Collection devices for obtaining cervical cytology samples (Review)

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ABSTRACT

Background
The large variation in disease detection rated with cervical smears may be partly due to differences in the sampling devices and the techniques of sampling.

Objectives
To assess whether the design of the cervical smear device affects rates of inadequate smears and the detection of disease; and whether the presence of endocervical cells in the smear affects disease detection.

Search strategy
We searched the Cochrane Gynaecological Cancer Group
trials register and MEDLINE up to July 1997. We also handsearched 16
journals.

Selection criteria
Randomised and quasi-randomised trials and non-randomised comparative studies comparing cervical smear collection devices in women attending for primary screening, colposcopy following an abnormal smear or colposcopy after treatment.

Data collection and analysis
Two reviewers independently abstracted data. Study quality was assessed.

Main results
Thirty-six trials and six observational comparative studies were included. The Ayre spatula was shown to be less effective compared with extended tip spatulas for collecting endocervical cells in eight trials (odds ratio 2.25, 95% confidence interval 2.06 to 2.44). Use of a spatula with the cytobrush was more effective than spatula alone at collecting endocervical cells (odds ratio 3.33, 95% confidence interval 3.05 to 3.63) and the same effect was present for adequate smear rates (odds ratio 1.51 95% confidence interval 1.19-1.92). Extended tip spatulas were also superior for the detection of dyskaryosis in seven trials (odds ratio 1.21, 95% confidence interval 1.10 to 1.33). Based on data from two trials and three observational studies, smears that contained endocervical cells were more likely to detect dyskaryosis, particularly in severe disease. The proportion of smears with endocervical cells present increased with increasing severity of the disease.

Authors' conclusions
Extended tip spatulas of various designs appear to be better for collecting endocervical cells than the commonly used Ayre spatula. The most effective combination appears to be the cytobrush with an extended tip spatula. The rate of detection of endocervical cells appears to be a valid and convenient surrogate for the ability to detect dyskaryosis and for adequate smear rates. The ability of the extended tip spatula with the cytobrush compared with the extended tip spatula alone to detect disease, needs to be evaluated in a trial.

PLAIN LANGUAGE SUMMARY

This review is no longer appropriate for update as liquid based cytology has superceded smear technology.

Commonly used spatula not the most effective for cervical screening.

Cervical screening (pap smear) is an effective way of detecting pre-cancerous abnormalities of the cervix (cervical intraepithelial neoplasia). Tests can be affected by the tester's skill and the design of the device used. Inadequate smears can produce incorrect results, causing stress and inconvenience to women having to undergo repeat screening. This review of trials found that the commonly used Ayre spatula is not as effective in collecting cells as the extended tip spatula. The most effective appears to be a combination of the cytobrush with an extended tip spatula.

BACKGROUND

Cervical screening has been proven to be effective in decreasing the incidence of invasive disease where comprehensive programmes exist (Parkin 1985; Duguid 1985). The effectiveness of cervical cancer screening programmes is limited in part by biological factors (such as the rate of progression of the disease), however, it is also partly under human control. For a disease with a long latent phase, the false negative rate is an important screening variable. The false negative rate associated with cervical smears varies from 55% (Mitchell 1988) to 1.5% (Van der Graaf 1987). This suggests that the false negative rate may be largely a function of interpretation and acquisition of cervical smears. The latter is a function of training and sampling device used. This review concentrates on the effectiveness of these devices.

Over recent years there has been a tendency to judge the adequacy of a cervical smear by the presence of endocervical cells, since this is a common (and therefore easily measured) endpoint which, if valid, could be useful in audit and health services research. That these cells reflect the adequacy of the smear is anatomically plausible, since the presence of such cells suggests that the transformation zone, from which premalignant change arises, has been sampled. The Report of the Working Party of the Royal College of Pathologists, British Society for Clinical Cytology and NHS Cervical Screening Programme (WPRCP 1995) recommend that information regarding the presence of metaplastic and/or endocervicals cells should be documented as they provide evidence of probable transformation zone sampling. Furthermore the Quality Assurance Guidelines For The Cervical Screening Programme for the U.K. (WPRCP 1995) recommend that greater than 80% of smears should contain such representative cells.

However, direct confirmation that the yield of endocervical cells correlates with the detection of dyskaryosis has been sought only within single and often underpowered studies. Therefore, we have used structured review and meta-analysis of randomised controlled trials and large observational studies to examine the question of whether the presence of endocervical cells is a surrogate for the quality of cervical sampling with regards to detection of disease and adequate cervical smears.

The design of cervical smear collection devices might influence inadequate smear rates. Inadequate smears have generally been defined as insufficient cellularity, poorly fixed, contaminated by blood, menstrual debris, inflammatory cells or spread too thickly. Inadequate cervical smears need repeating as there might be disease present. Paterson (Paterson 1984) demonstrated that a significant number of women who developed cervical cancer who had been screened, actually had inadequate cytology on screening smears. If the design of the cervical smear collection device influences inadequate smear rates, this might reduce costs to the health service and reduce stress and inconvenience for women having to have repeat screening.

There are many different designs of cervical smear collection devices. The characteristics of the collection devices examined in this review are summarised below:

Features of Spatulas:

AYRE: Wood
Advantages; cheap, easy to use, atraumatic, low incidence of blood contamination
Disadvantages; broad head may prevent sampling of canal, cells can get trapped into wood
AYLESBURY: Wood
Advantages; narrow head to enable access to the cervical canal, cheap, easy to use, samples endocervix and ectocervix
Disadvantages; cells might get trapped into wood
MILEX, ACCU-PAP, ROCKET, PAPLAST, ROLON: Plastic
Advantages: as Aylesbury, plastic prevents cells becoming embedded into spatula
Disadvantages: moderate cost
MULTISPATULA: Plastic, wide flat head with sliding central tip
Advantages: sliding tip allows sampling of all shaped cervices
Disadvantages: moderate cost
ARMOCERVICAL: Plastic, wide flat head with fixed central tip
Advantages: as Multispatula
Disadvantages: Moderate cost
CYTOPICK; Plastic
Advantages: cork screw design dislodges endocervical cells
Disadvantages: Moderate cost

Features of Specific Sampling Devices:

Endocervical Sampling Devices:

COTTON SWAB (Q-TIP)
Advantages; low cost, atraumatic, minimal discomfort
Disadvantages; cells can get trapped in fibres, only for endocervix
CYTOBRUSH
nylon fibres at tip of handle, fibres perpendicular to handle
Advantages; malleable fibres allow insertion into canal, nylon prevents cell entrapment, fibres are rigid can penetrate gland
Disadvantages; rigid fibres can be traumatic, can cause pain, metal wire in theory can perforate pregnancy sac

Ectocervical and Endocervical Sampling Devices

CERVEXBRUSH
Parallel plastic fibres at tip of handle, fibres are longer in the middle for endocervical sampling
Advantages; simultaneously samples ecto- and endo- cervix
Disadvantages: High cost
BAYNEBRUSH
Two cytological brushes arranged at right angles
Advantages; simultaneously samples ecto- and endo- cervix, malleable design adapts to all shaped cervices
Disadvantages; High cost, rigid fibres can be traumatic, metal wire in theory can perforate pregnancy sac
PROFILEBRUSH
Modified Cytobrush fibres at periphery are shorter to sample ectocervix
Advantages; simultaneously samples ecto / cervix,
Disadvantages; high cost, rigid fibres can be traumatic, metal wire in theory can perforate pregnancy sac

OBJECTIVES

1) To determine whether the presence of endocervical cells is a quality criterion in cervical cytology

2) To compare different sampling device ability to detect dyskaryosis and improve smear adequacy rates.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomised Controlled Trials (RCTs) using alternative cervical smear screening devices were identified by a) a computerised literature search, tracing references listed in the relevant articles and b) a manual search of appropriate journals. A trial was eligible for inclusion if it dealt with the ability of a cervical smear collection device to collect endocervical cells or dyskaryosis, and contained a control group which the authors claimed was created by a randomised procedure. The computerised MEDLINE search was conducted to identify all registered randomised trials comparing cervical smear devices before July 1997.

Types of participants

Women attending for primary screening, colposcopy following an abnormal smear or colposcopy after treatment.

Types of intervention

A trial was eligible for inclusion if it dealt with the ability of a cervical smear collection device to collect endocervical cells or detect atypia or dyskaryosis.

Types of outcome measures

A trial was eligible for inclusion if it dealt with the ability of a cervical smear collection device to collect endocervical cells, produce adequate smears and detect atypia or dyskaryosis in cervical smears.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

A computerised MEDLINE search was conducted to identify all registered randomised trials comparing cervical smear collection devices before July 1997
The method for identifying trials was as follows:
1 RANDOMIZED-CONTROLLED TRIAL in PT
2 RANDOMIZED-CONTROLLED-TRIALS
3 RANDOM-ALLOCATION
4 DOUBLE-BLIND-METHOD
5 SINGLE-BLIND-METHOD
6 CLINICAL-TRIAL in PT
7 explode CLINICAL-TRIALS
8 (clin* near trial*) in TI
9 (clin* near trial*) in AB
10 (singl* or doubl* or trebl* or tripl*) near (blind* or mask*)
11 (#10 in TI) or (#10 in AB)
12 PLACEBOS
13 placebo* in TI
14 placebo* in AB
15 random* in TI
16 random* in AB
17 RESEARCH-DESIGN
18 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #11 or #12
or #13 or #14 or #15 or #16 or #17
19 explode GENITAL NEOPLASMS, FEMALE
20 #18 and #19
21 TG=ANIMAL not (TG=HUMAN and TG=ANIMAL)
22 #20 not #21
23 PT=CONTROLLED-CLINICAL-TRIAL

24 #18 or #23
25 #24 and #22
26 #25 not #21
Our search strategy was similar to the one that is advocated by the Cochrane Collaboration (Dickersin 1994)

Observational studies examining the incidence and severity of cytological abnormality in cervical smears according to endocervical cell status were also identified.

Sixteen journals thought to be most likely to contain relevant publications were hand searched, (Acta Cytologica, Acta Obstetrica Gynecologica Scandanavia, Acta Oncologica, American Journal of Obstetrics and Gynaecology, British Journal of Cancer, British Journal of Obstetrics and Gynaecology, British Medical Journal, Cancer, Cytopathology, Diagnostic Cytopathology, Gynecologic Oncology, International Journal of Cancer, International Journal of Gynaecological Cancer, Journal of Family Practice, Lancet, Obstetrics and Gynaecology).

