The long and winding road from trial cost-effectiveness to cost-effective policy implementation

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Abstract

The introduction of screening programmes or changes to existing ones should be based on sound evidence of their effectiveness, feasibility and costs. A further prerequisite is that adequate mechanisms to monitor, maintain and improve quality are established. However, economic analyses designed to assess the cost-effectiveness of alternative screening strategies are typically based on the assumption that the option considered to be acceptable by policy makers would be rolled out nationally without much variation in practice.

In 1988 the NHS Cervical Screening Programme (NHSCSP) was set up using the Papanicolaou smear technology. Based on recent evidence in 2003 NICE produced guidance suggesting that liquid based cytology (LBC) should replace Pap smears. In addition, epidemiological studies have shown that Human Papilloma Virus (HPV) plays a major role in the development of pre-invasive and invasive cancer.

In this paper we explore scenarios for implementing changes to the existing cervical screening programme in England. Data were obtained from the ARTISTIC trial, which is examining the cost-effectiveness of HPV testing in addition to LBC in the NHSCSP. The trial is in Greater Manchester; it began in June 2001 and covers 25,000 women undergoing routine cervical screening.

From laboratory timing surveys carried out alongside the trial we have modelled strategies for implementing LBC screening within the existing NHS laboratory service. The same approach is applied to a hypothetical policy to include also HPV testing. Based on this work we can identify what types of additional evidence should be collected to improve the generalisability of screening trials.

Introduction

Screening as a method of early detection of diseases has played an important role in improving public health over the years. Although screening appears to be an appealing concept, the process of evaluating the appropriateness of a screening programme is not straightforward and should be carried out in view of the key criteria for adoption of such programmes. (1, 2)

Screening programmes for diseases are discretionary national programmes and as such they should be subjected to the highest of standards for evidence base. Policy makers increasingly demand evidence of the effectiveness, cost-effectiveness and feasibility of potential screening strategies. Once a strategy is approved a further prerequisite is that adequate mechanisms to monitor, maintain and improve quality are established. However, economic analyses designed to assess the cost-effectiveness of alternative screening strategies are typically based on the assumption that the option considered to be acceptable by policy makers would be rolled out nationally without much variation.

The purpose of this paper is threefold: 1/to explore the impact of introducing a new technology for cervical screening on the services providing the screening, 2/ to explore how options for implementation of a new programme relate to organisational service inefficiencies; 3/ to inform the economic analysis being carried out alongside an ongoing trial studying strategies for cervical screening in England with respect to data collection and analyses needed for improving the generalisability of the findings.

Background to the study

Screening for diseases

Screening as a form of secondary prevention of diseases has a very recent history. The first publications of the role of screening in the early detection of diseases are dated in the middle of the 20th century and the first centrally organised provision of such services was first introduced in the USA in the 1950s.

What identifies screening? Screening for diseases is a specific form of health service offered to the public and usually involves a simple and rapid test used to detect

diseases at early stages when there may be no obvious symptoms. Screening tests are not typically diagnostic tests; they only identify individuals with high probability of having a disease, so that further tests are needed to confirm the diagnosis. Screening affects large groups of individuals. It is either selective – targeting only high-risk groups, or mass screening – no selection is applied to the population groups.

Screening aims to provide benefits to three groups of individuals: 1/ those with the disease who are being screened and detected; 2/ those without the disease who are being screened and assessed as negative - they are reassured about the absence of the disease; and 3/ those who are not screened, but would benefit from the low prevalence of a disease, especially if it is communicable such as tuberculosis.

However, screening tests are not perfect. They may not be able to detect the disease in some individuals, or may wrongly present as positive in others. In addition, the process of screening may be unpleasant or posing some risk on the individual's health. Thus, the assessment of new screening programmes should relate both their benefits and harms against the cost. The UK National Screening Committee requires that a set of criteria should be met before screening for a condition is initiated. (See Table 1.)

The ARTISTIC trial

Cervical cancer is the second leading cause of cancer death in women around the world and the twelfth most common cause of cancer deaths in women in the U.K., where in 1988 the National Health Service Cervical Screening Programme (NHS CSP) was set up. Recently, NHS policy makers in England, Scotland and Wales have made various efforts to review the existing evidence and to commission prospective studies to provide further evidence on the benefits of new screening technologies for cervical cancer. Epidemiological studies have shown that Human Papilloma Virus (HPV) plays a major role in the development of pre-invasive and invasive cancer, thus the NHS HTA R&D Programme has funded a randomised controlled trial (ARTISTIC – A Randomised Trial in Screening To Improve Cytology) in order to examine the effectiveness and cost-effectiveness of HPV testing within the NHS CSP.

