HPV Primary screening

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In July 2016 the then Public Health Minister Jane Ellison announced that Human Papilloma Virus (HPV) primary screening would be implemented into the English cervical screening programme. HPV primary screening involves testing all cervical samples for HPV and undertaking cytology only on samples that are HPV positive. Nurses and Primary Care staff involved in cervical screening will therefore benefit from an understanding of the background to the introduction of HPV testing and the potential benefits of its introduction as a primary test in cervical screening.

Women aged 25-49 (24 ½ in England) are invited for cervical screening (previously referred to as smear test) every three years and screening is undertaken every 5 years in women aged 50-64. Cervical screening can detect early changes in cervical cells, which if left undetected and untreated could lead to cancer of cervix. It is estimated that cervical screening saves 4500 lives annually (NHSCSP, 2016). Cancer of the cervix is the twelfth most common cancer in women in the UK.

Background

The decision to implement HPV primary screening in the cervical screening programme follows on from the report of the ARTISTIC Trial (A randomised trial of HPV testing in primary cervical screening) (Kitchener et al 2009). The ARTISTIC trial was conducted in six pilot sites throughout England and investigated HPV as a primary screening test. The trial results provided evidence for the use of HPV testing in the cervical screening programme either in addition to cervical cytology or as a stand-alone test. The UK National screening programme (UKNSC) advises ministers and the NHS in the 4 UK countries about population screening and in February 2016, the UKNSC recommended the cervical screening programme should adopt HPV as a primary screening tool and sought ministerial approval, which was granted in July 2016.

Cervical screening identifies apparently healthy women who may be at increased risk of developing cervical cancer, early detection of cell changes enables better treatment and prognosis. A cervical screening test involves the visualisation of the cervix using

a speculum and obtaining a sample of the cervical squamo-columnar junction. A trained and competent registered professional can provide the appropriate communication, empathy, skill and assurance required for the individual woman to have confidence in the test (Public Health England, 2016).
Nurses and Primary Care staff involved in cervical screening will therefore benefit from an understanding of the background to the introduction of HPV testing and the potential benefits of its introduction as a primary test in cervical screening.

Currently, cervical screening involves the detection of abnormal epithelial cells from a sample of exfoliative cervical cells obtained using a cervexbrush and liquid based cytology (LBC) for sample saving. The discovery of the role of HPV in the development of cervical cancer in the early 1990's (Walboomers et al 1999) led to the inclusion of HPV testing in routine cervical screening in 2015 with HPV testing of samples in women with borderline or mild dyskaryosis (this is referred to a HPV triage). Women who test positive for HPV are referred to colposcopy.

HPV Primary Screening

Liquid-based cytology (LBC) was implemented in the UK in 2008 as a means for cervical sample saving, for transfer to a laboratory for testing; HPV primary screening can be conducted on an LBC cervical sample and a variety of tests are available for this purpose. Most of the tests are based on the detection of viral DNA. HPV DNA testing has been developed because a high-risk HPV positive test provides the basis for further investigation (Colposcopy) and possible treatment.

HPV is the term used to describe a collection of viruses that affect the skin and moist membrane that line the body's orifices such as the cervix, anus, mouth and throat. 99.9% of cervical cancers are caused by HPV (Wallboomers et al,1999). Anyone who is sexually active can contract HPV through contact with someone who already has the virus. Most people are infected with HPV at some point in their lives and HPV infection is so common that it can be considered a normal consequence of having sex. Most people are infected with HPV at some point in their lives. However, there are around eight high-risk types of HPV that are responsible for 90% of all cervical cancers. These are referred to High-Risk HPV types. Within the high-risk group, types 16 & 18 are responsible for about 70% of cervical cancers. The remaining 20% of leisons are associated with HPV types 31,33,34,45,52 & 58 (DeSanjose 2010). If undetected and left untreated these changes can lead to cervical intraepithelial neoplasia (CIN) and cancer of cervix. (see diagram 1).

