What is the right age for cervical cancer screening?

“...less attention has been given to the age at which cervical screening could reasonably stop.”

The question as to what the right age is for beginning cervical screening has received much attention in recent months following the tragic death of Jade Goody from cervical cancer at the age of 28 years, and the consequential campaigning by national newspapers for the age at which women are first invited to screening in England to be lowered from 25 to 20 years.

Far less attention has been given to the age at which cervical screening could reasonably stop, although it is an equally important question.

Decisions regarding when to screen are complex and require a careful balancing of the benefits and harms of screening, as well as the costs. Such balancing is inherently difficult because it is impossible to say how many anxious women or how many premature births balance out one cancer. There is no completely correct answer to the question ‘what is the right age for cervical screening?’, but there are some clearly wrong answers. The precise ages at which women are invited for screening is not fully evidence-based. Nevertheless, the reason behind such policy decisions should be rational and transparent.

“The harms of cervical screening are mostly minor in comparison with having cervical cancer; however, some of them are extremely common.”

When considering the benefits and harms of screening, it is useful to consider the ideal cervical screening test. The ideal test would be one that could be applied infrequently and would identify all women who, without intervention, would develop cervical cancer (prior to the next screen) and would not identify any women who would not develop cancer. Thus the ultimate goal for cervical screening is not the identification of high-grade cervical intraepithelial neoplasia (CIN), but a reduction in cancer. It is clear that the majority of such diseases would never progress to cancer [2], and recent research demonstrates that very little high-grade CIN in women aged in their early 20s would progress to cancer within 5 years if untreated [3]. We could identify women at (relatively) high risk of developing cervical cancer at some time in the future by screening teenagers for human papillomavirus (HPV) DNA, but since there is no simple treatment for HPV infection, few people favor such an approach. Rather, it is better to wait for the majority of infections that are transitory to clear and then screen older women to identify those who are more likely to have a persistent infection and who are therefore more likely to benefit from intervention. Similarly, there is no advantage to treating a case of high-grade CIN at 21 rather than 27 years of age if there is little or no chance of it progressing to cancer by 27 years of age, and if the same disease could be treated with no more side-effects and equal likelihood of success in the older woman. Indeed, if by 27 years of age many of the cases that were present at 21 years of age will have spontaneously cleared, then there may be considerable advantage to waiting.

The goal of cervical screening is to prevent cervical cancer. This is achieved by identifying and treating precancer. A secondary benefit of
The benefits of cervical screening have been demonstrated time and again in observational studies. In the UK, cervical cancer mortality and incidence rates fell sharply after the introduction of an organized screening programme in 1988.

The benefits of cervical screening have been demonstrated time and again in observational studies. In the UK, cervical cancer mortality and incidence rates fell sharply after the introduction of an organized screening programme in 1988. Furthermore, case-control studies have demonstrated a clear association between screening and a reduced risk of cervical cancer [8,9]. Historically, these benefits were felt to justify screening, and the decision as to when to start screening should have been based on the age at which cervical cancer became a reasonably common disease. In England in the early 1980s, the incidence of cervical cancer per 100,000 women-years was approximately two in women aged between 20 and 24 years, 11 in women aged between 25 and 29 years and 20 in women aged between 30 and 34 years. More recently, our group has shown that cervical screening is not equally effective at all ages [10]. The latest analysis involving over 4000 cases of cervical cancer in women aged between 20 and 64 years failed to detect any benefit of screening women aged between 20 and 24 years in terms of the reduction in cervical cancer or in the reduction of frank (i.e., stage 1B or worse) cervical cancer [11]. This is in stark contrast to the situation in older age groups, where cervical screening is associated with a reduction in all cervical cancers of between 60 and 80%, and a reduction of advanced (i.e., stage 2 or worse) cervical cancer of between 80 and 95%. (There were very few cases of advanced cervical cancer during the time period in focus.)

