Guidance Note 14
HPV reflex testing in primary care

Rationale for HPV reflex testing
The aetiological role of HPV infection among women with cervical cancer is now clearly established. The recognition of the fact that, in the absence of viral DNA, cervical cancer does not develop is of considerable practical importance within a screening Programme. Follow up studies of screened women with and without cervical abnormalities have indicated that the continuous presence of HR-HPV is necessary for the development, maintenance and progression of CIN disease. Conversely, women found to be HR-HPV negative with cytology of either ASCUS or LSIL are highly unlikely to develop CIN in the intervening recall period.

HPV testing within CervicalCheck
Since 2012 CervicalCheck has used HPV testing in colposcopy services to allow women categorised as low-risk for development or recurrence of CIN to be discharged without the requirement for annual surveillance smear tests for up to 10 years. (Refer to Guidance note 7 for further details).

Since April 2015 CervicalCheck uses HPV testing as an adjunct test when low-grade abnormalities (ASCUS or LSIL) are detected on cytology specimens. The laboratory tests these samples for the presence of certain types of the HPV virus (hr-HPV) which are associated with CIN and cervical cancer. The additional information provided by this reflex HPV test is used to determine the recall recommendation for these women.

The benefits of adjunct HPV testing in the presence of low grade cytological abnormalities (ASCUS / LSIL) include:
- reduction in unnecessary repeat tests for women who are HPV negative
- expedited referral to colposcopy for women who are HPV positive and who may require treatment.
- reassurance for those women who are HPV negative that the cellular abnormalities in the smear test are not considered clinically significant.

What do the test results mean?
- The test identifies HPV high-risk types (16,18, 31,33,35,39,45,51,52,56,58,59,66, & 68) at clinically relevant levels.
- Women who test negative for these types of HPV will be given a recommendation of ‘routine recall’ 3 years or routine recall 5 years. This reflects the low risk of developing high grade CIN in those intervals.
- Women who test positive for these HPV types will be given a recommendation of ‘refer to colposcopy’. They will have a colposcopy to determine if treatment is required.

It is important to remember that HPV infection is usually a self-limiting infection and many women referred to colposcopy do not have CIN requiring treatment and therefore can be safely recalled in three years.

Smeartaker role and responsibilities
- Give a clear explanation of HPV infection and the rationale for HPV testing at the time the smear test is taken (note: every smear test has a potential for reflex HPV testing).
- Dispatch the smear sample to the laboratory in 5 working days.
- Provide counselling and give a clear explanation of the screening test results and management recommendations, where needed.
- Adhere to CervicalCheck recommendations for the management of screening.
- Refer the woman to colposcopy as indicated.

Important points for counselling woman about HPV infection and testing
- HPV infection is very common and most sexually active people will have been exposed to it at some time in their lives.
- Most infections are cleared by the immune system in less than 2 years.
- Some types of HPV infections, if not cleared by the immune system, are associated with the development of changes in the cells of the cervix. When these types of HPV are found, a further examination at the colposcopy clinic is required.
- The vast majority of HPV infections do not lead to cervical cancer. Cervical cancer is a rare outcome of a very common viral infection.
• Regular screening and attending colposcopy appointments (when advised) is key to prevention of cervical cancer.
• Vaccinated women still require regular screening. Current HPV vaccines only protect against the HPV types responsible for 70% of cervical cancers.
• Women who are on annual surveillance post-colposcopy treatment may be returned to routine recall if their smear test shows a low grade abnormality and tests negative for HPV, thus superseding earlier colposcopy recommendations.

Sample text for counselling women about their HPV test result

If the test results are ASCUS/LSIL, HPV Negative
“... Your sample was tested for the types of HPV that are associated with cervical cancer, and this test was negative. This is very reassuring and a recall for screening in (3 or 5 years) is appropriate”

If the test results are ASCUS/LSIL, HPV Positive
“... An early colposcopy, where a specialist can take a closer look at the cervix will determine whether the cervix has developed any significant changes. If changes are detected you will be managed in colposcopy until a treatment is performed or the changes get better by themselves. If no changes are found, you will be discharged back to me for your cervical screening. Most HPV infections will have resolved by the time the next smear test is due in three years”

The explanation given by the smear-taker should include why they are being referred to colposcopy, how long they can expect to wait, and what investigations may happen there.

CervicalCheck letters to women

• When no abnormality is detected on smear test, women are advised of their result in the CervicalCheck letter. These women will not have had a reflex HPV test.
• When the hr-HPV test is negative, women are advised to contract their smear-taker in the CervicalCheck letter. The letter tells them when their next screening test is due.
• When women have abnormal results requiring colposcopy, they are advised to contact their smear-taker in the CervicalCheck letter. This includes women whose smear tests have been reflex tested for HPV and are found to be HPV positive.
• The About Your Smear Test Result leaflet is enclosed with all letters advising women that the result of the test has been received by the doctor or nurse who took the smear test.

References

Resources
1. HPV and Cervical Screening Fact Sheet
2. Cytology Terminology Table
4. CervicalCheck triage will lead to earlier detection, Drs. G Flannelly & C. Burns, GP Forum. April 2015 (reproduced with the kind permission of Forum, Medmedia Ltd.)
5. eLearning module (accredited with CPD points) on the Screening Service learning portal. It is accessible from the health professionals section of CervicalCheck website.
Process Flowchart for HPV reflex testing (HPV triage)

**Screening**

- Smear test
  - ASCUS or LSIL?
    - Yes: Reflex HPV test
      - HPV subtypes detected: Referral to colposcopy
        - Attendance at colposcopy service
          - Colposcopy and/or biopsy
            - CIN2 / CIN3: Treatment
              - Management of post-treatment women
            - CIN1: No treatment
              - Management of women with low grade abnormalities
            - No CIN: Discharge: re-call in 3 years*
              - *regardless of age
      - HPV subtypes not detected: Routine re-call in 3 or 5 years*
        - *dependent upon age & screening history
    - No: No change in management for negative, high grade or unsatisfactory cytology

*No change in management for negative, high grade or unsatisfactory cytology
*dependent upon age & screening history

*regardless of age