METHODS OF THE REVIEW

Randomised controlled trials were analysed for the method of randomisation, characteristics of the patients and the source of recruitment, the presence or absence of endocervical cells obtained by smear devices, blood contamination and inadequate smears and the presence or absence of dyskaryosis/atypia.
Observational studies examining the incidence and severity of cytological abnormality in cervical smears according to endocervical cell status were analysed

DESCRIPTION OF STUDIES

Characteristics of Trials Identified

Thirty-six randomised trials were identified. In all but two trials endocervical cells were used as an outcome, whereas the rate of detection of dyskaryosis was included in only 19 trials. Trial characteristics included year of publication, origin, number of patients included, number and type of collection devices, method of randomisation, source of patient recruitment and whether endocervical cells, blood contamination, inadequate smears or dyskaryosis was used as an outcome measure.
Six non-randomised trials of cervical smear collection devices with respect to detection of endocervical cells and dyskaryosis were also identified
(Elias 1983; Mauney 1990; Mitchell 1988 (b); Vooijs 1986; Vooijs 1985). Twelve randomised controlled trials (35%) were exclusively identified by handsearching.
Patients were recruited from four principal sources:
1. primary screening centres i.e. general practice, student health centres, genito-urinary clinics and general gynaecological clinics.
2. colposcopy clinics, patients with a recent history of abnormal cervical cytology.
3. colposcopy clinics and gynaecology clinics, after treatment of confirmed cervical dysplasia.
4. antenatal clinics.

Nineteen of the randomised controlled trials identified compared the ability of cervical smear collection devices to detect abnormal cervical cytology. Unfortunately, the results from individual publications were not presented in a uniform manner. In some studies, cytological abnormality was reported with all grades of dyskaryosis grouped together, in others low or high grades were distinguished while yet others distinguished all grades of severity, i.e. cytological atypia, mild, moderate, severe or invasive carcinoma. This heterogeneous classification of the different grades of dyskaryosis restricted comparisons of the abilities of devices to detect different grades of abnormality. Nevertheless the trial results permitted comparisons of rates of detecting dyskaryosis per se. None of the trials differentiated between squamous or glandular cytological atypia.

Studies investigating the incidence of dyskaryosis in smears with and without endocervical cells are included in the latter part of the analysis. Only three of these studies (Kristensen 1989; Szarewski 1990; Szarewski 1993 (b)) were randomised controlled trials. Therefore, we sought to augment these data with evidence from five observational studies. Three of these (Elias 1983; Vooijs 1985; Vooijs 1986) appeared to use data derived from the same study population. We therefore selected the results from Voojis (Vooijs 1985) as this was the largest study. Mitchell et al 1993 examined the results of all the smears reported by the Victorian Cytology Service, Australia during the years 1987-1991. During 1987 and 1988, smears were classified as being endocervical positive if they contained any columnar or squamous metaplastic cells. However, more stringent criteria were introduced in 1989 requiring the identification of at least ten or more endocervical cells for smears to be classified as endocervical cell positive. During 1990 and 1991 practitioners were instructed to use Cytobrushes in combination with spatulas and cervix samplers (designed to sample the ectocervix and endocervix simultaneously) on all non-pregnant women.

METHODOLOGICAL QUALITY

The method of randomisation (an important source of bias) was not described in nine studies (Buxton 1987, Hamblin 1985; Hjersing 1991; Kavak 1995, Kristensen 1989; Metcalf 1994 (a); Schettino 1993; Selvaggi 1991; Waddell 1990). Sixteen trials were quasi-randomised, allocating smear device by either a fixed period of time, by group, by file number, or by alternate assignment. In 11 trials allocation of sampling device was truly random and was assured either by sealed envelopes or computer generated allocation.

Randomisation was used to allocate a specific collection device to an individual patient or to determine the order of more than one

collection device to be used on the same patient. The advantage of the former trial design is that only one collection device is used on a specific patient where as the latter design may permit interaction between the individual trial spatulas depending on their order. Giles, Johnson, Pistofides and Schettino (Giles 1991; Johnson 1991; Pistofides 1988; Schettino 1993) randomized the order of collection devices to be used on individual patients but made no comment if the order of the devices influenced actual results. Hjersing (Hjersing 1991) demonstrated that if a Cytobrush was used prior to a spatula, then the total proportion of smears containing endocervical cells was greater than if the devices were used in the opposite sequence. Waddell (Waddell 1990) compared the Ayre spatula to the Cervexbrush; again, if the Cervexbrush was used first, this enhanced the Ayre's ability to collect cells from the transformation zone. The ability of the Cervexbrush to collect endocervical cells was not influenced by the previous sampling by the Ayre spatula. In a RCT specifically designed to investigate whether the order of collection devices influenced smear adequacy, Noel (Noel 1993) compared the Ayre and ectocervical brush sampling before and after endocervical sampling: sampling the endocervix and then the ectocervix produced more ectocervical smears containing endocervical cells. Vierhout (Vierhout 1987) used both the Multispatula and Ayre spatula on the same patient in random order, the efficacy of both devices was enhanced when they were used as the second collection device.

The issue of statistical power is raised by three authors (Koonings 1992; Paraiso 1994; Pretorius 1991) and they achieved the number of patients required to show a pre-specified difference in the ability of different devices to collect endocervical cells.
Johnson (Johnson 1991) combined the results of the Cytobrush and CervexBrush as they were similar, but this prevented the use of their data in this review as we could not assess the performance of the individual devices.

The classification and terminology of cytological abnormality varied in the identified studies. In some studies, cytological abnormality was reported with all grades of atypia/dyskaryosis grouped together, in other low and high grades were distinguished while yet others distingushed all grades of severity i.e. cytological atypia, mild, moderate, severe or invasive carcinoma. The heterogenous classification of the different grades of dyskaryosis restricted comparison of the abilities of devices to detect different grades of abnormality. Nevertheless the trial results permitted some comparisons of rates of detecting dyskaryosis.

RESULTS

1. Which Devices Are Best At Collecting Endocervical Cells?

1.1. Classical Ayre compared with extended tip spatulas. Eight randomised controlled trials were identified comparing the classical Ayre spatula with extended tip spatulas. Hughes compared three extended tip spatulas with Ayre design. The study by Stock (Stock 1988) compared a plastic Accu-Pap collection device of an Ayre design with an extended tip Accu-Pap spatula. Wolfendale (Wolfendale 1987) compared the Ayre with an extended tip spatula and used cellular content scores based on the presence of endocervical cells, cervical mucus and metaplastic cells from the transformation zone to grade the spatula performance, the extended tip spatula produced better cellular scores. All trials demonstrated that an extended tip spatula is superior to the classical Ayre design spatula in harvesting endocervical cells OR 2.15 95% CI (1.98-2.34). The same significant effect was found when only the primary screening trials were included (Bounds 1976; Goorney 1989; Szarewski 1990; Vierhout 1987; Woodman 1991) OR 2.13 95%CI (1.94-2.32).

1.2. Spatulas of all designs compared with spatulas with endocervical sampling devices or combination devices. In all trials, excluding Hamblin (Hamblin 1985), comparing simple spatulas with spatulas with a specific endocervical sampling device or a combination device, demonstrated that the yield of endocervical cells was better with the latter instruments. Spatula and Cytobrush, Cervex brush compared with Spatula OR 3.48 95%CI (3.20-3.78) and 1.57 (1.42-1.73) respectively. Hamblin (Hamblin 1985) suggest that the extended tip plastic Milex spatula was better than a wooden spatula and cotton swab. However, in this study randomised patients had their cervices wiped to remove cervical mucus prior to sampling and this might have been effected by this pre-treatment. It should be noted that Garite (Garite 1978) demonstrated that the spatula and Cotton Swab was superior to a spatula alone. However, there were insufficient data in the publication to include their results in our comparisons.

1.3. Spatula and cotton swab compared with spatula and cytobrush The comparison of these two cervical smear collection techniques is the most heavily investigated in the medical literature by randomised trials (101RCTs). It is clear that the combination of a spatula and Cytobrush was significantly superior to the spatula and Cotton Swab OR 3.58 95% CI (3.26-3.93). The significance was slightly increased by only including the primary screening trials (Boon 1989, Deckert 1988, Kristensen 1989; McCord 1992; Neinstein 1989; Paraiso 1994; Pretorius 1991; Schettino 1993) OR 3.62 95% CI (2.99-4.36).

1.4. Spatula and Cytobrush compared with combination devices. Four combination devices; Bayne Brush, Cervex Brush, Profile Brush and Cytopick specifically designed to sample both the ectocervix and endocervix are compared with the combination of a spatula and Cytobrush. In each case, the combination of the spatula and Cytobrush proved to be superior to the Cervex brush, Bayne Brush and Cytopick. The Profile Brush proving to be marginally superior in the single trial making this comparison (Data presented in analysis section).

1.5. Spatula and cotton swab compared with the Bayne Brush. The Bayne Brush proved to be consistently better than the spatula and

Cotton Swab in three studies (Data presented in analysis section).

1.6. Ayre and bulb aspirator compared with Ayre and Cytobrush. In one trial the Ayre spatula was used in conjunction with the rarely employed Bulb Aspirator and compared with the Ayre and Cytobrush. As might be expected the latter technique was the superior (Data presented in analysis section).

2. 1 Which Devices Are Best At Avoiding Contamination By Blood?

Devices specifically designed to enhance sampling of the endocervical canal are more likely to cause cervical trauma resulting in bleeding, which may, if heavy, interfere with diagnosis. Two trials comparing the Ayre spatula to extended tip spatula gave sufficient data to compare the effect of cervical 'trauma' by these devices on the resultant cervical smears. Bounds (Bounds 1976) reported the incidence of red cells on cervical smears taken with Armocervical and Ayre spatulas; the extended tip spatula produced more red cell contamination, OR 1.99 95% (1.47-2.7). Goorney (Goorney 1989) reported the number of inadequate smears as a result of red or pus cells contamination when using an Ayre or an Aylesbury spatula. The Aylesbury spatula produced more inadequate smears in this respect; OR 3.16 95% C.I.(1.8-5.6).
Paraiso, McCord and Koonings (Paraiso 1994; McCord 1992; Koonings 1992) all demonstrated more red cell contamination when using the Cytobrush in comparison with the Cotton Swab. None of the contaminated smears in the trial conducted by Paraiso (Paraiso 1994) prohibited cytological assessment. In this trial the population consisted only of pregnant women, whereas the trial by McCord (McCord 1992) included 33% non-pregnant women. A high incidence of red cell contamination may be expected when sampling the more vascular cervix in pregnancy. Dotters (Dotters 1988) noted spotting of blood after the use of the Cytobrush in 20% of pregnant women compared with 2.5% of non-pregnant women. However, Koonings (Koonings 1992) found little difference in the incidence of bleeding in their group of non-pregnant women.

2.2 Which Devices Are More Likely To Produce Adequate Smears?

Ten trials recorded the inadequate smear rate for each collection device under evaluation. (For ease of interpretation the results have been illustrated as adequate smear rates). The devices that prove to be better at collecting endocervical cells also had better adequate smear rates. Cervexbrush versus spatula OR 1.08 95% CI (0.97-1.21), Spatula and Cytobrush versus Cervexbrush OR 1.58 95% CI (1.28-1.95) and Spatula and Cytobrush versus Spatula and Swab OR 1.68 95% CI (1.17-2.41).

3. Do Those Devices Which Detect A Higher Proportion Of Endocervical Cells Also Detect A Higher Incidence Of Dyskaryosis?

