
Monograph:
Turner, J., Brennan, A. and Dixon, S. (1999) Final Report to the NHS Cervical Screening Programme. Report. ScHARR Other Reports . ScHARR (School of Health And Related Research), University of Sheffield , Sheffield. ISSN 1900752107

Final Report to the NHS Cervical Screening Programme

The Costs and Outcomes of Cervical Re-screening

Janette Turner
Alan Brennan
Simon Dixon

ISBN: 1 900752 10 7

Published by the Sheffield School of Health and Related Research, University of Sheffield.

Executive Summary

The examination of cervical smear tests is a subjective process which requires the application of personal judgement by screeners and pathologists. In recent years a number of quality control mechanisms and standards for reporting have been introduced into cytology laboratories to try and minimise the risk of errors in cervical smear examination and reporting. Nevertheless, there have been several high profile incidents relating to errors in cervical cytology services which, in some cases, have led to some women developing cancer shortly after a 'negative' cervical smear. There have subsequently been large scale re-examinations of slides within centres in order to identify other false-negatives.

The consequences of unacceptably high error rates are serious both in terms of the health effects on women and public confidence in the screening programme. In addition the re-screening process is costly to the NHS. At present there do not exist any estimates of the costs and effectiveness of re-screening exercises. However, it is important to have some understanding of the cost-effectiveness of this mass re-examination of cervical smears to inform future policy on the management of these incidents. This report presents the findings of a modelling study to assess the costs and potential effectiveness of cervical re-screening exercises.

The principle aims of the project were to construct a model that is capable of :

1. Describing current screening practices in terms of workload, costs, and outcomes

2. Estimating how costs and outcomes change as a result of undertaking a mass re-screening of slides.

A spreadsheet model was developed using data sources which included existing documented guidance, information from centres where previous re-screening exercises had taken place and national costing information on cervical screening services. The model was systematically tested for internal coherence and validity was tested against previous re-screening exercises.

A series of re-screening scenarios were then analysed using the model to produce estimates of the likely costs of the re-screening exercise and the outcomes in terms of the number of additional false negative cases found in different categories based on the classification system for cervical smear abnormalities. The key variables tested were differences in the size of the suspected error and differences in the size of the re-screening exercise.

The principle findings were:

- A critical factor is the sample size used to estimate the scale of the problem before a decision about mass re-screening is made. If sample sizes are small there is extreme variability around the central estimate of the number of additional false negative cases that may be detected.

- Cost is a major driver in the screening process and is very variable ranging from £89,000 to £41,000 for a 10,000 slide re-screen.

- There is an exponential relationship between the size of the error and the cost per additional moderate or worse case detected. This ranges between a cost per case of more than £12,000 for a 0.05% error, to £332 for an error rate of 2%.

- If a re-screening is a public exercise costs can increase by almost 25%

- Rapid review only followed by detailed examination of suspected cases can reduce the costs of re-screening by 50%. However, a high sensitivity of rapid review is required to make this option a viable alternative.

The decision about whether or not to re-screen slides where a reporting problem has been identified is not an easy one to make. There is no single combination of factors that can be identified which will determine at which point a re-screen should take place. The model developed for this study can provide important information which take account of both the scope and degree of error that is potentially present. This, in conjunction with other pertinent local issues, can then inform the decision making process.

The following factors should be taken into account when assessing the need for a major re-screening exercise:

- The significance of a potential error should be estimated before any re-screen takes place. The critical factor is whether or not an error detected is sufficiently greater than that which is within acceptable limits to be of concern. Where the error rate detected is at the margin of standard reporting benchmarks, the costs of detecting each additional false negative will be high.

- Consideration should be given to the degree of error. Severe abnormalities present the most risk to patients and this should be the primary focus of any decision about the need for a re-screening exercise. If mild abnormalities are the problem it may be more cost effective to recall women for a routine examination earlier.

- When the significance of an error has been identified the model should be used to provide estimates of the likely consequences in terms of both costs and outcomes. This will provide information of the outputs in relation to the size of the exercise to be undertaken.

1. Introduction

1.1 Background

The primary objective of the NHS cervical screening programme is to reduce the incidence of and mortality from cervical cancer. The screening tool is the cervical smear test, which is examined, interpreted and reported on in cytology laboratories. This is a subjective process which requires the application of personal judgement by screeners and pathologists and as such is therefore always open to error. In recent years a number of quality control mechanisms and standards for reporting[1] have been introduced into cytology laboratories to try and minimise the risk of errors in cervical smear examination and reporting. Nevertheless, there have been several high profile incidents relating to errors within various cervical cytology services[2]. The most notable of these incidents have led to some women developing cancer shortly after a 'negative' cervical smear. This has led to large scale re-examinations of slides within centres in order to identify other false-negatives.

The consequences of unacceptably high error rates are serious. For a small number of women there are significant health effects which, at worst, can result in premature death from a treatable condition. For a much larger number of women there may be no or relatively small health effects but the re-screening process, particularly if this is a public exercise, subjects them to a period of personal anxiety. Such events undermine public confidence in the screening programme and the re-screening process is costly to the NHS. It is therefore important to have some understanding of the cost-effectiveness of this mass re-examination of cervical smears to inform future policy on the management of these incidents.

1.2 Previous Research

A search of electronic information databases produced numerous citations of research into the cost-effectiveness of cervical screening. However, much of this work has been concerned with the effectiveness of screening programmes and their ability to reduce the incidence of cervical cancer in populations[3].

More specifically, there has been work to model the cost-effectiveness of different strategies of re-screening cervical smears that have been classified as negative during primary screening. Both Kaminsky[4,5] and Raab[6] have investigated the relative effectiveness of a policy of 10% re-screening of negative slides compared to the alternative strategy of rapid review of 100% of negative slides. However, this work is concerned with quality control mechanisms within a screening programme. So, whilst they are useful in terms of describing the technical development of models to investigate different screening strategies, they were not designed to investigate the mass re-screening of cervical smears that have previously been examined by the normal screening process. As such they cannot provide any evidence of the cost-effectiveness of this type of screening. All of the research found during the literature search was concerned with the normal screening process. No studies were found which specifically addressed the issue of the mass re-examination of cervical smears to identify erroneously classified specimens that have been previously screened. So, despite the importance of this issue, there do not exist any estimates of the costs and effectiveness of such mass re-examinations. Thus there remains a need to assess the cost-effectiveness of re-screening and to utilise the findings within the guidelines that are currently being devised to help cervical cytology centres handle such incidents.

1.3 Purpose of this Report

This research report summarises project work undertaken by the School of Health and Related Research to model the costs and potential effectiveness of cervical re-screening exercises. The work was commissioned in late 1998 by the national co-ordinator of the screening programme, Mrs Julietta Patnick. The project report summarises the project process and includes:

- A description of the mathematical model.

- Summary of the available data on key parameters in the model.
- The model results for a number of typical scenarios.
- Conclusions.
- Recommendations.

1.4 Project Brief

The principle aims of the project were:

1. To construct a model that is capable of describing the current screening practices in selected centres in terms of their workload, costs, and outcomes.
2. Estimate how costs and outcomes change as a result of undertaking a mass re-screening of slides.

In particular, it was intended that the model would:

- Enable estimates of the likely costs of the re-screening exercises to be made.
- Given initial information on the likely scale and the source of error the model should produce an estimate of the likely numbers of cases to be found by different categories.
- Provide helpful information to the National Screening Office and local staff in deciding whether or not a re-screening exercise is worth while.
- Provide a tool for use by the National Screening Office and/or the local management in considering different ways in managing a re-screening process.

1.5 Project Process

The key elements of the project process were as follows:

- An in-depth literature search on cervical screening and cervical re-screening in order to understand the evidence base, to examine whether previous models have been undertaken and to provide estimates of key parameters within the model to be developed.
- Questionnaires were sent to four sites which had recently undertaken cervical re-screening. These were followed up with telephone interviews and a site visit to one hospital.
- Examination of existing documented guidance.
- Analysis of data from previous re-screening exercises provided by local sites.
- Development of a conceptual model diagram of how the normal screening and re-screening process works and confirmation and refinement of this through discussion with key contacts.
- Development of a quantified model.
- Systematic testing of the quantified model for internal coherence
- Validity testing against previous re-screening exercises
- Development of a series of scenarios to analyse using the model
- Analysis of results of using the model
- Reporting of conclusions

2. Structure of the Model

The model was developed in several stages.

2.1 Normal Screening Reference

The first stage was to develop a spreadsheet model that describes existing normal screening practices. The data that this baseline model is built on are:

- Unit cost data from the NAO Financial Audit of Cervical Cytology and Colposcopy Services[7]
- Current salary scales for cytoscreeners, checkers (based on BMS grade) and pathologists
- Centre throughput
- Centre abnormality rates
- National standards for cervical screening and reporting [1]
- Percentage of slides referred through from screeners through to checkers and pathologists (taken from a small number of centres).

