National Institute for Health and Clinical Excellence

Colonoscopic surveillance
Guideline Consultation Comments Table
27 May – 24 June 2010

Stakeholder	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
Airedale NHS Foundation Trust	Full	2.4	39 -44	This section ends with Recommendation 1.1.2 "Offer colonoscopic surveillance using chromoscopy to people with IBD" although paragraph 2.4.4 remarks that no economic evaluation has been undertaken. The feeling in this facility is that the extra time and other costs involved will need to be funded for it to be implemented. Is it appropriate to make a firm recommendation without that economic evaluation?	Thank you for your comments. We have expanded the discussion in section 2.4.5 to discuss the fact that any additional costs of chromoscopy are likely to be offset by the need to take fewer biopsies.
Department of Health	Full	General	General	This stakeholder responded but did not have any comments to make.	Thank you for your comment.
Ferring Pharmaceuticals	Full	3.0	84	Although (as stated) chemoprevention is not covered within the scope of this guideline, we feel that the research recommendations should include the evaluation of 5-aminosalicylates (5-ASA's) along with folic acid and aspirin as a preventative strategy in patients at risk of colorectal cancer (those with IBD or polyps). Many patients with IBD, specifically with mild-moderate ulcerative colitis will be maintained on 5-ASA therapy, most commonly mesalazine. In this light, the research recommendations should include 5-ASA's as a chemoprevention measure. A number of clinical studies have reported on a protective association between 5-ASA and colorectal cancer (CRC). A meta-analysis by Velayos F et al (2005) reported on 9 studies containing 334 cases of CRC, 140 cases of dysplasia, and a total of 1932 subjects. Five studies reported CRC outcomes alone, two studies reported separate cancer and dysplasia outcomes, and two studies reported a combined outcome of CRC and dysplasia. Pooled analysis showed a protective association between use of 5-ASA's and CRC or a combined endpoint of CRC/dysplasia. REF: Velayos F et al. Am J Gastroenterol 2005; 100:1345-1353.	This reference to chemoprevention has been removed.

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				As stated on the French Summary of Characteristics for Pentasa oral formulations (mesalazine) the above meta-analysis showed that the riskof CRC was about 50% lower in patients taking 5-ASA regularly than in those taking 5-ASA improperly or not at all.	
NETSCC-HTA (Referee 1)	Full	2.2.4	20	**1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached)** Line 21. The authors developed an economic evaluation model for screening for people with inflammatory bowel disease. The model seems to account for a sub-group of individuals at high risk (e.g. those with dysplasia). The authors acknowledged this and this limitation and other seem to have been taken into account when developing the guideline.	Thank you for your comment.
NETSCC-HTA (Referee 1)	Full	General	General	**2.1 Please comment on the validity of the work i.e. the quality of the methods and their application (the methods should comply with NICE's Guidelines Manual available at http://www.nice.org.uk/page.aspx?o=guidelinesmanual).** The authors followed the NICE guidelines for conducting economic evaluations. This is usual practice for this type of analyses.	Thank you for your comment.
NETSCC-HTA (Referee 1)	Full	2.2.4	23	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** The authors reported the results of the probabilistic sensitivity analyses (PSA) in a curious manner. This reviewer prefers the classical way of reporting the probability of the intervention being cost effective at alternative values of willingness to pay (WTP) for an extra unit of effectiveness (extra QALY). I am not sure what the authors are reporting in Table 3 (also in Table 5).	Thank you for your comment. We have rewritten the results of the PSA to quote the probability of being cost effective at £20,000 and £30,000 per QALY gained.
NETSCC-HTA (Referee 1)	Full	2.2.4	23	Are the cost and QALY figures within these tables: 1) mean of the means when running Montecarlo simulation on the model a number of times? In this case, credible intervals around incremental cost and incremental QALYs might be more useful for the decision maker.	Thank you for your comments. The cost and QALY figures are mean results from a deterministic analysis and the mean output from a probabilistic simulation. The difference between the deterministic and probabilistic analysis has been identified as