The trial is taking place in Greater Manchester and began in June 2001. The study population comprises 25,000 women aged 20-64 who are attending general practices for routine cervical screening. Women are randomised 3:1 to the HPV result being revealed (study arm) or concealed (control arm) and will be followed for two screening rounds at a 3-year interval. The first screening round was completed in 2003 and the second round began in July 2004.

The economic evaluation alongside the trial will provide evidence on the costs and benefits of adding HPV testing to the liquid based cytology (LBC) technology for smear taking, to estimate the effectiveness and costs of HPV as a stand-alone test, and address methodological and logistic issues of HPV testing from a NHS perspective. The benefit measures in the cost-effectiveness analysis will be in terms of high-grade smears detected, and extrapolated to estimate life-years gained and quality adjusted life years gained.

Assessment of changes to existing screening programmes

The core set of criteria, summarized in table 1, refers to the case of new screening programmes, while an existing screening programme may undergo a number of changes during the time of its operation. These may be related to adjustments of the programme as it is being widely implemented, or may reflect the developments in the knowledge about the disease and the availability of new technologies for prevention, detection and treatment of the disease. Thus, a screening programme is an evolving system rather than a fixed model of services.

The assessment in ARTISTIC is based on the assumption that if a given strategy is accepted by policy makers it will be rolled out nationally within the existing service structure. However, we have to take into account that when the trial began the existing services were configured around the use of the conventional Papanicoloau (Pap) smear technology, while in the trial smears are being taken and slides are being prepared using the LBC technology. In addition, although NICE recommended in 2003 that LBC should replace the conventional Pap method, (3) the new technology is only now being rolled out in local CSPs. Thus, for the duration of the remainder of the trial NHS cytology laboratories will be undergoing substantial technological

adjustments, and when the ARTISTIC results are reported in 2007 the economic analysis should be relevant to the screening offered at that point in time.

Methods

In the NHS, cervical smears taken from women in general practices, community clinics and hospital departments are transported to cytology laboratories for analysis. Within the laboratories there are two key stages: preparation of the specimens ready for analysis (i.e. slide preparation), and interpretation of the slides, this work being performed primarily by cytoscreeners.

Impact of LBC on laboratory cytoscreening workloads

We assessed the impact of LBC on the cytoscreening workloads in cytology laboratories by means of self-timed surveys. These were three one-week surveys held at three month intervals in November 2001, and February and May 2002 at the two laboratories taking part in ARTISTIC. The surveys in the larger laboratory covered both LBC and conventional screening activities. At the beginning of each survey week each smear reader was given an envelope containing about 80 forms and a stop clock. The smear readers were instructed to fill in a form for every slide receiving primary or secondary screening during the 5-day survey period. The form identified the type of cytology being used (conventional or LBC), type of screening being performed (primary or secondary), time in minutes for screening the slide using the microscope, and for reporting the results on the computer.

Scenarios for LBC policy implementation

We modelled best case/worst case scenarios for the implementation of the new LBC slide preparation technology within the NHS CSP. Data on the structure and workload of cytology laboratories were obtained from national statistics. The two main (and competing) manufacturers of LBC equipment and consumables are Surepath and ThinPrep®. In ARTISTIC ThinPrep® products are being used. Costs of ThinPrep® slide preparation based on leasing the equipment were obtained from the manufacturer. The quickest routes between laboratories within each geographical region, were estimated using their postcodes. Distances were obtained either from the official NHS web site or using the 'Travel and Driving Directions' service provided by www.multimap.com .