Rapid review of all negative slides rather than a 10% re-screen of negatives was the quality control mechanism built into the model given that this is now the nationally recommended practice for laboratories which undertake cervical smear screening.

The model separates out clearly the different processes of the screening process:

- *Primary screening* – This is the first, detailed microscopic examination of the whole of the smear slide by a cytoscreener.
- *Rapid review* – A second, rapid examination of all slides classified as negative or inadequate after the primary screen. At this stage all smears confirmed as negative and inadequate are reported.
- *Checking* – Re-examination of all slides with suspected abnormality following the first two steps of the screening process. At this stage additional smears may be reported as negative or inadequate.
- *Reporting by a pathologist* – The final, detailed examination and reporting of smears identified as potentially abnormal.

At each of the first three stages of the process the model examines the likely flow through of the number of slides examined into categories defined as negative, borderline, inadequate or suspected abnormal cases. At the pathologist stage, the suspected abnormal cases are refined further into mild, moderate and severe dyskaryosis, glandular neoplasia and invasive cancer.

The model was constructed to reflect a screening process that assumed the national expected standard of a sensitivity of 85-95% for primary screening. It also produced results in each category of smear classification equivalent to the national averages reported in the 1996/7 DoH statistical bulletin for the cervical screening programme in England[8]. These outputs were also within the reference ranges for achievable standards for smear reporting[1], namely:

Smear result	Achievable standard
Moderate and severe	1.6% +/- 0.4%
Mild and borderline	5.5% +/- 1.5%
Inadequate	7.0% +/- 2.0%

This model therefore reflects the proportions of smears examined at each stage of the screening process that represents normal flow through the laboratory. However, all parameters of this baseline model are capable of being altered, and as such, can describe any centre in the UK. The model is reproduced in Appendix 1.

2.2 Re-screening process

An algorithm was then constructed which describes the re-screening process. Re-screening is defined as the mass re-examination of cervical smears previously screened and reported on during the normal cervical screening process. This is given in Appendix 2.

This provided the basic framework for the development of the re-screening model. For the spreadsheet model the detail at each point in the algorithm was expanded, using the same format as the normal screening model. However, the flow through the cytology laboratory system is likely to be different for a re-screening exercise than for the normal screening process. The purpose of the re-screen is to detect additional false negative smears. A substantial proportion of abnormal smears will have already been detected during the normal screening round, so at re-screen the proportion of abnormals found will be lower than the normal expected range. The actual proportion will depend on the size of the original error. At re-screen two possible alternatives may exist:

1. A greater proportion of smears will be reported as negative at the primary screening or checking stages resulting in a smaller proportion of the total number of smears going to the pathologist stage.
2. Because the exercise is a re-screen, there may be a lower threshold for slide referral to make sure no abnormals are missed. Consequently the proportion of slides seen by checkers and/or pathologists may increase.

Ideally, the flow through the re-screen model would be most robust if based on actual data from a re-screening exercise. At the start of the project, our intention was to collect this data from centres where re-screening had taken place and to use this to develop the model. However, although centres where re-screening exercises have taken place in the recent past have been very co-operative in releasing data to the project team, the record keeping process during re-screening exercises has not been comprehensive. For example, details of the proportions of slides passed from screeners to checkers are not available. Also, some data is unavailable to the laboratory undergoing re-screening as re-screening of slides has primarily been done by external laboratories. Consequently we have had to make some assumptions about flow through. These are based on those used for the normal screening model but adjusted to take into account the different proportions of outputs in each outcome category using observed data from re-screening exercises.

In the first instance a reference model was constructed using data from the re-screening exercise at one centre (Centre A). Flow throughs were assumed to be of the same order as the normal screening process with the exception that the relative proportions of negatives and inadequates were weighted towards negatives. This reflects the findings of other re-screening exercises but will vary depending on whether negatives only or negatives and inadequates are re-screened. The relatively small proportion of inadequates, compared to the level reported following the normal screening process, may also be a consequence of a greater tendency to produce a definitive result during a re-screen.

The basic model structure is set out in Appendix 3. This is a printout of the existing spreadsheet model. The cells with bold borders are the input parameters which can be varied. The model takes as its first set of inputs an estimate of the existing error rates. Error rates refer to the proportion of

slides that had an abnormality but were classified as negative (false negatives). The scale of the problem will depend on several factors;

- Whether there is a single screener or whole laboratory problem
- The size of the error
- How long the problem has existed for.

However, all of these factors can be taken into account by the model by adjusting either the error rate itself or by entering different values for the size of the re-screening sample. This is explained in more detail in section 4.

2.3 Costing Methods

Having constructed the re-screening model to reflect activity and outputs, costs were added to the spreadsheet.

One method would have been to simply use previously derived costs per slide for the normal screening process and add this to the model assuming the simple relationship that the costs of a re-screen would be a function of the fixed cost per slide and the number of slides re-screened. However, as we have already stated, the re-screening process, and particularly flow through the laboratory, are likely to be different form the normal screening process. As a result the cost per slide will vary from the normal screen and will also vary within re-screens depending on the error rate. We have therefore estimated costs for each stage of the screening process rather than for the overall process, which will allow these variations to be accounted for. As such these costs are considered to be more accurate reflections of resource use than "standard" unit costs quoted by laboratories.

Costs have been estimated using National Audit Office (NAO) data and current salary scales for cytoscreeners, BMR grades, (checkers) and pathologists. Only direct costs have been used at this stage, that is, excluding overheads and capital. The reason for this is that a re-screen will not typically have an opportunity cost in terms of these cost components.

The costs for each stage of the screening process were derived using the following steps:

1. NAO average costs per slide were disaggregated into labour costs and laboratory costs.

2. Laboratory costs were then calculated on a "per view" basis, that is a cost for each stage of the screening process.

3. Labour costs were updated for current salary scales and also calculated for a "per view" cost.

4. A total unit cost for each stage of the screening process was then made by adding steps 2 & 3

5. All screening costs have been calculated on the basis of 8 smears read per hour for primary screening, checking and pathologist. Rapid review costs have been calculated on the basis of 2 minutes per rapid review.

A summary of the costs used for each stage of the screening process is given in table 1

Table 1 - Cost per view labour, laboratory and unit costs for 4 stage screening process

	Labour Cost (£'s)	Laboratory cost (£'s)	Unit cost (£'s)
Primary screen	1.01	2.1	3.11
Rapid Review	0.27	2.1	2.37
Checking	1.72	2.1	3.82
Pathologist	4.92	2.1	7.02

The model has been constructed so that for any scenario inputted a unit cost per slide for the given re-screening exercise is calculated as is the cost per case detected for abnormal results.

The costs in the model reflect average costs. However, it is known that there is wide variation in the costs of cervical screening across UK laboratories[2] and as a consequence the costs of a re-screen may also vary. One of the centres that we contacted that has undergone a re-screening exercise reported that quotes from external laboratories for re-screening cervical smears ranged from £1.50 to £10 per slide. It is therefore useful to make comparisons of cost at different levels and some tables in the analysis show both average costs derived by the model and also 10th and 90th percentile costs derived from the NAO cost data. Cost per slide for the 10th and 90th percentiles are £4.10 and £8.90 respectively.

Re-screening exercises incur additional costs other than the actual cost of the screening itself. If a problem is found, legal costs and administrative costs (essentially the costs of sending letters to patients and GPs) will be incurred. If a public exercise ensues, then additional costs for the provision of services such as telephone helplines will arise. These elements have been costed separately using data supplied by Centre A and are summarised in table 2.

Table 2 – Additional costs of a re-screening exercise

Item	Cost (£'s)
Helpline – phone points, phone lines, handsets	2,304
Legal fees	9,860
Postal costs	225
Other items	46
Total	12,435

These costs were associated with a re-screening exercise of just under 10,000 slides and add an estimated additional cost of £1.25 per slide re-examined.

3. Sampling to Establish the Scale of the Problem

It should be emphasised that the model itself does not estimate the scale of the problem. This will need to be done by an initial audit or re-screening exercise. Once sample data is available to estimate the scale of the problem the error rates can be inputted in to the model. The model can then be used to estimate costs and likely numbers of patients in different outcome categories. The statistical aspects of a typical sampling exercise are summarised below:

Table 3 - A sampling example

Sample Size (N)	2000
Moderate or Severe cases discovered (A)	10
Error rate – central estimate (P=A/N)	0.005
Upper confidence limit	0.0081
Lower confidence limit	0.0019
Total number of slides to be re-screened	10,000
Central estimate of moderate or severe cases (P x 10,000)	50
Upper confidence interval for severe cases.	81
Lower confidence interval for severe cases.	19

The formulae for establishing the upper and lower 95% confidence limits for the error rate are:

Upper confidence interval for error rate $U = P + 1.96x \sqrt{(Px(1-P)/N)}$

Lower confidence interval for error rate $L = P - 1.96 x \sqrt{(Px(1-P)/N)}$

These formulae give the confidence interval for the error rate and are valid when the calculation of Px(1-P)xN is greater than 5. The upper and lower confidence intervals for the actual number of cases likely to be detected in a full re-screen are established by multiplying the upper and lower estimates of the error rate by the total number of smears (in our example this was 10,000).

