Options for Screening for Colorectal Cancer in the Royal Air Force: A Cost-effectiveness Evaluation

Wg Cdr K Daniels
MA, MSc, MRCGP, DAvMed, RAF
Officer Commanding Medical Wing

Princess Alexandra's RAF Hospital, Wroughton, Swindon, Wilts SN4 0QJ

Dr M McKee
MD, MRCP, FFPHM
Consultant Adviser in Public Health Medicine

Health Services Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT

SUMMARY:- Colorectal cancer (CRC) is the second most common form of malignancy, causing death after late presentation in two-thirds of cases. Early detection makes curative treatment likely. Faecal occult blood tests (FOBTs) detect some pre-symptomatic CRCs and their precursor lesions, adenomatous polyps. A trial showed reduced mortality in USA volunteers aged 50-80 with regular FOBTs; both this and the Nottingham population based trial detected earlier-stage CRCs.

Current US guidelines recommend annual digital rectal examination and FOBTs from age 40. FOBTs have been included in the USAF examination of aircrew for several years. Day-case colonoscopy, with appropriate biopsy excision, is the first-choice follow-up investigation. This study aims to investigate the design of any programme to introduce FOBTs as part of the RAF's existing schedule of Periodic Medical Examinations (PMEs) and Screenings, and the age groups to be included, rather than the decision as to whether or not it should be commenced. The analysis therefore examines the cost per cancer detected. The information required to evaluate subsequent outcomes, such as cost per life-year saved, is not available for the RAF population so speculative extrapolation from other data is not attempted.

Over a third of RAF personnel are under the age of 25, nearly three-quarters under 35 and over four-fifths under 40. Over a quarter of the 4 RAF CRC cases pa occur under age 40 and two-thirds under 50. The most cost-effective age at which to introduce FOBTs in the RAF is 40, regardless of the following parameters.

Assuming FOBT sensitivity of 55% and positivity 5%, FOBT costing 23p and colonoscopy £175, starting FOBTs RAF-wide at age 40 would cost annually £35,968 and £15,881 per CRC case detected. The FOBT contribution to the costs is extremely small and the importance of maximising sensitivity and specificity very great. Hence dietary modification, and using a test or combination of tests with higher sensitivity and/or lower false-positivity, even if much more expensive, would be highly cost-effective, reducing the above costs substantially. Counting as "cases" persons with adenomas reduces the cost per "case" detected by about 75%.

A pilot study is proposed concerning the introduction on selected stations of FOBTs with RAF PMEs/Screenings, from age 40, to determine: sensitivity and false-positivity rates for single and serial FOBTs, and the predictive value of positive tests, in RAF screenees; the annual cost; the costs per CRC case, and per CRC-plus-adenoma case, detected; possibly, an estimate of the cost per life-year saved; and, hence, whether the programme should be extended to all RAF personnel.

FOB screening from age 40 would miss the quarter of RAF CRC cases which occur in personnel under 40. Identification is therefore recommended now of personnel at high risk for CRC, because of personal or family history, at all PMEs/Screenings, regardless of age, with the subsequent offer of serial FOBTs annually and regular colonoscopy. Two half-yearly FOBTs, done with PMEs/Screenings and half-way through the 5 year interval, would detect almost as many CRCs as annual testing, missing only half as many as 5-yearly testing.

This analysis provides information on the costs and consequences of various FOB screening strategies for the RAF and other Services. Similar principles can be applied to develop informed strategies for other screening

Introduction

Colorectal cancer (CRC) is the second most common form of malignancy (after lung cancer) in the UK (1). About two-thirds of patients die (2) but, if detected early when it is still confined to the bowel wall, the 5 year survival rate exceeds 80%. In an unselected population, tests for faecal occult blood (FOB) can detect cancers at a pre-symptomatic stage (3) as well as adenomatous polyps, the precursor lesions for CRC (3, 4). Two large controlled trials have suggested that a FOB screening programme may reduce mortality. Mandel *et al* (5) reported a 33% (95% confidence intervals 13-50) reduction in mortality in volunteers aged 50-80 offered annual testing. Interim results from a British population-based trial show a change in stage distribution, consistent with an improvement in survival of up to 23% (6). After a positive faecal occult blood test (FOBT), colonoscopy is the preferred investigation because it detects early cancers and adenomas more sensitively and reliably than either barium enema or flexible sigmoidoscopy and allows simultaneous biopsy-excision (7).

