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Low-Dose CT Screening Pilot

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The Cost-Effectiveness Of The Manchester 'Lung Health Checks', A Community-Based Lung Cancer

Low-Dose CT Screening Pilot.

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Highlights

The use of CT to screen for lung cancer remains hotly debated

We explored the cost-effectiveness of screening in a targeted community setting

By updating evaluation methodology used in UKLS we ensure consistency of findings

We find the use of community screening to be cost-effective

Abstract

Background

Previous evaluations of low-dose CT (LDCT) lung cancer screening programmes have taken very

different approaches in the design of the informative trials and the methods applied to determine

cost-effectiveness. Therefore, it has not been possible to determine if differences in cost-

effectiveness are due to different screening approaches or the evaluation methodology. This study

reports the findings of an evaluation of the first round of a community-based, LDCT screening pilot

Manchester, applying previously published methodology to ensure consistency.

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Methods

Using the economic evaluation method reported in the UKLS trial, applying Manchester specific evidence where possible, we estimate the cost-effectiveness of LDCT for lung cancer. Estimates of the total costs and quality adjusted life years (QALYs) were calculated.

Results

The Manchester programme cost £663,076, diagnosed 42 patients with lung cancer resulting in a gain in population health of 88.13 discounted life years, equivalent to 65.85 QALYs. This implied an incremental cost-effectiveness ratio of £10,069/QALY.

Conclusions

We found the Manchester programme to be a cost-effective use of limited NHS resources. The findings suggest that further research is now needed not as to whether LDCT screening is cost-effective but under what conditions can it improve patient health by the most while remaining cost-effective.

Introduction

In recent years the debate over the value of screening for lung cancer has intensified with the conclusion of a number of high cost randomised trials from around the world, including NLST, UKLS, and NELSON.[1-3] Based largely on the results of NLST the US Preventive Services Task Force (USPSTF) recommended screening with LDCT in 2013.[4] This has been followed by similar statements from other countries including the Chief Executive of the NHS in the UK, Simon Stevens, in 2017 [5] and the recent European position statement.[6] However, formally Simon Stevens's statement differs from the views currently held by the UK National Screening Committee (NSC) who's most recent review in 2006 concluded such screening was not recommended.[7] Whilst another review is due upon the publication of the NELSON trial, the debate over the worth of a screening programme is far from settled.

The intrinsic appeal of such screening programmes is clear, with lung cancer causing around 35,600 deaths every year in the UK[8], a level that has stayed stubbornly high. Despite knowledge of the risk factors the majority of patients still present with advanced disease[5] when curative treatment options are limited.

It has been argued that despite the evidence of mortality benefit shown in NLST continued caution is required due to the issues associated with high false positive rates typically reported in screening trials.[9] Such concerns around the relative merits of the benefits of an intervention compared to its harms can be addressed through economic evaluation, which explicitly employs validated methods to consider the health and cost implications of all affected parties in a single statement of cost-effectiveness. Furthermore, the recent study by Field et al.[10] looking at which areas of the screening debate were yet to be fully resolved highlighted cost-effectiveness as 'amber' meaning 'requiring further research', highlighting a limited pool of cost-effectiveness analyses.

This paper seeks to expand on the existing pool of cost-effectiveness studies by evaluating the results of the recently conducted community-based lung cancer screening pilot in deprived areas of

Manchester.[11] In doing so it also provides evidence on the only 'red' category of the twelve considered by Field et al., that of the recruitment of patients in 'hard-to-reach' deprived communities, addressing the role of community based lung health checks and the use of mobile LDCT units.

The Pilot Programme Being Evaluated

The Manchester 'Lung Health Check' (LHC) pilot programme was designed to address both the health burden associated with lung cancer but also to reduce the barriers to participation in those at greatest risk by reducing travel time and increasing convenience.[11] Ever smokers aged 55 to 74 registered at one of the participating GP practices (14 across Manchester) were invited to have a LHC at convenient community venues, where respiratory symptoms, spirometry and 6-year lung cancer risk (using PLCO_{M2012}) were assessed. Those found to have a 6-year lung cancer risk of ≥1.51% were eligible for and offered LDCT screening. This consisted of annual screening over two rounds including an immediate scan in a co-located mobile CT scanner.

Of 16,402 invitations to participate, 2,541 LHCs were conducted, with 1,384 going on to have a LDCT. The pilot diagnosed 42 patients with lung cancer with 63% stage I, 17.4% stage II, 8.7% stage III, and 10.9% stage IV. Using historic controls a statistically significant stage shift was demonstrated compared to those with symptomatic presentation.

