CervicalCheck triage will lead to earlier detection

The CervicalCheck programme is introducing a new triage process for women with low grade abnormalities, write Grainne Flannelly and Criona Burns

THIS MONTH, CERVICALCHECK WILL INTRODUCE a change to improve the screening process for women found to have low-grade abnormalities (LSIL and ASCUS). The introduction of HPV triage will provide timely reassurance and earlier detection of cell changes which require treatment.

What will change?

When low-grade cytological abnormalities are detected in the smear test, the programme laboratories will test the residual sample for infections with certain types of the human papillomavirus (HPV) which are more likely to be associated with CIN.

This change in policy is called HPV triage. The additional information provided by this test will be used to plan the next step in the programme for these women.

Why is this change needed?

HPV triage should make cervical screening more efficient and effective for women with low-grade cytological abnormalities. Low-grade abnormalities are a common finding and were present in 6.96% of CervicalCheck smear tests in 2014. Most of these women do not have high-grade CIN or AIS and the low-grade changes resolve spontaneously over time.

Up to now these women have been managed with repeat smear tests at shorter intervals, with referral to colposcopy only if these changes persisted. The need for multiple repeat tests can be worrying and inconvenient for women and can be associated with a lack of compliance and the risk of default. There is also the possibility of a delay in the diagnosis and treatment of women who have high-grade CIN/AIS or indeed the tiny minority of women who have early cancerous changes.

The use of a test for certain HPV infections will provide real time information and reassurance for women who have a very low risk of cancer, reducing the need for repeat smear tests. A positive HPV test will result in more women having to have a colposcopy but it is expected that as many as 50% of women assessed at colposcopy will have no CIN detected. These women can be reassured that they have a low risk (< 5%) of developing CIN within three years. Up to now these women would have had multiple follow-up visits before being discharged. This change is informed by new evidence from the UK which confirms that these women can be safely discharged from colposcopy and advised to have a repeat smear test in the community in three years.

What additional information is provided by HPV triage?

Women without an infection with these types of HPV (negative result) are at a very low risk of developing CIN in the near future. These women will be recommended to have a repeat smear test in three or five years depending on their age. Women who test positive for these HPV types will be referred for a further examination at a CervicalCheck colposcopy service. This is to check whether these women have already developed high-grade CIN or AIS.

How will this change affect CervicalCheck stakeholders?

Women

All women who have a CervicalCheck smear test sign the consent section of the cervical cytology form. The information sheet attached to the form will inform them of the potential need for a HPV test in some circumstances. Women with a smear test result which is not LSIL or ASCUS will be managed as before.

Women with LSIL/ASCUS will get a letter to make contact with their smeartaker. A combined result will be issued to the smeartaker. This will focus on the next step – referral to colposcopy or routine screening. It is likely that more women will be referred to colposcopy for assessment. Women who have a confirmed abnormality on the cervix will be managed accordingly within colposcopy. Women who have been assessed and who have no confirmed abnormality will be reassured and discharged with the advice that they need a repeat smear test in three years. The cytology and HPV results will be communicated with the follow-up recommendation in the usual way.