Although FOB testing has been a regular part of the US Air Force examination of aircrew for several years, it is not currently part of the RAF's programme of Periodic Medical Examinations (PMEs) and Screenings - carried out 5-yearly for ground personnel under the age of 50, and annually for aircrew and air traffic controllers of any age plus all those over 50. Comparability with the US Air Force and civilian airlines has been a major influence on the content of RAF aircrew PMEs, increasing pressure to introduce FOB screening for the RAF population. However, evidence on the efficacy and cost-effectiveness of FOBTs cannot be translated directly to the RAF context: the published studies have been undertaken on older age groups (8) and the medical infrastructure is different. This study aims to inform decisions about the format of any programme to introduce FOBTs for CRC as part of the RAF's existing schedule of PMEs and Screenings, and the age groups to be included.

Methods

Determination of the population at risk

Figures for the RAF population by age band and sex (as at June 1994) were obtained from the Directorate of Information Systems (DAIS), Headquarters Personnel and Training Command, RAF Innsworth. Current and predicted strengths 1994-2005 (by age group for officers but length of service for airmen [other ranks]) and 5 yearly average ages of RAF personnel since 1975 were obtained from the Defence Analytical Services Agency (DASA).

Determination of expected age-sex incidence of CRC in the RAF

As there are no major occupational or socio-economic factors associated with the incidence of CRC (2), age specific rates among the general population, derived from cancer registration (ICD codes 153.x & 154.x) and census data (9), were applied to the age-sex distribution of the RAF population.

Determination of actual incidence of CRC in the RAF

Details of past and current cases of CRC in RAF personnel were extracted manually from the Cade Unit records at RAF Halton. Tumour site, age at and date of presentation, and Dukes's stage and outcome where known, were ascertained for 103 cases of CRC occurring in RAF personnel over the period Jan 1969 - Jun 1994. The date and cause of death for those who survived until retiring from the RAF was often not available. The Dukes's stage was not recorded in the earlier cases, but wherever possible this was inferred from the operation and histology notes.

Calculation of costs and other parameters

Costs of FOBT kits were supplied by the Defence Medical Equipment Depot (DMED). Estimates of FOBT sensitivity and false positivity rate were derived from published literature. Costs of colonoscopy and related investigations were derived from the NHS Management Executive (NHSME) CRC Needs Assessment Review (2). It has been assumed that the likely number of colonoscopies (initial estimate approximately 200 per year dependent on assumptions) and other investigations to be undertaken - by salaried staff - will not require significant additional capital resources.

Choice of outcome measure

As with all diagnostic technologies, there is hierarchy of outcomes. This analysis examines the cost per cancer detected as the analysis seeks to inform the design of any screening programme rather than the decision as to whether or not it should be introduced. Furthermore, the information required to evaluate subsequent outcomes, such as cost per life-year saved, is not available for the population in question and attempts to extrapolate from other data, while possible, would be highly speculative.

Identification of options

If it is decided to introduce a CRC screening programme to the RAF, three questions require answers. First, what form should the screening take? Second, at what age should it commence? Third, how often should it take place?

This analysis is constrained considerably by the existing medical infrastructure in the RAF. A variety of CRC screening strategies is possible, including: FOBT testing with follow-up of those found to be positive; FOBTs supplemented with 3-5 yearly barium enema (10, 11, 12) or 60 cm flexible sigmoidoscopy (13, 14, 15), usually after two negative examinations, from 50 years; once-only flexible sigmoidoscopy at age 55-60, with colonoscopic surveillance of the 3-5% with high-risk adenomas (16); and 10-yearly flexible sigmoidoscopy, starting either at age 55 (17) or as early as 40 (18).

