

# **Evaluation of HPV/LBC**

## **Cervical Screening Pilot Studies**

**First report to the Department of Health on  
evaluation of LBC (December 2002)**

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## **SUMMARY AND CONCLUSIONS**

1. As part of a pilot study, three sites in England have converted fully to using liquid based cytology (using two different technologies), and to using HPV triage in women with borderline/mildly dyskaryotic smears to determine the timing of referral to colposcopy, during a 12 month period.
2. This evaluation is of the pilot studies, and is not intended to be a full review of the other literature. The pilot studies were not designed as a formal comparison of the different technologies.
3. This report is an interim evaluation based primarily on the first six months of the 12 month pilots study period. It addresses only the effect and costs of LBC. More detailed information will be included in the final report, which will also include evaluation of the costs and effects of HPV triage. HPV triage will have affected rates and outcomes of referral to colposcopy in women with mild/borderline smears during this first six month period. However, those for moderate and severe dyskaryosis will not have been affected during this period.
4. The introduction of LBC resulted in a clear reduction in the reported rate of inadequate smears (from 9% to 1 – 2%). The rate of inadequate smears in the pilot was lower in the site using SurePath™ than in those using ThinPrep™. However, changes in reporting of smears lacking evidence of transformation zone sampling may also have had an effect on the inadequate rate. The long-term effect of the reduction in the rate of inadequate smears cannot be assessed from these data.
5. There was no clear evidence of any impact of LBC on the detection rates of borderline smears or of mild dyskaryosis, or of an overall impact, across all sites, on rates of moderate and severe dyskaryosis. For the latter there was a difference between sites, with an increase in the sites using ThinPrep™ combined (greater in one of these sites than the other) and a decrease in severe dyskaryosis in that using Surepath™, but possible reasons for this require further exploration before a difference between technologies can be inferred. In addition, the comparison of results for the pre-pilot and pilot periods may be confounded by a number of factors such as the effects of training and use of different smear taking equipment.
6. There was some evidence of a ‘learning curve’ effect, with higher rates during the first two months of the pilots.
7. There was a reduction in the rate of smears reported as showing glandular neoplasia. It is not clear whether such lesions are now being reported as negative, or as high grade dyskaryosis. The cytological reasons and implications of this reduction need further investigation.
8. It is not possible to estimate sensitivity directly from the pilot studies, since to do so would require knowledge of false negative screening results. However results on rates of moderate and severe dyskaryosis and provisional results on positive predictive value suggest that, for the sites combined, sensitivity is no lower with LBC than conventional cytology.
9. In our baseline estimate the cost per smear is slightly higher with ThinPrep™ than with conventional cytology (by £1.31 to £1.47 depending on the preparation machine used) and slightly lower with SurePath™ than conventional cytology (by £0.92).

10. There is uncertainty about the extent of any time-savings in primary care from using LBC. The above estimate uses a time-saving of 5 minutes. Using a conservative estimate of time-savings of 1 minute with LBC compared to conventional the costs per smear are higher for all LBC technologies (ranging from £1.23 to £3.62). Further research on primary care timings is urgently needed.
11. The results are influenced by our estimates of the consumable costs of the LBC technology in the marketplace once the pilot study has been concluded, and these are inevitably uncertain.
12. The costs of transportation, storage and training costs after a full conversion are similar between LBC and conventional cytology.
13. Preparation staff costs are a small component of total costs per smear. They vary between the technologies and are higher for the SurePath™ machine and the T2000™, although Cytoc have suggested that our estimate for the T2000™ is too high, and this needs further investigation.
14. The productivity of laboratories increased with LBC because 9% more slides can be primary screened per hour; the number of formal breaks remained unchanged.
15. The reduction in the inadequate rate with LBC will reduce the overall costs of screening as fewer smears have to be taken, prepared and read. For example, with a reduction in the inadequate rate from 9% to 1.6%, a laboratory processing 30,000 slides a year with conventional cytology would have a reduction in workload of 2,220 slides per annum. Nationally, the workload would be reduced from 4.2 million slides per annum to 3.9 million slides per annum.
16. The reduction in the inadequate rate will also be of considerable benefit to women in terms of reducing anxiety, uncertainty and the need for repeat smears.
17. The introduction of LBC has resulted in a reduction in the backlog of smears at laboratories, and hence in reporting times of smears.
18. Overall LBC is cost saving across both technologies. In the baseline scenario LBC is between £1 million and £10 million cheaper nationally than the estimated annual cost of £91 million for conventional cytology, the size of the reduction depending on the LBC technology. (Our estimate for conventional cytology excludes costs of items such as colposcopy and histology, and hence differs from that of the National Audit Office)
19. The overall costs include primary care costs of smear taking and administration where LBC is cost saving compared to conventional cytology. However, these potential savings may be difficult to realise financially and not transferred to the laboratories.
20. Uncertainty remains about the extent of time-savings in the primary care consultation time due to the methods of data collection. In a scenario using the baseline results except for the primary care time-savings, which are reduced to one minute, the change running costs nationally ranges from a saving of £1.9 million to an increased cost of £7.3 million depending on the technology.
21. The difference in overall costs of screening and treatment with LBC compared to conventional discounted over a life-time is small. These differences are mainly influenced by both the differences in smear costs and the proportions of inadequate smears that need to be repeated.

22. Re-estimated cost effectiveness results using costing and inadequate rate data from the pilot sites indicate that both the T3000™ and the PrepStain™ system are cost dominant at baseline, that is, they are both more effective and cost less per person than conventional cytology. At baseline the incremental cost per life year gained of the T2000™ compared to conventional cytology is £270.
23. Implementation of LBC was achieved successfully at all three pilot sites, although conversion was phased in two of the sites, largely due to delays in training.
24. The cost of smear taker time to convert if LBC were to be implemented nationally is estimated at a one off cost of £2.9 million, with additional costs of up to £1.5 million for co-ordinators and materials. However, these costs may be reduced depending on how a switch to LBC is implemented.
25. Total laboratory conversion costs (including training of both smear takers and smear readers) are estimated as £10.1 million nationally, or £72,100 for a laboratory reporting 30,000 smears annually. Again these costs may be subject to variation dependent on the way LBC is implemented. They include the cost of sending off the backlog of conventional smears which could be viewed as a cost of the current system
26. The implementation of LBC has been received favourably both by smear takers in primary care and by laboratory staff.

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## **1. INTRODUCTION**

Approximately 3.5 million women are screened each year in England as part of the NHS cervical screening programme. Since the introduction of the call/recall programme in 1988, it is estimated that the programme prevents between 1100 and 3900 cases of invasive cervical cancer in the UK each year<sup>1</sup>. Currently, approximately 10% of all smears are reported as inadequate and need to be repeated.

### **1.1 Liquid based cytology**

Liquid based cytology (LBC) involves an altered slide preparation technique, by not making a smear of the material obtained on the spatula/collection device, but placing it in a preservative fluid in order to generate a suspension of cells that is subsequently used to deposit a thin layer of cells on the slide. The technique is believed to produce a more representative sample of the specimen, and to reduce contamination by blood cells, pus and mucus.

Research evidence has suggested that the use of LBC could provide significant and important benefits over existing technology. A review carried out for the HTA in 1999/2000 concluded that it is likely that the technique will reduce the number of false-negative test results, reduce the number of unsatisfactory specimens and may decrease the time needed for examination of specimens by cytologists<sup>2</sup>. Guidance issued by NICE in June 2000 recommended that pilot projects of LBC should be undertaken and evaluated before national implementation is considered. In particular, there is a lack of knowledge on the costs and cost-effectiveness of the techniques.

The two most widely studied technologies for LBC preparation are SurePath™ (formally Autocyte®), (TriPath Imaging Inc.) and ThinPrep™ (Cytoc UK). The differences between the technologies are described in Section 4. LBC is now widely used in the USA, and much of the current literature is based on studies there. It is understood both technologies have FDA approval, the form of which is not contained in this report. By comparison, the New Zealand NSCP has recently decided not to purchase or endorse liquid-based cytology for its population-based screening programme in the light of a report by New Zealand Health Technology Assessment<sup>3</sup>. This report was a systematic review of the literature on effectiveness and cost effectiveness of automated and semi-automated cervical screening devices. The review of LBC concluded that the lack of verification of test results meant that clinical effectiveness for detection of high-grade abnormalities could not be reliably determined.

In the UK there has been some debate in the literature during the past two years on the advantages of LBC, and the extent to which reported differences from conventional cytology represent a true improvement<sup>4 5</sup>. In January 2002, a report on pilot studies of LBC carried out in Scotland Programme<sup>6</sup> concluded that training of laboratory staff and smear takers was feasible, that reduced workload and increased productivity were demonstrated in laboratories, and that there was a sharp reduction in the unsatisfactory smear rate and improved detection of high grade lesions. A decision to implement LBC technology in Scotland has now been made. All laboratories in the Scottish pilot used the ThinPrep™ technology. Approximately 30,000 LBC and conventional smears were examined over a six month period, but no data on histological outcomes of colposcopy are yet available. A pilot of LBC is also in progress in Wales.

The English pilots by contrast include more than one technology, and are also examining the effect of HPV triage for women with mildly dyskaryotic or borderline lesions.

## **1.2 HPV triage**

Human Papilloma Virus (HPV) has been found to be present in close to 100% of all cervical cancers<sup>7</sup>. Primary research has indicated a tendency for HPV positivity to be associated with high grade CIN in women with borderline nuclear change or mild dyskaryosis, and HPV testing has therefore been proposed as a means of classifying such women into groups at higher and lower risk. An HTA review concluded that available evidence supported limited introduction of the test to improve the management of women with borderline or mildly dyskaryotic smears<sup>8</sup>. However, the negative predictive value of the test requires further study.

## **1.3 The pilot studies**

In 2000, bids were invited from laboratories/health authorities to carry out pilot studies which would include both the use of LBC, and HPV testing to triage women with mild/borderline smears, with the aim of improving management of these women and reducing the numbers referred for colposcopy. (An original plan to include one site piloting HPV triage alone was dropped since no bids were received for this option). The sites selected are referred to in this report as sites A, B and C. Sites A and B process around 55,000 smears annually, whilst site C processes around 30,000. There are two different products using LBC technology included in the pilot; sites A and C are using ThinPrep™, whilst site B is using SurePath™. The original design of the pilot studies is described in the protocol (Appendix 3). Due to high rates of HPV positivity and referral to colposcopy in the first few months of the pilot, the protocol was subsequently amended for women below 35. Those HPV positive were only referred for colposcopy if they remained positive or showed mild dyskaryosis or worse at 6 months. (Appendix 4) However, site B continued with the original protocol. The studies were designed to recruit women over a 12 month period. Those women with a mild/borderline smear who were HPV negative would have a repeat smear 6 months later, whilst those HPV positive would be referred for immediate colposcopy. The evaluation was therefore planned over a two year period to allow results of repeat smears at 6 months to be included. The original intention was for training of smear takers and smear readers and conversion of laboratories to take place over a three month period between January and March 2001, and for full conversion to take place from April 2001. However, due largely to delays in training, this was only achieved in site C, and in sites A and B it was not until July 2001 that the majority of smears were taken using LBC. This not only delayed the availability of data from the pilots but also meant that there was not a clear 3 month 'run in period' as originally planned.

## **1.4 The evaluation**

This independent evaluation was commissioned by the DH Research, Analysis and Information Division.

The main aims of the evaluation are to study:

- i) the effect of LBC and HPV on rates of repeat smears (which will result both from changes in inadequate rates and sensitivity due to LBC and from HPV triage); rates of referral for colposcopy and histological diagnosis of different degrees of CIN
- ii) the effect on costs of changes in these rates
- iii) the effect on laboratory workload, throughput and costs
- iv) the psychological impact of HPV testing/triage

- v) the impact of the above on the cost-effectiveness of LBC and HPV
- vi) the practical and organisational implications of introducing LBC and/or HPV triage, including training and transition costs

None of the above gives an assessment of the impact of the pilots on the effectiveness of screening in terms of the impact on rates of invasive disease or mortality. In particular, the pilots will not provide information on the sensitivity of LBC. Modelling will be used, however, to address the impact on cost-effectiveness. Estimation of sensitivity requires data on false negative screening results, which are not available from the pilot studies.

This report is concerned only with the evaluation of LBC. The final report will cover the evaluation of HPV triage, together with further information on LBC, which it has not been possible to include in the current report.

For LBC, the key aims are to describe/estimate

- i) the rates of different degrees of dyskaryosis reported on smears
- ii) the effect on the rate of inadequate smears
- iii) the rate of repeat smears (which will be dependent on the above)
- iv) the effect on referral rates for, and outcomes of, colposcopy
- v) positive predictive values for different smear categories
- vi) the effect on laboratory workload and throughput
- vii) the cost implications of the above (repeat smears, referral rates, laboratory and transport costs)
- viii) the practical and organisational implications of the above, including training costs

#### **Subsidiary aims include**

- i) the monitoring of training requirements of all levels of staff, assessing the implications both for retraining existing staff and training of new staff, and staff proficiency
- ii) monitoring effect on rate of GP consultations
- ii) assessing patient and staff satisfaction

As previously stated, the full evaluation is scheduled to last for two years.

This interim report focuses on the effect of the introduction of LBC. It is not yet possible to study the effect of HPV triage, as this will require results of repeat smears at 6 months and subsequent colposcopy, and data on these are not yet available. Since the management of women with borderline and mild smears has changed as a result of HPV triaging, it is therefore not possible to study the effect of LBC on the positive predictive value of these smear categories, although in the final report the separate effects of LBC and of HPV triage will be modelled.

This report therefore focuses on the impact of LBC on smear outcomes and on the cost-effectiveness of the technique. Issues related to training, and practical aspects will be considered in more detail in the final report.

The evaluation primarily compares results for the 12 month pre-pilot period with those from the pilot period for each site. Once the pilot studies had been running for over 6 months, the smears included in different categories will have been affected by the immediate referral of HPV positive women to colposcopy. Analysis of the effect of LBC therefore concentrates on the first six months of the pilot period.

#### Limitations of the evaluation

This evaluation only covers the results of the pilot studies. It does not attempt to review evidence from elsewhere on the use of LBC; which was not within the remit of the evaluation.

The pilot studies were designed to investigate the logistics and the effect of introducing liquid based cytology and HPV triage for women with mild/borderline smears. However, due to the study design it is not possible to separate the effect of LBC from those which may arise due to other changes, such as the use of different smear taking equipment, and the training given to smear takers and smear readers. In addition, within any one laboratory rates of different smear categories will vary over time.

#### Outline of report

In section 2, the methods of data collection are described. Section 3 presents the results of the epidemiological evaluation, and section 4 reports the results of the cost assessment. In section 5, the effects and cost information are combined and the results of a cost-effectiveness model described. Section 6 addresses the transitional costs associated with conversion and implementation. (The logistics of these will be discussed more fully in the final report).

## **2. METHODS OF DATA COLLECTION**

### **2.1 Routine data**

2.1.1 Cytology Laboratory: Routine KC61 (cervical cytology & outcome of gynaecological referrals) returns have been obtained from cytology laboratories for the entire pre-pilot year, and monthly throughout the pilot. Parts A & B provide data on rates of inadequate smears and of different smear categories by age and source of smear. Part B, which gives results by age group, is restricted to smears from GP and NHS community clinics. Part C provides data on outcome of gynaecological referral from which the positive predictive values (PPV) for each smear category are calculated for referrals during April to June each year.

2.1.2 Health Authority & PCG/T: Routine KC53 (Health Authority Recall) returns for the pre-pilot year and quarterly throughout the pilot were obtained from all the relevant health authorities or, recently, from Primary Care Groups and Trusts.

2.1.3 Colposcopy Clinic: Routine KC65 (Colposcopy Clinic Referrals, Treatments & Outcomes) quarterly returns were obtained from colposcopy units for the pre-pilot year and throughout the pilot.

### **2.2 Individual data**

Anonymised individual data on all abnormal smears during the 12 month pre-pilot and the pilot period have been obtained from each site. These consist of an identifier, date of birth and hospital number (to enable linkage with colposcopy and virology data), date of smear, smear result, HPV status, and management (referral to colposcopy or repeat smear).

Individual data on all inadequate smears reported in the pre-pilot and pilot periods were also collected to provide information on persistent inadequates. The cytology laboratories also supplied data on repeat smears, including age and previous smear history (i.e. previous inadequate, mild, borderline and whether 1<sup>st</sup> or 2<sup>nd</sup> etc).

Results on individual smear reader performance for each individual regarding number of smears read, primary screener sensitivity and specificity (i.e. true negatives/(true negatives + false positives)), based on rapid review were obtained.

Individual data were also collected on patients referred to colposcopy in the pre-pilot and pilot period. Identifying data such as hospital number and date of birth enabled these data to be linked to cytology records. Data items included date of colposcopy, referral smear and date referral smear taken, biopsy type (if taken), histology, treatment method and future plan.

The number of failsafe reminders sent to women who failed to attend a repeat smear or colposcopy appointment was also collected from various sources (depending on who records the data and sent out the letters). In site C this was obtained from the cytology laboratory, but for the other two sites it was collected from the Health Authority system.

### **2.3 Questionnaires**

Questionnaires were devised to gather data on staff satisfaction with the training and subsequent confidence. Four separate questionnaires were devised for smear takers at GP practices, LBC

preparation staff, smear readers and staff who carry out HPV testing. Smear taker questionnaires were sent out to 120 randomly selected GP practices. The LBC preparation, smear reader and HPV testing questionnaires were sent out to each individual responsible for those tasks at all three pilot sites.

## **2.4 Record sheets**

Training data record sheets were issued to sites at the beginning of the pilot for cytology laboratory staff, smear readers and takers. Smear taker trainers were asked to record the following for each training session: date, time and place of session (including number of hours), trainers involved (number and qualifications), additional expenses (such as room hire, travel, consumables etc) and attendees (number per staff grade).

Cytology staff responsible for LBC preparation, and smear readers were asked to complete record sheets outlining their staff grade, date of training, task, number of hours spent on task, place training carried out and any additional comments. Staff were also asked to record time spent in assessment following training and time dedicated to setting up/testing equipment prior to the pilot.

Training records were also obtained from Dr Lesley Turnbull at the cytology training school in Liverpool giving the anonymised results for each of the induction course, consolidation course (and supplementary consolidation course), interim test (and repeat interim test), and performance review, together with a combined score of the training for each individual.

Record sheets sent out with questionnaires were used to collect information from smear takers on time spent taking the LBC smear and preparing it for the laboratory. These data were recorded for 5 smear appointments per smear taker.

Smear readers were asked to record over a 3 week period the time spent per day on each of the following tasks: primary screening LBC slides, review of LBC slides, and checking slides (if relevant), together with number of slides screened in each of the 4 categories, total hours worked per day and total time spent on breaks. This recording process took place between January and April 2002.

Staff responsible for LBC preparation were asked to record timings for 10 batches of sample preparation using each of the T3000™, and slide staining machine and the SurePath™ machine. As the T2000™ machine was not being used when the data were collected, these estimates were collected through interviews with staff. Batch size, total time operating machine, time spent processing batches and any time devoted to other activities was recorded for each batch.

Staff performing the HPV testing were asked to record timing for denaturing samples and for conducting and administration time for the Digene Hybrid Capture 2 test in each of 10 batches. Batch size, total time operating machine, time spent processing batches and any time devoted to other activities was also recorded for each batch.

## **2.5 Semi-structured interviews**

Semi-structured interviews were carried out to gather various information on training, workload, implementation, organisation, quality assurance mechanisms, financial information and ideas for future implementation. Visits were made to each site in December 2001 to meet with representatives from the following groups: smear taker trainers, cytopathologists, lab managers, smear readers, HPV staff and colposcopists. Questions to be asked were sent to the relevant staff to be interviewed prior to the visits so that they could discuss them with colleagues and gauge consensus opinions. Main points from the interviews have now been collated and summarised.

### **3. EPIDEMIOLOGICAL EVALUATION**

The results in this section are primarily based on comparisons of the first 6 months of the pilot period with the 12 month pre-pilot period (01/04/2000 – 31/03/2001). Because of the phased introduction of LBC, the six month periods included at each site are: sites A and B: 01/07/ 2001 – 31/12/2001, site C: 01/04/2001 – 30/09/2001. Sites A and C were using ThinPrep™, and site B using Surepath™.

During this period, site A had a 5 year recall policy, and site B had a 3 year recall policy; site C had changed from a 3 year to 4.5 year policy with effect from April 1998. However, since women invited under the later policy would not be screened before October 2002, this change should not affect the results of the pilot.

Results on numbers and percentages of smears in different categories are taken from KC61 part B (which includes only GP and NHS community clinic smears), and restricted to the age range 20 to 64. Rates for different smear categories (other than inadequates) are presented as percentages of adequate smears. The category ‘severe dyskaryosis’ includes that of ‘? invasive’ in tables 1-15. Results have been analysed for the age groups 20-34, 35-49 and 50-64.

The pilot period data have been primarily restricted to the first six months of the pilot at each site in order to avoid confounding of results by the effect of HPV testing. This will influence the proportion of smears in the second 6 month period which are repeats, and hence potentially the proportions of smears in different results categories, since those with borderline or mild dyskaryosis and HPV positive (under the original protocol) will have been referred for immediate colposcopy. However, data for the remainder of the pilot period beyond the initial 6 months have also been analysed and results are presented in Tables 2, 6, 8 and 10.

In order to study the possibility of a ‘learning curve’ effect as laboratories become familiar with LBC, monthly results have been studied over this period, and analyses performed excluding the first two pilot months from each site.

The three previous pre-pilot years (April 1997/March 98 – April 1999/March 2000) have also been examined in order to provide larger numbers and to detect any trends in rates at individual sites. (The use of different age groupings prior to 1997/98 makes comparisons with earlier years difficult.) Detailed data by individual site and year for the pre-pilot period are presented in Tables 11 and 13 to 15.

#### **3.1 Rates of inadequate smears**

Table 1 shows the rates of inadequate smears in the pre-pilot and pilot periods. For all sites combined there is an 82.7% reduction (RR (rate ratio) 0.173, 95% CI 0.162, 0.186) in the rate of inadequate smears in the 6 month pilot period (9.1% pre-pilot vs. 1.6% pilot,  $p < 0.0001$ ). There is a significant reduction in each of the three age groups. However, the reduction in the rate of inadequate smears with increasing age which is apparent with conventional cytology is no longer apparent in the pilot study. The observed reduction with LBC is therefore greatest (85.8%) in the age group 20-34 (RR 0.142, 95% CI 0.127, 0.159) and least (73.2%) in the age group 50-64 (RR 0.266, 95% CI 0.230, 0.306). The difference in the reduction by age group is significant ( $p < 0.0001$ ).

Comparing the 6 months pilot period with the four years pre-pilot a similar reduction of 83.7% is observed (RR 0.162, 95% CI 0.151, 0.173), with a similar differential effect with age. There was some evidence of a decreasing trend with time in the pre-pilot years (Table 11).

Table 1 also gives the results for individual sites. The reduction in the rates of inadequates is significantly greater in site B than in the other two sites, (both for comparisons with 1 year and 4 year pre-pilot data) and the inadequate rate in the 6 month pilot period is significantly lower in this site than in the other two sites.

The inadequate rate in the first 6 months of the pilot was highest in the first two months (Table 2). Excluding these two months, the reduction compared with the pre-pilot period was 84.8% (RR 0.152, 95% CI 0.140, 0.166). In both sites A and B the inadequate rate dropped further in the second 6 months of the pilot.

### **3.2 Rates of borderline smears**

The overall rate of borderline smears, as a rate of adequate smears is significantly lower in the 6 month pilot period than in the pre-pilot period (Table 3), (RR 0.852, 95% CI 0.813, 0.893), the rate of borderlines decreasing from 5.4% to 4.6%. The reduction increases significantly by age, with a 27% reduction in the oldest age group, (RR 0.734, 95% CI 0.652, 0.825). There is no evidence of a difference in this reduction by site (Table 5). However, in two of the pilot sites, the rate of borderline smears was high in the first month of the pilot (Tables 4 and 6).

There is no evidence of a reduction in the 6 month pilot period compared with the total 4 years pre-pilot when rates are expressed as a percentage of adequate smears (4.7% pre pilot vs. 4.6% pilot, RR 0.981, 95% CI 0.941, 1.022). For this latter comparison there is a significant reduction in the oldest age group (RR 0.892, 95% CI 0.801, 0.991) (Table 3) and in site B only (RR 0.904, 95% CI 0.847, 0.964) (Table 5). However, pre-pilot rates increased between 1998/99 and 2000/01 (Table 12).

### **3.3 Rates of mild dyskaryosis**

There is no difference in the rate of mildly dyskaryotic smears in the 6 month pilot period, if rates are expressed as a percentage of adequate smears (2.3% pre-pilot vs. 2.4% pilot, RR 1.051, 95% CI 0.933, 1.123) (Table 3). There was no evidence of a differential effect by age. However, there was a significant increase in site C (2.5% pre-pilot vs. 3.1% pilot, RR 1.342, 95% CI 1.192, 1.510) (Table 6).

When compared with the total 4 year pre-pilot period, there is a significant increase in the rate when expressed as a percentage of adequate smears, (2.0% pre-pilot vs. 2.4% pilot, RR 1.228, 95% CI 1.158, 1.301) (Table 1), with significant increases in the youngest age-group and in site C. However, again rates had been increasing between 1998/99 and 2000/01 (Table 12).

### **3.4 Borderline / mild combined**

Combining the results of borderline and mild smears, there is a small but significant reduction in the rate as a percentage of adequate smears (7.7% pre-pilot vs. 7.0% pilot), the reduction increasing with age, and not observed in site C. Whilst this reduction is more pronounced if the first two months of the pilot are excluded, the rate falling to 6.7%, rates increased again to 7.5% in the second six month period.

However, compared with the 4 years pre-pilot, the rate in the 6 month pilot period was significantly higher (6.7% pre-pilot vs. 7.0% pilot), but the increase only being observed in site C (Table 6).

### **3.5 Rates of moderate and severe dyskaryosis**

Overall, across all sites, there was no significant increase in the rates of moderate and severe dyskaryosis separately or combined for the six month pilot period when expressed as a percentage of

all adequate smears. The combined rates are 1.42% pre-pilot vs. 1.51% pilot, RR 1.064, 95% CI 0.977, 1.157 (Table 3). Again, rates were highest (1.74%) in the first two months of the pilot.

