

Bowel Cancer Services: Costs and Benefits

Summary Report to the Department of Health

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APRIL 2007



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Acknowledgements

This project was commissioned by the Policy Research Programme at the Department of Health.

The authors would like to acknowledge the detailed clinical input of Professor David Sebag-Montefiore, Cookridge Hospital, Leeds; Professor Matt Seymour, Cookridge Hospital, Leeds; Dr Rob Glynne-Jones, Mount Vernon Hospital, Middlesex; Dr Graeme Poston, Royal Liverpool University Hospital, Liverpool; Dr Greg Wilson and Dr Mark Saunders, The Christie Hospital, Manchester; Professor David Radstone, Weston Park Hospital, Sheffield, Professor Peter Franks, Dr William Hamilton, Professor Bill Heald, Basingstoke, Dr Robin Kennedy, Mrs Jackie Mann, Basingstoke Dr Eva Morris, NYCRIS and Dr Merv Rees, Basingstoke.

The authors are also grateful to the advisory group which the Department of Health set up to provide expert advice on the study. This was chaired by Professor Mike Richards (National Cancer Director) and the independent members were Tim Elliott, Professor Alastair Gray, Lynn Faulds Wood, Professor David Forman, Dr Rob Glynne-Jones, Marion Kerr, Economic Advisor, Dr Sue Moss, Professor John Northover, Professor Matt Seymour, Professor Bob Steele, Dr Ursula Wells and Dr Andrew Veitch.

Summary Report

1.1 INTRODUCTION

Bowel cancer, also known as colorectal cancer causes a substantial number of deaths in England each year. Historically, survival rates for patients with bowel cancer in England are lower than those in many countries of Europe and North America.

Against the backdrop of the desire by the Government to improve cancer services, as laid out in The National Health Service (NHS) Cancer Plan of September 2000¹, the Policy Research Programme of the Department of Health has initiated a study to estimate the costs and benefits of bowel cancer services in England. In particular, the Department of Health wishes to examine how to allocate future investment in bowel cancer services to deliver optimal benefit to patients at an acceptable economic cost.

This research has been developed in response to the Department of Health objectives and aims to identify expenditure at a national level in England on bowel cancer services as a whole, as well as expenditure on the different elements of service provision. The study also seeks to quantify the likely costs and benefits of different options for the development of bowel cancer services.

This is a summary report of the methodologies and findings from the main report produced for the Department of Health. The main report provides a more comprehensive description of the methodologies and further detailed results. Accompanying this report is a literature review conducted to populate the economic models presented herein.

1.1.1 Scope of the Research

The Department of Health identified two distinct phases of research:

- The first phase was to investigate the overall activity and expenditure on bowel cancer within the NHS (as well as affiliated organisations, such as hospices) as well as the patient outcomes that result from this activity;
- The second phase was to investigate what improvements in outcomes might be achievable at what cost and in what timescale.

The Department of Health has also specified a number of areas that should be addressed by the research including:

- Earlier presentation and improved assessment in primary care;
- Optimising diagnostic services;
- Optimising potentially curative treatments;

¹ Department of Health September (2000) 'The NHS Cancer Plan: A plan for investment, a plan for reform.'

- Optimising palliative treatment and care.

The outputs of this study are intended to assist healthcare decision planners and policy makers in allocating resources optimally. A recent King's Fund report (2006) identified four key gaps in the achievement of the NHS Cancer Plan (2000):

- The development of baseline knowledge and information on cancer services and understanding current and future resource requirements;
- Balancing prevention and treatment of cancer to avoid inequities;
- Balancing treatment and palliation;
- Guidance on high-cost drugs.

This project seeks to draw together existing evidence on these aspects of the current bowel cancer service provision and to provide a framework for assessing the potential of future options for change. Finally, it is hoped that the methodology might provide a template to facilitate comparisons of expenditure at a network level and internationally.

This research study has been undertaken as a collaboration between York Health Economics Consortium (YHEC) at the University of York, and the Health Economics and Decision Science Group from the School of Health and Related Research (SchARR) at the University of Sheffield.

1.2 BACKGROUND TO BOWEL CANCER IN ENGLAND

Bowel cancer includes cancerous growths in the colon, rectum and appendix (cancer of the appendix has not been considered within the current study). The cancer cells may spread to nearby lymph nodes (local recurrences) and also to more remote lymph nodes and other parts of the body (metastatic recurrences). The liver and the lungs are common sites for metastatic spread. The most common symptoms on presentation are blood on or mixed with stools; change in bowel habit; anaemia; weight loss, nausea and anorexia; and abdominal pain. However, these symptoms are not exclusively associated with bowel cancer and are associated with a variety of benign conditions which are prevalent in the general population. Importantly, some symptoms may not become apparent until the cancer is at an advanced stage, by which time the prognosis is poor. Patients are likely to develop a variety of physical and psychological symptoms during the life of the disease Seymour *et al.* (1997).

1.2.1 Epidemiology of Bowel Cancer

Bowel cancer is the third most common cancer in England after breast cancer and lung cancer, accounting for around 12% of all cancers in England. In 2003, approximately 27,800 new cases were registered in England. Around 71% of bowel cancers develop in the colon, with the remaining 29% developing in the rectum (ONS 2003).

Rectal cancer is more common in men than women. In 2003, the rates of newly diagnosed cases of bowel cancer for England were 62.3 for men and 49.5 for women per 100,000 population. The probability of developing bowel cancer increases sharply with age. In individuals below the age of 40 years, the risk is very low, with an incidence rate of 4.9 per 100,000 population in men and 4.0 per 100,000 population for women. However, between the ages of 40-49 years, the incidence rate rises to 20.9 per 100,000 population in men and 16.5 per 100,000 population in women. This increases further to over 396.5 per 100,000 population in men and 236.3 per 100,000 population in women aged 75 years and above, ONS (2005). The median age of patients at diagnosis is 72 NBOCAP (2005).

There is not only age- and sex-specific incidence, but also a regional specific incidence, which shows a range per 100,000 from 41.4 in London to 77.6 in the North East for men and from 36.4 in London to 61.1 in the South West for women. These differences reflect not just lifestyle and environmental factors, but also the underlying demography, with London having a younger population.

1.2.2 Survival

Prognosis is strongly related to the stage of cancer at diagnosis; late-stage cancers are associated with poorer survival, more intensive and disfiguring treatments, and increased morbidity. Furthermore, patients diagnosed at an earlier stage are more likely to undergo successful resection and may be cured. Importantly, the treatment of patients with bowel cancer focuses not just on improving survival, but also on morbidity. Whilst surgery and subsequent adjuvant therapies are often associated with favourable outcomes, many patients will eventually develop advanced disease and distant metastases, which typically present within two years of the initial treatment. In around 15% of cases, patients will present with advanced disease, and 50% of these patients will present with liver metastases.

Based on published sources, the overall five-year survival rate for patients with colon cancer is reported to be 47.6% for men and 47.4% for women. The overall five-year survival rate for patients with rectal cancer is estimated to be 48.7% for men and 51.35% for women² based on data for people diagnosed between 1996 and 1999 Coleman 2004. However, mortality rates vary according to both age and stage of disease at presentation. Mortality rates are higher for men than women, as shown in Table 1.3.

² This study considered cancer 5-year survival for some of the most recent cohorts of patients with bowel cancer that were split by colon and rectal cancer.

1.3 METHODOLOGY

1.3.1 Overview

The modelling approach used was underpinned by the design and population of a treatment pathway for the management of patients with bowel cancer. The research has also been supported by an Advisory Group established by the Department of Health, and by the use of a large number of external advisers, contacted independently by the research teams.