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				2) or just mean cost and effects when using the values for the mean for the probability distributions attached to the model parameters? If this is the case, then, the difference between the deterministic and probabilistic results are most likely due to the particular way the probability distributions were defined for the PSA (e.g. the most likely values from the probability distributions not being equal to the value used in the deterministic analysis).	a calculation error in the model and has now been corrected. The two results are now in greater concordance with each other.
NETSCC-HTA (Referee 1)	Full	2.2.4	23	Furthermore, It is not clear what a higher or lower ICER in the PSA compared with the deterministic analysis would tell the researcher. Therefore, I believe the authors should explain their interpretation point better (with the appropriate references) or they should opt to report their PSA in the classical way (e.g. reporting in the Tables the probability from the Cost effectiveness acceptability curves for alternative values of WTP for a QALY, for instance, 10,000; 20,000; 30,000; 50,000)	Thank you for your comment. The difference between the deterministic and probabilistic analysis has been identified as a calculation error in the model and has now been corrected. The two results are now in greater concordance with each other. We have rewritten the results of the PSA to quote the probability of being cost effective at £20,000 and £30,000 per QALY gained.
NETSCC-HTA (Referee 1)	Full	2.2.4	30	The author stated "The probabilistic sensitivity analysis suggests that colonoscopic surveillance in intermediate and high-risk groups has a probability of being cost effective of 52.9%." The authors should state at what value of WTP for a QALY.	Thank you for your comment. The difference between the deterministic and probabilistic analysis has been identified as a calculation error in the model and has now been corrected. The two results are now in greater concordance with each other. We have also quoted the threshold at which the probabilities of being cost effective are quoted.
NETSCC-HTA (Referee 1)	Full	2.2.4	29 & 30	The authors refer to appendix 7 but the health economic model for polyps is reported in appendix 8.	Thank you for your comment. This has been changed to the appropriate reference.
NETSCC-HTA (Referee 1)	Full	general	general	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** The economic evaluations presented showed several limitations. This was acknowledged by the authors	Thank you for your comment.

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				and considered when making final recommendations.	
NETSCC-HTA (Referee 1)	Full	2.5 & 2.5.4	50	I was expecting that sensitivity analyses on the economic model would be able to add information to help decision making on this question. Is this a limitation of the modeling approach?	Thank you for your comment. The sensitivity analysis for the IBD health economic model tried to quantify the uncertainty regarding the high risk group specifically for which yearly surveillance was recommended. This model could only inform decision making for the high risk group.
NETSCC-HTA (Referee 1)	Full	Appendix 8	58 -63	Tables 10 to 14 show 'IR and HR' strategy with very low ICER (Table 11) or dominating the 'No Surveillance' strategy. However, Figure 6 shows huge uncertainty in the incremental QALY results. Depending on the parameter values sampled from the attached probability distributions 'IR and HR' strategy could end up being more effective by almost 3 QALYs or loosing around 2,5 QALYs. I do not think this issue is fully reflected in the report.	Thank you for your comment. The difference between the deterministic and probabilistic analysis has been identified as a calculation error in the model and has now been corrected. The two results are now in greater concordance with each other. In addition, the results have now changed so the section has had to be rewritten.
NETSCC-HTA (Referee 2)	Appendix 1	4.4	6	**1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached)** I feel the work does not address the outcomes listed in the scope with insufficient justification for the use of alternative outcome measures.	Thank you for your comments. The outcomes in the scope (a): `Progression to colorectal cancer', (b): `Stage at presentation', (c): `Progression or regression of dysplasia at most recent follow-up of IBD', (d): `Overall mortality or survival' and (e): `Reported adverse effects of colonoscopic surveillance techniques' have been used for the clinical review. The information from the clinical review and the outcomes (e), (f): `Health-related quality of life (related to colonoscopic surveillance) and (g): `Resource use and costs' have been used for economic analysis. The review question 1 used the outcomes a, b and d from the scope. The outcomes b