For individual sites, there was a significant increase in site C (RR 1.403, 95% CI 1.188, 1.655) (Table 7) in the 6 month pilot period compared to the 12 months pre-pilot. There was a non-significant 11% decrease in the rate of moderate and severe dyskaryosis in site B compared to the pre-pilot period, and a significant 17% increase in sites A and C combined (RR 1.17%, 95% CI 1.055, 1.300) compared to the pre-pilot period. This is largely due to differences in the rates of severe dyskaryosis, for which the increase in sites A and C combined (RR 1.381, 95% CI 1.187, 1.605) and the decrease in site B (RR 0.655, 95% CI 0.523, 0.814) are both significant. However, the increase is greatest in site C, which had the lowest rate of moderate and severe dyskaryosis combined in the pre-pilot period

Compared with the 4 years pre-pilot period, there was a significant overall increase across all sites in the rates of moderate and severe dyskaryosis combined in the six month pilot period (1.38% pre-pilot vs. 1.51% pilot, RR 1.093, 95% CI 1.016, 1.175). The increase was greatest in the youngest age group, and again mainly observed in site C; the rate of moderate and severe dyskaryosis combined increased slightly between 1997/98 and 1999/2000 (Tables 12 and 14).

### **3.6 Glandular neoplasia**

There was a significant decrease in the rate of glandular neoplasia in the 6 month pilot period. Expressed as a percentage of adequate smears the rate decreased from 0.08% to 0.04% (RR 0.496, 95% CI 0.292, 0.807) (Table 3). This did not vary by age group or by site (Table 4, 9 and 10). These results are similar when the 6 month pilot period was compared with 4 years pre-pilot.

### **3.7 Repeat smears**

Because of the effect of HPV triage in the pilots on the number of repeat smears, being taken due to a previous abnormal smear the effect of LBC on this number cannot be studied directly. However, from the results observed, the effect of LBC on repeat smears will be mainly driven by the difference in inadequate rates.

### **3.8 Referral to colposcopy**

In the pre-pilot period, referral to colposcopy will have resulted from either:

- a) smears with moderate dyskaryosis or worse (irrespective of previous smear history)
- b) smears with borderline / mild dyskaryosis in women with 1 or 2 previous borderline / mild smears.
- c) persistent inadequate smears.

In the pilot period (prior to the change in protocol in sites A and C) women with borderline / mild dyskaryosis who were HPV positive will also have been referred after a single abnormal smear. Those with previous borderline / mild dyskaryosis in this first six months will also have been HPV tested and those testing positive or those with two results of mild dyskaryosis referred for colposcopy. (see flow chart in Appendix 3)

The introduction of LBC alone (without HPV triage) would therefore only immediately affect the referral rate to colposcopy if there is a change in the rates of moderate and severe dyskaryosis, or if there is a change in the rate of borderline/mild dyskaryosis in women having repeat smears. Changes in the rates of borderline/mild dyskaryosis would also have an impact after subsequent repeat smears. The latter effects, together with possible effect of referrals in women with persistent inadequate

smears, require further data and modelling and will be addressed in the final report. However, preliminary analysis of the data received so far suggests that there will be little change in the number of women with persistent inadequate smears.

Tables 16 to 18 shows the known outcomes of colposcopy in women referred due to moderate or severe dyskaryosis during the first 6 months of the pilot period for each pilot site. These have been restricted to one episode per woman in each period (taking most severe colposcopy outcome) and to LBC slides for the pilot period. It should be noted that these data are still provisional, as some colposcopy data are outstanding. In addition, the numbers of women referred will not equate to those reported in the different smear categories in the earlier tables, since they will include referrals from smears from different sources, (e.g. hospital and GUM clinics) whereas the numbers from KC61 are only those from GP/NHSCC smears. The proportion of smears from other sources varies between sites, but the comparison between the rates of moderate and severe dyskaryosis for the pre-pilot and pilot periods within each site for smears from all sources (and all ages) is similar to the results presented above.

It has not been possible in the time available to prepare this report to separate PPVs for smears taken for different reasons (e.g. routine vs. repeat smears).

As discussed earlier, PPVs for persistent borderline/mild dyskaryosis will be affected by HPV triage; these will be modelled for LBC only in the final report.

PPVs for both moderate and severe dyskaryosis are presented in Table 19. The positive predictive value (PPV) is generally calculated as the percentage of seen referrals with moderate dyskaryosis or worse which are CIN2 or worse on histology. The PPV calculated in this way is 71.7% (1177/1641) pre-pilot and 74.6 % (687/921) for the pilot period.

PPVs for CIN3 or worse are also calculated for use in the cost-effectiveness model (Section 5). There are non-significant increases in the PPVs of moderate and severe dyskaryosis. The PPV of moderate and severe dyskaryosis combined for CIN 3+ was 49.7% (816/1641) and 51.6% (475/921) in the pre-pilot and pilot periods respectively.

Data on primary reader sensitivity after rapid review do not suggest any difference with LBC: mean sensitivity for high grade lesions for the pre-pilot and 6 month pilot periods was 98.8% vs. 98.3%, 98.5% vs. 96.9% and 97.7% vs. 96.9% respectively for the three sites.

### **3.9 Discussion**

Interpretation of these results needs to bear in mind that, due to the study design, it is not possible to separate the effect of LBC from those which may have been due to other changes. These include the use of different smear taking equipment and the training given to both smear takers and smear readers, and the effect of these may vary between the sites. The longer screening interval in site A might also affect both pre-pilot and pilot rates of different smear categories.

There is evidence of a large reduction in the percentage of smears reported as inadequate using LBC technology, with an overall reduction of the order of 80%. There is also some evidence that the rate of reported inadequates is lower in the site using SurePath™ than in the two using ThinPrep™. Rates with LBC are 2% with ThinPrep™ and 0.9% with SurePath™ in the first six month period of the pilot studies (with a similar difference if later months are included). By contrast the inadequate rate for England and Wales for 2000/1 was 9.7%, with the 10th – 90th percentile range reported as 6.2% – 13.1%. The reduction in inadequate rate with increasing age apparent with conventional cytology is no longer apparent with LBC.

However the site using SurePath™ also moved to new reporting guidelines, under which endocervical cells are not essential for an adequate smear, at the same time as introducing LBC, and report that 8.5% of all their adequate LBC smears lacked transformation zone sampling. The other two sites had already introduced the new guidelines before the start of the pilot. However there has been no evidence nationally of a significant fall in inadequate rates with the new guidelines.

There is an immediate benefit to women from a reduction in the number of inadequate smears, with the resulting inconvenience due to the need for a repeat smear and the anxiety caused. The longer-term effect will depend on whether the reduction in inadequates has an impact on the detection of CIN, and cannot be determined from the data available from these studies.

If the number of women with persistent inadequate smears is also reduced this would affect referrals to colposcopy, but preliminary data show no evidence of this. This will be considered further in the final report.

There is no clear evidence of a difference in rates of smear categories from borderline to severe dyskaryosis when expressed as a percentage of adequate smears. Whilst there was an increasing trend with time for borderline lesions in the pre-pilot period rates were higher in the latter half of the pilot period (5.2%), when they might perhaps have been expected to fall due to referral of HPV positive women. There is also a change in the variation in rates with age. There was some evidence of an increase in rates of mild dyskaryosis, but this could reflect an increasing trend over a five year period.

Compared with the 12 month pre-pilot period there was a small reduction in the overall rate of borderline/mild lesions in the first 6 month pilot period. However, the rate in the pilot period of 7.0% compares with a rate in England and Wales of 6.6% for 2000/1, with the 10-90th percentile range as 4.2% - 9.4%. The rate for the 12 month pilot period is 7.4%.

There is no clear evidence of an overall change across all sites in rates of moderate and severe dyskaryosis, where again rates had been increasing slightly over the past few years. The rates in the pilot period are 1.5% for both the first 6 months and the total 12 months, compared with a rate in England & Wales of 1.4% in 2000/1, with the 10-90th percentile range of 0.9% - 1.8%. There is some evidence that the rate of severe dyskaryosis may have fallen in the site using Surepath™ with the introduction of LBC, and that in the sites using ThinPrep™ combined may have increased. However, possible reasons for this require further exploration before it can be attributed to a difference between technologies. The increase is greatest in site C, which had the lowest rates in the pre-pilot period. The pilot period for this site also included the months of May and June 2001, when a storyline in the television 'soap' Coronation Street may have resulted in an increase in smears in women not recently screened, and hence an increase in the rates of dyskaryotic smears, a result which can be observed in Tables 6 and 8. Excluding the results for these two months, there is no significant difference between the pilot and pre-pilot period. Because the other two sites converted later, their results do not include this period.

Data were obtained from each site on a monthly basis in order to study trends and the possibility of a 'learning curve' effect. Any such effect will be further complicated by the fact that site C converted fully to LBC earlier than the other two sites, and these two were not unaware of site C's early results.

Rates of borderline (and borderline/mild combined) smears fell following the first two months of the pilot, but then increased during the second six month period. By contrast the rate of moderate/severe dyskaryosis increased in the first two months but then returned to pre-pilot rate.

Whilst there was some evidence of a differential effect on rates of all degrees of smear abnormality with age (with a tendency to an increase at younger ages), this could again be a reflection of trends over time. There is a possible suggestion of a 'learning curve' effect, with slightly high initial rates in the first few months of the pilot, rates by month and particularly within individual sites are variable and there is no clear trend.

The decrease in the reporting of glandular neoplasia is significant, but further investigation is necessary to determine whether this merely reflects a change in interpretation and terminology, and whether such abnormalities are now 'missed' or reported in a different category. In site A there is a suggestion of an increase in glandular lesions reported on histology in the pilot period.

It is not possible to measure sensitivity directly with the data available from these pilot studies, although there is no evidence of a decrease in sensitivity or detection of CIN 3.

However, in order to inform the cost-effectiveness model from the results on positive predictive value and detection rates of different categories some predictions can be made. Assuming that the true (underlying) rate of CIN 3 remains the same, an increase in the PPV of moderate / severe dyskaryosis for CIN 3 from 50% to 52%, combined with an unchanged detection rate of 1.4%, and an initial sensitivity for CIN 3 of 50%, would give an increase in sensitivity to 52% (with an assumed corresponding decrease in the diagnosis of CIN 3 from borderline / mild smears). These definitions have been used to reflect those used in the cost-effectiveness model in Section 5 of this report.

### **Section 3 – Tables**

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**Table 1 Inadequate smears by age and site (GP/NHSCC smears only)**

Age group	A			B			C			All sites		
	all smears	inadequate smears	%	all smears	inadequate smears	%	all smears	inadequate smears	%	all smears	inadequate smears	%
<b>20-34</b>												
<b>1997-2001</b>	78625	10489	13.3	78886	7268	9.2	52984	5835	11.0	210495	23592	11.2
<b>2000-2001</b>	18917	2205	11.7	18019	1856	10.3	9759	922	9.5	46695	4983	10.7
<b>Pilot (6m)</b>	7595	158	2.1	8206	75	0.9	6261	101	1.6	22062	334	1.5
<b>35-49</b>												
<b>1997-2001</b>	70104	7622	10.9	74651	6691	9.0	46531	4302	9.2	191286	18615	9.7
<b>2000-2001</b>	17759	1572	8.9	18131	1819	10.0	9874	786	8.0	45764	4177	9.1
<b>Pilot (6m)</b>	7015	137	2.0	8124	73	0.9	6140	118	1.9	21279	328	1.5
<b>50-64</b>												
<b>1997-2001</b>	41341	3454	8.4	45405	2581	5.7	32440	2349	7.2	119186	8384	7.0
<b>2000-2001</b>	11135	846	7.6	11482	677	5.9	7140	397	5.6	29757	1920	6.5
<b>Pilot (6m)</b>	3957	67	1.7	5126	51	1.0	3845	104	2.7	12928	222	1.7
<b>Total</b>												
<b>1997-2001</b>	190070	21565	11.3	198942	16540	8.3	131955	12486	9.5	520967	50591	9.7
<b>2000-2001</b>	47811	4623	9.7	47632	4352	9.1	26773	2105	7.9	122216	11080	9.1
<b>Pilot (6m)</b>	18567	362	2.0	21456	199	0.9	16246	323	2.0	56269	884	1.6

**Table 2 Inadequate smears by month and site (GP/NHSCC smears only)**

Pilot month	A			B			C			All sites		
	all smears	inadequate smears	%	all smears	inadequate smears	%	all smears	inadequate smears	%	all smears	inadequate smears	%
<b>1</b>	2468	71	2.9	1268	10	0.8	1749	40	2.3	5485	121	2.2
<b>2</b>	2685	60	2.2	2448	51	2.1	3223	66	2.0	8356	177	2.1
<b>3</b>	2935	43	1.5	3981	32	0.8	3213	52	1.6	10129	127	1.3
<b>4</b>	3949	57	1.4	4660	30	0.6	2937	52	1.8	11546	139	1.2
<b>5</b>	3843	72	1.9	5381	53	1.0	2571	64	2.5	7952	189	2.4
<b>6</b>	2687	59	2.2	3718	23	0.6	2553	49	1.9	8958	131	1.5
<b>1<sup>st</sup> 6 mths</b>	18567	362	2.0	21456	199	0.9	16246	323	2.0	52426	884	1.7
<b>7</b>	4111	64	1.6	4739	22	0.5	2748	53	1.9	11598	139	1.2
<b>8</b>	3697	79	2.1	3818	21	0.6	2680	48	1.8	10195	148	1.5
<b>9</b>	3771	77	2.0	4918	36	0.7	1837	49	2.7	10526	162	1.5
<b>10</b>	3673	25	0.7	3780	14	0.4	3189	92	2.9	10642	131	1.2
<b>11</b>	4204	24	0.6	5435	42	0.8	2747	62	2.3	12386	128	1.0
<b>12</b>	3102	24	0.8	3853	23	0.6	2527	48	1.9	9482	95	1.0
<b>Total</b>												
<b>1997-2001</b>	190070	21565	11.3	198942	16540	8.3	131955	12486	9.5	520967	50591	9.7
<b>2000-2001</b>	47811	4623	9.7	47632	4352	9.1	26773	2105	7.9	122216	11080	9.1
<b>Pilot (12m)</b>	41125	655	1.6	47999	357	0.7	31974	675	2.1	117255	1687	1.4

**Table 3 Adequate smears by smear category and age (GP/NHSCC smears only)**

Age Group	total adequates		borderlines		mild dyskaryosis		moderate dyskaryosis		severe dyskaryosis		glandular neoplasia	
	n		n	%	n	%	n	%	n	%	n	%
<b>20-34</b>												
<b>1997-2001</b>	186903		10506	5.6	6356	3.4	2186	1.2	2090	1.1	108	0.06
<b>2000-2001</b>	41712		2662	6.4	1726	4.1	582	1.4	450	1.1	33	0.05
<b>Pilot (6m)</b>	21728		1284	5.9	959	4.4	303	1.4	281	1.3	6	0.03
<b>35-49</b>												
<b>1997-2001</b>	172671		7838	4.5	2212	1.3	691	0.4	1009	0.6	131	0.08
<b>2000-2001</b>	41587		2202	5.3	607	1.5	176	0.4	256	0.6	29	0.07
<b>Pilot (6m)</b>	20951		884	4.2	280	1.3	103	0.5	105	0.5	8	0.04
<b>50-64</b>												
<b>1997-2001</b>	110802		3735	3.4	664	0.6	167	0.2	358	0.3	103	0.09
<b>2000-2001</b>	27837		1140	4.1	217	0.8	50	0.2	65	0.2	23	0.08
<b>Pilot (6m)</b>	12706		382	3.0	96	0.8	23	0.2	22	0.2	7	0.06
<b>Total</b>												
<b>1997-2001</b>	470376		22079	4.7	9232	2.0	3044	0.65	3457	0.74	342	0.07
<b>2000-2001</b>	111136		6004	5.4	2550	2.3	808	0.73	771	0.69	85	0.08
<b>Pilot (6m)</b>	55385		2550	4.6	1335	2.4	429	0.77	408	0.74	21	0.04

**Table 4 Adequate smears by smear category and month (GP/NHSCC smears only)**

Pilot month	adequates		negatives		borderlines		mild dyskaryosis		moderate dyskaryosis		severe dyskaryosis		glandular neoplasia	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<b>1</b>	5364		4818	89.8	314	5.9	136	2.5	53	1.0	39	0.7	4	0.07
<b>2</b>	8179		7412	90.6	370	4.5	251	3.1	77	0.9	67	0.8	2	0.02
<b>3</b>	10002		9110	91.1	443	4.4	282	2.8	67	0.7	92	0.9	8	0.08
<b>4</b>	11407		10491	92.0	525	4.6	227	2.0	91	0.8	72	0.6	1	0.01
<b>5</b>	11606		10680	92.0	530	4.6	227	2.0	86	0.7	78	0.7	5	0.04
<b>6</b>	8827		8131	92.1	368	4.2	212	2.4	55	0.6	60	0.7	1	0.01
<b>1<sup>st</sup> 6mths</b>	55385		50642	91.4	2550	4.6	1335	2.4	429	0.8	408	0.7	21	0.04
<b>7</b>	11459		10389	90.7	580	5.1	283	2.5	110	1.0	92	0.8	5	0.04
<b>8</b>	10046		9225	91.8	460	4.6	235	2.3	64	0.6	56	0.6	7	0.07
<b>9</b>	10364		9430	91.0	534	5.2	244	2.4	77	0.7	70	0.7	9	0.09
<b>10</b>	10511		9524	90.6	612	5.8	231	2.2	75	0.7	65	0.6	4	0.04
<b>11</b>	12258		11204	91.4	635	5.2	271	2.2	68	0.6	76	0.6	4	0.03
<b>12</b>	9387		8578	91.4	465	5.0	228	2.4	56	0.6	56	0.6	4	0.04
<b>Total</b>														
<b>1997-2001</b>	470376		432222	91.9	22079	4.7	9232	2.0	3044	0.65	3457	0.74	342	0.07
<b>2000-2001</b>	111136		100918	90.8	6004	5.4	2550	2.3	808	0.73	771	0.69	85	0.08
<b>Pilot (12m)</b>	119410		108992	91.3	5836	4.9	2827	2.4	879	0.74	823	0.69	54	0.05

**Table 5 Borderline and mild dyskaryosis by age: individual pilot sites  
(GP/NHSCC adequate smears only)**

Age Group	A				B				C						
	adequate smears	border-line	mild dyskaryosis		adequate smears	border-line	mild dyskaryosis		adequate smears	border-line	mild dyskaryosis				
	n	n	%	n	%	n	n	%	n	%	n	%			
<b>20-34</b>															
<b>1997-2001</b>	68136	3424	5.0	2325	3.4	71618	4904	6.9	2511	3.5	47149	2178	4.6	1520	3.2
<b>2000-2001</b>	16712	966	5.8	602	3.6	16163	1220	7.6	710	4.4	8837	476	5.4	414	4.7
<b>Pilot (6m)</b>	7437	428	5.8	267	3.6	8131	518	6.4	323	4.0	6160	338	5.5	369	6.0
<b>35-49</b>															
<b>1997-2001</b>	62482	2725	4.4	923	1.5	67960	3365	5.0	814	1.2	42229	1748	4.1	475	1.1
<b>2000-2001</b>	16187	791	4.9	241	1.5	16312	911	5.6	221	1.4	9088	500	5.5	145	1.6
<b>Pilot (6m)</b>	6878	273	4.0	64	0.9	8051	346	4.3	97	1.2	6022	265	4.4	119	2.0
<b>50-64</b>															
<b>1997-2001</b>	37887	1212	3.2	279	0.7	42824	1533	3.6	218	0.5	30091	990	3.3	167	0.6
<b>2000-2001</b>	10289	402	3.9	90	0.9	10805	438	4.1	74	0.7	6743	300	4.5	53	0.8
<b>Pilot (6m)</b>	3890	86	2.2	15	0.4	5075	169	3.3	39	0.8	3741	127	3.4	42	1.1
<b>Total</b>															
<b>1997-2001</b>	168505	7361	4.4	3527	2.1	182402	9802	5.4	3543	1.9	119469	4916	4.1	2162	1.8
<b>2000-2001</b>	43188	2159	5.0	933	2.2	43280	2569	5.9	1005	2.3	24668	1276	5.2	612	2.5
<b>Pilot (6m)</b>	18205	787	4.3	346	1.9	21257	1033	4.9	459	2.2	15923	730	4.6	530	3.3

**Table 6 Borderline and mild dyskaryosis by month: individual pilot sites  
(GP/NHSCC adequate smears only)**

Pilot Month	A				B				C						
	adequate smears	border-line	mild dyskaryosis		adequate smears	border-line	mild dyskaryosis		adequate smears	border-line	mild dyskaryosis				
	n	n	%	n	%	n	n	%	n	%	n	%			
<b>1</b>	2397	107	4.5	51	2.1	1258	96	7.6	37	3.0	1709	111	6.5	48	2.8
<b>2</b>	2625	97	3.7	52	2.0	2397	93	3.9	65	2.7	3157	180	5.7	134	4.2
<b>3</b>	2892	118	4.1	52	1.8	3949	185	4.7	108	2.7	3161	140	4.4	122	3.9
<b>4</b>	3892	168	4.3	68	1.8	4630	256	5.5	75	1.6	2885	101	3.5	84	2.9
<b>5</b>	3771	199	5.3	70	1.9	5328	238	4.5	93	1.8	2507	93	3.7	64	2.6
<b>6</b>	2628	98	3.7	53	2.0	3695	165	4.5	81	2.2	2504	105	4.2	78	3.1
<b>1<sup>st</sup> 6mths</b>	18205	787	4.3	346	1.9	21257	1033	4.9	459	2.2	15923	730	4.6	530	3.3
<b>7</b>	4047	181	4.5	96	2.4	4717	282	6.0	113	2.4	2695	117	4.3	74	2.8
<b>8</b>	3618	146	4.0	86	2.4	3797	192	5.1	75	2.0	2632	122	4.6	74	2.8
<b>9</b>	3694	150	4.1	76	2.1	4882	304	6.2	110	2.3	1788	80	4.5	58	3.2
<b>10</b>	3648	199	5.5	57	1.6	3766	258	6.9	99	2.6	3097	155	5.0	75	2.4
<b>11</b>	4180	181	4.3	75	1.8	5393	330	6.1	125	2.3	2685	124	4.6	71	2.6
<b>12</b>	3078	107	3.5	40	1.3	3830	254	6.6	104	2.7	2479	104	4.2	84	3.4
<b>Total</b>															
<b>1997-2001</b>	168505	7361	4.4	3527	2.1	182402	9802	5.4	3543	1.9	119469	4916	4.1	2162	1.8
<b>2000-2001</b>	43188	2159	5.0	933	2.2	43280	2569	5.9	1005	2.3	24668	1276	5.2	612	2.5
<b>Pilot (12m)</b>	40470	1751	4.3	776	1.9	47642	2653	5.6	1085	2.3	31299	1432	4.6	966	3.1

**Table 7 Moderate and severe dyskaryosis by age: individual pilot sites  
(GP/NHSCC adequate smears only)**

Age Group	A				B				C						
	smears	moderate dyskaryosis		severe	smears	moderate dyskaryosis		severe	smears	moderate dyskaryosis		severe			
	n	n	%	n	n	n	%	n	n	n	%	n	%		
<b>20-34</b>															
<b>1997-2001</b>	68136	1027	1.5	619	0.9	71618	713	1.0	1073	1.5	47149	446	1.0	398	0.8
<b>2000-2001</b>	16712	279	1.7	157	0.9	16163	196	1.2	206	1.3	8837	107	1.2	87	1.0
<b>Pilot (6m)</b>	7437	117	1.6	90	1.2	8131	106	1.3	77	1.0	6160	80	1.3	114	1.9
<b>35-49</b>															
<b>1997-2001</b>	62482	325	0.5	374	0.6	67960	215	0.3	418	0.6	42229	151	0.4	217	0.5
<b>2000-2001</b>	16187	88	0.5	105	0.6	16312	54	0.3	99	0.6	9088	34	0.4	52	0.6
<b>Pilot (6m)</b>	6878	45	0.7	36	0.5	8051	33	0.4	25	0.3	6022	25	0.4	44	0.7
<b>50-64</b>															
<b>1997-2001</b>	37887	80	0.2	63	1.7	42824	41	0.1	201	0.5	30091	46	0.2	88	0.3
<b>2000-2001</b>	10289	22	0.2	16	0.2	10805	13	0.1	37	0.3	6743	15	0.2	12	0.2
<b>Pilot (6m)</b>	3890	3	0.1	5	0.1	5075	14	0.3	8	0.2	3741	6	0.2	9	0.2
<b>Total</b>															
<b>1997-2001</b>	168505	1432	0.85	1062	0.63	182402	969	0.53	1692	0.93	119469	643	0.54	703	0.59
<b>2000-2001</b>	43188	389	0.90	278	0.64	43280	263	0.61	342	0.79	24668	156	0.63	151	0.61
<b>Pilot (6m)</b>	18205	165	0.91	131	0.72	21257	153	0.72	110	0.52	15923	111	0.69	167	1.05

**Table 8 Moderate and severe dyskaryosis by month: individual pilot sites  
(GP/NHSCC adequate smears only)**

Pilot Month	A				B				C						
	smears	moderate	severe	dyskaryosis	smears	moderate	severe	dyskaryosis	smears	moderate	severe	dyskaryosis			
	n	n	%	n	%	n	%	n	n	%	n	%			
<b>1</b>	2397	33	1.4	21	0.9	1258	7	0.6	7	0.6	1709	13	0.8	11	0.6
<b>2</b>	2625	24	0.9	7	0.3	2397	21	0.9	14	0.6	3157	32	1.0	46	1.5
<b>3</b>	2892	22	0.8	13	0.5	3949	26	0.7	36	0.9	3161	19	0.6	43	1.4
<b>4</b>	3892	27	0.7	27	0.7	4630	38	0.8	17	0.4	2885	26	0.9	28	1.0
<b>5</b>	3771	39	1.0	33	0.9	5328	38	0.7	23	0.4	2507	9	0.4	22	0.9
<b>6</b>	2628	20	0.8	30	1.1	3695	23	0.6	13	0.4	2504	12	0.5	17	0.8
<b>1<sup>st</sup> 6mth</b>	18205	165	0.9	131	0.7	21257	153	0.7	110	0.5	15923	111	0.7	167	1.0
<b>7</b>	4047	58	1.4	50	1.3	4717	32	0.7	25	0.5	2695	20	0.7	17	0.6
<b>8</b>	3618	21	0.6	23	0.6	3797	29	0.8	20	0.5	2632	14	0.5	13	0.5
<b>9</b>	3694	33	0.9	27	0.7	4882	33	0.7	33	0.7	1788	11	0.6	10	0.6
<b>10</b>	3648	25	0.7	27	0.7	3766	24	0.6	21	0.6	3097	26	0.8	17	0.5
<b>11</b>	4180	21	0.5	23	0.6	5393	30	0.6	35	0.6	2685	17	0.6	18	0.8
<b>12</b>	3078	22	0.7	15	0.5	3830	20	0.5	19	0.5	2479	14	0.6	22	0.9
<b>Total</b>															
<b>1997-2001</b>	168505	1432	0.85	1062	0.63	182402	969	0.53	1692	0.93	119469	643	0.54	703	0.64
<b>2000-2001</b>	43188	389	0.90	278	0.64	43280	263	0.61	342	0.79	24668	156	0.63	151	0.61
<b>Pilot (12m)</b>	40470	345	0.85	296	0.73	47642	321	0.67	263	0.55	31299	213	0.68	264	0.84

