available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

Review

A literature review of assumptions on test characteristics and adherence in economic evaluations of colonoscopy and CT-colonography screening

Paul van Gils[a,*], *Matthijs van den Berg*[b,f], *Henk van Kranen*[c,g], *Ardine G. de Wit*[d,e,h]

[a]*Centre for Prevention and Health Services Research, National Institute of Public Health and the Environment, P.O. Box 1, 3723 BA Bilthoven, The Netherlands*
[b]*Centre for Public Health Forecasting, National Institute of Public Health and the Environment, P.O. Box 1, 3720 BA Bilthoven, The Netherlands*
[c]*Center for Nutrition and Health (CVG), National Institute of Public Health and the Environment, P.O. Box 1, 3720 BA Bilthoven, The Netherlands*
[d]*Centre for Prevention and Health Services Research, National Institute of Public Health and the Environment, P.O. Box 1, 3720 BA Bilthoven, The Netherlands*
[e]*Julius Centre University Utrecht, The Netherlands*

ARTICLE INFO

Article history:
Received 9 October 2008
Received in revised form 22 January 2009
Accepted 28 January 2009
Available online 2 March 2009

Keywords:
Colorectal cancer
Colonoscopy
CT-Colonography
Cost-effectiveness
Screening
Adherence
Sensitivity
Test characteristics

ABSTRACT

Colorectal cancer screening is an effective public health strategy for decreasing colorectal cancer mortality. Since many screening modalities exist, it needs to be determined what the most cost-effective strategy is. The aim of this review is to summarise the available cost-effectiveness evidence for colonoscopy versus CT-colonography screening, and to pay special attention to assumptions regarding test characteristics and adherence. A literature search resulted in twelve economic evaluations that could be included in the review. The incremental cost-effectiveness ratios of colonoscopy and CT-colonography versus no screening remained under €20,000 and €30,000 per life year gained, respectively. Although, both screening modalities were cost-effective according to most international thresholds, in most of the economic evaluations colonoscopy seemed more cost-effective than colonography screening. In many studies, model assumptions on major parameters (e.g. screening uptake) were more positive than real life data suggest. None of the models included indirect costs, which disproportionally favoured the relative cost-effectiveness of colonoscopy. For a good comparison of both screening methods, it is necessary that the assumptions used in economic evaluations are realistic, and include all costs.

* *Corresponding author:* Tel.: +31 302748581; fax: + 31 30 274 4407.
E-mail addresses: paul.van.gils@rivm.nl (P. van Gils), matthijs.van.den.berg@rivm.nl (M. van den Berg), henk.van.kranen@rivm.nl (H. van Kranen), ardine.de.wit@rivm.nl (A.G. de Wit).
[f] Tel.: +31 30 2743349; fax: +31 30 274 4450.
[g] Tel.: +31 30 274 3573; fax. +3130 274 4446.
[h] Tel.: + 31 30 274 3206; fax: + 31 30 274 4407.
0959-8049/$ - see front matter
doi:10.1016/j.ejca.2009.01.032

1. Introduction

Colorectal cancer is one of the most frequent cancers in European countries. In 2006 in Europe, 3,191,600 incident cases of cancer were diagnosed. In women, colorectal cancer is the second form of cancer diagnosed (13.1%) after breast cancer (28.9%). In men, colorectal cancer is the third frequent cancer diagnosed (12.8%) after prostate cancer (20.3%) and lung cancer (17.2%). Colorectal cancer is the second most common cause of cancer related mortality (12.2% of total cancer mortality) after lung cancer (20%), followed by breast cancer (7.8%) and stomach cancer (6.9%).[1] The aim of colorectal cancer screening is to decrease mortality caused by this disease. This can be reached by detecting and removing adenomas, a pre-cancerous lesion.[2] By screening, pre-malignant lesions and also cancer can be detected in an earlier stage than at the moment that a patient becomes symptomatic. It is known that colorectal cancer diagnosed in an earlier stage has a better a survival chance than discovered in a later stage.[3] The 5-year survival rate is 93% for stage I, 82.5% for stage II, 59.5% for stage III and 8.1% for stage IV.[4–6] Based on observational research, it is concluded that the removal of adenomas by colonoscopy reduces the risk on cancer with 75%.[7,8] Taking into account that most of the cases of colorectal cancer (>80%) start by a malign transformation of an adenoma to an adenocarcinoma, the early detection and removal of adenomas, before they develop to cancer, is a well-established method preventing colorectal cancer.

