

Colorectal Cancer Screening - Financial Aspects



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Health Care Cost-effectiveness

- ✓ Many variables
- ✓ New regimens: improvement in %, costs in multiples
- ✓ Easy to start the discussion, difficult to predict the costs
- ✓ Example from different issue: capital punishment in California 1990 – 2012

Penalties 13, **costs ???**

Methodological Background

- ✓ Markov model
- ✓ Cost-effectiveness:
Average costs per life-years saved (ACER)
- ✓ Incremental cost-effectiveness ratio in comparison to other strategy:

Table 1 Parameters incorporated in the model

Parameters included into our model	Empirical values (%)	Reference
Probability of polyps at the age of 50 years	25.0	[1]
Low-risk polyps	20.4	[1]
High-risk polyps	4.6	[1]
Probability of CRC at the age of 50 years	1.3	[1]
Localized CRC	0.7	[1]
Regional CRC	0.3	[1]
Distant CRC	0.3	[1]
Year-to-year transition probabilities		
Normal epithelium – low risk polyp	1.0	[1]
Low risk polyp – high risk polyp	2	[1]
High risk polyp – localized CRC	5	[1]
Localized CRC – regional CRC	28	[1]
Regional CRC – distant CRC	63	[1]
Annual CRC-specific mortality		
Localized CRC	0.2	[1]
Regional CRC	3.2	[1]
Distant CRC	56.6	[1]
Colonoscopy sensitivity for the low risk polyp	85	[1,10]
Colonoscopy sensitivity for the high risk polyp and CRC	95	[1,10]
FOBT sensitivity for a polyp	10	[1,10]
FOBT sensitivity for CRC	33	[1,10]
CE sensitivity for a polyp	76	[11]
CE sensitivity for CRC	76	[11]
Compliance of FOBT	83	[4]
Compliance of first colonoscopy	60	[1,10]
Compliance of second colonoscopy	100% of first colonoscopy	NA
Compliance of CE	75	[12]

CAPS, capsule endoscopy; CRC, colorectal carcinoma; FOBT, fecal occult blood test; NA, nonapplicable.

Projections of the Cost of Cancer Care in USA

2010 – 2020

Population > 65 years: **40 mill**→**65 mill**

Cancer survivors: **13.8 mill**→**18.1 mill**

Costs of care: **124.57**→**157.77 bill USD (27%)**

Prostate cancer increase: **42%**

Breast cancer increase: **32%**

Changes due to population changes

Biologics and Costs

FU/LV	63\$
FOLFOX	11,889\$
FOLFOX + bevacizumab	21,033\$
FOLFIRI + cetuximab	30,675\$

↑ total costs 4,600 → ↑ 1,4 m survival

Capacity of the Procedures

Procedure/country	USA 2002	Aim	Czech
Flex sigmo	2.8 mil	9.5 mil	35,000 → 1 mil
Colonoscopy	14.2 mil	22.4 mil	200,000 → 6 mil

Seef LC et al. Gastroenterology 2004

Main Costs of Bowel Cancer Services in England

CRC – approximately 13,000 deaths per year

Component	£ milion 2005	Proportion %
Screening FOBT	113	10
Diagnosis	291	27
Primary treatment (surgery, oncology)	200 (colon 129, rectum 71)	18
Follow-up, recurrence	271	25
Stoma care	52	5
Palliative care	119	10
High risk paptients (FAP, HBPCC)	54	5
Total	1,100	100

Bernding MW et al. Intern J Techno Assess H Care 2010

Main Costs of Bowel Cancer Primary Care in England

CRC – approximately 13,000 deaths per year

Treatment	£ Colon	£ Rectal
Primary Surgery	4,616	5,980
Chemotherapy/Radiotherapy	11,209	7,726
Per patient	8,808	12,037