The study has been undertaken within three phases:

- The set up phase. This has included the design of the generic patient pathway, using literature, previous work and expert opinion. The generic patient pathway has also been discussed at the Bowel Cancer Action Group (BCAG) meeting of November 2005 and the first Project Advisory Group Meeting in February 2006;
- Phase One. Refining and populating the pathway, to estimate current costs and benefits of activity and expenditure;
- Phase Two. Identifying potential options for service reconfiguration. Developing and populating a simulation model to assess the impact of options on the expected costs and benefits of the bowel cancer service.

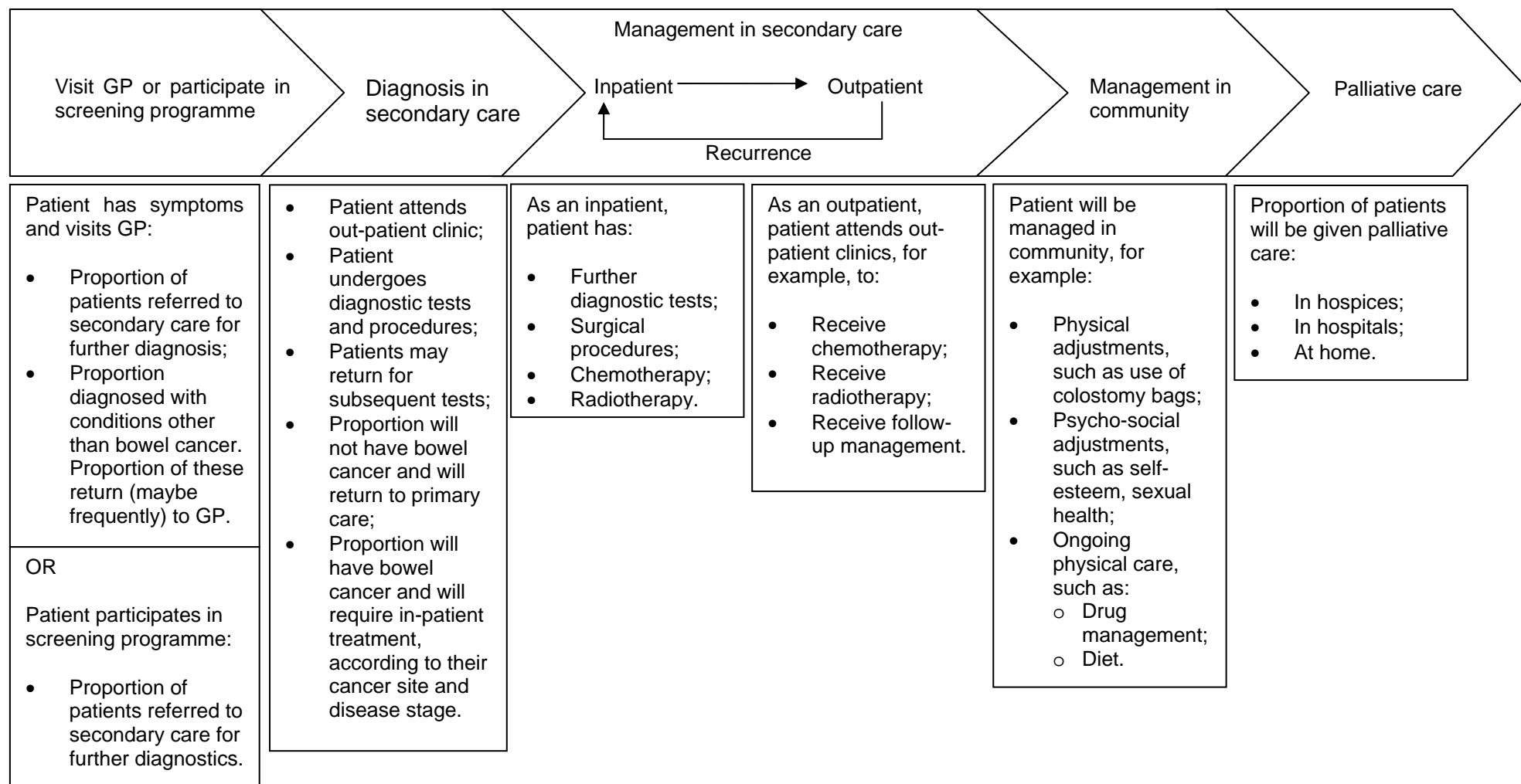
The generic patient pathway was based upon extensive clinical collaboration and consultation taking as its starting point previous research undertaken by SchARR for a series of Technology Assessments for the National Institute for Health and Clinical Excellence (NICE) and the colorectal cancer screening options appraisal Tappenden *et al* (2007). Work on phases one and two, as of necessity, overlapped considerably. Most of the data collected and utilised is common across the two models. The models have been validated against external data sources and calibrated against one another. Where the evidence base is weak or where data does not exist, a process of elicitation has been undertaken using clinical experts in the field.

Additionally, the research team have completed a literature review as part of the research in order to populate the baseline and options models. A report of the findings of the literature review is available as an accompanying report. Trueman *et al*. (2007).

1.3.2 The Patient Pathway

An overview of the patient pathway and the approach adopted has been presented here. The approach adopted follows the options for presentation, diagnosis, and treatment for patients with bowel cancer, including palliative care. Figure 1.1 provides a high-level illustrative pathway for a patient at normal risk. During the research study, the pathway was expanded and developed in detail for each of the phases described. Separate pathways were developed for colon and rectal cancer patients, and those who are at an increased-risk of developing bowel cancer, i.e. those with FAP, Hereditary Non-Polyposis (HNPPC), pre-identified adenomatous polyps, ulcerative colitis and Crohn's disease, these are described in detail in the main report.

Figure 1.1: High level illustrative pathway for patients with bowel cancer



1.3.3 Baseline Model

The patient pathways have been used as the basis for the structure of a model of the baseline costs and benefits. The baseline model is implemented in Excel and full details can be found in section 2 of the main report (Trueman *et al* 2007). Each node in the pathway has been populated with current evidence relating to:

- Activity, including number or percentage of patients following a particular treatment option in the model;
- Costs, applied to the activities in the pathway;
- Outcomes, as a result of the activities in the pathway.

1.3.4 Options Model

The treatment patient pathways have also been used as the basis for a simulation model to estimate the costs and outcomes associated with each of the options. The options model was implemented using discrete event simulation methods using the software package SIMUL8. The simulation operates on an individual patient-level basis with each individual being assigned a set of characteristics.

1.3.5 Expert Elicitation to Populate Areas where Current Evidence is Insufficient

Owing to a lack of empirical evidence in a number of areas, several of the model parameters and details of the models structure were elicited from experts. The elicitation was supported by Bayesian Elicitation of Expert Probabilities (BEEP) collaborative research team (<http://www.shef.ac.uk/beep/index.html>). Novel methods of elicitation were used focussing on determining probabilistic judgements for key parameters in the model in the presence of important covariate structures.

1.4 CURRENT BASELINE COSTS AND ACTIVITY

1.4.1 Introduction

The baseline models purpose was to estimate the total annual costs, activities and outcomes of current treatment for bowel cancer in England. These estimates are based on a modelling exercise, which is a distinct exercise from the development of the options model. Whilst the models are consistent, their objectives and outputs are quite different, with the baseline model providing an estimate of the total costs of current services for bowel cancer and the options model simulating the expected costs of outcomes of various service reconfigurations for a hypothetical cohort of patients with bowel cancer.

The two models are based on the patient pathways described in detail in the main report and the Literature Review which accompanies the main report. A process of validation of the models has been completed to ensure that the models are consistent, in terms of their predicted outcomes and estimates of cost.

1.4.2 Methodology

The baseline pathway was populated with activity data for each node and an appropriate cost. Uncertainty in parameter estimates were taken into account using Monte Carlo sampling techniques. The costs and their respective 95% confidence intervals were then estimated for each stage of the treatment pathway.