It has been demonstrated that extended tip spatulas are consistently better than the classical Ayre spatula at collecting endocervical cells. Extended tip spatulas also proved to be superior for the detection of dyskaryosis OR 1.21 95%CI (1.1-1.33). The same direction of effect was demonstrated if we only included the primary screening trials (Bounds 1976; Goorney 1989; Wolfendale 1987) OR 1.19 95% CI (1.02-1.39).
Cervexbrush compared with a spatula proved to be significantly superior at detecting dyskaryosis OR 1.13 95% CI (1.05-1.20), exclusion of the only trial by Waddell (Waddell 1990) which included colposcopy clinic patients also demonstrated a significant effect in primary screening OR 1.13 95% CI (1.05-1.22).
The combination of a spatula and Cytobrush has been demonstrated to be the best method at providing endocervical cells. Unfortunately there were insufficient trials recording dyskaryosis to provide significant improvements. Comparison of a spatula and Cytobrush to using a spatula alone also demonstrated a similar effect OR 1.07 95% CI (0.97-1.16). For primary screening trials (Boon 1989; Hjersing 1991; Szarewski 1993 (b)) OR 1.09 95% CI (0.94-1.28), the point estimate is in the expected direction. Pooled results suggesting again that the device which was superior at collecting endocervical cells was also superior at detecting dyskaryosis. Similarly, the comparison between the spatula and Cytobrush and spatula and Cotton Swab did not have sufficient statistical power to demonstrate moderate improvements in detection rates, but again, the direction of the effect is as predicted for the ability sampling devices to harvest endocervical cells OR 1.17 95% CI (0.92-1.45). For primary screening (Boon 1989; Pretorius 1991; Schettino 1993) the OR 1.3 95% CI (0.97-1.74).

4. Are Individual Smears Which Contain Endocervical Cells More Likely To Detect Dyskaryosis?

Studies were examined which gave the incidence of dyskaryosis in smears which did or did not contain endocervical cells. In all of these cases the smear was satisfactory apart from the lack of endocervical cells. The RCTs by Kristensen and Szareweski (Kristensen 1989; Szarewski 1990; Szareweski 1993) and the observational studies by Mauney, Mitchell, and Voojis (Mauney 1990; Mitchell 1988 (b); Vooijs 1985) gave data in this form. Mauney, Mitchell and Voojis gave the incidence of severe dyskaryosis in endocervical cell positive and negative samples. Mauney and Voojis listed the incidence of dyskaryosis for all grades, while Kristensen gave the incidence of dyskaryosis as a whole. We have selected the information from the years 1988 and 1989 from the five year study (1987-1991) by Mitchell for two reasons. First, for the year 1987, data were incomplete and secondly, the studies by Mauney and Voojis (Mauney 1990; Vooijs 1985) evaluated cervical smears taken exclusively by spatulas.

Dyskaryosis was much more likely to be detected when individual smears contained endocervical cells. The detection of cytological abnormality generally and of severe dyskaryosis specifically, are both enhanced if endocervical cells were present. These results could mean: 1) dyskaryosis is more common in cervices which more frequently shed endocervical cells, 2) dyskaryosis, when present, is more likely to be detected if the smear is endocer-

vical cell positive because the transformation zone is more likely to have been sampled, 3) both of the above. We take these points further in the discussion.

5. Does The Association Between Endocervical Cells And Dyskaryosis Change With The Degree Of Cytological Abnormality?

We were interested to see if the association between the endocervical cells detection rate and dyskaryosis varied by degree of abnormality. We therefore compared detection rates of different grades of dyskaryosis taken with extended tip spatulas to smears taken with classical Ayre designed spatulas, spatula and Cytobrush versus spatula alone and the spatula and Cytobrush versus spatula and Cotton swab. In each case the method that proved better at collecting endocervical cells was not only more likely to detect dyskaryosis, but it was more likely still to detect the highest grades of cytological abnormality, although the differences were small and statistically not significant. Not all RCTs gave information on grade of dyskaryosis and the power of these comparisons is therefore low. We, therefore, conducted a further analysis of the data of observational studies in order to demonstrate any association between the degree of dyskaryosis and the presence of endocervical cells on individual cervical smears. Voojis and Mauney (Vooijs 1985; Mauney 1990) provided data on the incidence of cytological atypia and the different grades of dyskaryosis in otherwise satisfactory smears with and without endocervical cells. The odds of detection of cytological abnormality according to endocervical cell status increased progressively with the severity of the disease. Furthermore, the proportion of smears with endocervical cells present increased with increasing disease severity. In each study significantly higher proportions of positive smears were found in association with progressively higher grades of disease .

DISCUSSION

This systematic review has identified a number of randomised controlled trials investigating the performance of 16 cervical smear collection devices. Extended tip spatulas of various designs have been demonstrated to be better at collecting endocervical cells that the classical Ayre design, yet the Ayre spatula is commonly used. The combination of the Cytobrush with an extended tip spatula is the best combination. Use of two devices may be too cumbersome for routine smearing in busy surgeries, but we should at the least replace the Ayre spatula with a simple extended tip device. In pregnancy the physiological state of the cervix reduces the ability of smear devices to collect endocervical cells (Hamblin 1985). McCord and Paraiso (McCord 1992; Paraiso 1994) both demonstrated that the spatula and Cytobrush, Cervex Brush and Bayne Brush were superior to extended tip spatulas or spatulas in combination with a cotton swab in pregnant women. Paraiso (Paraiso 1994) demonstrated that the Cytobrush and Cervex Brush produced more bleeding compared with the spatula or cotton swab but this did not significantly effect the ability of the cytologist to assess the smear.

In post menopausal women the cervix becomes stenotic and the upper limit of the transformation zone often migrates up into the cervical canal. Representative cells of the transformation zone and columnar epithelium are therefore more difficult to obtain. In the trials by Hjersing, Kristensen and Longfield (Hjersing 1991; Kristensen 1989; Longfield 1993) the devices that prove to be better at collecting endocervical cells in young women were also better at collecting these cells in women over 50 years of age.

The collection devices that were better at collecting endocervical cells were also less likely to produce inadequate smears (blood and inflammatory cell contamination, insufficient material). Repetition of cervical smears obviously increases the cost of screening and can be stress provoking for the women requiring a repeat smear.

Having identified the devices which were more effective at collecting endocervical cells, we examined whether or not these devices that were better at collecting these cells were also superior in the detection of cytological abnormality. The comparison of extended tip spatulas with Ayre design demonstrated a significant increased rate of detection of cytological abnormalities with extended tip spatulas. The trials investigating spatula alone compared with the spatula and Cytobrush, and spatula and Cytobrush compared with spatula and Cotton Swab did not achieve statistical significance after meta-analysis, but the direction of effect suggested that the better methods of collecting endocervical cells were also better at the detection of cytological abnormality. Comparison of the Cervexbrush with a spatula did demonstrate a significant increase in detection. The same effect was demonstrated when we examined the trials evaluating devices used in primary screening.
Furthermore, this effect was more marked when comparing the different devices ability to detect higher grades of abnormality, albeit not significantly.
The Report of the working party of the Royal College of Pathologists, British Society for Clinical Cytology and NHS Cervical Screening Programme (WPRCP 1995) recommends that women who have had treatment for cervical intraepithelial neoplasia should have endocervical sampling with an endocervical brush as well as ectocervical sampling if the transformation zone is not visible as a consequence of treatment. The findings of this review suggests that this is the optimum method of ensuring transformation zone sampling.

Although only three randomised controlled trials compared the detection of dyskaryosis in cervical smears with and without endocervical cells (all 3 RCTs suggested increased detection of disease in endocervical positive smears), combination of these results with those derived from observational studies shows that the detection of dyskaryosis is more likely with smears that contain endocervical cells. This could be a biased comparison if there is an inter-

action between these two events (i.e. if a factor which is associated with dyskaryosis is also, independently, associated with a high prevalence of endocervical cells). Age could be such a factor; postmenopausal women, for example, are less likely to yield endocervical cells. However, they also have a relatively low risk of cervical intra-epithelial neoplasia and these two factors may therefore balance out. If not, the bias may not be sufficient to account for the strength of the association between the presence of endocervical cells on a slide and the detection of dyskaryosis.

The association between the yield of endocervical cells and detection of dyskaryosis in the RCTs would tend to confirm that the association between detection of endocervical cells and dyskaryosis in the observational studies is not incidental. We therefore have several reasons for believing that the presence of endocervical cells should indeed increase the likelihood of detecting cervical dyskaryosis on the basis of 1) adequate sampling of the transformation zone 2) concordance of results of RCTs when the outcome is presence of endocervical cells or dyskaryosis 3) observational studies which showed that the likelihood of detecting dyskaryosis among endocervical cell positive smears, when the dyskaryosis is of more severe degree.

Only the study by Kivlahan and Ingram (Kivlahan 1986), has followed up women who had endocervical positive and negative smears, to see whether the negative group had a higher rate of dyskaryosis on follow-up smears. This study suggested that there was no difference in detection of cytological atypia between the two groups suggesting that there was no increase in detection of disease in endocervical positive smears. The incidence of dyskaryosis after two endocervical positive smears was 2.7% (14/311) versus 3.2% (14/429) among those with endocervical negative smears. To show a 25% difference in dyskaryosis rates between endocervical cell positive and negative women (from 4% to 5%) would require follow-up of over 17,000 women.

Lastly, training of samplers improves the yield of endocervical cells (Buntinx 1993). This supports the Report of the Working Party of the Royal College of Pathologists, British Society for Clinical Cytology and NHS Cervical Screening Programme (WPRCP 1995) and the Bethesda Report (USA) that ' the clinician ultimately determines what is adequate sampling for an individual patient'. It is the responsibility of the clinician to ensure adequate sampling of the transformation zone.

It is highly plausible that our findings are, at least in part, the result of a true association between the presence of endocervical cells and the chance of detecting any lesion that may be present.

The heightened awareness that cervical adenocarcinoma is preceded by pre-invasive disease is resulting in the more frequent diagnosis of glandular atypia (Laverty 1988; Howe 1991; Vincenti 1991). Smears that lack endocervical cells will fail to provide the opportunity to screen for glandular atypia. The Ayre spatula has been found to be ineffective in the detection of glandular epithelial neoplasia (Boon 1981). Whereas collection devices designed to enhance endocervical cell collection are likely to detect glandular abnormality (Boon 1987). This is a further argument in favour of extended tip spatulas and of the validity of endocervical cells as a marker for the ability of a device to detect both squamous and glandular dyskaryosis.

AUTHORS' CONCLUSIONS

Implications for practice

This review is no longer appropriate for update as liquid based cytology has superceded smear technology.