**Table 9 Glandular neoplasia by age: individual pilot sites  
(GP/NHSCC adequate smears only)**

Age Group	A			B			C		
	smears n	glandular neoplasia n	%	smears N	glandular neoplasia n	%	smears n	glandular neoplasia n	%
<b>20-34</b>									
<b>1997-2001</b>	68136	40	0.06	71618	52	0.07	47149	16	0.03
<b>2000-2001</b>	16712	11	0.07	16163	17	0.11	8837	5	0.06
<b>Pilot (6m)</b>	7437	2	0.03	8131	3	0.04	6160	1	0.02
<b>35-49</b>									
<b>1997-2001</b>	62482	57	0.09	67960	53	0.08	42229	21	0.05
<b>2000-2001</b>	16187	16	0.10	16312	9	0.06	9088	4	0.04
<b>Pilot (6m)</b>	6878	2	0.03	8051	2	0.02	6022	4	0.07
<b>50-64</b>									
<b>1997-2001</b>	37887	23	0.06	42824	40	0.09	30091	40	0.13
<b>2000-2001</b>	10289	10	0.10	10805	6	0.06	6743	7	0.10
<b>Pilot (6m)</b>	3890	1	0.03	5075	2	0.04	3741	4	0.11
<b>Total</b>									
<b>1997-2001</b>	168505	120	0.07	182402	145	0.08	119469	77	0.06
<b>2000-2001</b>	43188	37	0.09	43280	32	0.07	24668	16	0.06
<b>Pilot (6m)</b>	18205	5	0.03	21257	7	0.03	15923	9	0.06

**Table 10 Glandular neoplasia by month: individual pilot sites  
(GP/NHSCC adequate smears only)**

Pilot Month	A			B			C		
	smears	glandular neoplasia		smears	glandular neoplasia		smears	glandular neoplasia	
	n	n	%	N	n	%	n	n	%
<b>1</b>	2397	1	0.04	1258	0	0.00	1709	3	0.18
<b>2</b>	2625	0	0.00	2397	0	0.00	3157	2	0.06
<b>3</b>	2892	1	0.03	3949	5	0.13	3161	2	0.06
<b>4</b>	3892	0	0.00	4630	0	0.00	2885	1	0.03
<b>5</b>	3771	2	0.05	5328	2	0.04	2507	1	0.04
<b>6</b>	2628	1	0.04	3695	0	0.00	2504	0	0.00
<b>1<sup>st</sup> 6mths</b>	18205	5	0.03	21257	7	0.03	15923	9	0.06
<b>7</b>	4047	2	0.05	4717	3	0.06	2695	0	0.00
<b>8</b>	3618	3	0.08	3797	1	0.03	2632	3	0.11
<b>9</b>	3694	6	0.16	4882	2	0.04	1788	1	0.06
<b>10</b>	3648	1	0.03	3766	1	0.03	3097	2	0.06
<b>11</b>	4180	1	0.02	5393	2	0.04	2685	1	0.04
<b>12</b>	3078	1	0.03	3830	2	0.05	2479	1	0.04
<b>Total</b>									
<b>1997-2001</b>	168505	120	0.07	182402	145	0.08	119469	77	0.06
<b>2000-2001</b>	43188	37	0.09	43280	32	0.07	24668	16	0.06
<b>Pilot (12m)</b>	40470	19	0.05	47642	18	0.04	31299	17	0.05

**Table 11 Inadequate smears by age and site for 4 years pre-pilot**

Age group/ Year	A			B			C			All sites		
	all smears	n	inadequate smears %	all smears	n	inadequate smears %	all smears	n	inadequate smears %	all smears	n	inadequate smears %
<b>20-34</b>												
<b>1997/98</b>	21422	3584	16.7	21490	1691	7.9	16777	2138	12.7	59689	7413	12.4
<b>1998/99</b>	19433	2544	13.1	20851	1785	8.6	15911	1797	11.3	56195	6126	10.9
<b>1999/00</b>	18853	2156	11.4	18526	1936	10.5	10537	978	9.3	47916	5070	10.6
<b>2000/01</b>	18917	2205	11.7	18019	1856	10.3	9759	922	9.5	46695	4983	10.7
<b>35-49</b>												
<b>1997/98</b>	19620	2762	14.1	19133	1469	7.7	13275	1358	10.2	52028	5589	10.7
<b>1998/99</b>	16101	1807	11.2	19353	1567	8.1	12319	1284	10.4	47773	4658	9.8
<b>1999/00</b>	16624	1481	8.9	18034	1836	10.2	11063	874	7.9	45721	4191	9.2
<b>2000/01</b>	17759	1572	8.9	18131	1819	10.0	9874	786	8.0	45764	4177	9.1
<b>50-64</b>												
<b>1997/98</b>	10725	1098	10.2	11363	618	5.4	8290	763	9.2	30378	2479	8.2
<b>1998/99</b>	9097	720	7.9	11592	621	5.4	7749	654	8.4	28438	1995	7.0
<b>1999/00</b>	10384	790	7.6	10968	665	6.1	9261	535	5.8	30613	1990	6.5
<b>2000/01</b>	11135	846	7.6	11482	677	5.9	7140	397	5.6	29757	1920	6.5
<b>Total</b>												
<b>1997/98</b>	51767	7444	14.4	51986	3778	7.3	38342	4259	11.1	142095	15481	10.9
<b>1998/99</b>	44631	5071	11.4	51796	3973	7.7	35979	3735	10.4	132406	12779	9.6
<b>1999/00</b>	45861	4427	9.7	47528	4437	9.3	30861	2387	7.7	124250	11251	9.1
<b>2000/01</b>	47811	4623	9.7	47632	4352	9.1	26773	2105	7.9	122216	11080	9.1

**Table 12 Adequate smears by age for 4 years pre-pilot  
(GP/NHSCC adequate smears only)**

Age Group/ Year	all smears		borderlines		mild dyskaryosis		moderate dyskaryosis		severe dyskaryosis		glandular neoplasia	
	n	N	%	n	%	n	%	n	%	n	%	
<b>20-34</b>												
<b>1997/98</b>	52276	2753	5.3	1606	3.1	534	1.0	555	1.1	27	0.05	
<b>1998/99</b>	50069	2435	4.9	1494	3.0	526	1.1	590	1.2	25	0.05	
<b>1999/00</b>	42846	2656	6.2	1530	3.6	544	1.3	495	1.2	23	0.05	
<b>2000/01</b>	41712	2662	6.4	1726	4.1	582	1.4	450	1.1	33	0.08	
<b>35-49</b>												
<b>1997/98</b>	46439	2022	4.4	542	1.2	168	0.4	247	0.5	26	0.06	
<b>1998/99</b>	43115	1501	3.5	525	1.2	146	0.4	265	0.6	46	0.11	
<b>1999/00</b>	41530	2113	5.1	538	1.3	201	0.5	241	0.6	30	0.07	
<b>2000/01</b>	41587	2202	5.3	607	1.5	176	0.4	256	0.6	29	0.07	
<b>50-64</b>												
<b>1997/98</b>	27899	891	3.2	181	0.65	34	0.1	110	0.4	21	0.08	
<b>1998/99</b>	26443	698	2.6	95	0.36	36	0.1	88	0.3	32	0.12	
<b>1999/00</b>	28623	1006	3.5	171	0.60	47	0.2	95	0.3	27	0.09	
<b>2000/01</b>	27837	1140	4.1	217	0.78	50	0.2	65	0.2	23	0.08	
<b>Total</b>												
<b>1997/98</b>	126614	5666	4.5	2329	1.8	736	0.6	912	0.7	74	0.06	
<b>1998/99</b>	119627	4634	3.9	2114	1.8	708	0.6	943	0.8	103	0.09	
<b>1999/00</b>	112999	5775	5.1	2239	2.0	792	0.7	831	0.7	80	0.07	
<b>2000/01</b>	111136	6004	5.4	2550	2.3	808	0.7	771	0.7	85	0.08	

**Table 13 Borderline and mild dyskaryosis by age for 4 years pre-pilot: individual pilot sites  
(GP/NHSCC adequate smears only)**

Age Group/ Year	A				B				C						
	smears	border-line		mild dysk.		smears	border-line		mild dysk.		smears	border-line		mild dysk.	
	n	n	%	n	%	n	n	%	n	%	n	n	%	n	%
<b>20-34</b>															
<b>1997/98</b>	17838	921	5.2	633	3.6	19799	1220	6.2	568	2.9	14639	612	4.2	405	2.8
<b>1998/99</b>	16889	693	4.1	550	3.3	19066	1103	5.8	578	3.0	14114	639	4.5	366	2.6
<b>1999/00</b>	16697	844	5.1	540	3.2	16590	1361	8.2	655	4.0	9559	451	4.7	335	3.5
<b>2000/01</b>	16712	966	5.8	602	3.6	16163	1220	7.6	710	4.4	8837	476	5.4	414	4.7
<b>35-49</b>															
<b>1997/98</b>	16858	780	4.6	259	0.5	17664	755	4.3	170	1.0	11917	487	4.1	113	1.0
<b>1998/99</b>	14294	453	3.2	220	0.4	17786	661	3.7	186	1.1	11035	387	3.5	119	1.1
<b>1999/00</b>	15143	701	4.6	203	0.6	16198	1038	6.4	237	1.5	10189	374	3.7	98	1.0
<b>2000/01</b>	16187	791	4.9	241	1.5	16312	911	5.6	221	1.4	9088	500	5.5	145	1.6
<b>50-64</b>															
<b>1997/98</b>	9627	314	3.3	87	0.9	10745	318	3.0	57	0.5	7527	259	3.4	37	0.5
<b>1998/99</b>	8377	168	2.0	42	0.5	10971	321	2.9	23	0.2	7095	209	2.9	30	0.4
<b>1999/00</b>	9594	328	3.4	60	0.6	10303	456	4.4	64	0.6	8726	222	2.5	47	0.5
<b>2000/01</b>	10289	402	3.9	90	0.9	10805	438	4.1	74	0.7	6743	300	4.4	53	0.8
<b>Total</b>															
<b>1997/98</b>	44323	2015	4.5	979	2.2	48208	2293	4.8	795	1.6	34083	1358	4.0	555	1.6
<b>1998/99</b>	39560	1314	3.3	812	2.1	47823	2085	4.4	787	1.6	32244	1235	3.8	515	1.6
<b>1999/00</b>	41434	1873	4.5	803	1.9	43091	2855	6.6	956	2.2	28474	1047	3.7	480	1.7
<b>2000/01</b>	43188	2159	5.0	933	2.2	43280	2569	5.9	1005	2.3	24668	1276	5.2	612	2.5

**Table 14 Moderate and severe dyskaryosis by age for 4 years pre-pilot: individual pilot sites  
(GP/NHSCC adequate smears only)**

Age Group/ Year	A				B				C			
	Smears moderate		severe dyskaryosis		Smears moderate		severe dyskaryosis		Smears moderate		severe dyskaryosis	
	n	n %	n %	n %	n	n %	n %	n %	n	n %	n %	n %
<b>20-34</b>												
<b>1997/98</b>	17838	258 1.5	134 0.8		19799	180 0.9	320 1.6		14639	96 0.7	101 0.7	
<b>1998/99</b>	16889	231 1.4	163 1.0		19066	159 0.8	292 1.5		14114	136 0.9	135 1.0	
<b>1999/00</b>	16697	259 1.6	165 1.0		16590	178 1.1	255 1.5		9559	107 1.1	75 0.8	
<b>2000/01</b>	16712	279 1.7	157 0.9		16163	196 1.2	206 1.3		8837	107 1.2	87 1.0	
<b>35-49</b>												
<b>1997/98</b>	16858	78 0.5	88 0.5		17664	55 0.3	116 0.7		11917	35 0.3	43 0.4	
<b>1998/99</b>	14294	62 0.4	84 0.6		17786	49 0.3	111 0.6		11035	35 0.3	70 0.6	
<b>1999/00</b>	15143	97 0.6	97 0.6		16198	57 0.4	92 0.6		10189	47 0.5	52 0.5	
<b>2000/01</b>	16187	88 0.5	105 0.6		16312	54 0.3	99 0.6		9088	34 0.4	52 0.6	
<b>50-64</b>												
<b>1997/98</b>	9627	15 0.2	20 0.2		10745	11 0.1	64 0.6		7527	8 0.1	26 0.4	
<b>1998/99</b>	8377	16 0.2	19 0.2		10971	7 0.1	46 0.4		7095	13 0.2	23 0.3	
<b>1999/00</b>	9594	27 0.3	14 0.1		10303	10 0.1	54 0.5		8726	10 0.1	27 0.3	
<b>2000/01</b>	10289	22 0.2	16 0.2		10805	13 0.1	37 0.3		6743	15 0.2	12 0.2	
<b>Total</b>												
<b>1997/98</b>	44323	351 0.79	242 0.55		48208	246 0.51	500 1.04		34083	139 0.41	170 0.50	
<b>1998/99</b>	39560	309 0.78	266 0.67		47823	215 0.45	449 0.94		32244	184 0.57	228 0.71	
<b>1999/00</b>	41434	383 0.92	276 0.67		43091	245 0.57	401 0.93		28474	164 0.58	154 0.54	
<b>2000/01</b>	43188	389 0.90	278 0.64		43280	263 0.61	342 0.79		24668	156 0.63	151 0.61	

**Table 15 Glandular neoplasia by age for 4 years pre-pilot: individual pilot sites  
(GP/NHSCC adequate smears only)**

Age Group/ Year	A glandular neoplasia			B glandular neoplasia			C glandular neoplasia		
	smears n	n	%	smears n	n	%	smears n	n	%
<b>20-34</b>									
<b>1997/98</b>	17838	6	0.03	19799	14	0.07	14639	7	0.05
<b>1998/99</b>	16889	9	0.05	19066	15	0.08	14114	1	0.01
<b>1999/00</b>	16697	14	0.08	16590	6	0.04	9559	3	0.03
<b>2000/01</b>	16712	11	0.07	16163	17	0.11	8837	5	0.06
<b>35-49</b>									
<b>1997/98</b>	16858	9	0.05	17664	10	0.06	11917	7	0.06
<b>1998/99</b>	14294	22	0.15	17786	21	0.12	11035	3	0.03
<b>1999/00</b>	15143	10	0.07	16198	13	0.08	10189	7	0.07
<b>2000/01</b>	16187	16	0.10	16312	9	0.06	9088	4	0.04
<b>50-64</b>									
<b>1997/98</b>	9627	2	0.02	10745	12	0.11	7527	7	0.09
<b>1998/99</b>	8377	4	0.05	10971	15	0.14	7095	13	0.18
<b>1999/00</b>	9594	7	0.07	10303	7	0.07	8726	13	0.15
<b>2000/01</b>	10289	10	0.10	10805	6	0.06	6743	7	0.10
<b>Total</b>									
<b>1997/98</b>	44323	17	0.04	48208	36	0.07	34083	21	0.06
<b>1998/99</b>	39560	35	0.09	47823	51	0.11	32244	17	0.05
<b>1999/00</b>	41434	31	0.07	43091	26	0.06	28474	23	0.08
<b>2000/01</b>	43188	37	0.09	43280	32	0.07	24668	16	0.06

**Table 16 Outcome of referral to colposcopy. Site A**

(NB CIN3 includes high grade CGIN and adenocarcinoma in situ, CIN2 includes low grade CGIN ( Nos in brackets))

**Pre-pilot (12months)**

Referral Smear	Total seen	Outcome						No CIN/ HPV	Inad. biopsy	No biopsy
		Squamous carcinoma	CIN 3	CIN 2	CIN 1	Other	HPV only			
Moderate	360	3	123 (9)	112 (6)	33	0	43	46	0	0
Severe	242	8	165 (22)	35 (3)	7	2	9	16	0	0
? Invasive	11	2	8 (1)	0	0	0	0	1	0	0
G. neoplasia	25	5	10 (9)	3 (1)	0	0	4	3	0	0

**Pilot (6 months)**

Referral Smear	Total seen	Outcome						No CIN/ HPV	Inad. biopsy	No biopsy
		Squamous carcinoma	CIN 3	CIN 2	CIN 1	Other	HPV only			
Moderate	189	1	67 (10)	65 (6)	17	4	18	15	2	0
Severe	153	7	116 (11)	17 (3)	0	1	5	7	0	0
? Invasive	3	0	2 (2)	0	0	0	0	1	0	0
G. neoplasia	11	2	5 (4)	1	1	0	0	2	0	0

**Table 17 Outcome of referral to colposcopy. Site B**

(NB CIN3 includes high grade CGIN and adenocarcinoma in situ, CIN2 includes low grade CGIN ( Nos in brackets))

**Pre-pilot (12 months)**

Referral Smear	Total seen	Outcome						No CIN/ HPV	Inad. biopsy	No biopsy
		Squamous carcinoma	CIN 3	CIN 2	CIN 1	Other	HPV only			
Moderate	298	2	95	98	58	33	0	12	0	0
Severe	341	0	195 (3)	62	35	38	0	11	0	0
? Invasive	38	7	24	0	6	0	0	0	1	0
G. neoplasia	33	0	12 (6)	3	3	9	0	0	0	6

**Pilot (6 months)**

Referral Smear	Total seen	Outcome						No CIN/ HPV	Inad. biopsy	No biopsy
		Squamous carcinoma	CIN 3	CIN 2	CIN 1	Other	HPV only			
Moderate	169	2	45	57	27	1	23	14	0	0
Severe	101	3	61 (3)	21(1)	11	0	0	4	0	1
? Invasive	7	1	5	0	0	0	0	1	0	0
G. neoplasia	10	0	3	1	1	1	0	4	0	0

**Table 18 Outcome of referral to colposcopy. Site C**

(NB CIN3 includes high grade CGIN and adenocarcinoma in situ, CIN2 includes low grade CGIN ( Nos in brackets))

**Pre-pilot (12 months)**

Referral Smear	Total seen	Outcome						No CIN/ HPV	Inad. biopsy	No biopsy
		Squamous carcinoma	CIN 3	CIN 2	CIN 1	Other	HPV only			
Moderate	107	1	32	35	22	4	10	2	1	0
Severe	154	7	106 (1)	13	4	5	12	7	0	0
? Invasive	5	2	3	0	0	0	0	0	0	0
G. neoplasia	27	3	3 (3)	0	0	10	1	7	3	0

**Pilot (6 months)**

Referral Smear	Total seen	Outcome						No CIN/ HPV	Inad. biopsy	No biopsy
		Squamous carcinoma	CIN 3	CIN 2	CIN 1	Other	HPV only			
Moderate	133	0	55	44	10	5	13	5	0	1
Severe	123	5	90 (2)	6	6	2	8	5	0	1
? Invasive	2	0	1	0	0	1	0	0	0	0
G. neoplasia	20	1	4 (3)	0	0	7	2	6	0	0

**Table 19 Positive predictive value of referral to colposcopy**

Smear Category	PPV (CIN 3 +)		PPV (CIN 2 +)		
	Pre-pilot (12 months)	Pilot (6 months)	Pre-pilot (12 months)	Pilot (6 months)	
Moderate dyskaryosis	A	35.0% (126/360)	36.0% (68/189)	66.1% (238/360)	70.4% (133/189)
	B	32.6% (97/298)	27.8% (47/169)	65.4% (195/298)	61.5% (104/169)
	C	30.8% (33/107)	41.4% (55/133)	63.6% (68/107)	74.4% (99/133)
	Total	33.5% (256/765)	34.6% (170/491)	65.5% (501/765)	68.4% (336/491)
Severe dyskaryosis/ ?invasive	A	71.5% (183/253)	76.2% (125/156)	86.2% (218/253)	91.0% (142/156)
	B	59.6% (226/379)	64.8% (70/108)	76.0% (288/379)	84.3% (91/108)
	C	74.2% (118/159)	76.8% (96/125)	82.4% (131/159)	81.6% (102/125)
	Total	66.1% (527/791)	74.8% (291/389)	80.5% (637/791)	86.1% (335/389)
Moderate dyskaryosis or worse (including glandular neoplasia)	A	50.5% (324/638)	56.2% (200/356)	74.3% (474/638)	79.5% (283/356)
	B	47.2% (335/710)	41.8% (120/287)	70.1% (498/710)	69.3% (199/287)
	C	53.6% (157/293)	56.1% (156/278)	70.0% (205/293)	74.1% (206/278)
	Total	49.7% (816/1641)	51.6% (475/921)	71.7% (1177/1641)	74.6% (687/921)

## **4. RUNNING COSTS OF LBC COMPARED TO CONVENTIONAL CYTOLOGY**

In this section, we consider the running costs of LBC compared to conventional cytology. By running costs we mean 1) the costs incurred in primary care, including taking of smears and administration of letters; 2) equipment and labour involved in the preparation of slides; and 3) consumables, smear reading, and other laboratory costs. We are concerned here with costs incurred by the NHS, and have therefore not included estimates of costs associated with women's time and anxiety; these are likely to be reduced with LBC if there is a reduction in the need for repeat smears.

There is also a one-off transition cost of converting laboratories to the new technique and in training staff. These costs will be considered separately in Section 6. Once staff have been trained in LBC, subsequent training costs are likely to be similar to conventional cytology for both smear readers and smear takers.

Comparing the running costs of LBC with those of conventional cytology is complex. Use of LBC technology may result in reductions in the staff time involved in smear taking and smear reading. However, preparation staff time, equipment and consumable costs are likely to be greater with LBC, although some of these costs (such as equipment and consumable costs) can only be indicative at this stage. In this section, each of these costs is analysed to obtain an estimated total cost per slide, and the uncertainties around these estimates are addressed using sensitivity analysis.

Differences in the overall costs of screening may also occur between the two techniques due to differences in screening results. In particular a reduction in inadequate smears with LBC will reduce the need for repeat smears, generating a cost saving. This will be considered in Section 5, where the costs and effects of conventional versus LBC screening programmes are compared in a cost-effectiveness analysis.

### **4.1 Primary care costs**

Over 86% of smears are taken in a general practice setting<sup>9</sup>. Conventionally the smear taker (generally a practice nurse) uses a spatula to collect a sample. The sample is then smeared on a cytology slide, a fixative is applied, and the slide is then left to dry and subsequently labelled. With LBC, the smear taker obtains a sample using a broom-like device. The broom is then placed in a plastic vial containing a preservative solution and labelled. There is a slight difference between the technologies: with SurePath™ the broom is left in the vial and with Cytoc the broom is removed after depositing the sample. As taking an LBC sample is easier for the smear taker than preparing a cytology slide, this potentially reduces the consultation time.

The pilot site laboratories provided the consumables required for smear taking, both historically with conventional kits and for LBC. These costs will be considered in Section 4.4. LBC vials can be stored at room temperature and, as with conventional cytology, there is no need for refrigeration. LBC vials were collected using the same hospital van system as with conventional smears at all three pilot sites.

To estimate the workload and cost per smear of consultation using LBC a questionnaire was sent to a random sample of general practices across all three pilot sites. To obtain comparative data for conventional cytology a questionnaire was also sent to a random sample of GP practices in Oxfordshire. As part of both questionnaires, smear takers were asked to state their profession and to record the total time for smear taking consultations with five women. At the pilot sites smear takers also had to give information to the women about HPV testing and the pilot study; the time to do this was recorded and subtracted from the total consultation time.

Table 4.1 reports the unit cost per minute of General Practitioner and practice nurse time using national unit cost data from the Personal Social Services Research Unit (PSSRU) <sup>10</sup>, at £1.43 and £0.37 per minute respectively. Results from the smear taker questionnaire indicated that practice nurses took 80% and GPs 20% of smears, and we used these ratios to combine the staff unit costs in order to give a weighted smear taker cost of £0.58 per minute. Neither the questionnaire nor site visits produced any reason to assume that the staff mix of smear takers may be different using LBC compared to conventional cytology.

**Table 4.1: Unit cost of smear taker time**

Staff	Unit cost per minute of consultation time
Practice nurse	£0.37
General Practitioners	£1.43
<b>Weighted smear taker cost</b>	<b>£0.58</b>

In table 4.2, the average consultation times collected from the smear taker record sheets are presented (total number of observations n=333 for LBC and n= 135 for conventional cytology). Total consultation times were on average 8 minutes 35 seconds using LBC compared to 13 minutes 20 seconds with conventional smears. This statistically significant difference, of almost 5 minutes per smear was also found in sub-analyses of GP and practice nurse smear takers, and for the different LBC technologies. For practice nurses only; smear taker times were 8:22 (95% CI 7:49, 8:55) for LBC compared to 13:26 (95% CI 12:40, 14:13) for conventional. For Cytoc the average smear taking time was 8:14 (95% CI 7:33,8:55) and for SurePath™ 8:35 (95% CI 7:44, 9:27).

This difference is reflected in the average cost per smear, which has been calculated by multiplying the weighted smear taker unit cost (in table 4.1) by the consultation times. This results in a reduced cost per smear taking consultation of £4.93 compared to £7.66 with conventional cytology.

**Table 4.2: Total consultation time and average cost of taking an LBC smear**

	LBC	Conventional
<b>Total consultation time in minutes: seconds average (95% c.i.)</b>	8:35 (8:06, 9:05)	13:20 (12:06, 14:04)
<b>Average cost for taking a smear</b>	£4.93	£7.66

It is likely that LBC reduces the average consultation time because the smear taker does not have to prepare a cytology slide. However, it is possible that this difference has been over-stated due to the method of data collection. First, the questionnaires used to record times in the pilot site sample were in different geographical areas to the questionnaires used to record conventional cytology times, and some unobserved bias may have entered the analysis. Second, when estimating the time to take a smear using LBC, the time involved in explaining about the pilot study and HPV testing were estimated and subtracted.

