

**Supplementary Material 13 – Economic synthesis**

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**Table 1. Table of excluded studies**

<b>Reason for exclusion</b>	<b>Excluded studies (refs)</b>
Not children	N=13 <sup>1-13</sup>
No relevant economic outcomes reported	N=23 <sup>14-36</sup>
Not functional constipation	N=9 <sup>37-45</sup>
Not a relevant intervention	N=3 <sup>46-48</sup>
Evidence already included within another source	N=2 <sup>49, 50</sup>

**Table 2. Table of on-going studies**

Study (refs)	Aim	Methods / Trial register number	Participants	Interventions	Outcomes	Additional notes
Breukink and Dirksen <sup>51, 52</sup>	Compare the effectiveness of sacral neuromodulation with personalised conservative treatment in patients with idiopathic slow-transit constipation who are refractory to conservative treatment.	RCT NCT02961582	Adolescents (14-17 years) and adults N=67	1. Sacral neuromodulation 2. Personalised conservative treatment: optimal (least invasive) treatment which may include a combination of laxative / medication and /or colonic irrigation depending on patient preference	Primary: treatment success at 6 months, Secondary outcomes include defecation frequency, reduction in straining and sense of incomplete evacuation, constipation severity, fatigue, constipation-specific quality of life, generic quality of life, adverse events, resource use/costs, cost effectiveness and budget impact	Estimated that the study will complete in Dec 2021
Capra et al. 2003 <sup>53</sup>	To investigate the effectiveness of dietary interventions in chronic constipation	SR protocol	Children and adults with constipation	Plan to include interventions provided by dietary strategy only (e.g. bulk, stimulant, osmotic and softening laxatives); also plan to include dietary plus laxative interventions.	Examples of outcomes: Frequency and /or consistency of bowel actions/week, improvement in symptoms, reduction in abdominal pain, any requirement for breakthrough laxatives and costs	JBI protocol published in 2003. Full SR not available. Email sent to lead author to see if the SR has been published.
Cao 2012 <sup>54</sup>	To assess the efficacy and safety of acupuncture therapy for chronic constipation	SR protocol (Cochrane)	Children and adults with a diagnosis of constipation	Plan to include any types of acupuncture therapy (e.g., body acupuncture, auricular acupuncture, scalp acupuncture, electroacupuncture, or acupressure).	Primary outcomes: global improvement of clinical symptoms; improvement in clinical symptoms. Secondary outcomes include Quality of life, transit time measurement, functional rectoanal evaluation or electromyography; cost effectiveness, number and types of adverse events	Protocol. Full review not published. Email sent to authors requesting further information
Newham 2015 <sup>55, 56</sup>	The Children and Young People's Health Partnership (CYPHP) Evelina London model: Four stages: 1. Pseudoanonymised	Cluster RCT NCT03461848	Children and young people  Planned recruitment n=4000	1. CYPHP Evelina London Model: "Universal services offer, Paediatric hotlines, Education and training for health professionals, Online decision support tools and guidelines, Young people-friendly access to primary care, and Resilience training in schools, Targeted services offered dependent on need. Children with any of the	Economic outcomes: Cost assessment of the CYPHP Evelina London model, cost savings in relation to any decrease in health service use and cost-effectiveness of the model in terms of utility in relation to HRQOL of CYP	Constipation is one of four tracer conditions that is being evaluated in this cRCT. Protocols for different stages of this study have been