There is far less evidence regarding the appropriate age for discontinuing routine cervical screening. A woman who has never been screened would probably benefit from screening so long as she is likely to live for at least another 10 years. However, since most HPV infections occur in young women and the incidence of new high-grade CIN is low in older women, the accepted view is that there is less benefit in screening previously well-screened older women. Some years ago, van Wijngarden and Duncan suggested that screening could stop at 50 years of age in women who had had two consecutive negative smears at 3-yearly intervals, with the last one no more than 2 years previously [17,18]. Their reasoning was that very few such women...
had high-grade CIN detected in subsequent screens. More recent studies have failed to reproduce their results and most countries feel that the evidence to stop screening at age 50 years is too weak to implement such a policy.

Whether or not it is worthwhile to continue screening beyond 65 years of age is a relatively unstudied question. It is only in North America that screening over the age of 65 is at all common and we know of no studies that specifically look at its benefits. We have previously highlighted that cervical cancer rates seem to increase sharply after the age of 70 years and we know of no studies that specifically look at its benefits. We have previously highlighted that cervical cancer rates seem to increase sharply in several countries approximately 10 years after screening ceases, and this alone makes the study of screening in older women worthwhile. With increasing discomfort from arthritis associated with smear taking and the difficulty in obtaining an adequate sample for cytology owing to a lack of estrogen in older women, there is little enthusiasm for continued screening beyond the ages of 60 or 65 years. Nevertheless, the idea of having one screen at approximately 60 years of age and a final one some 10 years later has never been evaluated.

In summary, we believe that the case against cervical screening in teenagers is overwhelming. Screening of women aged between 20 and 24 years is hard to justify and should only be undertaken with informed consent from the woman. Screening between 25 and 59 years has a substantial effect on preventing cervical cancer and downstaging those cases that it fails to prevent. Screening beyond the age of 65 years may be beneficial but should only be undertaken within a properly monitored research study.

Financial & competing interests disclosure
Jack Cuzick (on behalf of Jack Cuzick, Peter Sasieni and Alejandra Castanon) received a small grant from the NHS Cervical Screening Programme (England) to write two reports on issues relating to whether the age at first invitation to cervical screening should be lowered from 25 to 20 years. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. No writing assistance was utilized in the production of this manuscript.

Bibliography
Papers of special note have been highlighted as:
• of interest
•• of considerable interest
• Following-up 948 untreated women with cervical intraepithelial neoplasia 3 and assessed the progression rates to cancer.
•• Extensive meta-analysis including 27 studies that investigated at the association between large loop excision of the transformation zone and preterm delivery, low birth weight and premature rupture of membranes.
• Provides estimates of what future trends in mortality would have been in the absence of screening.
•• Population-based case-control study of over 2500 cervical cancer screenings that found that screening was far less effective in preventing stage 1B or worse cervical cancer in women aged between 20 and 34 years than it was in preventing cervical cancer in older women.
•• Confirmed the findings of [9]. Comprised over 4000 cases and applied a different statistical method to the data. The focus was on age at screening.


**Affiliations**

- Peter Sasieni
  Cancer Research UK centre for Epidemiology, Mathematics & Statistics, Wolfson Institute of Preventive Medicine, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ, UK
  Tel.: +44 20 7882 3544
  Fax: +44 20 7882 3890
  p.sasieni@qmul.ac.uk

- Alejandra Castañon
  Cancer Research UK centre for Epidemiology, Mathematics & Statistics, Wolfson Institute of Preventive Medicine, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ, UK
  Tel.: +44 20 7882 3544
  Fax: +44 20 7882 3890
  a.castanon@qmul.ac.uk

- Jack Cuzick
  Cancer Research UK centre for Epidemiology, Mathematics & Statistics, Wolfson Institute of Preventive Medicine, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ, UK
  Tel.: +44 20 7882 3504
  Fax: +44 20 7882 3890
  j.cuzick@qmul.ac.uk