Using Whole Disease Modelling to inform economic recommendations for the detection, diagnosis, treatment and follow-up of colorectal cancer

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INTRODUCTION

Conventional economic evaluation typically involves piecewise comparisons of competing technologies at a single isolated point in a broader care pathway. This study assesses the value of simulating whole disease and treatment pathways to provide a common economic basis for informing resource allocation decisions across an entire disease service. This "Whole Disease Modelling" approach was applied to the evaluation of technologies for the detection, diagnosis, treatment and follow-up of colorectal cancer with the intention of informing NICE's colorectal cancer clinical guideline[1] (see Box 1).

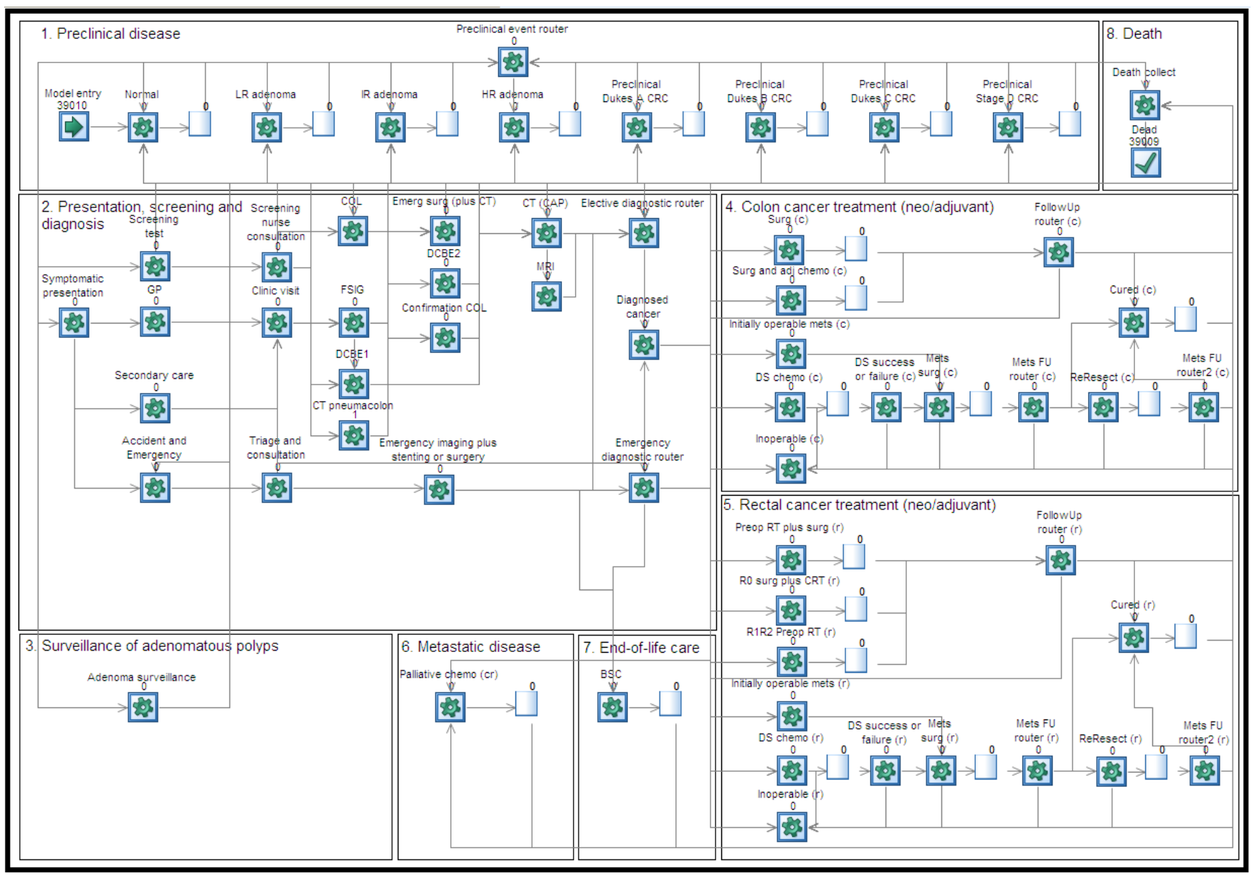
Box 1 Topics included in the scope of the NICE colorectal cancer clinical guideline