The most important factor in taking satisfactory cervical smears is the ability of the practitioner to perform the test accurately (Cecchini 1989; Buntinx 1993). As shown by this review, the design of the cervical smear collection device also significantly influences the yield of representative cells and the detection of cytological atypia. The replacement of the Ayre spatula with extended tip spatulas should be mandatory for mass screening since this is an inexpensive way to improve sampling. In the United Kingdom the presence of endocervical cells is not routinely used to assess the adequacy of a cervical smear. The evidence from the observational studies suggests that endocervical negative smears are less likely to detect any cytological abnormality which may be present, especially if the abnormality is severe. The introduction of more stringent assessment of cervical smears based on endocervical cell status and the repetition of endocervical negative smears might not be justified in the light of the present resources. However, assessment of endocervical cells appears to be a valid method to audit an aspect of the overall quality of a cervical smear screening program and to compare different devices.

Implications for research

The combination of a spatula and cytobrush has been demonstrated to be the most effective method of collecting endocervical cells. However there were relatively few high quality trials evaluating the detection of disease. We would advocate a further primary screening trial evaluating the ability of an extended tip spatula and cytobrush to detect disease (and the financial implications) with an extended tip spatula alone.

NOTES

This review is now over four years old and is currently being modified in accordance with the current quality criteria and to improve the clarity of presentation.

POTENTIAL CONFLICT OF INTEREST

None known.

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Boon 1989
Methods	Quasi-randomisation, allocation by week Randomisation used to allocate collection device to a specific women
Participants	Primary screening, Netherlands 22,515 women 5 experienced practitioners performed all smears
Interventions	Modified Ayre Spatula (extended-tip spatula) Spatula and Cytobrush Cytopick Spatula and Swab Cervexbrush
Outcomes	Endocervical cells present on smears Detection of cytological abnormality (recorded as mild/ moderate or severe)
Notes	
Allocation concealment	B – Unclear

Study	Bounds 1976
Methods	True randomisation, allocation by week Randomisation used to allocate collection device to a specific women
Participants	Primary screening: U.K. 982 women
Interventions	Ayre Armocervical spatula
Outcomes	Endocervical cells present on smear Detection of Cytological Abnormality (recorded as atypia, dyskaryosis)
Notes	
Allocation concealment	A – Adequate

Study	Buxton 1987
Methods	Not Stated
Participants	Colposcopy Clinic
Interventions	Ayre Ayre+Cytobrush
Outcomes	Endocervical cells Detection of cytological abnormality
Notes	
Allocation concealment	B – Unclear

Study	Deckert 1988
Methods	Quasi-randomisation by weekly allocation

	Randomisation used to allocate collection device to a specific women
Participants	Primary screening: U.S.A 402 women
Interventions	Ayre and Swab Milex (Extened Tip Spatula) Ayre and Cytobrush
Outcomes	Endocervicals present on smear
Notes	
Allocation concealment	A – Adequate

Study	**Dey 1996**
Methods	Quasi-randomisation, allocation by group Randomisation used to allocate collection device to a specific women
Participants	Primary screening: UK 15882 women
Interventions	Aylesbury Cervexbrush
Outcomes	Detection of cytological abnormality (recorded as borderline, mild, moderate, severe) Inadequate smears (as defined by British Society of Clinical Pathology)
Notes	
Allocation concealment	A – Adequate

Study	**Dotters 1988**
Methods	Quasi-randomisation, allocation by file number Randomisation used to allocate collection device to a specific women
Participants	Primary screening: U.S.A. 403 women
Interventions	Baynebrush Spatula and swab
Outcomes	Endocervical cells present on smear
Notes	
Allocation concealment	D – Not used

Study	**Elias 1983**
Methods	Comparative study investigating the incidence of dyskaryosis according to endocervical cell status
Participants	Cervical screening programme: Netherlands 62,375 cervical smears, 5,298 excluded post menopausal cervix not visible 55,853 adequate smears
Interventions	Cervical smears with or without endocervical cells
Outcomes	Presence of cytological abnormality
Notes	
Allocation concealment	D – Not used

Study	**Fokke 1993**
Methods	Quasi-randomisation, allocation by month

	Randomisation used to allocate collection device to specific women
Participants	Primary screening: Netherlands 279 women
Interventions	Ayre Ayre and Cytobrush Cervexbrush
Outcomes	Endocervical cells present on smear
Notes	
Allocation concealment	B – Unclear

Study	**Garite 1978**
Methods	Quasi-randomisation, allocation by month Randomisation used to allocate collection device to a specific women
Participants	Primary screening: U.S.A. 710 women
Interventions	Ayre Ayre and Swab
Outcomes	Endocervical cells
Notes	
Allocation concealment	D – Not used

Study	**Giles 1991**
Methods	True randomisation, allocation by computer generation Randomisation used to determine order of collection device to be used on same patient
Participants	Colposcopy clinics, patients with a recent history of an abnormal smear Colposcopy clinics, patient who have had confirmed and treated cervical dysplasia and are attending follow-up clinics U.K. 254 women
Interventions	Aylesbury Multispatula
Outcomes	Endocervical cells present on smear Detection of cytological abnormality (recorded as dyskaryosis)
Notes	
Allocation concealment	D – Not used

Study	**Goorney 1989**
Methods	Quasi-randomisation allocation by month Randomisation used to allocate collection device to specific women
Participants	Primary Screening: U.K. 4080 women
Interventions	Aylesbury Ayre
Outcomes	Endocervical cells present on cervical smear Detection of cytological abnormality (recorded as atypia, borderline, mild, moderate, severe)
Notes	

Characteristics of included studies (*Continued*)

Allocation concealment	A – Adequate

Study	**Hamblin 1985**
Methods	Method of randomisation not stated Randomisation used to allocate collection device to specific women
Participants	Primary Screening: U.S.A. 254 women
Interventions	Ayre and swab Milex Spatula (Extended Tip Spatula)
Outcomes	Endocervical cells present on cervical smear
Notes	
Allocation concealment	B – Unclear

Study	**Hjersing 1991**
Methods	Method of randomisation not stated Randomisation used to determine the order of more than one collection device to be used on the same patient
Participants	Primary screening: Sweden 197 women
Interventions	Papaplast (extended tip spatula) Ayre and Cytobrush
Outcomes	Endocervical cells present on cervical smear Detection of cytological abnormality (recorded as mild, moderate, severe)
Notes	
Allocation concealment	B – Unclear

Study	**Hughes 1992**
Methods	True randomisation, allocation by sealed envelopes Randomisation used to determine the order of more than one collection device to be used on the same patient
Participants	Colposcopy clinics, patients who have had confirmed and treated cervical dysplasia and are attending follow-up clinics U.K. 856 women
Interventions	Ayre Aylesbury Multispatula (extended-tip) Rocket (extended-tip) Cytobrush
Outcomes	Endocervical cells present on cervical smears
Notes	Duplicated to allow comparisons of extened tip spatulas in analysis
Allocation concealment	A – Adequate

Study	**Hughes 1992 (a)**
Methods	True randomisation, allocation by sealed envelopes Randomisation used to determine the order of more than one collection device to be used on the same patient
Participants	Colposcopy clinics, patients who have had confirmed and treated cervical dysplasia and are attending follow-up clinics

	U.K. 856 women
Interventions	Ayre Aylesbury Multispatula (extended-tip) Rocket (extended-tip) Cytobrush
Outcomes	Endocervical cells present on cervical smears
Notes	Duplicated to allow comparisons of extened tip spatulas in analysis
Allocation concealment	A – Adequate

Study	**Hughes 1992 (b)**
Methods	True randomisation, allocation by sealed envelopes Randomisation used to determine the order of more than one collection device to be used on the same patient
Participants	Colposcopy clinics, patients who have had confirmed and treated cervical dysplasia and are attending follow-up clinics U.K. 856 women
Interventions	Ayre Aylesbury Multispatula (extended-tip) Rocket (extended- tip) Cytobrush
Outcomes	Endocervical cells present on cervical smears
Notes	Duplicated to allow comparisons of extened tip spatulas in analysis
Allocation concealment	A – Adequate

Study	**Kavak 1995**
Methods	Not stated
Participants	Patients attending Obstetric and gynaecological clinics
Interventions	Cervexbrush Ayre+Cytobrush Ayre+Cotton swab
Outcomes	Endocervical cells
Notes	
Allocation concealment	B – Unclear

Study	**Koonings 1992**
Methods	True randomisation, allocation by random tables Randomisation used to allocate collection device to a specific women
Participants	Primary screening and colposcopy clinics, patients with a recent history of an abnormal cervical smear 310 women U.S.A.
Interventions	Milex (extended-tip spatula) and Cytobrush Milex and swab
Outcomes	Endocervical cells present on cervical smears Detection of cytological abnormality (recorded as low or high grade, cancer)

Characteristics of included studies (*Continued*)

	inadequate smears (defined as excess inflammatory/ red blood cells, insufficient material)
Notes	
Allocation concealment	A – Adequate

Study	**Kristensen 1989**
Methods	Method of randomisation not stated Randomisation used to allocate collection device to specific women
Participants	Primary screening, antenatal clinics: Denmark 849 women
Interventions	Ayre and Cytobrush Ayre and swab
Outcomes	Endocervical cells present on cervical smear
Notes	
Allocation concealment	B – Unclear

Study	**Longfield 1993**
Methods	True randomisation, allocation by computer generation Randomisation used to allocate collection device to specific women
Participants	Primary screening and colposcopy clinics, patients who have had confirmed and treated cervical dysplasia and are attending follow-up clinics U.K. 985 women
Interventions	Ayre and Cytobrush Profilebrush
Outcomes	Endocervical cells present on cervical smear Detection of cytological abnormality (recorded as atypia, low or high grade, carcinoma)
Notes	
Allocation concealment	A – Adequate

Study	**Mauney 1990**
Methods	Comparative study investigating the incidence of dyskaryosis according to endocervical cell status
Participants	Cervical screening: U.S.A. 36,853 cervical smears, 3,315 excluded inadequate data cervix not visible 32, 801 adequate smears
Interventions	Cervical smears with or without endocervical cells
Outcomes	Presence of cytological abnormality
Notes	
Allocation concealment	D – Not used

Study	**McCord 1992**
Methods	True randomisation, allocation by computer allocation Randomisation used to allocate collection device to specific women
Participants	Primary screening: U.S.A. 2015 women
Interventions	Ayre and Cytobrush Ayre and Swab Cervexbrush

Characteristics of included studies (*Continued*)

	Baynebrush
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormality (borderline+dyskaryosis) Inadequate smears (defined as excess inflammatory/ red blood cells, insufficient material)
Notes	
Allocation concealment	A – Adequate

Study	**Metcalf 1994 (a)**
Methods	Method of randomisation not stated Randomisation used to allocate collection device to specific women
Participants	Colposcopy clinics, patients with a recent history of an abnormal cervical smear 1063 women U.K.
Interventions	Ayre Aylesbury Multispatula (extended-tip spatula) Ayre+Cytobush
Outcomes	Detection of cytological abnormality (recorded as dyskaryosis)
Notes	Duplicated to allow comparisons of extened tip spatulas in analysis
Allocation concealment	B – Unclear