Bernding MW et al. Intern J Techno Assess H Care 2010

Cancer Management and Reimbursement in Germany

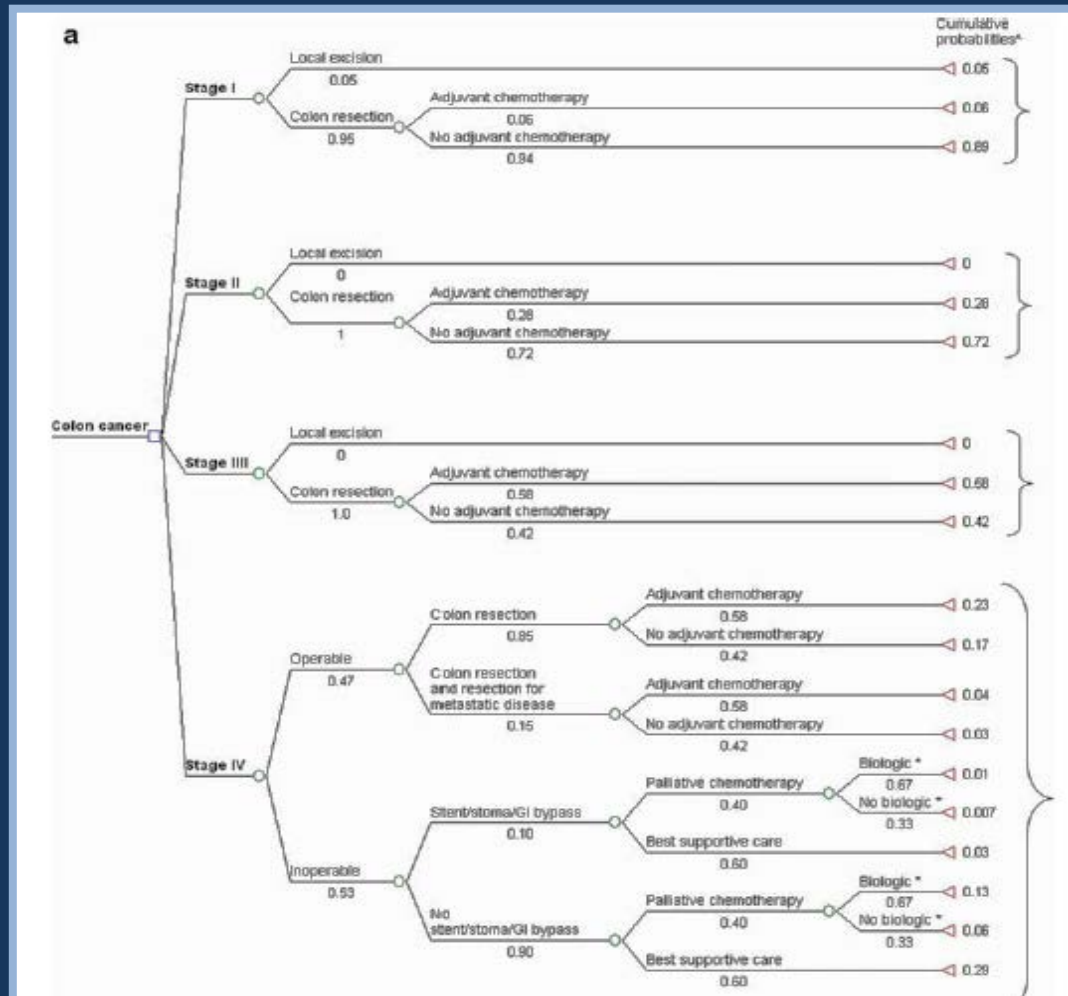
Table 1 Total health care, cancer care and pharmaceutical expenditure in Germany in 2002, 2004 and 2006. Results presented in million € [9]

	Total health care [€]	Total cancer care [€]	CRC (C18, C20) care [€]	Breast cancer care [€]	Prostate cancer care [€]	Total pharmaceutical [€]	Cancer pharmaceutical [€]
2002	218,871	11,408	1,445	1,564	1,203	31,957	1,018
2004	224,651	13,024	1,665	1,596	1,269	31,212	1,097
2006	236,002	14,579	1,750	1,906	1,396	34,721	1,354
Change (2002–2006) in %	+7.8	+27.8	+21.1	+21.9	+16.0	+8.6	+33.0

Von der Schulenburg J-M et al. Eur J Health Econ 2010

Costs of Care for CRC in Ireland

1,498 annual deaths, Markov model, 3 hospital databases



Costs of Care for CRC in Ireland

Table 3 Summary of costs^a of managing colorectal cancer^b by site, stage and disease phase (€ 2008), base-case estimates and 95% confidence intervals (CI) from probabilistic sensitivity analysis