Results

Cytology laboratory workloads

Although there was a four-fold difference in the annual screening workloads of the two survey laboratories, their LBC primary screening workloads for the ARTISTIC trial were relatively similar. The mean total times for primary screening in the larger laboratory during the first survey were 7 minutes 25 seconds for Pap slides and 6 minutes 35 seconds for LBC slides, a statistically significant difference ($p<0.001$). The time saving of nearly 1 minute by the LBC method occurred during the microscopy examination of the slides. When considering LBC screening practice over time, in both laboratories the mean time spent on primary microscopy screening of LBC slides was reduced by almost 50 seconds ($p<0.001$) between the first and second surveys, but there was no further improvement between the second and third surveys. Finally, there was a 2-minute difference between the laboratories in the mean time spent on primary microscopy screening of LBC slides in each survey, the mean times overall being 5 minutes 2 seconds for the larger laboratory and 3 minutes 5 seconds for the smaller laboratory ($p<0.001$). Mean hourly primary screening rates (covering both time spent at the microscope and reporting times) were calculated. The mean hourly rate for Pap slides was 9 per hour; for LBC slides the hourly means were 12.4 slides in the larger laboratory and over 20 slides in the smaller laboratory.

LBC policy implementation

There were 156 cytology laboratories in England in 2000-2001 with a total workload of 4,089,440 slides. (4) However, laboratories varied in size and the number of slides screened with a mean of 26,214 (SD=13,614) slides (see figure 1). Two laboratories screened more than 80,000 slides, while 140 (90%) had a workload of 40,000 or less. The yearly workload of laboratories is related to the cost per slide according to the quotes obtained from the manufacturer. This can be explained with the capacity of the LBC equipment needed by the laboratories for the production of slides. ThinPrep® markets two types of prep machines: T2000 and T3000. The capacity for T2000 is 40,000 samples per year and for T3000 around 80,000. Also, T2000 is less automated, thus, more labour intensive. (5) Since the majority of laboratories have a relatively small capacity it appears that the configuration of laboratories will have significant impact on costs; savings may be achieved by concentrating slide preparation activities in fewer laboratories. We explored this further by carrying out

best case/worst case scenario analysis. Table 2 and figure 2 summarise the cost of preparation of a slide using either T2000 or T3000 and including the labour costs.

'Worst-case' scenario

The worst-case scenario assumes that although there is a case for economies of scale when the LBC technology is introduced, each laboratory in fact acts separately in the leasing and use of the prep machine. As a result laboratories with an annual workload of less than 20,000 tests would lease a T2000, and the rest would lease the fully automated T3000. The total annual cost of slides for this scenario will be £23,200,000, of which £1,200,000 is needed for staff operating the prep machines.

'Best-case' scenario

The best-case scenario assumes that it is possible that laboratories share workloads and prep machines so that the lowest cost per slide is achieved. We estimated that this is possible if T3000 machines are leased and used at their full capacity. The cost for this scenario is £19,400,000. When the labour cost is added the total sum reaches £20,240,000. In addition there will be some transport costs from the laboratories where the prep machines are based.

'Plausible case' scenario

The best-case scenario does not account for the geographical distribution of laboratories and thus a different scenario had to be developed. In this scenario laboratories within each geographical region were studied with regards to their proximity to other laboratories and their annual workload. The purpose was to identify a central site to place the prep machine, and satellite laboratories to achieve a given economy of scale. When there were no laboratories at less than 30 miles distance from a laboratory, it was assumed that it would adopt the cheapest option given its annual workload. We also assumed that if more than two laboratories are using the same prep machine it would be based in the laboratory with the optimum total driving distance. However, if two laboratories shared the equipment the cost would be independent of which one takes the central role.

Under this scenario we identified 55 central sites with varying numbers of satellite laboratories. Eight T2000 and 48 T3000 prep machines had to be leased with one site

leasing one machine of each kind. The total cost of the plausible scenario was £20,400,000, exceeding the best scenario by £160,000 only. Transport costs were not considered. Regions that most benefited from this scenario were London and the Northern and Yorkshire regions.

Table 3 compares the costs of the three scenarios and the type and quantity of prep machines that should be leased. The plausible scenario can save about £2,800,000 per year to the NHS CSP compared to the worst-case scenario where laboratories operate individually. Since screening programmes are long-term health expenditures we calculated the present value of these savings for the next 20 years using a discount rate of 3.5%. (See Fig. 3) Thus, the present value for the first five years will be £16,356,000, while for 20 years the savings go over £50 million.