Activity data was mainly derived from 2003-4 national data (e.g. Hospital Episode Statistics), supplemented with data from national audits, literature and expert opinion. The activity data has been ordered in a hierarchy of the quality of the source of data which are as follows:

1. Hospital Episodes Statistics (HES) and Office for National Statistics (ONS);
2. National Audits such as NBOCAP;
3. Locally published data, such as NYCRIS;
4. Locally collected data;
5. Published literature;
6. Elicitation of expert judgement;

Costs are reported at 2004-5 price levels and were mainly derived from NHS reference costs, published literature and NICE technology appraisals. A list of the sources of all costs is as follows:

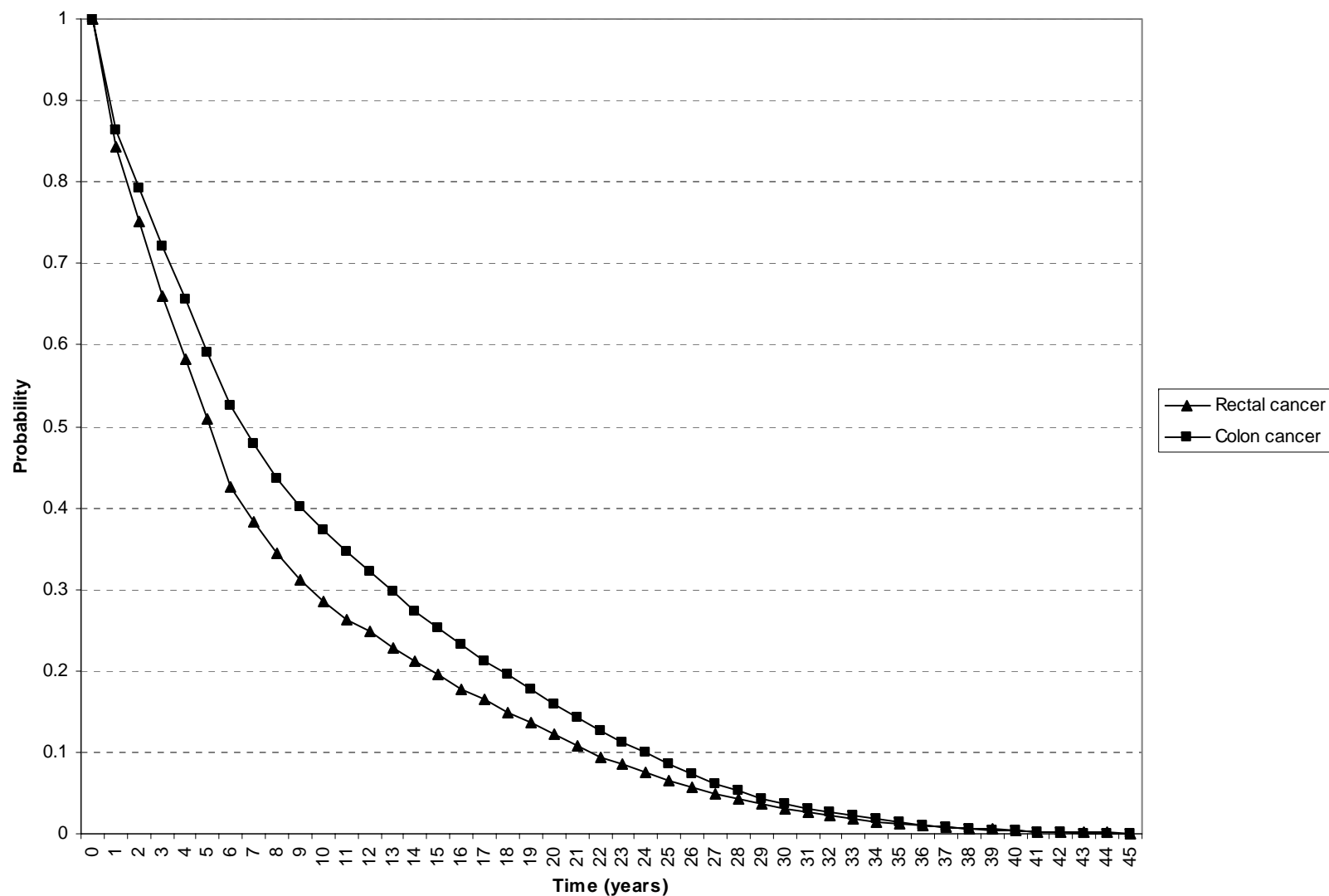
7. NHS Reference costs published by the Department of Health;
8. Standard costs collected and published annually by Curtis and Netten (2005);
9. Published literature;
10. Local sources and expert opinion.

The modelled overall survival curves used for the model are presented in Figure 1.2. The options model was used to estimate overall survival curves for colon cancer patients and rectal cancer patients for use in the baseline activity and cost model. These are modelled overall survival curves and are best estimates of current survival given the current baseline. These were based on data derived from a number of sources (CRO7 2006, Mawdsley 2005, FOCUS 2004, MOSAIC 2004, X-ACT 2005, COST 2004 and ONS 2003.). The one-, three- and five-year overall survival³ rates for rectal cancer are 84%, 66% and 51%, respectively. The one-, three- and five-year survival rates for colon cancer are 86%, 72% and 59%, respectively.

³ These are the estimated survival curves from the model.

Figure 1.2: Overall survival for Colon and Rectal cancer patients

Overall survival for Colon and Rectal Cancer Patients



The activity and costs associated with each element of the pathway have been estimated along with the key intermediary outcomes. Summaries of all the literature from which evidence was extracted can be found in the literature review report which accompanies this report.

1.4.3 Baseline Costs and Activity Results:

Table: 1.1: Estimated Annual Costs of Bowel Cancer Services in England (2006)

		Colon Mean Cost (£)	Rectal Mean Cost (£)	Total Mean Cost (£)
Col	Row	1	2	3
A	Diagnosis	£14,622,657	£5,972,634	(£20,595,291)
B	Primary Treatment	£128,759,653	£71,868,979	(£200,628,632)
C	- Surgery	(£67,477,601)	(£35,704,009)	
D	- CT/RT	(£61,282,052)	(£36,164,970)	
E	Follow-up (surveillance)	£17,562,685	£6,840,229	(£24,402,914)
F	Recurrence	£185,533,600	£61,119,695	(£246,653,295)
G	- Chemotherapy	(£175,848,853)	(£56,898,483)	
H	- Surgery	(£9,684,747)	(£4,221,212)	
I	Stoma	£24,328,903	£27,747,664	(£52,076,567)
J	Palliative	£80,399,658	£38,153,322	(£118,552,980)
K	- Interventions	(£66,733,715)	(£30,410,599)	
L	- End of Life care	(£13,665,943)	(£7,742,723)	
M	Annual cost of all patients with bowel cancer (A+B+E+F+I+J)	£451,207,156	£211,702,523	£662,909,679
N	Diagnosis costs in non-cancer patients			£270,129,193
O	Screening Cost (additional year 1 cost.)			£112,828,886
P	Increased-risk patients			£53,758,184
Q	Total Cost of Illness (M3+N3+O3+P3)			£1,099,625,942

Table 1.1 summarises the estimated costs of bowel cancer services in England. Throughout the discussion of the model results, the cells within this table have been referenced by column and row. For example the total cost of illness can be found in cell (Q3).

The costs and activities have been calculated separately for rectal and colon cancer, as well as normal and increased-risk patient groups, including patients with FAP, HNPCC and Ulcerates Colitis and Crohn's disease. Finally, a separate calculation has been made for the

costs of patients who were referred with suspected cancer but were subsequently found not to have cancer⁴. An estimate of the cost of the introduction of screening has been included for the 5-years.