Site	Stage I	Stage II	Stage III	Stage IV	Overall stage weighted cost
Colon cancer (95% CI)	€ 23,462 (€22,818–€24,459)	€ 35,059 (€25,904–€51,227)	€ 48,186 (€36,469–€67,970)	€ 31,744 (€26,966–€39,872)	€37,417 (€29,871–€50,618)
Rectal cancer (95% CI)	€ 24,089 (€16,284–€38,492)	€ 40,950 (€32,754–€55,430)	€ 49,987 (€41,233–€66,492)	€ 45,237 (€40,292–€53,196)	€43,502 (€36,872–€55,402)
Colorectal cancer (95% CI)	€ 23,688 (€20,900–€28,590)	€ 37,180 (€30,285–€48,032)	€ 48,835 (€40,548–€62,582)	€ 36,602 (€32,774–€42,962)	€39,607 (€33,843–48,980)
Treatment phase	Stage I	Stage II	Stage III	Stage IV	Overall stage weighted cost
Diagnosis	€ 1,634	€ 1,634	€ 1,634	€ 1,634	€ 1,634
Treatment	€ 18,550	€ 32,900	€ 45,407	€ 33,656	€ 35,918
Follow-up	€ 3,503	€ 2,646	€ 1,794	€ 1,311	€ 2,055

^a Future costs discounted at 4% per annum

^b All cancers that are not detected through screening; assuming 64% of cancers arise in the colon and 36% in the rectum and 11% are stage I, 25% stage II, 35% stage III and 29% stage IV

Costs of Care for Colorectal Cancer

Procedure	Ireland €	Czech €
Outpatient visit	169	19
Biopsy/histopathology	130	
CT scan, thorax, abdominal, pelvis	250	270
Colonoscopy	649	200 (+ aver. polypectomy)
MRI	467	
PET	1,700	800
Colon resection	17,974	2,000
FOLFIRI + cetuximab 5 months	59,265	10,000

Tilson L et al. Eur J Health Econ 2011

Cost-effectiveness of Screening – USA Task Force

CRC – approximately 53,000 deaths per year

Metaanalysis, 180→7 articles

Incremental cost-effectiveness ratio per
life year saved 10 000 – 25 000 \$

Current models provide insufficient evidence

Additional data needed: adherence, complications, biology

Pignone M et al. Ann Intern Med 2002

Factors Responsible for Heterogeneity

- ✓ Biological behaviour
- ✓ Dwell time
- ✓ Screening adherence
- ✓ Adverse effects (colonoscopy)
- ✓ Direct (indirect) costs only

Cost-effectiveness of Screening - Canada

Markov model, ICER – incremental cost-effectiveness ratio per quality-adjusted life year

Test	FOBT/y	FIT/y	Colonoscopy
Incidence reduction	44%	65%	81%
Mortality reduction	55%	74%	83%
ICER	9 159\$	611\$	6 133\$

Colonoscopy yielded the greatest benefit

Cancer Management and Reimbursement in Germany

- ✓ Incidence 73
- ✓ Mortality 26.7 in men
- ✓ Colonoscopy – quality assurance
- ✓ Waiting for colonoscopy 63 days
- ✓ Colonoscopy reimbursement 193 Euro

Von der Schulenburg J-M et al. Eur J Health Econ 2010

CRC Screening: a Recent Economic Evaluation

Table 5. Cancer outcomes and number of screening tests required during the lifetimes for a hypothetical 100,000 average risk patient cohort.

Screening Test	<i>n</i> Cancers Overall ^a	<i>n</i> Cancer Deaths	<i>n</i> Primary Screening Tests	<i>n</i> Colonoscopies	Cost Of Screening And Managing CRC (CAN\$)
FIT-high	1,290	432	819,178	56,541	2,004
FIT-mid	1,393	457	822,077	53,909	1,833
CTC	1,796	593	188,315	58,354	2,409
Colonoscopy	1,825	624	155,210	N/A	2,100
Flex Sig	2,036	699	189,135	49,484	2,263
FIT-low	2,634	918	871,986	31,597	2,005
FDNA-SDT2	3,129	1,143	331,090	20,805	2,491
FOBT-low	3,457	1,250	889,168	21,805	2,195
FOBT-high	3,890	1,368	902,299	15,089	2,084
FDNA-SDT1	4,131	1,530	331,699	14,548	2,720
No screening	4,857	1,782	n/a	n/a	1,901