Methodological approach

A major limitation of the existing literature on the cost-effectiveness of a lung cancer screening programme is the variation in methodology used. As an example, the cost-effectiveness studies linked to two of the large trials, NLST and UKLS, reported very different base-case results \$81,000/ Quality Adjusted Life Year (QALY) (roughly £60,000 in 2018 values)[12] and £8,466/QALY.[2] However, the extent to which this is the result of different programme designs or the impact of different evaluative methodologies is unclear due to different methodological approaches being used for the evaluations.

These are just two of the large array of literature on cost-effectiveness of lung cancer screening, all facing similar issues of a lack of comparability of methods. [13-18]

To ensure comparability of the evaluation of the Manchester LHC pilot with other trials, the economic evaluation conducted for the UKLS trial analysis was reconstructed. The UKLS method was chosen for a number of reasons including, primarily, its relevance to a UK setting but also the accessibility of the methods and validity as a reference point since its independence from the trial, reducing the risk of inherent bias in the approach and assumptions used.[19]

The methodological approach, hereafter the 'UKLS method', as with any evaluation approach, has limitations which it is important to be aware of. Most notably these include the assumption driven estimation of lead time, the simplistic approach to quality of life adjustment, and the assumption linking earlier stage diagnosis with gains in survival as a result of screening compared to symptomatic presentation. These are considered in more detail during the presentation of the model in the next section and are explored through sensitivity analysis in this study.

Methods

As details of the UKLS method are published extensively elsewhere [2, 19] this section is limited to a brief overview of the methods, with a focus on the differences in the parameter values used in this study compared to UKLS.

The core approach

The UKLS method takes a two part approach to the estimation of the costs and benefits associated with a screening programme, defining an algebraic formula to determine the total additional cost implications alongside a life table approach to estimating the impact of the programme on the expected years of life lived by each patient. The estimated life years (LY) are then adjusted by an estimate of the quality of life the affected patients would be expected to have to give an estimate of the QALYs.

The estimation of incremental total cost seeks to combine the three main cost factors: the cost of conducting the screening programme, the cost implications of diagnosing and treating a true positive, and those of diagnosing a false positive. These are combined using the function:

 $CS + NP (I_{TP}+T) + NF \cdot I_{FP}$

Where:

CS – the cost of conducting the screening programme

NP - the number of true positives in the cohort

I – the cost of the investigation of a positive screen result which is considered separately for true positives, I_{TP} , and false positives, I_{FP} .

T – the net additional cost of treating a screen detected cancer, compared to a symptomatic presentation (this takes into account the lead time to presentation)

NF – The number of false positives picked up by the programme

The assumption is therefore made that all true negatives and false negatives imply no change in the cost implications compared to a scenario where no screening programmes were available beyond the cost of the screen itself. This is certainly accurate for true negatives, who would not be expected to change how they interacted with the NHS, but it could be argued that false negatives (i.e. those with cancer who are not identified by the screen) are less likely to seek care for suspected lung cancer at a later date. However, it is not possible to incorporate an estimate of this, as both the rate of false negatives and the change in their actions as a result are largely unknown in this setting.

In keeping with best practice, all costs and benefits are discounted at a rate of 3.5% per year, and a NHS and PSS perspective is taken on costs, and population health, measured in terms of QALYs for the benefits.[20]

Parameter estimates

Costs

As discussed above in order to estimate the additional cost implication of screening we need to know:

the cost of conducting the screening programme, the number and cost implications of true positives,

and the number and cost implications of false positives.

The costs of conducting the screening programme are reported in Table 1, where all frequencies and

unit costs have been directly observed from the Manchester LHC pilot and therefore represent 'real

world' estimates. The costs exclude the non-recurrent project costs associated with setting up the

pilot (estimated at £315,000, funding a programme office that was tasked with exploring evidence

and designing the pilot rather than directly running a screening service) and, as noted elsewhere, are

limited to the first 3 month follow-up scan.

[Table 1 here]

The cost of treating true positive and false positive results combines the observed number of each of

these from the programme (42 true positives, 39 false positives) with an estimate of the unit cost

incorporating diagnostics to confirm or contradict the initial scan and the subsequent treatment for

true positives. The cost of diagnostic workup after the CT was estimated using frequencies of activities

reported by the pilot, combined with unit cost estimates provided by University Hospital of South

Manchester (UHSM) are reported in Table 2. It should be noted that the unit costs differ from National

NHS Reference Costs as they represent the local costs rather than national averages. Estimates

suggest that the use of the NHS Reference Costs (2015/16)[21] would result in the total cost of the

programme to be £12,000 lower.