In addition to the recorded timings, we also asked smear takers when completing the smear taker questionnaire for their views on consultation time (see appendix question 11): ‘Considering LBC alone (excluding time for giving information about the pilot or HPV testing) how does the consultation time when taking smears with LBC compare to conventional smears?’ From 82 responses: 0% replied “much slower - more than 2 minutes”, 8.5% replied “slightly slower”, 48.8% “no difference”, 32.9% “slightly quicker and 9.7% “much quicker - more than 2 minutes”. Thus those indicating LBC was quicker than conventional outnumbered by 5:1 those indicating it was slower, but the average change across all respondents was a reduction in time of just under 1 minute.

To reflect the uncertainty as to whether there is a true reduction in smear taker time of 5 minutes we have also presented a scenario where smear-taking time is only reduced by one minute in a sensitivity analysis in section 4.8.

The administration of results letters to women was managed differently across the pilot sites. At some sites/health authorities, letters were sent via the health authorities directly to the women. At others, the administration of letters was mainly managed by general practice and the results were sent to the smear taker who then informed the woman.

Assessment of the different administration options is beyond the scope of this evaluation. With the abolition of health authorities in spring 2002 the optimal method of letter administration, will need further assessment. Clearly it is likely that there will be economies of scale benefits in having letter administration co-ordinated in larger centres.

The introduction of LBC is unlikely to affect administration costs greatly, although the overall administration cost will be reduced due to the reduction in repeat smears due to inadequates. The cost of administration of letters to the women has been assumed to be £3 per smear in this analysis.

## **4.2 Slide preparation equipment cost**

With conventional cytology, slides are prepared and labelled by smear takers when they take the smear. Once slides have been transported to the cytology laboratory, they are stained before being interpreted by smear readers. Slides are stained using a semi-automated slide stainer that dips the slides in dye. On completion, some machines automatically fit a cover slip over the slide. Staining machines vary in capacity and the extent of automation and information was available on two types of machine in different pilot sites. Here, we present data from a slide-staining machine at one pilot site.

With LBC, the preparation of slides is more complex and time-consuming, as the sample has to be transferred from suspension in a liquid onto a cytology slide before staining. Two manufacturers supplied the pilot sites with LBC equipment: Cytyc (the T2000<sup>TM</sup> and T3000<sup>TM</sup> machines) and Tripath Imaging Inc. (PrepStain<sup>TM</sup> system). The processes involved in preparing slides vary between the equipment.

*T2000<sup>TM</sup>* This is a semi-automated processor that can be used to prepare one sample at a time. After preparation of a slide using the T2000<sup>TM</sup> it is still necessary to stain the slide in the same way as with conventional slides. The T2000<sup>TM</sup> was only used for a brief period at the pilot sites for the general screening programme, and was subsequently replaced by a T3000<sup>TM</sup> machine.

*T3000<sup>TM</sup>* This is a fully automated machine for slide preparation. Once loaded it can be left until the cycle is complete. Again, slides must still be stained using the same equipment as with conventional cytology.

*SurePath<sup>®</sup> PrepStain<sup>TM</sup>* system Prior to loading samples on the PrepStain<sup>TM</sup> system vials must be shaken, transferred to test tubes and centrifuged. The PrepStain<sup>TM</sup> system transfers the liquid from the test tube to cytology slides and automatically stains them.

Table 4.3 presents information on the capacity of the different slide preparation machines. Estimates of the maximum capacity per batch and of batch duration were collected from each pilot site using preparation record sheets. As the T2000<sup>TM</sup> machine was not being used when the data were collected, these estimates were collected through interviews with staff. Maximum capacity per shift and per year have been estimated based on an 8 hour shift, using the machines 5 days a week for 50 weeks per year.

**Table 4.3: Capacity of preparation equipment**

Technology	Maximum capacity per batch	Batch duration	Maximum capacity per shift	Maximum capacity per year
<b>T3000™</b>				
T3000™	80	2.5 hours	240	60,000
<b>T2000™</b>				
T2000™	1	4 mins	120	30,000
<b>PrepStain™ system</b>				
Preparation	48	1hour +	288	72,000
PrepStain™ machine	48	1 hour 10mins	288	72,000
<b>Slide stainer</b>				
Slide stainer	40	1 hour	320	80,000

The table shows that the maximum capacity of the different machines varies substantially. A T2000™ has a maximum capacity of 30,000 slides per annum, compared with 60,000 for the T3000™ and 72,000 for the PrepStain™ system. We have assumed that initially SurePath™ vials are prepared and then the PrepStain™ system is run six times in a day, the T3000™ three times a day. None of the sites were using machines at full capacity and therefore a full evaluation of the implications of this is not possible. The cost per slide will be cheaper if the machines are being used closer to full capacity.

In table 4.4 we report the cost of using equipment in preparation centres that process 30,000 slides a year and 60,000 slides per year. In the 60,000 per year processing laboratory only one T3000™ or the PrepStain™ system would be required as opposed to two T2000's™. However, as the T2000™ machine was not being used when the data were collected, estimates of time per batch were collected through interviews with staff. If the T2000™ time per batch increased potentially annual capacity would be higher.

To calculate the purchase and maintenance costs of LBC equipment, we have estimated in consultation with the NHS Purchasing and Supply Agency the costs likely to prevail in the marketplace once the pilot study has been concluded; these costs should be viewed as indicative. The purchase cost of a staining-machine was supplied by one pilot site only and it has been suggested that this may be a low estimate. Purchase costs of equipment have been divided by a 5-year lifespan and maintenance costs added to give an annual cost. Unless actual data were available, it has been assumed that maintenance costs will be equivalent to 10% of the purchase cost per annum. There are various purchasing options for equipment other than outright purchase which have not been considered in detail; however, in the sensitivity analysis in section 4.8 we consider lower and higher cost equipment scenarios.

Annual costs have then been divided by preparation centre sizes; here 30,000 and 60,000 have been used as illustrative examples to obtain a cost per slide.

**Table 4.4 Cost per slide of preparation equipment**

Technology	Machine total cost		Cost per slide	
	Purchase cost	Annual maintenance cost	30,000 slide preparation centre	60,000 slide preparation centre
<b>Conventional cytology</b>				
Staining machine	£8,000	£800	£0.08	£0.04
<b>Total</b>	<b>£8,000</b>	<b>£800</b>	<b>£0.08</b>	<b>£0.04</b>
<b>T3000™</b>				
Staining machine	£8,000	£800	£0.08	£0.04
T3000™	£95,000	£9,500	£0.95	£0.48
<b>Total</b>	<b>£103,000</b>	<b>£10,300</b>	<b>£1.03</b>	<b>£0.52</b>
<b>T2000™</b>				
Staining machine	£8,000	£800	£0.08	£0.04
T2000™	£30,000	£2,500	£0.28	£0.28
<b>Total</b>	<b>£38,000</b>	<b>£3,300</b>	<b>£0.36</b>	<b>£0.32</b>
<b>PrepStain™ system</b>				
PrepStain™ system	£45,000	£4,200	£0.44	£0.22
<b>Total</b>	<b>£45,000</b>	<b>£4,200</b>	<b>£0.44</b>	<b>£0.22</b>

As table 4.4 indicates, a cost saving is demonstrated through having larger preparation centres. The cost of a staining machine, a T3000™ or the PrepStain™ system is reduced by 50% in preparation centres that are processing 60,000 slides per annum compared to those processing 30,000. Although, as the T2000™ is estimated to have a capacity of 30,000 slides per annum as calculated in table 4.3 the same cost savings do not accrue through having larger preparation centres.

For convenience, we have used 30,000 and 60,000 as our example laboratory sizes. If the PrepStain™ system was used at full capacity estimated at 72,000 slides per year then the equipment cost per slide would fall from £0.22 to £0.18. If the preparation equipment was only used to prepare 15,000 slides per year instead of 30,000 slides per year, then the equipment cost per slide would rise from £1.03 to £2.06 for the T3000™, from £0.36 to £0.73 for the T2000™ and from £0.44 to £0.88 for the PrepStain™ system.

It should be borne in mind that currently in England approximately 75% of laboratories currently process under 30,000 slides per year<sup>9</sup>. Having preparation equipment in every laboratory in England is likely to be an expensive option, and an alternative would be to have preparation centres at one laboratory serving one or two other satellite laboratories: this and other options have not been evaluated as part of this study. The costs presented above for preparation centres dealing with 60,000 smears per annum represent a low cost scenario as no transportation or logistical costs have been included for transferring slides between cytology laboratories and preparation centres. For example, more administrative staff time would be required to record the smears received and to organise the distribution of the slides back to satellite laboratories.

It is important to note that the final post-pilot costs of equipment and consumables are still in negotiation between suppliers and the Department of Health. It is recognised that there may be price changes before this publication goes to press, and prices will also depend in part on the extent to which preparation machines are shared between laboratories.

It is also possible that there are other suitable suppliers beyond those considered in this pilot. Finally, there are many considerations in choosing suppliers including additional services provided such as training, and their capacity to implement and support LBC across many laboratories. A full assessment of supplier suitability is beyond the remit of this evaluation.

### 4.3 Slide preparation labour costs

The labour costs involved in preparing slides vary between the technologies. With conventional cytology, the slide is prepared in general practice before arrival at the laboratory, and consequently the preparation time only includes staining the slides. With LBC, the preparation time varies depending on which technology is used. Both the T2000<sup>TM</sup> and the PrepStain<sup>TM</sup> are semi-automated systems, with the T2000<sup>TM</sup> slides have to be loaded individually and with PrepStain<sup>TM</sup> samples have to be transferred to vials. The T3000<sup>TM</sup> is a fully automated machine and can prepare 80 slides at a time. With both of the T2000<sup>TM</sup> and T3000<sup>TM</sup> technologies the slides also have to be stained before interpretation by the smear readers. With the PrepStain<sup>TM</sup> system the preparation process is more labour intensive than the T3000<sup>TM</sup>, involving the preparation of small vials for the PrepStain<sup>TM</sup> machine. However, the PrepStain<sup>TM</sup> machine both prepares the slides and stains them.

The cost per minute of preparation time can be calculated from the annual salary of a whole time equivalent (wte) at the midpoint of the Whitley Council pay scales for a Medical Laboratory Assistant (MLA), which is £10,106, and by assuming that a wte works 46 weeks a year and a 37.5 hour week. It is also assumed that a MLA or other staff on equivalent pay scales prepares all slides. The resulting labour cost per minute is £0.10.

Table 4.5 shows the average time to prepare a slide using the different technologies – from record sheets (although the T2000<sup>TM</sup> was collected through interviews with staff). Preparation times vary, with conventional cytology taking 15 seconds per slide and the T2000<sup>TM</sup> 4 minutes 15 seconds per slide. Preparation staff costs per slide are then calculated by multiplying the time to prepare a slide by the unit cost of preparation labour time at £0.10 per minute.

**Table 4.5 Staff total time and cost for preparing a slide**

Technology	Batch size	Preparation time	Time per slide	Preparation staff cost per slide
<b>Conventional</b>				
Staining machine loading and unloading	80	00:20:00	00:00:15	£0.02
<b>Total</b>			<b>00:00:15</b>	<b>£0.02</b>
<b>T3000<sup>TM</sup></b>				
T3000 <sup>TM</sup> loading and unloading	80	00:30:00	00:00:23	£0.04
Staining machine loading and unloading	80	00:20:00	00:00:15	£0.02
<b>Total</b>			<b>00:00:38</b>	<b>£0.06</b>
<b>T2000<sup>TM</sup></b>				
T2000 <sup>TM</sup> loading and unloading	1	00:04:00	00:04:00	£0.39
Staining machine loading and unloading	80	00:20:00	00:00:15	£0.02
<b>Total</b>			<b>00:04:15</b>	<b>£0.41</b>
<b>PrepStain system<sup>TM</sup></b>				
PrepStain system <sup>TM</sup> preparation of vials and loading and unloading machine	48	01:30:00	00:01:52	£0.20
<b>Total</b>			<b>00:01:52</b>	<b>£0.20</b>

Labour costs for preparing slides vary, from £0.02 per slide with conventional cytology to £0.41 with the T2000™.

#### 4.4 Consumable costs

Consumable costs include those involved in the smear taking, and other consumables involved in the preparation process, such as staining fluids and filters. Both in the LBC pilot and historically at the pilot site laboratories, cytology laboratories have paid the consumable costs.

For conventional cytology, consumable costs include the cost of the smear taker kit provided to smear takers (including slides, fixative, mailers, spatulae and form) and staining fluid for the staining machine. The average cost of a conventional kit was collected at all three pilot sites and ranged from £0.12 to £0.17. In table 4.6 the mid-point of the range is reported. These consumable costs vary slightly due to different suppliers. Estimates for the cost per slide of staining fluid were estimated using data from one pilot site on total expenditure on staining fluid divided by the number of slides processed.

For LBC technologies, the consumable packs include LBC collection vials and solution, and consumables for operating the preparation equipment including filters and fluids. The additional cost of fluid for staining has conventionally been added to the consumable costs of the T2000™ and T3000™. For the PrepStain™ system the consumable cost is inclusive of staining fluid. As with LBC capital equipment, we have based our calculations on estimates made by us in consultation with the NHS Purchasing and Supplies Agency of the likely costs of consumables in the marketplace once the pilot study has been concluded, and these should be seen as indicative costs. In our sensitivity analysis we consider the effect of a range of values for these costs.

**Table 4.6 Indicative unit costs of consumables**

<b>Technology</b>	<b>Consumable cost per slide</b>
<b>Conventional cytology</b>	
Consumable pack	£0.15
Fluid for staining machine	£0.12
<b>Total</b>	<b>£0.27</b>
<b>T3000™</b>	
Cytec® consumables pack	£3.95
Fluid for staining machine	£0.12
<b>Total</b>	<b>£4.07</b>
<b>T2000™</b>	
Cytec® consumables pack	£3.95
Fluid for staining machine	£0.12
<b>Total</b>	<b>£4.07</b>
<b>PrepStain system™</b>	
SurePath™ consumables pack	£2.00*
<b>Total</b>	<b>£2.00</b>

\*Since writing this report we have been informed this will possibly increase to £2.50; this level of increase is included in the sensitivity analysis below.

#### 4.5 Smear reader costs

The appearance of LBC slides is different from conventional cytology slides and therefore it has been suggested that smear reading time may differ between the two technologies. In the cytology laboratory, once slides are prepared they are subject to primary screening. Primary screening is usually done by either cytoscreeners or level one Biomedical Scientists (BMS1). Negative and inadequate slides are then subject to rapid review. Abnormal slides are sent for checking in the form of a full interpretation. 'Checking' is usually done by higher grade BMSs in the laboratory and by pathologists. 'Checking' differs from rapid review as it involves a full re-screen.

To assess the workload implications of LBC, smear readers were asked to complete record sheets for three consecutive weeks. The record sheets assessed the total hours worked, and the time spent on different screening activities (primary screening, checking and rapid review). This provided information on time taken and the proportion of different grades of staff involved in each activity, from which weights could be derived for costing purposes. These weights were then multiplied by the unit cost per hour for each staff grade to estimate a cost per hour for each type of screening activity and the results are given in table 4.7. Unit costs per hour for each staff grade were calculated by taking midpoints of Whitley council salary pay scales, and assuming a 37.5 hour working week and 46 weeks per year. Costs of pathologists have been taken from Netten et al 2001<sup>10</sup>.

**Table 4.7 Unit costs for staff activity**

Activity	Unit cost per hour
Weighted primary screening cost	£9.62
Weighted rapid review cost	£10.93
Weighted 'checking' cost	£33.55

The unit cost per hour of 'checking' are higher than the primary screening costs and rapid review costs, as these only involve higher staff grades.

Data from the record sheets were also used to estimate the number of smears screened per hour for each smear reading activity: primary screening, rapid review and checking. These data were only available from one pilot site for conventional cytology; however, this pilot site was not significantly different from the other two sites in terms of LBC slides read per hour, suggesting it is not untypical. No significant differences in smear reading times were found between the two technologies. The number of smears read per hour, and the costs associated with smear reading times, are presented in table 4.8.

**Table 4.8 Average (95% c.i.) number of slides screened per hour, and staff cost per slide**

Screening stage	Total smears read per hour		Average cost per slide	
	LBC	Conventional	LBC	Conventional
Primary screening	9.04 (8.8, 9.3)	8.3 (7.8,8.8)	£1.06	£1.15
Rapid review	44.1 (42.1, 46.2)	46.7 (43.7,49.7)	£0.25	£0.23
Checking*	12.4 (11.4, 13.4)	9.5 (8.8,10.4)	£0.67	£0.87
<b>Total</b>			<b>£1.99</b>	<b>£2.26</b>

\*Based on estimate that 25% of slides are checked

For primary screening and checking, smear readers are able to read more slides per hour using LBC than with conventional cytology, but to undertake slightly fewer rapid reviews per hour. It was

assumed that the staff mix performing primary screening, rapid review and checking is the same for conventional slide reading and LBC.

A cost per slide of each activity was derived by dividing the average number of smears read per hour by the unit costs in table 4.7. From discussion with laboratory staff about 25% of slides are subject to 'checking' (although there is some inter laboratory variation) and hence 25% of the cost of checking one slide has been added to the cost per average slide. It is assumed that the percentage of slides checked is the same for LBC and conventional cytology. The table shows that the total reading costs per slide including primary screening, rapid review and checking average £1.99 with LBC and £2.26 with conventional cytology.

The productivity of the laboratory may increase with LBC because the number of slides that can be read per hour could increase from 8.3 to 9.0. At the pilot sites the number of formal breaks remained unchanged. The views of smear readers on the need for breaks are reported in Appendix 1. At all three pilot sites the productivity of primary smear reading increased by 9%.

The Scottish evaluation found similar times to read conventional smears as found in this study; however, LBC timings were different, with 11 slides per hour recorded in the Scottish study. This would represent an increase of primary smear reading by 25%. It may be that the smear readers at the English pilot sites were still on a learning curve, and that there will be further increases in the number of slides read. We use the higher estimates in the best-case scenario sensitivity analysis.

In this analysis we have assumed that the proportion of slides 'checked' is the same between LBC and conventional cytology, and have taken a 25% checking rate. It is possible that there may be some variation between the proportion of slides "checked" nationally; however we have not examined other baseline rates. In our sensitivity analysis we have examined the possibility that the proportion of slides being checked is different between LBC and conventional: in the best case we have assumed a 20% reduction in the proportion of LBC slides checked based on anecdotal evidence. This figure is high, but does illustrate that total costs per smear are not particularly sensitive to differences between LBC and conventional in the proportion of slides checked.

LBC not only affects the productivity of the laboratory, it also affects the overall number of slides that need to be screened. The decrease in the inadequate rate reported in section 3 will also affect the total smear reader workload because fewer slides in total will need interpretation. Using data on the average inadequate rate the number of slides that need interpretation will be reduced by 7%. See section 5.

At one pilot site a significant reduction in workload was also recorded due to reduced numbers of double smears. This is a practice in conventional cytology whereby smear takers prepare two cytology slides at the same time from one woman. With LBC it is no longer necessary to take two smears. However, nationally the practice of double smear taking for conventional cytology is now being discouraged for most cases and we have not incorporated the effect of double smear taking in this analysis.

#### **4.6 Other laboratory costs**

Other laboratory costs include overheads, smear readers' and MLA time on other activities, other staff costs such as managers who are not smear readers, clerical staff and trainee smear readers.

In interviews with laboratory management staff, no reasons were identified why, once a laboratory had been fully converted, overhead costs should differ between LBC and conventional technology. Overheads include building rental, storage space, and transport arrangements and were similar for conventional as for LBC.

In section 6.2 some further logistical and organisational issues are identified. Although LBC samples can be stored in the laboratory at room temperature and at the pilot sites they were stored in the preparation or administration area on racks, it was suggested that it would be better to have a separate storage area due to health and safety issues regarding the flammability; the disposal of the residual vials from the SurePath™ process was carried out via a route suitable for combined clinical and chemical waste whereas ThinPrep™ had a collection system for used vials; due to the extra expense and the limited shelf life of LBC, more comprehensive stock monitoring was introduced at some of the pilot sites. However, we have not included costs for these items.

Overhead costs are hard to identify accurately as cytology laboratories are also involved in other activities such as non-gynaecological work. In table 4.9, our estimates of average overhead costs are presented from data from one pilot site.

In order to estimate costs per smear spent on other activities, costs spent on slide preparation and reading have been subtracted from total costs. A total cost of smear readers time (excluding pathologists) and MLA time was calculated by multiplying the total number of whole time equivalent staff by the midpoints of Whitley council salary pay scales for the pre-pilot year. The total staff costs were divided by the total number of slides processed in the pre-pilot year to estimate total staff costs per conventional slide (data was used from two laboratories). In section 4.3 and 4.5 the cost per slide of MLA time loading and unloading the slide preparation equipment and smear reading time has been estimated at £0.02 and £2.26 respectively. These costs have been subtracted from the total cost per smear to estimate a cost per smear spent on other activity.

Primary screeners reported that they were screening slides for approximately 60% of their working time, with the remainder attributable to breaks and administration. The number of breaks was not changed between conventional cytology and LBC. Senior smear readers spent a smaller proportion of their working time reading smears and many had other responsibilities such as management.

There are a number of other staff involved including managerial, administrative and clerical staff who do not read smears themselves. Slides read by trainee smear readers have to be 'checked' by trained smear readers and therefore trainee smear readers impose an additional staff cost. The average costs of these staff were calculated across two of the pilot sites.

During the pilot site studies there was also a management burden associated with being a pilot site. However, no reasons were identified why the management cost per slide would be very different with LBC compared to conventional cytology once the laboratory had made a full transition to the new technique. Again administration and clerical workload is similar per slide for both LBC and conventional, the extent of automation of administration systems varied between the sites and is likely to vary nationally. Trainee smear readers undergo training for two years to become cytoscreeners and need to read a minimum of 5000 slides to qualify. There is unlikely to be a difference in training times between LBC and conventional cytology if they only trained in one technique.

In table 4.9 other laboratory costs are presented. There is likely to be some national variation in these costs between laboratories depending on the staffing arrangements in place, however, few reasons were identified as to why these costs would vary between LBC and conventional cytology.

**Table 4.9: Other laboratory costs per smear**

Item	Cost per smear
Overhead costs	£1.61
*Smear reader cost (for time not interpreting slides)	£4.15
MLA's (for time apart from using slide preparation equipment)	£0.48
Other staff including managers, trainees and administration staff	£2.18
<b>Total</b>	<b>£8.42</b>

\*Does not include pathologists

#### 4.7 Total cost per smear for conventional cytology and LBC

Drawing together the different components of cost set out in detail above, Table 4.10 shows a summary of the total cost per smear of conventional cytology and the various LBC technologies examined.

**Table 4.10: Summary of total costs per smear for conventional cytology and LBC**

Item	Technology			
	Conventional	LBC		
		T3000 <sup>®</sup>	T2000 <sup>®</sup>	PrepStain system <sup>®</sup>
Smear taker staff cost	£7.66	£4.93	£4.93	£4.93
Administration cost	£3.00	£3.00	£3.00	£3.00
Preparation equipment cost	£0.04	£0.52	£0.36	£0.22
Preparation staff cost	£0.02	£0.06	£0.41	£0.20
Consumable cost	£0.27	£4.07	£4.07	£2.00
Smear reading cost	£2.26	£1.99	£1.99	£1.99
Other laboratory costs	£8.42	£8.42	£8.42	£8.42
<b>Total</b>	<b>£21.68</b>	<b>£22.99</b>	<b>£23.15</b>	<b>£20.76</b>
<b>Difference to conventional</b>		<b>£1.31</b>	<b>£1.47</b>	<b>-£0.92</b>

Note: Assumes equipment used at 60,000 slide capacity

The total cost per smear using conventional cytology is estimated to be £21.68. The cost per smear of each of the T3000<sup>TM</sup> and T2000<sup>TM</sup> LBC technologies examined is slightly more than this, while the cost per smear of PrepStain<sup>TM</sup> LBC technology is slightly less. The main explanation for these results is that the LBC technologies have significantly higher consumable costs and preparation costs, but also have substantially lower labour costs associated with LBC smear taking, these two factors largely cancelling each other.

Both equipment and consumable costs are based on estimates made by us in consultation with the NHS Purchasing and Supply Agency of the likely costs in the marketplace once the pilot has concluded, and should be seen as indicative costs.

These costs are based on the assumption that equipment is used to process 60,000 slides per annum however, most laboratories in England process less than 30,000 slides a year. If a model is used where preparation is conducted at one laboratory and serve other laboratories these costs represent a low cost

scenario as no transportation or logistical costs have been included for transferring slides between cytology laboratories and preparation centres.

#### **4.8 Sensitivity analyses**

Our estimate of the smear labour costs is based on comparative observations of total consultation time recorded in the smear taker questionnaire: (sent to a random sample of practices using LBC at all three pilot sites, and a random sample of practices outside of the pilots where conventional smears are taken). To calculate the total consultation time for LBC we subtracted the time to explain about the pilot and HPV testing, and it may be that we have overestimated the difference between consultation time for LBC compared to taking a conventional smear.

In the questionnaire to smear takers who were using LBC, we also asked whether or not they thought it was quicker to take a smear using LBC than conventional cytology. On average, respondents indicated that it was about 1 minute quicker (see appendix 1). Table 4.11 shows how the results obtained in this section are affected if the time involved in taking a smear is not 5 minutes but just 1 minute faster than conventional. In this scenario LBC would become between £1.23 and £3.62 (depending on the technology) more expensive per smear than conventional cytology.

The results are influenced by our estimates of the consumable costs of the LBC technology in the marketplace once the pilot study has been concluded, and these are inevitably uncertain. To reflect this uncertainty we have varied the cost of each supplier's consumables independently over a range from 50% more to 50% less of our baseline estimate, and report the results in table 4.12. The table confirms that these consumable costs do have a significant effect on the incremental costs of LBC compared to conventional cytology, and on the relative total costs of the different LBC technologies considered.

In table 4.13 a worst-case scenario is presented. In this case smear taking times are only one minute faster and the worst case values for preparation and laboratory variables are used. All LBC consumable costs are 50% higher and all LBC equipment costs are 20% higher, and it is assumed that preparation equipment is used in laboratories processing 30,000 slides a year. Preparation staff costs have been increased by 5% and smear reader costs have been assumed to be the same for conventional and LBC.

In the worst-case, LBC costs between £2.83 and £6.50 more per smear than conventional cytology, with variation in the size of the difference depending on which equipment is used. In this scenario, cost per smear is higher for the T3000™ compared to the T2000™ because it is assumed that the preparation centres are only processing 30,000 slides a year. Variations in equipment and consumable costs outweigh any differences in laboratory staff costs.