^a*n* cancers overall include symptomatic and screen found CRC.
doi:10.1371/journal.pmed.1000370.t005

CRC Screening: a Recent Economic Evaluation

A metaanalysis, 55 publications, 32 models

Cost-effectiveness of Colorectal Cancer Screening

Table 2. Preferred Strategy From Incremental Cost-effectiveness Analysis (US Dollars) at Different Thresholds of Willingness-to-Pay for a Life-year Gained for the 7 Models That Evaluated the 4 US Colorectal Cancer Screening Strategies Recommended Since 1997

Study: First Author, Year (Reference No.) ^a	Willingness-to-Pay for a LYG			
	\$10,000/LYG	\$20,000/LYG	\$50,000/LYG	\$100,000/LYG
Frazier, 2000 (35)	No screening	FSIG	FSIG + gFOBT	FSIG + gFOBT
Khandker, 2000 (37)	No screening	No screening	FSIG	COL
Song, 2004 (20)	gFOBT	gFOBT	gFOBT	gFOBT
Vijan, 2007 (23)	gFOBT	COL	COL	COL
Wagner, 1995 (18)	No screening	COL	COL	FSIG + gFOBT
Zauber (MISCAN), 2009 (22)	gFOBT	FSIG + gFOBT	FSIG + gFOBT	COL
Zauber (SimCRC), 2009 (22)	COL	COL	COL	COL
Zauber (CRC-SPIN), 2009 (22)	COL	COL	COL	COL

Abbreviations: COL, 10-yearly colonoscopy; FSIG, 5-yearly flexible sigmoidoscopy; gFOBT, annual guaiac fecal occult blood test with Hemoccult II (Beckman Coulter, Inc., Brea, California); LYG, life-year gained.

^a The paper by Zauber et al. (22) contained analyses from 3 independently developed colorectal cancer models: MISCAN, SimCRC, and CRC-SPIN.

Conclusion: SCR screening was cost effective and even cost-saving.

The exceptions: DNA testing, CT colonography, capsule endoscopy

Lansdorp-Vohelaar I et al. Epidemiol Rev 2011

Screening Costs Analysis

Process – three phases

- ✓ Recruitment (mail invitation, organization, evaluation)
- ✓ Screening (kits, FOBT assay)
- ✓ Assessment (FOBHT positive subjects recall, colonoscopy, biopsy, reporting)

Items

- ✓ Staff (endoscopists, nurses, lab technicians, anaesthesiologists)
- ✓ Equipment (computers, instruments and accessories)
- ✓ Consumables (stationary, accessories for FOBT and preparation)
- ✓ Services (histology. Laundry and steriloization)
- ✓ General expences (elektricity, calls, heating)

Cost-effectiveness of Mailings to Promote CRC screening

21,860 patients, 11 health centers, RCT

A tailored letter, educational brochure, test kit at baseline and 6 months later

44% vs. 38%

Cost of the intervention: 5.48 USD

ICER: 94 USD/additional patient screened

Sequist TD et al. Med Care 2010

Various Targeted Invitations Cost-effectiveness

Tailored print material, test kit, delivering a reminder call

Invitation	Incremental cost, USD	% screened
Usual care	-	32,56
Tailored 1	42.04	45,74
Tailored 2	107.90	43.78
Tailored 3	158.35	48.45

Larson DR et al. Am Cancer Society 2007

Colonoscopies Conducted at the four Study Centers: Recent Czech Experience

Study center	1	2	3	4
Number of colonoscopies	1359	1000	541	500
Completeness (caecum intubation), %	93	90	89	90
Ileum intubation, %	87	80	73	73
Screening colonoscopies, (%)	369 (27.1)	101 (10.1)	55 (10.2)	40 (8.0)