Topic A	Effective diagnostic modalities in establishing a diagnosis of colorectal cancer in patients referred with suspicious symptoms.
Topic B	Tumour staging for defining treatment in patients with colorectal cancer.
Topic C	Curative treatment for patients with stage I or polyp cancer.
Topic D	Treatment for patients presenting as emergencies with the symptoms of colorectal cancer.
Topic E	The sequence of local and systemic treatments in patients presenting with locally-advanced colorectal cancer.
Topic F	The sequence of local and systemic treatments in patients presenting with synchronous metastatic disease.
Topic G	Effectiveness of pre-operative a) short course radiotherapy and b) chemo-radiotherapy in treating patients with rectal cancer.
Topic H	For patients with stage II and III rectal cancer, the indications for adjuvant chemotherapy after surgery.
Topic I	For patients with high-risk stage II colon cancer, the indications for adjuvant chemotherapy after surgery.
Topic J	The sequence of ablation, surgery, regional therapy and systemic therapy, to achieve cure or long-term survival in patients with apparently incurable metastatic disease.
Topic K	Clinical indications for performing liver metastasectomy in patients with colorectal cancer metastasised to the liver.
Topic L	Clinical indications for performing extrahepatic metastasectomy in patients with colorectal cancer.
Topic M	Chemotherapy for patients with advanced and metastatic disease
Topic N	Methods and frequencies of follow-up after potentially curative treatment for colorectal cancer.
Topic O	Colorectal-specific support for patients diagnosed with colorectal cancer.

METHODS

A patient-level simulation model[2] was developed using SIMUL8 software (see Figure 1). The model simulates disease and treatment pathways from preclinical disease through to detection, diagnosis, adjuvant treatment, follow-up, treatments for metastases and supportive care. The model was populated using randomised controlled trials, observational studies, audit data, health utility studies, costing sources and expert opinion. Unobservable natural history parameters were calibrated against published data (incidence, stage at diagnosis, probability obstruction and adenomas prevalence) using Bayesian MCMC methods. Economic analysis was undertaken using (1) standard cost-utility decision rules within each guideline topic, and (2) constrained optimisation across all modelled topics.

Figure 1 The colorectal cancer Whole Disease Model



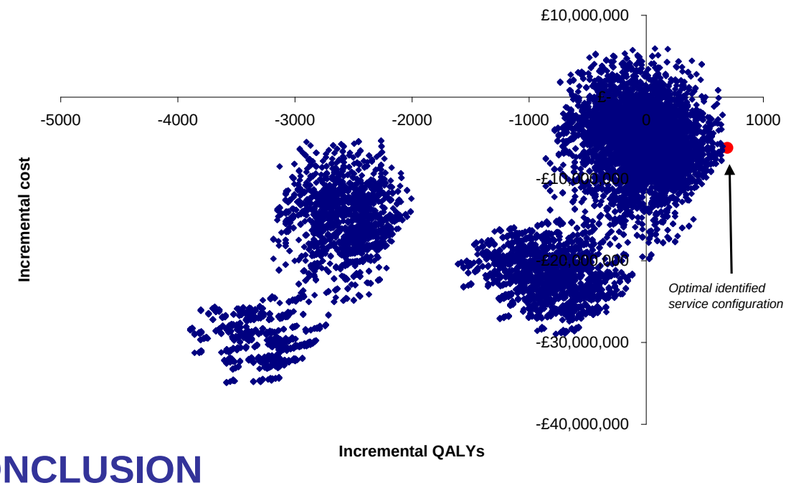
RESULTS

The NICE guideline included fifteen individual economic evaluation topics. Under usual processes, conventional piecewise economic modelling would have been used to evaluate between one and three guideline topics. In contrast, the Whole Disease Model provided a consistent platform for the economic evaluation of eleven of the fifteen guideline topics, ranging from alternative diagnostic technologies through to cytotoxic treatments for metastatic disease. The constrained optimisation analysis identified a configuration of colorectal services which was expected to maximise QALY gains without exceeding current expenditure levels.