Smeartakers

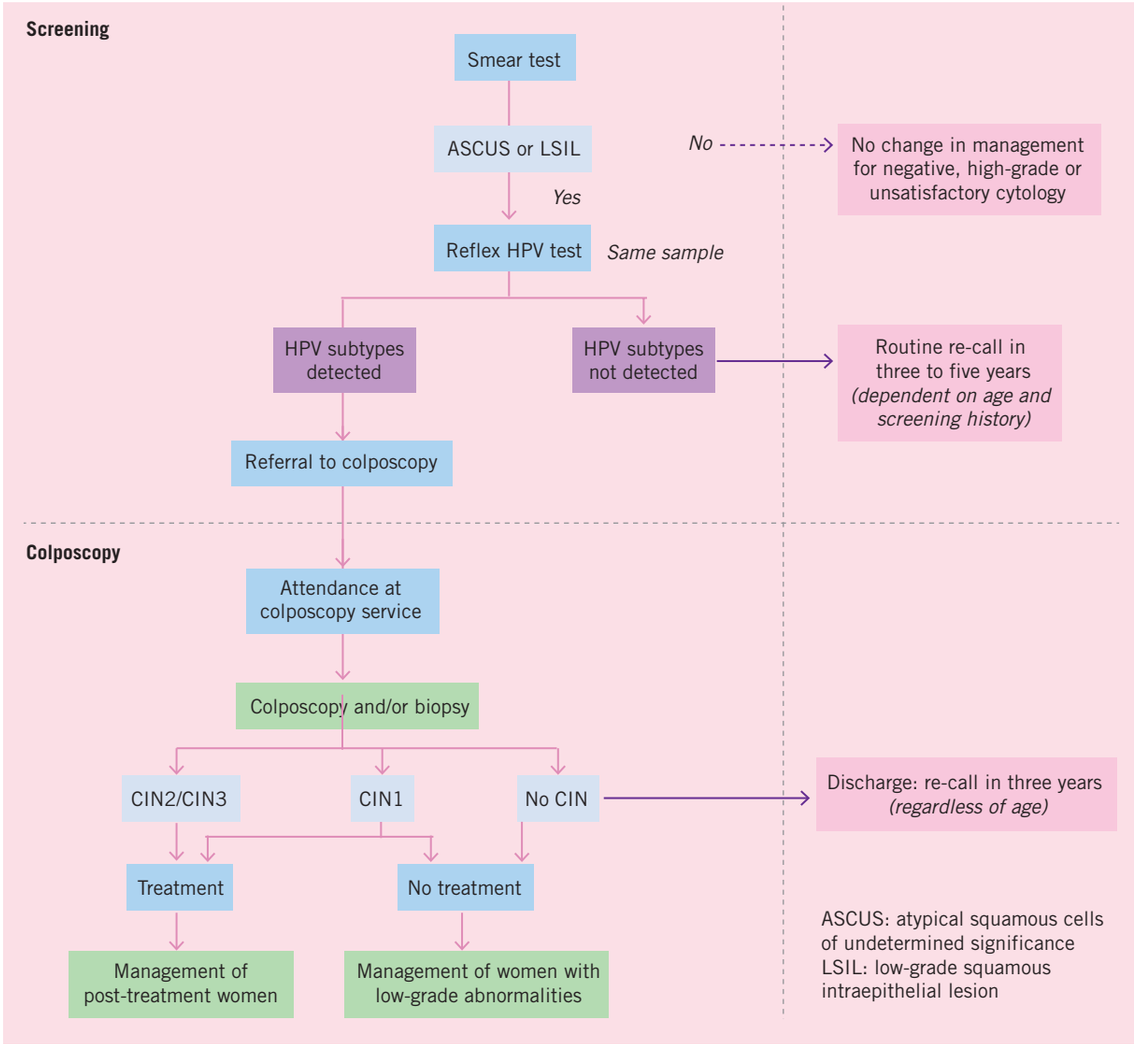
Smeartakers have a crucial role to play in the communication of the smear test result to the woman. Up to now this has involved the communication of the cytology result alone. The communication of the HPV result will be a relatively new experience for most smeartakers as to date HPV tests have been performed in colposcopy services only.

CervicalCheck is developing educational materials and communication tools and has already distributed a document entitled 'HPV Information' in November 2014 to familiarise smeartakers with HPV testing and to help them explain the process to women.

This year's clinical updates delivered by the CervicalCheck screening training unit will focus on HPV triage in order to support smeartakers who deliver cervical screening in primary care during the changes to and implementation of HPV triage in 2015.

Smeartakers should be aware that greater numbers of referrals to colposcopy may result in longer waiting times for women. While CervicalCheck will commission an additional 3,250 slots for new referrals, it is anticipated that there may be pressure in some geographical areas during the settling-in period.

Figure 1: HPV triage of low-grade abnormalities



The provision of sufficient quality-assured colposcopy capacity has been one of the key priorities of the CervicalCheck programme with a growth in new patient slots from a pre-programme national allocation of 9,000 slots to a national allocation of 16,500 slots since 2008. This has resulted in significant improvements in the waiting times for colposcopy for women.