In table 4.14, a best-case scenario is presented where reduction in smear taking time is 5 minutes and also the most favourable estimates for preparation and laboratory costs are presented. The equipment and consumables are reduced by up to 20% and 50% respectively. The smear reader times are based on data from the Scottish pilots where screeners were reading 11 slides an hour and a 20% decrease in the proportion of slides checked has been assumed. Preparation staff costs are 5% lower in this scenario. In the best-case scenario the LBC technologies are between £0.97 and £2.29 less per slide than conventional cytology.

**Table 4.11: Sensitivity analysis of baseline results with respect to smear taker time**

Assuming smear taker consultation time only 1 minute quicker for LBC

Item	Technology			
	Conventional	LBC		
		T3000 <sup>Ô</sup>	T2000 <sup>Ô</sup>	PrepStain <sup>™</sup>
<i>Baseline</i>				
Smear taker staff costs	£7.66	£4.93	£4.93	£4.93
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£22.99</b>	<b>£23.15</b>	<b>£20.76</b>
<b>Difference to conventional</b>		<b>£1.31</b>	<b>£1.47</b>	<b>-£0.92</b>
<i>Smear taker time only one minute quicker with LBC compared to conventional</i>				
Smear taker staff cost	£7.66	£7.08	£7.08	£7.08
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£25.14</b>	<b>£25.30</b>	<b>£22.91</b>
<b>Difference to conventional</b>		<b>£3.46</b>	<b>£3.62</b>	<b>£1.23</b>

Note: Assumes equipment used at 60,000 slide capacity

**Table 4.12: Sensitivity analysis of baseline results with respect to consumable costs**

Item	Technology			
	Conventional	LBC		
		T3000 <sup>Ô</sup>	T2000 <sup>Ô</sup>	PrepStain <sup>™</sup>
<i>Baseline</i>				
Consumable costs	£0.27	£4.07	£4.07	£2.00
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£22.99</b>	<b>£23.15</b>	<b>£20.76</b>
<b>Difference to conventional</b>		<b>£1.31</b>	<b>£1.47</b>	<b>-£0.92</b>
<i>Cytoc consumable costs reduced by 50% and SurePath<sup>™</sup> baseline consumable costs</i>				
Consumable costs	£0.27	£2.04	£2.04	£2.00
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£20.95</b>	<b>£21.11</b>	<b>£20.76</b>
<b>Difference to conventional</b>		<b>-£0.72</b>	<b>£0.16</b>	<b>-£0.92</b>
<i>Cytoc consumable costs increased by 50% and SurePath<sup>™</sup> baseline consumable costs</i>				
Consumables costs	£0.27	£6.11	£6.11	£2.00
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£25.02</b>	<b>£25.18</b>	<b>£20.76</b>
<b>Difference to conventional</b>		<b>£3.35</b>	<b>£3.51</b>	<b>-£0.92</b>
<i>SurePath<sup>™</sup> consumable costs reduced by 50% and Cytoc baseline consumable costs</i>				
Consumables costs	£0.27	£4.07	£4.07	£1.00
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£22.99</b>	<b>£23.15</b>	<b>£19.76</b>
<b>Difference to conventional</b>		<b>£1.31</b>	<b>£1.47</b>	<b>-£1.92</b>
<i>SurePath<sup>™</sup> consumable costs increased by 50% and Cytoc baseline consumable costs</i>				
Consumables costs	£0.27	£4.07	£4.07	£3.00
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£22.99</b>	<b>£23.15</b>	<b>£21.76</b>
<b>Difference to conventional</b>		<b>£1.31</b>	<b>£1.47</b>	<b>£0.08</b>

Note: Assumes equipment used at 60,000 slide capacity

\*Since writing this report we have been informed this will possibly increase to £2.50; this level of increase is included in the sensitivity analysis below.

**Table 4.13: Sensitivity analysis worst-case scenario**

Item	Technology			
	Conventional	LBC		
		T3000 <sup>Ô</sup>	T2000 <sup>Ô</sup>	PrepStain <sup>TM</sup>
Smear taker staff cost	£7.66	£7.08	£7.08	£7.08
Administration cost	£3.00	£3.00	£3.00	£3.00
Preparation equipment cost	£0.04	£1.24	£0.44	£0.53
Preparation staff cost	£0.02	£0.06	£0.44	£0.21
Consumable cost	£0.27	£6.11	£6.11	£3.00
Smear reading cost	£2.26	£2.26	£2.26	£2.26
Other laboratory costs	£8.42	£8.42	£8.42	£8.42
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£28.17</b>	<b>£27.74</b>	<b>£24.50</b>
<b>Difference to conventional</b>		<b>£6.50</b>	<b>£6.07</b>	<b>£2.83</b>

Note: Assumes equipment used at 30,000 slide capacity

**Table 4.14: Sensitivity analysis best-case scenario**

Item	Technology			
	Conventional	LBC		
		T3000 <sup>Ô</sup>	T2000 <sup>Ô</sup>	PrepStain <sup>TM</sup>
Smear taker staff cost	£7.66	£4.93	£4.93	£4.93
Administration cost	£3.00	£3.00	£3.00	£3.00
Preparation equipment cost	£0.04	£0.41	£0.26	£0.18
Preparation staff cost	£0.02	£0.06	£0.39	£0.19
Consumable cost	£0.27	£2.04	£2.04	£1.00
Smear reading cost	£2.26	£1.66	£1.66	£1.66
Other laboratory costs	£8.42	£8.42	£8.42	£8.42
<b>Total cost per smear</b>	<b>£21.68</b>	<b>£20.52</b>	<b>£20.71</b>	<b>£19.38</b>
<b>Difference to conventional</b>		<b>-£1.15</b>	<b>-£0.97</b>	<b>-£2.29</b>

Note: Assumes equipment used at 60,000 slide capacity

## **5. TOTAL COSTS AND COST EFFECTIVENESS**

In section 5.1 the overall running costs of LBC compared to conventional cytology are assessed taking into account the costs savings due to the reduction in the inadequate rate. In section 5.2 the cost effectiveness of LBC is considered by re-estimating the cost effectiveness results from a previous model using the additional information on inadequate rates and the costs of screening obtained from the pilot sites.

### **5.1 Total running costs for a local service and nationally**

The total running cost of LBC compared to conventional cytology is influenced by the unit cost per smear, but also by the number of smears that need to be processed. In section 4, the unit costs of LBC and conventional cytology were estimated. In section 3, a reduction in the inadequate rate with LBC was reported. This will reduce the overall costs of screening as fewer smears have to be taken, prepared and read. For example, with a reduction in the inadequate rate from 9% to 1.6%, a laboratory processing 30,000 slides a year with conventional cytology would have a reduction in workload of 2,220 slides per annum. Nationally, the workload would be reduced from 4.2 million slides per annum to 3.9 million slides per annum.

In table 5.1, the total running costs for a local service are presented for a laboratory that processed 30,000 slides per year and the associated primary care costs. Overall LBC is cost saving across both technologies. However these costs include primary care costs of smear taking and administration and in reality the savings accruing in primary care may not be transferred to the laboratory.

In table 5.2 the total running costs nationally are presented. This analysis is based on preparation equipment being used at 60,000 slides per year. In the baseline scenario LBC is between £1 million and £10 million cheaper than the estimated annual cost of £91 million for conventional cytology, the size of the reduction depending on the LBC technology. (Our estimate of the national cost of conventional screening is lower than the estimate of £141m given by the National Audit Office<sup>12</sup> in a 1998 report; however, our estimate does not include the costs of items such as colposcopy and histology costs, which are included in the NAO report, and once these differences are accounted for our estimated national running costs of the conventional cytology programme are very similar to the NAO estimate.)

In section 4, the uncertainty surrounding the estimates of unit costs were identified and presented in a sensitivity analysis. In particular, uncertainty remains about the extent of time-savings in the primary care consultation time due to the methods of data collection (see section 4.1). In tables 5.3 and 5.4, the baseline scenario is repeated except for the primary care time-savings, which are reduced to one minute. In this scenario, the increased running costs nationally range from a saving £1.9 million to an increased cost of £7.3 million depending on the technology.

There is also considerable uncertainty about the likely cost of LBC consumables in the marketplace following the completion of the pilot site evaluations. In table 4.12 in the previous section we presented the cost per smear when the consumable costs of each supplier was varied independently. In table 5.5 and 5.6 we present overall costs for a local service and nationally at these varying consumable costs.

In tables, 5.7-5.10 the total running costs for a local service and nationally are presented for the worst case and best case scenarios. The same assumptions have been used for these scenarios as in section 4.8. In the worst case adoption of LBC would result in a national cost increase in the screening programme's annual costs of between £4.3 million and £18.5 million depending on the technology; in

the best case the screening programme's annual costs would fall by between £10.5 million and £15.6 million.

**Table 5.1 Total running costs for a local service**

Item	Technology cost			
	Conventional	LBC		
		T30000 <sup>0</sup>	T20000 <sup>0</sup>	PrepStain <sup>0</sup>
Smear taker staff cost	£229,700	£137,000	£137,000	£137,000
Administration cost	£90,000	£83,300	£83,300	£83,300
Preparation equipment cost	£1,200	£14,300	£9,000	£6,100
Preparation staff cost	£700	£1,700	£11,500	£5,500
Consumable cost	£8,100	£113,100	£113,100	£55,600
Smear reading cost	£67,900	£55,200	£55,200	£55,200
Other laboratory costs	£252,700	£234,000	£234,000	£234,000
<b>Total</b>	<b>£650,300</b>	<b>£638,600</b>	<b>£643,100</b>	<b>£576,700</b>
<b>Difference to conventional</b>		<b>-£11,700</b>	<b>-£7,200</b>	<b>-£73,600</b>

Note: Assumes equipment used at 60,000 slide capacity and assumes the workload for a laboratory processing 30,000 conventional slides per annum is reduced to 27,780 slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.2 Total running costs nationally**

Item	Technology cost (1000's)			
	Conventional	LBC		
		T30000 <sup>0</sup>	T20000 <sup>0</sup>	PrepStain <sup>0</sup>
Smear taker staff cost	£32,200	£19,200	£19,200	£19,200
Administration cost	£12,600	£11,700	£11,700	£11,700
Preparation equipment cost	£200	£2,000	£1,300	£900
Preparation staff cost	£100	£200	£1,600	£800
Consumable cost	£1,100	£15,800	£15,800	£7,800
Smear reading cost	£9,500	£7,700	£7,700	£7,700
Other laboratory costs	£35,400	£32,800	£32,800	£32,800
<b>Total</b>	<b>£91,100</b>	<b>£89,400</b>	<b>£90,100</b>	<b>£80,900</b>
<b>Difference to conventional</b>		<b>-£1,700</b>	<b>-£1,000</b>	<b>-£10,200</b>

Note: Assumes equipment used at 60,000 slide capacity and assumes the annual national workload of 4.2 million conventional slides is reduced to 3.9 million slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.3: Total running costs for a local service: sensitivity analysis of main results with respect to smear taker time**

Item	Technology cost			
	Conventional	LBC		
		T30000 <sup>Ô</sup>	T20000 <sup>Ô</sup>	PrepStain <sup>Ô</sup>
<i>Baseline</i>				
Smear taker staff cost	£229,700	£137,000	£137,000	£137,000
<b>Total</b>	<b>£650,300</b>	<b>£638,600</b>	<b>£643,100</b>	<b>£576,700</b>
<b>Difference to conventional</b>		<b>-£11,700</b>	<b>-£7,200</b>	<b>-£73,600</b>
<i>Smear taker time only 1 minute quicker for LBC compared to conventional</i>				
Smear taker staff cost	£229,700	£196,700	£196,700	£196,700
<b>Total</b>	<b>£651,000</b>	<b>£698,700</b>	<b>£703,100</b>	<b>£636,400</b>
<b>Difference to conventional</b>		<b>£47,700</b>	<b>£52,100</b>	<b>-£13,600</b>

Note: Assumes equipment used at 60,000 slide capacity and assumes the workload for a laboratory processing 30,000 conventional slides per annum is reduced to 27,780 slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.4: Total running costs nationally: sensitivity analysis of main results with respect to smear taker time**

Item	Technology cost (£1000's)			
	Conventional	LBC		
		T30000 <sup>Ô</sup>	T20000 <sup>Ô</sup>	PrepStain <sup>Ô</sup>
<i>Baseline</i>				
Smear taker staff cost	£32,200	£19,200	£19,200	£19,200
<b>Total</b>	<b>£91,100</b>	<b>£89,400</b>	<b>£90,100</b>	<b>£80,900</b>
<b>Difference to conventional</b>		<b>-£1,700</b>	<b>-£1,000</b>	<b>-£10,200</b>
<i>Smear taker time only 1 minute quicker for LBC compared to conventional</i>				
Smear taker staff cost	£32,200	£27,500	£27,500	£27,500
<b>Total</b>	<b>£91,100</b>	<b>£97,700</b>	<b>£98,400</b>	<b>£89,200</b>
<b>Difference to conventional</b>		<b>£6,600</b>	<b>£7,300</b>	<b>-£1,900</b>

Note: Assumes equipment used at 60,000 slide capacity and assumes the annual national workload of 4.2 million conventional slides is reduced to 3.9 million slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.5: Total running costs for a local service: sensitivity analysis of baseline results with respect to consumable costs**

Item	Technology cost			
	Conventional	LBC		
		T30000	T20000	PrepStain
<i>Baseline</i>				
Consumable costs	£8,100	£113,100	£113,100	£55,600
<b>Total</b>	<b>£650,300</b>	<b>£638,600</b>	<b>£643,100</b>	<b>£576,700</b>
<b>Difference to conventional</b>		<b>-£11,700</b>	<b>-£7,200</b>	<b>-£73,600</b>
<i>Cytec consumable costs reduced by 50% and SurePath™ baseline consumable costs</i>				
Consumable costs	£8,100	£56,500	£56,500	£55,600
<b>Total</b>	<b>£650,300</b>	<b>£582,000</b>	<b>£586,500</b>	<b>£576,700</b>
<b>Difference to conventional</b>		<b>-£68,300</b>	<b>-£63,800</b>	<b>-£73,600</b>
<i>Cytec consumable costs increased by 50% and SurePath™ baseline consumable costs</i>				
Consumables costs	£8,100	£169,600	£169,600	£55,600
<b>Total</b>	<b>£650,300</b>	<b>£695,100</b>	<b>£699,600</b>	<b>£576,700</b>
<b>Difference to conventional</b>		<b>£44,800</b>	<b>£49,300</b>	<b>-£73,600</b>
<i>SurePath™ consumable costs reduced by 50% and Cytec baseline consumable costs</i>				
Consumables costs	£8,100	£113,100	£113,100	£27,800
<b>Total</b>	<b>£650,300</b>	<b>£638,600</b>	<b>£643,100</b>	<b>£549,000</b>
<b>Difference to conventional</b>		<b>-£11,700</b>	<b>-£7,200</b>	<b>-£101,300</b>
<i>SurePath™ consumable costs increased by 50% and Cytec baseline consumable costs</i>				
Consumables costs	£8,100	£113,100	£113,100	£83,300
<b>Total</b>	<b>£650,300</b>	<b>£638,600</b>	<b>£643,100</b>	<b>£604,500</b>
<b>Difference to conventional</b>		<b>-£11,700</b>	<b>-£7,200</b>	<b>-£45,800</b>

Note: Assumes equipment used at 60,000 slide capacity and assumes the annual national workload of 4.2 million conventional slides is reduced to 3.9 million slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.6: Total running costs Nationally: sensitivity analysis of baseline results with respect to consumable costs**

Item	Technology cost			
	Conventional	LBC		
		T3000 $\hat{O}$	T2000 $\hat{O}$	PrepStain $\hat{O}$
<i>Baseline</i>				
Consumable costs	£1,100	£15,800	£15,800	£7,800
<b>Total</b>	<b>£91,100</b>	<b>£89,400</b>	<b>£90,100</b>	<b>£80,900</b>
<b>Difference to conventional</b>		<b>-£1,700</b>	<b>-£1,000</b>	<b>-£10,200</b>
<i>Cytc consumable costs reduced by 50% and SurePath™ baseline consumable costs</i>				
Consumable costs	£1,100	£7,900	£7,900	£7,800
<b>Total cost</b>	<b>£91,100</b>	<b>£81,500</b>	<b>£82,200</b>	<b>£80,900</b>
<b>Difference to conventional</b>		<b>-£9,600</b>	<b>-£8,900</b>	<b>-£10,200</b>
<i>Cytc consumable costs increased by 50% and SurePath™ baseline consumable costs</i>				
Consumables costs	£1,100	£23,700	£23,700	£7,800
<b>Total cost</b>	<b>£91,100</b>	<b>£97,300</b>	<b>£98,000</b>	<b>£80,900</b>
<b>Difference to conventional</b>		<b>£6,200</b>	<b>£6,900</b>	<b>-£10,200</b>
<i>SurePath™ consumable costs reduced by 50% and Cytc baseline consumable costs</i>				
Consumables costs	£1,100	£15,800	£15,800	£3,900
<b>Total cost</b>	<b>£91,100</b>	<b>£89,400</b>	<b>£90,100</b>	<b>£77,000</b>
<b>Difference to conventional</b>		<b>-£1,700</b>	<b>-£1,000</b>	<b>-£14,100</b>
<i>SurePath™ consumable costs increased by 50% and Cytc baseline consumable costs</i>				
Consumables costs	£1,100	£15,800	£15,800	£11,700
<b>Total cost</b>	<b>£91,100</b>	<b>£89,400</b>	<b>£90,100</b>	<b>£84,800</b>
<b>Difference to conventional</b>		<b>-£1,700</b>	<b>-£1,000</b>	<b>-£6,300</b>

Note: Assumes equipment used at 60,000 slide capacity and assumes the annual national workload of 4.2 million conventional slides is reduced to 3.9 million slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.7: Total running costs for a local service: sensitivity analysis worst-case scenario**

Item	Technology cost			
	Conventional	LBC		
		T3000 $\hat{O}$	T2000 $\hat{O}$	PrepStain $\hat{O}$
Smear taker staff cost	£229,700	£196,700	£196,700	£196,700
Administration cost	£90,000	£83,300	£83,300	£83,300
Preparation equipment cost	£1,200	£34,300	£12,100	£14,700
Preparation staff cost	£700	£1,800	£12,100	£5,800
Consumable cost	£8,100	£169,600	£169,600	£83,300
Smear reading cost	£67,900	£62,900	£62,900	£62,900
Other laboratory costs	£252,700	£234,000	£234,000	£234,000
<b>Total</b>	<b>£650,300</b>	<b>£782,600</b>	<b>£770,700</b>	<b>£680,700</b>
<b>Difference to conventional</b>		<b>£132,300</b>	<b>£120,400</b>	<b>£30,400</b>

Note: Assumes equipment used at 30,000 slide capacity and assumes the workload for a laboratory processing 30,000 conventional slides per annum is reduced to 27,780 slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.8: Total running costs nationally: sensitivity analysis worst-case scenario**

Item	Technology cost (£1000's)			
	Conventional	LBC		
		T3000 $\hat{O}$	T2000 $\hat{O}$	PrepStain $\hat{O}$
Smear taker staff cost	£32,200	£27,500	£27,500	£27,500
Administration cost	£12,600	£11,700	£11,700	£11,700
Preparation equipment cost	£200	£4,800	£1,700	£2,100
Preparation staff cost	£100	£300	£1,700	£800
Consumable cost	£1,100	£23,700	£23,700	£11,700
Smear reading cost	£9,500	£8,800	£8,800	£8,800
Other laboratory costs	£35,400	£32,800	£32,800	£32,800
<b>Total</b>	<b>£91,100</b>	<b>£109,600</b>	<b>£107,900</b>	<b>£95,400</b>
<b>Difference to conventional</b>		<b>£18,500</b>	<b>£16,800</b>	<b>£4,300</b>

Note: Assumes equipment used at 30,000 slide capacity & that annual workload of 4.2 million conventional slides is reduced to 3.9 million slides with LBC due to a reduction in inadequate rate from 9 to 1.6%

**Table 5.9: Total running costs for a local service: sensitivity analysis best-case scenario**

Item	Technology cost			
	Conventional	LBC		
		T3000 $\hat{O}$	T2000 $\hat{O}$	PrepStain $\hat{O}$
Smear taker staff cost	£229,700	£148,000	£148,000	£148,000
Administration cost	£90,000	£90,000	£90,000	£90,000
Preparation equipment cost	£1,200	£12,400	£7,800	£5,300
Preparation staff cost	£700	£1,800	£11,800	£5,700
Consumable cost	£8,100	£61,100	£61,100	£30,000
Smear reading cost	£67,900	£49,900	£49,900	£49,900
Other laboratory costs	£252,700	£252,700	£252,700	£252,700
<b>Total</b>	<b>£650,300</b>	<b>£615,900</b>	<b>£621,300</b>	<b>£581,600</b>
<b>Difference to conventional</b>		<b>-£34,400</b>	<b>-£29,000</b>	<b>-£68,700</b>

Note: Assumes equipment used at 30,000 slide capacity and assumes the workload for a laboratory processing 30,000 conventional slides per annum is reduced to 27,780 slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

**Table 5.10: Total costs nationally: sensitivity analysis best-case scenario**

Item	Technology cost £1000's			
	Conventional	LBC		
		T3000 <sup>0</sup>	T2000 <sup>0</sup>	PrepStain <sup>0</sup>
Smear taker staff cost	£32,200	£19,200	£19,200	£19,200
Administration cost	£12,600	£11,700	£11,700	£11,700
Preparation equipment cost	£200	£1,600	£1,000	£700
Preparation staff cost	£100	£200	£1,500	£600
Consumable cost	£1,100	£7,900	£7,900	£3,900
Smear reading cost	£9,500	£6,500	£6,500	£6,500
Other laboratory costs	£35,400	£32,800	£32,800	£32,800
<b>Total</b>	<b>£91,100</b>	<b>£79,900</b>	<b>£80,600</b>	<b>£75,500</b>
<b>Difference to conventional</b>		<b>-£11,200</b>	<b>-£10,500</b>	<b>-£15,600</b>

Note: Assumes equipment used at 60,000 slide capacity and assumes the annual national workload of 4.2 million conventional slides is reduced to 3.9 million slides with LBC due to a reduction in the inadequate rate from 9 to 1.6%

## **5.2 Re-estimating cost effectiveness results using Payne model**

As part of the report in July 2003 we will assess the cost-effectiveness of using both LBC and HPV together. In this report we consider only LBC. To date, only Payne et al (2000)<sup>11</sup> have modelled the cost-effectiveness of LBC in the UK (based on the published work of Sherlaw-Johnson 1994<sup>12</sup>). In this section, we re-analyse their cost effectiveness results using their model but also incorporating the new evidence from the pilot sites, and consider the effect of the new evidence on the previous cost effectiveness estimates.

Payne et al (2000)<sup>11</sup> presented a state transition Markov model (based on the published work of Sherlaw-Johnson, (1994)<sup>12</sup> in order to compare the cost effectiveness of LBC with conventional smears. For a full description of the model please refer to Payne et al (2000)<sup>13</sup>; a brief summary is provided in Appendix 2. Payne et al. estimated a number of cost effectiveness results. They estimated that the incremental cost per life year gained at £1,198 for conventional cytology compared to no screening and £1,096 for LBC compared to conventional cytology, for a 5 year screening interval.

Data from the pilot provide little further information on many of the parameter estimates used in the model, and therefore we have used their baseline estimates for each parameter when re-analysing the cost-effectiveness results unless stated. However, we have adjusted the parameter estimates on the inadequate rates and costs in light of data from the pilot.

The evaluation team did not have any influence over the design of the pilots. It is important to stress that this was not a trial, and it is not possible to obtain sensitivity and specificity estimates. To estimate sensitivity and specificity it would be necessary to either collect both conventional and liquid based samples from the same woman in a cohort study or alternatively use a randomized control trial. Payne uses the following baseline estimates for changes in the sensitivity of LBC compared to conventional cytology; a 15% improvement in the detection of CIN1/CIN2 for LBC and a 2% sensitivity improvement in the detection of CIN3 and invasive cancer.

However, in section 3 of this report we compared the different rates of smear results in the pilot and pre-pilot year and positive predictive values at colposcopy for moderate and severe results. We concluded that the evidence from our data is compatible with the baseline changes in sensitivity.

The results of the pilot suggest that at least for moderate and severe results the specificity of LBC is comparable to that of conventional cytology. Therefore the baseline estimate used in Payne's model of a 0% change in specificity is not unreasonable.

The results from the pilot suggest that there is an 80% reduction in the inadequate results with both ThinPrep™ and SurePath™. This is equivalent to a reduction from 9% to 1.6% and is greater than the baseline estimates used in the Payne model. There is a slight difference between the two technologies with the inadequate rate 0.9% for SurePath™ and 2.0% for ThinPrep™.

The inadequate rate has a large influence on the overall costs of screening as it reduces the total number of smears that need to be taken, processed and interpreted. We use the pilot sites estimates of the inadequate rate when re-estimating the cost effectiveness results.

Payne's marginal costs are based on consumable and equipment costs alone. Our estimates of the marginal cost per smear of LBC from the pilot are presented in section 4.7 and range from -£0.92 to £1.47 at baseline depending on the technology used. In section 4.8 in the sensitivity analysis the uncertainty surrounding these marginal costs estimates are presented. In particular, the two key drivers in the marginal costs are the savings in primary care smear taking time and the cost of LBC consumables. Under a scenario where primary care consultation time is only one minute faster with LBC compared to conventional our estimated marginal cost per smear ranges from £1.23 to £3.62 across the technologies. In the worst-case scenario the marginal costs of LBC per smear range from £2.83 to £6.50 compared to conventional and in the best-case scenario from a marginal saving of between £0.97 and £2.29. It should be stressed that the best case and worse case scenarios include varying the consumable costs by 50%, reflecting the uncertainty regarding the consumable costs that are likely to prevail in the marketplace once the pilot site evaluation is completed.

Our baseline cost for conventional cytology - £21.68 per smear - is significantly less than the figure used by Payne et al. We have not included target payment to GPs which accounts for a substantial part of the Havelock costs used by Payne et al, as target payments are paid to GPs for achieving screening a certain percentage of coverage and there would be no difference between conventional and LBC smears. We have used an activity based costing method for identifying smear taker and laboratory costs and our estimates are comparable with other studies<sup>13</sup>.

