Review report of MTG36: Peristeen transanal irrigation system for managing bowel dysfunction

This medical technology guidance was published in February 2018.

All medical technology guidance is usually reviewed 3 years after publication, unless NICE become aware of significant new information before the expected review date.

This review report summarises new evidence and information that has become available since this medical technology guidance was published, and that has been identified as relevant for the purposes of this report. This report will be used to inform NICE's decision on whether this guidance will be updated, amended, remain unchanged (static list) or withdrawn.

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1. Original objective of guidance

To assess the clinical and cost effectiveness of Peristeen anal irrigation system to manage bowel dysfunction.

2. Current guidance recommendations

The current recommendations as outlined in NICE MTG36 (NICE 2018) are:

1.1 The case for adopting Peristeen for transanal irrigation in people with bowel dysfunction is supported by the evidence. Peristeen can reduce the severity of constipation and incontinence, improve quality of life and promote dignity and independence.

1.2 Peristeen may not be suitable for all people with bowel dysfunction. It may take several weeks before a person is comfortable with using Peristeen, and some people may choose to stop using it. Peristeen is therefore most effective when it is offered with specialist training for users, carers and NHS staff, and structured patient support.

1.3 Cost modelling for Peristeen is uncertain, but it is likely that Peristeen provides additional clinical benefits without costing more than standard bowel care.

3. Methods of review

Update searches, based on the original EAC searches for this guidance, were conducted by information specialists at NICE on 23rd June 2021 and covered the period March 2017 to June 2021. Details are provided in Appendix D.

NICE gIS searches identified 566 records, from which duplicates were removed (n=138). Search results provided to Cedar were imported into Endnote (n=428). The company submitted a list of 25 potentially relevant studies, and clinical experts identified 13. The company results included 5 references which had not been identified by the literature searches, and 2 more were added by clinical experts. Following de-duplication, a total of 435 publications were included for title and abstract sift. References provided by the company and clinical experts were cross-checked against the Endnote library.

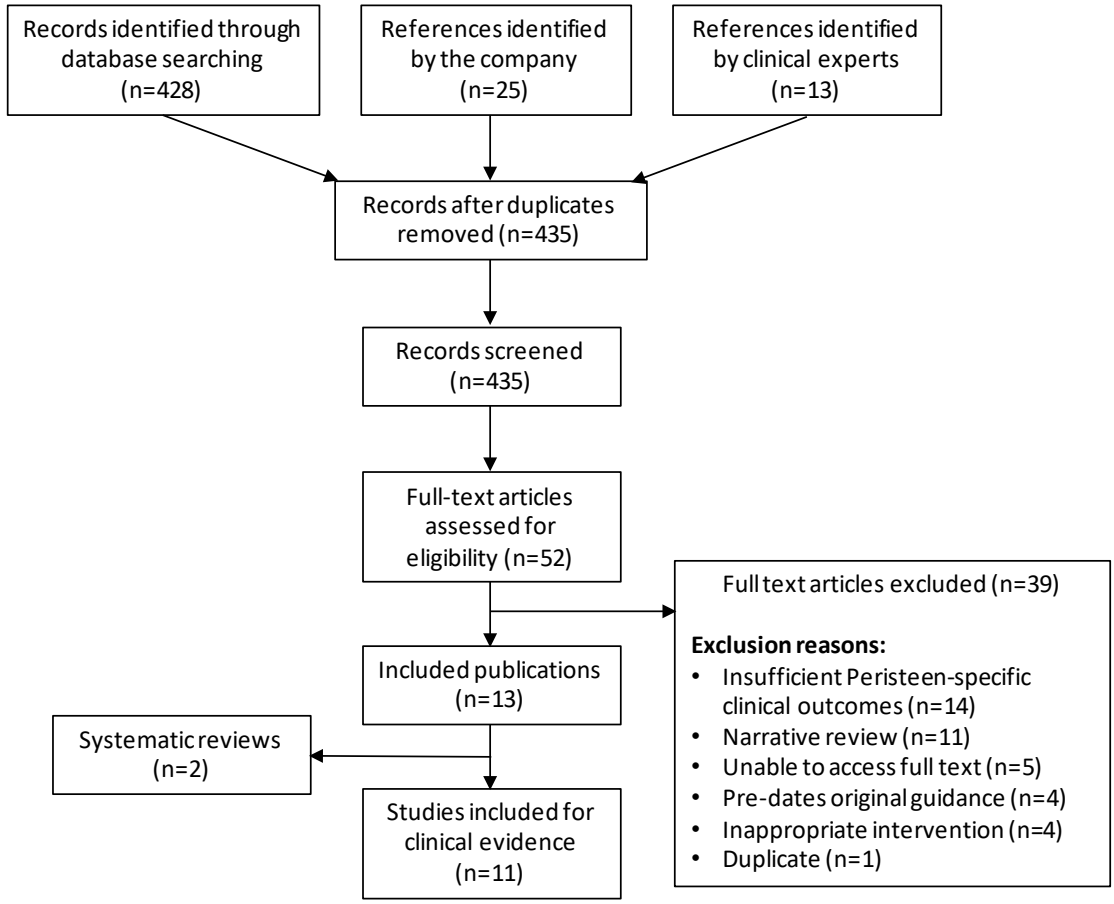
One researcher reviewed all records and 52 were selected as being relevant for full review. A second researcher reviewed the 52 selected publications to confirm relevance. Following review by second researcher, 11 studies were considered relevant for inclusion. The full text of all 11 studies was obtained; outcomes were reviewed and are summarised in Appendix C, together with EAC comments.

