



postnote

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CERVICAL CANCER

Cervical cancer is the twelfth most common cancer in women in the UK and the second most common worldwide. It causes around 1,000 deaths each year in the UK. Cervical screening programmes have reduced mortality rates by 62% between 1987-2006. From autumn 2008, a UK-wide programme will immunise adolescent girls using a new vaccine against a sexually-transmitted virus that can cause cervical cancer. This note gives an overview of cervical cancer prevention strategies, including vaccination, and the issues arising.

Cervical cancer

Incidence and mortality

In the UK in 2005 (the most recent year for which data are available) there were 2,800 diagnoses of invasive cancer of the cervix, accounting for 2% of all female cancers and 950 deaths. It was the third most common cancer in under 35s, with 670 new diagnoses in 2004.¹

Human Papilloma Virus

The Human Papilloma Virus (HPV) is one of the most common sexually transmitted infections; 30% of females are infected within two years of becoming sexually active.² While most HPV infections show no clinical symptoms, persistent infection with a high-risk HPV type causes almost all cervical cancers. Of the 100 HPV types, 40 infect the genital tract and are sexually acquired. Thirteen of these are known high-risk types that cause cervical cancer, of which two (16 and 18) are responsible for over 70% of all cervical cancer cases in the UK. High-risk HPVs also cause other, less common, non-cervical cancers. Two low-risk HPV types (6 and 11) cause approximately 90% of anogenital warts. Other factors can impact on the risk of cervical cancer through increasing the risk of HPV infection and/or increasing the risk of progression to cervical cancer. They include smoking, sexual activity at a young age, number of sexual partners, oral contraceptives and socio-economic factors.

Cervical cancer prevention strategies

Women are offered free cervical screening to detect and treat cervical abnormalities or lesions (Box 1).

The programme calls and recalls women between the ages of 25-64 for regular screening. Screening has

Box 1. NHS cervical screening programme

The UK's screening programme does not test for cervical cancer, but uses a method to detect early cervical cell abnormalities which, if left untreated, could lead to cancer. In England, free screening is offered to all women aged 25-64 (from age 20 in Wales and Scotland) at different intervals (every three to five years, depending on a woman's age). In 2006-07 (England) 4.3 million women of all ages were invited for screening, with 3.4 million women screened.⁴ This means that 79% of women eligible for screening attended at least once in the last five years.

reduced cervical cancer incidence and prevents ~4,500 deaths each year. Estimated savings are £36,000 per life saved and £18,000 per cancer prevented.³ The programme and treatment costs are estimated at £157 million a year in England. The percentage of women screened in the last five years has been falling slightly over the last decade, mainly in lower age groups. Data for 2006-7 show that this is the second year it has dropped below 80% since the early 1990s. This is of concern as there is strong evidence that the death rate is lower in women first screened at a young age.

Human Papilloma Virus vaccines

Two vaccines are licensed in the UK and both are highly effective at preventing infection by the HPVs they cover:

- Cervarix (GlaxoSmithKline) protects against two HPV types 16 and 18 (this is a bivalent vaccine);
- Gardasil (Merck) protects against HPV types 16 and 18, as well as 6 and 11 which can cause anogenital warts (this is a quadrivalent vaccine).

The vaccines protect only against HPV infection by the types indicated; they do not have any therapeutic effect in women already infected with these HPV types at the time of vaccination. Both vaccines provide some cross-protection against other, closely related HPV types. To be most effective, three doses of vaccine should be given, optimally within six months. There is no evidence that brands are interchangeable. Best protection occurs if females are vaccinated prior to becoming sexually active. Long-term follow-up research will assess the longevity of immunity and whether booster doses will be needed.

There is concern that if immunity wanes, women may not be protected through their teens and early 20s, when they may be at highest risk of acquiring HPV infection. Cervarix recipients have been monitored for six years; there is no evidence that their immunity is waning.

UK policy on HPV vaccination

Several countries have HPV vaccine programmes including USA, Australia, Canada (some provinces) and New Zealand. In 2007, the Joint Committee on Vaccination and Immunisation (JCVI) advised the Department of Health (DH) that HPV vaccination should be offered to females aged 12-13 with a catch-up campaign for those up to 18 years. Vaccinating all women over 18 was not considered cost-effective, although the DH is considering whether some high-risk groups of women might benefit.

