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Adequacy of cervical cytology sampling with the Cervex brush and the Aylesbury spatula: a population based randomised controlled trial

Paola Dey, Stuart Collins, Minaxi Desai, Ciaran Woodman

Centre for Cancer Epidemiology, University of Manchester, Manchester M20 4QL
Paola Dey, lecturer in public health
Stuart Collins, statistician
Ciaran Woodman, professor of public health and cancer epidemiology

Department of Cytopathology, Christie Hospital NHS Trust, Manchester M20 4QL
Minaxi Desai, consultant cytopathologist

Correspondence to:
Dr Paola Dey, Centre for Cancer Epidemiology, Christie Hospital NHS Trust, Manchester M20 4QL.

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Abstract

Objective—To compare the adequacy of cervical cytology sampling with two sampling instruments commonly used in primary care—namely, the Aylesbury spatula and the Cervex brush.

Design—Pair matched, population based randomised controlled trial.

Setting—86 general practices and family planning clinics in Greater Manchester.

Subjects—15 882 cervical smears taken from women aged 20-64 years as part of the national cervical screening programme.

Interventions—Participating centres were allocated to sample with either the Cervex brush or the Aylesbury spatula.

Main outcome measure—Inadequate smear rate.

Results—5.4% and 5.5% (433/8086 and 426/7796) of smears taken with the Cervex brush and the Aylesbury spatula respectively were reported as inadequate (odds ratio 0.95; 95% confidence interval 0.74 to 1.22).

Conclusion—The Cervex brush offers no advantage over the Aylesbury spatula in reducing inadequate smear rates in the primary care setting.

Introduction

Inadequate cervical smears are not only a cause of needless anxiety and inconvenience to women but are also an additional cost to the NHS. Attempts to reduce the rate of inadequate smears have focused on improving the competence of smear takers and the design of sampling instruments, but these instruments have rarely been evaluated in population based settings. We compared the adequacy of cytological sampling in a primary care setting with two commonly used instruments, the Cervex brush and the Aylesbury spatula.

Methods

The unit of randomisation was a general practice or family planning clinic. Fifty four general practices and 32 family planning clinics in Greater Manchester participated. Participating centres were stratified by primary care setting (general practice or family planning clinic) and then pair matched for their rate of inadequate smears during a preceding six month period (the "historical inadequate smear rate"). Within each pair one centre was randomly allocated to use the

Table 1—Appearance of study smears (expressed as numbers (percentages) of smears)

Smear result	Cervex brush (n = 8086)	Aylesbury spatula (n = 7796)
Inadequate†	433 (5.4)	426 (5.5)
Negative	6736 (83.3)	6641 (85.2)
Abnormal	917 (11.3)	729 (9.4)
Borderline	415 (5.1)	342 (4.4)
Mild dyskaryosis	289 (3.6)	240 (3.1)
Moderate dyskaryosis	118 (1.5)	82 (1.1)
Severe dyskaryosis	95 (1.2)	65 (0.8)

†Overall rate of inadequate smears for laboratory during study 5.8%.

Cervex brush and the other to use the Aylesbury spatula. The study ran for nine months in 1994, including a one month run in period to allow familiarisation with the allocated instrument. All smear takers were offered training and given written instructions on the use of their allocated instrument.

Compliance of centres was monitored by comparing the number of smears returned by each centre with the number of instruments supplied from a central location. As a further check we visited all centres at least once. Smear takers recorded when an instrument other than the one allocated had been used, and a random sample of 10% of smear forms was examined to estimate how often this occurred.

Smears from women attending the participating centres were processed and reported by the Christie Hospital NHS Trust Cytopathology Laboratory, which screens around 150 000 smears a year. Cytoscreeners were blinded to the instrument used. The primary end point was the inadequate smear rate. An inadequate smear was one that failed to meet the criteria of the British Society for Clinical Cytology.¹

The study was approved by the local research ethics committees of participating centres.