[Table 2 here]

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To estimate the additional treatment costs associated with the true positive diagnoses it was necessary to estimate both the cost profile for the true positive patients given they were diagnosed earlier (i.e. due to the screen), denoted C_{CT}, compared to had they been otherwise been diagnosed later, C_{SP}. Given the lack of long-term follow up in the pilot both costs are based on estimated treatment pathways. Both are estimated by applying stage and intervention specific unit cost estimates from CRUK[22] alongside estimates of the stage distribution, either from the pilot (to inform C_{CT}) or from an estimate of the stage distribution of the population without the programme, here using ONS data, to inform C_{SP}. C_{SP} is additionally adjusted for discounting, as the costs will occur at a later date. The average time to symptomatic presentation used to inform the discount rate is estimated by a weighting of the stage-specific lead times reported later in this section. C_{SP} is also adjusted for background mortality, as patients may have died before symptomatic presentation. The frequency of the various treatment strategies and associated unit costs is reported in Table 3. For the symptomatic group patients are assumed to present at a stage distribution that matches the national average, [23] the stage specific unit treatment cost is estimated using the stage specific averages from the CT arm of the model given in Table 3.

[Table 3 here]

Benefits

As discussed earlier the benefits of screen-detection versus symptomatic presentation are estimated by adapting the survival model referenced and applied by the UKLS study.[19]

The estimation of benefit uses actuarial tables which estimate the probability of dying in any given year for a number of different states of being (for this model gender and presence and stage of cancer).[23] Estimates of the life expectancy of each true positive lung cancer case are made at an individual patient level assuming both the cancer was diagnosed using the screening test, and that if the screening test had not been available the cancer would have presented symptomatically at a later

date. An estimate of the stage specific time between the identification at screening and symptomatic presentation is incorporated to account for lead time bias.

This approach can be characterised using Figure 1, reproduced from Whynes.[19] It shows the estimated relationship between survival curves (along axes of age (A) and number who survive (N)) of three cohorts: 'normal' survival curve based on life expectancy of the overall population; screened cohort; symptomatic cohort. Survival of the symptomatic cohort beyond the point of diagnosis at A_{SP} decays rapidly compared to both the normal cohort and the screened cohort which is diagnosed (and therefore treated) at an earlier point A_{CT} .

Using this approach it is therefore possible to estimate the LY gains from screening by considering the difference between the areas under the two lung cancer survival curves (screened and symptomatic). Doing so at a patient level, as done in our study and in the UKLS analysis (Whynes originally took a single cohort approach), allows for the adjustment of the model to differences in gender, the age of presentation, and the stage of presentation. The incremental LYs are then adjusted for the expected quality of life experienced by the patient.

[Figure 1 here]

To account for the higher level of mortality associated with deprivation in Manchester compared to the UK, we calculated the survival curves specific to Manchester residents. For each individual diagnosed with screen-detected lung cancer we constructed a statistical table for (a) symptomatic presentation, and (b) CT-screened presentation, factoring in published stage and gender specific 1 year and 5 year survival rates. The UKLS approach to stage specific survival, using evidence from the literature, is used to inform the screen detected survival rates, and updated estimates from the Office for National Statistics (ONS) for the symptomatic presentation curves (the original UKLS analysis used

an older version of the same source). These values are reported in Table 4. Stage 4 cancers are assumed to have the same survival rate as observed in the symptomatic presentation group whether diagnosed symptomatically or by screening. This implies no health benefit in identifying patients at stage 4 through screening. An exponential decay function is fitted to the two time points for each stage of cancer.

[Table 4 here]

In addition to modelling the difference in survival time given symptomatic or screen detection the model takes account of the lead time of each stage of disease, i.e. the time between identification at screening and any symptomatic presentation. While some authors have sought to estimate the lead time precisely, [24] these estimates are, due to the unobservable nature of a patient's lead time, highly assumption based and in need of further development. This model takes the same approach as used in UKLS that lead times can be estimated from the difference in the ages between symptomatic presentation and the screen detected programme (roughly 3, 2, 1, and 0 years for stage 1 to 4). To account for the significant uncertainty in these estimates the UKLS approach incorporated into the model lead times twice these observed rates (so 6, 4, 2, and 0). This assumption biases against CT screening (i.e. are conservative) as shorter lead times imply that lung cancer progresses more quickly between Stages 1 and 4, making the benefits of early stage diagnosis greater as without it lives and life years are lost very quickly.