Five studies reported outcomes of particular relevance to the economic model, and have been summarised in Section 4.4. Two systematic reviews were also checked against the list of included papers to make sure all relevant studies had been identified.

Of the 25 studies highlighted by the company, reasons for exclusion were: insufficient Peristeen-specific clinical data (n=5); systematic review (n=2); outcome measures not within scope (n=1); pre-dated original guidance (n=1); not English language (n=1); study protocol (n=1); unable to access full text (n=1).

Searches were also conducted for ongoing and/or unpublished trials in ClinicalTrials.gov, ISRCTN and WHO International Clinical Trial Registry Platform (ICTRP).

Figure 1: PRISMA Flow Chart



4. New evidence

4.1. Changes in technology

The original NICE guidance evaluated evidence for the Peristeen TAI (transanal irrigation) system. In July 2021 the company introduced a new version of the system into the NHS, named Peristeen Plus. As a class 1 medical device, a Declaration of Conformity was issued to verify the CE-mark status of Peristeen Plus in January 2021. Peristeen was discontinued at the end of 2021, after transitioning to the new technology.

Recent literature searches and enquiries did not identify published evidence of clinical outcomes from the new 'Peristeen Plus' version. The company has stated that the alterations to the system do not change its functionality, but instead provide usability improvements. These include new connections, a new dial design, more intuitive symbols on the control unit, and a temperature indicator on the water bag. Feedback from patients, healthcare professionals and carers informed the revisions, with the aim of making the product easier to use (especially for those with dexterity issues or visual impairment). Evidence of this feedback was shared with NICE.

One clinical expert confirmed that the two versions (Peristeen and Peristeen Plus) are likely to be equivalent, and that evidence underpinning Peristeen's safety and effectiveness would be applicable to Peristeen Plus.

The original Peristeen TAI system was designed to be used only with a balloon catheter. Peristeen Plus can be used with either a balloon catheter or a cone catheter, both having the same indication for use (people with faecal incontinence, chronic constipation, and/or time-consuming bowel management procedures). The company informed us that "the cone catheter is a recent addition to the Peristeen Plus range and provides another option for patients who may have challenging anatomical needs such as LARS (Low Anterior Resection Syndrome), patients who may be fragile after extensive bowel surgery, or indeed patients who find the balloon catheter unsuitable". The cone catheter is expected to be available to the NHS from April 2022. This review only considers evidence supporting use of Peristeen with a balloon catheter – any future updates to the guidance should consider inclusion of new evidence from people using the cone catheter.

