Changes to the cervical cancer screening program in Australia

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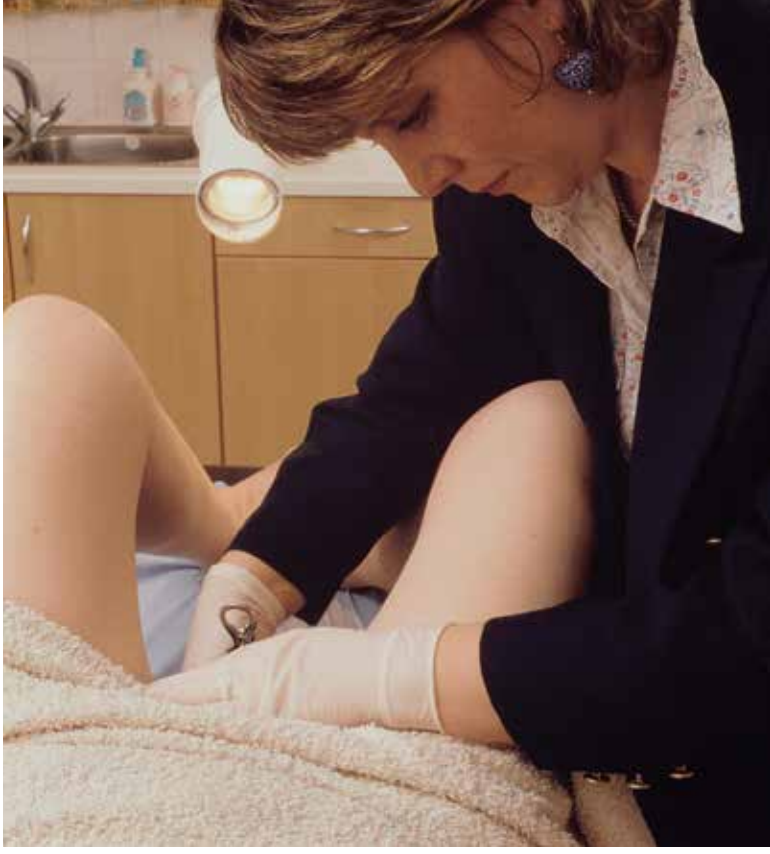

Recommended changes in the Renewed National Cervical Screening Program due to be introduced in Australia in May 2017 include replacing the Pap smear with a cervical HPV test that includes partial HPV genotyping for the highest oncogenic risk types and conducting this screening every five years between the ages of 25 and 69 years.

Australia is the first country in the world to announce large-scale changes to cervical screening as a direct response to the successful implementation of human papillomavirus (HPV) vaccination. Since the National HPV Vaccination Program began in 2007, a significant reduction has been seen in the prevalence of confirmed high-grade cervical abnormalities in young women. This, together with an accumulation of international evidence on the greater sensitivity of HPV testing (detection of HPV in cervical cells) compared with Pap testing (detection of abnormal or potentially abnormal cells from a cervical sample) in the detection of cervical intraepithelial neoplasia grade 2 or higher (CIN2+) lesions, has led to the development of new recommendations on cervical screening. These recommendations emerged from an evidence-based process of review and are that:

- HPV screening is conducted every five years in women aged 25 years and older
- women are discharged from screening when they reach their early 70s.

The impact of HPV vaccination

Since the start of the HPV vaccination program in young females in 2007, vaccination uptake has been approximately 71 to 72% for three-dose coverage in 12 to 13-year-old girls, and catch-up vaccination in 18 to 26-year-old women has achieved coverage rates of 30 to 50%.[1,2] Quadrivalent vaccine, which protects against the two types of HPV implicated in 70% of cervical cancers (HPV 16 and 18), as well as two types responsible for most anogenital warts (HPV 6 and 11), is used in the vaccination program. Since 2013, boys aged 12 to 13 years have also been vaccinated at school (with an initial two-year catch-up to Year Nine). Via herd immunity, male vaccination is expected to further reduce infections and high-grade cervical abnormalities among women.[3]