From the pilot data we have established revised estimates for the inadequate rates and costs of both conventional and LBC technology. In table 5.11 we present our cost effectiveness results using these new estimates and Payne's baseline estimates for all other parameters in the model for a 5 year screening interval.

**Table 5.11 Re-estimated cost effectiveness results using baseline pilot data**

	Conventional	LBC:			
		T3000 <sup>TM</sup>	T2000 <sup>TM</sup>	PrepStain <sup>T</sup> <sub>M</sub>	Average
<b>Total cost per person:</b>	£69.78	£69.62	£70.05	£62.91	£67.52
<b>Incremental cost per person (compared to conventional)</b>	-	-£0.16	£0.27	-£6.87	-£2.26
<b>Total life years per person:</b>	39.607	39.609	39.609	39.609	39.609
<b>Incremental life years gained(compared to conventional)</b>	-	0.001	0.001	0.001	0.001
<b>Incremental cost per life year gained (compared to conventional)</b>		Dominates*	£270	Dominates*	Dominates*

Assumes machines used at 60,000 capacity

\*Dominates = lower cost and higher effectiveness. In this circumstance it is inappropriate to calculate an incremental cost effectiveness ratio.

The total lifetime discounted cost per person of screening using conventional technology is £69.78, including all screening and treatment costs. The equivalent cost using LBC technology is slightly higher with the T2000<sup>TM</sup> at £70.05 (note the baseline assumes machines are used at 60,000 capacity), and slightly lower with the PrepStain<sup>TM</sup> system and T3000<sup>TM</sup> at £62.91 and £69.62 respectively. The T2000<sup>TM</sup> appears more expensive in this scenario as it is assumed machines are used at 60,000 capacity. The incremental total lifetime cost per person of LBC compared to conventional screening ranges from £0.27 to -£6.87.

Using Payne's assumed estimates of the improvement in sensitivity and specificity from switching from conventional cytology to LBC, the incremental life years gained through using LBC compared with using conventional cytology is: 0.001 life years (less than one day). (The total life years gained per person screened using conventional cytology compared with no screening programme are 0.135 life years, and using LBC are 0.136 life years.)

Our results indicate that both the T3000<sup>TM</sup> and the PrepStain<sup>TM</sup> system are cost dominant at baseline, that is, they are both more effective and cost less per person than conventional cytology. The incremental cost per life year gained of the T2000<sup>TM</sup> compared to conventional cytology is £270. In comparison to no screening the incremental cost per life year gained is £497 for conventional cytology. Payne et al estimated that the incremental cost per life year gained at £1,198 for conventional cytology compared to no screening and £1,096 for LBC compared to conventional cytology, for a 5 year screening interval. Our results differ from Payne et al because we have used lower estimates of total cost per smear for conventional cytology and lower estimates for the difference in cost of LBC and a greater reduction in the inadequate rate (see discussion above).

In section 4.8 we identified a number of different scenarios in which the marginal costs of LBC technologies would vary. In particular we examined the effect of smear taker time varying and consumables prices as these are key areas of uncertainty. In table 5.12 we present estimates of the cost effectiveness under worst-case and best-case scenario as defined in section 4.8.

**Table 5.12 Re-estimated cost effectiveness results using pilot data under different cost scenarios**

	Conventional	T3000™	T2000™	PrepStain™ M
<b>Total Cost per person (baseline):</b>	£69.78	£69.62	£70.05	£62.91
Worst case scenario (Table 4.13)	-	£83.80	£82.62	£73.05
Best case scenario (Table 4.14)	-	£62.89	£63.39	£59.21
<b>Incremental cost per person compared to conventional</b>				
Worst case scenario (Table 4.13)	-	£14.02	£12.84	£3.27
Best case scenario (Table 4.14)	-	-£6.89	-£6.39	-£10.57
<b>Incremental life years gained compared to conventional</b>				
Table 4.12		0.001	0.001	0.001
<b>Incremental cost per life year gained</b>				
Worst case scenario (Table 4.13)	-	£14,020	£12,840	£3,450
Best case scenario (Table 4.14)	-	Dominates*	Dominates*	Dominates*

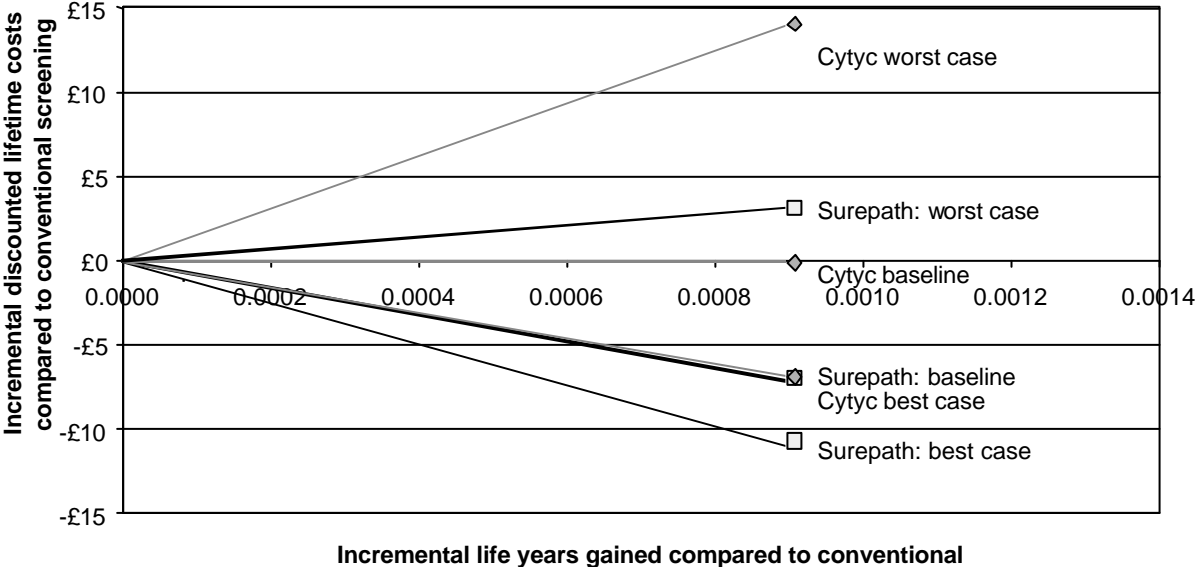
\* Dominates = lower cost and higher effectiveness. In this circumstance it is inappropriate to calculate an incremental cost-effectiveness ratio.

In the best case and at baseline all technologies dominate conventional screening, as they both cost less and are more effective.

In the worst case scenario the incremental cost-effectiveness of LBC compared to conventional varies between £3,450 and £14,020 per life year gained. It is stressed that the worst-case scenario includes increasing consumable costs by 50% above the baseline estimates, reflecting uncertainty about market prices. Due to the small differences in incremental life years gained, the incremental cost effectiveness ratios are sensitive to changes in the marginal costs between the technologies.

In figure 5.1 these results are presented graphically on a cost effectiveness plane.

**Figure 5.1: Incremental discounted lifetime costs and life years compared to conventional**



In conclusion, re-estimating Payne's<sup>13</sup> cost effectiveness results using data from the pilot sites indicates that both the T3000™ and the PrepStain™ system dominate conventional cytology at baseline: that is, they are both more effective and cost less per person than conventional cytology. At baseline the incremental cost per life year gained of the T2000™ compared to conventional cytology is £270.

In the best-case scenario all three technologies are more effective and cost less than conventional cytology. In the worst-case scenarios the incremental cost per life year gained compared to conventional varies between £3,450 and £14,020. The worst-case scenario includes increasing consumable cost by 50% above our baseline estimate.

## **6. CONVERSION AND IMPLEMENTATION COSTS**

The implementation of LBC would require a number of transitional costs concerning training of smear takers, smear readers and other laboratory staff, and re-organisation and re-equipment of laboratories.

We consider these as one-off or transition costs of changing from conventional cytology to LBC, as the longer-term training requirements for LBC would be similar to conventional cytology, and the longer-term equipment costs have already been estimated in section 4.

The time to convert a laboratory to reading only LBC slides varied between 3-9 months. The main factors affecting the overall set up time were:

- The time to train all the smear takers in the laboratory catchment area.
- Having sufficient laboratory staff to cover the backlog as others attended the training programme and the time smear readers took to be certified in LBC.

In the following section, the resource and cost implications of converting both smear takers and cytology laboratories to LBC are discussed.

### **6.1 Converting Smear takers**

The main logistical implication of converting smear takers to LBC technology is the need to provide them with training and information on how to take a LBC sample. In the pilot sites a qualified nurse, either from the health authority or a Primary Care Trust, co-ordinated the training and information at each laboratory with the support of Marie Curie Cancer.

The strategy towards training varied slightly between the pilot sites. At two of the pilot sites training was mainly provided via an external course, where at least one smear taker from each practice was invited to attend and information was then cascaded to colleagues at the practice. The other pilot site initially trained a small group of practice nurses, who then visited individual practice training staff. Information packs were distributed by the primary care co-ordinators. The suppliers of LBC also provided training materials for inclusion in the information packs. In this report we only consider the training given in primary care as they take the majority of smears.

As part of the smear taker questionnaire to a random sample of GP practices at pilot sites, questions were asked about the location and duration of training sessions in LBC. Training was provided for HPV testing and LBC in the same session. In the smear taker questionnaire respondents were asked about the length of the LBC training separately. These data are presented in table 6.1.

**Table 6.1: Type of training session attended and length of training in LBC.**

Training time	Type of training session			Total
	External training session	Trainer at practice	Colleague at practice	
Less than 30 mins	6	10	11	27
30 mins-1 hour	15	10	4	29
1-2 hours	14	3	0	17
More than 2 hours	10	0	0	10
<b>Total</b>	<b>45</b>	<b>23</b>	<b>15</b>	<b>83</b>

On average training time for LBC only was about an hour. Training times varied between the different training session locations, and were longest for external training and shortest for training

delivered by a colleague at the practice. There is an added opportunity cost of travel time to attend the external training session, but practice based training incurs additional travel time for a trainer to attend each practice.

### Cost of smear taker time

In table 6.2, a total cost of smear taker time has been estimated based on an average training session time of 1 hour (based on the data from table 6.1) multiplied by the staff unit costs. The staff unit costs for General Practitioners and practice nurses are based on national unit cost estimates as presented previously in table 4.1. The resulting cost is £22 for the time of practice nurses undergoing training and £84 for general practitioners undergoing training.

**Table 6.2 Costs of staff time while undertaking LBC training, per smear taker**

Staff	Cost of staff time training in LBC
Practice nurses	£22
General practitioners	£84

In table 6.3, the total staff time costs of training all General Practitioners and practice nurses in England has been estimated by multiplying the costs in table 6.2 by the total number of staff in England<sup>14</sup>. An underlying assumption is that all General Practitioners and practice nurses would be trained. This may be an over-estimate as in some practices not all staff may take smears. However, this may be offset in part by the cost of training other smear takers not in general practice. These figures have been standardised for a local service serving a laboratory currently processing 30,000 slides per year by dividing the national figures by the total number of smears processed.

**Table 6.3 Staff costs of providing smear takers with LBC training, for a local service and national total.**

Staff	Per 30,000 laboratory		Nationally	
	Number	Cost (£1,000s)	Number	Cost (£1,000's)
GP	210	17.6	29,389	2,468
Practice nurses	139	3.0	19,455	419
<b>Total</b>	<b>349</b>	<b>20.6</b>	<b>48,844</b>	<b>2,887</b>

Table 6.3 shows that, for an average laboratory processing 30,000 smears per year, 139 practice nurses and 210 General Practitioners would need to be trained at a cost of about £21,000 in staff time. Nationally this translates to nearly 50,000 staff and £2.9 million of staff time.

### Other costs of converting smear takers

As well as the cost of staff time for smear takers themselves there are costs in providing the training itself. At the pilot sites the training co-ordinators provided training in both HPV and LBC, with a considerable administrative workload on the co-ordinators or their assistants in sending out the information packs including information on HPV and the different referral routes. In total this was estimated at about 4-6 months of a wte time, but when considering LBC alone this workload is likely to be reduced.

The workload on the training co-ordinator is also influenced by whether they visit each smear taking centre or hold external training sessions. In addition, other staff may be involved in helping with the training, including trained cytology nurse advisors (only some Primary Care Trusts have these), Marie

Curie Cancer nurses, who provided training at some centres and suppliers, who may provide training as part of an overall package.

In table 6.4, a cost of smear taker training has been estimated. This is based on the budget given to Marie Curie Cancer for the pilots and costs of trainers from the health authority at each pilot site. These costs have then been averaged and an estimate for a laboratory processing 30,000 slides a year calculated. These costs include training in HPV testing and may be reduced if training is given in LBC only.

The cost of information packs also depends on whether these are provided by the suppliers, centrally by the National Cervical Screening Programme or locally. In table 6.4 an assumption of training material at £2 per smear taker has been used as a baseline estimate. To calculate the cost per laboratory or nationally the training pack cost has been multiplied by the number of smear takers estimated in table 6.3.

**Table 6.4: Training co-ordinator costs and training material costs**

Item	Total costs	
	Per 30,000 Laboratory (£1,000's)	Nationally (£1,000's)
Training material for primary care	0.7	98
Training co-ordinator primary care	10.4	1,454
<b>Total</b>	<b>11.1</b>	<b>1,552</b>

In summary, it is likely that training material and training co-ordinator costs will be approximately £11,100 per laboratory or £1.5million for England as a whole. However, this estimate may be quite high as it also includes cost of training smear takers in providing information about HPV testing.

**6.2 Logistical and organisational implications for laboratories**

A number of logistical and organisational changes in converting from conventional cytology to LBC were identified:

- Travel expenses and accommodation for training schools
- Dealing with the backlog of conventional smears
- Structural changes for installation of preparation equipment
- Changes to bar-coding system

Finance managers at each site provided costing information for each item. To compare between the pilot sites the costs have been standardised for a laboratory that processes 30,000 smears per year. Minimum, maximum and average cost estimates are presented in table 6.5.

**Table 6.5: Laboratory conversion costs for standardised laboratory processing 30,000 slides per year**

Item	Costs (£1000's)		
	Minimum	Maximum	Average
Travel expenses and accommodation for training school	1.0	5.0	2.6
Sending off backlog	4.6	24.5	14.2
Structural changes to fit the preparation equipment	1.5	6.0	3.3
Changes to the bar-coding system	0.0	5.1	2.0
<b>Total</b>	<b>7.1</b>	<b>40.6</b>	<b>22.2</b>

*Travel to and accommodation for training school:* Each laboratory paid for the cost of sending smear readers to the training school and their accommodation. However, they did not contribute towards the cost of the training school itself. The costs varied primarily due to distance from the training school. Smear reader training is discussed in more detail in section 6.3.

*Sending off the backlog of conventional slides to other laboratories or paying staff overtime:* Prior to starting LBC, all three pilot sites had a backlog of conventional slides to be read. This backlog also increased whilst the sites were converting to LBC and cytology staff were being trained. To deal with the backlog conventional slides were either sent off to other laboratories and/or staff did overtime. Pilot sites with a fuller staff complement were able to absorb the backlog more readily and hence the cost is lower. However, although the total cost of sending smears away varied there was a similar cost per smear sent away of £5 per slide.

*Structural changes:* In order to fit the preparation equipment in the laboratory it was necessary to alter the laboratories. The cost of these alterations varied between the laboratories due to the space currently available.

*Bar coding:* Conventional cytology slides are currently usually labelled manually by the smear-taker. With LBC it is necessary to label the slides with a bar code for use in the preparation machines, and at all sites this necessitated changes to the existing system. In the pilot, one supplier provided bar-coding machines free of charge.

*Other organisational and logistical issues:*

We have not identified costs for the following items however, the following other issues were also raised at interview.

LBC samples can be stored in the laboratory at room temperature. At the pilot sites they were stored in the preparation or administration area on racks. However, it was suggested that it would be better to have a separate storage area due to health and safety issues regarding the flammability of the samples.

There was an additional constraint imposed in the pilots by the HPV testing, which should be done within three weeks of processing of the sample.

The disposal of the residual vials from the SurePath™ process was carried out via a route suitable for combined clinical and chemical waste. ThinPrep™ had a collection system for used vials.

At some laboratories there had been little prior recording of the smear taker kits that were sent out to General Practice. Due to the extra expense and the limited shelf life of LBC, more comprehensive stock monitoring was introduced at some of the pilot sites.

Organisational and logistical issues will be considered in more detail in the final report.

### **6.3 Cost of converting smear readers and preparation staff**

The appearance of LBC slides differs significantly from conventional slides. Therefore, it is necessary for all smear readers to be trained and tested in the new technique. The pre-requisites for the training were that staff should be fully trained in conventional smear microscopy and be qualified to sign out negative and inadequate smears.

This is a one off cost for the laboratories and national training schools. For qualification as a Cytoscreener there is a two-year training period, and for a BMS 5000 smears must be read. These training requirements are similar whether trainees are learning to read conventional or LBC slides.

The training to convert smear-readers trained in conventional cytology to LBC consisted of four stages:

- **Initial Induction Course:** held at the Liverpool and Edinburgh Cytology Training Schools, in which individuals looked at 6 test sets over a three day period.
- **Consolidation Course:** in which trainees were given 200 slides to review over a period of 1-4 weeks back at their own pilot sites.
- **Test Sets** – This consisted of 20 slides (5 marks given per slide) and individuals were required to obtain a score of 80% or above.
- **Performance Review**– This was the final stage of the training, in which individuals were given 200 further slides (this gives primary screener sensitivity). Pathologists had an abridged version.

Smear reader training times were collected from training log-books at each pilot site and are presented in table 6.6. On average, the training time for smear readers varied between 41 hours (pathologists have an abridged performance review) and 56 hours (cytoscreeners). In total, 55 smear readers were trained from the pilot sites 17 cytoscreeners, 25 BMSs and 13 pathologists.

**Table 6.6: Average smear reader training times at the pilot sites (in hours)**

Training stage	Average training time		
	Cytoscreeners	BMSs	Pathologists
Initial induction course	21.0	21.0	21.0
Consolidation slides	17.7	14.3	14.0
Test sets	2.0	2.0	2.0
Performance review	15.3	17.0	4.0*
<b>Total</b>	<b>56.1</b>	<b>54.3</b>	<b>41.0</b>

\*Pathologists had a different performance review package.

The introduction of LBC in the laboratory also requires training for staff that prepare slides for the smear readers to use (usually these are Medical Laboratory Assistants MLAs). With conventional cytology the slides just have to be stained on arrival at the laboratory. LBC requires the use of equipment to convert the liquid sample collected by the smear takers into a cytology slide.

The training period for preparation slides lasted approximately a day, at some of the sites this was followed up with some further short sessions for trouble shooting.

Table 6.7 reports the cost of staff time for per staff member for reading and preparing (MLAs only) LBC slides. Cost have been calculated by multiplying the average training times reported in table 6.6 by the staff unit costs. Staff unit costs for laboratory staff, have been estimated by using the mid-point on their pay-scale and assuming that a full time member of staff works 37.5 hours per week and 46 weeks per year. The Pathology costs are from national unit cost estimates (Netten et al 2001) <sup>10</sup> for a hospital consultant and include overheads.

**Table 6.7: Staff time training costs by grade of staff-per grade of staff**

Laboratory staff	Hours training	Cost per hour	Total cost
MLA	8	£5.86	£44
Cytoscreener	56	£8.17	£458
BMS1	54	£10.34	£562
BMS2	54	£13.34	£725
BMS3	54	£15.91	£865
BMS4	54	£18.64	£1,011
Pathologists	41	£64.00	£2,624

To estimate the total costs of staff training if LBC were to be rolled out nationally the total number of staff in England <sup>15</sup> were multiplied by the costs in table 6.7. Data were not available on the number of pathology staff nationally and are therefore based on number of pathologists trained in the pilot. These figures have also been presented for an average laboratory currently processing 30,000 per year. The total cost of staff time estimates averages at £9,500 per laboratory processing 30,000 slides a year, or £1.3 million as shown in table 6.8.

**Table 6.8: Staff time training costs-per laboratory and nationally**

Staff type	Per 30,000 laboratory		Nationally	
	Number	Cost (£1000's)	Number	Cost (£1000's)
MLA	1.4	0.06	199	9
Cytoscreener	3.7	1.7	514	235
BMS1	2.4	1.3	331	186
BMS2	1.9	1.4	271	196
BMS3	1.0	0.8	137	118
BMS4	0.3	0.3	39	39
Pathologists	2.8	7.3	392	1029
<b>Total</b>	<b>12.1</b>	<b>9.5</b>	<b>1701</b>	<b>1336</b>

We have not evaluated in detail the costs of cytology training schools. Training was provided by two training schools and they were given a budget of £30,000 to train 55 smear readers. This is equivalent to £545 per smear reader. Based on 11 smear readers per 30,000 laboratory from table 6.8 this is equivalent to £5,995 per laboratory. However, the cost of training a smear reader in a national roll out will be dependent on the number of training schools and programme of training. The cost of training preparation staff was included by both suppliers of equipment and came as part of the overall equipment cost package.

## 6.4 Summary conversion costs

Table 6.9 provides a summary of all costs identified above, for a single laboratory and for the country as a whole. The cost of conversion is £39,300 per laboratory including provision of training and structural and organisational changes. The cost of smear taker time training is considerable at £20,600 and smear reading about £12,900 per laboratory processing 30,000 slides. Translated nationally the overall cost of converting to LBC would be £10 million.

**Table 6.9: Conversion costs per laboratory and nationally**

Item	Conversion costs	
	Per 30,000 laboratory (£1000's)	Nationally (£1000's)
<b>Conversion costs</b>		
Training material for primary care	0.7	98
Training co-ordinator primary care	10.4	1,456
Smear reader training school & follow up	6.0	839
Travel & accommodation for training school	2.6	370
Sending off backlog	14.2	1,992
Structural changes for preparation equipment	3.3	467
Changes to bar-coding system	2.0	280
<b>Sub Total</b>	<b>39.3</b>	<b>5,500</b>
<u>Staff training time</u>		
Smear takers	20.6	2,887
MLA	0.06	9
Cytoscreener	1.7	235
BMSs	3.8	540
Pathologists	7.3	1,029
<b>Sub Total</b>	<b>33.5</b>	<b>4,771</b>
<b>Total</b>	<b>72,851</b>	<b>10,270</b>

However, these costs may well over estimate the true cost of converting to LBC. In table 6.10 a best-case scenario is presented. The cost of training co-ordinators may be reduced by up to 50% as training need only be provided in LBC and these costs include the costs of providing training in giving information about HPV and developing training materials that could be produced nationally. We do not know the true costs of providing smear reader training and have used the figures provided in the budget, but these costs also include the costs of developing smear reading training materials in the best case we have assumed smear reader training costs could be reduced by 20%.

There was also considerable variation across the pilots about the costs of converting the laboratory in this best case we use the minimum estimates for each item. There is also potential that staff time costs for training could be reduced. In particular if not all GPs are trained in smear taking and GPs receive internal training at the practice lasting 30 minutes rather than attending an external training course. Assuming only three quarters of GPs were trained in smear taking and the training time was 30 minutes the total cost of smear taker time would be reduced from over £20,000 to just under £10,000.

In summary, under a best-case scenario conversion costs to LBC could potentially be halved with the costs of structural and organisational changes to laboratories plus provision of training totalling £2.5 million and costs of staff time £3.1 million.

**Table 6.10: Conversion costs per laboratory and nationally best-case scenario.**

Item	Conversion costs	
	Per 30,000 laboratory (£1000's)	Nationally (£1000's)
<b>Conversions costs</b>		
Information material for primary care	0.7	98
Training co-ordinator primary care	5.2	728
Smear reader training school and follow up	4.8	<b>671</b>
Travel to & accommodation at training school	1.0	141
Sending off backlog	4.6	649
Structural changes for preparation equipment	1.5	209
Changes to bar-coding system	0	0
<b>Sub Total</b>	<b>17.8</b>	<b>2,496</b>
<b>Staff training time</b>		
Smear takers	9.6	1.3
MLA	0.06	9
Cytoscreener	1.7	235
BMSs	3.9	540
Pathologists	7.3	1039
<b>Sub Total</b>	<b>22.5</b>	<b>3,157</b>
<b>Total</b>	<b>40.3</b>	<b>5,652</b>

## **7. DISCUSSION**

Because of the limitations imposed by the nature and design of the pilot studies, some of the results of the evaluation must be interpreted with caution. In particular, it is not possible to study directly the effect of LBC technology on the sensitivity of screening or its effectiveness in preventing invasive cervical cancer, since no data are available on the follow-up of negative smears. The simultaneous introduction of HPV triaging for women with borderline or mildly dyskaryotic smears also confounds any analysis of the outcome in such women.

We have presented results from the three sites separately, and where possible compared the two different technologies used, but confounding by other differences between the sites cannot be excluded in any such comparison. These include different methods of training of smear takers and timing of changes to different reporting systems. One site also changed its recall policy to three years before the introduction of the pilot, although this should not have affected detection rates in the timescale of the pilot study.

The evaluation is a two year project, but a detailed report on the LBC aspects of the pilots has been specifically requested at this stage. However, it has not been possible in this timescale to include all aspects of LBC which have been studied, and any additional data will be presented in the final report in 2003. This will include analysis of population coverage (from KC53 returns), examination of failsafe workload, and the implications for quality assurance, as well as more detail on issues related to training and the logistics of implementation.

There is clear evidence of a large reduction in the rate of reporting of inadequate smears. The rate of reporting of such smears appears lower in the SurePath™ site than in those using ThinPrep™. However, the SurePath™ site has also implemented new reporting guidelines with the introduction of LBC, and has reported a high percentage of 'satisfactory' smears lacking evidence of transformation zone sampling. The pilot studies will not provide information on outcomes of women with negative smears which might otherwise have been called inadequate. However, the reduction in inadequates is of benefit both in terms of reduced laboratory (and smear taker) workload, and to women in reducing the distress and anxiety related to an inadequate result and need for a repeat smear.

The effect of LBC technology on other rates is less clear. Results from other studies have suggested improved sensitivity for CIN 3, and the Scottish pilots reported an improved detection of high grade lesions of between 3-9 per 1000 women tested.

