3. FOLLOW-UP, CLINICAL TESTING (with symptoms), HIGH-RISK GROUPS: new test scheme

3.1. Overview

TABLE 2: NEW TEST SCHEME : FOLLOW-UP, CLINICAL TESTING (WITH SYMPTOMS) AND HIGH-RISK GROUPS

FOLLOW-UP			
	Test type	**Frequency reimbursement**	**Notification advising phycisian**
Diagnostic or therapeutic follow-up	Cytology and/or HPV-test (not to be interpreted as cotesting)	One reimbursement/calendar year, both for cytology and HPV-testing	Temporary high-risk with the possibility of testing twice per calendar year (e.g. in HSIL without treatment)
CLINICAL/DIAGNOSTIC			
Clinical testing (with symptoms)[2]	Cotesting (cytology + HPV)	No limitation	Notification with reimbursement of one diagnostic cotest
HIGH-RISK GROUPS			
DES[3] AIS[4]	Cotesting (cytology + HPV)	No limitation Recommendation: yearly	Notification with reimbursement of all requir tests
Others[5] (immunocompromised)	HPV-test or cytology, depending on age	No limitation Recommendation: 3-yearly HPV-test or yearly cytology, depending on age[◊]	Notification with reimbursement of all requir tests

[2] indication: postmenopausal blood loss, abnormal therapy-resistant uterine blood loss, unexplained postcoital blood loss

[3] DES=diethylstilbestrol: synthetic estrogen prescribed to pregnant women between 1938 and 1971 to prevent miscarriage. The daughters of DES-treated women are at higher risk of cancers including cervical cancer.

[4] AIS=adenocarcinoma in situ

[5] UPDATED DEFINITION vs nomenclature: all patients with immunosuppression (HIV positives (CD4 <350/µl or HIV RNA >200 cp/ml), after organ transplantation, after allogenetic stem cell transplantation, systemic lupus erythematosus, congenital primary immune deficiency, or patients under long-term continued immunosuppressants) require more frequent screening, as long as the immunosuppressive treatment is continued.

[◊] Cfr 3.4: Screening, triage and follow-up in high-risk populations

3.2. Follow-up: diagnostic or therapeutic

For diagnostic or therapeutic follow-up, one HPV test and one cytology can be reimbursed per calendar year. The nomenclature refers to '**The scientific guidance for therapeutic follow-up**, validated and published by Sciensano in consensus with the professional and scientific associations concerned', as further elaborated below (cfr. Chapter 5).

The treating physician must respect the scientific guidance when prescribing the necessary test or tests and when switching back to the regular testing scheme. In some cases e.g. HSIL without treatment, six-monthly follow-up may be appropriate. Via notification to the advisory physician of the insurance company (cfr. 3.5; cfr. mammoscreening), reimbursement can be made twice per calendar year. This is a one-off notification that remains valid as long as stricter follow-up is required. The insured then falls into the category of "temporary high-risk".

3.3. Clinical testing (with symptoms)

In case of clinical symptoms, testing can be done at any time outside the screening protocol. The indications are clearly defined in the nomenclature:

- postmenopausal blood loss
- abnormal therapy-resistant uterine blood loss
- unexplained postcoital blood loss

A notification is remitted to the consulting physician of the insured's insurance company specifying the indication, with entitlement to reimbursement for one co-test in the context of the attested clinical episode. A notification form – for each clinical event - will be provided (cfr. 3.5).

3.4. Screening, triage and follow-up in high-risk populations

High-risk groups benefit from more extensive reimbursement subject to notification to the insured's advisory physician at the insurance company. This notification states the indication giving entitlement to unlimited reimbursement of the HPV test and cytology. This is a one-time notification of a permanent nature. A notification form will be provided (cfr. 3.5).

- For DES exposed, an annual cotesting is recommended (this is a diminishing group).
- For persons with AIS, see specific guidance underneath, or cfr. 5.2.7.
- Immunocompromised patients (other high-risk group in Table 2) are recommended to have an HPV test (National Reference Center (NRC) for Human papillomavirus | sciensano.be; *cave: mRNA test not to be used for HIV+ women, cfr. WHO guidance (21)*) every three calendar years (after 30y of age). A more detailed screening schedule specifically for 21-29 years and from 30 years onwards is explained below.