The importance of sample size in the estimation of the scale of the problem cannot be over estimated. For example, if a sampling exercise is done which finds an error rate of 0.5% i.e. 1 in 200, the confidence intervals can be quite wide if the sample size is less than 2000. This is illustrated below.

Table 4 - Confidence intervals for different sample sizes where the error rate discovered is 1 in 200 (i.e. 0.50%)

Confidence intervals for the likely numbers of moderate / severe cases detected in a 10000 rescreen for different sample sizes where the error rate discovered is 1 in 200 (i.e. 0.50%)			
Sample Size	Lower Confidence Interval	Central Estimate	Upper Confidence Interval
200	0	50	148
500	0	50	112
1000	6	50	94
2000	19	50	81
5000	30	50	70
10,000	36	50	64

Recommendation - There is extreme variability around the central estimate when sample sizes are small. It is recommended that a statistician should be involved in establishing whether the error rates detected are significant.

4. A Model Example

4.1 Example of basic results

Figure 1 shows the main input and output variables from the model. The cells with bold borders are the variable sample size and error rates.

Figure 1 – Re-screening model input and output screen

Cervical rescreening model					
Inputs in blue, data from other Notes denoted by numbers,					
Key Inputs					
Suspected level of error following sampling exercise		Central Estimate	Upper CI	Lower CI	
Sample Size (n)	2000				
Moderates or worse (a)	10				
Borderline / mild	58				
For moderates or worse p = a/n	0.00500				
Moderates or worse	50	50	81	19	
	0.50%	0.50%	**0.81%**	**0.19%**	The confidence interval calculations are valid if p*(1-p)*n > 5 --------->
Borderline / mild	290	290			9.95
	2.90%	2.90%			
Total number of smears to be rescreened	10,000				
Normal error rates					
Primary screen	90% b				
Rapid review	90% b				
Checker	95% b				
Pathologist	99% b				
Outputs		Central	Upper	Lower	
Cases detected					
Moderates/severes		47	75	18	
Borderline/mild		270	268	268	
Rescreening costs		£56,558	£56,374	£55,870	
Cost per case detected (moderate + severe only)		**£1,215**	**£754**	**£3,168**	
cost per case - all		£179	£164	£195	

A user should enter data into the 4 cells with a border i.e.:

- Sample size for the sample undertaken.
- Percentage error discovered in moderates and severes.
- Percentage error discovered in borderline and mild.
- Total number of smears to be re-screened.

This data together with the unit cost data (cells M95 and N95 in Appendix 3) allows the calculation of the expected number of cases that would be detected in the full re-screen and the costs.

The output section shown in Figure 1 gives

- the expected number of moderate, severe, borderline and mild cases.
- the re-screening costs and
- the costs per case detected.

In the example shown the cost per moderate or severe case detected is £1,215. Given the uncertainty in the error rate following the sample of 2000 this could range to anything from £754 per case detected to £3,168. This example serves to illustrate the importance of both the sample size and the error rate in determining the likely cost per case detected.

4.2 Sensitivity Analysis of the Impact of Error Rate and Sample Size on the Cost per Moderate or Severe Case Detected

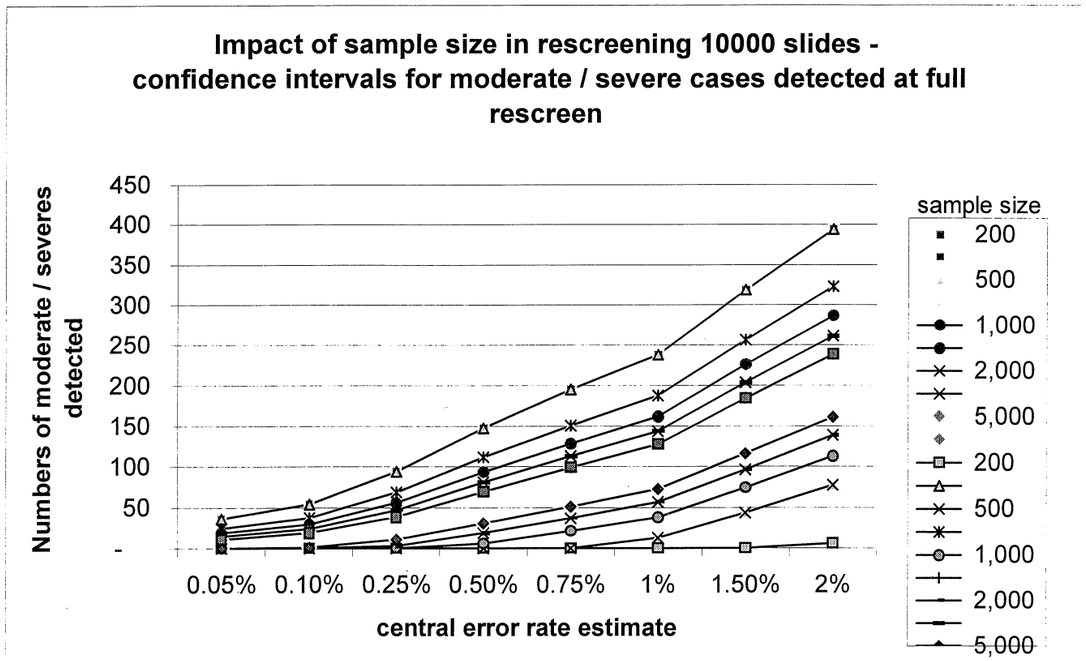
We have undertaken a sensitivity analysis on the number of moderate and severe cases that might be detected at a full re-screen of 10,000 slides given:

a) variations in the central error rate estimate

b) variations in the sample size undertaken to establish this error rate estimate.

Figure 2 shows that the lower the sample size the wider the confidence intervals in the number of cases detected. With a sample size as small as 2000 for example, even an error rate of 2% (1 in 50) would still give estimates of the likely numbers of cases detected at a full re-screen of between 0 and 400.

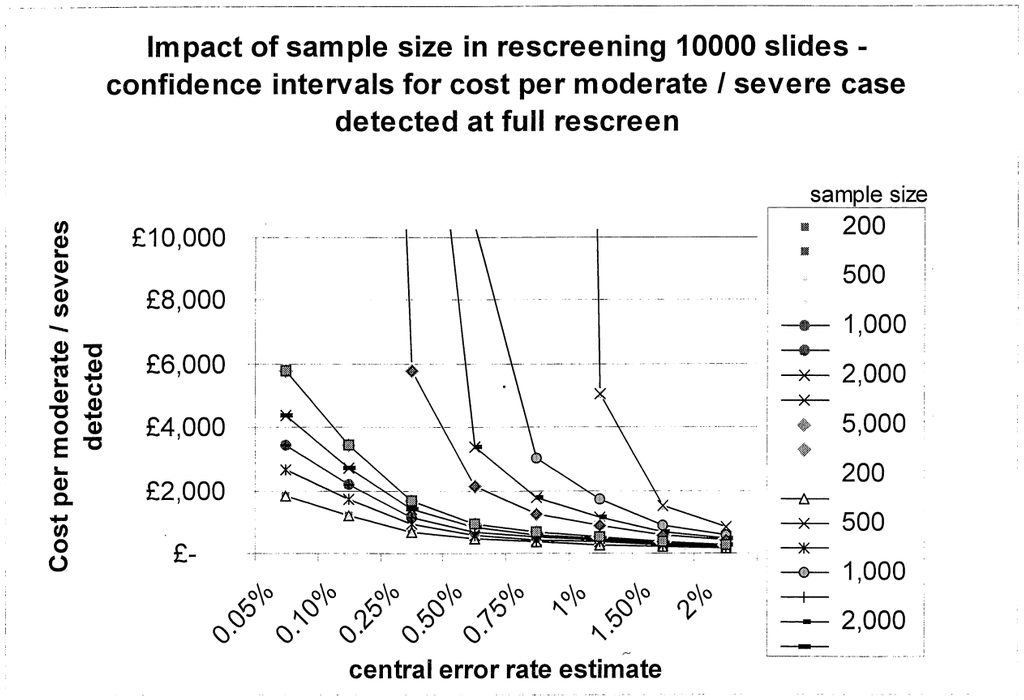
Figure 2 Impact of sample size in re-screening 10000 slides on cases detected



Having undertaken this sensitivity analysis we would certainly recommend that for a re-screen as large as 10,000 a sample size of around 2000 would probably be necessary before deciding on a full re-screen exercise. However, all situations will vary and it is recommended that a statistician be brought in to establish a relevant sample size for the first sample.