Between 1/3/2017 and 22/06/2021, 57 adverse events had been reported to the FDA medical devices (MAUDE) database relating to the Peristeen TAI system or its components (Peristeen bag/rectal catheter). The majority appear to be reports of bowel perforations.

4.2. Changes in care pathways

Since publication of the original NICE guidance, there have not been any substantial changes to care pathways in which Peristeen is used.

There is some new guidance from professional bodies. The Royal College of Nursing includes a description of TAI, with its indications and contraindications, when discussing conservative management and interventions to improve and maintain bowel function (RCN Bowel Care 2019).

The International Continence Society includes TAI as a treatment option within several clinical pathways, including the conservative management of faecal incontinence in adult patients; specialised management of urinary incontinence in children with bowel dysfunction; and management of faecal incontinence in neurological patients (ICS Standards 2019).

4.3. Results from the MTEP research commissioning workstream

Not applicable. No research was commissioned.

4.4. New studies

Systematic reviews

Two new systematic reviews had been highlighted by the company. Mekhael et al. (2021) included 27 studies, 19 of which were published before the original NICE guidance (MTG36). One did not include any outcomes of transanal irrigation (Brochard et al., 2019), and two did not report outcomes separately for Peristeen (Etherson et al., 2017; Juul et al., 2017). The Rosen et al. (2019) RCT and follow-on cohort study Rosen et al. (2020) were based on use of Peristeen within the initial 3 months following rectal surgery – when its use is contraindicated. Three of the papers matched those identified by our recent literature searches, and have been considered in this guidance review (Bildstein et al., 2017; Enriquez-Navascues et al., 2019; Martellucci et al., 2018).

The systematic review by Musco et al. (2020) selected a total of 31 papers, 25 of which predated the original NICE guidance (MTG36). One paper was a summary of the evidence used to develop the original NICE guidance (Dale et al., 2019). Four papers were out of scope as they did not report outcomes from transanal irrigation or Peristeen (Brochard et al., 2019; Deng et al., 2018; Parkinson Study Group, 2017; Weiner et al., 2017). One paper was relevant for inclusion in this guidance review, having also been identified during our literature search (Bildstein et al., 2017).

Included studies

Relevant studies include: 1 randomised controlled trial in adults; 3 case series in adults (2 prospective, 1 retrospective); 6 case series in children (3 prospective, 3 retrospective), and 1 comparative observational mixed-methods study. Details of the 11 included studies and their clinical outcomes can be found in Appendix C.

All included studies reported favourable outcomes associated with use of the Peristeen TAI system, although there was heterogeneity of study design, quality, and indicators used to illustrate effectiveness. This narrative summary focuses in particular on clinical evidence which may contribute towards addressing uncertainties relating to the economic model including: frequency of TAI; incidence of faecal incontinence, urinary tract infections, and pressure ulcers; training costs; reliance on carers; and longer-term outcomes such as the need for stomas. We also include data relating to treatment adherence/discontinuation. Five studies provided information about these outcomes (Bildstein et al., 2017; Furuta et al., 2021; Lallemant-Dudek et al., 2020; McCarthy et al., 2020; McCutchan et al., 2018).

Bildstein et al. (2017)

This retrospective case series reported findings from a study of 108 adults with constipation (the predominant symptom in 60% of patients) or faecal incontinence (40% of patients). The main causes were listed as neurological disease (38%), slow transit constipation (16%), obstructed defaecation syndrome (26%), and pudendal neuropathy (10%). Participants were instructed to perform TAI using Peristeen daily or every 2 days, with frequency being revised after 1 month if necessary. After 12 months, 46/108 (43%) participants continued to use TAI. Others had been lost to follow-up (n=12); failed training (n=5); died (n=1), or discontinued treatment (n=44). Reasons for discontinuation were reported as technical problems (n=16), “inefficacy” (n=18), or “too-many constraints” (n=10). At final follow-up (median 16 months, range 1-67), discontinuation of TAI had led to an invasive surgical procedure for 18 patients (37%): Malone antegrade continence enema (n=6); sigmoid colostomy (n=4); ileostomy (n=1); coloproctectomy (n=1); rectoplexy (n=2); sacral nerve stimulation (n=3); artificial bowel sphincter (n=1).