Overall resources, both financial and organisational, in the RAF mean that a programme based on initial screening with FOBTs is the only practical and readily available option. Day-case colonoscopy is the first-choice follow-up investigation.

It has been assumed that FOBT screening would only be considered as part of the existing programme of medical Screenings and PMEs. These involve contact by all RAF personnel with the medical services 5-yearly for ground-duty personnel aged 30-50, and annually for aircrew and air traffic controllers plus all those over 50. It has also been assumed, on grounds of cost-effectiveness, that a programme would treat those having more regular examinations (10% of the total) in the same way as other personnel. The options are therefore to start FOBTs at one of the ages 30, 35, 40, 45, 50, 55 or 60 - screening appreciably fewer personnel with each 5 year increase in the start-age.

Analysis

A model was developed using a Quattro-123 spreadsheet to calculate the costs per CRC detected of introducing FOBTs with PMEs/Screenings from various ages. The baseline model can be expressed as:

$$\frac{\text{Cost}}{\text{Cases detected}} = \frac{\text{(Number in age group} \times \text{Cost of FOBT)} + \text{(Number FOBT positive} \times \text{Cost of colonoscopy)}}{\text{Population} \times \text{Incidence} \times \text{FOBT sensitivity} \times \text{Adjustment for screening intervals}}$$

Sensitivity analyses were undertaken to test the effect of parameter variation, within ranges based on published evidence, on the degree of precision of the cost estimates.

Results
I - Input Parameters
RAF population at risk

The total strength of the RAF (officers and airmen combined) by age group and sex, provided by DAIS as at 24 June 1994, is shown in Table 1, which also gives the cumulative and reverse cumulative totals, for both sexes combined, from the lower and upper age limits respectively. There is a large preponderance of personnel in the younger age bands, with over a third of the population being under the age of 25, nearly three-quarters under 35 and over four-fifths under 40. The average age of the RAF has been within the range 30.5 ± 0.9 years since 1975. Projections for the period 1994-2005 show very little change in the age distribution throughout this period, although the RAF's total strength is likely to be reduced by 11% following the Defence Costs Study. However, despite the predicted reduction in numbers, it is not anticipated that the age structure of the RAF population will alter appreciably over the next decade.

Expected age-sex incidence of CRC in the RAF

The calculation of the predicted percentage distribution of cases presenting from each age group within the present RAF population is shown in Table 2. CRC in the general population is rare below the age of 40 and its incidence rises steeply with age, particularly in those aged over 50 (2). However, because the RAF population is so dominated by those in the younger age bands, the expected age distribution of case rises gradually from the age of 20, reaching over 21% in each of the 40-44 and 45-49 age groups, peaking at 24% in the 50-54 age band, and falling off steeply with age (because of very rapidly shrinking numbers) thereafter.

Actual incidence and prognosis of CRC in the RAF

The distribution of age at presentation for the 101 cases, discovered in the Cade Unit's records, of CRC occurring in RAF personnel during the 25½ years Jan 1969 - June 1994 is shown in Figure 1 and the final column of Table 2. There is a close approximation between the current predicted and historical actual

Table 1
RAF Total Strength (Officers & Airmen) by Age Group and Sex – 24 June 1994

Age Band	Male	Female	Totals	Cumulative Totals		Reverse Cumulative Totals	
				No	%	No	%
15-19	411	118	529	529	0.72	73631	100
20-24	22795	3870	26665	27194	36.9	73102	99.3
25-29	13455	1150	14605	41799	56.8	46437	63.1
30-34	10919	721	11640	53439	72.6	31832	43.2
35-39	7669	348	8017	61456	83.5	20192	27.4
40-44	6966	132	7098	68554	93.1	12175	16.5
45-49	3064	50	3114	71668	97.3	5077	6.90
50-54	1785	12	1797	73465	99.8	1963	2.67
55-59	156	0	156	73621	99.99	166	0.23
60-64	10	0	10	73631	100	10	0.01
Total	67230	6401	73631	–	–	–	–