After the introduction of vaccination, Australia experienced rapid falls in vaccine-included HPV type infections, including anogenital warts and histologically confirmed cervical high-grade precancerous abnormalities (CIN2/3). From 2004 to 2012, rates of CIN2/3 decreased by 53% for women aged younger than 20 years. For women aged 20 to 24 years, from 2004 to 2012, rates of confirmed CIN2/3 were stable until 2010 and then decreased by 21% in the following year.[4]

Cytology screening – reaching its limits

Australia's National Cervical Screening Program (NCSP) currently recommends two-yearly cytology using the Pap test in all women who have ever been sexually active and are aged between 18 to

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KEY POINTS FOR GPS ON THE RENEWED CERVICAL SCREENING PROGRAM

- The Renewed National Cervical Screening Program is expected to reduce incidence and mortality from cervical cancer by over 20%, and is estimated to reduce cervical screening episodes from 26 to 11 over a woman's lifetime.
- The HPV screening test will become available on the Medicare Benefits Schedule.
- To conduct an HPV test, a cervical sample will still need to be taken. The sample will be placed directly into a liquid-based medium with no need to prepare and fix a slide.
- It remains important to sample the transformation zone of the cervix in order to optimise the sensitivity of the HPV test and the reflex liquid-based cytology, if required.
- Reflex liquid-based cytology will be performed on all HPV-positive cervical samples. Women with HPV 16/18 will be referred for colposcopy immediately; in this situation the reflex liquid-based cytology result will inform management at colposcopy.
- Until May 2017, women eligible for cervical screening should be offered the two-yearly Pap smear, with the exception of eligible women attending Victorian practices enrolled in the Compass Clinical Trial (which is comparing 2.5-yearly Pap test screening with five-yearly HPV screening in an HPV-vaccinated population; http://www.compasstrial.org.au)
- It is important to encourage all age-eligible HPV-vaccinated women to continue to participate in cervical screening, as the vaccine does not protect against all known HPV types that may cause cervical cancer.

20 years and 69 years. Screening participation rates over a two-year period are 58%, and around 83% of all eligible women are screened every five years.[4] Since its introduction in 1991, the NCSP has been very successful in reducing the incidence and mortality from cervical cancer in Australia, which fell by around 50% in the first decade.[5]

However, in the second decade of the screening program, cervical cancer incidence and mortality have plateaued. Although Australia has one of the lowest incidences of cervical cancer in the world, it is likely that the cytology screening program has reached its limits. This is mainly due to the continuing difficulties of reaching some groups of women (including those in remote and rural communities) for two-yearly screening, along with the ongoing limitations of cervical cytology in the detection of adenocarcinoma and its precursor, adenocarcinoma-in-situ.[4]

The review process

The rapid impact of the vaccination program in reducing high-grade cervical abnormalities prompted a major review of Australia's cervical screening program, known as Renewal, which was announced in November 2011. In the first phase of Renewal, the Australian government's Medical Services Advisory Committee (MSAC) commissioned a systematic review of the international evidence. A modelling approach was then used to combine the international evidence on vaccine efficacy with local information on vaccination and screening behaviour.

The Renewal modelling predicted that switching to five-yearly HPV screening with partial genotyping from the age of 25 years would be both life-year and (potentially) cost saving, and that this would be the most favourable screening approach overall for both vaccinated and unvaccinated women. It also predicted that the use of partial HPV genotyping would result in up to 22% further reductions in cervical cancer incidence and mortality compared with the current screening program, if retaining a screening end-age of 70 years.[6] These findings form the basis of the screening recommendations for the Renewed NCSP, which will commence in Australia on 1 May 2017.

The renewed program also includes the use of HPV self-collection, which will be offered only to women who have never been screened or have been underscreened because of cultural or logistic reasons, with the aim of improving overall participation rates among these groups. It has been estimated that a single self-collected test at age 30 years in a previously unscreened women could reduce her lifetime risk of cervical cancer by about 40%; however, if a women has regular five-yearly screening with clinician-collected samples, the lifetime risk reduction would be over 90%.[7]

National clinical management guidelines are being developed using NHMRC processes, facilitated by the Cancer Council Australia Clinical Guidelines Network. The draft clinical management guidelines for the renewed program were released for public consultation in March 2016.[8] The final guidelines will be released prior to the program's transition in May 2017.