	<p>population-based evaluation for all CYP;</p> <p>2. patient reported outcome with constipation identified as one of the ‘tracer’ conditions; 3. Process evaluation and 4. Economic evaluation</p>			<p>tracer conditions will be offered pathway-based care including early intervention for physical and related mental health needs, paediatric nursing support, care plans shared with schools, medication reviews, and peer-led parenting support. Self-management support, social support signposting, and safety-netting are offered to all”</p> <p>2. Enhanced usual care: “Universal services offer, Paediatric hotlines, Education and training for health professionals, Online decision support tools and guidelines, Young people-friendly access to primary care, and Resilience training in schools, Self-management support, social support signposting, and safety-netting are offered to all”.</p>	<p>Specific objectives of the economic evaluation are:</p> <p>(1) To quantify the differences in resource use and costs linked to professional contacts and services delivered in managing the tracer conditions between the CYPHP Evelina London model and EUC.</p> <p>(2) To assess secondary healthcare contacts and costs to the NHS.</p> <p>(3) To evaluate cost-effectiveness by combining evidence on cost impacts and HRQOL outcomes for CYP with tracer conditions.</p>	<p>reported.</p> <p>Primary study completion date was 31/12/2020 only one abstract has been published<sup>14</sup> with limited data. Email sent to authors requesting further information about timelines for this project.</p>
Protheroe 2004 <sup>57</sup>	To assess the effect of the introduction of a primary care-based intervention for children with constipation compared to conventional hospital-based management.	RCT ISRCTN07833068	Children aged 2-15 years	<ol style="list-style-type: none"> <li>1. Nurse-led service</li> <li>2. Conventional hospital-based management</li> </ol>	<ol style="list-style-type: none"> <li>1. Clinical outcomes: remission and relapse of symptoms</li> <li>2. Quality of life/patient and parental satisfaction</li> <li>3. Cost benefits: on-going treatment, nurse contacts, out-patient visits and hospital admission</li> </ol>	Clinical trial registry entry. Start date: 04/2003; end date: 03/2004. No publications found and an email has been sent to the PI to clarify status.
Van Biervliet et al. 2019 <sup>58</sup>	Long-term (at least 12m follow-up) results of transanal irrigation using a rectal balloon in children on continence, independence and cost effectiveness as primary	SR protocol	Children aged 4- 18 years	Plan to include longer-term studies (at least 12-month follow-up). Includes observational and experimental studies with >12-month follow-up.	<ol style="list-style-type: none"> <li>1. Continence (i.e., no involuntary stool loss in the last 6 months)</li> <li>2. Independence</li> </ol>	Not clear whether this protocol is actually considering costs. Not listed as outcomes although it is mentioned in the aims. An email has been sent seeking clarification.

	outcomes and quality of life, compliance and safety as secondary outcomes.					
Woodward et al. 2009 <sup>59</sup>	To assess the efficacy and safety of reflexology for the treatment of chronic idiopathic constipation	SR protocol	Male or female patients of any age	Planned to include studies of reflexology treatment for chronic constipation. Reflexology treatments need to be carried out by a qualified practitioner.	<p>Primary outcomes: global or clinical improvement as defined by the included studies (e.g., clinical symptoms frequency of defecation, straining, lumpy or hard stools, sensation of incomplete evacuation, sensation of anorectal blockage, manual manoeuvres to facilitate defecation, pain, and bloating). Secondary outcome measures will include:</p> <ol style="list-style-type: none"> <li>1. anxiety and depression;</li> <li>2. quality of life;</li> <li>3. need for rescue medication such as laxatives or rectal evacuants;</li> <li>4. transit time measurement (radio-opaque markers), functional recto-anal evaluation (proctoscopy, anorectal manometry, defecography) or electromyography;</li> <li>5. cost effectiveness; and</li> <li>6. any adverse events.</li> </ol>	Protocol published in the Cochrane Library. Full SR not available at present.

