Cervical Cancer Screening—An Alternative Viewpoint

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In 1968 Wilson and Jungner outlined the criteria which need to be satisfied before the implementation of any mass screening programme1. It is questionable whether cervical screening passes this set of tests2. Nevertheless the pressure from the media to “Take the Screen Test” is enormous and cervical screening is an integral part of the Government’s vision of medical practice3. This article asks two questions; firstly, what is the evidence that younger women can benefit from screening and secondly what is the evidence that the screening programme has benefited the women of this country as a whole.

DOES CERVICAL SCREENING BENEFIT YOUNG WOMEN?

Two of Wilson’s criteria were that the disease should pose an important health problem and that its natural history should be well known1. Evaluation of these criteria with respect to cervical cancer in younger women will allow us to assess the threat posed by the disease and how sure we can be that our interventions will be beneficial.

Of the 4 million women aged between 15 and 24 in 1987 in England and Wales4, 8 died from cervical cancer5. 1 in 60,000 women aged between 15 and 34 died from the disease6. Distressing as each individual case may be, cervical cancer in young women is not a major health problem. A nationwide screening programme cannot and should not be expected to prevent these deaths. Sensitivity is inversely proportional to specificity and so the costs, both to the tax payer and well women in the programme, would be unacceptably high. It is misleading to quote relative percentage increases in deaths and conclude that “many young women now come into high-risk groups” without at the same time quoting absolute risk values. Naturally if there were evidence that the early detection and treatment of lesions in young women would protect against the development of invasive cancer later in life then the quest to find these lesions would assume more importance. However the absence of randomised controlled trials means that the natural history of cervical cancer is very poorly understood. The significance of various lesions, especially in younger women, is uncertain. “Implicit in the nomenclature of cervical intraepithelial neoplasia (CIN) is the concept of tumour progression7” but the evidence concerning the long term outcome of such lesions is conflicting and unreliable. Studies of the progression of CIN are plagued by selection bias, inadequate follow up, difficulties in terminology8 and marked observer variation, even among expert histopathologists9. As a result it has been estimated that frank malignancy develops in anywhere between 0.17% and 70% of cases10.

Some series suggest that regression of the different ‘pre-malignant’ lesions is the norm in younger women11,12. Carcinoma in situ (CIS) is far more common than invasive carcinoma and has a peak frequency many decades earlier13,14. This suggests that either the two conditions are unrelated or that a small amount of CIS lesions convert into invasive cancer and take a very long time to do so. If progression does occur then the Walton report concluded that CIS takes more than 10 years to become invasive and dysplasia an average of 45 years15. If this is the case then a couple of screens around the age of 30 should pick up almost all of the lesions which had started at an early age and would ultimately be life threatening.

A nationwide screening programme cannot and should not be expected to protect against the extremely rare, rapidly invasive subgroup of cancers and the predominance of such cancers in younger women has been questioned by Robertson et al16.

HAS CERVICAL SCREENING BENEFITED THE POPULATION?

The efficacy of cervical cancer screening in the UK will never be known for certain as a randomized controlled trial has never been carried out. Such a trial would now be unethical. Therefore we are left with two methods of evaluating the outcome of screening: case control studies and observations on the temporal relationship between the onset of screening in a region and any reduction in mortality.

Case Control Studies

One trial of this type was carried out in North East Scotland and claimed to show that screened women were 2.3 times less likely to develop symptomatic cervical cancer than unscreened women (unmatched analysis, 95% confidence interval: 1.0–5.3)17. However this study was particularly susceptible to selection bias as controls were chosen retrospectively and only matched with respect to age. Several studies have shown that the likelihood of attending screening is inversely proportional to the chance of developing cervical cancer18,19. Consequently such a trial cannot discern what percentage of the observed difference in incidence rates, if any, was due to the screening process—it may have been due to the inherently more favourable risk profiles of attenders.

Observations On Screening Effort and Mortality Reduction

Several studies have observed regional mortality reductions but to conclude that these were due to cervical screening is tenuous. In Scotland, following the introduction of screening in one region, incidence fell by 25% in screened women (aged 20–69) but by 39% in those women not screened (aged 70 and over)20. Another review documents the decreasing death rates from cervical cancer since 1968 and attributes them to screening, but fails to report that rates were falling before the onset of screening21. It is inconsistent to disentangle age specific mortality reductions and say these are attributable to the screening process, while citing lack of effect in those age groups most intensively screened as a reason for more screening.

Furthermore regional observations are unsatisfactory: national programmes should produce results discernible at a national level. Figure 1, shows the death rates from cervical cancer from 1950 for all women aged over 15. As is clearly shown the onset of screening in the mid 1960’s has had no discernible effect on the rate at which deaths were declining.