USE OF GROUP RANDOMISATION

Randomisation by group was used to allocate women to sampling with the Cervex brush or the Aylesbury spatula. This method of randomisation facilitated recruitment of a sample large enough to investigate small differences in our primary end point and increased the likelihood of compliance with the study protocol. Group randomisation is particularly useful when evaluating preventive strategies, but statistical implications mean that standard methods for sample size estimation and analysis are no longer appropriate.

Observations on subjects within the same group cannot be assumed to be independent but in general will be correlated. For example, women attending a particular practice may be more likely to share demographic characteristics which make them more or less likely to have an inadequate smear. In these circumstances each subject contributes less information under group randomisation than when the subject is the unit of randomisation.

As a consequence larger sample sizes are required.

When estimating the variance of test statistics it is necessary to account for this within group dependence. This can be achieved by incorporating a variable which measures within group dependence—the intraclass correlation coefficient, derived from the appropriate analysis of variance design.² This coefficient is restricted to values between zero and 1, larger values corresponding to greater within group dependence. A value of zero implies that all observations in the same group can be considered independent; a value of 1 implies that dependence is total and the group behaves as a single individual. For binary outcomes, values of the coefficient are typically low. However, when large groups are randomised, as in this study, even very weak dependence corresponding to values close to zero can substantially alter estimates of variance.

The Cervex brush costs 15.5p and the Aylesbury spatula 3p. Hence given a rate of inadequate smears in the population of 6% and the cost of repeating an inadequate smear of £11.25³ a reduction of 1.5% in inadequate smears would more than outweigh the extra cost of the Cervex brush. As 86 centres were available for randomisation and the intraclass correlation coefficient based on historical data was 0.006, a sample of 15 000 smears was required to detect a difference of 1.5% at the 5% level of significance (two sided) with a power of 90%.

The difference in rate of inadequate smears between the groups was compared by using the odds ratio. A Mantel-Haenszel statistic adapted for the group randomised design was used to test the significance of the odds ratio⁴ and 95% confidence intervals constructed.²

Results

A total of 15 882 smears from women aged 20-64 years were available for analysis; 8086 (51%) were taken by centres allocated the Cervex brush (6122 by general practices, 1964 by family planning clinics) and 7796 (49%) by centres allocated the Aylesbury spatula (5541 by general practices, 2255 by family planning clinics). We estimated that only 1.3% of the smears were taken with a sampling instrument other than the one allocated. All smears were retained in their original study arm for analysis. The mean ages of women in the Cervex brush and Aylesbury spatula arms were 36.0 and 35.5 years respectively. The mean number of smears contributed by each centre was 185 and the intraclass correlation coefficient 0.008.

Of the smears taken with the Cervex brush and the Aylesbury spatula, 5.4% (433/8086) and 5.5% (426/7796) respectively were reported as inadequate (odds ratio 0.95 (95% confidence interval 0.74 to 1.22); $P = 0.62$) (table 1), suggesting no difference between the instruments in the adequacy of cytological sampling. Inadequate smear rates varied between nil and 18.7% in the centres allocated the Cervex brush and between 1.2% and 17.4% in centres allocated the Aylesbury spatula.

Subgroup analysis compared inadequate smear rates across the different primary care settings and across centres with a high historical inadequate rate (>12%), a moderate historical inadequate rate (6-12%), and a low historical inadequate rate (<6%). No significant differences were observed (table 2).

Discussion

So far as we can ascertain this is the first population based randomised controlled trial comparing the Cervex brush and the Aylesbury spatula. Eligibility of participating centres was determined by their willingness to accept randomisation, not by the competence of

Table 2—Inadequate smear rates by sampling instrument, primary care setting, and historical inadequate smear rate of participating centre

Subgroup analysis (No allocated Cervex brush, No allocated Aylesbury spatula)	Inadequate smear rate (%)		Odds ratio (95% confidence interval)
	Cervex brush	Aylesbury spatula	
Primary care setting:			
General practice (n = 6122, n = 5541)	5.7	5.5	1.01 (0.77 to 1.33)
Family planning clinic (n = 1964, n = 2255)	4.4	5.3	0.74 (0.39 to 1.42)
Historical inadequate smear rate of centre:			
Low (<6%) (n = 2041, n = 1712)	4.5	5.3	0.78 (0.38 to 1.57)
Moderate (6-12%) (n = 4767, n = 5092)	5.0	4.9	1.06 (0.80 to 1.40)
High (>12%) (n = 1278, n = 992)	6.7	7.1	0.85 (0.44 to 1.63)

