Appendix 1 - parametric and structural assu

General

Author	Tappenden et al
Year of publication	2006
Modelling methodology (as described in paper)	State transition model
Cycle length	1 year
Primary measure of clinical benefit	QALYs gained
Perspective	UK NHS
Start age for simulation cohort	30 years
Time horizon	Until dead
Stopping age for screening/surveillance	80
Discount rate for costs	3.5%
Discount rate fost health outcomes	3.5%

Primary screening modalities included in evaluation

FOBT options?	Yes
FSIG options?	Yes
DCBE options?	No
COL options?	No

Natural history assumptions (baseline)

Proportion of cancers arising from prior adenoma	100%
Health state definitions	Normal epithelium, Low risk
Separate health states for distal and proximal bowel	Yes
Adenoma/CRC prevalence at model start	0% at age 30.
TP Normal to adenoma	Age dependent. Based on 6
TP Normal to CRC (de novo)	N/a
TP Low-risk to high-risk adenoma	0.02
TP High-risk to CRC	0.03
TP CRC progression	Dukes' A-B (0.58), Dukes' B
Probability of cancer diagnosis	Dukes' A (0.07), Dukes' B (
Probability of cancer death	Dukes' A (0), Dukes' B (0.0
Higher recurrence rates given history of prior adenoma	Yes

Treatment assumptions

Polypectomy undertaken at point of screening?	Yes

Test characteristics (baseline)

Unrehydrated FOBT sensitivity (low risk/small adenoma)		0.05
Unrehydrated FOBT sensitivity (high risk/large adenoma		0.05
Unrehydrated FOBT sensitivity (cancer)	0.41	
Unrehydrated FOBT specificity	0.985	
Rehydrated FOBT sensitivity (low risk/small adenoma)	N/a	
Rehydrated FOBT sensitivity (high risk/large adenoma)	N/a	
Rehydrated FOBT sensitivity (cancer)	N/a	
Rehydrated FOBT specificity	N/a	
Proportion of bowel visualised by FSIG	N/a. Left and right sided pol	
FSIG sensitivity (low risk/small distal adenoma)	0.76	
FSIG sensitivity (high risk/large distal adenoma)	0.97	
FSIG sensitivity (distal cancer)	0.97	
FSIG specificity	1	
COL sensitivity (low risk/small adenoma)	0.76	
COL sensitivity (high risk/large adenoma)	distal = 0.97, proximal = 0.9	
COL sensitivity (cancer)	distal = 0.97, proximal = 0.9	

COL specificity	1.00
DCBE sensitivity (low risk/small adenoma)	N/a
DCBE sensitivity (high risk/large adenoma)	N/a
DCBE sensitivity (cancer)	N/a
DCBE specificity	N/a
Follow up assumptions	
Follow-up schedule modelled	3-yearly COL for high-risk p
Participation	
Compliance rate for screening	60%
Compliance rate for follow-up	80%
Was compliance modelled as independent of previous p	Yes
Health outcome valuation	
Health state definitions (utility values)	No cancer (0.91), Dukes' A
Sensitivity analysis	
Description of simple sensitivity analyses	Discount rates, screening a
Was probabilistic sensitivity analysis undertaken?	Monte carlo sensitivity anal
Calibration/validation methods	
Methods for calibration	Ranges informed by literatu
Costs	
Cost of FOBT (single test)	£11.74
Cost of FSIG	£51.60
Cost of DCBE	N/a
Cost of COL	£188.40
Cancer treatment costs	Dukes' A (£8,299.24), Duke

umptions used within previous CRC screening mod

Neilson et al	Sonnenberg et al	Frazier et al
2003	2002	2000
Markov model	Markov process	Markov model
1 year	1 year	1 year
QALYs gained	Life years saved	Life years gained
UK NHS	US third-party payer	US societal
50 years	50 years	50 years
Until dead	Until dead	Until dead
Not reported	Not reported	85
6.0%	3.0%	3.0%
1.5%	3.0%	3.0%
Yes	Yes	Yes
No	Yes	Yes
No	No	Yes
No	Yes	Yes
100%	Not reported	100%
Polyp/cancer free, low risk polyp	CRC, status after FOBT, status	Low risk adenoma, high risk ade
No	No	Yes
0.26	Taken from 2 autopsy studies. V	21% adenoma prevalence at ag
0.01	0.01	Logistic regression based on 6 a
N/a	N/a	N/a
0.02	N/a	0.02
0.05	N/a	0.05
Dukes' A/B to Dukes C/D (0.4)	N/a	Localized-regional CRC (0.28), l
Dukes' A/B (0.25), Dukes' C/D (	N/a	Localized (0.25), Regional (0.55
Dukes' A/B (0.002), Dukes' C/D	Without screening, 40% CRCs a	Localized (0.002), Regional (0.0
Yes	N/a	Yes
Yes	Yes	Yes
0.1	N/a. Only CRC is modelled as "t	0.1
0.1	N/a. Only CRC is modelled as "t	0.1
0.33	0.40	0.33
0.97	0.975	0.97
N/a	N/a	0.1
N/a	N/a	0.1
N/a	N/a	0.6
N/a	N/a	0.9
N/a	45% detectable by FSIG	N/a. Left and right sided polyps a
N/a	N/a	0.85
N/a	N/a	0.95
N/a	N/a	0.95
N/a	N/a	1
0.85	N/a	0.85
0.95	N/a	0.95
0.95	N/a	0.95