Study	**Metcalf 1994 (b)**
Methods	Method of randomisation not stated Randomisation used to allocate collection device to specific women
Participants	Colposcopy clinics, patients with a recent history of an abnormal cervical smear 1063 women U.K.
Interventions	Ayre Aylesbury Multispatula (extended-tip spatula) Ayre+Cytobush
Outcomes	Detection of cytological abnormality (recorded as dyskaryosis)
Notes	Duplicated to allow comparisons of extened tip spatulas in analysis
Allocation concealment	A – Adequate

Study	**Mitchell 1988 (a)**
Methods	Comparative study investigating the incidence of dyskaryosis according to endocervical cell status
Participants	Cervical smears taken during cervical screening programme Victoria, Australia No exclusions 1987-8 cervical smears classified as being endocervical cell positive if they had any endocervical or metaplastic cells 1989 onwards: more stringent classification, smears had to have at least 10 endocervical cells present 1990 -1991 practioners were instructed to use Cytobrushes with spatulas or collection devices specifically designed to sample the endocervix on all non-pregnant women 1987: 262,721 smears, 260,869 adequate smears 1988 252,950 smears, 250,661 adequate smears 1989 238,164 smears, 236,449 adequate smears

	1990 255,836 smears, 254,415 adequate smears 1991 256,419 smears, 255,185 adequate smears
Interventions	Smears with and without endocervical cells
Outcomes	Presence of cytological abnormality
Notes	1989 data presented against this duplicate citation to alllow comparison in review
Allocation concealment	D – Not used

Study	**Mitchell 1988 (b)**
Methods	Comparative study investigating the incidence of dyskaryosis according to endocervical cell status
Participants	Cervical smears taken during cervical screening programme Victoria, Australia No exclusions 1987-8 cervical smears classified as being endocervical cell positive if they had any endocervical or metaplastic cells 1989 onwards: more stringent classification, smears had to have at least 10 endocervical cells present 1990 -1991 practioners were instructed to use Cytobrushes with spatulas or collection devices specifically designed to sample the endocervix on all non-pregnant women 1987: 262,721 smears, 260,869 adequate smears 1988 252,950 smears, 250,661 adequate smears 1989 238,164 smears, 236,449 adequate smears 1990 255,836 smears, 254,415 adequate smears 1991 256,419 smears, 255,185 adequate smears
Interventions	Smears with and without endocervical cells
Outcomes	Presence of cytological abnormality
Notes	1988 data presented against this citation
Allocation concealment	D – Not used

Study	**Neinstein 1989**
Methods	Quasi-randomised allocation by file number Randomisation used to allocate collection device to specific women
Participants	Primary screening: U.S.A. 111 women
Interventions	Ayre and Cytobrush Ayre and swab
Outcomes	Presence of endocervical cells on smear
Notes	
Allocation concealment	A – Adequate

Study	**Noel 1993**
Methods	Method of randomisation not stated Randomisation used to determine the order of more than one collection device to be used on the same patient
Participants	Primary screening: U.S.A. 663 women
Interventions	Ayre Curved Brush before / after straight brush Cervexbrush
Outcomes	Endocervical cells present on cervical smear

Notes	
Allocation concealment	B – Unclear

Study	**Paraiso 1994**
Methods	True randomisation, allocation by computer generation Randomisation used to allocate collection device to specific women
Participants	Antenatal clinics: U.S.A. 352 women
Interventions	Extended- tip spatula and swab Extended- tip spatula and Cytobrush Cervexbrush
Outcomes	Presence of endocervical cells Detection of cytological abnormality (recorded as all grades of dyskaryosis) Inadequate smears (insufficient material)
Notes	
Allocation concealment	A – Adequate

Study	**Partoll 1993**
Methods	True randomisation, allocation by sealed envelopes Randomisation used to allocate collection device to specific women
Participants	Colposcopy Clinics, patients with a recent history of an abnormal cervical smear U.S.A. 230 women
Interventions	Ayre and swab Ayre and Cytobrush
Outcomes	Presence of endocervical cells on cervical smear
Notes	
Allocation concealment	A – Adequate

Study	**Pistofides 1988**
Methods	True randomisation, allocation by sealed envelopes Randomization used to determine the order of more than one collection device to be used on the same patient
Participants	Colposcopy clinics, patients with a recent history of an abnormal cervical smear: U.K. 158 women
Interventions	Ayre Multispatula (extended- tip spatula)
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormality (recorded as mild, moderate, severe dyskaryosis)
Notes	
Allocation concealment	A – Adequate

Study	**Pretorius 1991**
Methods	Quasi-randomisation, allocation by file number Randomisation used to allocate collection device to specific women
Participants	Primary Screening: U.S.A.

Characteristics of included studies (*Continued*)

	11061 women
Interventions	Ayre and Cytobrush Ayre and swab Baynebrush
Outcomes	Presence of endocervical cells Detection of cytological abnormality (recorded as atypia, mild, moderate, severe dyskarosis) Inadequate smears (defined as excess inflammatory/ red blood cells, insufficient material)
Notes	
Allocation concealment	A – Adequate

Study	**Schettino 1993**
Methods	Method of randomisation not stated Randomisation used to determine the order of more than one collection device to be used on the same patient
Participants	Primary screening: Italy 89 women
Interventions	Ayre and swab Ayre and Cytobrush
Outcomes	Presence of endocervical cells on cervical smears Detection of cytological abnormality (recorded as all grades of dyskaryosis)
Notes	
Allocation concealment	B – Unclear

Study	**Selvaggi 1991**
Methods	Method of randomisation not stated Randomisation used to allocate collection device to specific women
Participants	Colposcopy clinics, patients with a recent history of an abnormal cervical smear Colposcopy clinics, patients who have had confirmed and treated cervical dysplasia and are attending follow-up clinics U.S.A. 192 women
Interventions	Ayre and Cytobrush Ayre and bulb aspirator
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormalities (recorded as atypia and all grades of dyskaryosis)
Notes	
Allocation concealment	B – Unclear

Study	**Stock 1988**
Methods	Quasi-randomisation, allocation by code Randomisation used to allocate collection device to specific women
Participants	Colposcopy Clinics, patients who have had confirmed and treated cervical dysplasia and are attending folow-up clinics U.S.A. 200 women
Interventions	Extended-tip Spatula Extended-tip Accu-Pap Standard Accu-Pap

Characteristics of included studies (*Continued*)

Outcomes	Presence of endocervical cells on cervical smear
Notes	
Allocation concealment	A – Adequate

Study	**Szarewski 1990**
Methods	Quasi-randomisation, allocation by group Randomisation used to allocate collection device to specific women
Participants	Primary screening, U.K 6991 women
Interventions	Ayres Aylesbury Cervexbrush Spatula+Cytobrush
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormality (recorded as all grades of dyskaryosis) Inadequate smears (defined as excess inflammatory/ red blood cells, insufficient material)
Notes	
Allocation concealment	D – Not used

Study	**Szarewski 1991**
Methods	Quasi-randomisation, allocation by month Randomisation used to allocate collection device to specific women
Participants	Colposcopy Clinics, patients who have had confirmed and treated cervical dysplasia and are attending follow-up clinics U.K. 802 women
Interventions	Ayre and Cytobrush Cervexbrush
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormality (recorded as atypia, mild, moderate, severe dyskaryosis) Inadequate smears (defined as excess inflammatory/ red blood cells, insufficient material)
Notes	
Allocation concealment	A – Adequate

Study	**Szarewski 1993 (a)**
Methods	Quasi-randomisation, allocation by month Randomisation used to allocate collection device to specific women
Participants	Primary screening, U.K 14,172 women
Interventions	Aylesbury Rolon (Extended- tip Spatula) Cervexbrush Spatula+Cytobrush
Outcomes	Endocervical cells present on smears Detection of cytological abnormality (recorded as all grades and moderate/severe)
Notes	
Allocation concealment	A – Adequate

Characteristics of included studies (*Continued*)

Study	**Szarewski 1993 (b)**
Methods	Quasi-randomisation, allocation by month Randomisation used to allocate collection device to specific women
Participants	Primary screening: U.K 14,172 women
Interventions	Aylesbury Rolon (Extended-tip spatula) Cervexbrush Spatula+Cytobrush
Outcomes	Endocervical cells present on smears Detection of cytological abnormality (recorded as all grades and moderate/severe) Inadequate smears (defined as excess inflammatory/red blood cells, insufficient material)
Notes	Duplicated to allow comparisons of extened tip spatulas in analysis
Allocation concealment	A – Adequate

Study	**Vierhout 1987**
Methods	Quasi-randomisation Randomisation used to determine the order of more than one collection device to be used on the same patient
Participants	Primary screening: Netherlands 236 women
Interventions	Ayre Multispatula
Outcomes	Presence of endocervical cells on cervical smear
Notes	
Allocation concealment	A – Adequate

Study	**Vooijs 1985**
Methods	Comparative study investigating the incidence of dyskaryosis according to endocervical cell status
Participants	Cervical screening: Netherlands 120,218 cervical smears, 30,764 exclusions post-menopausal cervix not seen 85,406 adequate smears
Interventions	Cervical smears with or without endocervical cells
Outcomes	Presence of cytological abnormality
Notes	
Allocation concealment	D – Not used

Study	**Vooijs 1986**
Methods	Comparative study investigating the incidence of dyskaryosis according to endocervical cell status
Participants	Cervical Screening: Netherlands women screened twice 34,600 smears, exclusions post-menopausal cervix not visible 30,555 adequate smears
Interventions	Cervical smears with and without endocervical smears
Outcomes	Presence of cytological abnormality
Notes	
Allocation concealment	D – Not used

Study	Waddell 1990
Methods	Method of randomisation not stated Randomisation used to allocate collection device to specific women
Participants	Primary screening, colposcopy clinics, patients with a recent history of an abnormal cervical smear, colposcopy clinics, patients who have had confirmed and treated cervical dysplasia and are attending follow-up clinics U.K. 280 women
Interventions	Cervexbrush Ayre
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormality (recorded as atypia, all grades of dyskaryosis) Inadequate smears (as defined by British Society of Clinical Pathology)
Notes	
Allocation concealment	B – Unclear

Study	Wolfendale 1987
Methods	Quasi-randomisation, allocation by month Randomisation used to allocate collection device to specific women
Participants	Primary screening: U.K. 17781 women
Interventions	Ayre Extended- tip spatula
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormality (recorded as all grades of dyskaryosis)
Notes	
Allocation concealment	A – Adequate

Study	Woodman 1991
Methods	Quasi-randomisation allocation by week Randomisation used to allocate collection device to specific women
Participants	Colposcopy clinics, patients with a recent history of an abnormal cervical smear, Colposcopy clinics, patients who have had treated cervical dysplasia and are attending follow-up clinics U.K. 533 women
Interventions	Ayre Rocket (extended-tip spatula)
Outcomes	Presence of endocervical cells on cervical smear Detection of cytological abnormality (recorded as all grades of dyskaryosis)
Notes	
Allocation concealment	A – Adequate

Characteristics of excluded studies

Study	Reason for exclusion
Johnson 1991	Combined the results of Cytobrush and Cervexbrush as they were similar, this prevented the use of the data as we could not assess the performance of the individual devices