Key messages

- Inadequate cervical smears cause anxiety and inconvenience for women and are an additional cost to the NHS
- Cervical sampling instruments have rarely been formally evaluated in population based settings
- Group randomisation is useful when evaluating community based interventions but requires modified statistical techniques
- The Cervex brush offers no advantage over the Aylesbury spatula in reducing rates of inadequate smears when used in primary care

smear takers; hence the findings are likely to be generalisable to the screening programme. In addition, the findings are consistent with those of the only other randomised controlled trial of these sampling instruments, undertaken in a more narrowly defined study population of young women attending a single family planning clinic.⁵ Though other studies have suggested that the Cervex brush may improve the adequacy of smears taken by less competent smear takers,⁶ this was not substantiated by subgroup analysis in this study (table 2).

The Christie Hospital NHS Trust Cytopathology Laboratory routinely used the British Society for Clinical Cytology statement on cell content of cervical smears to define the adequacy of cytological sampling. Other researchers evaluating the effectiveness of sampling instruments have used the presence of endocervical cells to define the adequacy of smears.⁶⁻⁸ This is an unreliable predictor, and its use as the sole criterion of adequate sampling is no longer recommended.^{1 9 10}

Smears taken with the Cervex brush were more likely to contain cytological abnormalities (table 1). However, the difference was of only borderline significance (odds ratio 1.19 (95% confidence interval 1.00 to 1.41); $P = 0.05$) (table 3). Furthermore, the pre-randomisation stratification was based on historical inadequate smear rates and not on previous rates of cytological abnormality. Therefore, the study design does not guarantee a balanced distribution of risk factors for cytological abnormality between the groups.

We chose the rate of inadequate smears rather than the rate of detection of cytological abnormality as our primary measure of sampling efficacy for the following reasons. Cytological examination has detection accuracy rather than diagnostic accuracy, and there is

imperfect correspondence between the severity of epithelial abnormality predicted by cytological findings and that found histologically in cervical tissue. There is much uncertainty surrounding the natural course of early cervical neoplasia, and high rates of spontaneous regression of minor cytological abnormalities have been reported.¹¹ In addition, more efficient sampling may merely advance the time of detection of abnormality without influencing outcome. In these circumstances it is difficult to quantify the benefits to the NHS and women of the earlier detection of epithelial abnormalities of uncertain malignant potential.

Our results do not support the routine use of the more expensive Cervex brush to reduce inadequate smear rates in the cervical cytology screening programme.

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ONE HUNDRED YEARS AGO

THE ETHICS OF THE ARMY MEDICAL QUESTION.

The full significance of the present crisis in army medical affairs is apt to be overlooked by the mere casual observer. Such a one may, indeed, be excused if he hastily arrives at the conclusion that present difficulties are merely the revival of old contentions, and possess only limited interest. But, while the struggle is old and has been long drawn out, its present phase has really wider and deeper issues than previous disputes, not alone to the State and the army, but to society at large.

The present deadlock means simply: Medical men decline to serve in the army in a position of military and social inferiority to other officers, especially the so-called combatant, in so far as that the inferiority depends upon

army status. It is only a sign of the times, of the social revolt against mere artificial distinctions between men otherwise equal and indistinguishable. The army is about the last entrenchment held by the old feudal spirit, and it is against that the present struggle is directed.

The controversy is thus as interesting to the sociologist as it is dangerous to the efficiency of the army, and doubtless embarrassing to the statesmen who come between the disputants, and have certain responsibilities for both. It is its bearing on the well-being of the land forces of the Crown that invests it with a national importance little comprehended or even suspected by the civilian uninitiated into army affairs.

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