Finally, to adjust for patients' quality of life after the development of cancer we adjust the estimated life years gained by an expected quality of life score, consistent with the approach taken by UKLS. Adjusting the life years by a quality of life score indicative of a cancer sufferer would risk biasing the benefit of diagnosing and treating patients earlier as many survive cancer and those who do not would experience the quality of life implications whether they were diagnosed through screening or

symptomatically. Therefore a quality of life adjustment indicative of an age adjusted typical person was used, 0.7472 as used in UKLS from estimates by Kind et al.[25]

Results

Bringing the Cost Elements Together

In the methods section we defined the formula "NS + NP (I_{TP} +T) + NF · I_{FP} " as defining the incremental cost of the screening programme. Using the methods outlined this resolves into:

Total additional cost = £566,013 + 42 · £1,579 + 39 · £788

= £566,013 + £66,323 + £30,740

= £663,076

This shows that the cost of conducting the screen, £566,013, was the largest cost component, compared to the cost of diagnosing and net additional cost of treating the true positives, £66,323, and of diagnosing false positives, £30,740.

Health Benefits of the Screening Programme

Based on the survival assumptions described above, we find that the total undiscounted Life Years gained through screening are estimated to be 128.24 LYs, 88.13 LYs when discounting is applied. Table 5 shows the number of people diagnosed as true positives in the trial, according to stage and gender, alongside the average estimate LY gains (undiscounted) as a result of the screening programme. When discounting rules are applied the average estimated LYs gained across the 42 true positive patients is 2.10.

[Table 5 here]

The table highlights the significant benefits of identifying patients earlier, with an average gain of up to 4.19 years, significant considering the average age of this population was 67.6. It also highlights the importance of early diagnosis, with a large decrease in expected gains as the stage moves from 1 to 2 or 3 and then to 4, where there is no gain expected from screening.

Adjusting the LY gained by patients' expected quality of life results in a QALY gain of 65.85.

Combining the Costs and Benefits

Conventionally the result of a cost-effectiveness analysis is reported as the incremental cost-effectiveness ratio (ICER) in terms of the additional cost of an intervention and in terms of the additional gain in QALYs. The resultant ICER is then compared to a 'cost-effectiveness threshold' which is used to determine the point at which a new intervention would represent a worthwhile use of finite NHS resources. In the UK a threshold value of £20,000 to £30,000/QALY is most often used, due to its use by the National Institute for Health and Care Excellence (NICE) in their decision making process. However, recent quantitative research has argued that this value should be closer to £13,000/QALY.[26] The analysis described in this paper results in an ICER of £10,069/QALY, below any of the threshold values considered appropriate, and therefore suggesting that, under the base-case assumptions, the Manchester pilot represents a cost-effective use of NHS resources.

Uncertainty analyses

While the base-case analysis represents a best estimate of the expected lifetime costs and benefits of the Manchester LHC pilot, there are inevitably areas of uncertainty that, to some extent can be explored through uncertainty analysis. We conducted two scenario analyses to explore the sensitivity of the results to changes in the base case assumptions, relating to the modelled survival times and the lead times.

As with the UKLS approach we modelled the mortality rates of CT and symptomatically presenting patients using a decay function applied to data on one and 5 year survival from the literature (for CT)

and the ONS (for symptomatic presentation). The nature of the informative data makes traditional probabilistic sensitivity analysis difficult as we have no robust estimates of the standard error.[27] As a result, we explored the sensitivity of the model to the CT mortality rates by adjusting the estimated time dependent rates, using a hazard ratio. This found that applying a hazard ratio of 0.5 (i.e. reducing the annual mortality rate for CT detected patients by half) reduced the ICER to £5,801/QALY. Similarly a hazard ratio of 1.5 resulted in an ICER of £26,837.

In addition, a scenario analysis in which we weakened the bias against screening by reducing the lead times estimates to 3, 2, 1 and 0 years for stage 1-4 respectively was conducted. These values most closely reflect the point estimates that were considered most likely in the UKLS model, but which were adjusted in the base case to ensure a conservative analysis. This scenario reduces the ICER to £5,579/QALY as the benefits of diagnosing a lung cancer earlier increase. This is due to the increased speed at which the cancer is assumed to develop through the stages and therefore the risk of mortality under a reliance on symptomatic presentation. In a related scenario we identified that the lead times would need to increase to 8.0, 5.4 and 2.7 for the screening programme to no longer be cost effective (assuming the same relative size of the lead times).