**Table 3. Table of economic outcomes for formal economic evaluations**

Abbreviations: NR: not reported

Study  [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
Guest and Clegg 2006 <sup>60</sup>  [Cost minimisation analysis]	“To compare the costs and consequences of using oral macrogol 3350 plus electrolytes compared with enema’s and suppositories and nasogastric administration of macrogol lavage solution in treating paediatric faecal impaction in Australia”	Conducted from perspective of Australian Commonwealth and parents	Estimated direct healthcare costs and clinical consequences of disimpaction of faecally impacted children (aged between 4 – 11 years) and managing them over 12 weeks.	Data sources included: literature searches supplemented by information about treatment patterns and associated resource use from interviews with clinicians (n=14)	Decision model input based on a variety of laxatives used across the 12-week interval including macrogol 3350, enema’s, suppositories, NG admin of macrogol, and senna. Commonwealth resource used included outpatient physician visits, outpatient nurse visits, hospitalisation, diagnostic and lab tests. Parent funded resource use included cost of prescription laxatives. Utility estimates were	NR	NR	Reported that oral macrogol 3350 is an effective treatment for faecal disimpaction, “taking 4-8 days to effectively disimpact a child compared with 3-12 days for enemas and suppositories, 3-6 days for manual evacuation and 0.2-4 days if PEG 3350 was given via NG. Level of health gain at 12 weeks post-disimpaction is the same irrespective of treatment and maintenance chosen. QALY 0.20 (95% CI: 0.17-0.23); based on the decision model the expected Commonwealth cost is primarily affected by initial treatment selected initially. Parents costs were comparable. Authors noted that potential benefits of oral macrogel administered to the child (less distressing) compared with alternatives

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
					based on published studies (see page 9). Costs from the Manual of Resources and AR-DRGs (AUS\$) at 2003-04 prices – see Table 2 in paper for more details about individual unit costs.			
Guest 2007 <sup>61</sup> [Cost minimisation analysis]	“To compare clinical and economic impact of using macrogol 3350 plus electrolytes in an outpatient setting compared to enemas and suppositories and manual evacuation to treat paediatric faecal impaction”	NR  Resource costs based on hospital costs only so implies healthcare only.	Clinical and resource data were extracted from case notes. These included: A&E admission, costs of labs (e.g. bloods) and diagnostic tests (e.g. x-rays, ultrasound), cost of outpatient visits (nurse, physician) and cost of telephone consultation	Data sources included retrospective case note review from 5 centres in Wales and England. Cohort (n=224 children) included children aged 2-11 years with intractable constipation who had initially received either macrogol 3350 or enemas/ suppositories or manual evacuation for disimpaction.	Decision model input based on macrogol 3350 or enemas/ suppositories or manual evacuation for disimpaction. Utility costs were based on published literature; unit resource costs (2005/6) reported in Table 1.	NR	NR	Expected number of QALYs at 3 months (irrespective of treatment) was 0.21 (95% CI: 0.18, 0.24) and level of health gain was the same irrespective of treatment modality. No significant differences between treatments in terms of outpatient visits but fewer hospital admissions in children treated with macrogol. (“(0.1 versus 1.4 and 1.0 for enemas and suppositories and manual evacuation respectively; p < 0.05) and occupied fewer bed days. Total NHS cost of disimpaction and subsequent maintenance of

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
				Covered the period of disimpaction and 12 weeks post-disimpaction.				children initially treated with macrogol 3350 was estimated to be 694 pounds sterling (95% CI: 496 pounds sterling; 892 pounds sterling). This compared with 2759 pounds sterling (95% CI: 1266 pounds sterling; 4252 pounds sterling) and 2333 pounds sterling (95% CI: 1609 pounds sterling; 3058 pounds sterling) for those who initially received enemas and suppositories or underwent a manual evacuation, respectively.” Cost of subsequent management was broadly similar between groups, but cost of initial treatment was substantially cheaper for children treated with macrogol. They concluded that “clinically effective and cost-effective treatment for the disimpaction of children suffering from faecal impaction compared to enemas and suppositories or a manual evacuation, and has the potential to release



Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
NICE 2010 (A) <sup>62</sup> [Cost minimisation analysis]	Cost analysis for disimpaction assuming high, medium and low levels of effectiveness to consider whether the cost of higher priced treatments that were more effective would be offset by savings due to lower failure rates than cheaper alternatives	Not stated by appears to be healthcare only	Treatment costs and hospitalisation costs. Modelled different treatment pathways including oral pharmacological treatments, in various preparations and dosages, as well as other methods of treatment such as suppositories, enemas and manual evacuation. Two different starting doses were considered (lowest and highest reported on the BNF for Children (BNFC) website for each pharmacological treatment.	Data based on a “a hypothetical case of a constipated child age 5 years treated in a primary care setting with no indication of a serious underlying disorder after history and physical examination. The time frame is the first 3 months after first referral (disimpaction followed by maintenance up to 3 months).”	Resources use was calculated for each pathway, including pharmacological treatment costs and hospitalisation costs (related to manual evaluation and enemas only). Costs relate to the different starting doses published on the BNFC website (accessed December 2008).	NR	Additional QALYs ICER for PEG 3350 plus electrolytes was 0.00126 £20032 in the first 3 months of treatment.  PEG 3350 plus electrolytes would need to increase the effectiveness by 0.021 to be more cost effective than senna at the £20,000 per QALY threshold. PEG 3350 plus electrolytes base dosage with 0.3 success rate is cheaper than senna base dosage with 0.2 success rate (£444 versus £501).	healthcare resources” “_cost of disimpaction by success rate model showed that treatments with a high chance (80%) of success cost less than treatment with a low chance of success (20%), regardless of the price of drugs used or the dose provided. Also, the cost of failure (changing doses, combining drugs and manual evacuation as a last resort) was a far greater determinant of overall cost than the cost of initial treatment.”

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
NICE 2010 (B) <sup>62</sup> [Cost effectiveness/cost-utility analysis]	“Conducted an analysis of a macrogol (PEG plus electrolytes alone) to assess the cost effectiveness of different doses of treatment”	NHS perspective	Daily doses, daily dose for a 25 kg child, number of sachets/days, costs of each sachet, 5 days of treatment cost, success rate and four different doses.	Clinical outcomes and treatment doses came from a randomised controlled trial (RCT) conducted in the US (Youssef et al. 2002)	Baseline cost analysis of PEG 3350 plus electrolytes by dose of treatment showed that dose 3 (1 g/kg, 4 sachets per day) was the preferred option. “This is obvious since dose 3 costs less than the higher dose alternative (dose 4) but has the same reported level of effectiveness”	NR	ICER for dose 4 was £20238 “Data suggests a higher dose of treatment with higher success rate and higher short-term disimpaction costs (i.e cost of success, see dose 3) is more cost-effective than lower doses at lower initial pharmacological costs which are less effective and therefore require costly intervention when they fail. However, given the NICE threshold for cost effectiveness of £20,000 per QALY, the effectiveness of	“analysis by dose of PEG 3350 plus electrolytes showed that highly effective strategies will lead to cost savings due to the high downstream costs of invasive treatment requiring hospitalisation that are saved. Effectiveness is determined both by the type of drug used and by the dose given. The data we have been able to identify on doses of treatment suggest that higher doses of PEG 3350 plus electrolytes that lead to effectiveness levels of 95% compared with 55% for lower doses would be cost saving to the NHS.”