Figure 3 shows confidence intervals for the cost per moderate or severe case detected for different sample sizes.

Figure 3 - Impact of sample size in re-screening 10000 slides on cost per case



Even for the larger sample size of 5000, the confidence interval in the cost per moderate/severe detected can be very wide if the central error rate estimate is low. This again emphasises the need for careful consideration of the size of the initial sampling exercise before the decision about whether or not to carry out a full re-screen is made.

5. Model validation

In addition to the sensitivity analysis around sampling problems, a series of validation exercises were carried out to test the robustness of the model. This comprised entering the error rates detected in both the reference model (centre A) and two other re-screening exercises (centres B & C). The results in each classification category for smear results produced by the model was compared with those actually found in the re-screen. The results of these validation tests are given below.

A comparison of the actual re-screen results and those produced by the model for centre A (reference model) is given in table 5.

Table 5 - Comparison of actual and model results for each category of cervical smear outcome - Reference model (centre A)

	Actual	%	Model	%	Difference	%
Negative	9578	96.52	9590	96.64	-12	-0.12
Inadequate	12	0.121	23	0.22	-11	-0.099
Borderline	288	2.9	170	1.7	118	1.2
Mild Dyskaryosis	0	0	99	1.0	99	-1.0
Borderline + Mild	**288**	**2.9**	**269**	**2.7**	**19**	**0.2**
Moderate Dyskaryosis	28	0.282	23	0.24	5	0.042
Severe Dyskaryosis	12	0.12	15	0.15	-3	-0.03
? Invasive	0	0	1	0.01	-1	-0.01
Glandular Neoplasia	5	0.05	2	0.02	3	-0.03
Moderate or worse	**45**	**0.452**	**41**	**0.42**	**4**	**0.032**
Total	9923		9923			

There are two main points to consider when comparing the actual and model values in each category. Firstly, the actual values are the final values of a re-screen and therefore represent the 100% outcome of the screening process. Any erroneous results, for example additional undetected false negatives, cannot be identified from the data provided. The model however, has been constructed assuming that 100% of abnormalities cannot be detected. The screening assumptions of, for example 90% of negatives remain negative after rapid re-screening, have been incorporated. As a result the model will always produce slightly smaller estimates than the actual data as a degree of error is built in to each stage of the screening process which precludes the identification of all false negative results.

Secondly, there are differences between actual and model values in individual outcome categories. This is because the error rate has been entered on the basis of 2 broad categories only (borderline/mild, moderate or worse) and not as error rates for specific categories. However, these differences may be of small consequence if it is assumed that the clinical management is the same within these broad categories. So, although there is an apparent difference between, for example, borderline and mild categories in the actual and model values presented, the total number and proportion in this broad category is actual similar.

The same is true for the broad categories of negative/inadequates and moderates or worse. In reality, the actual spread between individual categories within these broad bands could be quite variable. We are therefore confident that, within the broad categories which reflect clinical

management choices, the model is robust in its ability to accurately estimate the likely number of cases that will be detected for a given error rate.

The modelling exercise was repeated for two other re-screening exercises. These are presented in tables 6 and 7.

Table 6 - Comparison of actual and model results for each category of cervical smear outcome - (Centre B re-screen)

	Actual	%	Model	%	Difference	%
Negative	8254	98.5	8254	98.5	0	0
Inadequate	12	0.14	20	0.2	-8	-0.06
Borderline	62	0.74	47	0.6	15	0.14
Mild Dyskaryosis	18	0.22	27	0.3	-9	-0.08
Borderline & Mild	**80**	**0.96**	**74**	**0.9**	**6**	**0.06**
Moderate Dyskaryosis	15	0.18	16	0.19	-1	-0.01
Severe Dyskaryosis	15	0.18	10	0.12	5	0.06
? Invasive	0	0	1	0.008	-1	-0.008
Glandular Neoplasia	0	0	1	0.17	-1	-0.17
Moderate or worse	**30**	**0.36**	**28**	**0.326**	**2**	**0.034**
Total	8376			8376		

The Centre B model shows similar results to the reference model and produces the same proportions of cases detected in the broad categories for both actual and modelled values.

Table 7 - Comparison of actual and model results for each category of cervical smear outcome - (Centre C re-screen)

	Actual	%	Model	%	Difference	%
Negative	5655	87.8	5941	92.2	-286	-4.4
Inadequate	265	4.1	15	0.2	251	3.9
Negative & inadequate	**5920**	**91.9**	**5956**	**92.4**	**-36**	**-0.5**
Borderline	350	5.4	267	4.2	82	1.2
Mild Dyskaryosis	105	1.6	156	2.4	-51	-1.8
Moderate Dyskaryosis	21	0.33	34	0.53	-13	-0.2
Severe Dyskaryosis	36	0.56	22	0.34	14	0.22
? Invasive	3	0.05	2	0.023	1	0.027
Glandular Neoplasia	5	0.08	3	0.05	2	0.03
Total	6440		6440			

The final example reveals a much larger proportion of inadequate results in the actual values obtained from a re-screen although the total proportion of negatives andin adequates remains similar. The model is sufficiently flexible that this can be accounted for and adjustments made for any scenario where it is envisaged that the relative proportions of negatives to inadequates is likely to be substantially different from the reference model.

The analysis comparing the estimated outcomes produced by the model with those found in previous re-screening exercises show a high level of agreement. The model can produce a different distribution across specific outcome categories. However, for the broad categories which are significant in terms of clinical management, the results are robust. We are therefore confident that the model developed is an accurate and valid representation of the screening process for mass re-examination of previously screened cervical smears.

6. Model results for typical re-screening scenarios

6.1 Basic results

Typical scenarios entered into the model provide estimates of the expected number of additional abnormal cases detected for different sizes of re-screening exercise.

The values in tables 8 and 9 have been estimated using a reference error rate corresponding to that found in the reference re-screening exercise. This corresponds to 0.45% for moderates or worse and 2.9% for borderline or mild cases. Detection rates at each stage (screener, checker, pathologist) have been calculated using the national standards e.g. 85-95% of negatives confirmed as negatives after rapid review.

Table 8- Outputs From Re-screening Range 10000 - 100000 Using Reference Error Rates

	Negative	inadequate	b/line	mild dyskaryosis	moderate dyskaryosis	severe dyskaryosis	invasive	glandular neoplasia
10000	9664	23	171	99	24	15	1	2
20000	19328	47	342	199	47	31	2	4
30000	28992	70	513	298	71	46	3	6
50000	48321	117	854	497	118	77	5	10
100000	96641	234	1709	994	237	154	10	21

As expected there is a linear relationship between the size of re-screen and the number of cases detected when the error rate is fixed. Similarly the total cost of re-screening increases in a linear fashion as cost per case is constant for any given error rate. This is illustrated in table 9.

Table 9 - Costs For Re-screening Of Slides Range 10000 - 100000 Using Reference Error Rates

	Total cost	Cost per case Moderate or worse	Cost per case All abnormals	Total cost 90th percentile*	Total cost 10th percentile*
10000	£60,602	£1446	£194	£88,900	£41,000
20000	£121,204	£1446	£194	£177,800	£82,000
30000	£181,806	£1446	£194	£266,700	£123,000
50000	£303,009	£1446	£194	£355,600	£164,000
100000	£606,020	£1446	£194	£889,000	£410,000

*using data from the NAO survey. These unit costs will not vary with error rate.

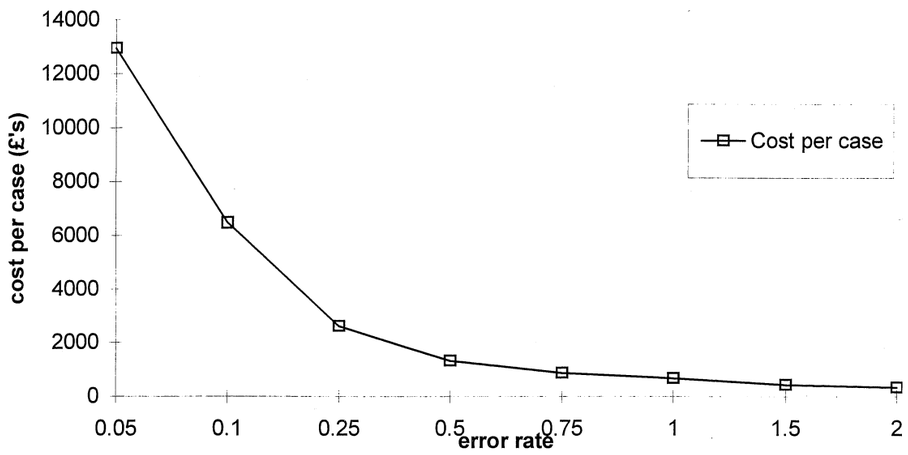
The principal choice to be made is at what size threshold does a major re-screening exercise become a cost effective option? The key factor is the number of slides to be re-screened. However, the choice will also be influenced by the size of the error itself. This is illustrated in table 10 and figure 4.