The overall results from the present evaluation suggest any increase is likely to be at the lower end of this range. Although there is some evidence of a decrease in the detection of high grade lesions in the site using Surepath™ and of an increase in the sites using ThinPrep™, a detailed examination of possible implications of different technologies on detection rates and a review of all the available evidence on this is beyond the scope of this report. It is also not possible to allow for the influence of confounding factors such as the effect of training or use of different equipment, to that used in the pre-pilot period either as overall rates or comparisons between sites. However, there is also a suggestion of an improved positive predictive value with LBC, which could reflect either a true increase in the sensitivity of the test, or an improved discrimination of the reporting of moderate/severe dyskaryosis compared with borderline/mild in identifying CIN 2/3 compared with lesser abnormalities.

The reduction in the reported rate of glandular neoplasia requires further investigation of the cytological reasons, and to determine how slides previously reported in this way may now be classified. The reduction could reflect such lesions now being reported as squamous, or alternatively being undetected and reported as negative.

It should be noted that any changes in the terminology used for reporting of smears in the future, unrelated to LBC, will make it difficult to monitor the effect of any transition to LBC if both are implemented during a similar time period.

The effect of the introduction of LBC on costs is driven primarily by the reduced cost of smear taking in primary care, a difference in cost which was not considered in the HTA analysis. In our baseline estimates the cost per smear of ThinPrep™ is slightly higher than conventional (£1.31 higher with T3000™ and £1.47 higher with T2000™) and slightly lower than conventional with SurePath™ PrepStain system (-£0.92). These estimates were based on a difference in smear taking consultation time of 5 minutes for LBC compared to conventional. This was estimated from self-recorded timings by smear takers. However, when LBC smear takers were asked to state how much quicker they thought it typically took to take a smear with LBC, in general they reported the average of the responses indicated that LBC was only 1 minute quicker. Therefore we have also presented an alternative scenario, and in this case the costs per smear of all LBC technologies are slightly higher than conventional techniques (ranging from £1.23 to £3.62.)

The results are influenced by our estimates of the consumable costs of the LBC technology in the marketplace once the pilot study has been concluded, and these are inevitably uncertain. To reflect this uncertainty we have varied the cost of each supplier's consumables independently over a range from 50% more to 50% less of our baseline estimate. The results confirm that consumable costs do have a significant effect on the incremental costs of LBC compared to conventional cytology, and on the relative total costs of the different LBC technologies considered.

In our analysis it was difficult to accurately record differences in the administration costs of letters from primary care. In part this was due to the abolition of health authorities during the pilot period. In our analysis we have made an assumption of £3 administration costs per smear. Little reason was identified why administration costs per smear would vary between LBC and conventional cytology.

In the HTA report the cost to health authorities of target payments to GPs has also been included in the overall costs of smears. Target payments are based on the proportion of women screened within a General Practice population and are used as an incentive payment; they are unlikely to vary between LBC and conventional screening and we have excluded them from our analysis.

The HTA analysis also identified that storage, transportation and training costs may be higher with LBC compared with conventional. However, we found little evidence for changes in these costs. LBC vials are stored at room temperature and transportation arrangements were the same for collecting vials as opposed to slides. There is a one off cost of converting smear takers and smear readers from conventional to LBC; however, after a full conversion (as costed in section 6) training costs are likely to be similar between LBC and conventional.

The HTA report did not include changes in the costs of staff time in the laboratory of preparing and reading slides and these have been included in our evaluation. Preparation staff costs vary between the technologies and are higher for the PrepStain™ system and the T2000™; however, they are a small component of total costs per smear. In the pilot sites the T2000™ was not used at the main preparation equipment, our estimates of staff time come from interview, Cytoc have suggested that an estimate of 4 minutes per slide is too high, and a preparation time of 2 minutes has been quoted<sup>16</sup>; this needs further investigation.

Our results indicate that LBC will increase the productivity of laboratories because the number of slides that can be read per hour will rise from 8.3 to 9.0 and the number of formal breaks will remain unchanged. At all three pilot sites the productivity of primary smear reading increased by 9%. Feedback from the sites obtained from the interviews suggested they viewed throughput to have increased slightly as a result of LBC, although there was also a view that rapid review of slides now

took longer, as the whole slide was re-examined. Smear readers commented that whilst obvious negatives were easier to read, abnormal could take longer with LBC.

The workload of the laboratories is not only affected by changes in smear reading time but also by reductions in the number of slides that need to be processed. The large decrease in the inadequate rate will also affect the total smear reader workload because fewer slides in total will need interpretation. The number of slides that need interpretation will be reduced by about 7%.

The combination of these effects has resulted in considerable reduction in the backlog of smears at the pilot sites. This is of importance both in terms of improving staff morale, and in potentially reducing overall staffing requirements at a time when there are staff shortages.

The increase in primary smear reading time was slightly lower than recorded in the Scottish evaluation. However, we found in a sensitivity analysis that these differences in smear reading times had relatively small effects on total cost per smear.

The workload of the laboratories is not only affected by changes in smear reading time but also by reductions in the number of slides that need to be processed. The large decrease in the inadequate rate will also affect the total smear reader workload because fewer slides in total will need interpretation. The number of slides that need interpretation will be reduced by about 7%.

The difference in costs of smear taking time and the reduction in smear reader costs partly offsets the increased costs of equipment and consumables with LBC. However, there is a significant difference in costs between the two suppliers.

The overall costs of LBC compared to conventional are also affected by the reduced inadequate smears that need to be repeated. In the pilots lower estimates of inadequate rates were identified than those used in the HTA model at baseline. The difference in overall costs of screening women with LBC compared to conventional discounted over a lifetime are very similar.

The reduction in the inadequate rate with LBC will reduce the overall costs of screening as fewer smears have to be taken, prepared and read. For example, with a reduction in the inadequate rate from 9% to 1.6%, a laboratory processing 30,000 slides a year with conventional cytology would have a reduction in workload of 2,220 slides per annum. Nationally, the workload would be reduced from 4.2 million slides per annum to 3.9 million slides per annum.

Overall LBC is cost saving across both technologies. In the baseline scenario LBC is between £1 million and £10 million cheaper than the estimated annual cost of £91 million for conventional cytology, the size of the reduction depending on the LBC technology. However these costs include primary care costs of smear taking and administration and in reality the savings accruing in primary care may not be transferred to the laboratory. Our estimate of the national cost of conventional screening is lower than that estimated by the National Audit Office<sup>12</sup> because our estimate does not include items such as colposcopy and histology costs.

Re-estimates of Payne's<sup>13</sup> cost-effectiveness results using data from the pilot sites indicates that both the T3000™ and the PrepStain™ system are cost dominant at baseline, that is, they are both more effective and cost less per person than conventional cytology. At baseline the incremental cost per life year gained of the T2000™ compared to conventional cytology is £270. In the best-case scenario all three technologies are more effective and cost less than conventional cytology. In the worst-case scenarios the incremental cost per life year gained compared to conventional varies between £3,450 and £14,020. The worst-case scenario includes increasing consumable costs by 50% above our baseline estimates.

In our analysis we have excluded the transition and implementation costs of converting to LBC from our analysis, however, if LBC were implemented nationally these costs would be sizeable. These costs include training smear takers and readers and logistical changes to the laboratories.

The cost of training smear takers will depend in part on how it is rolled out. The main cost driver is the cost of GP staff time. Smear takers reported that they were satisfied with the training in LBC smear taking at all three pilot sites whether they had attended external training courses, a trainer came to their practice or they received training from a colleague.

The main logistical costs of converting to LBC for laboratories were: the cost of travel and accommodation at training schools, dealing with the backlog of conventional smears whilst smear readers were training, structural changes for installation of preparation equipment and changes to bar coding systems. It is arguable whether cost of processing the backlog of conventional smears is a strict conversion cost or a cost of the current system that by converting to LBC the cost will simply be brought forward in time however, in this analysis we have included it as a conversion cost. It was also suggested that increased stock control for smear takers was needed for LBC vials compared to conventional cytology due to more their differences in shelf life and their increased cost.

Again the total costs of smear reader training will depend on how it is implemented nationally. There was a view that smear reader training (for primary readers) could have been slightly longer and could have incorporated more revisiting of 'the basics', and there was a preference for more local training. Lack of training materials contributed to the delay in full conversion. There was considerable pressure on the pilot sites to convert to LBC within a short timescale, and if a decision were made to implement LBC nationally a realistic and achievable timetable would be essential. This is particularly true for laboratories that are short of staff. In particular, pathologists will be involved in many other tasks apart from cervical screening, and taking time for training in LBC may be difficult particularly if there are staff shortages. Capacities of both training schools and of suppliers to install equipment were also flagged up as potential issues in interviews.

The costs of preparation equipment were considered as part of the unit costs. For both the T3000™ and SurePath PrepStain™ system machines economies of scale would accrue through using the machines to prepare 60, 000 slides per year compared to 30, 000 slides a year. The extent to which machines are shared between the cytology laboratories will influence the number of machines needed and therefore the costs. During the pilots each laboratory had its own equipment; however, further consideration is needed of the logistical implications of sharing preparation equipment between laboratories

The introduction of LBC should not be viewed alone, as the altered method of smear taking facilitates HPV testing, (and also other potential tasks), since HPV testing in a programme using conventional cytology would require a separate sample to be taken. LBC slides may also be more suitable for use in automated smear reading systems.

In general, the use of liquid based cytology is viewed favourably by staff at the pilot sites, both in the laboratory and in primary care this may largely reflect the overall workload reductions resulting from the new technology.

The full report of this evaluation will, as well as covering additional aspects discussed above, include modelling of the impact of LBC on the outcomes of borderline or mildly dyskaryotic smears.

## REFERENCES

1. Sasieni PD, Cuzick J, Lynch-Farmery E, and the National Co-ordinating Network for Cervical Screening Working Group. Estimating the efficacy of screening by auditing smear histories of women with and without cervical cancer. *Br J Cancer* 1996;**73**:1001-5.
2. Payne N, Chilcott J, McGoogan E. Liquid-based cytology in cervical screening: a rapid and systematic review. Southampton: The National Coordinating Centre for Health Technology Assessment,2000.
3. Broadstock M. Liquid-based cytology - an alternative international view. *Cytopathology* 2001;**12**:141-3.
4. Herbert A, Johnson J. Personal view. Is it reality or an illusion that liquid-based cytology is better than conventional cervical smears? *Cytopathology* 2001;**12**:383-9.
5. Moseley RP, Paget S. Liquid-based cytology: is this the way forward for cervical screening? *Cytopathology* 2002;**13**:71-82.
6. Scottish Cervical Screening Programme. Feasibility of Introducing Liquid Based Cytology. *Steering Group Report* 2002;
7. Schiffman M, Bauer H, Hoover R, et al. Epidemiologic evidence showing that HPV infection causes most cervical intraepithelial neoplasia. *J Natl Cancer Inst* 1993;**85**:958-64.
8. Cuzick J, Sasieni P, Davies P, et al. A systematic review of the role of human papilloma virus testing (HPV) in the cervical screening programme. *Health Technol Assess* 1999;**3**:1-196.
9. Department of Health. Statistical Bulletin: Cervical Screening Programme England:2000-2001. London:2001.
10. Netten A, Rees T, Harrison G. Unit costs of health and social care. University of Kent:2001.
11. Payne N, Chilcott J, McGoogan E. Liquid-based cytology in cervical screening: a rapid and systematic review. *Health Technol Assess* 2000;**4**:1-73.
12. Sherlaw-Johnson C, Gallivan S, Jenkins D, Jones MH. Cytological screening and management of abnormalities in prevention of cervical cancer: an overview with stochastic modelling. *J Clin Pathol* 1994;**47**:430-5.
13. Flannelly G, Campbell MK, Meldrum P, Torgerson DJ, Templeton A, Kitchener HC. Immediate colposcopy or cytological surveillance for women with mild dyskaryosis: a cost effectiveness analysis. *J Public Health Med* 1997;**19**:419-23.
14. Profile of UK General Practitioners. RCGP Information sheet. <http://www.rcgp.org.uk/rcgp/information/publications/information/rcf0001/rcf0001.asp> 2001;**1**:
15. NHS Cervical Screening Programme. A survey of non-medical staff within the cervical screening programme 1996-1999. Sheffield:2000.
16. Bur M, Knowles K, Pekow P, Corral O, Donovan J. Comparison of ThinPrep Preparations with Conventional Cervicovaginal Smears. *Acta Cytologica* 1995;**39**:631-42.
17. Havelock C. The cost of the cervical screening programme-an activity based approach. NHS Cervical Screening Programme,1994.

## **GLOSSARY**

**Cytoscreener-** Individual trained to read cytology slides (degree not required).

**Bio-Medical Scientists-** Biological sciences graduate trained to read cytology slides and also may have further responsibilities depending on level.

**Pathologist-** Medical Consultant of Pathology.

**Suppliers and equipment –**

Tripath Imaging Inc. - suppliers of SurePath™, uses PrepStain™ preparation system

Cytec – suppliers of ThinPrep™, uses T2000™ or T3000™ for preparation.

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## **Appendix 1 – Summary of staff satisfaction with training**

### **Smear Taker Questionnaire**

(140 Questionnaires sent out. 84 completed questionnaires returned 60% response rate. 16 filled in by GP's, 66 by practice nurses and 2 by nurse practitioners.)

Question 6: Who provided your training in taking LBC smears (and providing information about the HPV test)?

<b>Training providers</b>	<b>Responses</b>
External session	45
Internal Colleague	15
Trainer @ practice	23
Trainer @ practice & external session	1

(This question was answered on all questionnaires.)

Question 7a: Please estimate the time your training took for LBC

<b>Time spent training for LBC</b>	<b>Responses</b>
<30Min	27
30min-1hr	29
1-2hrs	18
>2hrs	10

(This question was answered on all questionnaires.)

Question 8: How satisfied were you with the training that you received in taking an LBC smear?

<b>Satisfaction with LBC</b>	<b>Responses</b>
1 – Not at all satisfied	0
2	1
3	9
4	27
5 – Extremely satisfied	47

(This question was answered on all questionnaires.)

Question 11: Considering LBC alone (excluding time for giving information about the pilot or HPV testing) how does the consultation time when taking smears with LBC compare to conventional smears?

<b>Time quicker?</b>	<b>Responses</b>
Much slower + 2mins more	0
slightly slower	7
no difference	40
Slightly quicker	27
Much quicker – 2mins less	8

(All answered this question.)

### **LBC Preparation Staff Questionnaire**

(9 questionnaires sent out and 9 completed questionnaires returned 100% response rate.)

Question 5: How long did your training in LBC slide preparation take with external trainers (trainers not from the laboratory)?

<b>Duration of training</b>	<b>Responses</b>
No external training	3
30 minutes	1
1 hour	4
2 hours	1

(All responders answered this question.)

Question 6. How satisfied were you with the external training?

<b>Satisfaction with training Satisfactory</b>	<b>Responses</b>
Not applicable	3
1 – Not at all satisfied	0
2	0
3	3
4	1
5 – Extremely satisfied	2

(All responders answered this question.)

Question 7: Did you have any further training in LBC technology with colleagues at your laboratory? Everyone answered this question and had had some form of additional training within the laboratory.

Question 8: If yes, how many days of training did you have with colleagues at your laboratory in LBC slide preparation?

<b>Number of extra days</b>	<b>Responses</b>
1 day	7
2 days	1
7 days	1

(All answered this question.)

Question 9: How satisfied were you with training provided with your colleagues in the laboratory?

<b>Satisfaction with training</b>	<b>Responses</b>
1 – Not at all satisfied	0
2	0
3	1
4	5
5 – Extremely satisfied	3

(All answered this question.)

### **Smear reader questionnaire**

(48 questionnaires sent out. 38 completed questionnaires returned. 79% response rate.)

Question 5. How satisfied were you with the initial induction course in LBC at the external centre?

<b>Satisfaction with Induction Course</b>	<b>Responses</b>
No response	1
1 – Not at all satisfied	3
2	6
3	13
4	12
5 – Extremely satisfied	3

(1 individual did not answer this question)

Question 6: How satisfied were you with the consolidation course (review of 200 slides at you laboratory)?

<b>Satisfaction with Consolidation Course</b>	<b>Responses</b>
No response	2
1 – Not at all satisfied	2
2	7
3	12
4	15
5 – Extremely satisfied	0

(2 individuals did not answer this question)

Question 7: How satisfied were you with the test sets?

<b>Satisfaction with Test Sets</b>	<b>Responses</b>
No response	3
1 – Not at all satisfied	0
2	6
3	12
4	15
5 – Extremely satisfied	2

(2 individuals did not answer this question)

Question 8: How satisfied were you with the performance review?

<b>Satisfaction with Performance Review</b>	<b>Responses</b>
No response	5
1 – Not at all satisfied	1
2	7
3	8
4	16
5 – Extremely satisfied	1

(5 individuals did not answer this question. NB. Consultants did not do this stage of the training.)

Question 10: Do you feel as confident reading LBC slides as conventional cytology?

Confident with LBC?	Responses
Yes	35
No	3

(All answered this question.)

Question 14: Overall LBC slides are easier than conventional cytology to read?

Overall LBC Easier	Responses
No Response	1
1 – Strongly disagree	0
2	0
3	3
4	19
5 – Strongly agree	15

(All answered this question.)

Question 16: Do you think there is a need to change the number of breaks that you have when reading liquid based cytology slides compared to conventional cytology?

Change breaks?	Responses
Yes	22
No	16

(All answered this question.)

Question 17: If yes, (to question 16) how many extra breaks per 2 hour session compared to conventional smears?

How many long extra breaks (min)	Responses
0	20
5	2
10	11
20	3
30	1

( 1 individual did not answer this question.)

## Appendix 2 – Description of Payne model

The Payne model uses a number of parameters including management variables, discount rates, disease natural history and effectiveness of cervical cancer treatment; these are presented in table A1.

Table A1 Key parameters: management variables, discount rates, disease natural history and effectiveness of cervical cancer treatment

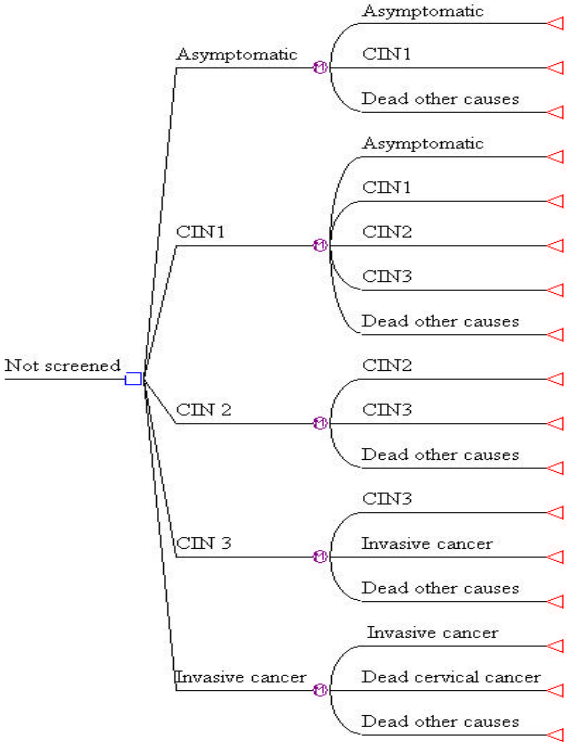
Parameters used in Payne model	Baseline	Minimum	Maximum
<b>Management variables</b>			
Female population	100000		
Start age (years)	18		
First screen at age (years)	21		
Last screen at age (years)	64		
Policy	B		
Screening interval	3	2	5
<b>Discount rates</b>			
Costs	6	0	10
Health Benefits	1.5	0	10
<b>Disease natural history and treatment (6 month progression rates) (%)</b>			
Progression rates from clear to CIN1	0.12		
Progression rates from CIN1 To Clear	2		
Progression rates from CIN1 To CIN2	6		
Progression rates from CIN1 To CIN3	2.5		
Progression rates from CIN2 To CIN3	15		
Progression rates from CIN3 to invasive cancer	1		
Progression factor	100		
Incidence factor	100		
<b>Effectiveness and mortality (%)</b>			
Effectiveness of cervical conisation	90	80	100
Effectiveness of hysterectomy	85	75	95
Screen-detected cancers suitable for conisation – stage 1A1 carcinomas	30	10	50
6 month ,mortality rates associated with invasive cancer	2		4

The Payne model follows a cohort of 100,000 women starting from aged 18, with the first screening when they are 21 years old and the final screen at 64. The baseline screening policy is that women with a moderate/severe test result would proceed directly to colposcopy and women with a borderline/mild results would be re-screened at 6 months. The baseline time interval between screening rounds is every 3 years; however, the model allows other options such as screening every 5 years to be explored.

The natural history of disease aspect of Payne’s model has five distinct health states. The probability of transferring between states is calculated at 6-month time intervals. Pre-invasive cancer is defined by three categories of cervical intraepithelial neoplasia: CIN 1, CIN 2 and CIN 3.

The model assumes that a woman is disease free (clear) until the onset of CIN 1. Without interventions a woman is assumed to progress through each pre-invasive stage to invasive cancer. With no interventions women with pre-invasive cancer can only regress to a disease free state if they have CIN 1 and not with higher grades. As some lesions are fast growing, the model represents this with a proportion of women moving directly from CIN 1 to CIN 3.

Figure A1: Natural history of disease model Payne (2000)/ Sherlaw Johnson 1994



A criticism of this natural history of disease model has been that it assumes that incidence rates of pre-invasive cancers are independent of age despite evidence to the contrary. Sherlaw-Johnson et al <sup>12</sup> acknowledge in their paper that the model is over simplified in this respect; however, since publishing this work they have developed the model significantly.

In Payne’s model age specific mortality from all causes was estimated from the Government Actuary Department’s life tables for women in England and Wales for 1992-1994. Assumptions have also been made about the effectiveness and mortality of cervical cancer treatment.

In table A2, the screening characteristics used in Payne’s model are presented. The estimates of conventional smear test results and other test characteristics based on estimates from the published literature.

Table 5.2: Screening characteristics

Parameters used in Payne model	Baseline	Minimum	Maximum
<b>Test characteristics</b>			
Conventional smear test results (%)			
Specificity of test	98	96	100
False borderline/mild result	1.8	0.9	2.7
False moderate/severe result	0.2	0.1	0.3
Proportion of CIN 1 lesions that give:			
Negative test result	57	42	72
Borderline/mild results	39	24	54
Moderate/severe result	4	2	6
Proportion of CIN 2 lesions that give:			
Negative test result	63	50	76
Borderline/mild results	22	10	34
Moderate/severe result	15	10	20
Proportion of CIN 3 lesions that give:			
Borderline/mild results	50	40	60
Moderate/severe result	50	40	60
Proportion of invasive cancers that give			
Borderline /mild result	60	50	70
Moderate/severe result	40	30	50
<b>Other test characteristics (%)</b>			
Inadequate conventional smear slides	9	7	11
Inadequate rate with LBC	3	1	5
CIN 1/ CIN 2 sensitivity improvement with LBC	15	5	25
CIN 3/ IC sensitivity improvement with LBC	2	0	4
Improvement in specificity with LBC techniques	0	-1	1
Percentage of women who take up screening	85	80	90

In the Payne model proportions of cancers that give different test results are presented. There is then assumed to be an overall improvement in test result sensitivity with LBC; the baseline estimate for specificity of the test is the same as for conventional cytology.

Inadequate smears are incorporated under the assumption that inadequate slides require an immediate re-screen; and are then assumed to be adequate. Inadequate rates differ between LBC and conventional cytology.

In table A3 the cost estimates used for screening and treatment of invasive cancer are presented.

Table A3 Cost parameters used in Payne model

Parameters used in Payne model	Baseline	Minimum	Maximum
<b>Costs</b>			
Cost per conventional smear	55	35	75
Marginal cost for liquid based sample	3.5	0	7
Cost of colposcopy and conization	185	135	235
Cost of surgical treatment of invasive cancer	1700	1000	2400

In Payne's model the costs of conventional smears are based on <sup>17</sup> uplifted to 1999 values baseline estimate of cost per smear is £55. This study was based on activity based costing. Costs per smear include GP costs, Health Authority (including target payments to GPs) and cytology laboratory costs.

The marginal costs of LBC are based on equipment and consumable costs alone. Costs of colposcopy and treatment are taken from the published literature.

Payne et al. estimated a number of cost effectiveness results. They estimated that the incremental cost per life year gained at £1,198 for conventional cytology compared to no screening and £1,096 for LBC compared to conventional cytology, for a 5 year screening interval.

## **Appendix 3 – Pilot Protocol**

### **LBC PILOT STUDIES USING HUMAN PAPILLOMA VIRUS (HPV) TESTING AS TRIAGE**

H C Kitchener, J Patnick, M P Vessey

#### **BACKGROUND**

##### **HPV testing as a triage**

Human Papilloma Virus (HPV) has been found to be present in close to 100% of all cervical cancers<sup>1</sup>. Primary research has indicated that HPV positivity tends to be associated with high grade CIN in a population of women with borderline nuclear change or mild dyskaryosis. HPV testing has therefore been proposed as a means of distinguishing a higher risk group from a very low risk group among such women. An HTA review concluded that HPV testing could not currently be recommended for primary screening for which further research was needed. The evidence did support limited introduction of the test in order to improve the management of women with smears showing borderline nuclear change or mild dyskaryosis<sup>2</sup>. A report from the Kaiser Permanente<sup>3</sup> provides further evidence for this approach. Nine hundred and ninety five women with ASCUS smears had repeat smear, HPV testing, colposcopy and, if required, histopathological diagnosis. There were 65 high grade lesions, of which 7 were HPV high risk type negative and fifteen showed a normal smear result. Four would have been missed at first review by the criteria of both smear  $\leq$ ASCUS and HPV-ve, which indicates a very high negative predictive value for the test in this setting.

Thus the negative predictive value of HPV testing can help to identify which women in this category do not require immediate referral for colposcopy. There is, however, still some uncertainty about the negative predictive value of the test in the presence of persistent mild dyskaryosis and the safety associated with reduced surveillance. This particular aspect of HPV screening needs to be carefully evaluated in pilot studies. Viewed overall, however, it seems extremely likely that the introduction of HPV testing for triage of women with smears showing borderline nuclear change or mild dyskaryosis would be cost effective for the NHS by reducing referral to colposcopy and would therefore reduce anxiety for some women.

The question of the most appropriate way to deal with HPV positive results and associated psychological issues would benefit from further research. The MRC funded TOMBOLA study, which started recruitment of women in December 1999, should be able to address these issues for women with borderline nuclear change and mild dyskaryosis.