With the introduction of HPV primary testing women who are HPV negative will be returned to routine recall (3 or 5 yearly depending on age). A result which is HPV negative places a woman at very low risk of developing cervical cancer (Walboomers et al, 1999). Diagram 1 illustrates the process from initial test to outcome.

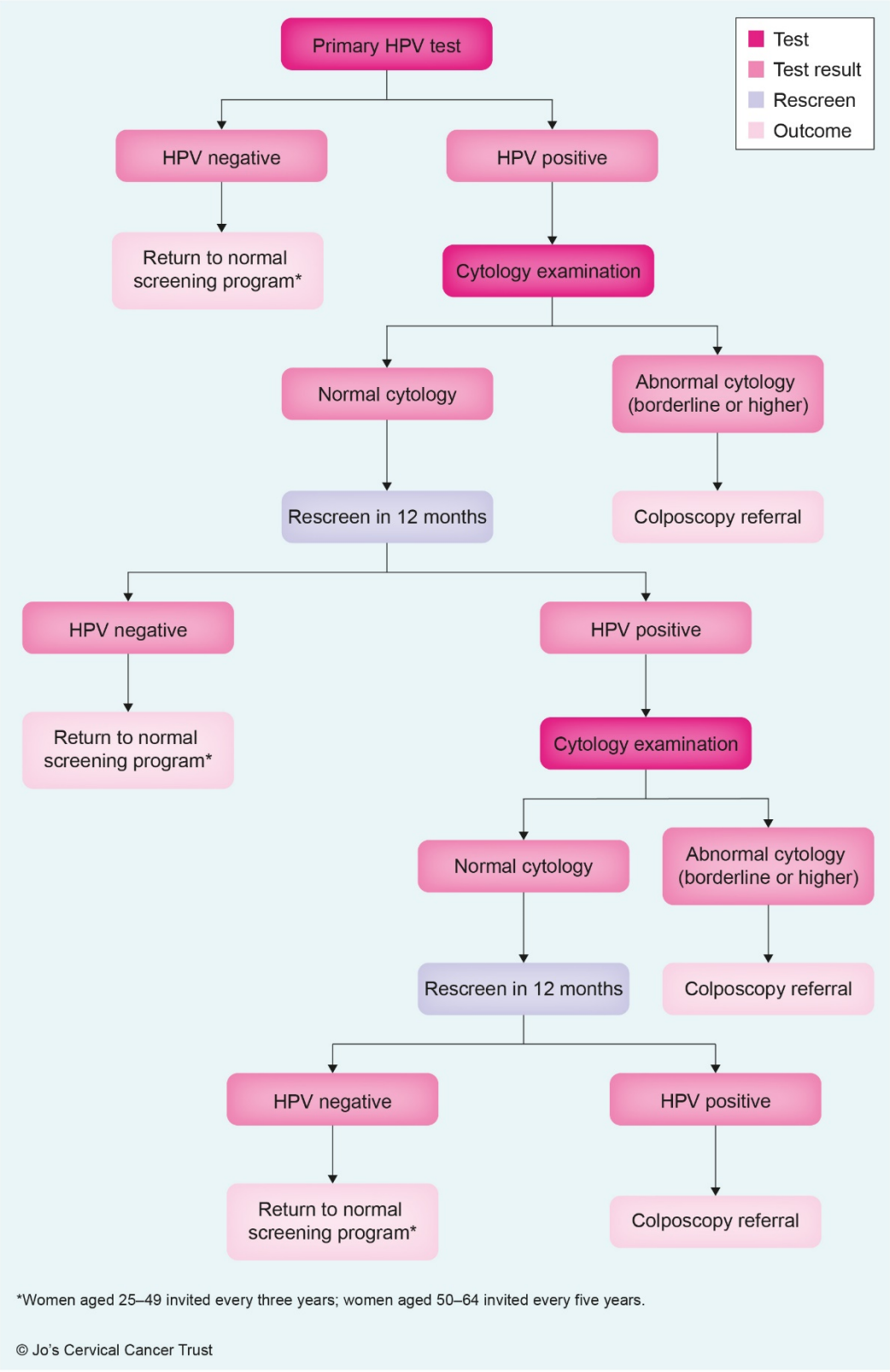

Diagram 1 Reproduced with permission from Jo's cervical cancer trust.