Table 10 - Impact Of Different Suspected Error Rates For Moderate Or Worse - 10000 Re-screen.

% Error Rate	Number of cases detected	Cost per case at model unit costs .(£'s)	Cost per case at 90th percentile costs (£'s)*	Cost per case at 10th percentile costs (£'s)*
0.05	5	12,945	17,780	8,200
0.1	9	6,477	9,877	4,555
0.25	23	2,596	3,865	1,783
0.5	47	1,303	1,891	872
0.75	70	871	1,270	586
1.0	93	656	956	441
1.5	140	440	635	293
2.0	186	332	478	220

*using data from the NAO survey. These unit costs will not vary with error rate.

Figure 4 - Cost per case detected (moderate or worse) for different levels of error



In this scenario the error rate for one category, for example moderates or worse, is varied whilst the rate for the other category (borderline/mild) remains constant. There is an exponential relationship between the size of the error and the cost per case detected, that is, as the error rate becomes smaller, the cost of identifying each additional case becomes progressively larger. Here the choice to be made is at what point the cost of detecting an additional case outweighs any benefits to be gained from detecting that case.

The costs per case detected also vary if both categories of error change. This is illustrated in table 11.

Table 11 - Impact Of Varying Suspected Error Rates For Borderline Or Mild And Moderate Or Worse On Cost Per Case Detected (Moderate Or Worse) - 10000 Re-screen.

Moderate or worse	Borderline or mild					
Error rate	0.5	1.0	2.0	3.0	4.0	5.0
0.05	£12510	£12601	£12782	£12963	£13144	£13324
0.1	£6260	£6305	£6395	£6486	£6576	£6667
0.25	£2509	£2527	£2564	£2600	£2636	£2672
0.5	£1259	£1268	£1286	£1304	£1322	£1341
1.0	£634	£639	£648	£657	£666	£675
1.5	£426	£429	£435	£441	£447	£453

The cost per case detected for moderate or worse increases as the size of the error for that variable decreases and also as the size of the error for borderline/mild cases increases even when the moderate or worse error remains fixed. This reflects the additional slides examined during the process from primary screen to pathologist stage and hence the additional costs incurred during the screening process. There is wide variation in costs per case detected ranging from in excess of £10000 where error rates are small to less than £500 where error rates are large. This matrix can be expanded for a greater number of combinations and from this a suitable threshold for re-screening could be identified.

6.2 Effects of adding costs of a public exercise

All the costs presented so far reflect only the re-screening process itself. However, if the size of the error is sufficiently large and weighted towards moderate dyskaryosis or worse necessitating the recall of a large number of women for either repeat smear or further investigation then additional costs will be incurred as a result of the re-screening exercise becoming public. We have attempted to quantify these additional costs, however complete data for the additional costs of a public exercise were only available from one centre (Centre A). This centre provided costs for administration, telephone helplines and legal fees and these accounted for an additional £1.25 per slide rescreened.

Table 12 shows the additional estimated costs that may result from a public re-screening exercise.

Table 12 - Additional Estimated Costs Of A Public Re-Screening Exercise For Different Sizes Of Re-Screen

Size of re-screen	Total cost at model unit cost - internal (£s)	Additional cost of public exercise (£'s)	Total cost at model unit cost - public (£s)
10000	60,602	12,500	73,102
20000	121,204	25,00	146,204
30000	181,806	37,500	219,306
50000	303,009	62,500	365,509
100000	606,018	125,000	731,018

The results show that a public re-screen adds considerable costs to the exercise. However, these figures should be interpreted with caution. The additional costs have been based on a single re-screening exercise and are hence, limited in their generalisability. Furthermore, there may be economies of scale as the size of the re-screen increases. For example, the costs of providing telephone helplines may be the same or similar for a 10,000 or 20,000 res-creen and this would produce a reduction in the additional costs per slide. In the absence of any other data these economies are, at present, impossible to quantify. Nevertheless these estimates do illustrate the magnitude of increase that is possible if a public re-screening exercise is undertaken.

6.3 Use of rapid review as a primary screening process

All of the scenarios described so far have been analysed using the standard screening model of a primary, full screen of slides followed by rapid review of negatives as an internal quality control mechanism. However, it is possible that, for the purposes of a mass re-screen of slides that have already been through the normal screening process once, rapid review as a primary screen could provide an effective an less costly means of detecting additional false negative smears which require further review. This is a process similar to rapid pre-screening where cervical smears are rapidly viewed as the first stage in the screening process to detect slides with potential abnormalities which are then examined in more detail. It has been suggested that this is a useful way of, for example, clearing a backlog of slides to ensure that patients with abnormal results are offered early treatment[9].

The extent to which this is a viable alternative to the full screening process depends on the sensitivity of rapid review, that is, the ability to detect smears with abnormal cells present. A review of the literature has shown wide variation in the reported sensitivity of rapid review as both a pre-screening and quality control tool. Estimates have ranged from 100%[9] to 54%[10] sensitivity for moderate and severe abnormalities. Sensitivity for low grade lesions (borderline or mild changes) tends to be lower[9]. There is also variability in sensitivity between individual screeners[11].

Clearly, with such variation in sensitivity, the use of rapid review without full primary screening remains questionable. Nevertheless it would be useful to provide some comparison of a rapid review based re-screen with the full re-screening process described so far. We have therefore adapted the spreadsheet model to one in which rapid review is the first stage in the re-screening process. We have then run this model, using the reference error rates, for different levels of

sensitivity reported in the literature. For each of these scenarios the cost per case detected for moderate or worse results and the total cost of a 10,000 slide re-screen have been calculated. The results are presented in table 13.

Table 13 - Effects of using rapid review as the primary screening method on total cost and cost per case detected – 10000 slide re-screen

Sensitivity	No. moderate & severe cases detected	No. moderate & severe cases present	Cost per case (£'s)	Total cost of re-screen (£'s)
100%[9]	42	45	716	30,302
92%[12]	39	45	773	30,114
88%[13]	37	45	806	30,020
67%[11]	28	45	1041	29,526
54%[10]	23	45	1279	29,221

Using rapid review only as the primary screening method produces a substantial reduction in costs when compared to the full re-screening model estimates for a 10000 slide re-screen of a cost per case of £1446 and total costs of £60,602. Where a high sensitivity is achievable this may be a more cost-effective option. However, if sensitivity is low then although costs are reduced there is a high chance of some cases of moderate or severe abnormalities remaining undetected. It is also likely that a much larger number of low grade abnormalities will remain undetected although this may be of less clinical significance. If rapid review as a primary screening method were considered for a re-screening exercise then it would be prudent to only use laboratories that have already made, or are willing to make, robust estimates of their sensitivity for this technique.

7 - Impact of re-screening on morbidity and mortality

7.1 Introduction

The principle outcome measured in this study is additional abnormal cases detected. There are, of course, other potential consequences and a re-screening exercise will have cost and health implications that go well beyond the identification of cases. Costs will be incurred by the additional investigations, tests and surgery where required. Additional outcomes in terms of mortality (for example, life years saved from detecting an abnormality at re-screen that could have progressed if left until the next routine screen) or morbidity (for example, avoiding a hysterectomy by detecting an abnormality early enough to be treated locally) could also be present. Knowing these longer term costs and outcomes would be useful to decision makers and so the possibility of extending the basic re-screening model was investigated. However, incorporating these effects into the model proved too complex to perform within the remit of this project. A number of factors influence the process of trying to estimate these additional outcomes including:

- How long the screening problem has existed for (and hence how long false negative smear tests have been undetected for)
- Whether the problem is a single screener or whole laboratory problem
- The normal screening interval - 3 years or 5 years
- The uncertainties around the relationship between an abnormal cervical smear and progression to disease (or not)
- Variation in progression rates where disease does occur.

The result of the uncertainties around each of these factors means that a complex model would need to be developed which could take account of all these facts and produce reliable estimates of mortality and morbidity outcomes. We have taken advice from experts in this field who have confirmed that at present no such model exists and that to produce one would entail a substantial amount of work.

We have nevertheless produced some preliminary ideas about how such a model could be developed and these are presented below. However these should be viewed as a first step only and hence as a simple framework from which a more substantive and accurate model could be developed.

7.2 Model Structure

The basic model structure would be based around referral patterns following the findings at re-screen. Expert opinion was sought to discover these referral patterns, and a simplified clinical pathways model was produced from these consultations. This is given in figure 5 overleaf.