Furuta et al. (2021)

Furuta et al. (2021) investigated the impact of Peristeen on gut microbiota in 11 children with spina bifida and intractable constipation. The mean (± SD) total NBDS (neurogenic bowel dysfunction score) was 15.6 (± 4.1) at baseline, and 11.1 (±4.6) at 3 months (p=0.009) The mean (± SD) faecal

incontinence scores at baseline and after 3 months were reported as 5.0 (± 3.7) and 3.7 (± 3.4) respectively (p=0.108); according to the NBDS questionnaire (Krogh et al., 2006), both of these values would correspond with faecal incontinence occurring fewer than 4 times each month.

The presence of perianal skin problems contributes 3 points to the NBDS, and may be related to the incidence of pressure ulcers (an outcome of interest in the economic model). Furuta et al. (2021) reported mean (± SD) perianal skin problem scores at baseline (0.9 ± 1.4) and 3 months (0.2 ± 0.8). This did not represent a statistically significant difference (p=0.083), although the sample may not have been sufficiently powered for this purpose.

This was the only included study to report the incidence of urinary tract infections at baseline (n=9/11, 82%) and at 3-month follow-up (n=6/11, 55%). Again, this difference was not statistically significant (p=0.082) according to the authors.

Lallemant-Dudek et al. (2020)

This retrospective case series reported findings from the use of Peristeen in 149 children with faecal incontinence or constipation, with a minimum follow-up of 9 months (mean 14 ± 7.4 months). The mean time required for training was 1.5 hours (a median of 1.5 sessions). The prescribed frequency of irrigation varied, with 104/149 (70%) instructed to perform TAI “daily or every 2 days”. 129/149 (87%) were still using Peristeen at least 9 months after training. The mean time to discontinuation was 16 ± 8.4 months. Two (10%) of those who discontinued treatment did so because of reliance on a carer – other reasons included lack of motivation (n=9); poor tolerance (n=7); and difficulties performing the procedure (n=7). Factors associated with continued use of Peristeen included resolution of symptoms/continence (77.3%) and other reasons such as social wellbeing, comfort, self-sufficiency at care, and resolution of pain (22.7%). Ongoing adherence was also improved when at least one TAI procedure had been performed under nurse supervision during training (p=0.014), and when TAI was initially prescribed on a daily basis (p=0.04).

Although not compared for statistical significance, there were reductions in the proportions of people experiencing bowel symptoms between baseline and at follow-up (per protocol, at 9 or more months): prevalence of constipation changed from 82% to 31%; faecal incontinence from 87% to 39%; and daily incontinence fell from 65% to 5%.

McCarthy et al. (2020)

This prospective case series from the UK reports outcomes of Peristeen TAI use in 50 adults with neurogenic bowel dysfunction (as a consequence of

spinal cord injury). Despite weaknesses in the design of this study, it does provide some information about the incidence of faecal incontinence. The authors describe the proportion of respondents reporting frequency of "involuntary defaecation", although denominators are not provided and missing data may have biased the results. At baseline the proportions were: "A few times a year or less" (40%); "3-4 times a month" (26%); "1-6 times per week" (26%); and "Daily" (8%). After 8 weeks of treatment using Peristeen, outcomes in the same categories were: "A few times a year or less" (86%); "3-4 times a month" (4%); "1-6 times per week" (10%); and "Daily" (0%). Average total bowel dysfunction scores (range) were 20.1 (3-38) at baseline, and 8.8 (0-22) after 8 weeks. Mean Likert scale scores for emotional wellbeing and satisfaction with bowel management showed improvements over the same period, but these were not statistically verified.

McCutchan et al. (2018)

The main focus of this mixed-methods UK study was factors influencing adherence to TAI treatment. 21 adults with LARS were recruited, 15 of whom were treated with Peristeen; the other 6 people received standard care. Groups were not compared statistically, but scores for faecal incontinence (St Mark's questionnaire) and LARS were reported. Mean (range) scores for LARS in the Peristeen group were 35.9 (21-42) at baseline, and 17.7 (0-41) at 6-month follow-up. Over the same period, faecal incontinence scores reduced from 9.7 (2-15) to 3.2 (0.9).

