, using the Policy1-Cervix platform.

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de Sanjosé	Silvia	ISGlobal	Spain
Gravitt	Patti	National Cancer Institute	USA
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Europe	Lasierra	María
Western Pacific	Narayan	Elick
Europe	Lauby-Secretan	Beatrice
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Annex 2. Evidence-gathering teams and guideline task groups

Cumulative risk for cervical intraepithelial neoplasia 3+ and cancer	Modelling simulation for use of human papillomavirus DNA tests in screening according to genotyping level
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Didem Egemen	Michael Caruana
Pegah Rousta	Kate Simms
Nicolas Wentzensen	Daniela Rivas

Guideline Development Group (GDG) subgroup: preparation of evidence for full GDG discussion

Lead: Maribel Almonte

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Karel Blondeel
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Methodologist

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GDG members

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Additional experts

Silvia de Sanjosé
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Nicolas Wentzensen

Annex 3. Declarations of interests

WHO region	Last name	First name	Declared interests	Confidentiality agreement
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Africa	Bitilinyu	Joseph	None	Received
Africa	Botha	Hennie	None	Received
Africa	Bothwell	Guzha	None	Received
Africa	Chime	Christopher	None	Received
Africa	Chirenje	Z. Mike	None	Received
Africa	Chung	Michael	Declared/assessed/ approved	Received
Africa	Diop	Mamadou	None	Received
Africa	Kamfwa	Paul	None	Received
Africa	Mugo	Nelly	Declared/assessed/ approved	Received
Africa	Muzingwani	Laura	None	Received
Africa	Nakawala	Karen	None	Received
Africa	Yuma	Safina	None	Received
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The Americas	Arrossi	Silvina	Declared/assessed/ approved	Received
The Americas	Bento Claro	Itamar	None	Received
The Americas	Chavez	Karla	None	Received
The Americas	Darragh	Teresa	Declared/assessed/ approved	Received
The Americas	Eckert	Linda	None	Received
The Americas	Egemen	Didem	None	Received
The Americas	Gravitt	Patti	None	Received
The Americas	Matos	Andrea	None	Received
The Americas	Murillo	Raul	None	Received
The Americas	Picconi	María Alejandra	None	Received

WHO region	Last name	First name	Declared interests	Confidentiality agreement
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South-East Asia	Lumbiganon	Pisake	None	Received
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Western Pacific	Saville	Marion	Declared/assessed/ approved	Received
Western Pacific	Woo	Yin Ling	Declared/assessed/ approved	Received
Western Pacific	Zhao	Fanghui	None	Received

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