1.4.3.1 Total cost of illness

The total annual cost of illness is estimated to be £1.1bn (M3+N3+O3+P3). The total annual cost for people diagnosed with cancer is estimated at £662.9m, non-cancer patients at £270.1m, that is those suspected of bowel cancer but who are subsequently diagnosed negative, screening cost is estimated at £112.8m and the cost of increased-risk patients is £53.8m. The above costs include all of the component costs for those patients within a year that are currently being treated for bowel cancer. The first year cost of all newly diagnosed patients in a year is estimated to be £419.6m.

The largest cost as a proportion of the total cost of illness is the cost of diagnosis (A3+N3) which makes up 26.4% of the overall cost. The next significant cost is that of the prevalent patients follow-up cost (E3+F3) estimated to be 24.7% of the total cost of illness.

Table 1.2: Total cost, per patient cost and proportion of total cost estimates

Patients	Mean total cost (95% CI)	Mean per patient (95% CI)	Proportion of total cost
Diagnosis	£290.7m (£257.4m,£317.8m)	£379 (£335,£413)	26.44%
Rectal cancer treatment	£71.9m (£44.6m,£109m)	£12,037 (£11,110,£12,940)	6.54%
Colon cancer treatment	£128.8m (£79.6m,£195.1m)	£8,808 (£8,309,£9,314)	11.71%
Stoma cost	£52.1m (£31.7m,£81.3m)	£1,279 (£1,279,£1,279)	4.74%
Follow-up cost	£271.1m (£164.3m,£405.8m)	£11,183 (£9,448,£12,520)	24.65%
Palliative care cost	£118.6m (68.5m,193.2m)	£7,360 (£5,951,£8,851)	10.78%
Increased-risk cost	£53.8m (£53.8m,£53.8m)	£1,978 (£1,978,£1,978)	4.89%
Screening cost	£112.8m (£112.8m,112.8m)	-	10.26%
Total cost of illness	£1.1bn (£845.5m,£1.4bn)	-	100%

⁴ It is not strictly speaking appropriate to allocate all of this cost to bowel cancer services as it would be a part of the entirely appropriate GI services expenditure. However, the appropriate allocation to a bowel cancer label is highly uncertain and due to the scale of this expenditure it is better to include this otherwise hidden cost of the service.

1.4.3.2 Diagnosis of Bowel Cancer

The diagnosis cost includes the cost of referral and diagnosis of all patients who present via a GP, A&E or from elsewhere in secondary care. The total diagnosis cost consists of two main components, those that are diagnosed as bowel cancer patients and those that receive a negative diagnosis (described herein as non-cancer patients). A large proportion of the diagnosis cost is due to the cost of those patients in whom bowel cancer is suspected that subsequently receive a negative diagnosis. This can be explained firstly, by the large number of patients who are referred for diagnosis and subsequently are diagnosed negative and secondly the cost of the diagnostic procedures. The cost of the non-cancer patients going through diagnosis and returning as negative bowel cancer patients was £270.1m (N3). Those patients diagnosed with bowel cancer were estimated in the model to cost £20.6m for diagnosis (A3).

1.4.3.3 Rectal Cancer and Colon Cancer Primary treatment costs

The cost of primary treatment is £128.8m for colon cancer patients and £71.9m for rectal cancer patients. Table 1.3 shows that for both colon cancer and rectal cancer the majority of cost are accounted for, in roughly equal proportions, by the cost of surgery for the primary tumour and the cost of adjuvant chemotherapy. The surgery for the primary tumour includes the cost of stenting and the appropriate staging cost.

Table 1.3: Rectal and Colon cancer treatment costs

	Colon Cancer	Rectal Cancer
Primary surgery	£67.5m	£35.7m
- MRI Cost	(£0.0m)	(£1.6m)
- Surgery for primary tumour (inc. stenting and staging cost)	(£66.8m)	(£32.8m)
- Stoma reversal cost	(£0.7m)	(£1.3m)
Chemotherapy/Radiotherapy	£61.3m	£36.2m
- Pre-operative chemoradiotherapy	(£0.0m)	(£8.5m)
- Adjuvant chemotherapy	(£61.3m)	(£27.7m)
Total primary treatment (Primary surgery + CT/RT)	£128.8m	£71.9m
Per patient cost	£8,808	£12,037

The mean cost per patient for rectal cancer treatment is estimated to be £12,037 in comparison with the mean cost per patient with colon cancer treatment which is estimated to be £8,808. There are three main factors that explain why the rectal cancer surgery cost per patients was estimated to be greater than the colon cancer per patient cost:

- Firstly, there are a higher proportion of rectal cancer patients who undergo stomas and stoma reversal;

- Secondly, a proportion of rectal cancer patients undergo pre and post-operative chemoradiation;
- Thirdly, higher numbers of rectal cancer patients undergo adjuvant chemotherapy.

1.4.3.4 Follow-up cost

Table 1.4: Follow-up costs for colon and rectal cancer

	Colon Cancer Cost	Rectal Cancer Cost
Total surveillance cost	£17.6m	£6.8m
Total recurrence cost	£185.5m	£61.1m
- Metastatic: Chemotherapy	(£175.9m)	(£56.9m)
- Metastatic: Liver resection	(£9.7m)	(£2.4m)
- Local recurrence surgery	(£0.0m)	(£1.8m)
Total Follow-up cost (inc treatment for recurrence)	£203m	67.9m

Table 1.4 shows the total cost of colon cancer follow-up is estimated to be £203m, which comprises surveillance costs of £17.5m and recurrence treatment costs of £185.5m. The total cost of rectal cancer follow-up is £67.9m and is made up of the surveillance costs of £6.8m and recurrence treatment costs of £61.1m. For both types of patients the majority of the follow-up cost results from the subsequent treatment for metastatic recurrence by chemotherapy.

1.4.3.5 Stoma care cost

The stoma care cost has been estimated to be an annual cost of all prevalent permanent stoma costs related to bowel cancer. The total cost of stoma care is estimated to be approximately £52m (I3). This consisted of a stoma care cost of £27.7m for patients who have previously undergone rectal surgery and £24.3m for those patients who have previously undergone colon surgery. The mean cost per year was calculated as £1,279 per patient.

1.4.3.6 Palliative care cost

Table 1.5: Palliative care costs for colon and rectal cancer

	Colon Cancer	Rectal Cancer
Palliative Intervention costs	£66.7m	£30.5m
- Palliative chemotherapy	(£65.8m)	(£29.7m)
- Palliative stenting	(£0.29m)	(£0.12m)
- Palliative bypass	(£0.0m)	(£0.35m)
- Palliative stoma	(£0.63m)	(£0.09m)
- Palliative radiotherapy	(£0.0m)	(£0.15m)
End of life care	£13.7m	£7.7m
Total Palliative care cost	£80.4m	£38.2m

The estimated total palliative care cost for bowel cancer in England was £118.6m (Table 1.1; J3). This is comprised of £80.4m for the colon cancer and £38.2m for rectal cancer palliative care costs. The total palliative care costs have been presented in two components; the palliative intervention costs and the end of life costs for both colon and rectal cancer. The majority of the palliative intervention cost is a result of treatment by palliative chemotherapy for both colon cancer patients and rectal cancer patients.

1.4.3.7 Screening cost

The screening cost was estimated using the original screening appraisal model⁵. This model was updated for the costs used in the baseline bowel cancer model. The screening cost is an estimate of the first year costs of the programme screening for those aged between 60 to 69 years by Faecal Occult Blood testing (FOBT) and the resulting costs of treating the additional cancers detected by the programme. Table 1.6 shows that this cost is estimated at £112.8m and represents 10% of the overall cost of illness.

Table 1.6 shows the screening cost for five years after the introduction of the programme. The table shows the testing costs associated with the programme and then the subsequent treatment costs for the additional cancers detected by screening.

