

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 what would happen to 10,000 people participating in screening [1]. Investigating relative risks alone is insufficient since it does not take into account how common (or rare) the cancer is for a particular group. Consider three possible scenarios involving 10,000 women. For one scenario, there is no screening and 100 women get cancer; in another scenario, there is 3-yearly screening and ten cancers; and in a third scenario, there is 5-yearly screening and 20 cancers. Comparing

3-yearly with 5-yearly screening, one might say that 3-yearly screening halves the risk of cervical cancer. The added benefit, however, is ten cancers prevented, and, compared with no screening, this is an additional reduction of 10%.

When considering the benefits of cervical screening it is useful to consider the ideal 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

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cervical screening is to diagnose cervical cancer earlier when it can be more easily treated and with greater chances of cure. The harms of cervical screening are mostly minor in comparison with having cervical cancer; however, some of them are extremely common. Thus, substantial numbers of women are made anxious by abnormal screening tests; large numbers have their cervix excised or ablated and a proportion of those may subsequently have a preterm obstetric delivery as a consequence of this treatment [4].

“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 [5,6] and incidence [7] 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

in women in their early 20s and, as such, the confidence intervals were very wide; however, the point estimates were still consistent with screening having little or no effect.)

The harms of cervical screening are more common in young women. Smear abnormality rates in England in 2002–2003 (when women aged 20–24 years were still invited) were 15% in women aged between 20 and 24 years, 11% in women aged between 24 and 29 years and 4% in women aged between 50 and 54 years [12]. It has also been shown that, if anything, the anxiety caused by an abnormal smear is greater in a young woman than in an older woman. Similarly, the number of cases of high-grade CIN detected and treated as a result of screening falls substantially with age. In 2003 in England, there were nearly 4000 cases of CIN3 registered in women aged between 20 and 24 years; 5000 in women aged between 25 and 29 years; and just under 400 in women aged between 50 and 54 years [13]. Treatment of CIN is generally very safe, with immediate complications such as hemorrhaging being rare and more serious complications being extremely rare. Nevertheless, recent studies have found that pregnancies in women previously treated for CIN are more likely to result in preterm delivery than are pregnancies in women who have not been treated for CIN [4,14–16]. Since younger women are more likely to have pregnancies after treatment, delaying treatment for 10 years could have a substantial impact on the chances of a subsequent preterm delivery.

“...in older age groups ... cervical screening is associated with a reduction in all cervical cancers of between 60 and 80%.”

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 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.

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