Table 2
RAF 1994 Population, Predicted Annual Colorectal Cancer Registrations (Using OPCS Rates for 1988)
and Actual Cases 1969-94

Age Band	Sex	Population	Colorectal Cancer Rate Per 100000	Predicted Annual Colorectal Cancer Registrations		% of Predicted Overall Colorectal Cancer Cases	% of Actual Colorectal Cancer Cases 1969-94
				By Sex	Total		
15-19	M	411	0.26238	0.00108	0.00134	0.04	0
	F	118	0.22086	0.00026			
20-24	M	22795	0.42583	0.09707	0.11034	3.07	0.97
	F	3870	0.34292	0.01327			
25-29	M	13455	1.20072	0.16156	0.17267	4.80	3.88
	F	1150	0.96594	0.01111			
30-34	M	10919	1.97010	0.21512	0.22950	6.38	6.80
	F	721	1.99507	0.01438			
35-39	M	7669	6.56314	0.50333	0.52370	14.5	13.6
	F	348	5.85549	0.02038			
40-44	M	6966	11.0356	0.76874	0.78313	21.8	17.5
	F	132	10.9038	0.01439			
45-49	M	3064	24.9403	0.76417	0.77386	21.5	22.3
	F	50	19.3804	0.00969			
50-54	M	1785	48.4373	0.86461	0.86908	24.1	31.1
	F	12	37.3035	0.00448			
55-59	M	156	79.0883	0.12338	0.12338	3.43	2.91
	F	0	59.5371	0			
60-64	M	10	127.200	0.01272	0.01272	0.35	0.97
	F	0	91.6895	0			
Total	M	67230	–	3.51176	3.59972	100	100
	F	6401	–	0.08796			

distributions of age at presentation. The average incidence over this period, during which the RAF population was larger than now, has been 4.04 per annum, slightly greater than the current incidence predicted from national data of 3.60 per annum.

The stage distribution amongst the 87 RAF cases in which the Dukes's classification was either recorded or could be reliably deduced from the notes is shown in Table 3, where it is compared with the stage distributions in a clinically detected group of CRC patients in an
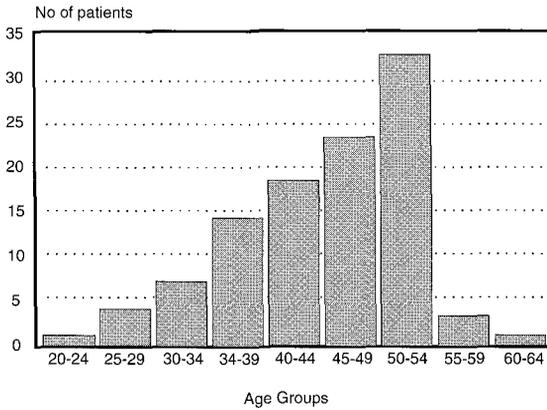
No of patients

Fig. 1. Frequency of Age at Presentation of Colorectal Cancer in the RAF – 103 Cases – 1969-94.

average UK district (19) and in the Nottingham trial (6). As can be seen, the RAF stage distribution is appreciably worse than that expected in an average district, with considerably more stage C and less stage B, as well as somewhat less stage A tumours. This may be a function of the difference in the age distributions of the populations concerned. At younger ages CRCs may be more aggressive; also, diagnosis may be later because of a lower index of suspicion. Using data on survival by stage (20), the table extrapolates to the likely change in 5 year survival as a result of the stage shift produced by screening (2). It will be seen that a potential 24% increase in the RAF 5 year survival rate, from 40.6% to 50.4%, is envisaged, even with the relatively low compliance rate achieved (53%) in Nottingham. However, in the RAF much higher compliance rates should be feasible, since FOB screening would be linked with the compulsory PME/Screening programme, so an increase in the 5 year survival rate greater than 24% should be attainable.