Table 1 Piecewise cost-effectiveness results estimated using the Whole Disease Model (300,000 simulated patients)

Topic	Option	Cost	QALY	Inc. cost	Inc. QALY	ICER (QALY)
Baseline service		**£105,486,388**	**14,636,144**	-	-	**-**
A	CT colonography	£102,244,329	14,636,316	£6,515,000	2488.98	**£2,618**
	FSIG→BE	£104,333,696	14,636,149	-	-	**Dominated**
	Baseline (COL)	£105,486,388	14,636,144	-	-	**Dominated**
	FSIG→COL	£95,729,329	14,633,827	-	-	**-**
C	TEMS	£101,186,651	14,636,392	-£4,299,737	248.62	**Dominating**
	Radical resection	£105,486,388	14,636,144	-	-	**-**
D_1	Baseline	£105,486,388	14,636,144	£311,207	144.72	**£2,150**
	No CT scan	£105,175,181	14,635,999	-	-	**-**
D_2	Baseline	£105,486,388	14,636,144	£311,207	144.72	**£2,150**
	No stenting	£105,175,181	14,635,999	-	-	**-**
E	All pre-op CRT	£106,231,677	14,636,458	£1,594,462	66.74	**£23,891**
	All pre-op RT	£104,637,215	14,636,391	-	-	**-**
	Baseline	£105,486,388	14,636,144	-	-	**Dominated**
	No pre-op adjuvant tx	£106,168,990	14,636,050	-	-	**Dominated**
F	Simultaneous resection	£105,395,195	14,636,144	-£91,193	0.00	**Dominating**
	Baseline (staged)	£105,486,388	14,636,144	-	-	**-**
G	All pre-op CRT	£106,231,677	14,636,458	£1,594,462	66.74	**£23,891**
	All pre-op RT	£104,637,215	14,636,391	-	-	**-**
	Baseline	£105,486,388	14,636,144	-	-	**Dominated**
H	Adjuvant chemo	£104,732,227	14,636,197	-£754,161	53.87	**Dominating**
	Baseline	£105,486,388	14,636,144	-	-	**-**
I	Baseline	£105,486,388	14,636,144	-£307,136	144.35	**Dominating**
	No adjuvant chemo	£105,793,524	14,635,999	-	-	**-**
J	Baseline	£105,486,388	14,636,144	£1,149,942	18.62	**£61,746**
	HAI	£104,336,446	14,636,125	£15,388,185	775.42	**£19,845**
	BSC only	£88,948,261	14,635,350	-	-	**-**
M	CAPOX→CAPIRI	£106,742,491	14,636,221	£1,955,623	12.19	**£160,437**
	FOLFOX→FOLFIRI	£110,673,827	14,636,221	-	-	**Dominated**
	CAPOX→CAP	£104,786,868	14,636,209	£7,249,769	246.14	**£29,454**
	FOLFOX→5-FU/FA	£108,673,497	14,636,209	-	-	**Dominated**
	Baseline (current mix)	£105,486,388	14,636,144	-	-	**Dominated**
	CAPIRI→CAPOX	£105,670,207	14,636,104	-	-	**Dominated**
	FOLFIRI→FOLFOX	£109,670,755	14,636,104	-	-	**Dominated**
	CAPIRI→CAP	£102,804,556	14,636,081	-	-	**Ext dom.**
	FOLFIRI→5-FU/FA	£106,596,878	14,636,081	-	-	**Dominated**
	CAP→IR	£97,537,099	14,635,963	-	-	**-**
	5-FU/FA→IR	£100,722,827	14,635,963	-	-	**Dominated**
N	Baseline	£105,486,388	14,636,144	£2,160,699	142.83	**£15,128**
	Relaxed follow-up	£103,325,689	14,636,001	-	-	**-**

Figure 2 Constrained maximisation using the Whole Disease Model (all 11 guideline topics)



CONCLUSION

This study demonstrates that Whole Disease Modelling is feasible and can allow for the economic analysis of virtually any intervention across a disease service within a consistent conceptual and mathematical infrastructure. The approach may be especially valuable in instances whereby a substantial proportion of a disease service has not previously been subjected to formal economic evaluation.

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