From these basic pathways it would be relatively simple to estimate the costs of referrals if service data were available. However, estimating mortality reduction from such a model is much more difficult due to uncertainties in defining the course of the disease itself and how changes in the time of discovery impact on disease progression. Despite these problems we have attempted to produce what should be considered as the simplest possible but clinically plausible model of health and outcome gains from re-screening.

A spreadsheet printout of the model, using hypothetical data, is given in appendix 4.

The model only estimates costs and benefits from patients classified as having moderate or severe cervical abnormalities following re-screen. It also ignores the consequences associated with women who are referred to a repeat smear in 6 months.

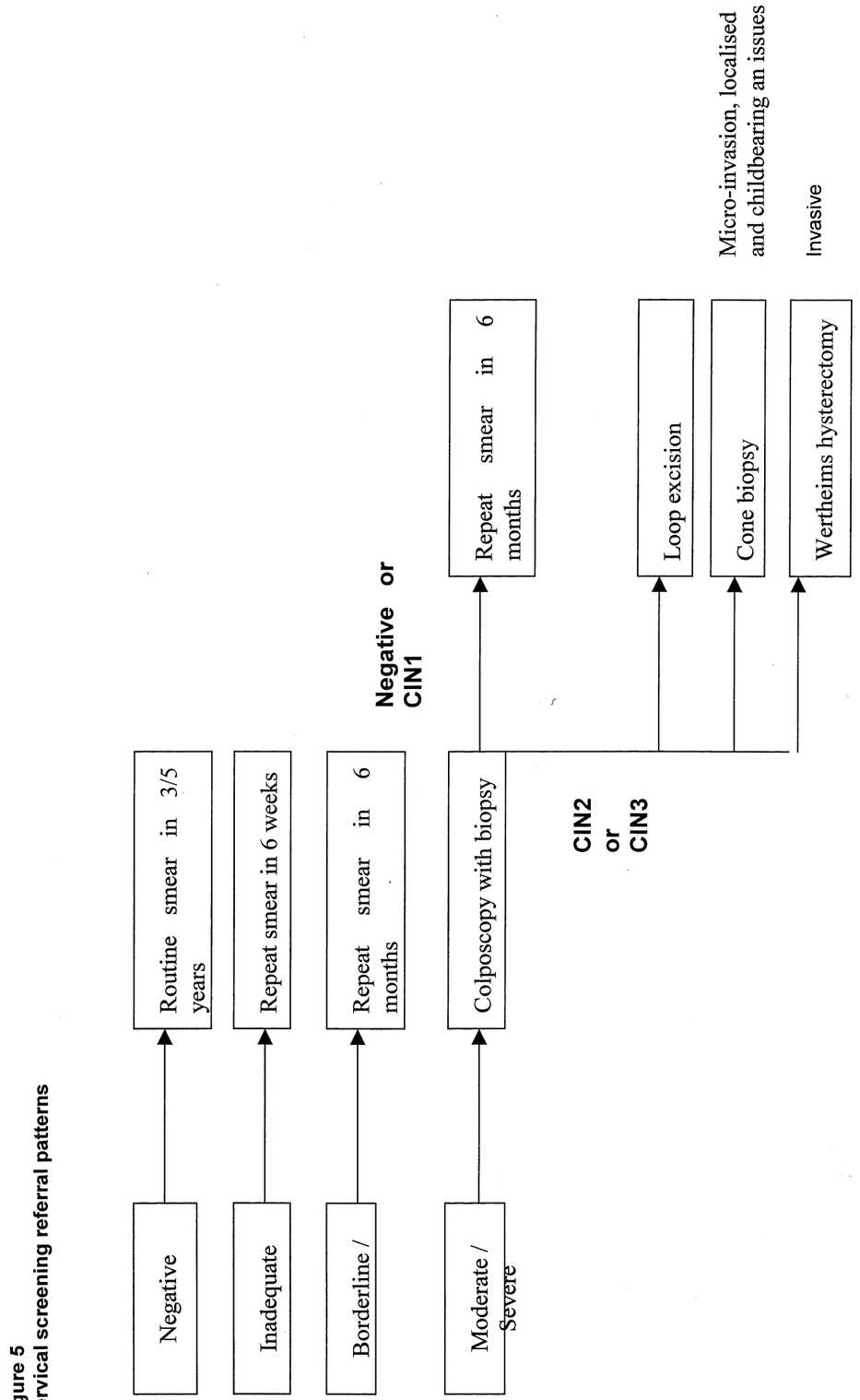


Figure 5
Cervical screening referral patterns

The health benefits of earlier detection are accrued by (a) a shift in diagnosis pattern at colposcopy , that is, a greater proportion of CIN2 or 3, and (b) a shift in referral patterns to surgery, that is, a greater number of invasive cancers requiring hysterectomy.

A key assumption is that life expectancy for each type of referral is the same for the re-screen and no re-screen scenarios. So, even if the disease has progressed as a result of the original error, as long as the referral and treatment is the same, then life expectancy is not changed.

7.3 Data requirements

Data on the normal clinical pathways following cytological findings are thought to exist, and preliminary contact was made with the British Society for Colposcopy and Cervical Pathology to identify recent audit data. Accurate data on life expectancies for an average woman completing each type of referral and treatment would be difficult to find although crude literature estimates which could be supplemented with clinical opinion may be available. Sufficiently accurate cost data for diagnostic and treatment procedures is available from NHS trusts.

The extent to which delays in cytological diagnosis impact on disease progression and treatment is unknown at present and hence would require further modelling. Similarly the size of the delay in producing the correct cytological diagnosis is unknown and can only be known when the full nature of the problem has been discovered, that is, after the re-screening exercise has been completed.

7.4 Limitations of the model

The structure of the model is considered to be clinically credible although fairly simplistic. The estimation of life years gained is very simplistic and excludes many potentially important issues.

We contacted colleagues at the Clinical Operational Research Unit, University College London, who are currently undertaking a large scale programme of modelling on cervical cancer[14] and asked their opinion on the task of estimating outcomes from cytological re-screening. They had serious reservations about the capability of any simple model producing useful approximations of outcomes. The principal concerns centred around the difficulties of modelling the complex dimension of disease progression. So, although disease progression is a key input into the model discussed here, it should be acknowledged that this has not been fully explored within the scope of this exercise.

There are also doubts about the value of such a model to decision makers. Disease progression, treatment shifts and mortality changes can only be estimated if the delay in cytological diagnosis is known. For example, if a problem in the screening process is quickly detected, and a re-screen undertaken promptly, then 3 or 4 years of progression could be avoided by not waiting until the next routine screen. If, however, the problem had existed undetected for several years then the interval could be much greater. The extent of the delay, and hence the effects, can only be established after a re-screen has taken place and as such this type of model cannot be used to aid the decision making process about whether or not to conduct a re-screening exercise.

7.5 Conclusion

It is possible to construct a simple model of clinical treatment pathways following cytological diagnosis but estimating outcomes is extremely difficult. Even if simplifying assumptions are used, the data required to populate the model are either not available (e.g. life expectancies) or require further modelling (e.g. disease and treatment progression).

Crucially, the costs and outcomes of the re-screen depend on the nature and size of the problem discovered at the re-screen itself. It is possible that the prior estimates of the size of the error used in the basic model could be used to inform an assessment of the possible outcomes of the problem. However, the resultant life-years model is not thought to be sufficiently robust to provide meaningful results given all the other sources of uncertainty.

8. Conclusions and Recommendations

Inconsistencies in the reporting of cervical smears result in major problems for the NHS screening programme. Failure to detect abnormalities that could potentially result in serious disease have consequences for both individual patients and the screening service as public confidence is diminished. The screening process has limitations and, at present, is conducted in such a way that there is inevitably a margin of error and hence, inaccurate test results as either false negatives or positives will always be present. The critical factor is determining at what point any suspected error rate falls outside acceptable limits. At this point the screening process could be considered to have failed and some action may be required.

Historically, the remedial action taken when such a situation exists has been to undertake a mass re-screening of smears to detect any abnormalities that have previously been reported as negative. As this report has shown, this incurs considerable costs to the NHS. Furthermore, depending on the scale of the problem and the size of the error, the costs in identifying a single additional abnormal case can be very variable. The major issue then is to find some way of determining at what point the costs of undertaking a major re-screening exercise are justified in terms of the likely detection of additional abnormal cases. This is further complicated by the degree of abnormality detected. Patient consequences are likely to be significantly different if a screening problem is failing to detect serious abnormalities rather than mild abnormalities which have a high chance of spontaneous regression. Re-screening because of the later problem could, in fact, result in some women being treated for abnormalities that may have disappeared by their next routine screen. Conversely, serious abnormalities that remain undetected for a long period of time present the risk of development of serious disease that, if treated early, could be prevented.

