

## ACOG guidelines on cervical screening: a step in the right direction

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The guidelines on cervical cytology screening of the American College of Obstetricians and Gynecologists (ACOG), recently published in *Obstetrics & Gynecology*<sup>1</sup> and summarized in the *New England Journal of Medicine*,<sup>2</sup> should be welcomed as a step in the right direction for America, which has traditionally put more emphasis on maximizing the potential benefits of screening rather than balancing the benefits against the harms and costs of screening.

Compared with previous ACOG guidelines, the new guidelines go some way to reducing the harms of over-screening, but they are still quite different from the policies adopted by most organized screening programmes. While it is entirely reasonable that different societies should weigh benefits and harms differently, we do not believe the substantial differences between the ACOG guidelines and European practice (within organized screening programmes) are evidence-based.

The ACOG guidelines follow the approach outlined by the US Preventive Services Task Force on the level of evidence. It is important however to distinguish between the *quality* of evidence and the *relevance and specificity* of the evidence. When the ACOG say that there is good and consistent scientific evidence to begin cervical screening at age 21, do they mean 'as opposed to at 18' or 'as opposed to not screening at all' or 'as opposed to starting at age 25'? Whereas we would agree that the evidence that it is better to start at 21 than at 18 is good, as is the evidence that it is better to start at 21 than not to screen at all, we know of no direct scientific evidence showing that cervical screening is effective in women aged 21–24 and indeed there is some evidence to the contrary. There is good evidence that cervical screening is substantially less effective at preventing cervical cancer in women in their twenties than it is at older ages.<sup>3</sup> Given the uncertain effectiveness of screening at ages 21–24, the low incidence of cervical cancer under age 25 and the substantial harms of screening young women, we believe that the harms outweigh the potential benefits. There is certainly no 'good evidence' to recommend cervical screening beginning at age 21.

The case for two-yearly (as opposed to three-yearly) screening in women aged 25–29 is stronger than the case for screening women aged 20–24 (at any interval), but again one needs to know what the 'strong evidence' cited by the ACOG supports. Are we to believe that the evidence is for two-yearly screening rather than annual screening or for two-yearly screening rather than three- (or even five-) yearly screening? Similarly in women aged 50–64 is three-yearly screening really justified or would five-yearly screening be equally as effective as suggested by our

analysis<sup>4</sup> of the English programme? What is needed is a careful review of the available evidence.<sup>3–8</sup>

It would be of interest to know the ACOG estimate of how many additional screening tests, in women aged 20–24, 25–29, and 30–49 are needed to prevent one additional cervical cancer compared with three-yearly screening from age 25. Further estimation of the number of additional preterm deliveries<sup>9</sup> resulting from the treatment of the extra cases of cervical intraepithelial neoplasia detected by the more intensive screening would be informative. Formal consideration of the harms and costs of the additional screening as well as the benefits would be useful to inform decision makers.

We note with interest that the ACOG conclude that 'based on limited and inconclusive scientific evidence' 'it is reasonable to discontinue cervical screening between 65 years and 70 years of age in women who have three or more negative cytology results in a row and no abnormal test results in the past 10 years'. Although this is not unreasonable and brings the US guidelines in line with European programmes, we know of no good evidence to support the cessation of cervical screening at age 65 (when cervical cancer is still relatively common compared with at younger ages) and indeed comparisons of age-specific cervical cancer rates between North America (where screening of elderly women is common) and Europe (where it is almost non-existent) would suggest that screening over the age of 65 is justifiable<sup>10</sup> albeit with longer intervals between screens.

The new guidelines also conclude that 'co-testing using the combination of cytology plus HPV DNA is an appropriate screening test...' and the recommendation that those who are negative on both tests 'should be rescreened no sooner than 3 years subsequently' is particularly welcome. The evidence however is that human papillomavirus (HPV) DNA testing alone is almost as sensitive as co-testing and that the advantages of co-testing are minimal.<sup>11</sup> The main disadvantage of HPV DNA testing is its lack of specificity for pre-cancer and the addition of cytology will only exacerbate this problem. There may be social and political reasons to favour co-testing over HPV alone, but we do not believe that there is scientific evidence to support such an approach.

Disappointingly these guidelines are still focused on the quantity of screening (from what age and how often) with not a single recommendation regarding the quality of screening. It has been known for some time that quality assurance is essential if cytology-based cervical screening is to reach its full potential. Recent literature shows how the sensitivity and specificity of cytology can be hugely variable even within controlled clinical trials.<sup>11–13</sup> It is generally agreed that the full benefits of cytology 'can only be

achieved if quality is optimal at every step in the screening process, from information and invitation of eligible target population, to performance of the screening test and follow-up, and, if necessary, treatment of women with screen-detected abnormalities'.<sup>14</sup>

Overall, the ACOG guidelines are a significant step in the right direction, but we feel it is important to point out that these are not fully 'evidence-based' guidelines. In particular we know of no evidence to prefer the ACOG guidelines to the generally less intensive guidelines of the organized European cervical screening programmes.

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## Colorectal cancer prevention through screening: population acceptance of flexible sigmoidoscopy

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The latest UK figures show that 37,514 people were diagnosed with colorectal cancer (CRC) in 2006 and 16,259 died from the disease, putting CRC second only to lung cancer as a cause of cancer death.<sup>1</sup> In 2006, the National Bowel Cancer Screening Programme was initiated, offering biennial faecal occult blood testing (FOBT) starting at age 60, with the aim of detecting CRC at an earlier stage when treatment is likely to be more effective.<sup>2</sup>

An even greater prize than finding early stage disease is to identify the precursor lesions and prevent cancer developing. This avoids the human and financial costs associated with surgery, chemotherapy and radiotherapy. The Cervical Screening Programme is an example of screening for precursor lesions. The primary test examines a sample of cervical cells; if neoplastic changes are observed, the woman is referred for a colposcopic examination during which the affected area of the cervix is removed under local anaesthetic. This programme is estimated to prevent thousands of cases of cervical cancer a year.<sup>3</sup>

Prevention of colorectal cancers through detecting and removing the precursor lesions (adenomatous polyps) may also be within reach. In the UK Flexible Sigmoidoscopy (FS) Trial, adults aged 55 to 64 years were randomized to either a single FS examination or usual care (no CRC screening was offered at that time in the UK). The 11-year follow-up results have just been published and showed a 43% reduction in CRC mortality and a 33% reduction in incidence among those attending for the test.<sup>4</sup> This is one of the most impressive cancer preventive outcomes ever reported in a trial, and the results will get better still if CRC incidence remains low in the screened group while continuing to rise with age in the controls.

Crucial to delivery of this protective effect at a population level is high uptake of FS. This is likely to be a challenge outside the trial context. Apart from the test itself, participants need to complete the bowel preparation at home because of the difficulty of doing it in a high-volume screening clinic. In the FS Trial, participants were sent an enema to