It concerns the following groups: *(UPDATED DEFINITION vs nomenclature) all patients with immunosuppression (HIV positives (CD4 <350/µl or HIV RNA >200 cp/ml), after organ transplantation, after allogenetic stem cell transplantation, systemic lupus erythematosus, congenital primary immune deficiency, or patients under long-term continued immunosuppressants) require more frequent screening as long as immunosuppressive treatment is continued.* These high-risk groups are explicitly mentioned in the nomenclature.

Adenocarcinoma in situ (AIS)

Remark: follow the expert guidance (cfr. 5.2.7).

- Follow-up after LEEP for AIS:
  - Co-test with high endocervical sampling (additional endocervical brushing)
    - every 6 months - for 3 years, followed by yearly - for another 2 years.
  - followed by HPV testing (with reflex cytology, if HPV positive)
    - every 3 years - for 25 years.

  Colposcopy for any abnormal result.

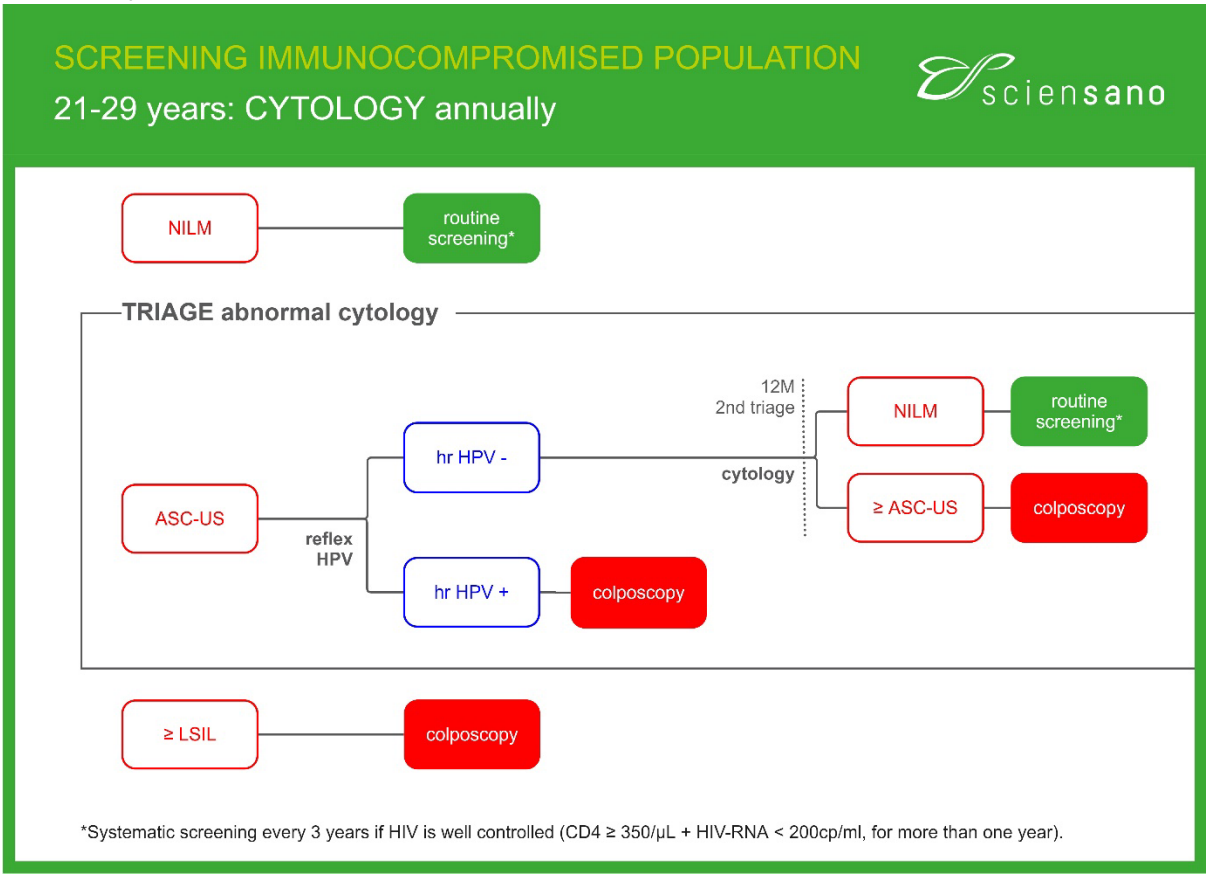
- Follow-up after hysterectomy for AIS:
  - HPV test at 12 and 24 months
  - Continued HPV follow-up
    - every 5 years - for 25 years.