1	N/a	1
N/a	N/a	0.3
N/a	N/a	0.5
N/a	N/a	0.7
N/a	N/a	0.86
3-yearly COL for high-risk patier	Colonoscopy undertaken every :	3-yearly COL for high-risk patier
60%	100%	60%
80%	100%	80%
Yes. Fall in participation modelle	Complete compliance assumed.	Yes
Adjustment for quality of life of 0	N/a	N/a
FOBT compliance rates, follow-u	FOB test characteristics, FOBT	All natural history parameters va
No	No	No
Natural history parameters base	None reported.	Natural history calibrated agains
£5	US $3.50	US $38
N/a	US $400.56	US $279 ($564 with polypectom
N/a	N/a	US $296
£127 (£138 with polypectomy)	US $695.95	US $1012 ($1519 with polypecto
Screen-detected: Dukes' A/B (£	Value not reported.	Localized CRC ($22,000) Regio

dels

Vijan et al	Ladabaum et al	Khandker et al
2001	2001	2000
Markov decision model	Markov model	(Dynamic) state transition mode
Not reported	1 year	Not clearly reported. First 20 ye
Life years saved	Life years gained	Life years gained
US third-party payer	US third-party payer	Not reported
50 years	50 years	50
Lifetime	30 years (Until age 80)	Until dead
Unclear	80	85
3.0%	3.0%	3.0%
3.0%	3.0%	3.0%
Yes	Yes	Yes
Yes	Yes	Yes
No	No	Yes
Yes	Yes	Yes
75%	90%	100%
Not clear. Appears to be normal	Normal, polyp, cancer (localized	Disease-free, hyperplastic polyp
No	No	Yes
0.2 adenoma prevalence	Prevalences at age 50: adenom	25% adenoma prevalence at ag
Incidence rates based on 5 auto	Age and gender specific, based	Based on models by Whynes ar
Not reported	Age and gender specific, based	N/a
N/a	N/a	N/a
10-year "dwell time" to CRC for	Age and gender specific, based	Rates for malignant transformati
2 years for progression through	2-year sojourn time in local, regi	Transition from local to regional
Disseminated cancer assumed t	Local (0.22/year over 2 years), r	Patients with advanced stages v
Localised (0.105), regional (0.3	Local (0.0174/year in first 5 year	Based on SEER data, values nc
Yes	Not reported	Yes
Yes	Yes	Yes
0.05	0.1	0.06
0.05	0.1	0.1
Localized cancer (0.30), region	0.4	0.6
0.975	0.92	0.92
N/a	N/a	N/a
N/a	N/a	N/a
N/a	N/a	N/a
N/a	N/a	N/a
55% neoplasia detectable by FS	50%	N/a
0.85	0.9	0.73
0.85	0.9	0.97
0.95	0.9	0.97
Not reported	0.95	0.92
0.85	0.9	0.79
0.85	0.9	0.85
0.95	0.95	0.97

Not reported	Not reported	1
N/a	N/a	0.67
N/a	N/a	0.82
N/a	N/a	0.84
N/a	N/a	0.75
3-yearly colonoscopy for patient	Surveillance colonoscopy every	Based on Winawer (1997). Depe
25% to 100% in base case.	25% in base case. 75% and 10(	100% assumed in base case. 2:
25% to 100% in base case.	Not reported	100% assumed in base case
Yes	No. Patients either comply with ;	Not reported
N/a	N/a	N/a
One- to three-way sensitivity an;	Varying assumptions concernin;	Focussed on key parameters of
No	Monte Carlo sampling was used	No
Model outputs validated against	Matched against SEER data. M(	Not reported
US $17	$10	US $11 - Under 65 / US $7 - Ov
US $225 ($240 with biopsy)	$206 ($377 with biopsy)	US $176 - Under 65 / US $94 - (
N/a	N/a	US $176 - Under 65 / US $175 -
US $550 (plus $215 if polypecto	$623 ($901 with biopsy)	US $670 - Under 65 / US $438 -
Localized CRC ($60,000) Regio	Local ($24,000) Regional ($31,0	Based on Fireman (Health Care