Cost of FOBTS for the RAF and of subsequent investigations

The FOBT most commonly used in the RAF is OKOKIT II, supplied by Hughes & Hughes Limited at a contract price of £14.20 for a set of 150 (9.5p per test). Haemoccult, supplied by Roehm Limited, is also obtainable through DMED but is more expensive, the contract price being £24.10 for a set of 60 (40p per test). Personnel costs of testing have been calculated as the full capitation costs of a senior aircraftman (£14,000 per annum) for the time taken to undertake one test, which is one minute when done in batches of at least four (information supplied by the Pathology Laboratory, RAF Wroughton). This equates to 13 pence per test, bringing the total cost of the OKOKIT II to 23 pence and that of the Haemoccult to 53 pence. Additional supply and transport costs are assumed to be negligible as they will involve existing transport channels. The costs of subsequent investigation (1992 prices) cited in the NHSME CRC Needs Assessment Review (2) are £175 for colonoscopy and £290 for a more comprehensive package of investigation for CRC (with 2-3 tests such as colonoscopy/X-ray/barium enema). These include NHS staff costs but it has been assumed that the figures for the RAF will be comparable.

Sensitivity of FOBT

The baseline FOBT sensitivity for CRC has been estimated to be 55%. This is within the range of 50-86% quoted in the NHSME CRC Needs Assessment Review (2), and corresponds most closely with the levels of 54% and 58% reported in 1990 and 1992 for non-rehydrated guaiac tests in preliminary results from the Nottingham trial (21, 22). Rehydration of guaiac FOBT slides only yields greater sensitivity at the price of lower specificity, ie higher false-positivity rates. It has been assumed that the uptake rate of FOBT screening will be 100%, somewhat higher than the rate achieved in the Nottingham

Table 3
Stage Distribution and Predicted 5-Year Survival of Colorectal Cancer Patients after Clinical Detection in an Average District & the RAF, and after Screening in the Nottingham Trial

Dukes's Stage at Diagnosis	Stage Distribution (%)			Survival Rate (%) (20)	Proportion Surviving to 5 Years (%)		
	Average district (19)	5-Year RAF 1969-1994	Notts trial post screen (6)		Average district	RAF 1969-1994	Notts trial post-screen
A	12	9.2	31	80	9.6	7.4	24.8
B	38	32.2	30	60	22.8	19.3	18
C	30	40.2	19	30	9	12.1	5.7
D	20	18.4	19	10	2	1.8	1.9
Total	100	100	100	–	43.4	40.6	50.4

population-based trial but justifiable in these somewhat different circumstances, because of the link with the PME/Screening programme.

Lead time

One study has reported a sensitivity of the Haemoccult II test of 50-66% for CRC diagnosed within 1 year of testing, 43-61% within 2 years and 25% within 4 years (23). It has therefore been assumed that, whatever the FOBT's sensitivity for CRCs that would have been diagnosed within the first year, it would have an additional sensitivity of two-thirds of the initial value for CRCs diagnosed between one and two years later, and one third of this level for CRCs diagnosed between two and three years later. These figures imply that FOBTs performed at 5-yearly PMEs/Screenings would be expected to detect CRCs at a total rate of twice that given by the annual incidence for that age group multiplied by the sensitivity.

Prevalence of positive FOBT results

The baseline prevalence of positive FOBT results has been assumed to be 5%, which corresponds with the rates for more sensitive guaiac tests reported by Castiglione *et al* in 1992 (24) and takes into account the latest figures from Nottingham (22), where non-hydration is recommended on grounds of cost-effectiveness.

II - Economic Evaluation

Comparison of cost-effectiveness of screening between age bands and with progressive inclusion of younger age bands.