There are different methods that can be used for screening on colorectal cancer: first, biomarkers such as the faecal occult blood tests (FOBT) and faecal or blood DNA tests; second, endoscope-based techniques such as sigmoidoscopy and colonoscopy; finally, imaging techniques such as CT-colonography or MRI-colonography. The Advisory Committee on Cancer Prevention of the European Union has advised the member states to use the FOBT and to offer it to men and women aged 50 years to 74 years, with an interval of 1–2 years. If the FOBT is positive, colonoscopy should be used as a follow-up of test positive cases.[9] In 2007, twelve European Member States have adopted FOBT screening (Bulgaria, Czech Republic, Finland, France, Hungary, Latvia, Portugal, Romania, Slovenia, Spain, Sweden, and the United Kingdom), six Member States use both FOBT and endoscopic tests for primary screening (Austria, Cyprus, Germany, Greece, Italy, Slovak Republic), and one European country only offers endoscopic screening (Poland).[9] In these countries, nationwide screening programmes have been implemented or started in 2007. In seven Member States, there is no programme (Belgium, Denmark, Estonia, Ireland, Luxembourg, Lithuania and Malta).[10] In the Netherlands trials are going on, and the implementation of population screening is planned for 2010.[11]

FOBT screening leads to a decrease of colorectal cancer related death, but the accuracy is low, especially in detecting adenomas in an early stage.[12,13] Although no RCT-evidence of endoscopy-screening is available for colorectal cancer mortality reduction, it has better sensitivity and specificity than FOBT-screening.[14] However, the uptake of endoscopy-screening is relatively low, because the test is invasive and carries the risk of a perforation. There is a growing interest in CT-colonography, since colonography combines the sensitivity and specificity of colonoscopy, with the non-invasiveness of biomarker-screening.

Many economic evaluations of colorectal cancer screening strategies were published in the recent years, especially comparing the cost-effectiveness of colonoscopy and CT-colonography. To project long term health gains and cost implications, these economic evaluations are all based on mathematical models. In economic modelling, assumptions have to be made for instance on test characteristics and adherence. Such assumptions have an important influence on the cost-effectiveness. Parameter uncertainty leads to uncertainty of the incremental cost-effectiveness ratio (ICER) and consequently to decision uncertainty.[15] The aim of this review is to summarise the available cost-effectiveness evidence for colonoscopy and CT-colonography screening, and to pay special attention to assumptions regarding test characteristics and adherence.

2. Methods

Economic evaluations were identified by searching PubMed for economic evaluations of colorectal cancer screening, in which colonoscopy and CT-colonography were compared with each other or to no screening. The search included the keywords 'colorectal cancer', 'cost-effectiveness', 'cost-utility', 'colonoscopy', 'endoscopy', 'CT-colonography', 'virtual colonoscopy', 'life years gained' and 'life years saved'. The initial search was restricted to articles published between 1 October 1997 and 1 October 2007, published in the English language. Over this period we found 34 articles. We followed the literature till 1 October 2008, but no new relevant articles were published. Relevant articles were selected based on title analyses and abstracts. Then we used reference tracking via the PubMed option 'related articles' and the references of articles retrieved. Based on the inclusion criteria (economic evaluation of colorectal cancer screening comparing colonoscopy and/or CT-colonography with each other or with no screening and sensitivity, specificity and adherence admitted in the model) 12 articles were included. The second search was performed for test characteristics found in research on the effectiveness of screening. We restricted this search to meta-analyses. The keywords used were 'colorectal cancer', 'faecal occult blood test', 'colonoscopy', 'endoscopy', 'CT-colonography', 'virtual colonoscopy', 'sensitivity' and 'specificity'. Finally, a literature search for adherence was done using the same search terms for different forms of colorectal cancer screening, combined with 'adherence', 'compliance' and 'participation'. Based on this search several trials that present the adherence of colorectal cancer screening were selected.

