# How can we develop a cost-effective quality cervical screening programme?

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*SUMMARY*

*This article discusses the evidence base underpinning the United Kingdom cervical screening programme and proposes that there is now sufficient evidence to suggest that too many women are screened too frequently. The financial savings generated from increasing the screening interval to five years and restricting routine screening to women aged 25 to 50 years may, we suggest, be better spent on improving the quality of the cervical screening programme. Re-awakening this debate must not however deflect energy and effort from recruiting women who have never been screened or further developing quality control systems. Any debate must also fully engage women of all ages as the key stakeholders in the decision-making process.*

***Keywords:*** *cervical screening programme; screening interval; cost effectiveness; cervical intraepithelial neoplasia.*

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## Introduction

EVIDENCE-BASED medicine should encompass regular review of the rationale and structure of all areas of health care, including screening programmes. The cost of the cervical screening programme (estimated as £132 million per year in the UK in 1998)[1] also creates a moral obligation to examine the cost effectiveness of this service. Cervical screening undoubtedly saves lives[2-4] yet, despite good coverage,[5] a significant proportion of cases of invasive disease are still not prevented.[4] Public confidence in screening may be attributable to misconceptions about the sensitivity of the test[6] but is also intermittently shaken by the publicity surrounding reports of false-negative smears.[7,8] The benefits of screening have been well publicised, but not the limitations of a single screening test. The relative benefits of prioritising resources to screening more women or minimising errors related to the sampling technique and interpretation of findings have not been quantified. Recent reviews[9-11] suggest that perhaps routine smear tests are being offered too frequently and to too many women.

This article aims to reopen the debate about the cervical screening programme[12,13] and revisit proposals to screen women only between the ages of 25 and 50 and once every five years.[2,14] We suggest that any financial savings should be redistributed to provide a quality service with better coverage which identifies pre-invasive lesions when they are present and adequately follows up women identified as having an abnormal smear. If we could provide a more cost-effective service, then any financial savings could be used to improve the quality of existing services. These issues need to be debated by and with women. This latter recommendation is not a knee-jerk response to increasing consumerism within the health service, but because the consequences of any modification to a longstanding health programme need to be understood and approved by its recipients.

## Cervical screening and the screening paradigm

The purpose of cervical screening is to identify cytological abnormalities in women before they develop clinically invasive carcinoma. The Papanicolaou smear is the primary method of screening for cervical cancer and is used to detect the early dysplastic cell changes that may be precursors to invasive disease. If such abnormalities are detected then women can have further diagnostic testing and treatment, which aims to prevent progression of the disease. The long pre-invasive stage during which the disease can be detected and cured makes cervical cancer an ideal condition for a screening programme.[15]

In other respects, however, cervical screening sits uneasily within the screening paradigm. Wilson[16] and Cadman[17]

argued that screening programmes should only be instituted when the benefits of screening outweigh the costs. Screening programmes should screen for common conditions where the natural history is known, for which there is an acceptable test and an effective treatment. The costs incurred by those who do not gain from the programme also need to be considered when weighing up the arguments for screening. Benefits and costs should be established through the 'gold standard' of a randomised controlled trial.

### *Natural history*

The natural history of cervical neoplasia is, nevertheless, still not well understood. Although it has been estimated that approximately one-third of cases of cervical intraepithelial neoplasia (CIN) III will progress to invasive cancer, if left untreated, over a period of 15 years,[18] estimates of the time to progression and spontaneous regression rates for the various grades of CIN vary substantially[19-23] and there is ongoing debate about the role of human papilloma virus (HPV) in the development of CIN.[24]

### *Effectiveness*

The effectiveness of cervical screening has never been assessed in a randomised controlled trial and its widespread introduction is based primarily on observational studies. Despite good coverage of the population, the success of the cervical screening programme in preventing cervical neoplasia is questionable and almost half of all invasive cervical cancers are diagnosed in women who have actively participated (i.e. had a smear in the past three to five years) in the screening programme.[4,25,26] In England and Wales, a national call-recall scheme was introduced in 1988[27] during which time coverage of the target population (women aged 20 to 64 years) was only 42%. Since 1992 coverage has been over 80%.[5] The incidence of cervical cancer remained relatively constant, despite considerable screening activity, until 1990. However, during the period 1990 to 1995 incidence fell consistently by an average of 6% per year.[2] Mortality fell relatively steadily from 1950 to 1990 by approximately 1.5% per year and, since that time, the rate of decline has increased threefold.[2] The interpretation of these trends in incidence and mortality, in relation to the introduction of screening programmes, is confounded by temporal variability in the intensity of screening and ascertainment of incident cases, misclassification of both incidence and mortality data, birth cohort effects, changes in sexual behaviour, and clinical practice.[2,28] Case-control studies are also subject to methodological limitations and cannot be considered to provide robust evidence for the value of screening. However, despite this lack of reliable evidence to support the effectiveness of cervical screening, during the past 30 years women have been constantly urged to participate in national programmes. The opportunity for assessing the level of benefit and cost of the current cervical screening programme through a randomised controlled trial has therefore now been missed.