The costs per case detected when starting screening at the various ages, for each of the 5 costing options are shown graphically in Figure 2. In all the models (i.e. regardless of FOBT sensitivity and positivity, and unit costs of colonoscopy & FOBT), the most cost-effective age band for screening is 45-49, followed in order by: 60-64; 40-44; 55-59; 35-39; 50-54; and lastly 30-34. This order reflects the interplay of increasing incidence with age and the frequency of PMEs/Screenings (and hence of FOBTs). Similarly, in all the models, assuming the RAF would not restrict FOB screening to its 10 personnel in the 60-64 age band, the most cost-effective age at which to introduce FOB screening of the whole RAF population is 40.
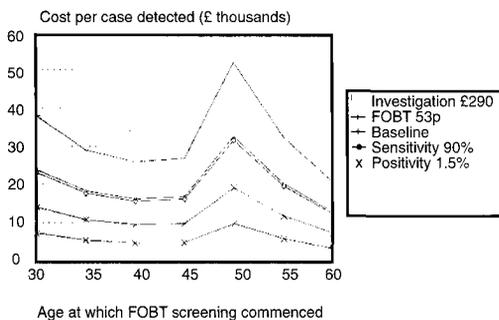

Cost per case detected (£ thousands)

Investigation £290
FOBT 53p
Baseline
Sensitivity 90%
Positivity 1.5%

Age at which FOBT screening commenced

Baseline value FOBT. Sensitivity 55%. Positivity rate 5% Unit costs. Colonoscopy £175; FOBT 23p

Fig. 2. Cost per Colorectal Cancer Case Detected with Various Screening Options

Baseline model

The model used to calculate the baseline figures is shown in tabular form in Table 4. FOBT sensitivity is *et at* 55% and the prevalence of positive tests at 5%. Unit costs are £175 for colonoscopy and 23 pence for FOBT (OKOKIT II). These parameters yield a cost per case detected when starting screening at age 40 of £15,881.

Sensitivity analysis

Model 2 assumes that all FOBT positive cases have a full investigation with 2-3 tests at a cost of £290 as described in the NHSME CRC Needs Assessment Review (2). However, this refers to the investigation of symptomatic patients, so is only likely to be incurred for the few cases with a positive finding on colonoscopy. Nevertheless, this model does demonstrate that the cost of investigating those who are FOBT positive is the major factor in determining the total cost and cost per case detected. A 66% increase in the cost of investigation produces a 64% increase in the cost per case detected, if doing FOB screening from age 40 onwards, to £26,049.

Model 3 assumes the use of the more expensive Haemoccult test (equivalent in price to using the OKOKIT II test serially on 4 days, which would increase sensitivity but also decrease specificity). The consequent quadrupling in the cost of the FOBT kits (and 130% increase in the overall FOBT cost) produces only a 3.3% increase in the cost per case detected, if starting FOB screening at 40, to £16,411. Hence if a better FOBT were to become available, with a better sensitivity (less CRCs missed) and/or a higher specificity (lower false positive rate and therefore fewer negative colonoscopies) it would be very cost-effective to use it, even if the FOBT itself were considerably more expensive. Such immunochemical tests, eg Hemeselect, are available and some trails have demonstrated their superiority (22, 24). Indeed, 1-day immunochemical testing is almost as specific as 3-day guaiac testing and Hemeselect is a more sensitive indicator of CRC in symptomatic subjects. Although the benefit of 1-day testing on screening acceptability is evident, the sensitivity of the newer tests is yet to be evaluated in a screening situation, with a proper study design and a larger sample size of asymptomatic patients.

Model 4 assumes an improvement in the specificity of FOBT and thus a reduction in the prevalence of positive FOBTs to 1.5%, a figure which accords with levels found in trials in asymptomatic populations using a 2-phase guaiac, then immunochemical scheme (25), or Haemoccult tests (26, 27). This reduces the cost per case detected by 68.2%, if starting FOB screening at age 40 years, to £5,049.

Model 5 involves setting the sensitivity at 90%, which has been achieved using non-hydrated Fecatwin (28) and Hemoccult (29), as well as Hemeselect (22). Identification of 90% of cases instead of only 55% reduces the cost per case detected by 38.9%, when starting screening at age 40, to £9,704.