Table 1.6: Total Screening Cost by year following implementation

	Year 1	Year 2	Year 3	Year 4	Year 5
Testing and Diagnostics	£50.3m	£50.2m	£49.8m	£49.8m	£49.6m
Treatment costs	£62.5m	£65.9m	£34.1m	£34.4m	£16.8m
Total Screening cost	£112.8m	£116.1m	£83.9m	£84.2m	£66.4m

1.4.3.8 Increased-risk groups cost

Increased-risk patients account for a small proportion (5.5%) of the cost of the total cost of illness, estimated to be £53.8m (P3). However, there is a high degree of uncertainty surrounding this as data sources to populate this aspect of the treatment pathway were limited.

⁵'Option Appraisal of population-based Colorectal Cancer Screening in England.' Tappenden P, Chilcott J, Eggington S, Patnick J, Sakai H and Karnon J. Gut Volume 56 issue 5 (2007)

1.5 OPTIONS MODEL

1.5.1 Option Model Outline

A number of potential options for evaluation have been identified based on discussions and subsequent correspondence with the Project Advisory Group (9th February 2006) and the English Bowel Cancer Working Group (23rd November 2005, plus previous meetings' minutes). The options are summarised below.

Access to services:

1. GP referral criteria;
2. Media campaign;
3. Emergency stenting;
4. Colonoscopy versus flexible sigmoidoscopy;
5. Colonoscopy completion rates.

Treatments:

6. Pre- versus post- operative radiotherapy;
7. Improve surgery/pathology;
8. Lap versus open;
- 9a. Alternative adjuvant chemotherapies;
- 9b. Alternative palliative chemotherapies
10. Enhanced recovery programme
11. Intensive versus relaxed follow-up
12. Increased liver/lung resection

Palliative care:

13. Increase palliative surgery.

A brief outline of the options assessed within the model follows.

1.5.1.1 Access to service options

Improving GP referral criteria (option 1), raising awareness in the general population of England via media campaigns (option 2) and implementing a screening programme (assessed separately) all aim to detect the disease at an earlier stage, and hence improve long term outcomes. However, for each of these options, there is also the potential for an increased number of patients to present without colorectal cancer to be drawn into the bowel cancer system; resulting in an increased workload with little benefit and with the potential for harm.

Around 15% of colorectal cancer patients present as an emergency, often due to obstruction of the bowel. Stenting may be used as a bridge to elective surgery (option 3) to improve operative mortality rates and reduce the number of people requiring stomas.

Patients are diagnosed at endoscopy, via either a flexible sigmoidoscopy or a colonoscopy. Complete colonoscopy allows for visualisation of the entire colon to the caecum, whilst flexible sigmoidoscopy only allows for the visualisation of the distal portion of the bowel, meaning cancers or polyps may not be detected. However, colonoscopy is more expensive, potentially more time consuming, more uncomfortable and more dangerous than sigmoidoscopy. The use of colonoscopy as against flexible sigmoidoscopy may be increased from around 70% to 90% (option 4). Colonoscopy completion rates may also be improved via national training programmes to reduce the number of barium enemas required following an inadequate colonoscopy (option 5).

1.5.1.2 Treatment options

Patient outcomes may be improved by improving surgical expertise or developing specialist pathology services (option 7), using laparoscopic instead of open surgery (option 8), or through the further development of chemotherapy regimens for adjuvant or palliative care (option 9). Trials also suggest that carrying out pre-operative instead of post-operative radiotherapy (CR07) (option 6) and using an intensive rather than relaxed follow up programme (FACS) (option 11) may improve patient outcomes. Implementing an Enhanced Recovery Programme (option 10) has been shown to have no negative effect on health outcomes whilst saving costs and beds, and increasing the use of liver and lung resection for metastatic disease may reduce recurrence rates (option 12). The majority of these options would incur staff training and resource costs.

1.5.1.3 Palliative options

There may be potential for increasing the use of palliative bypasses and stenting in patients with inoperable tumours, to replace best supportive care, which may lead to improvements in their quality of life (option 13).

1.5.2 Methods

The bowel cancer options model has been produced using the simulation software, SIMUL8, based on the patient pathways and data collected for the base case model, trial data, personal communication with experts and further literature. As the underlying model of the natural history of bowel cancer and the treatment pathways are complex, standard health economic modelling techniques such as simple decision analysis and Markov processes are not sufficiently flexible to accurately capture this level of detail for option modelling. Instead, a more sophisticated discrete event simulation (DES) approach has been used. This simulation model estimates the expected costs and resource use resulting from the diagnosis, treatment and follow-up of bowel cancer, as well as health outcomes such as number of cancers diagnosed, life years gained and Quality-Adjusted Life Years (QALYs) gained for the modelled population from the perspective of the UK NHS and PSS. In line with current practice, future costs and health outcomes are discounted at a rate of 3.5%.

It is important to note that other individuals besides those with sporadic bowel cancer consume resources within the bowel cancer service. The population included within the model (and hence the boundary around the modelled service) is any person presenting with bowel cancer symptoms or requiring the diagnostic services in England (with the exclusion of people who are at increased-risk of bowel cancer such as people with FAP, HNPCC, ulcerative colitis and Crohn's disease). The model includes 4 groups of patients:

1. People who are diagnosed with an underlying bowel cancer;
2. People who present to their GP or at A&E with symptoms of bowel cancer but have no underlying pathology;
3. People who present to their GP or at A&E with symptoms of bowel cancer with other non-malignant colorectal pathology e.g. diverticulitis, ulcerative colitis, haemorrhoids;
4. People in whom adenomatous polyps have been identified.

The model operates on an individual patient-level basis. Each individual is assigned a specific set of characteristics (age, fitness, health utility score, stage of disease, location of cancer, obstructions) before entering into the model which will influence the pathways that the individual patient follows (i.e. event probabilities), times to event occurrence, and the duration of events. Disease progression prior to diagnosis has been modelled using probabilities calibrated using the SchARR screening model. Disease-free and overall survival has been modelled using data from several trials according to stage and location of the cancer (Trueman *et al.* 2007 - Section 4). Operative mortality and death from other causes has also been explicitly modelled. Health utility scores are based on the absence or presence of colorectal cancer and the patient's age, rather than Dukes' stage due to limited evidence in this area (Trueman *et al.* 2007 - Section 4). Utility scores are decremented in the model to represent the reduced quality of life as a result of some of the interventions. However, in many cases there is no evidence around the way in which patient quality of life is affected; in most such cases no difference in quality of life has been assumed. First-order uncertainty (variation in the sample data) and second-order uncertainty (uncertainty surrounding the population mean) have been incorporated into the model using appropriate distributions. A schematic of the model is presented in Figure 4.1 overleaf and the model parameters can be found in the main report (Trueman *et al.* 2007 – Appendix C).

Many assumptions have been made throughout the patient pathways. These assumptions have been made explicit in the main report (Trueman *et al.* 2007 – Section 4 and Section 5 respectively) and have been shown to a number of clinicians during the project to verify that they are not inconsistent with current clinical opinion. Further research in a number of areas would reduce the large amount of model assumptions currently required.

Several parameters have been altered for each option individually and the model has been run 1250 times for each. The results present costs, LYs gained and QALYs gained for each option, as well as a number of secondary outcomes such as the cost at each stage of the pathway and the number of patients of each Dukes' stage for each option. The results have also been subjectively graded according to their uncertainty and implementability as an aid to understanding some of the advantages and disadvantages of each of the options. The

aim of this analysis is to provide an estimate of the effect of making changes to the current bowel cancer service. However, because of the large amount of uncertainty involved in the process, further research is required in order to validate the results and to allow a more in-depth analysis of the options.

The Department of Health has recommended that bowel cancer screening using faecal occult blood test (FOBT) for individuals aged between 60 to 69 years is to be rolled out imminently. Importantly, bowel cancer screening has the potential to both reduce the incidence of cancer and change the distribution of disease stage at the expense of increasing the use of diagnostic services and prospective treatment of people with polyps. Currently screening has been piloted, but has not been rolled out. The effect of implementing screening has been modelled for the 'competing' options (to improve GP referral criteria and to introduce a media campaign); however the remaining options will be discussed without the use of mathematical modelling because the effect upon the relative cost-effectiveness between the options is expected to be minimal.