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
							dose 4 has to rise by only 0.21% in order for this to be the preferred option, indicating that these results are highly sensitive to the effectiveness of the treatment”	
NICE 2010 (C) <sup>62</sup> [Cost minimisation analysis]	“decision analytic model of strategies for disimpaction and initial maintenance in the first three months of treatment with all combinations of treatments by pharmacological type, including drug and downstream cost data”	NHS perspective	“disimpaction model was developed assuming clinical equivalence of first line treatment for disimpaction to establish which group of pharmacological treatments, including all combinations of treatments and dose of treatments, including manual evacuation as a	Clinical outcomes and resource used values obtained from GDG consensus. Timeframe – 3 months	“All pharmacological treatments were assumed to be administered at home, while a hospitalisation was required for enemas and manual evacuation procedures see above. Hospitalisations and GP/nurse outpatient visits following disimpaction were considered equal across the treatment	NR	ICER: £20,708. “Threshold analysis showed that the effectiveness of PEG 3350 plus electrolytes would have to be 2.6% higher than the next best alternative (in this case senna) in order for it to be the preferred option on cost-effectiveness grounds”	“oral pharmacological alternatives were more than ten times cheaper than enemas which were assumed to be less effective and require hospitalisation. At a 20% failure rate, oral pharmacological treatment provided a mean benefit of 0.23 QALYs per child. The threshold analysis showed that the effectiveness of PEG 3350 plus electrolytes would have to be 2.6% higher than the next best alternative in order for it to be the preferred option on cost-effectiveness grounds”

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
			<p>last resort for disimpaction, provided care at the lowest cost to the NHS over the initial 3 months of treatment”</p> <p>136 possible treatment pathways were identified</p>		<p>options. Estimates of pharmacological treatment failure rates were agreed with the GDG members on a consensus base (table E.5). Daily doses and unit costs were derived from BNF children (last visited December 2008). When a range of doses was available, the lowest was considered as baseline dose. A higher dose was calculated applying a 25% increase to the baseline option, as advised by the GDG. Combinations of treatments included baseline doses for both</p>			

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					<p>options. Daily doses for the remaining maintenance period were calculated applying a 25% decrease to the disimpaction doses. Details of mean time to disimpaction, dosages, failure rate and hospitalisation unit costs are the same as those reported in table E.5. Total costs (for disimpaction phase, maintenance phase, and overall 3 month time frame) were calculated for all possible pathways and group options. Resource use data, mean time to disimpaction and failure rates for</p>			

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
					the different treatment options were obtained from discussions with the GDG (table E.5)."			
NICE 2010 (D) <sup>62</sup> [Cost effectiveness/cost-utility analysis]	“decision analytic model of strategies for ongoing maintenance after disimpaction (including treatment for reimpaction) in the following three months after disimpaction and initial maintenance, one year later and two years later”	NHS perspective	Used information from C above but created a separate model because of the large number of alternative pathways	“Model covered maintenance treatment (pharmacological and antegrade continent enema [ACE] procedure) for disimpacted children (age 2 to 11 years). The ACE strategy was included only as a last resort if other pharmacological strategies failed”. Two additional treatments which are only offered in the maintenance phase methylcellulose and liquid paraffin were factored into the model.	Drug doses were taken from BNFC (see table E.5). All other healthcare resources and failure rates were agreed by GDG consensus	NR	Compared with Senna:  Macrogol baseline dose (1 cycle – 3 months): ICER £21821  Macrogol baseline dose (4 cycles – 1 year): ICER £20370  Macrogol baseline dose (8 cycles – 2 years): ICER £22029  “an increase in effectiveness from 80% to just over 85% effectiveness in the first 3	“maintenance model showed that, unlike the disimpaction model, the cost of drugs in the pharmacological treatment alternatives had a greater impact on the total of care than hospitalisation, which widened the gap between the cheapest and most expensive options”