## **Liquid Based Cytology (LBC)**

Research evidence suggests that Liquid Based Cytology (LBC) could provide significant and important benefits. However, the quality of the evidence is variable and some areas of uncertainty remain. Although there is insufficient evidence to justify the nation-wide introduction of LBC technology at this time, it is likely that LBC will have the effect of reducing the number of false negative test results as well as the number of unsatisfactory specimens. In addition, it may decrease the time needed for examination of specimens by cytologists. NICE has recommended pilot studies to evaluate controlled introduction of LBC into the NHS cervical screening programme.<sup>4</sup>

In order to establish its contribution, a programme of pilot implementation projects of LBC will be undertaken, accompanied by a full review of the results at each stage

The technologies of LBC and HPV testing form a natural link in that the technology of the liquid based specimen allows an HPV test to be performed at a later date in the laboratory without the patient being required to provide a second sample. Therefore, the piloting of the two new technologies will be linked and assessed as part of the evaluation of each.

## **THE PILOTS**

### **Aims and objectives of the pilots**

**LBC:** These pilots are designed to evaluate all the effects, costs and practical implications of introducing LBC technology into the cervical screening programme, including the following:

1. the effect on test results (proportions of tests classified as inadequate, negative, borderline/mild dyskaryosis, moderate dyskaryosis, severe dyskaryosis or worse) and the consequent need for repeat screening, recall in less than three years and additional diagnostic investigation;
2. the extent to which productivity improvements in cytology laboratories are realised in routine practice, the acceptability of LBC to laboratory staff and their needs for training, and the identification of quality assurance guidance prior to full implementation;
3. the impact in the primary care setting with regard to the training of screening personnel, avoidance of repeat visits and ease of implementation;
4. the logistical implications of implementing LBC, including transport of specimens, storage, waste disposal and laboratory throughput.

**HPV testing as triage:** These pilots are designed to evaluate a number of issues associated with introducing HPV technology into the cervical screening programme as triage for smears showing borderline nuclear change and mild dyskaryosis including the following:

1. The extent to which HPV testing in women with low grade cytological changes reduces the need for colposcopy
2. The feasibility of performing a second test on women with low grade abnormalities. The options would be:
  - smear and specimen for every woman in case HPV testing is needed
  - recall to a second appointment for those with low grade cytological smear abnormalities for a swab to be taken for HPV testing
  - liquid based cytology to be used on all women in order that the HPV test can be carried out in the laboratory if appropriate
3. The positive predictive value of the HPV test in women with low grade smear abnormalities and the negative predictive value for women with persistent mild dyskaryosis
4. The public acceptability of HPV testing as part of the screening programme. This would need to be seen as a component of an improved cervical screening test and not a “sexually transmitted disease test”<sup>5</sup>. The anxiety of patients returned to normal recall after a negative HPV test despite an earlier abnormal smear would need to be monitored as would the anxiety caused to patients whose HPV test was positive and followed by immediate referral.
6. The piloting of a limited introduction of HPV testing would offer a learning opportunity concerning HPV testing and a means to assess the prevalence of HPV infection in the UK population with low-grade abnormalities. The impact of the introduction of testing on a laboratory could also be judged. Ideally, histological correlation of biopsy findings with the HPV findings would be included in order to confirm the accuracy of the result given UK cytology reporting standards and practices which differ somewhat from those of the US.

### **A two-stage approach**

As a first stage, there will be three pilot sites in England, each fully converted to LBC, but using one or other of two different manufacturers’ systems in order that experience can be gained with each of

the two major systems currently available in the UK (ThinPrep™ and Autocyte Prep). These sites will complement the recently announced four Scottish development sites. It is expected that Wales will also wish to establish a pilot development.

The LBC pilot sites will form the three pilot sites for HPV triage for borderline and mildly dyskaryotic smears. This pilot will last for 12 months.

HPV testing will not be added to the LBC pilot sites until the 3-month training and conversion period is concluded and the evaluation period has begun.

### **Site Selection**

The 3 sites to carry out the pilot are:

Norfolk and Norwich Hospital

Southmead Hospital, North Bristol NHS Trust

Royal Victoria Hospital, Newcastle

The sites were selected through a competitive process according to criteria which included size of service, quality assurance standards and current performance.

### **OUTLINE PROTOCOL**

#### **First stage: LBC**

During the first 6 months of the HPV triage pilot, there will be no impact on the number of repeat smears being received by the laboratory. This first 6 months will be the 6 months of the LBC evaluation period and therefore the numbers of referrals to colposcopy or for further repeat smears without HPV triage will be able to be modelled accurately.

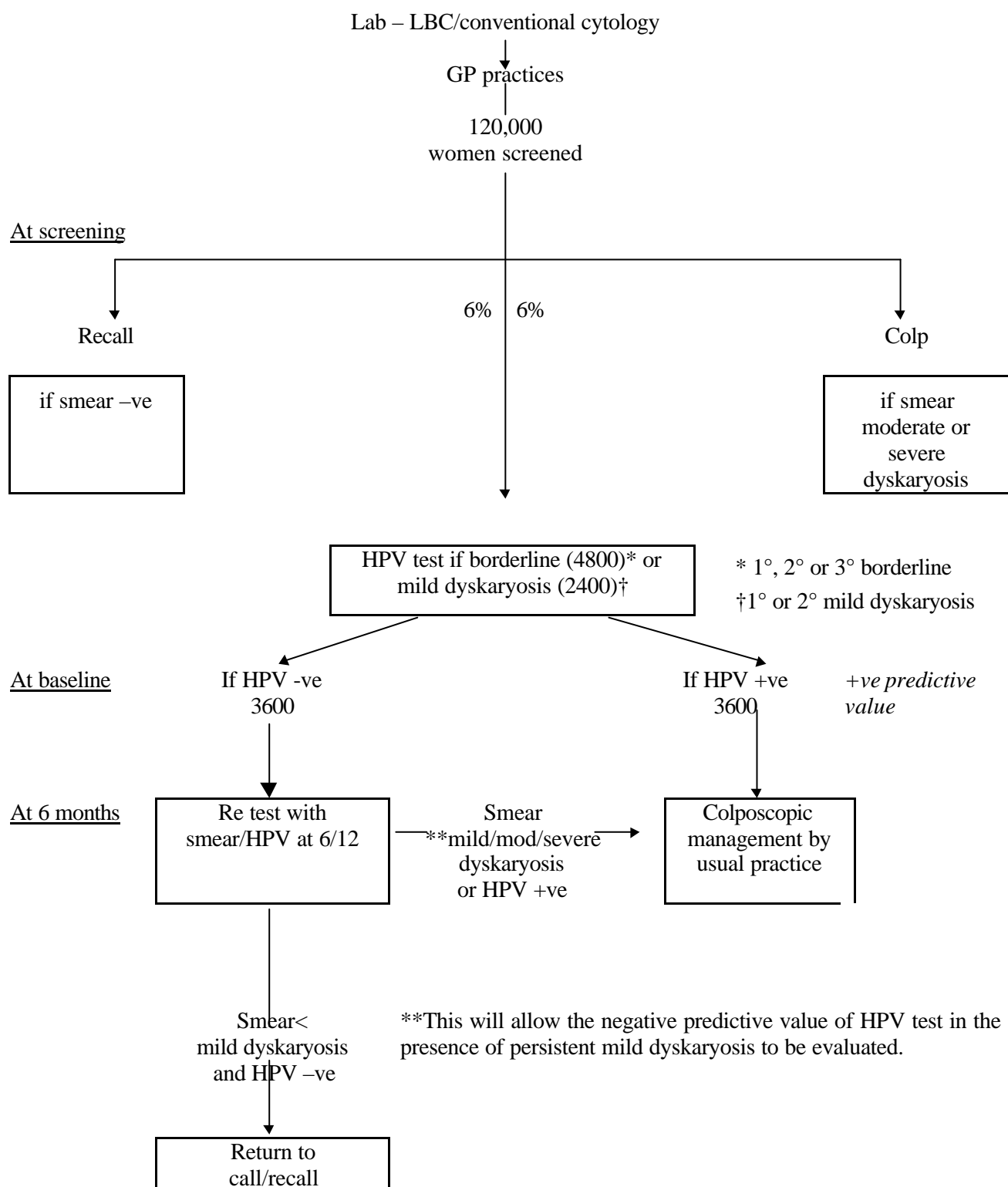
The evaluation of the first stage will take place over a 6-month period (the same duration as the Scottish demonstration sites). This will follow an initial training and conversion period of 3 months.

## **Second stage: HPV triage**

*The pilot would essentially replace assessment of low-grade abnormalities by colposcopy with assessment by HPV testing. Women whose index smear showed borderline nuclear change or mild dyskaryosis would also have material tested for high-risk HPV types. If liquid based cytology were to be used at primary screening, this would not require a second specimen to be taken. If HPV positive, they would be referred immediately to colposcopy.*

If the test showed they were HPV negative, then it is suggested that they should have a repeat smear in 6 months time, as now, **and** a second HPV test. If the apparent abnormality had **either** persisted as mild dyskaryosis **or** progressed to a high-grade smear (a very unlikely occurrence) **or** the women were now found to be HPV positive, they would then be referred for colposcopy. If the abnormality had regressed or was no worse than borderline nuclear change **and** the woman were HPV negative on both occasions then she could be discharged back to 3 yearly screening. If, during the course of the pilots, the second test proved to have a negligible yield, then if HPV triage were to be rolled out, the 6 month repeat could be discontinued. Similarly, referral for colposcopy of women who were HPV negative on both tests, but referred because of persistent mild dyskaryosis might prove to add nothing to a woman's care and this could then also be discontinued at roll-out.

### Flow chart of women at pilot sites



With 3 pilot sites and around 7,200 abnormalities we can compare LBC vs conventional smear, with good confidence. There should be around 4,800 borderlines and 2,400 mild, as follows:

1200 x 3° borderline

1600 x 2° borderline

2000 x 1° borderline

1000 x 2° mild dyskaryosis

1400 x 1° mild dyskaryosis

These should also allow good comparison in the context of positive predictive value when combined with HPV +ve test, in terms of identifying CIN3 at colposcopy.

## **EVALUATION**

Evaluators will be separately recruited by DH R&D. There will be a separate advisory structure for the evaluation to ensure independence of the ultimate report.

### **First stage: LBC**

The evaluation will consist of two parts; an evaluation of the training and conversion process, and an evaluation of the use of LBC as a functioning cervical cytology system. The evaluation of training and conversion will cover not only the necessary changes in the laboratory, but also the process in the primary care setting and in the colposcopy clinic. This period is expected to last three months to provide valuable information for an eventual rollout. The evaluation of LBC overall will aim to undertake a full review of all the effects, costs and practical implications of introducing LBC technology into the cervical screening programme over a 6 month period once the system has ironed out any initial problems and before any reduction in repeat smears due to HPV testing would have had an effect.

### **Second stage: HPV triage**

In order to ascertain the effect of the intervention, results obtained during the pilot will be compared with historical data from the same site in the previous year or immediately prior to the pilot's commencement as appropriate

## Effects

The following items should be considered:

1. Laboratory reporting profile over the 8 BSCC categories. It is expected that a laboratory using LBC should see a significant reduction in specimens reported as inadequate or borderline. This should consequently lead to a reduction in women undergoing cytological surveillance or being referred. In turn, there should be a reduction in the amount of anxiety created by the programme. The latter point may not need specific measurement since there is ample evidence that smear reports that are anything other than normal cause anxiety. The reduction in repeats and referrals may require modelling since the HPV triage pilots will be taking place in the same locations as the same time.
2. Productivity in the laboratory. The faster reporting time for LBC smears should lead to cytology screeners, checkers and pathologists reporting more smears than is currently possible. This will have the effect of reducing turn around times in laboratories which are often overlong. Some baseline information is available through the national office of the NHSCSP, but some local measurement in the pilot sites may be needed.

## Costs

The following should be monitored:

1. The expected reduction in the number of specimens due to a fall in repeat smears. This should reduce costs at the health authority, which generally organises call and recall, and in primary care, where the appointment is made and attended and the specimen collected and from where it is transported to the laboratory.
2. The laboratory costs. These may increase per specimen due to the fact that all preparation of the specimen now takes place in the laboratory and a more complex collection medium is used. However, greater productivity on the part of the laboratory manpower might compensate for an increase in material costs. Both medical and non-medical costs should be assessed.
3. The referral rate which would have normally been seen in the absence of HPV triage. This would be expected to decline following a fall in inadequate and borderline reports. However, a greater number of high-grade abnormalities might be found which required immediate referral. These effects would reflect the use of a more specific and/or more sensitive test respectively.
4. The cost of LBC based HPV testing.
5. GP consultations for discussion of results involving non-negative smears. These may decrease following a reduction in inadequate and borderline smears, but could increase if the number of high-grade smears rises or if women seek advice regarding the HPV test result.
6. Training costs both for laboratory and primary care staff.

### Practical implications

The training needs of laboratory and primary care staff will be monitored as part of the evaluation of the training and conversion stage. There should also be an evaluation of the length of time it takes staff to become proficient once they have completed initial training. During this stage, the following should be monitored:

1. Storage of vials both in primary care and in the laboratory
2. Transport of the specimens from collection to the laboratory
3. Laboratory handling characteristics
4. Equipment service and support
5. Disposal of the remaining specimens after reporting
6. Fatigue in reporting and optimum reporting time
7. Rapid review methodology
8. EQA mechanisms and protocols
9. Development of appropriate Quality Assurance tools
10. Development of teaching methodologies and libraries
11. HPV testing protocols
12. Physical requirements in the laboratory to accommodate LBC and associated equipment
13. Patient satisfaction. While the loss of anxiety following a reduction in the number of repeat smears and referrals can be modelled, patient attitude to the new technique and to the explanations they are offered when being tested should be monitored
14. Smear taker satisfaction. The attitudes of GP's, practice nurses, family planning clinic and colposcopy clinic staff to the new technique should be monitored
15. Laboratory staff satisfaction. The attitudes of laboratory staff to the new technique and its impact on their work should be monitored
16. Chlamydia testing protocols. This aspect might be subject to modelling

### Indicators of success

1. Reduction in no. of referrals for colposcopy
2. Reduction in no. of repeat smears required
3. Overall reduction in number of smears
4. Reduction in inadequates
5. Reduction in borderlines
6. Reduction in time to return to routine call/recall
7. Reduction in time to resolution/return to call/recall

8. Cost benefit analysis
9. Rate of underlying CIN lesion at referral to colposcopy (according to 1<sup>o</sup>, 2<sup>o</sup> or 3<sup>o</sup> smear)
10. Patient anxiety, acceptability and response to HPV testing

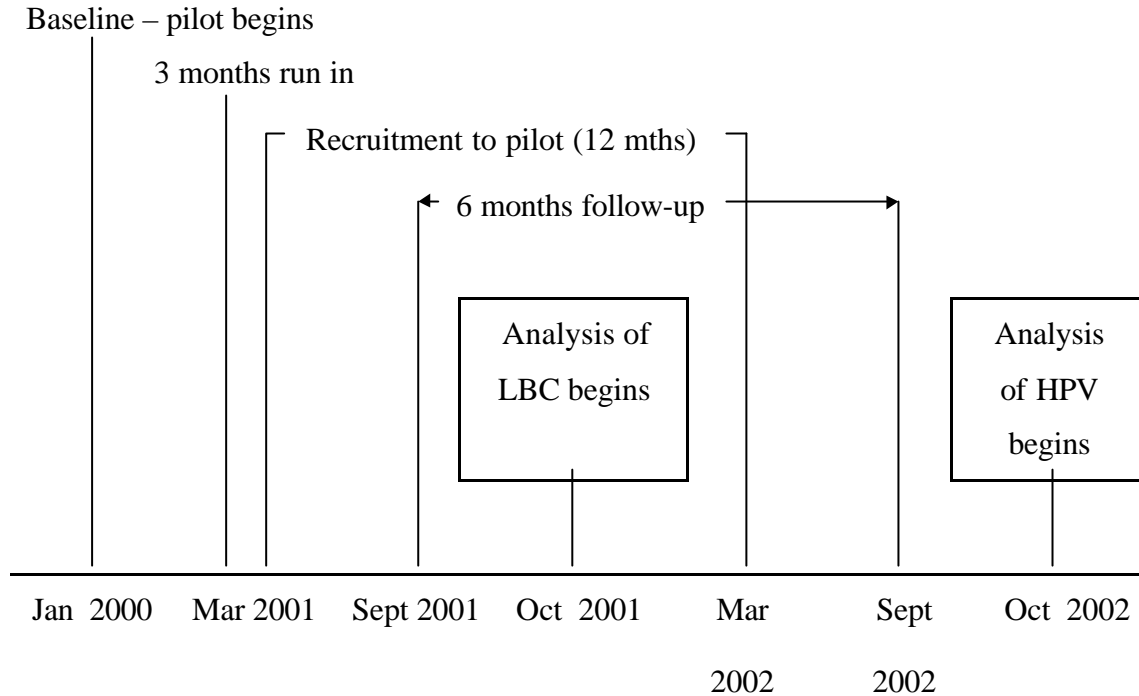
#### Supplementary/process questions

1. All results will be analysed by 5 year age groups in order to establish the cut-off points for effectiveness if any
2. The repeat HPV test at 6 months will be examined to ascertain if it adds anything to improve management
3. The referral for colposcopy of women who are twice HPV negative but show persistent mild dyskaryosis will be examined to ascertain if it adds anything to improve management
4. The viral load using picograms will be examined using modelling techniques to ascertain the appropriate cut-off point. During the pilot, 2 picograms will be used as the action point. ALL borderlines and milds will be HPV tested and an analysis made of 2<sup>nd</sup>/3<sup>rd</sup> milds and borderlines according to test history

A report will be made to NICE on the use of LBC by May 2002 at the latest.

## TIME MILESTONES

Baseline - Pilot begins  
- 3 months run in



## **REFERENCES**

1. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Munoz N. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol* 1999 Sep;189(1):12-9.
2. Cuzick J, Sasieni P, Davies P, Adams J, Normand C, Frater A, van Ballegooijen M, van den Akker E. A systematic review of the role of human papillomavirus testing within a cervical screening programme. *Health Technology Assessment* 1999, Vol 3 No. 14.
3. Manos MM, Kinney WK, Hurley LB, Sherman ME, Shieh-Ngai J, Kurman RJ, Ransley JE, Fetterman BJ, Hartinger JS, McIntosh KM, Pawlick GF, Hiatt RA. Identifying women with cervical neoplasia: using human papillomavirus DNA testing for equivocal Papanicolaou results. *JAMA* 1999 May 5;281(17):1605-10.
4. National Institute for Clinical Excellence. Guidance on the Use of Liquid Based Cytology for Cervical Screening, London, 2000

## **Appendix 4 – Protocol Amendment**

### **NHS Pilots of HPV triage Protocol amendment for women < 35 years**

The NHS Pilot studies of liquid based cytology (LBC) and HPV testing were designed to test whether LBC would bring significant advantages over conventional cytology and whether HPV testing could usefully identify women at very low risk who could avoid colposcopy. The pilot studies are proceeding satisfactorily but it has become clear that there is a considerable difficulty, which is that far more women than anticipated are testing HPV +ve with the HC II test. The recently published data from the ALTS trial in the United States have demonstrated HPV positivity using the same test in 90% of LSIL and 56% of ASCUS. Although these cannot be said to be equivalent to borderline and mild dyskaryosis in terms of morphology, they are similar in terms of risk of underlying high grade CIN. The early data from the pilots indicates HPV +ves in 90% of mild dyskaryosis and 50% of borderlines, figures which are consistent with the US data.

The problem with these rates is that the ‘immediate’ colposcopy examination, triggered by HPV +ve testing according to the original pilot protocol, is proving impossible to deliver in a timely manner. This partly relates to a prevalence of HPV due to testing of 1<sup>o</sup>, 2<sup>o</sup> and 3<sup>o</sup> borderline smears as well as women with mild dyskaryosis. If this were followed through, many women who are currently in a surveillance loop would be dealt with and their diagnosis resolved.

Nevertheless the protocol requires to be changed in order to stop accumulating even more HPV positive women (over 600 in Norwich and 350 in Bristol) who are awaiting colposcopy. These women will require to be colposcoped at additional clinics. It should be noted that around 70% of these HPV +ve women are under 35 years.

The Trial Steering Group met on 7<sup>th</sup> November 2001 to discuss the position. There was agreement on the following principles to reduce the colposcopy burden while at the same time preserving the aims of the Pilot studies:

1. The original protocol would still apply to women 35 and over.
2. In women below 35 years, there would not be immediate referral for colposcopy but only under the following circumstances
3. Maintenance of colposcopy for women who remain HPV +ve at 6 months

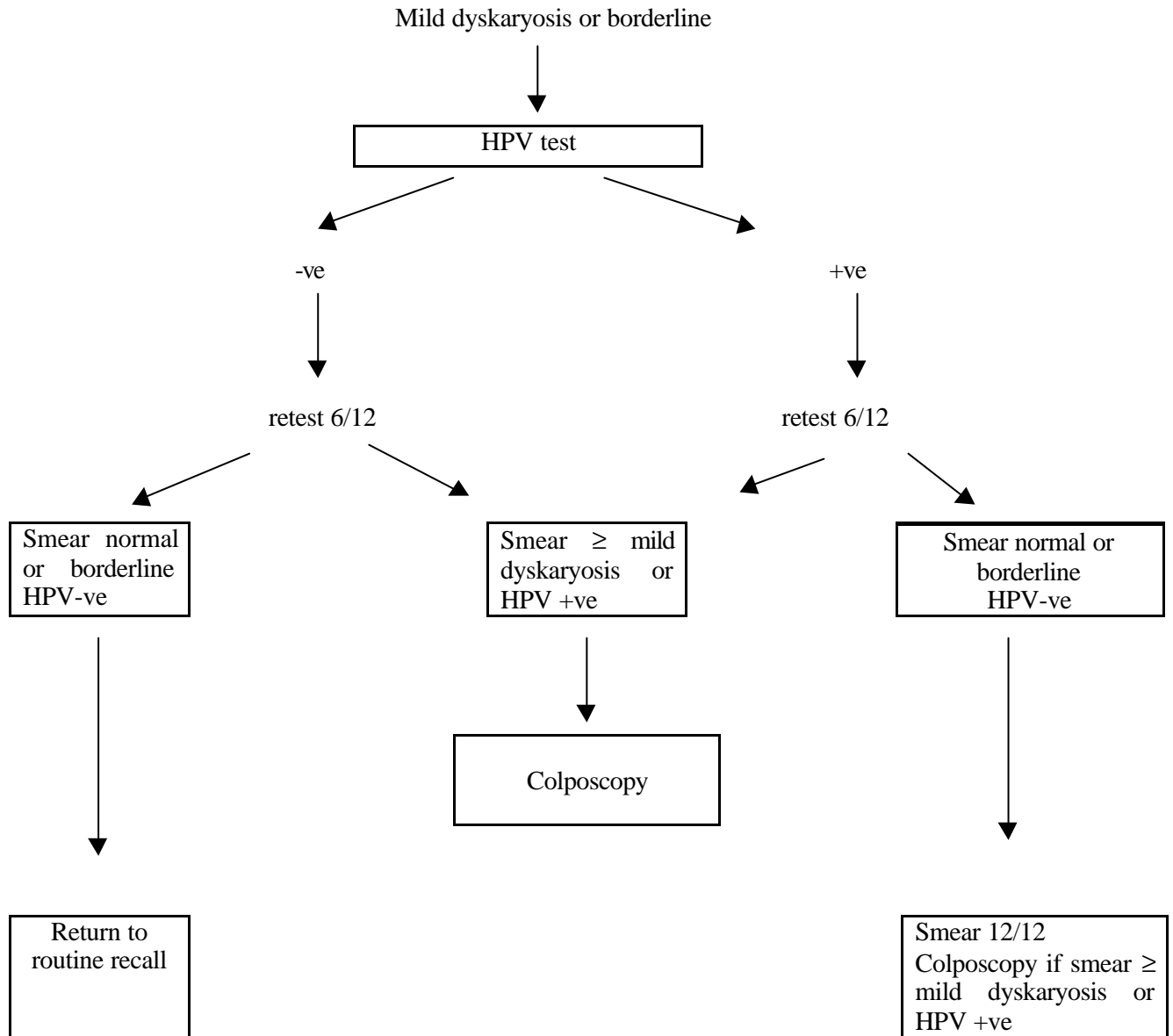
The criteria for colposcopy will apply to the following women:

- a) Mild dyskaryosis is maintained over 6 months
- b) HPV +ve is maintained over 6 months

This is illustrated in the accompanying flow chart (p.3). What these measures do is to defer colposcopy in such a way that although the overall number may not be greatly reduced (unless HPV +ves clear in a significant proportion) it will be more spread over time, allowing the immediate backlog to clear. There is still a challenge for colposcopy clinics but the data that will flow from successful prosecution of the protocol will be invaluable in determining future HPV testing policy for this large group of women.

**NHS Pilots of HPV triage**

**Protocol amendment for women < 35 years**



## **Appendix 5 – Steering Group Committee**

Professor Henry Kitchener, Professor of Gynaecological Oncology, Department of Obs & Gynae, St Mary's Hospital

Dr Patricia Wilkie, Member of RCPATH Patient Focus Group

Sir Charles Nightingale, National Screening Policy Team, Health Services Directorate

Professor Richard Lilford, Department of Public Health & Epidemiology

Mr Tim Elliott, Cancer Screening Policy Manager, Department of Health

Dr Ursula Wells, Principal Research Officer, R & D Directorate, Department of Health

Dr Sue Moss, Institute of Cancer Research

Dr Heather Cubie, R & D Director, The Royal Infirmary of Edinburgh

Professor Nick Wald, Wolfson Institute of Preventative Medicine

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Mrs Julietta Patnick, National Coordinator, NHS Cancer Screening Programmes

Mr Richard Winder, Deputy National Coordinator, NHS Cancer Screening Programmes

Dr Euphemia McGoogan, Patient Services Director, Department of Pathology, The University of Edinburgh

Dr Cerilan Rogers, National Coordinator, Breast Test Wales

Mrs Janet Rimmer, Secretariat, NHS Cancer Screening Programmes

Ms Isabel Gavin, Scottish Screening Programmes

Mr James Richards, NHS Purchasing & Supply Agency

Dr David Hicks, Consultant Physician, Genitourinary Medicine, Royal Hallamshire Hospital

Mr Patrick Walker, Consultant Gynaecologist, Colposcopy Department, Royal Free Hospital

Mr Alan Woodworth, NHS Purchasing & Supply Agency

Dr Karin Denton, Consultant Cytopathologist, Department of Pathology, Southmead Hospital

## **Appendix 6 – Advisory Group for the Evaluation of the LBC/HPV Pilot**

Professor Richard Lilford, Department of Public Health & Epidemiology, University of Birmingham

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