Interviews were carried out at baseline with 12 people who had accepted the offer of TAI, and with 5 of the comparator group. Follow-up interviews were carried out after 6 months with 11 people from the TAI group only; one person withdrew from treatment and declined to be interviewed.

Participants initially experienced problems with using the equipment properly, but gained confidence after a few attempts. One patient required additional telephone support from a nurse outside of their allocated outpatient appointment.

Most participants used TAI daily. Patients who completed treatment often described TAI as "life changing", and felt confident in their ability to pursue activities they had previously avoided as they regained complete control over their bowel movements. These benefits extended to spouses, who had previously forfeited social activities.

4.5. Ongoing trials

Searches identified 16 trial registration records which referred to TAI. One referred to a Swedish study comparing Peristeen TAI with medication for

people with LARS. Another study in Italy aimed to evaluate the impact of Peristeen TAI to treat constipation and faecal incontinence in people with multiple sclerosis. Details of these 3 studies are available in Appendix C.

Reasons for excluding the other 13 records were:

- Studies have now been published and were considered elsewhere in this review, n=3
- Record has not been updated within the search period, n=3
- Insufficient detail to confirm specific use of Peristeen, n=3
- TAI is not the main intervention (it is listed as one of multiple comparators), n=2
- Population focus is on management of urinary tract infections (UTIs) in people with neurogenic bladder, rather than on management of bowel dysfunction, n=1
- Trial terminated due to recruitment difficulties, n=1.

4.6. Changes in cost case

This review focused on recently published clinical evidence, and did not directly consider costs. A cost update review was carried out recently (November 2021), and is included in full in Appendix B. It concluded that Peristeen remained cost saving after the costs had been updated.

In the original economic analysis there was considerable uncertainty around the findings of the audit data upon which the model relied. The model was sensitive to frequency of TAI, pressure ulcer treatment, and frequency of faecal incontinence (although the economic model correction in the cost update found that the sensitivity of the model to frequency of faecal incontinence is reduced); there was limited clinical evidence around these variables. Evidence from long-term use, such as the need for stomas, was particularly lacking. Table 1 indicates possible alternate values for the key drivers in the model and the possible impact of new clinical data on cost savings.

Table 1. Possible impact of new clinical data on economic model

Clinical Input	Description	Value in Original Model	Possible New Values	Comment on the potential impact on cost savings
Faecal Incontinence	Faecal incontinence is used to calculate the number of anal plugs and incontinence pads required for the proportion of patients using them.	Mean incidence of faecal incontinence per week taken from audit data (Emmanuel et al. 2016) Peristeen: 1.5 per week Standard Bowel Care: 3.5 per week	McCarthy et al. (2020) reported incidence of faecal incontinence. At baseline the proportions were: "A few times a year or less" (40%); "3-4 times a month" (26%); "1-6 times per week" (26%); and "Daily" (8%). After 8 weeks of treatment using Peristeen, outcomes in the same categories were: "A few times a year or less" (86%); "3-4 times a month" (4%); "1-6 times per week" (10%); and "Daily" (0%).	Following a correction to the original economic analysis, the results were less sensitive to faecal incontinence than originally thought. A greater number of episodes of faecal incontinence experienced by a patient will lead to increased costs associated with managing the episodes. Even if the incidence of faecal incontinence was the same in both Peristeen and Standard Bowel Care, Peristeen remains cost saving (Making the incidence of faecal incontinence per week 3.5 in both arms decreases the cost savings from £5,144 to £4,722).
Frequency of TAI	The frequency of use of the Peristeen transanal irrigation system which	Patients use the device every other day (or 3.5 times a week). Based on data from a randomised trial (Christensen 2006) which reports frequencies	There may be differences between the *prescribed* frequency of irrigation, and the actual frequency with which patients use the device. Where frequency of irrigation is reported	Increased frequency of use will increase the costs associated with Peristeen and will reduce any cost savings. As discussed in the original assessment report, frequent use can result in