Occurrence of Polyps and Neoplasias by Age Group

Age	Colonoscopies	Patients with potential neoplastic lesions (both polyps and cancers) (%)	Patients with adenomas (%)	Patients with advanced adenomas (%)	Cancers (%)	Advanced neoplasia (%)
<40 ys	1274	99 (7.8)	20 (1.6)	10 (0.8)	2 (0.16)	12 (9.4)
40-45 yr	180	37 (20.5)	15 (8.3)	6 (3.3)	2 (1.1)	8 (4.4)
46-50 yr	249	141 (56.6)	63 (25.3)	25 (10.0)	5 (2.0)	30 (12.0)
>50 yr	1697	1196 (70.5)	819(48.3)	532 (31.3%)	115 (6.8)	647 (38.1)
Total	3400	1473 (48.3)	917(30.2)	573 (18.8)	124(3.64.1)	697 (20.52.9)

Location of Advanced Neoplasia

Neoplasia/location	Rectosigmoid	Descendens	Transversum	Caecum/ ascendens	Total
Advanced adenoma (%)	306 (50.0)	48 (7.8)	101 (16.5)	157 (25.6)	612
Carcinoma (%)	64 (52.4)	12 (9.8)	17 (13.9)	29 (23.8)	122
Advanced neoplasia, total (%)	370 (51.1)	60 (8.3)	118 (16.2)	186 (25.74.6)	724

Incidence of Colon Neoplasia in Asymptomatic Individuals

Author	N	Mean age (yr)	Advanced adenoma (%)	Cancer (%)
Johnson et al 1990	90	65	8.89	1.1
Rex et al 2000	121	60.5	2.48	0
Prajapati et al 2003	257	62	6.23	0.39
Imperiale et al 2004	4404	68.6	9.67	0.7
Pickhardt et al 2004	1201	57.8	3.89	0.16
Regula et al 2006	43042	50–66	5.9	0.9
Kim et al 2007	3163	58.1	3.7	0.13
Špičák et al 2011	565	50.5	14.2	2.78

Colonoscopy and Screening - Background

- ✓ Sufficient caecum intubation rate as the quality indicator
- ✓ Annusually high occurrence of neoplasia even below 50
- ✓ Surprisingly almost equal in both genders despote the official statistics
- ✓ Screening colonoscopies 10% of total procedures **only**