IMMUNOCOMPROMISED WOMEN - 21-29 year: TRIAGE ALGORITHM after a positive cytology screening (22-26)

For immunocompromised women, there was opted to start screening from the age of 21 instead of 25 as compared to the general population. In line with the general population, the screening test is a cytological test.

If Atypical Squamous Cells of Undetermined Significance are present (ASC-US), women should be further triaged using a reflex HPV test, in a 2-step process. This further specifies the risk of a high-grade lesion of the cervix.

FIGURE 3: SCREENING ALGORITHM FOR 21-29 YEAR OLDS, IN AN IMMUNOCOMPROMISED POPULATION **(version 1 - dd 20241015)**



- Immunocompromised women (aged 21-29 in the initial screening round) with a negative cytology result (NILM) are adviced for annual screening. The screening test offered varies according to the woman's age in the next screening round: cytology if under 30 years, an HPV test if the woman is 30 years or older in the meantime.

- Immunocompromised women with an ASC-US result are initially triaged using a reflex HPV test:
  - ➔ If negative for hr HPV, a 2nd cytological triage follows after 12 months:
    - Women with a cytological result of ASC-US or a more severe lesion are referred for colposcopy;
    - Women with normal cytology (NILM) are referred back to the annual screening schedule).
  - ➔ If positive for hr HPV, the woman is immediately referred for colposcopic examination.

- Immunocompromised women with a cytological result of LSIL or a more severe lesion (ASC-H, HSIL, SCC, AGC, AIS, AC) are immediately referred for colposcopic examination.

CAUTION

The screening interval is determined by the immune status for HIV/AIDS patients:

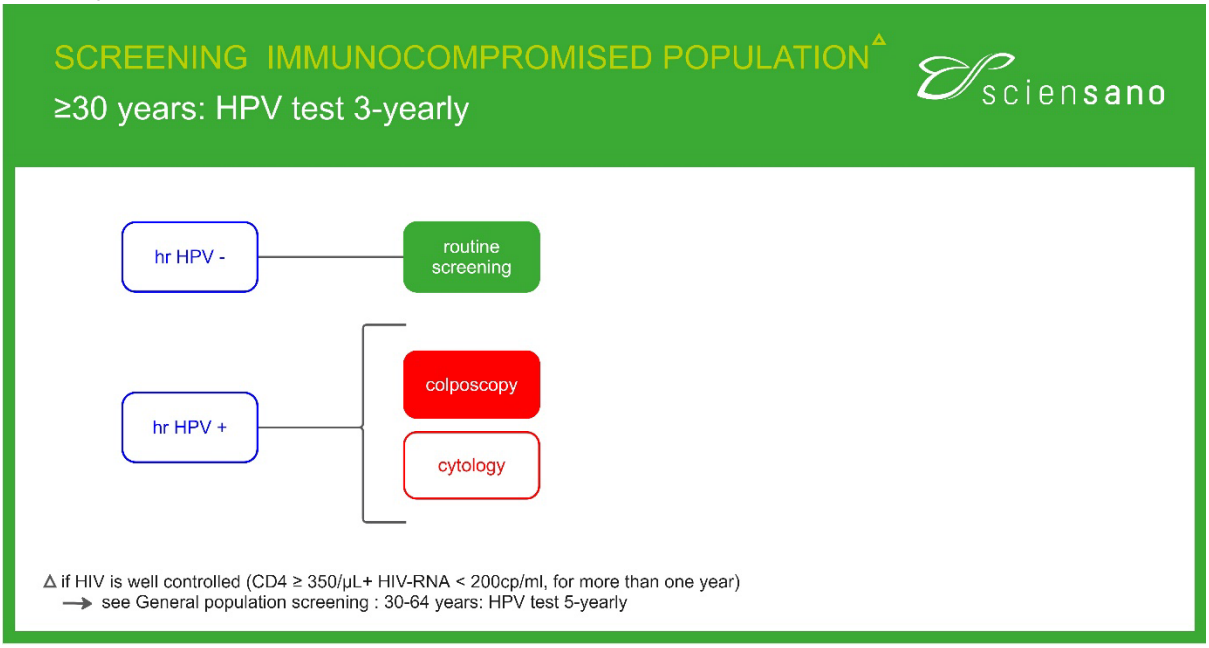
- ➔ **Annual cytology for all immunocompromised patients, uncontrolled HIV patients included (CD4 <350/µl or HIVRNA >200 cp/ml).**
- ➔ **3-yearly cytology for well-controlled - NOT immunocompromised - HIV patients (CD4 ≥350/µl and HIVRNA <200 cp/ml, for more than one year), cfr. 2.3 - general population.**