Clinical Input	Description	Value in Original Model	Possible New Values	Comment on the potential impact on cost savings
	can be very variable between patients. More frequent use will require additional packs of catheters and more rapid replacement of the system.	of 16.2% daily, 48.6% alternate days, 35.1% 1-3 times weekly giving a weighted mean of 3.5 times a week.	by studies, it is usually the prescribed frequency (for example, Lallemant-Dudek et al. 2020 report that 70% of people were instructed to perform TAI "daily or every 2 days"). The only included publication which reported actual frequency of use was a qualitative study (McCutchan et al, 2018), which simply stated that "most participants used rectal irrigation daily".	Peristeen becoming cost incurring.
Pressure Ulcers	Adverse events were identified as a key driver of the model and the EAC considered that the incidence and grade of pressure ulcers and the cost of treating them to be of particular importance.	The annual probability of patients needing hospitalisation was 28% for Peristeen, and 63% for standard care. For these patients, 20% were assumed to be admitted for pressure ulcer management, in both arms. The EAC noted concern that this value was too high. The assessment report noted that evidence suggested a lower rate of readmissions for pressure ulcers in patients with spinal cord injuries is reported as 3% (Vaidyanathan et al., 1998)) and for “skin problems” as 17% (Savic et al., 2000). The EAC	None of the recent evidence specifically referred to incidence of pressure ulcers. Furuta et al. (2021) reported mean (± SD) perianal skin problem scores at baseline (0.9 ± 1.4) and 3 months (0.2 ± 0.8), although the difference was not found to be significant (p=0.083). In the study reported by McCarthy et al., the proportion of people with perianal skin problems at baseline and 8 weeks were 15% and 5%, respectively.	The amended model remains relatively sensitive to the cost of pressure ulcer treatment, with a 25% variation for the one way sensitivity analysis resulting in incremental cost saving values of £3,685 to £6,603.

Clinical Input	Description	Value in Original Model	Possible New Values	Comment on the potential impact on cost savings
		also noted that the model assumes pressure ulcers are grade 4, and the reality may be a mix of severity.		
Adherence/ discontinuation rate	Some patients choose not to continue use of TAI, and others are unable to.	The original assessment report noted that there was a higher rate of discontinuation during the initial 6 months of use than subsequently. The EAC adjusted the model to give a variable transition probability for discontinuation. In the submitted model, at 2 years 93% of patients were using Peristeen. In the EAC model 69% of patients were still using Peristeen.	Several new papers reported compliance with TAI, and reasons for discontinuation of treatment are detailed in Appendix C. Bildstein et al. (2017) provided data at baseline, after training, and after 1, 4, 6, and 12 months of follow-up. After 12 months, 46/108 (43%) of adults continued to use Peristeen. Median time using TAI before discontinuation = 3 months (range 0.2-11 months). Lallemant-Dudek et al. (2020) found that 129/149 (87%) children were still using Peristeen at least 9 months after training. Those who had stopped using it (n=20) had done so at a mean of 16 ± 8.4 months. 25% of discontinuations occurred during the first 3 months; the remaining	Increased levels of early discontinuation will mean that the longer term benefits of Peristeen are not accrued. The impact on incremental cost is minimised however as there is an increased cost to deliver Peristeen, compared to standard care, and this increased cost continues, together with the increased benefits, for all patients who continue to use Peristeen.

Clinical Input	Description	Value in Original Model	Possible New Values	Comment on the potential impact on cost savings
			75% occurred during the second year of use.	

4.7. Other relevant information

None

5. Conclusion

The new clinical evidence is consistent with the recommendations in existing NICE guidance (Table 2), although we did not evaluate any possible impact on cost modelling. All included studies reported favourable outcomes associated with TAI, but there was substantial heterogeneity in populations and variability in outcome measures used, and the significance of the effect size was not always quantified. The new publications increase the quantity of supporting evidence, but the heterogeneity of study designs means that quality of the evidence remains limited. Formal critical appraisal of the quality of studies was not undertaken and it may not be appropriate to generalise outcomes across different populations

A recent cost update report (Appendix B) identified uncertainties about clinical parameters and assumptions applied in the economic model for Peristeen. In the original economic analysis there was considerable uncertainty around the findings of the audit data upon which the model relied. The model was sensitive to frequency of TAI, pressure ulcer treatment, and frequency of faecal incontinence, and there was limited clinical evidence around these variables. Evidence from long-term use, such as the need for stomas, was particularly lacking. Whilst the new clinical evidence provides some relevant data, including the requirement for surgical procedures after TAI, it is unlikely that recently reported outcomes would impact significantly on cost modelling.