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					and c were studied in review question 2. As the stage at presentation could not be detected by the surveillance technique, the number and size of adenomas etc. was used as for people with polyps, and the number and type of lesions for people with IBD due to their relevance to the long-term clinical outcomes and this has now been clarified within the guideline. Outcome e (adverse effects) was studied for all the review questions; however there were none seen in almost all the studies, where seen they were included in the analysis.
NETSCC-HTA (Referee 2)	Appendix 1	4.4	6	**2.1 Please comment on the validity of the work i.e. the quality of the methods and their application (the methods should comply with NICE's Guidelines Manual available at http://www.nice.org.uk/page.aspx?o=guidelinesmanual).** The validity of the work is affected by the choice of outcome measures in sections 2.3 and 2.4. Presence/numbers of adenomas on initial investigation do not feature in the list of pre-specified outcome measures which presumably were included in the scope because of their relevance to long term clinical outcomes and quality of life.	Thank you for your comments. As you have mentioned and as explained in the response above for the earlier comment, the guideline has been amended in the relevant sections to explain that these outcomes were used due to their relevance to the long term clinical outcomes.
NETSCC-HTA (Referee 2)	Full	2.5.2	51	Some studies included in the review of initiation and frequency of surveillance in patients with IBD address different issues. For example the meta-analysis by Eaden et al. described the incidence of CRC in IBD patients rather than focusing on surveillance intervals. Other research cited compared CRC rates in IBD patients compared with the general population or looked at risk factors for CRC development but again did not address the review question posed.	This section has been updated with a further evidence review which should clarify issues with which you have concerns.
NETSCC-HTA (Referee 2)	Full	2.2.2	16	The quality ratings used need more justification. In this example studies are rated as low/very low but in the preceding columns the criteria of consistency, direction, etc. were not marked as having serious problems leading one to assume these studies were ok.	Thank you for your comments. As per GRADE methodology, the individual studies are not assessed for quality but the

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				Overall much more detail is required on how the GRADE criteria were used to justify the quality ratings awarded.	evidence per outcome, which could be from one or more studies. The GRADE methodology is explained in `the guidelines manual' (2009) at www.nice.org.uk/GuidelinesManual'
NETSCC-HTA (Referee 2)	Full	2.2.2	13	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** It is unclear why all studies are scored as high quality using the Downs and Black criteria and then low quality when using GRADE profiles. This confuses and only one method of quality assessment should be applied (see point above).	The Downs and Black criterion was used by the Cochrane group to assess the individual studies. The GRADE methodology was used to assess the evidence by the outcomes by the Short Clinical Guidelines Technical Team. They are different systems with a different methodology so different assessments are not unanticipated. The paragraph does state that Downs and Black was used in the Cochrane review, rather than in the guideline.
NETSCC-HTA (Referee 2)	Full	2.2.2	17	(row 1, column 5) odds ratios should not be calculated for 5-year survival probabilities. 5-year survival rates are calculated based on methods for survival data, so application of odds ratios and relative risks to these is misleading	Thank you for your comments. The 5-year survival and 5-year CRC mortality was calculated by cancer survival analysis in the individual studies and the misleading odds ratios and relative risks have been removed as suggested.
NETSCC-HTA (Referee 2)	Full	2.2.2	18	(footnote) NNTB/H: should read number needed to treat to benefit/harm	Thank you for your comments. The footnote has been amended as suggested.
NETSCC-HTA (Referee 2)	Full	2.2.2	18	(footnote f): remove 'remaining non-significant' as the upper CI suggests that it's borderline.	Thank you for your comments. The footnote has been amended as suggested.
NETSCC-HTA (Referee 2)	Full	2.2.3	19	(plus other places throughout report): Avoid consistent use of 'Statistically significant' when 'significant' will suffice. Overall, more emphasis should be placed on effect size than significance when compiling evidence summaries. See existing NICE guidelines for	Thank you for your comments. The phrase 'statistically significant' is used where true to clarify that it is not just a large increase.