### *Frequency of disease*

Approximately 4.3 million smears are taken each year in England and Wales; the 8% classified as cytological abnormalities and 10% reported as inadequate (Table 1)[5] require either repeat smears, ongoing cytological surveillance or further colposcopic investigation. Less than 0.5% ($n$ = 18 729) of women screened are registered as having CIN III.[5,31] More than 34 000 women are referred for colposcopy each year and only 46% of these have a problem that requires treatment.[5] These high false-positive rates increase costs, the risk and discomfort of invasive procedures, and psychological distress.[29,30] Each year 3170 women develop cervical cancer[31] and 1100 women die from the disease,[32] representing 0.4% of all deaths in women.[2] Although these events are significant for each of the women and their families, the disease is relatively rare and represents, for example, only a small fraction of the number of women who are diagnosed or die from breast cancer.[31,32]

### *The test*

Estimates of the sensitivity (true positive rate) of the smear test range from 30% to 95% depending on the population studied; samples of women referred for previous cytological abnormality or with visible lesions have a high sensitivity, whereas low-prevalence screening samples demonstrate low sensitivity.[33-35] The most commonly quoted estimate for the sensitivity of screening is around 80%.[36] However, studies based on routine screening in low-prevalence areas estimate sensitivity to be much lower (average = 47%) and specificity (true negative rate) to be in the range of 86% to 100% (mean = 95%).[34] The sensitivity of the test is influenced by operational factors, including collecting and processing techniques. However, increased sensitivity (reducing errors in sampling and interpretation) may be at the expense of decreased specificity by increasing the number of false-positives. Estimates of false-negative rates range from 15% to 26%.[8,37] However, retrospective re-examinations of slides rarely reflect screening practice in real life. The calculation of sensitivity is further complicated since neither the number of true positives nor the number that would progress to invasive disease are known.[38] The positive predictive value (PPV) of a screening test is more clinically useful than sensitivity, as it indicates the probability of disease being present in those with a positive test result. A single smear showing moderate dyskaryosis or worse has a PPV for a diagnosis of CIN III or worse of 72% while persistent inadequate, mild or borderline smears have a PPV of only 20%.[5] However, the negative predictive value (NPV) of a smear test (the probability of not having the disease if the test is negative) is very high.[34]

## What is the issue?

Rationing is an emotive issue that understandably causes public disquiet and anxiety.[13] However, decisions on what level of services to provide need to be based on evidence of effectiveness, on information about who is likely to benefit and must take into account those who may be harmed.[39] Smear tests are currently offered to all women aged 20 to 64 years every three to five years in the UK.[5] We suggest that in the light of the current evidence it is necessary to reconsider the target population and the length of the screening interval and routinely screen only women aged between 25

*Table 1. Number and proportion of smears by source — England 1999-2000.*

| | Total smears | Inadequate | | Negative | | Borderline/mild | | Moderate dyskaryosis | | Severe or worse | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % |
| GP | 3 679 265 | 360 073 | 9.8 | 3 053 859 | 83.0 | 218 866 | 5.9 | 26 251 | 0.7 | 20 216 | 0.5 |
| NHSCC[a] | 186 987 | 19 429 | 10.4 | 151 532 | 81.0 | 13 229 | 7.1 | 1691 | 0.9 | 1106 | 0.6 |
| GUM[b] | 54 766 | 5846 | 10.7 | 38 083 | 69.5 | 9 321 | 17.0 | 1100 | 2.0 | 416 | 0.8 |
| Hospital[c] | 292 021 | 25 358 | 8.7 | 210 818 | 72.2 | 41 066 | 14.1 | 7580 | 2.6 | 7199 | 2.5 |
| Private | 28 009 | 1528 | 5.5 | 23 075 | 82.4 | 2892 | 10.3 | 250 | 0.9 | 264 | 0.9 |
| Other | 18 406 | 1976 | 10.7 | 14 455 | 78.5 | 1611 | 8.8 | 221 | 1.2 | 143 | 0.8 |
| Total | 4 259 454 | 414 210 | 9.7 | 3 491 822 | 82.0 | 286 985 | 6.7 | 37 093 | 0.9 | 29 344 | 0.7 |

[a]NHSCC = NHS community clinic; [b]GUM = genitourinary medicine clinic; [c]'Hospital' = NHS hospital. Source: Department of Health Statistical Bulletin 2000/30.[5]

and 50 years and only once every five years. Such changes may enable the health service to provide a more cost-effective service with improved quality.