There is necessarily a high level of uncertainty in the analyses presented in this report due to the sparsity of sometimes quite fundamental evidence. The probabilistic uncertainty within the marginal cost and quality of life results for the options is presented in Table 1.9. The uncertainty in the potential value of each of the options has been graded subjectively. This subjective grading tries to capture both the uncertainty captured in the probabilistic sensitivity analysis together with uncertainties in the structural assumptions underlying the model and the use of evidence within the model. These grades should all be interpreted within the overall high level of uncertainty indicated above.

Table 1.7: Uncertainty grade scale

Robust	1
Some uncertainty	2
Highly uncertain	3

Grade 1 suggests that we are fairly confident that the option is unlikely to provide any negative benefit and it is unlikely to be costly, despite the underlying uncertainties. Grade 2 suggests that there is some uncertainty in the model or the underlying evidence base that could lead to undermine the predicted potential for benefits. Finally, Grade 3 suggests that the results of the modelled option are highly uncertain and further research is required before any further validation is possible.

The level at which implementation is possible has also been graded.

Figure 1.3 Schematic of the options model

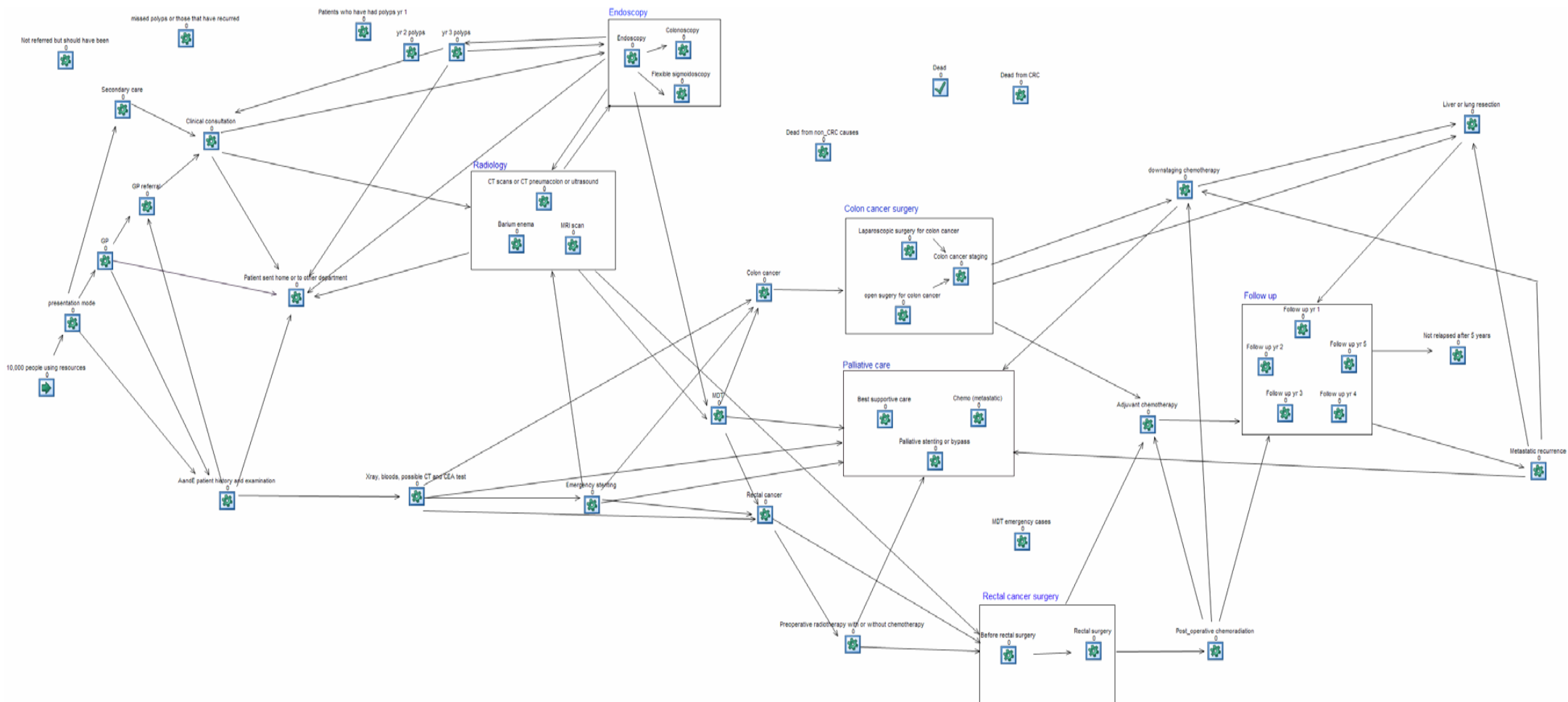


Table 1.8: Implementability grade scale

Implementable with modest development requirements	A
Developmental research on implementation required	B
Basic research required	C

Grade A is used for options where trials have already been run and the option has been piloted. Grade B suggests that the option has usually been trialled, but piloting has not yet begun. Finally, Grade C suggests that there are key gaps in the evidence available around the costs and/ or benefits of the option and further basic research is required in order to understand the potential of the suggested option.

1.5.3 Results

The results for the options are presented in Figure 1.4 and Table 1.9 overleaf. The table presents the estimates for both the base case and each of the individual options for a person consuming bowel cancer services which also includes those patients with a negative diagnosis of bowel cancer. The results presented include the total costs, life years gained (LYG), Quality Adjusted Life Years (QALYs), marginal LYG and marginal QALYs. The final columns of this table rank the costs and rank the QALYs in comparison with the baseline options model results. For example, the lowest marginal cost (-ive implies the option will be cost saving) and highest marginal QALY will receive a rank of 1.