The rationale for the introduction of HPV Primary screening as opposed to cytology is based on the greater sensitivity of the HPV to detect CIN and to address the inclusion of women who have received HPV vaccination (Kitchener, 2105). In the UK, HPV

primary prevention through vaccination of girls aged 12-13 commenced in September 2008 alongside a 3 year catch –up programme to target girls up to 18 years. The uptake rates for HPV vaccination in the UK has been high with 90% of girls aged 12-13 completing the course (Public Health England, 2013).

Results from the ARTISTIC trial

The ARTISTIC trial commenced in 2001 and involved six pilot sites in Manchester, Stockport, Wigan, Leith, Salford and Trafford and investigated the role of HPV testing within the national screening programme. The study population comprised of 25,000 women aged 20-64 who were attending general practices for routine cervical screening and who consented to having the HPV test (Kitchener & Almonte, 2006).

Moss & Gibney (2015) in their evaluation report of the ARTISTIC trial to the national screening committee collated the data received from all sites on HPV primary screening for samples received up to 31.10.2014. The data include a total of 167,919 primary HPV tests and 331,995 primary cytology samples. The pilot sites were partially converted to primary HPV screening and results for primary HPV testing are compared to those for primary cytology screening in the same sites.

Of the study population, 12.9% (21682) tested positive for HPV and subsequent colposcopy indicated that 2.9% (4841) had borderline dyskaryotic changes and a further 2.3% (2232) had dyskaryosis which was moderate or worse. They concluded that baseline screening by HPV primary testing achieves a higher detection rate for CIN 2 or worse.

Higher HPV positive rates were detected in women in the 25-29 age group. However HPV positivity will decline once the HPV vaccinated cohort reaches screening age from 2016 onwards (Moss & Gibney,2015). HPV vaccination was introduced in 2008 and is offered to girls aged 12-13 years, and included a catch-up programme for girls up to age 18 at the time of its introduction.

Kitchener (2015) reported that high-risk HPV testing is superior to cytology in terms of sensitivity for high grade cervical intraepithelial neoplasia (CIN). The risk of CIN 3+ developing in women found to have HR-HPV infection could be determined from the ARTISTIC trial data. HPV negative women had a 0.28% risk of CIN3+ over a 6 year period compared with women with High-risk HPV 16 which was associated with a 100 fold increase in the development of CIN3+.

Increase in screening intervals

Ronco et al (2014) in a follow-up study of the analysis of four European randomised controlled trials which compared HPV based screening for cervical cancer with cytology-based screening recorded that the incidence of cervical cancer was lower 5.5 years after a negative HPV test than 3.5 years after a negative cytology result,

indicating that 5 year intervals for HPV screening are safer than 3-year intervals for cytology.

Likewise data from the ARTISTIC trial specifically, indicated that 6 yearly screening until age 50 and 10 yearly screening over 50 would be as effective as the current three yearly (women aged 25-49)and five (women age 50-64) yearly screening intervals, thus potentially allowing women to be screened less frequently in the future.

Other potential benefits of HPV testing

Uptake of cervical screening continues to decline throughout the UK. In March 2016 the uptake of cervical screening in women aged 25-64 was 72.7%. This compares with 73.5% in 2015. Women in the 25-49 age group have the lowest attendance at 70.2% compared with 71.5% in 2015. Several reasons are quoted for non-participation including fear of the procedure, embarrassment, lack of clinic provision, lack of understanding of the risks of cervical cancer and the purpose of cervical screening (Kothari, 2016).

HPV testing can be carried out on a self-taken sample and HPV primary testing using self-sampling kits is a strategy that might encourage a number of women who have not attended for screening to gain information about their potential risk. Self-collected samples are already in use in the bowel screening and chlamydia screening programme. Racey et al (2013) in their systematic review of eight European studies of under-screened women found that compliance with HPV self-testing was significantly higher that with cervical cytology. However, with regards to HPV self-sampling Cadman et al (2015) in a study of Hindu women reluctant to attend for screening noted that efforts would need to be made to build the confidence of women regarding the quality of the sample they could collect.