## Which age group should be screened?

The age at which screening commences should be based on the onset of risk and duration of pre-invasive disease while allowing for the potential harms that can arise from false-positive results; such as over-treatment and anxiety. Performing smear tests on teenagers is particularly problematic since non-negative smears may result from normal developmental changes in the cervix.[40] Offering cervical screening to women under the age of 25 years is unlikely to be cost effective since the risk of invasive cancer is very low[31,32] while the prevalence of pre-clinical lesions is high.[41] There is a significant risk of over-treatment of incidental minor lesions in these young women,[42] the majority of which will spontaneously regress within five years. The more significant lesions will persist and subsequently be identified during the relatively long pre-clinical screen detectable duration (median duration approximately 14 years).[43]

Defining the appropriate upper age group for screening is more contentious. Almost maximal effectiveness is achieved by a programme that initiates screening at the age of 25 years and continues with three to five yearly screening to the age of 60 years.[44] However, the incidence of CIN in post-menopausal women, who have been previously screened, is exceptionally low and the PPV of an abnormal smear in the two years following a normal smear in this age group is less than 3% (best estimate = 0.9%).[45] There is a strong negative association between age and the probability of having a smear test result demonstrating severe dyskaryosis or worse[5] and it has been estimated that nearly 18 000 smear tests are required in women over 50 years to detect one new case of CIN III.[46] Modelling suggests that withdrawing women aged 50 years or over from the screening programme, if their current smear is negative and they have a recent history of regular, negative results, will generate financial savings of up to 25% for smear tests and 18% for colposcopy in addition to reducing the psychological distress associated with screening and false-positive results.[47] A large prospective cohort study estimates that 110 women require further investigation to identify one case of CIN in post-menopausal women.[45] However, the human cost of withdrawing women over the age of 50 years from the screening programme could be up to two additional cases of invasive cervical cancer per 100 000 women per year (90 cases per year in England and Wales, assuming 4.48 million women are aged 50 to 64 years).[32,47]

The difficulties of attempting to measure the psychological costs of screening and false-positive results (affecting a substantial number of women) and comparing these with the costs associated with a diagnosis of cancer (affecting a smaller number of women) are immense. New methods of measuring and equating harm and benefit need to be developed prior to recommending modifications to either the lower or upper age limit for routine screening. However, even if such methods are established, the additional morbidity associated with modifying the age group routinely screened may be an unacceptable cost in a society where decades of health promotion have promoted the value of cervical screening and where ageism and patriarchy are recognised problems. However, the substantial resources that may be saved by reducing the upper age limit could be diverted to other areas of the screening programme or invested in other areas of the health service.[47]

## At what interval should screening occur?

Screening should occur at sufficiently frequent intervals to detect abnormal cytology during the detectable pre-clinical phase of disease.[36] It has been estimated that it takes, on average, 10 to 15 years for early dysplasia to progress to CIN III[48] (best estimate = 14 years).[43] The proportion of cases of pre-invasive disease that are missed by screening is determined by the sensitivity of the test, the screening interval and the detection window; it is not affected by the incidence of disease. Incidence does, however, affect the cost-effectiveness of screening and is important in determining whether screening is worth the time and effort.[36]

The Department of Health currently recommends that a smear should be taken 'at least every five years'.[27] Health Authorities within the UK operate either three-yearly or five-yearly screening or a mixed programme of three to five-yearly screening depending on the woman's age.[5] The rate of cervical cancer is higher in women with an interval of more than three and a half years between smears compared with an interval of less than three-and-a-half years.[49] However, the majority of abnormal test results subsequent to a normal smear are false-positives, incurring a risk of unnecessary diagnostic procedures and distress. Increasing the recommended screening interval from three to five years has been suggested by many.[14,50,51] Five-yearly screening provides

comparable protection against invasive disease at a lower cost[41] and is further supported by evidence suggesting that the incremental sensitivity of the screening test decreases as the frequency of screening increases.[36] Modelling suggests that five-yearly screening would detect 90% of cervical cancers[43] and restricting five-yearly screening to women aged over 35 years is the most cost-effective option.[52] To minimise the possibility of false-negative smears failing to identify significant cytological abnormality, consideration could also be given to introducing variable screening intervals. For example, at the commencement of screening a three-yearly screening interval may be appropriate, the screening interval to be lengthened to five years after two or three consecutive normal tests.