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
							months of treatment (and less in the longer term) would make PEG 3350 plus electrolytes the more favourable option.	
Van der Wilt <sup>63</sup> [Cost effectiveness/cost-utility analysis]	“Assess the cost-effectiveness of sacral neuromodulation (SNM) compared with conservative treatment in children and adolescents with constipation refractory to conservative management”	Healthcare perspective with a time horizon of 3 years, and had a cycle length of 6 months	“Outcomes included defaecation frequency, ancillary treatment (laxatives, lavage, surgical procedures such as reoperation), complications and quality of life as measured by EQ-5D youth. The primary endpoint was frequency of defaecation as recorded by the patient in a 3-week bowel diary”.	Data collected from a cohort of 30 consecutive female patients who were referred to our centre for evaluation and possible SNM. Data regarding defaecation frequency were prospectively collected, with a median follow-up of 22.1 months. Markov probabilistic model was used, comparing costs and effectiveness of SNM and conservative	Utilisation of healthcare services and associated costs data collected based on information from children referred for evaluation and possible SNM (i.e asked about laxative use, outpatient visits and hospitalisations in the last 6 months) From this, resource use and costs associated with the health states ‘recurrent symptoms	NR	Mean incremental cost-effectiveness ratio was €12 328 per QALY (SD €4788).	Mean cumulative costs for the SNM group and the conservative treatment group were €17 789 (SD €2492) and €7574 (SD €4332) per patient, respectively. The mean quality adjusted life years (QALYs) in the SNM group was 1.74 (SD 0.19), compared with 0.86 (SD 0.14) in the conservatively managed group.  “This modelling study shows that in this specific population (ages 10–18 years), SNM can be a cost-effective option compared with continued conservative management”

Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
			Economic outcomes included costs of devices, healthcare usage, medication and consumables and cost of surgery.	treatment in children and adolescents aged 10–18 years with constipation refractory to conservative management.	requiring intermittent hospitalisation' and 'recurrent symptoms not requiring intermittent hospitalisation' were estimated.			
Van Summeren <sup>64</sup> [Cost effectiveness/cost-utility analysis]	Evaluated whether physiotherapy plus standard care was a cost-effective strategy in the management of children with CFC	An economic evaluation was performed alongside a pragmatic RCT with a follow-up of 8 months. Standard care comprised toilet training, nutritional advice, and laxative prescribing, whereas physiotherapy focused on resolving dyssynergic defecation.	Treatment success at 8 months (defined as the absence of CFC according to the Rome III criteria without laxative use); absence of CFC irrespective of continue laxative use; and societal costs	NR	NR	NR	ICERs to treat one extra patient successful with physiotherapy, confidence intervals were calculated with 5000 bootstrap replications. The ICER to treat one extra patient successful with physiotherapy was 24060 (95%CI; -16275 to 31390). For the outcome measure absence of CFC irrespective of continue laxative use, the	Abstract only. Details limited.  Authors concluded that physiotherapy as first line treatment for children in primary care is not cost-effective compared to standard care; longer term studies are required to see whether costs are reduced longer-term



Study [Type of economic evaluation]	Economic question	Perspective	Economic outcomes / model input	Data sources	Cost categories/ values and sources	Identification of benefits/ Benefit categories/ Benefit values	ICER	Key economic findings (as reported by the author)
							ICER was 1221 (95%CI -12905-10956)	

**Note:** NICE guidelines report four different economic analyses: (A) Cost analysis of treatments for disimpaction; (B) Cost-effectiveness of disimpaction by dose of a specific pharmacological treatment (PEG 3350 plus electrolytes), (C) Pharmacological treatment for disimpaction: comparing different alternatives; (D) Maintenance phase following disimpaction and initial management

**Table 4. CHEC Checklist**

Source: The Campbell Collaboration - Economics Methods Policy Brief. (p23: Adapted from Drummond 1996). Abbreviations: N: no, NA: Not applicable, P: partially reported, Y: yes

**Note:** NICE guidelines report four different economic analyses: (A) Cost analysis of treatments for disimpaction; (B) Cost-effectiveness of disimpaction by dose of a specific pharmacological treatment (PEG 3350 plus electrolytes), (C) Pharmacological treatment for disimpaction: comparing different alternatives; (D) Maintenance phase following disimpaction and initial management