Characteristics of excluded studies (*Continued*)

ANALYSES

Comparison 01. Presence of Endocervical Cells

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Extended Tip Spatula versus Classical Ayre	10	11443	Peto Odds Ratio 95% CI	2.25 [2.06, 2.44]
02 Multispatula versus Extended Tip Spatula	1	502	Peto Odds Ratio 95% CI	3.34 [2.07, 5.39]
03 Spatula+Cytobrush versus Spatula	6	25430	Peto Odds Ratio 95% CI	3.48 [3.20, 3.78]
04 Spatula+Cytobrush versus Cytopick	1	7547	Peto Odds Ratio 95% CI	2.69 [1.81, 3.99]
05 Cervexbrush versus Spatula	3	11582	Peto Odds Ratio 95% CI	1.57 [1.42, 1.73]
06 Spatula+Cytobrush versus Spatula+Swab	11	17358	Peto Odds Ratio 95% CI	3.58 [3.26, 3.93]
07 Spatula+Cytobrush versus Cervexbrush	6	18962	Peto Odds Ratio 95% CI	2.29 [2.05, 2.55]
08 Spatula+Cytobrush versus Baynebrush	2	8729	Peto Odds Ratio 95% CI	1.29 [1.12, 1.49]
09 Spatula+Cytobrush versus Profilebrush	1	979	Peto Odds Ratio 95% CI	0.97 [0.69, 1.34]
10 Baynebrush versus Spatula+ Swab	3	9032	Peto Odds Ratio 95% CI	3.37 [3.03, 3.76]
11 Spatula+Swab versus Spatula	2	12638	Peto Odds Ratio 95% CI	1.22 [1.07, 1.40]
12 Spatula+Cytobrush versus Bulb Aspirator	1	192	Peto Odds Ratio 95% CI	6.41 [2.88, 14.29]

Comparison 02. Adequate Smears

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Extended Tip Spatula+ Cytobrush versus Extended Tip Spatula	2	10861	Peto Odds Ratio 95% CI	1.51 [1.19, 1.92]
02 Cervexbrush versus Spatula	4	27297	Peto Odds Ratio 95% CI	1.08 [0.97, 1.21]
03 Spatula+Cytobrush versus Cervexbrush	4	11802	Peto Odds Ratio 95% CI	1.58 [1.28, 1.95]
04 Spatula+Cytobrush versus Spatula+Swab	5	8444	Peto Odds Ratio 95% CI	1.68 [1.17, 2.41]

Comparison 03. Detection of All Grades of Dyskaryosis

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Extended Tip Spatula versus Classical Ayre	5	6440	Peto Odds Ratio 95% CI	1.44 [1.19, 1.75]
02 Spatula+Cytobrush versus Spatula	7	26188	Peto Odds Ratio 95% CI	1.05 [0.95, 1.15]
03 Spatula+Cytobrush versus Spatula+Swab	5	14809	Peto Odds Ratio 95% CI	1.17 [0.92, 1.48]

04 Cervexbrush versus Spatula	5	34656	Peto Odds Ratio 95% CI	1.13 [1.05, 1.20]
05 Smears with Endocervical Cells versus those without	5	141245	Peto Odds Ratio 95% CI	1.89 [1.79, 2.00]

Comparison 04. Detection of Severe dyskaryosis

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Smears with Endocervical Cells versus those without	4	606282	Peto Odds Ratio 95% CI	3.21 [2.81, 3.66]

Comparison 05. Detection of Different Grades of Atypia/Dyskaryosis

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Extended Tip versus Classical Ayre Design : Mild/Moderate	3	20229	Peto Odds Ratio 95% CI	1.14 [0.96, 1.35]
02 Extended Tip versus Classical Ayre Design: Severe Dyskaryosis	3	20229	Peto Odds Ratio 95% CI	1.28 [0.99, 1.64]
03 Spatula+Cytobrush versus Spatula: All grades of Dyskaryosis	1	13282	Peto Odds Ratio 95% CI	1.24 [0.77, 1.99]
04 Spatula+Cytobrush versus Spatula: Mild/Moderate Dyskaryosis	1	13282	Peto Odds Ratio 95% CI	1.11 [0.64, 1.91]
05 Spatula+Cytobrush versus Spatula: Severe Dyskaryosis	1	13282	Peto Odds Ratio 95% CI	1.72 [0.68, 4.34]
06 Spatula+Cytobrush versus Spatula+Swab; Mild/Moderate Dyskaryosis	3	14361	Peto Odds Ratio 95% CI	0.97 [0.71, 1.33]
07 Spatula+Cytobrush versus Spatula+ Swab: Severe Dyskaryosis	3	14361	Peto Odds Ratio 95% CI	1.31 [0.86, 1.98]
08 Smears with Endocervical Cells versus those without: Atypia	2	119191	Peto Odds Ratio 95% CI	1.75 [1.63, 1.89]
09 Smears with Endocervical Cells versus those without: Mild/ Moderate Dyskaryosis	2	119181	Peto Odds Ratio 95% CI	1.86 [1.60, 2.17]
10 Smears with Endocervical Cells versus those without: Severe Dyskaryosis	2	119181	Peto Odds Ratio 95% CI	2.46 [1.76, 3.45]

INDEX TERMS

Medical Subject Headings (MeSH)

Clinical Trials; Uterine Cervical Neoplasms [*pathology]; Vaginal Smears [*instrumentation]

MeSH check words

Female; Humans

COVER SHEET

Title	Collection devices for obtaining cervical cytology samples
Authors	Martin-Hirsch P, Jarvis G, Kitchener H, Lilford R
Contribution of author(s)	P Martin-Hirsch, R. Lilford, H. Kitchener and G. Jarvis designed the review. R. Lilford and H. Kitchener supervised the conduct and analyses by P. Martin-Hirsch. P. Martin-Hirsch wrote the review with advice from the other investigators.
Issue protocol first published	/
Review first published	1998/1
Date of most recent amendment	21 August 2007
Date of most recent SUBSTANTIVE amendment	21 May 2000
What's New	This review is no longer appropriate for update as liquid based cytology has superceded smear technology.
Date new studies sought but none found	01 September 2006
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	16 August 2007
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GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Presence of Endocervical Cells, Outcome 01 Extended Tip Spatula versus Classical Ayre

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 01 Extended Tip Spatula versus Classical Ayre

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Bounds 1976	342/491	207/491		11.2	3.05 [2.37, 3.92]
Goorney 1989	669/2003	423/2077		37.0	1.94 [1.69, 2.23]
Hughes 1992	68/116	168/358		4.1	1.59 [1.05, 2.42]
Hughes 1992 (a)	98/129	165/358		4.4	3.32 [2.22, 4.97]
Hughes 1992 (b)	81/120	168/358		4.2	2.28 [1.51, 3.44]
Pistofides 1988	105/158	28/158		3.6	7.34 [4.70, 11.46]
Stock 1988	96/100	92/100		0.5	2.03 [0.63, 6.49]
Szarewski 1990	1403/1637	1341/1784		25.1	1.94 [1.64, 2.30]
Vierhout 1987	188/236	158/236		4.3	1.91 [1.27, 2.87]
Woodman 1991	142/285	59/248		5.8	3.02 [2.13, 4.29]
Total (95% CI)	5275	6168		100.0	2.25 [2.06, 2.44]

Total events: 3192 (), 2809 (Control)

Test for heterogeneity chi-square=49.33 df=9 p=<0.0001 I^2 =81.8%

Test for overall effect z=18.81 p<0.00001

Analysis 01.02. Comparison 01 Presence of Endocervical Cells, Outcome 02 Multispatula versus Extended Tip Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 02 Multispatula versus Extended Tip Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Giles 1991	233/253	189/249		100.0	3.34 [2.07, 5.39]
Total (95% CI)	253	249		100.0	3.34 [2.07, 5.39]

Total events: 233 (), 189 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=4.95 p<0.00001

Analysis 01.03. Comparison 01 Presence of Endocervical Cells, Outcome 03 Spatula+Cytobrush versus Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 03 Spatula+Cytobrush versus Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	4100/4142	8291/9140		31.6	3.75 [3.24, 4.34]
Buxton 1987	540/625	329/623		11.7	4.89 [3.84, 6.22]
Fokke 1993	82/92	59/87		1.3	3.55 [1.74, 7.26]
Hjersing 1991	94/106	83/107		1.3	2.20 [1.07, 4.49]
Szarewski 1990	1672/1769	1341/1784		20.3	4.49 [3.73, 5.39]
Szarewski 1993 (b)	3097/3341	2982/3614		33.8	2.52 [2.19, 2.91]
Total (95% CI)	10075	15355		100.0	3.48 [3.20, 3.78]
Total events: 9585 (), 13085 (Control)					
Test for heterogeneity chi-square=37.44 df=5 p=<0.0001 I^2 =86.6%					
Test for overall effect z=29.65 p<0.00001					

Analysis 01.04. Comparison 01 Presence of Endocervical Cells, Outcome 04 Spatula+Cytobrush versus Cytopick

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 04 Spatula+Cytobrush versus Cytopick

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	4110/4141	3336/3406		100.0	2.69 [1.81, 3.99]
Total (95% CI)	4141	3406		100.0	2.69 [1.81, 3.99]
Total events: 4110 (), 3336 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.92 p<0.00001					

Analysis 01.05. Comparison 01 Presence of Endocervical Cells, Outcome 05 Cervexbrush versus Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 05 Cervexbrush versus Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Szarewski 1990	1639/1801	1341/1784		30.2	3.09 [2.60, 3.68]
Szarewski 1993 (b)	3202/3823	2982/3614		62.4	1.09 [0.97, 1.23]
Waddell 1990	210/280	165/280		7.4	2.07 [1.45, 2.94]
Total (95% CI)	5904	5678		100.0	1.57 [1.42, 1.73]
Total events: 5051 (), 4488 (Control)					
Test for heterogeneity chi-square=94.23 df=2 p=<0.0001 I^2 =97.9%					
Test for overall effect z=9.18 p<0.00001					

Analysis 01.06. Comparison 01 Presence of Endocervical Cells, Outcome 06 Spatula+Cytobrush versus Spatula+Swab

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 06 Spatula+Cytobrush versus Spatula+Swab

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	4100/4142	2965/3200		14.7	5.72 [4.49, 7.28]
Deckert 1988	118/140	91/132		2.7	2.36 [1.35, 4.14]
Kavak 1995	57/111	26/125		3.0	3.80 [2.23, 6.48]
Koonings 1992	126/158	91/152		3.7	2.57 [1.58, 4.17]
Kristensen 1989	325/418	215/431		11.0	3.33 [2.52, 4.40]
McCord 1992	465/501	420/503		5.9	2.44 [1.66, 3.57]
Neinstein 1989	35/51	34/60		1.5	1.66 [0.77, 3.56]
Paraiso 1994	107/118	85/120		2.1	3.55 [1.87, 6.75]
Partoll 1993	77/89	84/114		1.8	2.18 [1.10, 4.31]
Pretorius 1991	3122/3409	2351/3206		52.8	3.59 [3.16, 4.08]
Schettino 1993	87/89	74/89		0.9	5.37 [1.98, 14.56]
Total (95% CI)	9226	8132		100.0	3.58 [3.26, 3.93]
Total events: 8619 (), 6436 (Control)					
Test for heterogeneity chi-square=29.01 df=10 p=0.001 I^2 =65.5%					
Test for overall effect z=26.97 p<0.00001					