It seems there are three possible explanations for this finding:
The second possible explanation of figure 1 is that screening has succeeded in curtailing what would otherwise have been a rising death toll from the disease. The steady decline of cervical cancer deaths shown in Figure 1 really goes against this hypothesis—is it really tenable to suggest (Fig. 2) that the onset of screening and its intensity coincided exactly, both in time and in magnitude, with an increase in the disease, to produce no overall effect? Furthermore it is often implied that the rise in overall deaths would have been caused by more cervical cancer deaths in younger women. However in 1964 only 1.4% of cervical cancer deaths occurred in women under 35—-the supposed 'increase' in deaths would have had to have been truly exponential, and simultaneous with the onset of screening, to annul a decrease of, say 30% of total deaths.

A Have Death Rates Been Recorded Inaccurately
There is little or no evidence to suggest that inaccurate recording of deaths rates can explain the trends shown in Fig. 1. A report in 1966 concluded that nearly all deaths from cervical cancer were registered and there has been no change in the international classification of the disease which may have been confounding. Retrospective scrutinisation of Cancer registration figures in the Dundee and Angus regions suggest a confounding factor in that ideally death rates should be expressed as a percentage of the total number of cervixes and not the total number of women. Hysterectomy rates have tripled in the age group 35-69 from 1963-1983, reaching about 14% in women aged 55-59. One would therefore automatically expect a decrease in cervical cancer deaths if there were fewer cervixes and this trend would owe nothing to screening.

B Has an Increase in Cervical Cancer Been Averted?
The concept of cervical cancer as a sexually transmitted disease and the proposed increase in promiscuity of young women, with less barrier contraception, is often cited as a reason to expect more cervical cancer. The increase in the amount of unprotected intercourse seems reasonable but obviously accurate figures are extremely hard to obtain. However as yet the evidence for a sexually transmitted, aetiologically important agent is unconvincing. When agents varying from Herpes Simplex virus to Syphilis and spermatozoa to smegma were considered "proof of carcinogenesis has been found to be lacking in every case". The spotlight has since turned to Human Papilloma Virus (HPV) but the epidemiological evidence implicating HPV is still "rather limited". As with Herpes Simplex Virus, it has been impossible to disprove that virus preferentially infects neoplastic tissue.

Cervical cancer is associated with sexual activity but to say that an increase in sexual activity would automatically result in an increase in cervical cancer is as justifiable as saying more grey hair would give more hip fractures. Associated factors are not necessarily causal.

The third possible explanation of Figure 1 is that screening for cervical cancer in the UK has been largely ineffective. A comprehensive analysis of screening effort and incidence and mortality from cervical cancer in Scotland, Wales and the 14 English Health regions for the last 20 years is consistent with the conclusion that "the screening programme has been largely unsuccessful." Faced with the lack of evidence to the contrary from both case control and observational studies this conclusion must be seriously considered.

In this light the detractions of screening assume relatively more importance. At least 10,000 excision biopsies are performed each year and the number of women traumatised by abnormal smears must be an order of magnitude greater. The cost of overassessment and overtreatment are not only financial; Luesley et al. studied a series of 915 women who had cone biopsies and they found that 13% had primary or secondary haemorrhages, 17% developed cervical stenosis and 4% subsequently suffered from abnormal pregnancies or infertility. Despite the diagnosis and treatment of tens of thousands of abnormal cervical smears over 25 years the first study of the psychosocial trauma associated with this activity was only published in 1988. Campion and co-workers found that a group of 56 women reported less spontaneous interest, frequency, arousal and orgasm, with more pain and negative feelings towards sex, 6 months after the diagnosis and treat-
ment of an abnormal cervical smear. These differences were highly statistically significant, when compared to a group of controls who were well matched for the same variables beforehand.

CONCLUSION
In England and Wales 40,000 smears and 200 excision biopsies are undertaken for every life saved—a grievously poor cost-benefit ratio. The cost of saving a life has been estimated at £300,000. The reasons for the failure of cervical screening are mainly organizational and administrative; in Nottingham fewer than two thirds of women received the recommended follow up. However other factors may also be important. The lack of effect on mortality after the treatment of so many 'pre-malignant' conditions must cast doubt on the 'dogma of progression'. The sensitivity of the test in the UK has been questioned on a day to day basis as well as in the much publicized tragedies in Liverpool and Oxford. Both of these observations raise the question of whether, in the search for certain pathological entities such as CIN, other aetologically important lesions have been overlooked.