To be able to compare the outcomes of economic evaluations with different base years and different currency units, all local currencies were first transferred to the Euro currency values of that time, following the advice of the Organisation for Economic Co-operation and Development and then recalculated with the price index 2006 of Statistics Netherlands.[16,17]

3. Results

Twelve economic evaluations describing colonoscopy and/or CT-colonography were included in this review. In three of them, colonoscopy was compared with no screening, in six evaluations colonoscopy was compared with CT-colonography and either colonoscopy or CT-colonography or both were compared with no screening.[i]

3.1. *Incremental cost-effectiveness ratio (ICER)*

In the base case scenario all studies used a third payers perspective, implying that only the direct medical costs were incorporated in the studies. The time horizon used, differed from 3 years[18] to 30 years,[19] 35 years[20] to a life time horizon.[21–29] All studies used a discount rate for both effects and cost of 3%. The ICERs of colonoscopy compared with no screening varied between dominant and €18,236, of CT-colonography compared with no screening between dominant and €27,839. The ICERs of colonoscopy compared with CT-colonography varied between dominant and €15,695. When a threshold of ⩾6 mm. (i.e. non-reporting of diminutive lesions) was used for CT-colonography, the ICER of colonoscopy compared with CT-colonography was €58,149 (Table 1). Model assumptions influence the ICER. For example, Sonnenberg and colleagues used a 100% adherence rate in their model. A decrease in adherence rate of 20% resulted in an increase in the ICER from €11,971 to €14,258.[23]

3.2. *Model assumptions used in economic evaluations*

3.2.1. *Sensitivity of colonoscopy*

When the sensitivity of colonoscopy was categorised in groups with polyp size <6 mm, 6–9 mm and >10 mm, the sensitivities were 80%, 85–94%, and 85–96%, respectively.[18,19,27,28] When the sensitivity of colonoscopy was reported by dividing polyps '<' or '⩾' 10 mm, the sensitivity was 85%, and 90–95%, respectively.[24,26,29] Khandker and colleagues used in their model a sensitivity of 79% for small polyps and 85% for large polyps.[20] Vijan and colleagues reported only the overall sensitivity of colonoscopy for polyps, without dividing in sizes: 85%.[25] The sensitivity for colorectal cancer was 95–97%.[19,20,22–25,27] The unweighted average sensitivity was 80% for polyps <6 mm, 88% for polyps 6–9 mm, and 91% for polyps ⩾10 mm (Table 1).

3.2.2. *Sensitivity of CT-colonography*

The sensitivity ranges in the models were 33–48% for polyps ⩽6 mm, 50–70% for polyps 6–9 mm and 71–82% for polyps ⩾10 mm.[18,19,26,27] Ladabaum reported a sensitivity of 70% for polyps <10 mm, and 75% for polyps ⩾10 mm.[24] The sensitivity for colorectal cancer was 95%.[19,24,27] Sonnenberg and colleagues reported an overall sensitivity of CT-colonography of 80%.[21] The unweighted average sensitivity for polyps <6 mm was 43%, for sizes between 6 and 9 mm the unweighted average sensitivity was 63%, and for polyps larger than 10 mm it was 80%. The unweighted average sensitivity for colorectal cancer was 95% (Table 1).

3.3. *Adherence*

The adherence in the models ranged from 50% to 100%. When colonoscopy was compared with CT-colonography, the same adherence for both screening methods was assumed in all models. The unweighted average adherence was 78%.