Analysis 01.07. Comparison 01 Presence of Endocervical Cells, Outcome 07 Spatula+Cytobrush versus Cervexbrush

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

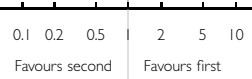
Outcome: 07 Spatula+Cytobrush versus Cervexbrush

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	4110/4142	2515/2627		10.4	5.35 [3.81, 7.50]
Kavak 1995	73/110	57/111		4.2	1.85 [1.09, 3.16]
McCord 1992	465/501	454/505		6.2	1.45 [0.93, 2.24]
Paraiso 1994	107/118	95/114		2.0	1.91 [0.89, 4.12]
Szarewski 1990	1672/1769	1639/1801		18.6	1.68 [1.31, 2.17]
Szarewski 1993 (b)	3097/3341	3202/3823		58.7	2.32 [2.01, 2.68]
Total (95% CI)	9981	8981		100.0	2.29 [2.05, 2.55]

Total events: 9524 (), 7962 (Control)

Test for heterogeneity chi-square=34.77 df=5 p=<0.0001 I^2 =85.6%

Test for overall effect z=14.85 p<0.00001



Analysis 01.08. Comparison 01 Presence of Endocervical Cells, Outcome 08 Spatula+Cytobrush versus Baynebrush

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

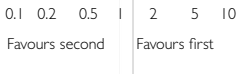
Outcome: 08 Spatula+Cytobrush versus Baynebrush

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
McCord 1992	465/501	454/505		10.7	1.45 [0.93, 2.24]
Pretorius 1991	3122/3409	3860/4314		89.3	1.27 [1.09, 1.48]
Total (95% CI)	3910	4819		100.0	1.29 [1.12, 1.49]

Total events: 3587 (), 4314 (Control)

Test for heterogeneity chi-square=0.28 df=1 p=0.60 I^2 =0.0%

Test for overall effect z=3.48 p=0.0005



Analysis 01.09. Comparison 01 Presence of Endocervical Cells, Outcome 09 Spatula+Cytobrush versus Profilebrush

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 09 Spatula+Cytobrush versus Profilebrush

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Longfield 1993	401/488	406/491		100.0	0.97 [0.69, 1.34]
Total (95% CI)	488	491		100.0	0.97 [0.69, 1.34]
Total events: 401 (), 406 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.21 p=0.8					

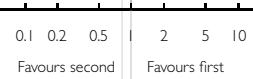
Analysis 01.10. Comparison 01 Presence of Endocervical Cells, Outcome 10 Baynebrush versus Spatula+Swab

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 10 Baynebrush versus Spatula+Swab

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Dotters 1988	206/212	120/191		4.8	9.17 [5.58, 15.08]
McCord 1992	459/506	420/503		8.7	1.90 [1.31, 2.75]
Pretorius 1991	3860/4314	2351/3306		86.5	3.38 [3.01, 3.80]
Total (95% CI)	5032	4000		100.0	3.37 [3.03, 3.76]
Total events: 4525 (), 2891 (Control)					
Test for heterogeneity chi-square=24.92 df=2 p=<0.0001 I^2 =92.0%					
Test for overall effect z=21.95 p<0.00001					



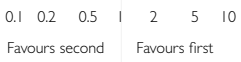
Analysis 01.11. Comparison 01 Presence of Endocervical Cells, Outcome 11 Spatula+Swab versus Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 11 Spatula+Swab versus Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	2965/3200	8290/9140		92.5	1.28 [1.11, 1.47]
Hamblin 1985	89/133	121/165		7.5	0.74 [0.45, 1.21]
Total (95% CI)	3333	9305		100.0	1.22 [1.07, 1.40]
Total events: 3054 (), 8411 (Control)					
Test for heterogeneity chi-square=4.32 df=1 p=0.04 I^2 =76.9%					
Test for overall effect z=2.90 p=0.004					



Analysis 01.12. Comparison 01 Presence of Endocervical Cells, Outcome 12 Spatula+Cytobrush versus Bulb Aspirator

Review: Collection devices for obtaining cervical cytology samples

Comparison: 01 Presence of Endocervical Cells

Outcome: 12 Spatula+Cytobrush versus Bulb Aspirator

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Selvaggi 1991	88/90	76/102		100.0	6.41 [2.88, 14.29]
Total (95% CI)	90	102		100.0	6.41 [2.88, 14.29]
Total events: 88 (), 76 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.55 p<0.00001					

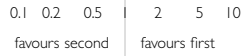
Analysis 02.01. Comparison 02 Adequate Smears, Outcome 01 Extended Tip Spatula+Cytobrush versus Extended Tip Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 02 Adequate Smears

Outcome: 01 Extended Tip Spatula+Cytobrush versus Extended Tip Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Szarewski 1990	1734/1769	1603/1637		25.3	1.05 [0.65, 1.69]
Szarewski 1993 (b)	3762/3841	3488/3614		74.7	1.71 [1.29, 2.25]
Total (95% CI)	5610	5251		100.0	1.51 [1.19, 1.92]
Total events: 5496 (), 5091 (Control)					
Test for heterogeneity chi-square=2.96 df=1 p=0.09 I^2 =66.3%					
Test for overall effect z=3.36 p=0.0008					



Analysis 02.02. Comparison 02 Adequate Smears, Outcome 02 Cervexbrush versus Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 02 Adequate Smears

Outcome: 02 Cervexbrush versus Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Dey 1996	7633/8066	7370/7796		63.3	1.02 [0.89, 1.17]
Szarewski 1990	1739/1801	1603/1637		7.3	0.60 [0.40, 0.91]
Szarewski 1993 (b)	3704/3823	3488/3614		18.5	1.12 [0.87, 1.45]
Waddell 1990	167/280	114/280		10.9	2.13 [1.53, 2.96]
Total (95% CI)	13970	13327		100.0	1.08 [0.97, 1.21]
Total events: 13243 (), 12575 (Control)					
Test for heterogeneity chi-square=24.77 df=3 p=<0.0001 I^2 =87.9%					
Test for overall effect z=1.43 p=0.2					

Analysis 02.03. Comparison 02 Adequate Smears, Outcome 03 Spatula+Cytobrush versus Cervexbrush

Review: Collection devices for obtaining cervical cytology samples

Comparison: 02 Adequate Smears

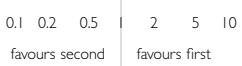
Outcome: 03 Spatula+Cytobrush versus Cervexbrush

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
McCord 1992	146/161	145/165		9.1	1.34 [0.66, 2.70]
Paraiso 1994	107/118	100/119		7.6	1.82 [0.85, 3.91]
Szarewski 1990	1734/1769	1739/1801		27.4	1.74 [1.16, 2.60]
Szarewski 1993 (b)	3762/3841	3709/3828		55.9	1.52 [1.15, 2.01]
Total (95% CI)	5889	5913		100.0	1.58 [1.28, 1.95]

Total events: 5749 (), 5693 (Control)

Test for heterogeneity chi-square=0.64 df=3 p=0.89 I^2 =0.0%

Test for overall effect z=4.25 p=0.00002



Analysis 02.04. Comparison 02 Adequate Smears, Outcome 04 Spatula+Cytobrush versus Spatula+Swab

Review: Collection devices for obtaining cervical cytology samples

Comparison: 02 Adequate Smears

Outcome: 04 Spatula+Cytobrush versus Spatula+Swab

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Koonings 1992	145/158	145/152		15.9	0.55 [0.22, 1.36]
Kristensen 1989	412/415	416/421		6.7	1.63 [0.41, 6.56]
McCord 1992	148/161	137/158		25.7	1.73 [0.85, 3.51]
Paraiso 1994	107/118	85/120		31.5	3.55 [1.87, 6.75]
Pretorius 1991	3411/3422	3306/3319		20.2	1.22 [0.55, 2.72]
Total (95% CI)	4274	4170		100.0	1.68 [1.17, 2.41]

Total events: 4223 (), 4089 (Control)

Test for heterogeneity chi-square=11.70 df=4 p=0.02 I^2 =65.8%

Test for overall effect z=2.82 p=0.005

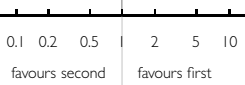
Analysis 03.01. Comparison 03 Detection of All Grades of Dyskaryosis, Outcome 01 Extended Tip Spatula versus Classical Ayre

Review: Collection devices for obtaining cervical cytology samples

Comparison: 03 Detection of All Grades of Dyskaryosis

Outcome: 01 Extended Tip Spatula versus Classical Ayre

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Bounds 1976	15/491	7/491		5.1	2.10 [0.90, 4.89]
Goorney 1989	72/2003	74/2077		33.6	1.01 [0.73, 1.40]
Metcalf 1994 (a)	51/199	79/330		22.0	1.10 [0.73, 1.65]
Pistofides 1988	149/158	129/158		8.0	3.30 [1.68, 6.49]
Woodman 1991	129/248	101/285		31.2	1.96 [1.39, 2.77]
Total (95% CI)	3099	3341		100.0	1.44 [1.19, 1.75]
Total events: 416 (), 390 (Control)					
Test for heterogeneity chi-square=15.82 df=4 p=0.003 I^2 =74.7%					
Test for overall effect z=3.75 p=0.0002					



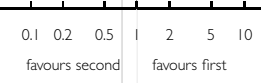
Analysis 03.02. Comparison 03 Detection of All Grades of Dyskaryosis, Outcome 02 Spatula+Cytobrush versus Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 03 Detection of All Grades of Dyskaryosis

Outcome: 02 Spatula+Cytobrush versus Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	29/4142	52/9140		4.0	1.24 [0.77, 1.99]
Buxton 1987	268/623	275/625		17.6	0.96 [0.77, 1.20]
Hjersing 1991	7/107	5/107		0.7	1.42 [0.44, 4.54]
Metcalf 1994 (a)	52/203	92/331		5.7	0.90 [0.60, 1.33]
Metcalf 1994 (b)	52/203	51/199		4.4	1.00 [0.64, 1.56]
Szarewski 1990	400/1769	380/1784		34.9	1.08 [0.92, 1.27]
Szarewski 1993 (b)	312/3341	317/3614		32.8	1.07 [0.91, 1.26]
Total (95% CI)	10388	15800		100.0	1.05 [0.95, 1.15]
Total events: 1120 (), 1172 (Control)					
Test for heterogeneity chi-square=2.20 df=6 p=0.90 I^2 =0.0%					
Test for overall effect z=0.98 p=0.3					



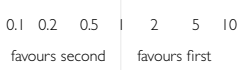
Analysis 03.03. Comparison 03 Detection of All Grades of Dyskaryosis, Outcome 03 Spatula+Cytobrush versus Spatula+Swab