Loeve et al	Ness et al	Whynes et al
2000	2000	1998
Microsimulation model	Discrete event simulation model	Semi-Markov
N/a	N/a	Annual
Presented as cost consequence	QALYs gained	QALYs gained
US private-healthcare provider (	US societal	UK NHS
50	40 years	50
Until dead	Until dead	Model allows for simulation to continue until
Screening options include possi	Not reported	74
3.0%	3.0%	6.0%
3.0%	3.0%	6.0%
No	No	Yes
Yes	No	No
No	No	No
Yes	Yes	No
100%	100%	83%
No lesion, adenoma ≤5mm, ade	N/a. Steps defined as normal tis	Healthy, adenoma, early asymptomatic CR(
Specific site of lesion modelled t	Yes	No
Simulated adenoma prevalence	0%	No
See above	Defined by piecewise age-deper	Based on Nottingham trial. Values not repor
N/a	Dependent on age, sex, pre-det	Based on Nottingham trial. Values not repor
Based on SEER data. Size distr	Dependent on age, sex, pre-det	N/a
Mean sojourn time of 20 years.	Dependent on age, sex, pre-det	Progressive polyps assumed to take 15 yea
Mean duration of cancer in prec	Dependent on age, sex, pre-det	Based on Nottingham trial. Values not repor
Total average diagnosis of 3.6 y	Time to emergence of symptom	Cancer diagnosis assumed to take 2 years t
Based on SEER data. Values nc	Based on survival curves from S	Based on Nottingham trial. Values not repor
Not reported	Unclear	Based on Nottingham trial. Values not repor
After positive test, all lesions are	Yes	Yes, as done within the Nottingham trial pro
N/a	N/a	N/a
N/a	N/a	FOBT assumed to detect true progressive a
N/a	N/a	Value not reported.
N/a	N/a	Value not reported.
N/a	N/a	Value not reported.
N/a	N/a	Value not reported.
N/a	N/a	Value not reported.
N/a	N/a	Value not reported.
Based on Kaiser Permanente da	N/a	N/a
75% in adenomas ≤5mm. 85% i	N/a	N/a
95% in adenomas ≥10mm.	N/a	N/a
95%	N/a	N/a
Specificity not reported	N/a	N/a
80% in adenomas ≤5mm. 85% i	.75 (small polyps)	Value not reported.
95% in adenomas ≥10mm.	0.8 (intermediate polyps), 0.85 la	Value not reported.
95%	0.95	Value not reported.

Specificity not reported	30% colonoscopies assumed to	Value not reported.
N/a	N/a	N/a
N/a	N/a	N/a
N/a	N/a	N/a
N/a	N/a	N/a
Persons in whom adenomas gre	3-yearly COL for high risk, 5-yea	Not reported in paper.
100%	Not reported	Based on the Nottingham trial. Basecase va
100%	Not reported	Based on the Nottingham trial. Basecase va
Not reported	Not reported	Decline in compliance modelled in line with
N/a	No cancer (0.91), Local colon ca	Taken from Whynes et al (Quality of Life Re
Dwelling time probability distribu	One-way sensitivity analysis var	5 simulations including empirical trial results
No.	No	No
Structural and parametric assun	Model fitted against SEER CRC	Not reported. Based on Nottingham trial.
N/a	N/a	Taken from Walker et al (Journal of Clinical
US $100	N/a	Taken from Walker et al (Journal of Clinical
N/a	N/a	Taken from Walker et al (Journal of Clinical
US $300 ($400 with polypectom	$303 (plus $159 for polypectom	Taken from Walker et al (Journal of Clinical
Costs for primary cancer treatm	Initial costs: Local ($16,051), Re	Taken from Whynes et al (British Journal of

l age 90

C, late asymptomatic CRC, early symptomatic CRC, late symptomatic CRC, screen-detected preclinical

rted
rted

ırs to develop to early-stage colorectal cancer.
rted
following early-stage colorectal cancer onset
rted
rted

ɔtocol.

ıdenoma with a probability of 20%.

alue not reported.
alue not reported.
Nottingham trial.

esearch, 1994). Health utility values not reported.

s, adjusted UK age/sex distribution, lifetime costs, compliance rates. Further sensitivity analysis explorin

Oncology, 1991). Values not reported
Oncology, 1991). Values not reported
Oncology, 1991). Values not reported
Oncology, 1991). Values not reported
Cancer, 1993). Values not reported

l disease, preclinical disease, clinical disease, death - other causes, death CRC

ıg impact of increasing cost of FOBT test, increasing colonoscopy cost, different costs for early- and late

e-stage colorectal cancer, annual screening options, lower survival differences between early- and late-

stage cancers, increased FOBT sensitivity and decreased FOBT specificit