Table 2: Potential Impact on Recommendations

MT36 Recommendation	Potential Impact on Recommendation
The case for adopting Peristeen for transanal irrigation in people with bowel dysfunction is supported by the evidence. Peristeen can reduce the severity of constipation and incontinence, improve quality of life and promote dignity and independence.	The EAC suggests that this recommendation does not need to be changed.
Peristeen may not be suitable for all people with bowel dysfunction. It may take several weeks before a person is comfortable with using Peristeen, and some people may choose to stop using it. Peristeen is therefore most effective when it is offered with specialist training for users, carers and NHS staff, and structured patient support.	The EAC suggests that this recommendation does not need to be changed.
Cost modelling for Peristeen is uncertain, but it is likely that Peristeen provides additional clinical benefits without costing more than standard bowel care.	The EAC suggests that this recommendation does not need to be changed.

Appendix A – Relevant guidance

Supplied by the NICE gIS team

NICE guidance – published

NICE guidelines (clinical, public health, social care, medicine practice guidelines, safe staffing)

Constipation in children and young people: diagnosis and management. (2010) NICE guideline CG99

All other NICE guidance and advice products

Naldemedine for treating opioid-induced constipation (2020) NICE technology appraisal guidance TA651

Irritable bowel syndrome with constipation in adults: linaclotide (2013) NICE evidence summary ESNM16

Naloxegol for treating opioid-induced constipation (2015) NICE technology appraisal guidance TA345

Laxatives (2015) NICE key therapeutic topic KTT1

Assessing motility of the gastrointestinal tract using a wireless capsule (2014) NICE interventional procedures guidance IPG502

Constipation in children and young people (2014) NICE quality standard QS62

Stapled transanal rectal resection for obstructed defaecation syndrome (2010) NICE interventional procedures guidance IPG351

Prucalopride for the treatment of chronic constipation in women (2010) NICE technology appraisal guidance TA211

NICE pathways

Constipation (2020) NICE Pathway

NICE guidance – in development

NICE guidelines (clinical, public health, social care, medicine practice guidelines, safe staffing)

None identified

All other NICE guidance and advice products

None identified

Guidance from other professional bodies

ICS Standards (International Continence Society, 2019)

Bowel Care: Management of lower bowel dysfunction, including digital rectal examination and digital removal of faeces (Royal College of Nursing, 2019)

Bladder and bowel care in childbirth (Royal College of Nursing, 2021)

Guidelines on the management of irritable bowel syndrome (British Society of Gastroenterology, 2021)

The management of adult patients with severe chronic small intestinal dysmotility (British Society of Gastroenterology, 2020)

Excellence in Continence Care (NHS England, 2018)

Guidelines for Pelvic Floor Biofeedback for Adults with Bowel Dysfunction (University Hospitals Birmingham NHS Foundation Trust, not dated)

IBD Standards Core Statements (IBD UK, not dated)

Appendix B – Costing report

Costing update report of MTG36: Peristeen transanal irrigation system for managing bowel dysfunction

This medical technology guidance was published in February 2018.

All medical technology guidance is reviewed 3 years after publication according to the process described in the MTEP Interim addendum on guidance reviews.

This report is part of the information considered in the guidance review. It describes an update of the cost model so that it reflects any new relevant information including revising the cost and resource parameters to current values. The results from the updated cost model are used to estimate the current savings associated with the use of the technology.

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6. Background

The company (Coloplast Ltd.) submitted a model that was based on a published model (Emmanuel et al. 2016). The submitted model was a Markov model with a 6-month cycle and a variable time horizon representing an average patient lifetime, depending on patients age selected at entry. Discounting was 3.5% and an NHS and social care perspective was used.