What are the changes to cervical screening?

The major changes to cervical screening in Australia recommended in the Renewed NCSP are listed below.

- From May 2017, the Pap smear will be replaced by a cervical HPV test that includes partial HPV genotyping for the highest risk types, HPV 16 and 18.
- Reflex liquid-based cytology will be performed on all HPV-positive cervical samples. However, women with HPV 16/18 will be referred for colposcopy immediately, irrespective of the reflex liquid-based cytology result; in this situation the reflex liquid-based cytology result will inform management at colposcopy.
- Women with other oncogenic HPV types (not HPV 16/18) will be triaged based on the liquid-based cytology result.
- All women aged 25 to 69 years, irrespective of whether they have been HPV-vaccinated, will be invited to have an HPV test every five years.

- The screening interval will be extended from two to five years because of the high negative predictive value of a negative HPV test result.
- Asymptomatic women aged 70 to 74 years who have been regularly screened up to the age of 69 years will have an HPV exit test before being discharged from the program.
- Women aged 70 years and older who have never been screened or have not had regular screening tests should have an HPV test if they request screening.
- Women of any age who have symptoms suggestive of cervical disease (including pain or bleeding) should have appropriate clinical assessment, which may include a cervical cytology test and an HPV test.

Key points for GPs regarding the renewed program are provided in the Box.

How safe is it to defer screening until age 25 years?

Even in completely unvaccinated populations, rates of invasive cervical cancer are low in women younger than 25 years of age.[4] Importantly, a substantial body of evidence has found that cervical screening in this age group has little or no impact on the risk of developing invasive cancer before the age of 30 years.[9] Almost all countries with organised screening programs recommend that cervical screening commences at age 25 or age 30 years, and the International Agency for Research on Cancer (IARC) recommends regular cervical screening begins at age 25 years. This achieves the best balance of benefits and harms for cervical screening.

It is important to note that the modelled evaluation for Renewal considered the impact of starting at age 25 years. Overall, the evaluation predicted a reduction of cervical cancer incidence of up to 22%; this reduction was predicted even if the population had never been offered HPV vaccination. Subsequent modelling, taking into account postcolposcopy management as recommended in the new clinical management guidelines, has predicted reductions of 31 to 36% in cervical cancer incidence and mortality in unvaccinated cohorts, and reductions of 24 to 29% in cohorts offered vaccination.[10]

In the postvaccination era, the risk of cervical cancer in women aged 25 years or less has been reduced even further.[11] In Australia, the prevalence of vaccine-included HPV type infections reduced by 77% in 18 to 24-year-old women from 2005–2007 (pre-vaccination) to 2010–2011 (i.e. this substantial reduction occurred within a few years after vaccination was introduced).[12] Furthermore, the impact of the vaccination program has not been confined to those women who have been personally vaccinated. Even before the

implementation of male vaccination, women experienced herd immunity because of the vaccination of other women in the community. The effect has been documented as a fall in vaccine-included HPV type prevalence in unvaccinated women aged 18 to 24 years that occurred by 2012.[11] The effect of herd immunity is expected to be further increased by the implementation of male vaccination in 2013.

Therefore, several factors have combined to support a starting age of 25 years in the Renewed NCSP, including:

- the relatively lower rates of cervical cancer in women less than 25 years of age
- the lack of evidence for the effectiveness of cervical screening in women less than 25 years of age
- the impact of HPV vaccination on further substantially lowering the risks of CIN2/3 and cervical cancer for both vaccinated and unvaccinated young women.

Conclusion

In the Renewed NCSP, partial genotyping will be performed to allow identification of vaccine-included oncogenic HPV types 16 and 18 at the time of screening, regardless of whether or not a woman has been offered vaccination.

Women testing positive for HPV 16 or 18 will be directly referred for colposcopy. Women with other oncogenic (not HPV 16/18) type infections (which are not vaccine-included) may be triaged to colposcopy depending on the result of the reflex cytology. Thus the program will be tailored to operate effectively for both older unvaccinated women and for younger women in cohorts offered vaccination in whom the rates of infection with the vaccine-included types have dropped dramatically. Women will be managed according to their HPV test outcome, whether vaccinated or not.