Review: Collection devices for obtaining cervical cytology samples

Comparison: 03 Detection of All Grades of Dyskaryosis

Outcome: 03 Spatula+Cytobrush versus Spatula+Swab

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	29/4142	18/3200		16.8	1.24 [0.70, 2.21]
Koonings 1992	82/158	81/152		28.4	0.95 [0.61, 1.48]
Paraiso 1994	8/118	8/120		5.5	1.02 [0.37, 2.80]
Pretorius 1991	48/3422	43/3319		32.9	1.08 [0.72, 1.64]
Schettino 1993	54/89	39/89		16.4	1.96 [1.09, 3.52]
Total (95% CI)	7929	6880		100.0	1.17 [0.92, 1.48]
Total events: 221 (), 189 (Control)					
Test for heterogeneity chi-square=4.08 df=4 p=0.40 I^2 =1.9%					
Test for overall effect z=1.31 p=0.2					



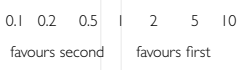
Analysis 03.04. Comparison 03 Detection of All Grades of Dyskaryosis, Outcome 04 Cervexbrush versus Spatula

Review: Collection devices for obtaining cervical cytology samples

Comparison: 03 Detection of All Grades of Dyskaryosis

Outcome: 04 Cervexbrush versus Spatula

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Dey 1996	917/8066	729/7796		41.9	1.24 [1.12, 1.38]
Szarewski 1990	401/1801	380/1784		17.4	1.06 [0.90, 1.24]
Szarewski 1993 (a)	380/3823	332/3389		18.2	1.02 [0.87, 1.19]
Szarewski 1993 (b)	380/3823	357/3614		18.9	1.01 [0.86, 1.17]
Waddell 1990	112/280	87/280		3.7	1.48 [1.04, 2.09]
Total (95% CI)	17793	16863		100.0	1.13 [1.05, 1.20]
Total events: 2190 (), 1885 (Control)					
Test for heterogeneity chi-square=10.25 df=4 p=0.04 I^2 =61.0%					
Test for overall effect z=3.54 p=0.0004					



Analysis 03.05. Comparison 03 Detection of All Grades of Dyskaryosis, Outcome 05 Smears with Endocervical Cells versus those without

Review: Collection devices for obtaining cervical cytology samples

Comparison: 03 Detection of All Grades of Dyskaryosis

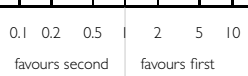
Outcome: 05 Smears with Endocervical Cells versus those without

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Kristensen 1989	16/635	3/206		0.3	1.62 [0.56, 4.65]
Mauney 1990	1041/26562	142/7273		16.3	1.79 [1.56, 2.06]
Szarewski 1990	1433/6055	112/936		11.8	1.97 [1.67, 2.33]
Szarewski 1993 (b)	1313/12219	68/1953		12.5	2.28 [1.94, 2.68]
Vooijs 1986	15162/80445	486/4961		59.1	1.83 [1.70, 1.97]
Total (95% CI)	125916	15329		100.0	1.89 [1.79, 2.00]

Total events: 18965 (), 811 (Control)

Test for heterogeneity chi-square=6.91 df=4 p=0.14 I^2 =42.1%

Test for overall effect z=21.92 p<0.00001



Analysis 04.01. Comparison 04 Detection of Severe dyskaryosis, Outcome 01 Smears with Endocervical Cells versus those without

Review: Collection devices for obtaining cervical cytology samples

Comparison: 04 Detection of Severe dyskaryosis

Outcome: 01 Smears with Endocervical Cells versus those without

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Mauney 1990	118/26562	8/7223		9.5	2.45 [1.60, 3.76]
Mitchell 1988 (a)	244/115850	69/120580		35.3	3.19 [2.56, 3.98]
Mitchell 1988 (b)	371/132850	70/117811		49.5	3.50 [2.90, 4.22]
Vooijs 1986	229/80445	2/4961		5.7	2.47 [1.42, 4.30]
Total (95% CI)	355707	250575		100.0	3.21 [2.81, 3.66]

Total events: 962 (), 149 (Control)

Test for heterogeneity chi-square=3.18 df=3 p=0.36 I^2 =5.8%

Test for overall effect z=17.35 p<0.00001

Analysis 05.01. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 01 Extended Tip versus Classical Ayre Design : Mild/Moderate

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

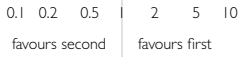
Outcome: 01 Extended Tip versus Classical Ayre Design : Mild/Moderate

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Goorney 1989	55/2003	54/2077		20.0	1.06 [0.72, 1.55]
Pistofides 1988	96/158	87/158		14.5	1.26 [0.81, 1.97]
Wolfendale 1987	191/7971	165/7862		65.5	1.14 [0.93, 1.41]
Total (95% CI)	10132	10097		100.0	1.14 [0.96, 1.35]

Total events: 342 (), 306 (Control)

Test for heterogeneity chi-square=0.35 df=2 p=0.84 I^2 =0.0%

Test for overall effect z=1.54 p=0.1



Analysis 05.02. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 02 Extended Tip versus Classical Ayre Design: Severe Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

Outcome: 02 Extended Tip versus Classical Ayre Design: Severe Dyskaryosis

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Goorney 1989	11/2003	16/2077		11.1	0.71 [0.34, 1.52]
Pistofides 1988	53/158	42/158		27.5	1.39 [0.86, 2.25]
Wolfendale 1987	87/7971	63/7862		61.4	1.36 [0.99, 1.88]
Total (95% CI)	10132	10097		100.0	1.28 [0.99, 1.64]

Total events: 151 (), 121 (Control)

Test for heterogeneity chi-square=2.54 df=2 p=0.28 I^2 =21.2%

Test for overall effect z=1.89 p=0.06

Analysis 05.03. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 03 Spatula+ Cytobrush versus Spatula: All grades of Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

Outcome: 03 Spatula+Cytobrush versus Spatula: All grades of Dyskaryosis

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	29/4142	52/9140		100.0	1.24 [0.77, 1.99]
Total (95% CI)	4142	9140		100.0	1.24 [0.77, 1.99]
Total events: 29 (), 52 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.90 p=0.4					

Analysis 05.04. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 04 Spatula+ Cytobrush versus Spatula: Mild/Moderate Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

Outcome: 04 Spatula+Cytobrush versus Spatula: Mild/Moderate Dyskaryosis

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	20/4142	40/9140		100.0	1.11 [0.64, 1.91]
Total (95% CI)	4142	9140		100.0	1.11 [0.64, 1.91]
Total events: 20 (), 40 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.36 p=0.7					

Analysis 05.05. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 05 Spatula+ Cytobrush versus Spatula: Severe Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

Outcome: 05 Spatula+Cytobrush versus Spatula: Severe Dyskaryosis

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	9/4142	12/9140		100.0	1.72 [0.68, 4.34]
Total (95% CI)	4142	9140		100.0	1.72 [0.68, 4.34]
Total events: 9 (), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.16 p=0.2					

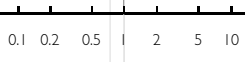
Analysis 05.06. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 06 Spatula+ Cytobrush versus Spatula+Swab; Mild/Moderate Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

Outcome: 06 Spatula+Cytobrush versus Spatula+Swab; Mild/Moderate Dyskaryosis

Study		Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Boon 1989	20/4142	14/3200		21.8	1.10 [0.56, 2.18]
Koonings 1992	32/147	36/143		34.2	0.83 [0.48, 1.42]
Pretorius 1991	35/3416	33/3313		44.0	1.03 [0.64, 1.66]
Total (95% CI)	7705	6656		100.0	0.97 [0.71, 1.33]
Total events: 87 (), 83 (Control)					
Test for heterogeneity chi-square=0.53 df=2 p=0.77 I^2 =0.0%					
Test for overall effect z=0.19 p=0.8					



Analysis 05.07. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 07 Spatula+ Cytobrush versus Spatula+ Swab: Severe Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

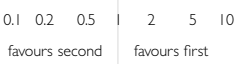
Outcome: 07 Spatula+Cytobrush versus Spatula+ Swab: Severe Dyskaryosis

Study	n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Boon 1989	9/4142	4/3200		14.4	1.69 [0.56, 5.05]
Koonings 1992	49/147	38/143		68.8	1.38 [0.83, 2.28]
Pretorius 1991	7/3416	8/3313		16.8	0.85 [0.31, 2.34]
Total (95% CI)	7705	6656		100.0	1.31 [0.86, 1.98]

Total events: 65 (), 50 (Control)

Test for heterogeneity chi-square=0.95 df=2 p=0.62 I^2 =0.0%

Test for overall effect z=1.26 p=0.2



Analysis 05.08. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 08 Smears with Endocervical Cells versus those without: Atypia

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

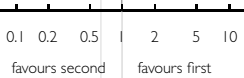
Outcome: 08 Smears with Endocervical Cells versus those without: Atypia

Study	n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Mauney 1990	238/26562	47/7223		6.6	1.34 [1.01, 1.78]
Vooijs 1986	14293/80445	469/4961		93.4	1.79 [1.66, 1.93]
Total (95% CI)	107007	12184		100.0	1.75 [1.63, 1.89]

Total events: 14531 (), 516 (Control)

Test for heterogeneity chi-square=3.68 df=1 p=0.05 I^2 =72.9%

Test for overall effect z=15.04 p<0.00001



Analysis 05.09. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 09 Smears with Endocervical Cells versus those without: Mild/Moderate Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

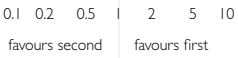
Outcome: 09 Smears with Endocervical Cells versus those without: Mild/Moderate Dyskaryosis

Study	n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Mauney 1990	685/26562	87/7223		78.1	1.85 [1.55, 2.20]
Vooijs 1986	640/80445	15/4951		21.9	1.91 [1.37, 2.65]
Total (95% CI)	107007	12174		100.0	1.86 [1.60, 2.17]

Total events: 1325 (), 102 (Control)

Test for heterogeneity chi-square=0.03 df=1 p=0.87 I^2 =0.0%

Test for overall effect z=7.93 p<0.00001



Analysis 05.10. Comparison 05 Detection of Different Grades of Atypia/Dyskaryosis, Outcome 10 Smears with Endocervical Cells versus those without: Severe Dyskaryosis

Review: Collection devices for obtaining cervical cytology samples

Comparison: 05 Detection of Different Grades of Atypia/Dyskaryosis

Outcome: 10 Smears with Endocervical Cells versus those without: Severe Dyskaryosis

Study	n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Mauney 1990	118/26562	8/7223		62.6	2.45 [1.60, 3.76]
Vooijs 1986	229/80445	2/4951		37.4	2.47 [1.42, 4.30]
Total (95% CI)	107007	12174		100.0	2.46 [1.76, 3.45]

Total events: 347 (), 10 (Control)

Test for heterogeneity chi-square=0.00 df=1 p=0.98 I^2 =0.0%

Test for overall effect z=5.23 p<0.00001