An Adapted Program of CRC Screening – Cost Benefit Analysis

N 109,213, compliance 83,1%

CRC 13,1%

Gross national product savings: 18,560 USD/person

Frič P et al. Hepato-Gastroenterol 1994

Comparison of Various Strategies for Colorectal Cancer Screening Tests

CRC – approximately 4,000 deaths per year

Parameters incorporated in the model

FOBT

Capsule endoscopy

Colonoscopy once per year

Colonoscopy twice per year

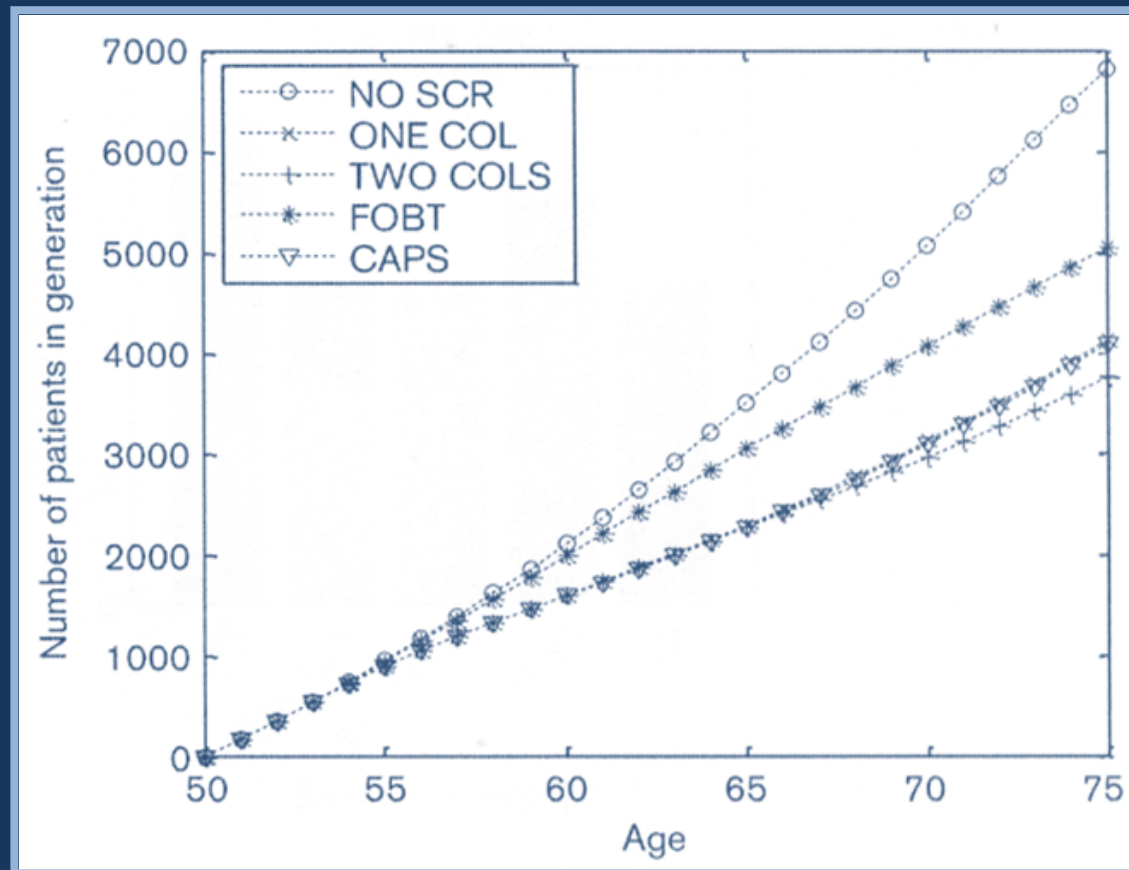
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Distant CRC	0.3	[1]
Year-to-year transition probabilities		
Normal epithelium – low risk polyp	1.0	[1]
Low risk polyp – high risk polyp	2	[1]
High risk polyp – localized CRC	5	[1]
Localized CRC – regional CRC	28	[1]
Regional CRC – distant CRC	63	[1]
Annual CRC-specific mortality		
Localized CRC	0.2	[1]
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Distant CRC	56.6	[1]
Colonoscopy sensitivity for the low risk polyp	85	[1,10]
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CE sensitivity for a polyp	76	[11]
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Compliance of FOBT	83	[4]
Compliance of first colonoscopy	60	[1,10]
Compliance of second colonoscopy	100% of first colonoscopy	NA
Compliance of CE	75	[12]

CAPS, capsule endoscopy; CRC, colorectal carcinoma; FOBT, fecal occult blood test; NA, nonapplicable.