The renewed cervical cancer screening program thus positions Australia as the first country to implement a truly integrated approach to screening in the context of vaccination. MT

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Note on sources

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Cervical cancer. Chapter in: National Cancer Prevention Policy, Cancer Council Australia. [Chapter revised in 2012 in consultation with Professor Karen Canfell (Director, Research Cancer Council NSW). Associate Professor Kristine Macartney (Deputy Director of Government Programs, National Centre for Immunisation Research and Surveillance) provided advice about HPV immunisation. Chapter externally reviewed by Professor Ian Frazer, Professor Ian Hammond and Associate Professor Marion Saville].

Canfell K. The Australian example: an integrated approach to HPV vaccination and cervical screening. HPV Today 2015 August; 34. Available online at: http://www.hpvtoday.com/revista34/09-The-Australian-Example.html (accessed May 2016).

References

1. Gertig DM, Brotherton JML, Saville AM. Measuring human papillomavirus (HPV) vaccination coverage and the role of the National HPV Vaccination Program Register, Australia. Sexual Health 2011; 8: 171-178.
2. Brotherton JM, Liu B, Donovan B, Kaldor JM, Saville M. Human papillomavirus (HPV) vaccination coverage in young Australian women is higher than previously estimated: independent estimates from a nationally representative mobile phone survey. Vaccine 2014; 32: 592-597.
3. Smith MA, Canfell K, Brotherton JM, Lew JB, Barnabas RV. The predicted impact of vaccination on human papillomavirus infections in Australia. Int J Cancer 2008; 123: 1854-1863.
4. Australian Institute of Health and Welfare. Cervical screening in Australia 2011-2012. Canberra: AIHW; 2014. Cancer series no.82. Cat. no. CAN 79. Available online at: http://www.aihw.gov.au/publication-detail/?id=60129546865 (accessed May 2016).
5. Simonella L, Canfell K. The impact of a two- versus three-yearly cervical screening interval recommendation on cervical cancer incidence and mortality: an analysis of trends in Australia, New Zealand, and England. Cancer Causes Control 2013; 24: 1727-1736.
6. Lew JB, Simms K, Smith M, et al. National Cervical Screening Program Renewal: effectiveness modelling and economic evaluation in the Australian setting (assessment report). Medical Services Advisory Committee Australia (MSAC) Application No. 1276. November 2013.
7. Smith M, Lew JB, Simms, K, Canfell K. Impact of HPV sample self-collection for underscreened women in the renewed Cervical Screening Program. Med J Aust 2016; 204: 194.
8. Cancer Council Australia Cervical Cancer Prevention Guidelines Working Party. Draft clinical management guidelines for the prevention of cervical cancer: public consultation draft. Sydney: Cancer Council Australia; 2016. Available online at: http://wiki.cancer.org.au/australiawiki/index.php?oldid=130637 (accessed May 2016; available for reference until the final guidelines are published).
9. Sasieni P, Castanon A, Cuzick J. Effectiveness of cervical screening with age: population based case-control study of prospectively recorded data. BMJ 2009; 339: b2968.
10. Canfell K, Hall M, Lew JB, et al. Modelled evaluation of the predicted benefits, harms and cost-effectiveness of the renewed National Cervical Screening Program (NCSP) in conjunction with these guideline recommendations. In: Cancer Council Australia Cervical Cancer Prevention Guidelines Working Party. Draft clinical management guidelines for the prevention of cervical cancer. Sydney: Cancer Council Australia; 2016. Available online at: http://wiki.cancer.org.au/australiawiki/index.php?oldid=130637 (accessed May 2016; available for reference until the final guidelines are published).
11 Tabrizi SN, Brotherton JM, Kaldor JM, et al. Assessment of herd immunity and cross-protection after a human papillomavirus vaccination programme in Australia: a repeat cross-sectional study. Lancet Infect Dis 2014; 14: 958-966.
12. Tabrizi SN, Brotherton JM, Kaldor JM, et al. Fall in human papillomavirus prevalence following a national vaccination program. J Infect Dis 2012; 206: 1645-1651.

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