Discussion

This economic evaluation of the Manchester Lung Health Check pilot found it to be a cost-effective use of NHS resources if the significant long-term benefits both to patient health and NHS expenditure were considered. A base-case ICER of £10,069/QALY was estimated, lower than both the conventional cost-effectiveness threshold used by NICE, and the recently estimated value of the threshold by Claxton et al. of £13,000/QALY.[26] This is comparable to the findings of the UKLS trial analysis which estimated an ICER of £8,466/QALY. The primary difference between this study and UKLS is the use of mobile scanners over fixed, hospital based, units. In this trial the cost per reported CT scan was £286, compared to an estimated cost of using a fixed unit of £232 (CT of up to three areas with contrast plus an MDT meeting from the NHS Reference Costs)[21], a difference of £54 per scan. However, while

hospital based screening is cheaper per scan it is likely that many patients who benefitted from this screen would have been put off from attending a hospital setting. As a result, it is not reasonable to assume that the results of this trial can be directly transferred to a hospital setting at a reduced cost.

The UKLS analysis additionally reported 95% confidence intervals around the cost and LYs by assuming normality and re-estimated the net cost using Monte-Carlo simulations, resulting in a confidence interval of £362,564 to £769,309 around their mean estimate of £565,498, and 2.6 to 3.9 LYs around a mean of 3.3 LYs. Combining these gave a 95% confidence interval for UKLS of £5,542 to £12,569/QALY around a mean of £8,466/QALY.

The methodology and characterisation of the normal distribution and the parameters incorporated was, nevertheless, unclear making replication impossible. Attempts were made to conduct a similar analysis through the Monte Carlo resampling of triangular distributions (considered more practicable due to their facilitation of a minimum and maximum), which resulted in a 95% confidence interval of £8,407 to £12,002/QALY.

We consider the estimated confidence intervals reported in this study and UKLS, give a misleading indication of the level of uncertainty present in the analysis. This is because the UKLS method, and indeed any approach based on a life table methodology, is unlikely to be able to fully incorporate the parameter uncertainty evident in the underlying model. This is due to the informative life tables typically only reporting point estimates of e.g. mortality risk, making any informative distribution applied purely speculative. Furthermore, while statistical methods such as bootstrapping are available to consider the impact of the screening programme identifying a different mix of patients, this can only ever be informed within the confines of the pilot or trial findings, which in this case are arguably too limited in size and scope to be informative about the true level of uncertainty. Therefore, while it is possible to attach confidence intervals, we do not consider that such an approach is informative of the true level of uncertainty, risking giving false confidence in a point estimate. In reality the cost-

effectiveness of such programmes, especially at relatively small scale, is hugely uncertain and dependent on many factors which, given the current level of research, are not robustly quantifiable.

The main strength of this analysis stems from its replication of the UKLS study, not only imbuing the benefits of the peer reviewed method by Whynes but allowing for the direct comparison of the results of the two studies. We also extended the scenario analyses conducted in UKLS by exploring the impact of changes to the modelled mortality rate, finding the result to be sensitive.

However, as with the UKLS study this analysis has a number of weaknesses. The reductive nature of the model, primarily considering the survival benefit of earlier stage lung cancer diagnosis with a quality of life adjustment for the life years gained with screening, implies a limited definition of benefit of the programme, failing to reflect the potential benefits of other factors including COPD diagnosis, or smoking cessation (advice given to all attendees). Furthermore, the analysis is limited by the scale and scope of the pilot, failing to reflect the impact of the screening past the first follow up at 3 months or whether a different screening criteria or approach in the same population would be more cost-effective.

Conclusions

This analysis applied the method devised by Whynes and used in the UKLS analysis to estimate the cost-effectiveness of the Manchester Lung Health Check pilot, finding it cost-effective at an ICER of £10,069/QALY. This is an important finding as it presents another validation of the cost-effectiveness of lung cancer screening but in a different setting and carried out differently to the UKLS.

Cost effectiveness, determined by the cost of screening and treatment and the benefits derived through increased longevity, is underestimated in the model through the conservative approach to lead times and exclusion of numerous health benefits beyond lung cancer diagnosis. Potential overestimates may emerge if survival rates of screened cases are lower than projected; this data

would become available in the future through longitudinal analysis of mortality among the screened cohort.