3.4. *Test characteristics and adherence in research on the effectiveness of screening*

3.4.1. *Sensitivity of colonoscopy*

A recent Dutch meta-analysis of back to back studies shows a miss rate of 21% for all polyps. Non-adenomateus polyps were more often missed than adenomas (27–22%). The sensitivity improves with increased polyp size: for little polyps (<6 mm) the miss rate is 26% (21–30%), for medium sized polyps (6–9 mm) this is 13% (8–20%) and for large polyps (>9 mm) 2% (1–8%).[14]

3.4.2. *Sensitivity of CT-colonography*

Mulhall and colleagues performed a meta-analysis including CT-colonography and colonoscopy. Thirty-three studies were included in the meta-analysis. Studies were only included if all the subjects who had undergone CT-colonography also underwent colonoscopy (as a reference standard). The pooled per-patient sensitivity of CT-colonography of big polyps (>9 mm) is about 85% (95% CI 79–91%). For medium sized polyps (6–9 mm) the pooled sensitivity is about 70% (95% CI 55–84%) and for little polyps (<6 mm) the sensitivity is about 48% (95% CI 25–70%).[30] Lansdorp-Vogelaar and colleagues recalculated the per-patient sensitivity given in this meta-analysis to per-polyp sensitivity. For polyps <6 mm the sensitivity was 29%, for medium sized polyps (6–9 mm), the per-polyp sensitivity was 66% and for large polyps (⩾10 mm) the per-polyp sensitivity was 87%.[31]

3.4.3. *Adherance*

In an Australian study performed by Scott and colleagues, a population (1400 subjects, randomly selected) with an average risk on colorectal cancer, was offered colorectal screening. One group was allocated to colonoscopy, the second group was offered to CT-colonography and the third group was allowed to a choice between both. The average adherence was 18% and there was no significant difference between the three groups.[32] The Multicentre Australian Colorectal-neoplasia screening Group performed a randomised comparative study offering one of six screening strategies: (1) FOBT, (2) FOBT and flexible sigmoidoscopy, (3) CT-colonography, (4) colonoscopy, (5 and 6) two groups were offered a choice of these strategies In one group, a FOBT kit was sent with the letter of invitation, while the other was required to request a FOBT kit by telephone if that was the test chosen. The average adherence was 21%. For CT-colonography it was 16% and for colonoscopy

[i] From the literature describing also other methods, only colonoscopy and CT-colonograpy data compared to doing nothing and to each other were used.

Table 1 – Colonoscopy compared with CT-colonography[a].

Study	Se/Sp colonoscopy	Se/Sp CT-colonography	Adherence	ICER (per Life Year Gained)
Sonnenberg (2000, 2002)	Se CRC:[b]		100%	CS[c] (10 yearly) versus no screening: €11,971
Khandker	Se small polyp: 79% Se big polyp: 85% CRC: 97% Sp: 100%		100%	CS versus no screening €22,672
Ness	Se: ⩽5 mm: 75% 6–9 mm: 80% ⩾10 mm: 85% CRC: 95%		100%	CS versus no screening: dominant
Frazier	Se: <10 mm: 85% ⩾10 mm: 95% Sp: 100%		60%	CS versus no screening €22,664[d]
Vijan (2001)	Se polyp: 85% CRC: 95%		100%	CS (age 50 and 60 years) versus no screening: €9261
Sonnenberg (1999)	Se CRC: [b]	Se: 80% Sp: 95%	65%	Screening every 10 year CS versus no screening: €12,237 CT versus no screening: €12,518 CS versus CT: €11,345
Ladabaum	Se: <10 mm: 85% ⩾10 mm: 90% CRC: 95% Sp: 85%	Se: <10 mm: 70% ⩾10 mm: 75% CRC: 95% Sp: 85%	75%	Screening every 10 year CS versus no screening: €18,236 CT versus no screening: €27,839 CS versus CT: dominant
Heitman	Se: 6–9 mm: 94% ⩾10 mm: 96% Sp: 100%	Se: 6–9 mm: 61% ⩾10 mm: 71% Sp: 84%	50%	Screening one time CS versus CT(at age 50 years): dominant
Hassan	Se: ⩽5 mm: 80% 6–9 mm: 85% ⩾10 mm: 90% CRC: 95% Sp: 90%	Se:⩽5 mm: 48% 6–9 mm: 70% ⩾10 mm: 85% CRC: 95%	65%	Screening every 10 year CS versus no screening: dominant CT versus no screening: dominant CS versus CT: €15,695
Pickhardt	Se: ⩽5 mm: 80% 6–9 mm: 85% ⩾10 mm: 90% CRC: 95% Sp: 90%	Se: ⩽5 mm: 48% 6–9 mm: 70% ⩾10 mm: 85% CRC: 95% Sp: 86%	65%	Screening every 10 year CS versus CT (using a 6 mm reporting threshold): €58,149
Vijan (2007)	<1 cm: 85% >1 cm: 95%	Se:1–5 mm: 33% 6–9 mm: 50% ⩾10 mm: 82% Sp: 91%	60%	Screening every 10 year 2D CT versus no screening: €16,762 3D CT versus no screening: €7906 CS versus no screening €7847 CS versus 3D CT: dominant