Discussion

In this paper we explored the impact of a new slide preparation technology on the cervical screening programme in England. This work was carried out as a part of the economic evaluation alongside the ARTISTIC trial and aimed to inform the analysis on what additional data should be collected to improve the generalisability of the trial findings to the NHS CSP. LBC differs from the conventional cytology in two aspects: 1/ we observed shorter screening times for LBC slides, and 2/ unlike the conventional cytology, LBC used equipment with huge capacity, that exceeded the individual needs of cytology laboratories. Since LBC is being introduced in the UK at present and there is limited evidence on its impact on the workload within laboratories and the overall structure of cytology services in England, we modelled scenarios for its implementation to measure the variations in costs related to each scenario.

The immediate benefit from shorter LBC screening times will be increased productivity that will reduce the waiting for results by women. In the long-run the shortage of staff will be less of an issue especially in laboratories using the automated T3000. The inter-laboratory variations in screening rates that we observed have been reported elsewhere, for instance, in the Scottish LBC pilots, (5) and in the 1999 survey of conventional screening patterns in English cytology laboratories undertaken

by the National Cervical Screening Committee. (6) The pilot studies in England also reported shorter screening times and observed lower rates of inadequate smears. (7)

The first report from an English pilot study on the role of LBC in the NHSCSP (undertaken in three laboratories) estimated a one-off cost of between £10.1 million and £10.3 million for the conversion from Pap smears to LBC in England, which equates to a cost of approximately £73,000 for a local laboratory processing 30,000 tests per annum. (The pilot was undertaken at the request of NICE.) These figures include the cost of training smear takers and laboratory staff, producing training material, sending off a backlog of samples, and structural changes to the laboratory. However, NICE considered that the capacity of laboratories has been overestimated, because 75% of laboratories in England currently process fewer than 30,000 samples per annum. The centralisation of sample processing may be the most effective organisation of services. If sample preparation using LBC were to be centralised in regional laboratories, consideration would need to be given to the logistics and costs associated with sample transport and communication of the central processing laboratories with the local reporting laboratories.

In the cost analysis for the trial we investigated the range of losses in terms of cost of the programme to the NHS under a set of implementation strategies with varying levels of efficiency/inefficiency. The results reported here suggest that efficient use of resources requires careful planning of the equipment leasing policy from the early stages, which will pay off in the long run. The best scenario is likely to be associated with logistical problems and high transportation costs. However, the worst-case scenario is possible, especially if laboratories are not encouraged to consider more efficient options of sharing equipment. That is why a plausible scenario was developed to illustrate the opportunities and to measure the potential for savings. The quotes obtained from the manufacturer were at a time when the technology was not used beyond the settings of on-going research studies. However, the increased demand for LBC may result in even greater savings if lower prices are negotiated. Still, transportation will add some costs to the total.

We used one LBC technology as an example, while there are some other options on the market. At present there is little evidence on their comparative efficiency. If more

than one technology is available on the market, the benefits from planning its use in relation to neighbouring laboratories may be greater.

We still face the question what evidence is needed to extrapolate beyond the trial setting and to inform policy makers. The two cytology laboratories in the trial are at the two extremes of the annual workload spectrum. It should be noted also that the NHS pathology services in England, covering all branches of pathology, are currently being reorganised in accordance with the Modernisation Agency's programme for pathology service improvement. (9) Thus, we are planning a national survey to provide us with a snapshot of the new cytology laboratory services configuration, and covering workloads, type of technology used, method of acquiring it (purchase, lease or other), arrangements with other laboratories, cost data and others.

Also, since ARTISTIC is studying the added value of HPV testing within cervical screening programmes, the economic study could explore the impact of the technology on the virology services. Although the yearly demand for such services would be much less than the demand for cytology services, given the current availability and capacity of virology laboratories, there may be insufficient supply of such services should HPV testing be introduced nationally.

The criteria for a screening programme may need to be revisited to account for changes made along screening programmes. With the increasing role of cost-effectiveness analysis, guidelines could be produced to formulate explicitly what economic evidence policy makers consider acceptable. Our findings suggest that in some screening programmes the cost analysis may have to consider amongst others the cost of the policy makers' decision on the method of a programme implementation.

In conclusion, with the changes the NHS CSP is undergoing at present and the findings of the ARTISTIC trial not that far away, the screening for cervical cancer in England has the potential to offer enhanced benefits to the female population. However, the efficient use of NHS resources during the implementation of the programme is in the hands of the policy makers.