Table 4
Resource Consequences of RAF Colorectal Cancer Screening Options – Baseline Model
FOBT: Sensitivity 55%; Positivity Rate 5% Units Cost: Colonoscopy £175; FOBT 23p

Age Bands	RAF Population	No FOB + PA	CRC Incidence	No of Cases axc	Cases Potentially Detected dxsensitivity	Lead Time Effect	Total Cases with Lead Time Effect dxf	Cases Potentially Detected with Lead Time Effect exf	No Scoped to Detect 1 Case b/h	Cost of Colono-scopies bxunit cost	Cost of FOBT Screening axunit cost	Total Cost j+k	Cost Case Detected l/h
	a	b	c	d	e	f	g	h	i	j	k	l	m
30-34	11640	116.4	0.000020	0.230472	0.1267596	x2	0.460944	0.253519	459.1368	20370.00	535.44	20905.44	82461.03
35-39	8017	80.17	0.000065	0.521105	0.28660775	x2	1.04221	0.573216	139.8601	14029.75	368.78	14398.53	25118.85
40-44	7098	70.98	0.00011	0.78078	0.429429	x2	1.56156	0.858858	82.64463	12421.50	326.50	12748.00	14842.97
45-49	3114	31.14	0.000249	0.775386	0.4264623	x2	1.550772	0.852925	36.50968	5449.50	143.24	5592.24	6556.55
50-54	1797	89.85	0.000484	0.869748	0.4783614	x1	0.869748	0.478361	187.8287	15723.75	413.31	16137.06	33734.06
55-59	156	7.8	0.00079	0.12324	0.067782	x1	0.12324	0.067782	115.0748	1365.00	35.88	1400.88	20667.43
60-64	10	0.5	0.00127	0.0127	0.006985	x1	0.0127	0.006985	71.58196	87.50	2.30	89.80	12856.12
Reverse Cumulative													
30-34		396.84		3.313431	1.82238705		5.621174	3.091646	128.3588	69447.00	1825.46	71271.96	23053.08
35-39		280.44		3.082959	1.69562745		5.160230	2.838127	98.8116	49077.00	1290.02	50366.52	17746.39
40-44		200.27		2.561854	1.4090197		4.118020	2.264911	88.4229	35047.25	921.24	35967.99	15880.53
45-49		129.29		1.781074	0.9795907		2.556460	1.406053	91.9524	22625.75	594.73	23219.98	16514.30
50-54		98.15		1.005688	0.5531284		1.005688	0.553128	177.4454	17176.25	451.49	17627.74	31869.18
55-59		8.3		0.13594	0.074767		0.13594	0.074767	111.0115	1452.50	39.18	1490.68	19937.66
60-64		0.5		0.0127	0.006985		0.0127	0.006985	71.58196	87.50	2.30	89.80	12856.12

Detection of pre-cancerous adenomatous polyps

FOBTs detect about three times as many persons with adenomatous polyps as with CRCs (3, 27, 30). Since many of these polyps are pre-cancerous (31), their removal at colonoscopy should prevent subsequent CRCs (27). Counting persons with adenomas as cases reduces the cost per case detected to about a quarter of the above figures.

Discussion

This model is, of necessity, a considerably simplified version of reality and the costs and outcomes are highly dependent on extrapolations from published data on older populations. In an ideal situation, decisions would be based on a randomised controlled trial of CRC screening supported by a comprehensive economic evaluation. This would provide much information that is unavailable at present, such as the cost per additional cancer detected in Dukes's stages A or B, and thus a more precise estimate of the additional cost per life-year saved. These would not necessarily show the same relationship in different age groups because of the increasing incidence of cancer, and possible variation of average survival after clinical detection of CRC, with age. In this study, the absence of several pieces of key information, such as the resources needed to investigate individuals presenting with interval cancers, precluded this calculation. Such a trial would have to be conducted within the RAF, since the specific age structure and deployment and cost of resources would not be generalisable. It has been assumed that such a trial

is unlikely, certainly within the time period within which decisions will be necessary. However, further research, in the form of a pilot study, could be undertaken to confirm that the above results can be applied to this population and to fill in some of the gaps in our knowledge. Nevertheless, within the limits of this study and the parameters examined in the sensitivity analysis, the most cost-effective age at which to introduce FOB screening appears to be 40, regardless of FOBT sensitivity & positivity and unit costs of colonoscopy & FOBT.