a All local currencies were first transferred to the Euro currency values of that time and recalculated with the index 2006.
b Sonnenberg did not use sensitivity in his models, but the efficacy preventing colorectal cancer (75%).
c CS: colonoscopy; CT: CT-colonography.
d Calculated by the authors' using data of the original table.

18%.[33] A recent Italian population-based randomised trial performed by Segnan and colleagues shows an adherence of colonoscopy of 27%.[34] In 2004, an editorial of this Journal concluded that 'compliance with colonoscopy in trials is below 30% and there is no country in the world where this level has become higher than 20%'.[35]

4. Discussion

Compared with doing nothing, both colonoscopy and CT-colonography were cost-effective, according to most international cost-effectiveness thresholds used (e.g. €50,000 per QALY). The ICERs ranged from dominant to €30,000. When colonoscopy was compared with CT-colonography, colonoscopy is the most cost-effective screening strategy. The ICERs varied from dominant to €16,000 per life year gained. One study reported an ICER above €50,000 per QALY, but this study used a 6 mm reporting threshold for CT-colonoscopy.

However, assumptions on major parameters influencing cost-effectiveness were far more positive than real life data suggest. The biggest difference between the assumptions made in economic evaluations and the data presented in the effect studies were seen in the adherence to screening. The average adherence in the economic evaluation models was 78%, while in trials the adherence of colonoscopy and CT-colonography was less than 30%. Although programmatic costs of screening were not considered in the studies, low

adherence still affects the total costs related to screening. The more members of the target population opt to forego the opportunity of screening, the higher the subsequent healthcare expenditures arising from treatment and terminal care of colorectal cancer cases. So, lower adherence implies less health benefits and more health care costs, and thus has a major influence on the cost-effectiveness. All sensitivity analyses done in the studies showed that a decrease in adherence results with an increase in the ICER, which means that an intervention becomes more expensive.

The sensitivity of both colonoscopy and CT-colonography for large polyps was underestimated in the models. The sensitivity for polyps smaller than 5 mm was overestimated for colonoscopy and for CT-colonography. The underestimation of the sensitivity of CT-colonography for large polyps means that in real life probably more polyps are found and therefore more colonoscopies are needed for the removal of the polyps, leading to both an increase in costs and in effects. This also influences the cost-effectiveness.

All economic evaluations were done from the third payers' perspective. That means that indirect costs, like productivity costs, were not included. For both colonoscopy and CT-colonography, a bowel preparation is necessary. The intestine has to be completely cleared, otherwise the miss rate will be too high. This preparation takes time from a patient, starting the evening before the examination with taking laxatives. Furthermore, for a colonoscopy almost every person gets a light anaesthetic (53%) or a total anaesthesia (30%).[36] So colonoscopy also costs recovery time, and one is not allowed to drive a car for the whole day. This generates additional productivity costs, and hence adopting a societal perspective (i.e. including these non-medical costs) has a negative influence on the cost-effectiveness of colonoscopy.[37] This has consequences for the ICER, comparing colonoscopy and CT-colonography, which becomes probably more favourable for CT-colonography. Based on the economic evaluations (from a third payers' perspective) colonoscopy is the most cost-effective method. However, a more societal perspective should be taken, thus including all indirect costs, we speculate that the CT-colonography would become more cost-effective in relation to colonoscopy. Such a societal perspective should also take into account the increase in capacity (e.g. endoscopists and pathologists) that would be needed with the various screening modalities.[35]

The present study shows that model assumptions on adherence are very unrealistic. These assumptions may have a major impact on the positive results of cost-effectiveness analyses. We speculate that real life effectiveness, in terms of number of colorectal cancer incidence and mortality will be less impressive than shown in the economic models. For a good comparison of both methods, it is necessary that the assumptions used in economic evaluations are realistic and include all relevant costs. An economic evaluation done from a societal perspective, including all direct and indirect medical and non-medical costs, is preferred. Only when the results of this kind of economic evaluations are available, it is possible for policy makers to take a well-informed decision which method for screening is the most worthwhile for the population.