The decision about whether or not to re-screen slides where a reporting problem has been identified is not an easy one to make. There is no single combination of factors that can be identified which will determine at which point a re-screen should take place and this study cannot provide a definitive answer to this question. Furthermore, this report has only considered the re-screening process itself. However, if a re-screen does take place there are longer term consequences for the screening service that also need to be considered. One service that has conducted a mass re-screening exercise has identified post re-screen effects that result from loss of confidence and low morale which include:

- Experienced cytoscreeners leaving the service
- Increased caution in the screening process resulting in an increase in the number of suspected smears being passed to the checking and pathologist stages
- Decreased efficiency as new cytoscreeners are recruited and trained – a process that can take up to three years.

All of these factors will have an effect both on costs and efficiency, that is, a laboratory's ability to cope with a specified workload, however to estimate the true cost of these effects would require a separate exercise.

What the work presented here can do is provide a method for estimating the likely costs and effects, in terms of additional cases detected, of a re-screening exercise before it takes place. The model developed here can provide important information which take account of both the scope and degree of error that is potentially present. This, in conjunction with other pertinent local issues, can then inform the decision making process. However, the decision about whether or not to proceed with a re-screen is ultimately one that has to be made by the providers of the screening service and those who purchase that service.

We recommend that the following factors be taken into account when assessing the need for a major re-screening exercise.

- The need to establish the significance of a potential error before any re-screen cannot be overemphasised. The critical factor here is whether or not an error detected is sufficiently

greater than that which is within acceptable limits to be off concern. Where the error rate detected is at the margin, and therefore small, the costs of detecting each additional false negative will be very high.

- Consideration should also be given to the degree of error, that is, whether it is mild or severe abnormalities that are being missed. It is severe abnormalities that present the most risk to patients and this should be the primary focus of any decision about the need for a re-screening exercise.
- If mild abnormalities are the problem it may be more cost effective to recall women for a routine examination earlier. However, this option cannot be investigated using the model presented here.
- Once the significance of an error has been identified the model developed here should be used to provide estimates of the likely consequences in terms of both costs and outcomes. This will provide information of the outputs in relation to the size of the exercise to be undertaken. Help can be provided with this exercise if needed
- The major driver is the unit cost of a screen. Previous re-screens have reported wide variation in the costs quoted for re-screening slides. The model can estimate the likely financial impact of different costs before any decision about where to re-screen is made.

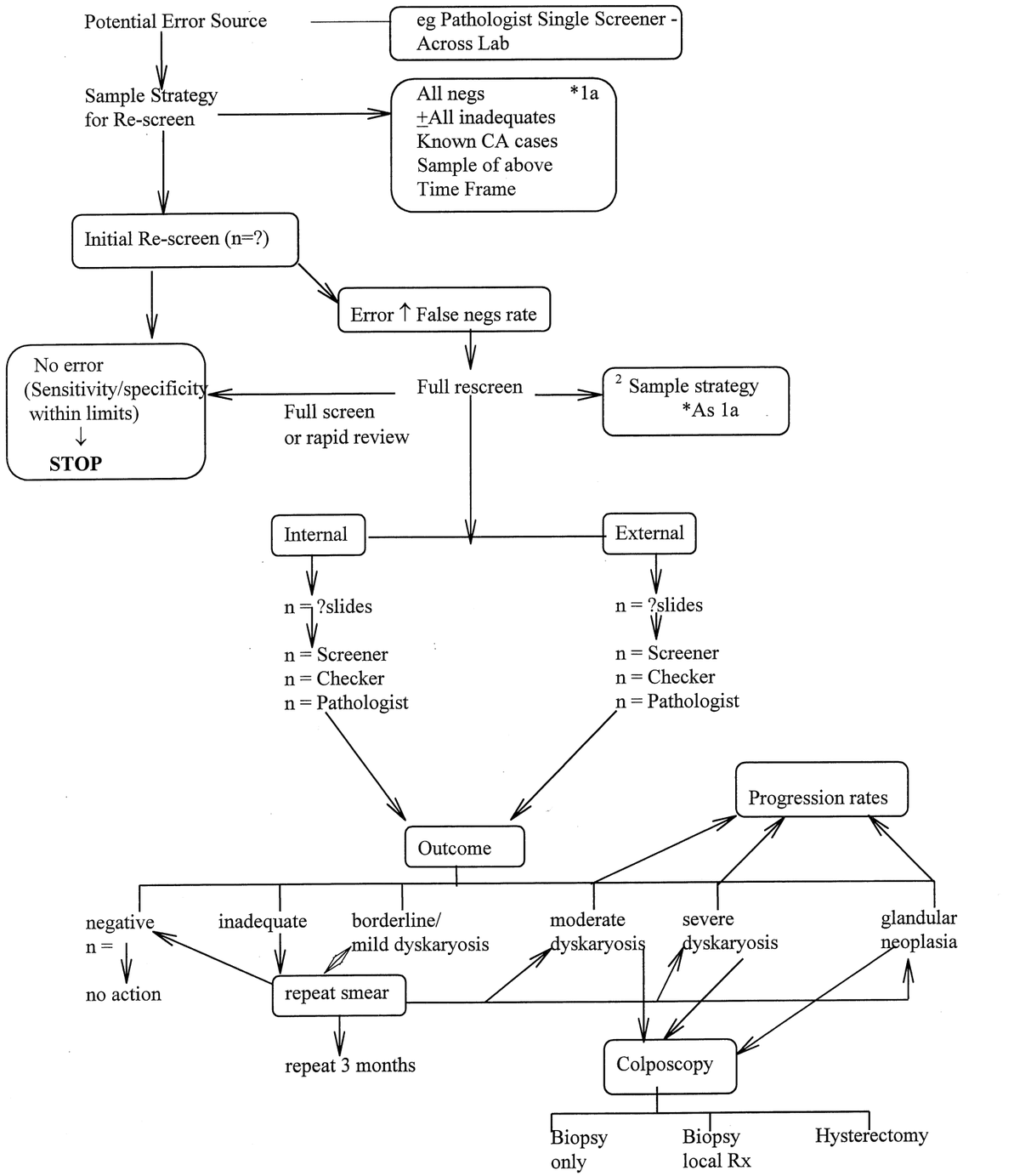
References

1. Herbert A. Achievable standards, benchmarks for reporting, criteria for evaluating cervical cytopathology. *Cytopathology* 1995; **6** supplement 2.
2. Report by the Comptroller and Auditor General. The performance of the NHS cervical screening programme in England. *National Audit Office* 1998; HMSO, London.
3. Gyrd-Hansen D, Holund B, Anderson P. A cost-effectiveness analysis of cervical cancer screening: health policy implications. *Health Policy* 1995; **34**: 35-51.
4. Kaminsky FC, Burke RJ, Haberle KR, Mullins DL An economic model for comparing alternative policies for cervical cytologic smear rescreening. *Acta Cytologica* 1995; **39**: 232-238.
5. Kaminsky FC, Burke RJ, Haberle KR, Mullins DL Rescreening policies in cervical cytology and their effect on detecting the truly positive patient. *Acta Cytologica* 1995; **39**: 239-245.
6. Raab SS. The cost-effectiveness of cervical-vaginal rescreening. *American Journal of Clinical Pathology* 1997; **108**: 525-536.
7. National Audit Office. Financial Audit: Costs of cervical cytology and colposcopy. 1997.
8. Department of Health. Cervical screening programme, England: 1996-7. Statistical Bulletin, 1997; London.
9. Baker A, Melcher DH. Rapid cervical cytology screening. *Cytopathology* 1991; **2**: 299-301.
10. Johnson SJ, Hair T, Gibson L, Ridley B, Wadehra V. An assessment of partial rescreening as an internal quality control method for cervical smears. *Cytopathology* 1995; **6**: 376-387.
11. Shield PW, Cox NC. The sensitivity of rapid (partial) review of cervical smears. *Cytopathology* 1998; **9**: 84-92.
12. Faraker CA. Partial rescreening of all negative smears: an improved method of quality assurance in laboratories undertaking cervical screening. *Cytopathology* 1993; **4**: 47-50.
13. Faraker CA, Boxer ME. Rapid review (partial rescreening) of cervical cytology. Four years experience and quality assurance implications. *J Clin Pathol* 1996; **49**: 587-591.
14. Sherlaw-Johnson C, Gallivan S, Jenkins D. Withdrawing low risk women from cervical screening programmes: mathematical modelling study. *British Medical Journal* 1999; **318**: 356-361.