With FOBT sensitivity of 55% & positivity rate of 5%, costs for colonoscopy of £175 & FOBT (OKOKIT II) of 23p, when starting screening at age 40 the annual cost is £35,968 and the cost per case detected is £15,881. With each parameter varied in turn, the costs per case detected are as shown in Table 5. The FOBT contribution to the costs is so small, and the importance of maximising sensitivity and specificity so great, that using a test or combination of tests with higher sensitivity and/or lower positivity, even if much more expensive, would be very cost-effective.

Dietary modifications both increase the sensitivity and reduce the false positivity of FOBTs (32, 33). A combined FOBT method, using an initial guaiac test, followed only in those testing positive by an immunochemical test, reduces the positivity rate to 1.6% without loss of sensitivity (25). Hence by incurring the extra cost of an immunochemical FOBT, though only on those guaiac-positive, the screening conditions outlined in model 4 could be achieved - with currently available tests and

Table 5
Effect of Parameter Variations on Cost-Effectiveness of RAF Colorectal Cancer Screening

Model	Features	Cost Per Cancer Detected	% Change in Cost Per Cancer Detected from Baseline
1	Baseline	£15,881	0
2	Investigation at £290	£26,049	+64%
3	FOBT @ 53p	£16,411	+3.3%
4	Increased specificity (only 1.5% of FOBT's positive)	£5,049	-68.2%
5	Increased sensitivity (to 90%)	£9,704	-38.9%

without overly burdensome dietary restrictions, providing it could be shown that an acceptably small number of CRCs/adenomas were present in the guaiac-positive immunochemical-negative group.

Using the baseline model, and assuming commencement at 40, CRC screening in the RAF would cost just under £36,000 annually in revenue and involve 200 colonoscopies per year. It would be expected to detect nine cases every four years and lead to a cure in three of these cases. However, such a policy would miss the quarter of RAF CRCs which occur in personnel under 40. Thus, a comprehensive policy to reduce mortality from CRC should also include those in younger age groups who can be identified to be at higher risk. This includes those: with familial adenomatous polyposis; with previous history of ulcerative colitis or colorectal adenoma; with two or more first degree relatives affected by CRC, or a single first degree relative developing CRC before the age of 55 or having multiple adenomatous polyps; in families affected by the family cancer syndrome (members developing colorectal, breast, ovarian or uterine cancer, especially at a young age); or who have had previous cholecystectomy or gallstones (34, 35, 36). Such a family or personal history should be sought at all PMEs/Screenings.

It would be possible to detect many more cancers with a more intensive screening programme. In particular, the published evidence on the effectiveness of screening has been based on annual rather than 5-yearly testing. This would, however, require a considerable change in the existing pattern of medical contact for those other than aircrew and air traffic controllers, with a considerable increase in total cost. After discussion with senior policy makers, this option is not believed to be feasible. It must be noted that, for thee reasons and others noted earlier, the results cannot be generalised to civilian practice.

Nevertheless, 2½-yearly FOBTs, done with PMEs/Screenings and half-way through the 5 year interval, would appear to retain the lead-time benefit and therefore detect almost as many CRCs as annual testing, missing only half as many as 5-yearly testing.

This analysis provides information on the costs of various FOBT screening strategies for the RAF, and other Services. Similar principles can be applied to develop informed strategies for other screening procedures, not only in Service populations but also in other comparable workforces and possibly their dependants as well. It does not seek to argue for or against the introduction of a Service-wide screening programme, since the final decision requires additional information, derived from a pilot study, and must be taken by senior policy makers in the light of available resources. Nevertheless, it indicates the consequences of various possible options.

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