Figure 1.4: Graph of Option Model Results

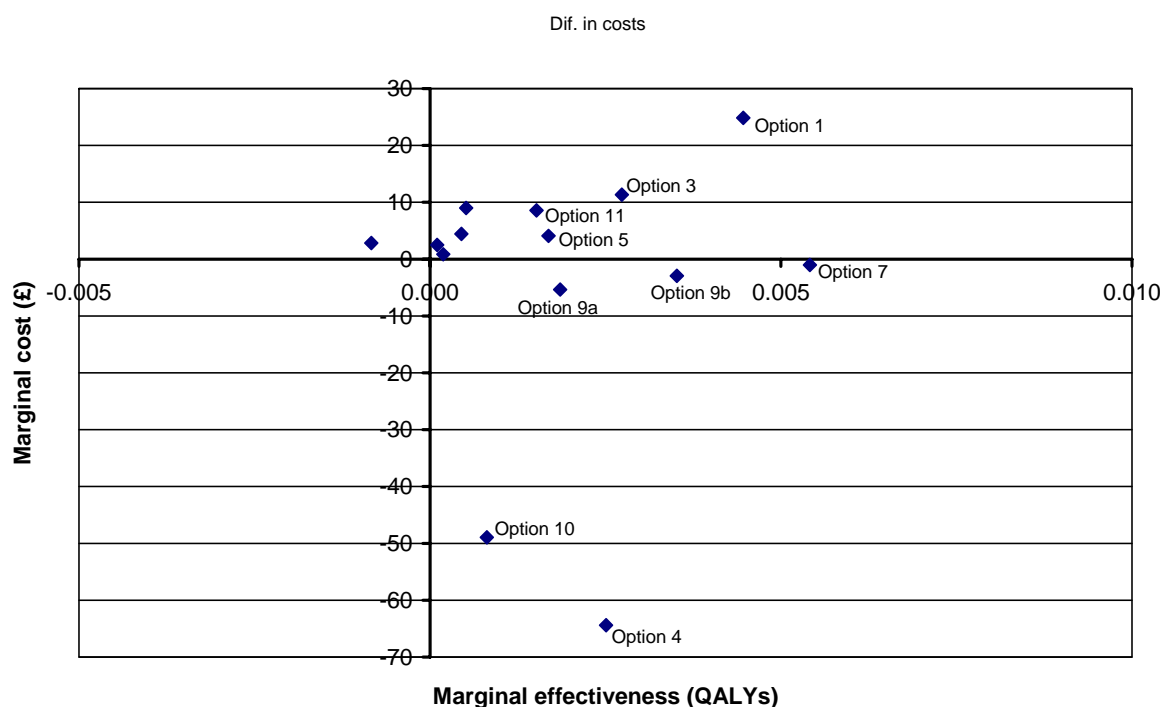


Table 1.9: The Option Model Results

Option	Cost (£)	Life years	QALYs	Marginal cost (£)	Marginal life years	Marginal QALYs	Cost rank	QALY rank	
--	Baseline	908.18	10.4691	8.1981					
1	GP referral criteria - sensitivity	933.02	10.4708	8.2026	24.85 (-32.33, 84.23)	0.0017 (-0.0724, 0.0722)	0.0045 (-0.0508, 0.0586)	14	2
2	Media campaign	909.50	10.4702	8.1986	1.32 (-64.38, 63.31)	0.0011 (-0.0772, 0.074)	0.0005 (-0.0601, 0.0567)	7	10
3	Emergency stenting	919.52	10.4731	8.2008	11.34 (-46.85, 65.58)	0.0040 (-0.0678, 0.0767)	0.0027 (-0.0525, 0.0589)	13	4
4	Colonoscopy versus flexi sig	843.79	10.4802	8.2006	-64.39 (-120.52, -11.54)	0.0111 (-0.0615, 0.0839)	0.0025 (-0.054, 0.0586)	1	5
5	Colonoscopy completion rates	912.29	10.4713	8.1998	4.11 (-49.75, 56.92)	0.0022 (-0.0725, 0.0765)	0.0017 (-0.0545, 0.0589)	10	7
6	Pre versus postop RT	912.64	10.4695	8.1986	4.46 (-46.71, 58.97)	0.0004 (-0.0674, 0.074)	0.0004 (-0.0527, 0.0566)	11	11
7	Improve surgery/pathology	907.15	10.4763	8.2035	-1.03 (-51.7, 45.75)	0.0072 (-0.0626, 0.0811)	0.0054 (-0.0481, 0.0617)	5	1
8	Lap versus open	911.01	10.4680	8.1973	2.84 (-53.97, 62.71)	-0.0011 (-0.0745, 0.0688)	-0.0008 (-0.0569, 0.0538)	9	14
9a	Alternative adjuvant chemotherapies	902.84	10.4714	8.2000	-5.34 (-31.83, 24.61)	0.0023 (-0.0596, 0.0647)	0.0019 (-0.0464, 0.05)	3	6
9b	Alternative palliative chemotherapies	905.24	10.4751	8.2016	-2.94 (-6.65, -0.31)	0.0060 (0.0006, 0.0128)	0.0035 (0.0004, 0.0074)	4	3
10	Enhanced recovery programme	859.25	10.4702	8.1989	-48.93 (-107.93, 12.75)	0.0011 (-0.0707, 0.08)	0.0008 (-0.0535, 0.0616)	2	9
11	Intensive versus relaxed follow up	916.75	10.4714	8.1996	8.57 (-54, 73.56)	0.0023 (-0.0697, 0.0781)	0.0015 (-0.0531, 0.0598)	12	8
12	Increased resection liver/lung	909.02	10.4695	8.1983	0.84 (-43.06, 41.23)	0.0004 (-0.0653, 0.0696)	0.0002 (-0.0501, 0.0536)	6	12
13	Increase palliative surgery	910.66	10.4691	8.1982	2.48 (1.12, 4.27)	0.0000 (0, 0)	0.0001 (0, 0.0002)	8	13

Figure 1.4 shows that the options to; (Option 2) introduce a media campaign; (Option 5) improve colonoscopy completion rates; (Option 6) use preoperative instead of postoperative radiotherapy; (Option 8) use laparoscopic rather than open surgery; (Option 12) increase liver/lung resection for metastatic disease; and (f) increase the use of palliative surgery do not have a large effect on either costs or QALYs of the system as a whole. However, there are a number of options which stand out as warranting further consideration. These are discussed below. The assumptions underlying all of the options can be found within the main report (Trueman *et al.* 2007 – Section 5).

1.5.3.1 Improving GP criteria

Assuming a cost of implementation of £20 per patient, the cost per QALY gained would be £5,566 and £3,969 for a 5% and 10% absolute improvement in sensitivity. If this cost per patient was doubled, the incremental cost per QALY gained would become £10,046 and £6,565 respectively. This option has been given a grade of 3C because there is little evidence surrounding the disease natural history and further research would be required around the way in which GP guidelines could be improved in order to increase sensitivity without decreasing specificity of the referral. Although a ‘competing’ option to screening, the SchARR screening model (Tappenden *et al.*, 2007) suggests that this option would still be considered as cost-effective by the National Institute for Health and Clinical Excellence (NICE) if the Fecal Occult Blood Test (FOBT) was rolled out throughout England. This analysis assumes that Dukes stage at diagnosis has the potential to be improved by revising GP referral criteria.

1.5.3.2 Emergency stenting

Increasing the use of emergency stenting from around 2% to 10% would have only a small effect on costs or outcomes due to the small amount of people that may potentially benefit from a stent. However, increasing the use of emergency stenting to 47.5% (the maximum percent achievable suggested by clinicians during elicitation exercises) increases both costs and outcomes further; with an estimated cost per QALY gained of £4,150. This option has been given a grade of 2A because there is a little uncertainty surrounding the cost of training and patient quality of life, but with additional training it could be implemented. The roll out of screening in England is expected to reduce the number of emergency presentations, hence reducing the effectiveness of this option. However, the cost of training surgeons may also be reduced if demographics allow. Therefore, whilst screening may reduce the total cost-effectiveness of this option, the relative cost-effectiveness per person should remain approximately the same.

1.5.3.3 Increasing the use of colonoscopy as an alternative to flexible sigmoidoscopy

This option is expected to dominate the base case scenario (i.e. the option produces a greater number of QALYs at a lesser cost than the base case scenario). This result is strongly dependent upon the assumed proportion of polyps/cancers a flexible sigmoidoscopy is able to detect and the disease natural history assumed within the model; both of which are based on limited evidence. However, this option has been given a grade scale of 2B since it is anticipated to be cost saving despite these uncertainties and relatively easily to implement

without much further work. Screening is expected to increase the use of colonoscopy due to the additional tests required following a positive FOBT. Therefore, capacity and resource constraints may cause difficulties in using additional colonoscopies when screening has been rolled out. However, the per-patient cost-effectiveness is unlikely to change significantly, unless many more diagnostic clinics are required to accommodate the additional colonoscopies.

1.5.3.4 Improving surgical expertise/ developing pathology services

Assuming that the cost of improving surgical expertise or developing pathology services is around £1500 per bowel cancer patient and that a hazard ratio of 0.7 can be applied to the disease-free survival curves, this option is dominating (decreases costs whilst improving outcomes) until the cost per bowel cancer patient becomes greater than around £2000. There is very little evidence surrounding the cost required in order to produce this effectiveness, particularly with regards to developing pathology services. However, trials have been run surrounding the effects of improving surgery on health outcomes (Martling *et al*, 2000). Therefore, the option to improve surgical expertise has been given a grade of 2A whilst the option to develop pathology services has been given a grade of 3B. Screening is not expected to have a significant effect upon the relative cost-effectiveness of this option.