## Screening a higher risk group?

There have been suggestions that women at increased risk of cervical cancer, defined by risk factors such as educational level, smoking status, oral contraceptive use and number of sexual partners, should be specifically targeted to improve the effectiveness of screening.[53] However, selective call of some groups of women would be potentially stigmatising and there are no population-based registers which would enable such groups to be identified routinely. Furthermore, there is no reason to believe that the rate of progression is greater in high-risk women and, therefore, there is no reason to screen them more frequently.[36,54]

## Quality not quantity?

To be of real value to women's health, financial savings accrued by a more cost-effective screening programme need to be invested in quality-control aspects of the existing service, both in primary care, where 90% of cervical smear tests are taken, and in secondary care.[5] It is known, for example, that the adequacy of the cervical smear is dependent on the expertise of the operator.[55,56] Currently, cytology laboratories report the proportion of inadequate smears to each general practice on request. However, audit might be more effective at the level of the individual smear taker. Practices or operators identified as having an above average inadequate smear rate need to be followed up with appropriate support and training.[57] If an abnormality is detected, then women should ideally be sent a personalised letter and explanatory leaflet from the practice, and be offered a consultation for further explanation and information. Although these enhancements are expensive in terms of primary care secretarial and clinical staff time, they have been shown to create less anxiety than receiving a standard computerised letter about a positive smear[58] and may lead to lower default rates from colposcopy.[59] The sampling device used also affects the effectiveness of the screening process. The Ayre's spatula is still commonly used in primary care yet is the least effective device and should be replaced by the more expensive but reliable extended tip spatula.[60,61] The skills of cytologists are also key to the cost-effectiveness of the screening programme.[62,63] High false-negative rates[4,8,25,26] may, for example, be related to low salaries, the stress of an unacceptably high workload or the need for greater training and supervision. If fewer smears are received, then the quality of reporting may improve.

## How could we improve quality?

The median waiting time for a suspected cervical cancer, from an urgent GP referral to first outpatient appointment, has recently been reported as 22 days, which is considerably longer than for many other tumour types (ovary — six days, lung — seven days, breast — nine days, colorectal — 13 days).[64] Money saved by reducing the number of smear tests (by restricting the age range or extending the interval) could indirectly help reduce the morbidity and mortality from cervical cancer by diverting funds into improving the care (e.g. waiting times) of those with a suspected positive diagnosis or by increasing the uptake of the screening programme. All screening programmes tend to have preferential uptake from the non-manual classes and those at highest risk of cervical cancer often have the lowest uptake rates.[65] Since the incidence of cervical cancer is higher in manual groups[66] it is possible that better uptake overall might lead to an increase in the rate of case detection and consequent increase in the rate of health gain.[67] Screening will also be more cost-effective in these higher prevalence groups, i.e. more cases will be detected for a given number of screening tests performed.[36] It has been estimated, for example, that increasing uptake from 70% to 80% would reduce the incidence of cervical cancer from 2.1 to 1.6 per 10 000[68] (i.e. a reduction by almost 15 cancers per year in the population of 0.25 million English women where uptake rates are currently less than 70%). Encouraging first-time attendance; that is, encouraging more women to participate rather than inviting the same women more often, may also enhance the cost-effectiveness of the screening programme.[43,51]

## Conclusions

Despite its poor fit within the screening paradigm, observational evidence suggests that organised cervical screening programmes are associated with reductions in incidence and mortality from cervical cancer. However, cervical cancer is a relatively rare disease, its natural history is not well understood and the smear test has low sensitivity, which results in many women being unnecessarily investigated and treated at a cost to their psychological health.

There is sufficient evidence to suggest that too many women are screened too frequently. While individual patient preferences must be considered, the financial savings generated from increasing the screening interval to five years and restricting routine screening to women aged 25 to 50 years, may be better spent on improving the coverage, set up, and diagnostic accuracy of the programme and the quality of the service given to those requiring further investigation and treatment. We do not believe that sufficient robust evidence currently exists to recommend such modifications to the existing programme. However, we do propose that there is sufficient uncertainty to warrant a re-appraisal of this screening programme. The data that are currently available should be collated and presented in a format that will enable all stakeholders — which obviously includes current users — to contribute to the debate about the optimal target group and screening interval. Re-awakening the discussions relating to the frequency of screening and appropriate age

range must not, however, deflect energy and effort from recruiting women who have never been screened or from further developing quality control systems.[69] It is also important that screening is not debated in isolation. It is just one part of the programme that aims to control the impact of cervical cancer, and how resources are allocated to each component of this programme must be considered. What is needed now is a debate with all stakeholders that centres on issues of quality as well as quantity.

## Declaration

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