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				examples.	
NETSCC-HTA (Referee 2)	Full	2.2.3.7	19	Please correct typo, it should be "compared with surveillance group"	Thank you for your comments. The guideline has been amended as suggested.
NETSCC-HTA (Referee 2)	Full	2.2.2	17	(row 1, column 5) odds ratios should not be calculated for 5-year survival probabilities. 5-year survival rates are calculated based on methods for survival data, so application of odds ratios and relative risks to these is misleading	Thank you for your comments. The 5-year survival and 5-year CRC mortality was calculated by cancer survival analysis in the individual studies and the misleading odds ratios and relative risks have been removed as suggested.
NETSCC-HTA (Referee 2)	Full	2.2.7	25	(lines 12-14) This implies people who died from colorectal cancer form the control group. This needs clarifying/correcting.	Thank you for your comment. The guideline has been amended to reflect this.
NETSCC-HTA (Referee 2)	Full	2.3.2	33	Please mention that a cross-over design was used in the trial by Dekker et al. for clarity (i.e. the 42 patients in the study received both procedures)	Thank you for your comment. This has been added.
NETSCC-HTA (Referee 2)	Full	2.3.7	36	(row 3, column 5) the odds ratio is the wrong way round leading to an incorrect conclusion in section 2.3.8.2 (that adenoma detection rate is 2 fold higher with conventional colonoscopy compared with alternative whereas the opposite is true).	Thank you for your comment. The odds has been adjusted to reflect section 2.3.8.2
NETSCC-HTA (Referee 2)	Full	2.3.7	36	(row 5) the no.'s and %'s presented from the Winnawer et al. study (cols. 3 and 4) do not seem to tally with those in evidence Table 2A and the paper. Also, the results in column 5 do not relate to the review outcomes but just contain material copied from the abstract of the paper.	Thank you for your comment. The Winnawer study carried out surveillance only on the people that were followed up from the original total population and the diagnostic efficacy of DCBE compared to conventional colonoscopy was estimated. This result was pooled from the study and presented in the GRADE profile. The evidence table shows the total number of colonoscopic examinations that was carried out
NETSCC-HTA (Referee 2)	Full	2.3.8.3	38	The 2nd sentence should be removed.	This sentence reflects the evidence as shown in the GRADE table.

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NETSCC-HTA (Referee 2)	Full	2.5.2	51	(line 10) delete the word 'pooled'	Removed as suggested
NETSCC-HTA (Referee 2)	Appendix 6 (review question)	2a	91	The description of the study by Inoue implies that polyps rather than patients were randomised. 205 polyps (127 in NBI group and 78 in control group). Please reword to clarify.	Thank you for your comment. We have reworded to clarify this.
NETSCC-HTA (Referee 2)	Appendix 6 (review question)	2b	102	(Outcome 1): Studies by Marion and Rutter should be removed from the meta-analysis, because all patients received both interventions (chromoscopy and conventional colonoscopy). Hence data are paired but the methods used assume independent samples (hence specifying a sample size of 204 instead of the correct 102)	We have used a similar analysis as in the Brown Cochrane review, which included back-to-back studies also. We have put these studies as a subgroup for clarity.
NETSCC-HTA (Referee 2)	Appendix 6 (review question)	2b	102	(Outcomes 2 to 7): outcome measures comprising no. of events per person should not be analysed using binary methods (either 0 or 1 events). If the no. of lesions per patient/biopsy follows a normal distribution then methods for continuous data can be used (i.e. wmds as used in the following section) otherwise alternative methods are needed. Overall, the data presented under outcomes 2 and 4 are very confusing because the overall sample size does not relate to the number of patients in the study.	We were not able to re-analyse as suggested as standard deviations (or other measure of spread) were not reported. These have been removed and the review updated accordingly.
NETSCC-HTA (Referee 2)	Appendix 6 (review question)	2b	108	Outcomes 2, 6 and 10: Comments made above also apply here.	These have been removed and the review updated accordingly.
NETSCC-HTA (Referee 2)	Full	2.2.5	25	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** It seems incorrect to say that there is clear evidence in favour of colonoscopic surveillance when the quality of this evidence is very low or low.	Thank you for your comments. The guideline has been amended to reflect that the evidence in favour of colonoscopic surveillance was low or very low.
NETSCC-HTA (Referee 2)	Full	2.4.3	43	These evidence statements are not reliable as they are based on misleading statistical analyses as detailed above.	Noted and these evidence statements have now been removed because of problems with the prior analysis.