IMMUNOCOMPROMISED WOMEN - ≥30 year: ALGORITHM after a positive HPV screening (22-26)

A 3-yearly primary HPV test is recommended for immunocompromised women aged 30 years and above. Women are screened until the age of 64 if the last HPV screening gives a negative result and no previous high-grade lesions or cancer were diagnosed.

There is NO triage taken up in this screening schedule, because of the high risk of lesion present.

FIGURE 4: SCREENING ALGORITHM FOR ≥30 YEAR OLDS, IN AN IMMUNOCOMPROMISED POPULATION **(version 1 - dd 20241015)**



- Immunocompromised women aged 30 years and above who test negative on the primary hr HPV screening test are adviced for 3-yearly screening.
- Immunocompromised women who test positive on the primary HPV test for any high-risk HPV type will be referred for colposcopy. Besides colposcopy, a reflex cytology will be performed.

CAUTION

Well-controlled - NOT immunocompromised - HIV patients (CD4 ≥350/µl and HIVRNA <200 cp/ml, for more than one year) aged 30 years and over are NOT covered by the immunocompromiseds screening schedule, but are referred to the screening schedule in the general population for the 30-64 age group, meaning a 5-yearly HPV test (cfr. 2.3).

3.5. Notification advising physician

One and the same nomenclature code is provided for high-risk group testing and testing on clinical indications (591835-591846 for cytology and 553674-553685 for HPV testing), without any age restriction. However, an expert-agreed testing frequency is recommended (cfr. 3.3-3.4). It is the responsibility of the treating physician to comply with the recommended testing frequency and with the recommended test type (cotesting in DES/AIS and HPV testing or cytology in immunocompromised groups, depending on age).

To obtain reimbursement for clinical/diagnostic testing as well as for high-risk groups, the prescribing physician will complete one single standardised notification form and ticks the corresponding indication. This notification puts a brake on any misuse of the clinical/diagnostic nomenclature as a parallel circuit to organised screening.

- For clinical symptoms, as listed in the nomenclature, one diagnostic cotest is reimbursed for the attested clinical indication.
- In high-risk groups, a one-time notification is transferred to the health insurance company where HPV testing and cytology are reimbursed as long as there is a high-risk condition.

A "temporary high-risk" category will also be created for a number of follow-up cases (cfr. 5.2), where follow-up is indicated twice per calendar year instead of once. Via notification to the advising physician of the insurance company, follow-up tests can then be reimbursed twice per calendar year. This is a one-off notification that applies for as long as stricter follow-up is required.

NOTIFICATION FORM - practicalities

French: https://www.inami.fgov.be/SiteCollectionDocuments/formulaire-notification-depistage-cancer-col-uterus.pdf
Dutch: https://www.riziv.fgov.be/SiteCollectionDocuments/formulier-notificatie-baarmoederhalsscreening.pdf

It is the responsibility of the requesting physician to send the notification form to the woman's health insurance fund (mutuality). This is the above paper version sent by regular mail*. The insurance fund (IF) 'flags' the woman when the form arrives (no approval or rejection, the document should only be delivered). This means the woman will be entitled to additional reimbursements and the NIHDI can check based on these notifications for (temporary) high-risk applications and possible misuse. The lab does not get any confirmation, but can provide an option on their application form where the requesting physician can tick that the notification form was sent to the IF.

The pseudocodes on the notification form are only for internal use at the health insurance fund/NIHDI and should not be used or passed on to anyone else.

**addresses from the mutualities can easily be found here:*
https://www.inami.fgov.be/fr/professionnels/autres-professionnels/mutualites/contactez-les-mutualites
https://www.riziv.fgov.be/nl/professionals/andere-professionals/ziekenfondsen/contacteer-de-ziekenfondsen