Conflict of interest statement

None declared.

Acknowledgement

This study was supported by ZonMw, the Netherlands organisation for health research and development.

REFERENCES

1. Ferlay J, Autier P, Boniol M, Heanue M, Colombet M, Boyle P. Estimates of the cancer incidence and mortality in Europe in 2006. *Ann Oncol* 2007;**18**(3):581–92.
2. Anderson WF, Guyton KZ, Hiatt RA, Vernon SW, Levin B, Hawk E. Colorectal cancer screening for persons at average risk. *J Natl Cancer Inst* 2002;**94**(15):1126–33.
3. Markowitz SD, Dawson DM, Willis J, Willson JK. Focus on colon cancer. *Cancer Cell* 2002;**1**(3):233–6.
4. Gollub MJ, Schwartz LH, Akhurst T. Update on colorectal cancer imaging. *Radiol Clin North Am* 2007;**45**(1):85–118.
5. Ballinger AB, Anggiansah C. Colorectal cancer. *Bmj* 2007;**335**(7622):715–8.
6. O'Connell JB, Maggard MA, Ko CY. Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. *J Natl Cancer Inst* 2004;**96**(19):1420–5.
7. Winawer SJ, Flehinger BJ, Schottenfeld D, Miller DG. Screening for colorectal cancer with fecal occult blood testing and sigmoidoscopy. *J Natl Cancer Inst* 1993;**85**(16):1311–8.
8. Hafner M. Conventional colonoscopy: technique, indications, limits. *Eur J Radiol* 2007;**61**(3):409–14.
9. Recommendations on cancer screening in the European union. Advisory committee on cancer prevention, . *Eur J Cancer* 2000;**36**(12):1473–8.
10. von Karsa L, Antilla A, Ronco G, et al. Cancer Screening in the European Union. *Report on the implementation of the Council Recommendation on cancer screening*. First Report. Luxembourg; 2008.
11. Bakkenist T, van den Berg M. Bevolkingsonderzoek naar dikkedarmkanker. *Stand van zaken juni 2008: projecten, expert meeting, literatuurstudie*. Bilthoven, Den Haag: RIVM, ZonMw; 2008.
12. Hewitson P, Glasziou P, Irwig L, Towler B, Watson E. Screening for colorectal cancer using the faecal occult blood test, Hemoccult. *Cochrane Database Syst Rev* 2007(1):CD001216.
13. Burch JA, Soares-Weiser K, St-John DJ, et al. Diagnostic accuracy of faecal occult blood tests used in screening for colorectal cancer: a systematic review. *J Med Screening* 2007;**14**(3):132–7.
14. van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E. Polyp miss rate determined by tandem colonoscopy: a systematic review. *Am J Gastroenterol* 2006;**101**(2):343–50.
15. Briggs A, Sculpher M, Claxton K. *Decision Modelling for Health Economic Evaluation*. Oxford: Oxford University Press; 2006.
16. CBS. Consumentenprijsindices (CPI) alle huishoudens, 2000=100 In: Heerlen: Centraal Bureau voor de Statistiek; 2007.
17. OECD. Purchasing Power Parities (PPPs) for OECD Countries since 1980. In: Organisation for Economic Co-operation and Development; 2007.
18. Heitman SJ, Manns BJ, Hilsden RJ, Fong A, Dean S, Romagnuolo J. Cost-effectiveness of computerized