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NETSCC-HTA (Referee 2)	Full	2.1	12	**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence.** The GRADE abbreviation needs spelling out (and more detail on these is required as described above).	Thank you for your comments. The full form of the GRADE abbreviation and more details has been added to the guideline as suggested.
NETSCC-HTA (Referee 2)	Full	2.3.2	31	(and other places) Repetition of the search strategy results (14,701 articles yielding 9544 unique articles) throughout the report could be avoided. I have assumed a single search strategy was applied across all research questions but this needs to be made clearer.	Thank you for your comments. A single strategy was applied for some of the review questions and the details for this are in appendix 5. To allow for completeness of each review question the search results have been retained for each question.
Royal College of Nursing	Full	General	General	The Royal College of Nursing welcomes this guideline. It is clearly set out and comprehensive.	Thank you for your comment.
Welsh Assembly Government	Full	General	General	This stakeholder responded but did not have any comments to make.	Thank you for your comment.

These stakeholder organisations were approached but did not respond

Association of British Insurers (ABI)
Association of Coloproctology of Great Britain and Ireland
BASO ~ The Association for Cancer Surgery
Beating Bowel Cancer
Belfast Health and Social Care Trust
Bowel Screening Wales
Brighton and Sussex University Hospitals Trust
British National Formulary (BNF)
British Society of Gastroenterology
British Society of Gastrointestinal and Abdominal Radiology (BSGAR)
British Society of Paediatric Gastroenterology, Hepatology & Nutrition (BSPGHAN)
Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)
Cancer Research UK

Cancer Screening Programmes London
Care Quality Commission (CQC)
Coloplast Limted
Commission for Social Care Inspection
Connecting for Health
Department for Communities and Local Government
Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)
Dorset Cancer Network
East Midlands Cancer Network
Ferring International Center
GE Healthcare
Gloucestershire Hospitals NHS Trust
Imperial College London
Institute of Biomedical Science
Leeds PCT
Liverpool PCT Provider Services
Luton & Dunstable Hospital NHS Foundation Trust
Macmillan Cancer Support
Medicines and Healthcare Products Regulatory Agency (MHRA)
Merck Sharp & Dohme Ltd
Ministry of Defence (MoD)
National Association for Colitis and Crohns Disease (NACC)
National Patient Safety Agency (NPSA)
National Public Health Service for Wales
National Treatment Agency for Substance Misuse
NHS Cancer Screening Programmes
NHS Clinical Knowledge Summaries Service (SCHIN)
NHS Direct
NHS Plus
NHS Quality Improvement Scotland
NHS Sefton
NHS Sheffield
NHS Western Cheshire
Norgine Pharmaceuticals Ltd
North East London Cancer Network
North of England Cancer Network
North Tees and Hartlepool Acute Trust
North West London Cancer Network

Northern Devon Healthcare NHS Trust
PERIGON Healthcare Ltd
Primary Care Society for Gastroenterology (PCSG)
psc-support
Randox Laboratories Ltd
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Midwives
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians London
Royal College of Radiologists
Royal College of Surgeons of England
Royal Society of Medicine
Sandwell PCT
Scottish Intercollegiate Guidelines Network (SIGN)
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence (SCIE)
Social Exclusion Task Force
Society and College of Radiographers
South Asian Health Foundation
South Tees Hospitals NHS Trust
UCLH NHS Foundation Trust
Welsh Scientific Advisory Committee (WSAC)
Western Health and Social Care Trust
York NHS Foundation Trust