Cervical cancer screening in older women

Should women over 65 be offered a catch-up HPV test?

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Most women in the UK aged over 65 years have never had a test for human papillomavirus (HPV). On present trends, about 5000 of these 6.5 million women will die from cervical cancer over the next 35 years (unpublished birth cohort projection from national death rates).

The NHS cervical screening programme has been among the most successful in the world, preventing an estimated 5000 deaths a year1 by offering regular cytology up to age 65. HPV testing of cervical samples has now replaced cytology for primary screening in many countries, including the UK. This was accompanied by an increase in the age of eligibility in Australia, where the upper age for screening has been increased to 74,2 and in Denmark, where all women born before 1948 have been offered an HPV test.3 But in England, where half of all cervical cancer deaths are now among women aged 65 years or over, screening is still stopped at age65.

The NHS programme justifies not screening women beyond age 64 because “it is highly unlikely that women over 64 who have been regularly screened will go on to develop the disease.”4 The proportion who will develop cervical cancer at age 65-84 is about 1 in 1200 among women who have been regularly screened and 1 in 200 among inadequately screened women.5 These are not negligible risks, and there is now evidence that more than half these cases and a larger proportion of deaths after age 65 might be prevented by one sensitive HPV test.

The introduction of primary HPV screening in England last year increased the cervical cancer detection rate in the first screening round by about 30%,6 and the long term cancer risk is much lower after a negative HPV result than after a negative cytology result.7 Women currently being discharged from the screening programme with a negative HPV result will therefore be at extremely low risk of developing cervical cancer. However, lifelong risk will be substantially higher in women who were screened only with cytology and exited the programme before 2019 with normal cytology results.

There is a strong case for offering these women a “catch-up” HPV test to detect the small proportion who are HPV positive (4% of women aged 69 or over in the Danish catch-up programme3). Uptake will be lower among women who were not screened adequately by the cytology programme,8 but about 40% of women now developing cervical cancer at age 65 or over had been screened regularly and were discharged from the programme with normal cytology results.9

A few women will acquire a new HPV infection after the age of 65, but the persisting risk associated with early age at first intercourse10 suggests that most cervical cancers in older women are the result of infections acquired many years previously. Although latent HPV infections sometimes lead to precancerous changes late in life,11 a large proportion of older women who are HPV positive may already have subclinical precancerous cells.

The ability of a single HPV test to detect these latent precancerous cells depends on test sensitivity. Five of the samples taken at recruitment to the ARTISTIC trial from the 13 women who were diagnosed with cancer more than four years later tested negative with the standard HPV Hybrid Capture 2 assay, but only one was negative when the samples were reanalysed by a PCR assay.12

Practicalities

The population benefit of a “catch-up” HPV test will depend on engaging and educating inadequately screened women,13 whose response rate may be low.8 The risk of cancer among women who have not been screened since age 50, many of whom have never been screened, is about six times higher than the risk among adequately screened women.5 Conventional screening in primary care involves speculum examination which can be painful in older women. Vaginal self-sampling, which yields higher response rates14 and has similar sensitivity for HPV detection, is likely to be the optimal testing strategy for women over 65.15

Women testing positive for HPV could either be referred straight to a gynaecologist or asked to provide a repeat self-sample 12 months later to identify those with persistent infection, the strongest predictor of underlying disease.16, 17

Colposcopy and biopsy are difficult in older women as most do not have a fully visible transformation zone. Current NHS guidelines do not recommend cone biopsy or large loop excision in women with persistent HPV but no apparent abnormality indicated by cytology or colposcopy. This does not seem appropriate given the low sensitivity of cytology seen in two Swedish studies in older women.14, 18 A qualitative review by Danish researchers reported that older women with persistent HPV, for whom the associated increased risk of preterm birth is no longer relevant, preferred a diagnostic cone biopsy to continued surveillanceeven if this proved to be overtreatment.19

Half the cervical cancer deaths in England now occur in women aged over 65 years. Studies in women aged up to at least 80 to determine whether self-sampling is the easiest and most effective option for HPV testing.

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