1.5.3.5 Improving adjuvant/ palliative chemotherapy

This option considers the necessary benefits and cost characteristics required of a hypothetical novel chemotherapy regime to provide a valuable improvement to the bowel cancer services. It is highly likely that a new chemotherapy would incur additional costs, particularly in terms of drug acquisition. A hazard ratio of 0.85 or 0.7 in disease free survival for a novel adjuvant chemotherapy would justify an additional cost of £200 or £400 per bowel cancer patient respectively. The marginal cost of a new palliative chemotherapy with similar survival characteristics to bevacizumab would need less than £100 per bowel cancer patient to be cost saving. This option has been given a grading scale of 2C because the interventions are hypothetical. Screening is expected to reduce the number of patients requiring chemotherapy, although the per-patient cost-effectiveness is expected to remain approximately the same.

1.5.3.6 Introducing an Enhanced Recovery Programme (ERP)

The model suggests that this option would dominate the base case since it is expected to be cost saving and have no negative effect on patient quality of life. This option has been graded at 1A since the evidence is relatively robust and ERPs have been trialled and piloted. The introduction of screening is again not expected to affect this option in terms of its relative cost-effectiveness.

Secondary model outcomes for all of the options are shown in Table 1.10 overleaf. This table shows the difference in each of the options' results from the base case results listed. Where zero difference is expressed there is no more than five units' difference in the results between the option and the base case. This table suggests that the proportion of each cancer stage and costs of each part of the pathway are predominantly affected by options 1, 2 and 4.

Table 1.10: Options Output for number of Patients

	Base case	Option													
		1	2	3	4	5	6	7	8	9a	9b	10	11	12	13
Mean time until death	5206	0	0	0	0	0	0	8	0	0	0	0	0	0	0
St dev of time until death	3454	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cost of diagnosis: _no cancer	17905	0	0	15	-6	0	6	8	18	0	0	7	13	19	0
Cost of diagnosis: _polyps	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cost of diagnosis: CRC	42	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cost of rectal cancer treatment	1948	47	40	0	-326	10	6	-26	0	-20	0	-41	7	0	0
Cost of colon cancer treatment	807	-6	0	-7	10	0	0	0	0	0	0	0	0	0	0
Total number of polyps	20329	22	-64	446	545	15	352	-802	63	-117	-109	-1744	298	9	89
Total number of cancers	15167	10 4	-19	-78	381	-24	6	-596	2322	-516	-94	45	254	11	81
No. of low risk polyps diagnosed	1645	21	-35	0	0	-14	0	0	0	0	0	0	0	0	0
No. of high risk polyps diagnosed	345	0	0	0	-33	0	0	0	0	0	0	0	0	0	0
No. of cancers treated electively	38	0	0	0	-20	-14	0	0	0	0	0	0	0	0	0
No. of elective Dukes A diagnosed	1607	19	-36	0	17	0	0	0	0	0	0	0	0	0	0
No. of elective Dukes B diagnosed	289	0	0	0	-28	0	0	0	0	0	0	0	0	0	0
No. of elective Dukes C diagnosed	43	0	0	0	-14	0	0	0	0	0	0	0	0	0	0
No. of elective Dukes D diagnosed	93	0	0	0	0	0	0	0	0	0	0	0	0	0	0
No. of emergency cases	90	0	0	0	0	0	0	0	0	0	0	0	0	0	0
No. of Dukes A (emergency)	64	0	0	0	-19	0	0	0	0	0	0	0	0	0	0
No. of Dukes B (emergency)	56	0	0	0	0	0	0	0	0	0	0	0	0	0	0
No. of Dukes C (emergency)	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0
No. of Dukes D (emergency)	19	0	0	0	0	0	0	0	0	0	0	0	0	0	0

1.5.4 Conclusion

The model suggests that the most economically attractive option for improving outcomes for bowel cancer patients is to increase the use of colonoscopy from 70% to 90% as an alternative to flexible sigmoidoscopy. Whilst the assumptions in the model may affect the extent to which this option will benefit patients, it is expected to improve health outcomes and produce cost-savings. Research concerning the probability of polyps and cancers being detected in patients with distal colon cancer would be valuable in further assessing the potential benefits of this option. The evidence for the Enhanced Recovery Programme suggests that this is likely to be cost saving with initial indications of a low associated risk of detrimental clinical outcomes. This option is again relatively robust and at an advanced stage of development for implementation.

The model suggests that the whilst the further development of GP referral criteria guidelines has the potential to improve long outcomes this option is highly uncertain due to the lack of evidence surrounding disease natural history and how symptoms related to disease natural history, together with uncertainty on the costs of implementation. It would also require substantial further research in order to assess how changes in referral criteria will affect GP referrals, so that specificity is not decreased as a result of increasing sensitivity since this would lead to worsened health outcomes.

Increasing the use of emergency stenting is expected to be very effective for a small number of patients consuming bowel cancer resources, but is associated with a relatively high cost. Options 7 and 9, to improve surgical resection and/or pathology and to improve adjuvant or palliative chemotherapies, are associated with improvements in health outcomes at a relatively low cost; providing that for option 7 the cost of improvements in pathology are not greater than the modelled costs, and for option 9 that the new chemotherapy regimens are not considerably more expensive than the current standard chemotherapies. All of these options would provide health benefits; however there is uncertainty surrounding the necessary costs required to provide the amount of health benefit. In the case of option 9, this will depend upon new and currently unknown chemotherapy costs and effectiveness.

Many of the options assessed within the model display huge variability due to the large amount of uncertainty associated with both the base case model and the options. The confidence intervals around the results suggest that it is unlikely that increasing the use of colonoscopy and introducing an Enhanced Recovery Programme will not be cost saving. However, since there is very little evidence regarding health utility scores for bowel cancer services, there is a considerable degree of uncertainty associated with all of these options in terms of their impact upon quality of life. This is a clear area in which further research would be merited.

The effect of introducing bowel cancer screening across England upon the value of the options is expected to be minimal, in that whilst the total costs and benefits of different options may be reduced slightly in a system with a higher level of preventative treatment the marginal impacts of many of the treatment options are not expected to be significantly different. Furthermore, the fact that the current FOBT test has been shown to have a low

sensitivity means that whilst the effect of the options around presentation and early referral are likely to be largely affected by the introduction of screening, the ScHARR screening model (Tappenden *et al*, 2007) suggests that they do have the potential to provide some benefit alongside screening using the FOBT 60-69 screening test.

1.6 LIMITATIONS OF THE ANALYSES

It is important to acknowledge that both the baseline model and the options model presented within this report are dependent on a considerable number of structural and parametric assumptions, which have been sourced from expert clinical advice and from evidence available within the literature. As with any mathematical model which attempts to synthesise a large yet incomplete evidence base, the results of the analyses are subject to a considerable degree of uncertainty.

Furthermore, the populations recruited into many of the clinical trials used to inform the model are likely to be fitter and younger than the English NHS bowel cancer population; therefore, it is likely that modelled clinical outcomes appear more favourable than would be observed for the general bowel cancer population. Consequently, when modelling the options which are expected to improve disease-free survival, their impact upon life years and QALYs gained may have been slightly underestimated.

1.7 FURTHER RESEARCH

Further research would be valuable in the following areas:

- Health related quality of life and utilities throughout the bowel cancer treatment pathways and disease natural history;
- Relationship between symptoms and histological state;
- Benefits of adjuvant chemotherapies;
- Understanding presentation, specifically time from onset of symptoms to presentation;
- Sensitivity of endoscopy;
- Relationship between distal polyps and proximal cancers;
- Costs of surgical techniques;
- Audit of current practice nationally;
- Prognosis for inoperable patients;
- Benefit of follow-up;
- Costs and benefits for increased and high risk groups.

Further explanation around each of these is given in the main report (Trueman *et al.*, 2007).

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