	<b>STUDY</b>	<b>Guest</b> <sup>60</sup>	<b>Guest</b> <sup>61</sup>	<b>NICE</b> <sup>62</sup> <b>A</b>	<b>NICE</b> <sup>62</sup> <b>B</b>	<b>NICE</b> <sup>62</sup> <b>C</b>	<b>NICE</b> <sup>62</sup> <b>D</b>	<b>Van der Wilt</b> <sup>63</sup>	<b>Van Summeren</b> <sup>64</sup>
1	The research question is stated	Y	Y	Y	Y	Y	Y	Y	Y
2	The economic importance of the research question is stated	Y	Y	Y	Y	Y	Y	Y	Y
3	The viewpoint(s) of the analysis are clearly stated and justified	Y	Y	N	N	Y	N	Y	N
4	The rationale for choosing alternative programmes or interventions compared is stated	Y	Y	Y	Y	Y	Y	N	N
5	The alternatives being compared are clearly described	Y	Y	Y	Y	Y	Y	N	N
6	The form of economic evaluation used is stated	Y	Y	Y	Y	Y	Y	Y	Y
7	The choice of form of economic evaluation is justified in relation to the questions addressed	Y	Y	Y	Y	Y	Y	Y	N
	<b>DATA COLLECTION</b>								
8	The source(s) of effectiveness estimates used are stated	Y	Y	N	Y	Y	Y	Y	Y
9	Details of the design and results of effectiveness study are given (if based on a single study)	NA	NA	N	P	P	P	Y	Y
10	Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies)	P	P	N	N	N	N	Y	P
11	The primary outcome measure(s) for the economic evaluation are clearly stated	Y	Y	Y	Y	Y	Y	Y	P
12	Methods to value benefits are stated	P	N	N	Y	N	Y	Y	Y
13	Details of the subjects from whom valuations were obtained were given	Y	NA	N	N	N	N	Y	P
1	Productivity changes (if included) are reported separately	NA	NA	NA	NA	NA	NA	NA	NA

4									
15	The relevance of productivity changes to the study question is discussed	NA	NA	NA	NA	NA	NA	NA	NA
16	Quantities of resource use are reported separately from their unit costs	Y	Y	Y	Y	Y	Y	Y	N
17	Methods for the estimation of quantities and unit costs are described	Y	Y	Y	Y	Y	Y	Y	N
18	Currency and price data are recorded	Y	Y	Y	Y	Y	Y	Y	N
19	Details of currency of price adjustments for inflation or currency conversion are given	Y	NA	NA	NA	NA	NA	Y	N
20	Details of any model used are given	Y	Y	Y	Y	Y	Y	Y	N
21	The choice of model used and the key parameters on which it is based are justified	Y	N	N	N	N	N	Y	P
	<b>ANALYSIS AND INTERPRETATION OF RESULTS</b>								
22	Time horizon of costs and benefits is stated	Y	Y	Y	Y	Y	Y	Y	N
23	The discount rate(s) is stated	N	N	N	N	N	Y	Y	N
24	The choice of discount rate(s) is justified	N	N	N	N	N	Y	Y	N
25	An explanation is given if costs and benefits are not discounted	N	N	N	N	N	NA	NA	N
26	Details of statistical tests and confidence intervals are given for stochastic data	Y	Y	N	N	N	N	Y	N
27	The approach to sensitivity analysis is given	Y	Y	N	N	N	N	Y	N
28	The choice of variables for sensitivity analysis is justified	Y	Y	N	N	N	N	Y	N
29	The ranges over which the variables are varied are justified	Y	Y	N	N	N	N	Y	N
30	Relevant alternatives are compared	Y	Y	Y	Y	Y	Y	P	N
31	Incremental analysis is reported	N	N	Y	Y	Y	Y	Y	Y
32	Major outcomes are presented in a disaggregated as well as aggregated form	Y	Y	Y	Y	Y	Y	Y	N

3 3	The answer to the study question is given	Y	Y	Y	Y	Y	Y	Y	Y
3 4	Conclusions follow from the data reported	Y	Y	Y	Y	Y	Y	Y	P
3 5	Conclusions are accompanied by the appropriate caveats	Y	Y	Y	Y	Y	Y	Y	Y

## References

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