tomographic colonography versus colonoscopy for colorectal cancer screening. *Cmaj* 2005;**173**(8):877–81.
19. Hassan C, Zullo A, Laghi A, et al. Colon cancer prevention in Italy: cost-effectiveness analysis with CT colonography and endoscopy. *Dig Liver Dis* 2007;**39**(3):242–50.
20. Khandker RK, Dulski JD, Kilpatrick JB, Ellis RP, Mitchell JB, Baine WB. A decision model and cost-effectiveness analysis of colorectal cancer screening and surveillance guidelines for average-risk adults. *Int J Technol Assess Health Care* 2000;**16**(3):799–810.
21. Sonnenberg A, Delco F, Bauerfeind P. Is virtual colonoscopy a cost-effective option to screen for colorectal cancer? *Am J Gastroenterol* 1999;**94**(8):2268–74.
22. Sonnenberg A, Delco F, Inadomi JM. Cost-effectiveness of colonoscopy in screening for colorectal cancer. *Ann Intern Med* 2000;**133**(8):573–84.
23. Sonnenberg A, Delco F. Cost-effectiveness of a single colonoscopy in screening for colorectal cancer. *Arch Intern Med* 2002;**162**(2):163–8.
24. Ladabaum U, Song K, Fendrick AM. Colorectal neoplasia screening with virtual colonoscopy: when, at what cost, and with what national impact? *Clin Gastroenterol Hepatol* 2004;**2**(7):554–63.
25. Vijan S, Hwang EW, Hofer TP, Hayward RA. Which colon cancer screening test? A comparison of costs, effectiveness, and compliance. *Am J Med* 2001;**111**(8):593–601.
26. Vijan S, Hwang I, Inadomi J, et al. The cost-effectiveness of CT colonography in screening for colorectal Neoplasia. *Am J Gastroenterol* 2007;**102**(2):380–90.
27. Pickhardt PJ, Hassan C, Laghi A, Zullo A, Kim DH, Morini S. Cost-effectiveness of colorectal cancer screening with computed tomography colonography: the impact of not reporting diminutive lesions. *Cancer* 2007.
28. Ness RM, Holmes AM, Klein R, Dittus R. Cost-utility of one-time colonoscopic screening for colorectal cancer at various ages. *Am J Gastroenterol* 2000;**95**(7):1800–11.
29. Frazier AL, Colditz GA, Fuchs CS, Kuntz KM. Cost-effectiveness of screening for colorectal cancer in the general population. *Jama* 2000;**284**(15):1954–61.
30. Mulhall BP, Veerappan GR, Jackson JL. Meta-analysis: computed tomographic colonography. *Ann Intern Med* 2005;**142**(8):635–50.
31. Lansdorp-Vogelaar I, van Ballegooijen M, Zauber AG, Boer R, Wilschut J, Habbema JD. At what costs will screening with CT colonography be competitive? A cost-effectiveness approach. *Int J Cancer* 2008.
32. Scott RG, Edwards JT, Fritschi L, Foster NM, Mendelson RM, Forbes GM. Community-based screening by colonoscopy or computed tomographic colonography in asymptomatic average-risk subjects. *Am J Gastroenterol* 2004;**99**(6):1145–51.
33. A comparison of colorectal neoplasia screening tests: a multicentre community-based study of the impact of consumer choice, . *Med J Aust* 2006;**184**(11):546–50.
34. Segnan N, Senore C, Andreoni B, et al. Comparing attendance and detection rate of colonoscopy with sigmoidoscopy and FIT for colorectal cancer screening. *Gastroenterology* 2007;**132**(7):2304–12.
35. Coebergh JW. Colorectal cancer screening in Europe: first things first. *Eur J Cancer* 2004;**40**(5):638–42.
36. Froehlich F, Harris JK, Wietlisbach V, Burnand B, Vader JP, Gonvers JJ. Current sedation and monitoring practice for colonoscopy: an International Observational Study (EPAGE). *Endoscopy* 2006;**38**(5):461–9.
37. Jonas DE, Russell LB, Sandler RS, Chou J, Pignone M. Value of patient time invested in the colonoscopy screening process: time requirements for colonoscopy study. *Med Decis Making* 2008;**28**(1):56–65.