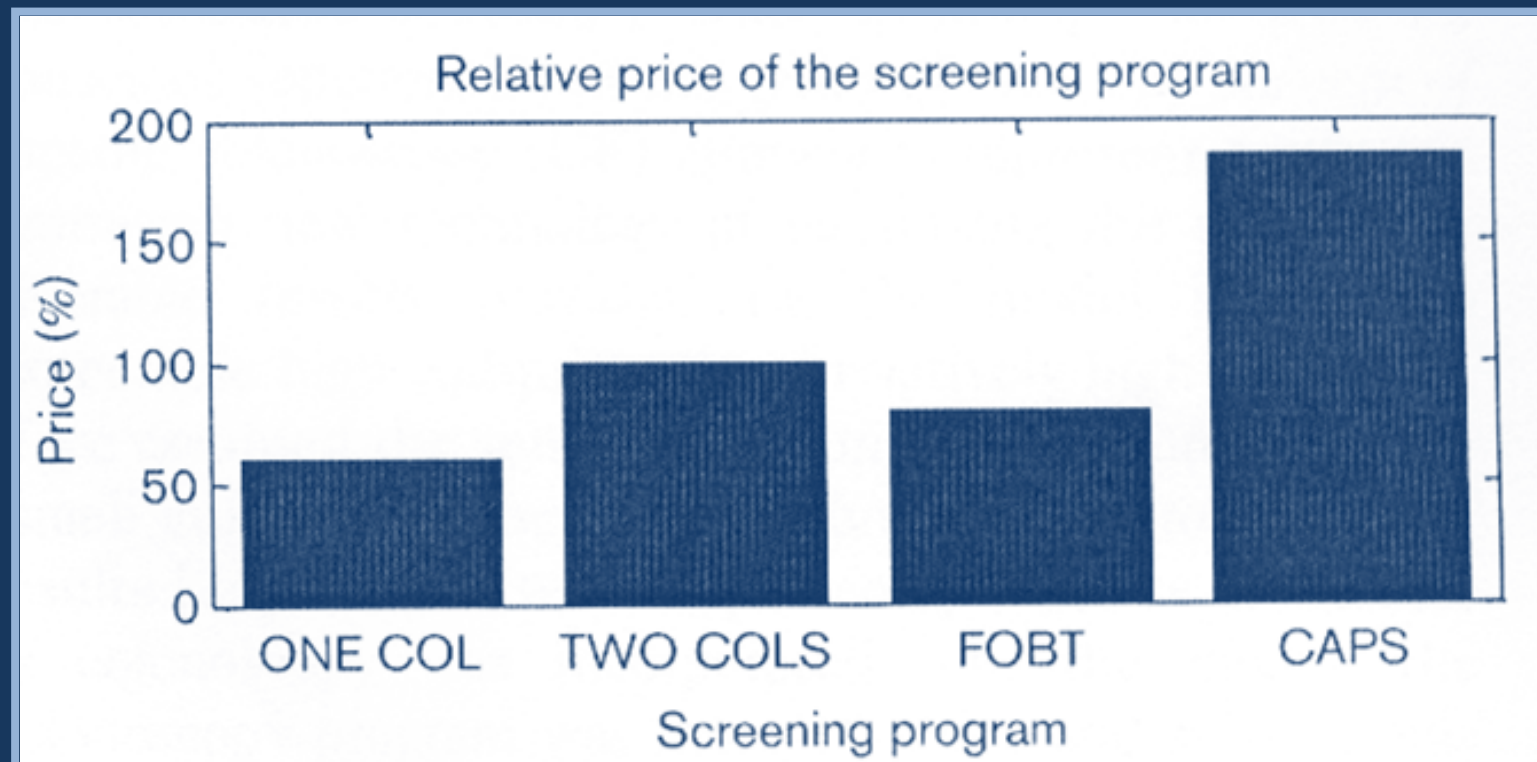
Comparison of Various Strategies for Colorectal Cancer Screening Tests

Deaths reduction vs. no screen in various strategies



Comparison of Various Strategies for Colorectal Cancer Screening Tests

Relative costs of screening programmes



Dutch Programme CRC Screening

Country of similar size

CRC incidence 2008 11.231

CRC mortality 2008 4,843

FIT biannually → colonoscopy

Participation 60% → deaths reduction 1,428 → increase of colonoscopies 50 %

Life-Year-Gained cost-effectiveness 2,200 USD

Cervical cancer Life-Year-Gained cost-effectiveness 11,300 USD

Conclusions

- ✓ Common finding: Colorectal cancer screening is cost-efficient
- ✓ Currently the highest increase of costs is due to biologics
- ✓ High proportion of costs due to diagnostic work-up
- ✓ Economy of screening – the ideal model does not exist
- ✓ Variable parameters & conditions – no universally applicable recommendation
- ✓ Current 10% of screening colonoscopies and low total number prevents significant contribution of screening

Costs of care for CRC in Ireland

1994 chemotherapy: 20%

2002 colon cancer chemotherapy: 35%

2002 rectal cancer chemotherapy: 50%

Tilson L et al. Eur J Health Econ 2011

CRC screening: a recent economic evaluation

A metaanalysis, 55 publications, 32 models

Cost-effectiveness of Colorectal Cancer Screening

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Cost-effectiveness of colorectal cancer screening

A metaanalysis

180 → 7 studies

FOBT, sigmoidoscopy, colonoscopy, barium

Pignone M et al. Ann Int Med 2002

Biologics and Costs

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FOLFIRI + cetuximab	30,675\$

↑ total costs 4,600/ 1 CRC patient → ↑ 1,4 m survival

Karaca-Mandic P et al. J Oncol Pract 2011

Costs of Care for CRC in Ireland

Average lifetime cost	39,607€
Rectal cancer	43,502€
Colon cancer	37,417€
Stage I	23,688€
Stage III	48,835€

Tilson L et al. Eur J Health Econ 2011

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Cost-effectiveness of colorectal cancer screening

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Screening vs. No scr. 10 – 25 000 \$ per year saved