References

1. Wilson JMG, Jungner G. Principles and practice of screening for disease.

Geneva,: World Health Organization; 1968.

2. Health Departments of the United Kingdom. The National Screening Committee Handbook of Population Screening Programmes. In. First Edition ed: National Screening Committee; 1998.

3. National Institute for Clinical Excellence. Guidance on the use of liquid-based cytology for cervical screening. Technology Appraisal 69, October 2003. London, National Institute for Clinical Excellence.

4. Cervical screening programme, England 2000-01, Statistical bulletin No.22; Department of Health; 2001.

5. Scottish Cervical Screening Programme. Steering Group Report on the feasibility of introducing liquid based cytology. January 2002. Edinburgh, Scottish Cervical Screening Programme, 2002.

6. NHS Cancer Screening Programmes (1999) The Second Survey of Non-medical Laboratory Staff working within the NHSSCP. (Unpublished report)

7. Moss SM, Gray A, Legood R, Henstock E. Evaluation of HPV/LBC Cervical Screening Pilot Studies. First report to the Department of Health on evaluation of LBC (revised January 2003). London, Institute of Cancer Research.

8. National Institute for Clinical Excellence. Guidance on the use of liquid-based cytology for cervical screening. Technology Appraisal 69, October 2003. London, National Institute for Clinical Excellence.

9. Department of Health (2004) Modernising Pathology Services, London, Department of Health.

Table 1. Criteria for appraising the viability, effectiveness and appropriateness of a screening programme. (2)

The condition	- should be an important health problem. - the epidemiology and natural history of the condition should be adequately understood and there should be a detectable risk factor, or disease marker and a latent period or early symptomatic stage. - all the cost-effective primary prevention interventions should have been implemented as far as practicable.
The test	- should be simple, safe, precise and validated - should be with known distribution of test values in the target population and a defined and agreed suitable cut-off level. - should be acceptable to the population. - there should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals.
The treatment	- there should be an effective early treatment or intervention leading to better outcomes than late treatment. - there should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered. - clinical management of the condition and patient outcomes should be optimized by all health care providers prior to participation in a screening programme.
The screening programme	- there must be evidence from high quality RCTs that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an "informed choice", there must be evidence from high quality trials that the test accurately measures risk. - should be clinically, socially and ethically acceptable to health professionals and the public. - the benefit from the screening programme should outweigh the physical and psychological harm. - the opportunity cost of the screening programme should be economically balanced in relation to expenditure on medical care as a whole. - there must be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards. - adequate staffing and facilities for testing, diagnosis, treatment and programme management should be made available prior to the commencement of the programme. - all other options for managing the condition should have been considered, to ensure that no more cost effective intervention could be introduced or current interventions increased within the resources available. - evidence-based information, explaining the consequences of testing, investigation and treatment, should be made available to potential participants to assist them in making an informed choice. - public pressure for widening the eligibility criteria for reducing the screening interval, and for increasing the sensitivity of the testing process, should be anticipated. Decisions about these parameters should be scientifically justifiable to the public.

Figure 1. Distrubution of cytology laboratories' annual workload in England in 2000-2001. (4)