APPENDIX I Normal Screening Process

Number of smears	91000								
Primary Screen								Unit Cost	Total Cost
Initial screen	Negative	Inadequat	Borderline / Mil	Moderate / severe		Source		£ 6.45	£ 587,060
	83.5%	4.0%	7.5%	5.0%	100.0%	England averages			
	75985	3640	6825	4550	91000			£ 3.11	£ 283,010
Rapid review of negative	75985								
	90.0%	4.7%	4.5%	0.75%	100.0%				
	68,387	3,571	3,419	570	75947			£ 2.37	£ 179,994
Rapid review of inadequate	3640								
	7.5%	90.0%	2.0%	0.5%	100.0%				
	273	3,276	73	18	3640			£ 2.37	£ 8,626.80
Total of primary screen process	68,660	6,847	10,317	5,138	90,962				
	75.5%	7.5%	11.3%	5.6%	100.0%				
			2.01						
Estimate of likely number of false negatives									
ie -ve or inadequate but should have been abnormal	using screener		using pathologist						
upper limit	95.0%								
	813		299						
lower limit	85%								
	2,727		1,003						
	5566								
Checker process									
Borderline / Mild	10,317								
	50.0%	5.0%	40.0%	5.0%	100.0%				
	5,159	516	4,127	516	10,317			£ 3.82	£ 39,411
	5.7%	0.6%	4.5%	0.6%	11.3%				
Moderate / severe	5,138								
	30.0%	4.0%	36.0%	30.0%	100.0%				
	1,541	206	1,850	1,541	5138			£ 3.82	£ 19,627
	1.7%	0.2%	2.0%	1.7%	5.6%				
	6,700	721	5,977	2,057	15,455				
	7.4%	0.8%	6.6%	2.3%	17.0%				
Pathologist									
	negative	inadequat	borderline	mild dyskaryosis	mod dyskaryosis	severe dyskaryosis	? invasive	glandular neoplasia	
Borderline / Mild	5,977								
	15.0%	0.0%	55.0%	25%	5%			100.0%	
	896	-	3,287	1,494	299	-	-	- 5,977	£ 7.02 £ 41,955
	1.0%	0.0%	3.6%	1.6%	0.3%	0.0%	0.0%	0.0% 6.6%	
Moderate / severe	2,057								
	0.0%	0.0%	15.0%	29.0%	25.0%	25.7%	1.8%	3.5% 100.0%	
	-	-	309	597	514	529	36	72 2,056	£ 7.02 £ 14,435
	0.0%	0.0%	0.3%	0.7%	0.6%	0.58%	0.04%	0.08% 2.3%	
	896	-	3,596	2,091	813	529	36	72 8,033	
	1.0%	0.0%	4.0%	2.3%	0.9%	0.58%	0.04%	0.08% 8.8%	
			5,686		**1,450**				
England average	83.80%	8.3%	4.0%	2.3%	0.9%	0.58%	0.04%	0.08% 100.0%	
Implied position	83.8%	8.3%	4.0%	2.3%	0.9%	0.58%	0.04%	0.08% 100.0%	
Treatment Options									
Routine follow up	76,256								
Repeat smear		13,255							
Colposcopy			1,450						

Appendix II. Algorithm for the Rescreening Process



Appendix III Cervical rescreening model

Inputs in blue, data from
Notes denoted by numbers,

Key Inputs

Suspected level of error following sampling exercise		Central Estimate	Upper CI	Lower CI	
Sample Size (n)	10000				
Moderates or worse (a)	45				
Borderline / mild	290				
For moderates or worse p = a/n	0.00450				
Moderates or worse	45	45	58	32	
	0.45%	0.45%	0.58%	0.32%	The confidence interval calculations are valid if p*(1-p)*n > 5 ------->
Borderline / mild	290	290			44.80
	2.90%	2.90%			
Total number of smears to be rescreened	10,000				

Normal error rates

Primary screen	90%	b
Rapid review	90%	b
Checker	95%	b
Pathologist	99%	b

Outputs	Central	Upper	Lower
Cases detected			
Moderates/severes	42	69	14
Borderline/mild	270	268	268
Rescreening costs	£60,600	£60,380	£59,890
Cost per case detected (moderate + severe only)	£1,446	£879	£4,138
cost per case - all	£194	£179	£212

Primary Screen

10,000

% found that are there to be found

	Negative	Inadequate	Borderline / Mild	Moderate / severe	Non-negative sub-total		Unit Co	Total Cost	% of total
			90%	90%	b				
True cases detected		0.0%	2.61%	0.41%	3.0%				
Extra suspected cases per slide seen		-	261	41	302		£ 3.11	£ 31,100	51%
		0.25%	1.25%	3.41%	4.9%	c			
Totals		25	125	341	491				
(% Total Review)	9,208	25	386	381	792				
	92.1%	0.3%	3.9%	3.8%	7.9%				

Rapid Review

Number of true cases undetected at this stage			29	5				
% found that are there to be found			90%	90%	b			
Number negatives smears	9,208							
(% Rapid Review)		0.0%	0.28%	0.04%	0.3%		£ 2.37	£ 21,822	36%
True cases detected		-	26	4	30				
Suspected cases per slide seen		0.01%	4.50%	0.75%	5.3%	d			
Totals	8,723	1	414	69	484				
(% Negatives review)	94.7%	0.0%	4.5%	0.8%	5.3%				
Number of inadequate	25						£ 2.37	£ 59	0%
		90.00%	2.00%	0.50%					
Suspected cases per slide	2	23	1	0	23				
Totals	8,725	23	801	450	1,275				
(% Total Review)	87.3%	0.2%	8.0%	4.5%	12.7%				

Checker process

Number of true cases included in this sample			287	45				
% found that are there to be found			95%	95%	b			
Number of smears	1,251						£ 3.82	£ 4,780	8%
		0.0%	21.8%	3.4%	25.2%				
True cases detected			273	42	315				
Extra suspected cases per slide seen		0.0%	1.88%	3.93%	5.8%	e			
		0	23	49	73				
Totals	847	0	311	94	404				
(% Check)	67.7%	0.0%	24.8%	7.5%	32.3%				
Totals 10000	9572	24	311	94	428				
(% Total Review)	95.7%	0.2%	3.1%	0.9%	4.3%				

Pathologist

% found that are there to be found			99%	99%	99%	99%	99%	99%	b			
	negative	inadequate	borderline	mild dyskaryosis	mod dyskaryosis	severe dyskaryosi	? invasive	glan neoplasi	Sub-total			
	404											
Total pathologist screen	92	-	171	99	23	15	1	2	404	£ 7.02	£ 2,838	5%
(% Total Review)	0.9%	0.0%	1.7%	1.0%	0.23%	0.15%	0.0%	0.021%	4.0%			
check 10,000												
Grand total	9,665		270		42							
	96.6%		2.70%		0.42%							
England average	83.80%	8.3%	4.0%	2.3%	0.9%	0.58%	0.04%	0.08%	100.0%			
										Totals	£ 6.06	60,600	100%

Treatment options

Routine follow up	Negatives	?	9,665
Repeat smear	inad/border/mild	?	294
Colposcopy	Moderate+	?	42
			10,000

Appendix 4 – Cervical screening life years model

Cervical screening life-years model

Summary	
Incremental cost of rescreening referrals	9,859
Incremental life-years gained from rescreening (discounted)	3
Incremental life-years gained from rescreening (undiscounted)	8
Cost per life-year saved (discounted life years)	3,277

Clinical pathways	*Referral patterns*		*Patient numbers*	*Expected life years per patient**	*Total life years*	*% numbers*	*Unit cost*	*Total cost*
Findings at re-screen								
Number of moderate/severes			100					
Colposcopy								
Proportion receiving colposcopy		99%	99				300	29,700
Proportion declining colposcopy		1%	1	20	20	1%		
Findings at biopsy								
Negative/CIN1	70%	69		21	1455	69%	0	-
CIN2/3	30%	30						
Referral								
Loop excision		80%	24	19	451	24%	300	7,128
Cone biopsy		5%	1	15	22	1%	2,000	2,970
Wertheims hysterectomy		15%	4	10	45	4%	5,000	22,275
Totals					*1994*	*100%*		62,073
			Total discounted life years		*1239*	*Total discounted cost*		62,073

Clinical pathways			*Patient numbers*	*Expected life years per patient**	*Total life years*	*% numbers*	*Unit cost*	*Total cost*
Findings at next screen (I.e. if re-screen did not take place)								
Number of moderate/severes missed at previous screen			100					
Proportion regressing to negative, borderline or mild	10%	10		21	210	10%	0	-
Colposcopy								
Proportion receiving colposcopy		99%	89				300	26,730
Proportion declining colposcopy		1%	1	20	18	1%		
Findings at biopsy								
Negative/CIN1	65%	58		21	1216	58%	0	-
CIN2/3	35%	31						
Referral								
Loop excision		79%	25	19	468	25%	300	7,391
Cone biopsy		5%	2	15	23	2%	2,000	3,119
Wertheims hysterectomy		16%	5	10	50	5%	5,000	24,948
Totals					*1985*	*100%*		*62,187*
			Total discounted life years		*1236*	*Total discounted cost*		*52,214*