The decision was based on unpublished clinical trial data, published papers, and peer-reviewed economic modelling of cost-effectiveness by the Health Protection Agency (HPA).⁵ The HPA concluded that either vaccine would be cost-effective with 70% or greater vaccine take-up in 12 year old females, assuming protection lasts 10 years or more. Up to 70% of cervical cancers could be prevented and up to 400 lives a year saved with either vaccine; if a quadrivalent vaccine was used, most cases of anogenital warts in both sexes would also be prevented.⁵ Vaccinating males was not cost-effective.

Choice of vaccine

The JCVI does not make recommendations about which vaccines to purchase. The contracts are awarded by the DH according to a range of criteria given different weights related to cost-effectiveness:

- quality of protection against cervical cancers caused by HPV types 16 and 18;
- duration of protection against cervical cancers caused by HPV types 16 and 18 for more than 10 years;
- protection against HPVs 6 and 11;
- quality of protection against other HPV types;
- manufacturing and supply arrangements.

The weight given to price per dose is not disclosed. Since Gardasil (quadrivalent) protects against HPVs for cervical cancer and anogenital warts it has a cost-effectiveness advantage, unless Cervarix (bivalent) is cheaper. The HPA's analysis concluded that for the bivalent vaccine to be chosen, it would have to cost £13-21 less per dose (depending on duration of protection) than the quadrivalent vaccine. This difference would amount to potential savings of £11.5-18.6m in the first year of the programme. The contract was awarded to GSK (Cervarix). This has been criticised by sexual health campaigners who believe that choosing the quadrivalent vaccine would also protect against anogenital warts.

The DH began the routine vaccination programme for 12-13 year old females in September 2008. Over the next three years, a catch-up campaign will vaccinate all girls aged 14-18, with 17-18 year olds offered the vaccine in 2008. A total of 1,800,000 doses will be purchased in year one. At least 80% take up is needed for full cost-benefits to be realised. Surveys of parents and a pilot vaccination project (Box 2) indicate broad support for the

Box 2. Parents' attitudes to HPV vaccination

Surveys suggest a low level of parental awareness of HPV, its association with cancer and of the HPV vaccine. 75% of mothers of 8-14 year old girls would accept the vaccine, whereas 19% were 'unsure'. There was reluctance from some to consider their adolescent daughters as potentially sexually active, and a preference for giving children information on cancer and HPV rather than messages about safe sex and sexually transmitted infections. Children under 16 who understand what is involved can give consent; ideally someone with parental responsibility will be involved.

A pilot study in 36 secondary schools found that take-up of the first 2 HPV vaccinations (Cervarix) was ~70%. There was lower take up in schools with a higher proportion of females from ethnic minority groups or by those entitled to free school meals.⁶ Other issues raised by parents were lack of knowledge about the vaccine; and safety concerns, particularly over possible adverse effects in the long-term; while a very small percentage felt that allowing vaccination meant they were condoning early sexual activity, increased promiscuity and unprotected sex.

vaccine. Insights gained from attitudinal research informed a range of government communication materials that were tested with girls and their parents.

Impacts of HPV vaccination

High vaccine coverage should result in fewer abnormal screening results and thus eventually reduce cervical cancer incidence. Outcomes will not become clear until females become eligible for cervical screening (2015 for those turning 18 in 2008 in England). The government will monitor vaccine coverage, safety and impact on HPV infections. The DH and cancer charities advise that women need to attend cervical screening regardless of their vaccination status, as one-third of cancers are caused by HPV types not covered by the vaccine.

HPV testing and the future of screening

Testing for HPV status is not currently recommended for primary cervical cancer screening. A large trial involving 25,000 women to assess the value of HPV testing as part of the cervical screening programme is ongoing. Future vaccines that protect against a wider range of HPV types may also be a consideration.

Endnotes

- 1 Cancer Research UK CancerStats website <http://info.cancerresearchuk.org/> accessed September 2008
- 2 *Immunisation against Infectious Disease - The Green Book*, Department of Health, 2008
- 3 J. Peto et al., *The Lancet*, 364, 2004
- 4 *Cervical Screening Programme (England) 2006-07*, National Statistics and NHS, www.ic.nhs.uk/
- 5 M. Jit et al, *British Medical Journal*, 337, 2008
- 6 L. Brabin et al., *British Medical Journal*, 336, 2008

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POST is grateful to all contributors and reviewers. For further information on this subject please contact the author, Dr Sarah Bunn, at POST.

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