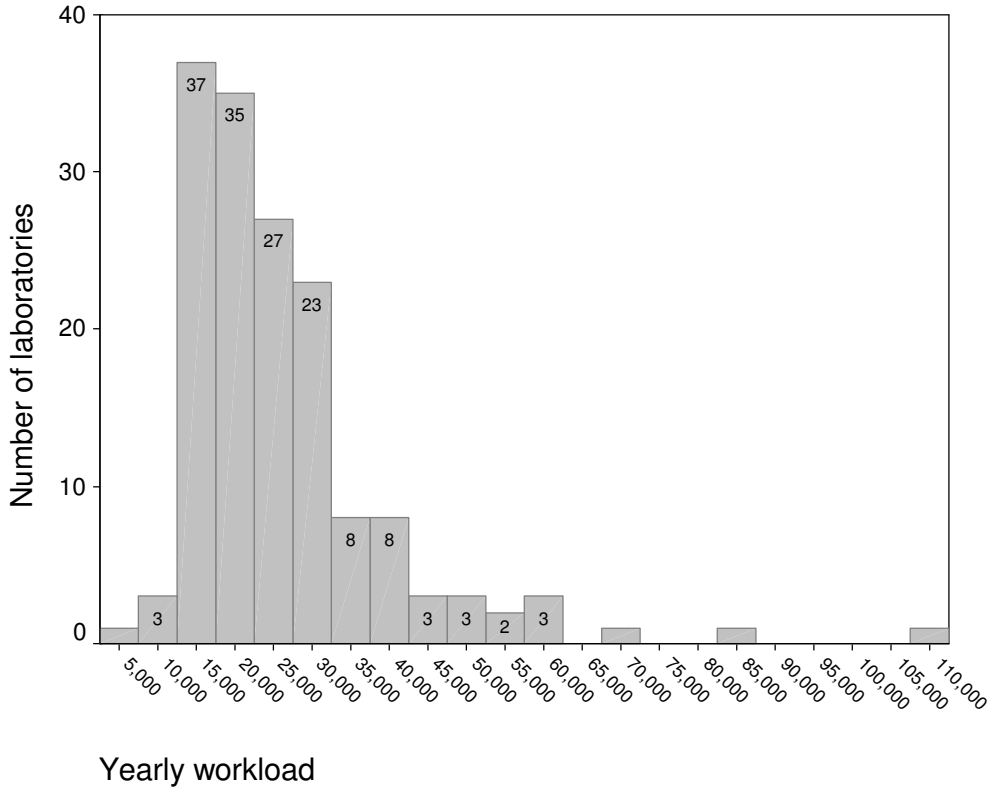

Table 2. Cost per slide in £ in relation to laboratory workload per year*.

Annual Workload	T2000	T3000
10,000	5.75	NA
15,000	5.43	
20,000	5.27	
25,000	5.18	5.89
30,000	5.12	5.66
35,000	5.07	5.5
40,000	5.04	5.38
50,000	NA	5.21
60,000		5.1
70,000		5.01
80,000		4.95

* - cost includes labour

Figure 2. Cost per test (£) according to yearly workload.

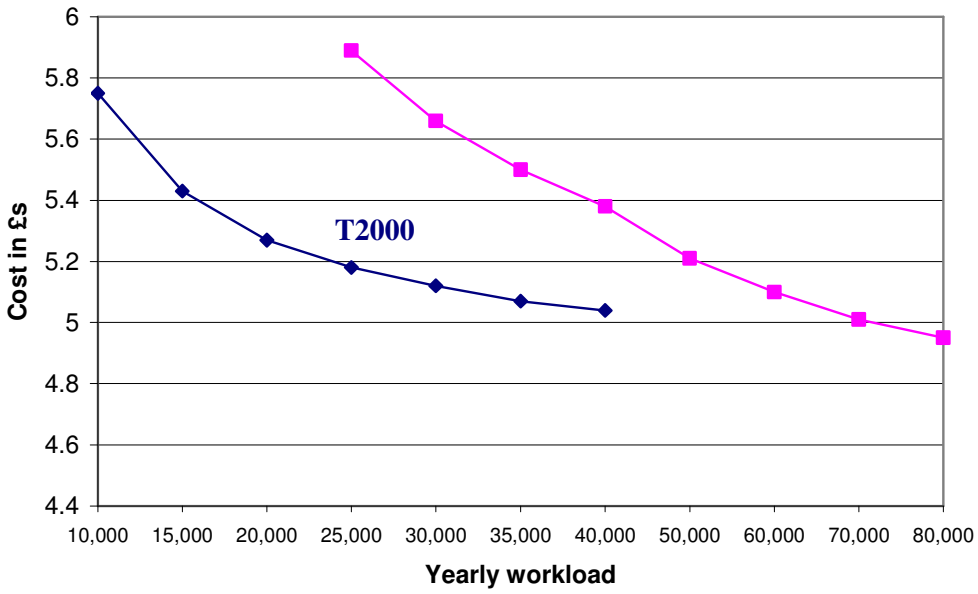

Table 3. Scenarios for LBC policy implementation.

	Number of T2000	Number of T3000	Total annual cost in £'000s	Savings compared to worst-case in £'000s
Best-case	0	51	20,240	2,960
Worst-case	65	91	23,200	NA
Plausible case	8	48	20,400	**2,800**

Figure 3. Present value of savings discounted at 3.5%.