Improvements in the programme have been promised with the new computerized recall system but the gross inadequacy of our population registers for the task of screening means that improvements will be very hard to achieve. Perhaps refinement is suggested after critical analysis of the case for screening in younger women. Faced with the lack of evidence that younger women will benefit from screening, even when an abnormality is detected, the amount of emotional trauma associated with each case, and the extreme rarity of cancer in this age group, is it not time to divert resources? Computer simulation programmes suggest that screening women under the age of 35 is particularly unrewarding and efficiency would be greatly increased by concentrating on older age groups. The almost inverse relationship between attendance and risk of cervical cancer is due to spend more effort on targeting services. Given the limited resources available more frequent screening would be counterproductive to the aim of more widespread screening. The IARC Working Group estimated that reducing the screening interval from 5 to 3 years would only produce a 7% extra reduction in mortality.

There is an ethical dimension to screening—it is fundamentally different from other aspects of medical care in that we go out into the community with an implicit promise of net benefit. Consequently informed consent is imperative. We should inform women of their absolute risks of dying from cervical cancer, our certainty (or lack of it) that we can improve these odds and the possible risks to their physical and emotional health. Such an approach may help to redress the imbalance that exists between the women at low risk who attend cervical screening and the women who need protection from cervical cancer but have never had a smear in their lives.

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1987–88. 1,468 applications on 88 days (16.7/day). 132 problems.
1988–89. 1,304 applications on 88 days (14.8/day). 134 problems.
1898–90. 1,419 applications on 87 days (16.3/day). 141 problems.

More than 75% of the problems are of an identical type and involve discrepancies in age on Forms A and B from the age given on the Certification of Death. I accept a difference of a year, since this can easily be due to lack of knowledge of the deceased’s precise birthdate; others I have to clarify.

Between 3 and 5% of the difficulties are due to the doctor signing Form B not answering the “pacemaker” question. This always results in a ‘phone call from me or the crematorium.

Two to 3% of “Cause of Death” answers are either unacceptable, or unclear. Occasionally there is a disparity between the answers on Forms B and C; these are usually resolvable with a ‘phone call or two. In other instances the case is referred to the Coroner, eg as in one case where the doctor on both forms gave death as due to “1a. Bronchopneumonia. 1b. Fracture of femur.” It is perhaps worth pointing out that this cause of death was accepted by the Registrar of Births and Deaths, otherwise the forms would not have come to me!!

Form A produces about 4% of the problems, but these, by virtue of the nature of the Form, are never due to medical insufficiency!

The question which causes most difficulty is one exclusively for the hospital doctor, and I see this mainly in my role as a Consultant Pathologist, rather than Medical Referee. Question 8A on Form B is a multi-part question, any part of which, when answered in the negative, causes the whole to become negative. The question itself concerns deaths of inpatients in Hospitals, the definition of a “hospital” being laid down (it is much wider than one might at first think); it goes on to enquire whether a post mortem has been held, and whether by a practitioner of five years full registration (who is not a relative of the deceased or a relative or partner of the doctor signing Form B) and whether the results of any post mortem are known to the doctor signing the Form. What is not clarified anywhere on either Form B or C is the implication of a “Yes” answer. In these circumstances there is no need for Form C! About 2.5% of the problems arise in this area. There would be more, but I manage to prevent almost any coming from my own hospital and presenting to the Referees.

The above problem is basically one of the design of the Forms (most of the questions seem to be unaltered from 1902). Another design defect is that, certainly on City of Bristol Forms, there is no question along the lines of “If you have discussed the case with the coroner and he has allowed you to issue the Death Certificate then please so indicate.” There are regular occasions when, from answers given on Form B, I know that the deceased died within a few hours of Hospital admission. Almost all Coroner’s wish to know of such cases, but in a significant percentage they will not order a post mortem and will allow the normal paper work to be completed (20% of Coroner’s cases don’t come to post mortem; Knight, 1987). Never-the-less the Coroner will record that he has been told of the case by completing a “Pink A” certificate. There is nothing on the Forms to prompt a doctor to record that he has discussed a case with the Coroner; in consequence I regularly inform the Coroner of these “sudden deaths”, only to be told that he knows about all almost of them! However, there is at least one Crematorium Authority, in The Wirral, where this question is asked. Perhaps there are others.

Other regular but occasional problems arise; examples are:

a. Doctors forgetting to sign the Form.
b. Cause of Death not filled in.
c. Admitting to a pecuniary interest in the death (this absolutely rules out the signatory! !)
d. Doctors on holiday and not available to sign Form B when no other doctor had looked after the deceased (the signatory must have given some clinical care prior to death.)
e. Questions left unanswered.

All in all, the current design of the Forms required for Cremation leaves something to be desired. The task of the Medical Referee could be eased with better protocols and, as long as the existing Cremation Law remains, there will continue to be an important role for Referees. Whether the existing Law is suitable for today’s is another matter. In 1971 the Broderick Report suggested basic changes; to date virtually nothing has happened.

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