Changes to Practice

Cervical screening is a well-established programme and new developments have been incorporated successfully into the programme since its inception in 1988. The introduction of HPV primary screening will require practitioners involved to be knowledgeable regarding the background and rationale for the planned changes in cervical screening provision and to be able to advise women about the changes to the programme and how this will impact on individual screening experiences.

The introduction of primary HPV screening will require significant changes to the existing screening programme. Public Health England (2016) have acknowledged that many aspects remain to be discussed including the introduction of a new cervical screening pathway taking into account the individual woman's screening result. New

IT systems will be required and Laboratory staff training and future laboratory workforce requirements will need to be considered.

As practitioners we should endeavour to remain informed about the proposed changes.

References

Cadman l Ashdown-Barr L Waller J Szarewski A 2015 Attitudes towards cytology and human papillomavirus self-sample collection for cervical screening among hindu women in London, UK: a mixed methods study Journal of Family Planning and Reproductive Health Care January 2015;Vol 41:Issue 1

DeSanjose S Quint WGV Alemany L Geraets DT Klaustermeier JE Lloveras B Tous S Felix A et al 2010 Human papillomavirus genotype attribution in invasive cervical cancer:a retrospective cross-sectional worldwide study. www.thelancet.com/oncology Vol 11 November 2010

Kothari, A 2016 *Strategies for increasing uptake of cervical screening.* Practice Nursing, 27 (11). pp. 546-548.

Racey CS, Withrow DR,Gesink D. 2013 Self-collected HPV testing improves participation in cervical cancer screening:a systematic review and meta-analysis. *Can J Public Health 2013;104:e159-66*

Ronco G,Dillner j, Elfstrom KM, Tunesi S, Snijders PJF, Arbyn M, Kitchener H, Segnan N, Gilham C, Giorgi-Rossi P, Berkhof J, Peto J, Meijer CJLM, and the International working group. 2014 Efficacy of HPV-based screening for prevention of invasive cervical cancer:follow-up of four European randomised controlled trials.*Lancet 2014;383:524-32*

Kitchener HC, Almonte M, Gilham C, Dowie R, Stoykova B, Sargent A, Roberts C, Desai M Peto J. 2009 ARTISTIC: a randomised trial of human papillomavirus (HPV) testing in primary cervical screening. *Health Technology Assessment 2009; Vol. 13: No. 51*

Kitchener HC,Almonte M et al. on behalf of the ARTISTIC Trial Study Group (2006) HPV testing in routine cervical screening: cross sectional data from the ARTISTIC trial, *British Journal of Cancer* 95(1):56-61.

Kitchener HC 2015 Report to the National Screening Committeehttps://legacyscreening.phe.org.uk/policydb_download.php?doc=555

Moss S Gibney A 2015 HPV PRIMARY SCREENING PILOTS: EVALUATION REPORT TO THE NATIONAL SCREENING COMMITTEE . FEBRUARY 2015
Centre for Cancer Prevention, Wolfson Institute, Queen Mary University of London

NHSCSP 2016 NHS Cervical Screening Programme Colposcopy and Programme management. Available from:
http://www/bsccp.org.uk/assetts/file/uploads/resources/NHSCSP-20-Colposcopy-and - programme-management-(3rd -edition)-(2).pdf

Public Health England 2013 National HPV Vaccination Coverage remains High and evidence shows Programme effective in protecting women's health. Tinyurl.com/PHE-HPV

Public Health England 2016 HPV Primary Screening in the cervical screening programme. Available at:http://phescreening.blog.gov.uk/2016/04/13/hpv-primary-screening –in the cervical–screening –programme

Public Health England 2016 NHS Cervical Screening Programme guidance for the training of cervical sample takers. Accessed at http://www.gov.uk/topic/population-screening-programmes

Walboomers J et al 1999 Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. Journal of Pathology;189:12-19