What is the scientific basis for HPV triage?

There are many different types of HPV virus and while 40 types affect the mucous membranes, only some 15 types are associated with the development of CIN.[1] Infections are very common, with the majority of women infected during their lifetime, 43% within 18 months of starting sexual activity.[2,3] Most infections however, are transient with the majority clearing within 18 months.[4] It is thought that many cases of low-grade cytological abnormalities and even CIN grade 1 represent physical manifestations of these transient infections with the resolution of these abnormalities mirroring that of the infection with HPV.[5]

Persistent infections (present for longer than 18 months) can lead to integration of the virus into the cervical cell nucleus and the development of high-grade lesions.[6] Transition from viral integration to invasive cancer is a slow process with a timeframe of up to between 10 and 15 years.[7] The use of HPV triage for women with ASCUS or LSIL has been evaluated in a recent meta-analysis against the traditional approach of repeating the cytology at an interval of six or 12 months.[8] HPV triage was found to be a more sensitive modality with the identification of more cases of high-grade CIN but was not very specific with a maximum positive predictive value of 33% for CIN2+.

Communication of results of screening tests has long been identified as a challenge, particularly where the results are not reassuring. The addition of information which includes HPV makes this process even more important.

Changes to be considered regarding existing HPV testing strategies in parallel with triage

The follow-up of women referred to colposcopy has changed significantly during the past two years. Combined smear and HPV tests have been in use both for post-treatment surveillance as well as for the management of women of uncertain risk in CervicalCheck colposcopy services. These changes have helped to identify women who are at low risk of CIN and the use of the high negative predictive value of HPV testing has facilitated earlier discharge of women to the community.

New information is now available which provides a context for a positive HPV result. The high chance of resolution of the infection following a single positive test as well as the low risk of CIN3 in the next four years suggests that women who have had a satisfactory assessment and have no CIN detected can be discharged from colposcopy after the first visit. It is estimated that this could represent up to 50% of women with LSIL/ASCUS. This is because HPV infection alone is not sufficient to cause CIN – the HPV DNA must integrate into the cell's nucleus to facilitate the production of cellular abnormalities. We now know that this integration happens only in a minority of cases. Information from the NHS cervical screening programme in England has shown that only 4.5% of women with LSIL/ASCUS who were HPV positive developed CIN3 within the subsequent four years.

HPV testing in the management of uncertainty

Since March 2014 CervicalCheck colposcopy services have been using a combined smear and HPV test to allow a more accurate definition of the risk of high-grade CIN. Women with results categorised as low risk (HPV negative and less than LSIL) were eligible for discharge from colposcopy and a return to routine screening. During the first nine months, 9,012 women had this combined test performed. No prior treatment was recorded in 7,030 women while a treatment more than 24 months earlier was recorded for 1,982. The test was categorised as low risk in 5,441 (60.4%) women, meaning that these women were suitable for discharge to the community for routine screening. This allows more effective use of resources as well as reducing unnecessary anxiety for women and the risk of default. A repeat colposcopic assessment was recommended in 3,571 (39.6 %) and the outcome for these women is being evaluated. These included women with LSIL who tested negative for HPV.

HPV testing in management of women following treatment for CIN

CervicalCheck provides treatment at colposcopy for high-grade cervical intraepithelial neoplasia (CIN) to over 4,000 women annually. Traditional follow-up for these women has included annual cytology for 10 years because of the increased risk of recurrence. New strategies including testing for subtypes of the human papillomavirus (HPV) allow a more accurate definition of this risk. Post-treatment HPV testing was introduced as part of CervicalCheck in 2012 with combined cytology and HPV tests at six and 18 months following the treatment. Women with results categorised as low risk (HPV negative and cytology of less than LSIL) were eligible for a return to routine screening.

More detailed information about HPV triage is available via **www.cervicalcheck.ie** in the health professional section. Clinical updates in eight regional locations are also available as an elearning module. The CervicalCheck programme office can be contacted at Freephone 1800 45 45 55. Further information on cervical screening is also available through online e-learning courses (accredited with CPD points – see CervicalCheck website).

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References available on request