Current model determine suboptimally

Pignone M et al. Ann Int Med 2002

Factors responsible for heterogeneity

- ✓ Biological behaviour
- ✓ Dwell time
- ✓ Screening adherence
- ✓ Adverse effects (colonoscopy)
- ✓ Direct costs only

Screening costs analysis

- ✓ Process – three phases
- ✓ Recruitment (mail invitation, organization, evaluation)
- ✓ Screening (kits, FOBT assay)
- ✓ Assessment (FOBHT positive subjects recall, colonoscopy, biopsy, reporting)
- ✓ Items
- ✓ Staff (endoscopists, nurses, lab technicians, anaesthesiologists)
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Health care cost-effectiveness

Many variables

New regiment: improvement in %, costs in multiples

Easy to start the discussion, difficult to finish

Example from different issue: capital punishment in California 1990 – 2012

Penalties 13, costs 4,000, 000, 000,-USD

Colonoscopies conducted at the four study centers

Study center	1	2	3	4
Number of colonoscopies	1359	1000	541	500
Completeness (caecum intubation), %	93	90	89	90
Ileum intubation, %	87	80	73	73
Screening colonoscopies, (%)	369 (27.1)	101 (10.1)	55 (10.2)	40 (8.0)

Colonoscopies in patients older than 40 years of age

	N (%)	Mean age (yr)	Patients with adenomas (%)	Patients with advanced adenomas (%)	Carcinomas (%)	Patients with advanced neoplasia (%)
Male	1225 (57.6)	57	511 (41.763.1)	355 (30.0)	70 (5.7)	425 (34.7)
Female	901 (42.4)	55	406 (45.6)	208 (23.1)	58.(5.8)	260 (28.9)
Family history	931 (43.8)	47±5.2	338 (36.3)	63 (6.8)	20 (2.1)	83 (8.9)
No Family History	1194 (56.2)	63±4.9	579 (48.6)	500 (44.6)	102 (8.5)	602 (50.4)
Diagnostic colonoscopy	1561	58	73 (47.0)	480 (30.71)	106 (6.8)	586 (37.5)
Screening colonoscopy	565	50	183 (32.3)	83 (14.7)	16 (2.8)	99 (17.5)
Male	320 (56.6)	51	89 (27.8)	49 (15.3)	12 (3.7)	61 (19.1)
Female	245 (43.4)	50	69 (28.2)	34 (13.8)	4 (1.6)	38 (15.5)
Primary (%)	320	49	78 (24.4)	40 (12.5)	7 (2.1)	47 (13.1)
Positive FOBT (%)	245	51	105 (42.8)	43 (17.6)	9 (3.7)	52 (21.2)
Negative FOBT (%)	336	50	64 (19.0)	16 (4.8)	9 (2.7)	25 (7.4)
Family history	301 (53.2)	45±4.6	33 (11.0)	10 (3.3)	3 (1.0)	13 (4.3)
No Family history	264 (46.8)	52±4.4	125 (47.3)	73 (27.6)	13 (4.9)	86 (32.6)

Location of advanced neoplasia

Neoplasia/location	Rectosigmoid	Descendens	Transversum	Caecum/ ascendens	Total
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Markov model, ICER – incremental cost-effectiveness ratio per quality-adjusted life year

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Telford JJ et al. CMAJ 2010

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- ✓ Metaanalysis, 180→7 articles
- ✓ incremental cost-effectiveness ratio per
- ✓ life year saved 10 000 – 25 000 \$
- ✓ Current models provide insufficient evidence
- ✓ Additional data needed: adherence, complications, biology

Pignone M et al. Ann Intern Med 2002

Incidence of colon neoplasia in asymptomatic individuals

Author	N	Mean age (yr)	Advanced adenoma (%)	Cancer (%)
Johnson et al 1990	90	65	8.89	1.1
Rex et al 2000	121	60.5	2.48	0
Prajapati et al 2003	257	62	6.23	0.39
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Pickhardt et al 2004	1201	57.8	3.89	0.16
Regula et al 2006	43042	50 – 66	5.9	0.9
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Špičák et al 2011	565	50.5	14.2	2.78

Colonoscopy and screening - background

- ✓ Sufficient caecum intubation rate as the quality indicator
- ✓ Annusually high occurrence of neoplasia even below 50
- ✓ Surprisingly almost equal in both genders
- ✓ Screening colonoscopies 25% of total procedures