Further research is needed not only to address the limitations of this analytical method and informative data, but also to go beyond the question of is screening cost-effective, to how can it be designed to be the most cost-effective, realising the greatest population health gain while remaining an effective use of limited NHS resources. These questions will begin to be addressed through the continued analysis of findings from the NELSON trial, the forthcoming Yorkshire Lung Screening Trial and additional NHS commissioned screening in Manchester.

Conflicts of interest

None of the authors have any conflicts of interest to declare.

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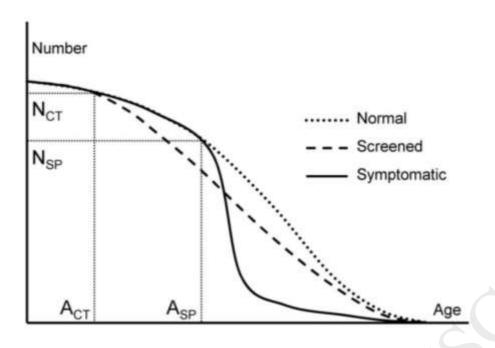


Figure 1: survival curves for the normal, screen, and symptomatically detected cancers, reproduced from Whynes[19]

Table 1: Cost of conducting the screening programme

Cost	Number of people	Unit cost	Total cost
Recruitment –	16,402	£2	£37,527
invitation letters			
Lung Health Checks	2,613 (2,541 of whom	£33	£86,425
	consented for further		
	data collection)		
Initial LDCT scan &	1,384	£286	£395,511
reporting			
3 month LDCT scan &	191	£244	£46,550
reporting			
Total			£566,013

Table 2: Diagnostic workup costs in the true and false positive groups

Test	Frequency	Unit cost	
	True Positives	False Positives	
	(n=42)	(n=39)	
Spiro/DLCO	34	23	95.04
Blood Sample	35	18	2.00
PET-CT	35	17	720.00
Percutaneous Lung	21	4	706.21
biopsy			
Staging EBUS	10	3	1,300.00
Diagnostic EBUS	1	0	1,300.00
Radial EBUS 1.7mm	3	0	650.19
Autofluorescence	2	9	650.19
bronchoscopy			
Other Sampling	4	0	706.21
Technique			
Echocardiogram	4	0	72.45
CPET	2	0	300.00
Other radiology	12	6	616.93

Table 3: Frequency of treatment and unit cost in the true positive group

			Surgery only	Surgery & Chemo	Chemo only	Radio only	Chemo & radio	Follow Up	Palliative	No Treatment
Number of stage and treatment intervention		Stage 1	21	0	0	3	0	26	0	2
	ntion	Stage 2	1	1	1	3	1	7	1	0
	nterver	Stage 3	0	3	0	0	1	4	0	0
	ment ii	Stage 4	0	0	2	1	1	5	4	1
	treat	Total	22	4	3	7	3	42	5	3
Ţ.		Stage 1	£5,359	£8,988	£3,629	£6,296	£9,925	£1,720	£3,581	£0
Cost per treatment category[22]	<u></u>	Stage 2	£5,359	£8,988	£3,629	£2,840	£6,469	£1,720	£3,581	£0
	;ory[22	Stage 3	£5,359	£8,988	£3,629	£2,390	£6,019	£1,720	£3,581	£0
	Stage 4	£1,645	£5,274	£5,699	£1,940	£7,639	£1,720	£3,581	£0	

Table 4: Survival rates used in the model

	1	Male survival	Female survival		
Stage	1 year	5 year	1 year	5 year	
Symptomatic pre	sentation (ONS)			
Stage 1 or later	34%	11%	40%	15%	
Stage 2 or later	27%	6%	31%	8%	
Stage 3 or later	23%	4%	26%	5%	
Screen detected (UKLS)				
Stage 1	90%	70%	90%	70%	
Stage 2	75%	40%	75%	40%	
Stage 3 55%		22%	55%	22%	
Both - Stage 4	23%	4%	26%	5%	

Table 5: Stage distribution and estimated LY gains (undiscounted) from screening

Gender	Stage 1	Stage 2	Stage 3	Stage 4	All
Female	19 (4.10)	1 (2.04)	1 (1.90)	3 (0)	24 (3.41)
Male	7 (4.44)	6 (1.78)	3 (1.52)	2 (0)	18 (2.57)
All	26 (4.19)	7 (1.82)	4 (1.61)	5 (0)	42 (3.05)