The technology in the model was Peristeen in addition to standard bowel care, as required, and the comparator was standard bowel care. Standard bowel care could include diet and bowel habit advice, medication (oral drugs, suppositories and enemas), disposable pads and anal plugs, muscle training/bowel retraining, biofeedback and electrostimulation, digital stimulation and manual evacuation. It should be noted that the type of treatment a person receives is highly dependent on their personal preference, ability and the carer support available to them.

The company provided product prices for inclusion in the model and clinical inputs were taken from audit data from 3 UK hospitals. The audit data was for a heterogenous group of patients including those with spinal cord injuries, multiple sclerosis, cauda equina and spina bifida. Paediatric patients under the age of 17 years were not included in the model.

The company included a number of assumptions in the cost modelling. The EAC made some adjustments to these and the final assumptions in the assessment report included:

- All patients enter the model at age 30. Mortality was added by the EAC.

- The probability of ceasing to use Peristeen was assumed to be constant, whereas data from published studies (Passananti et al., 2016) shows a higher probability of reverting to standard bowel care in the first few months of using Peristeen. The EAC added a higher probability of cessation during the first year.

- Adverse events are included, but it is assumed that adverse events are reflected as a proportion of the hospitalisations recorded in the audit database and in the number of patients discontinuing Peristeen. Hospital admissions are assumed to be split equally between gastrointestinal infections, pressure ulcers, falls or trauma, abdominal pain and UTI. Bowel perforation is not explicitly included.

- There is a description of patients who are prescribed off-label medications (Lubiprostone and Prucalopride, L/P) however these patients are not included in any of the model calculations.

- The model is stated as being for a patient with SCI, and patients are assumed to be homogeneous, whereas the audit data is actually made up of patients with several different diagnoses, who are likely to have different outcomes.

- The model assumes that variables are constant over time for all patients. Many variables are likely to change with age for all patients, and will also change over time for patients with progressive diseases such as multiple sclerosis.

- Transition probabilities for patients who start using Peristeen, and then revert to SBC are assumed the same as probabilities in the SBC arm.

The EAC consider that these assumptions remain valid at this time however as there is potentially a large volume of new clinical evidence (see section 2). Some of these assumptions may need to be revised following a review of the clinical evidence.

The company base-case was for a male patient with spinal cord injuries and resulted in cost savings of £21,768 per patient.

During guidance development the EAC identified a number of changes to be made to the model comprising corrections to the model and changes which were considered potential improvements in the accuracy of the model. Key changes were:

- incorporating the costs of standard care for people who stop using Peristeen within the Peristeen arm

- adjusting transition probabilities

- changing the costs of pressure ulcers and urinary tract infections

- adding background mortality.

A full list of changes can be found in the EAC Assessment Report (section 4.4). The EAC base case resulted in greatly reduced cost savings of £2,867 per patient. The key driver in the model was frequency of use of Peristeen (or number of catheters required).

As part of this review process, the EAC noticed an additional error and a small number of inaccuracies that had not been previously identified. This was

reported to NICE, and the EAC then carried out further checks on the model structure, including checking calculations and recreating sections of the model.

7. Changes made to correct the 2017 model

A number of changes were made, all of which applied to both arms of the model and were errors in the original company submission:

- Remove double counting of anal plugs and incontinence pads
- Split follow-up costs for 3rd line treatment between the three potential treatment options
- Include full costs for adverse events for 3rd line and stoma care states
- Ensure calculation for stoma arrivals remains positive at longer time horizons

	Peristeen cost	SBC cost	Incremental
EAC base case 2017	£96,381	£99,248	**-£2,867**
Post corrections	£79,561	£85,188	**-£5,627**

The key driver, from one-way sensitivity analysis, remains the frequency of use of the Peristeen system. The sensitivity of the model to frequency of faecal incontinence is reduced.
The quality of the clinical data used in the model remains poor and should better clinical data become available the accuracy of the model could be improved.

The corrections made by the EAC to the 2017 cost analysis increase the reported cost savings with Peristeen and do not therefore impact the recommendations made by NICE in the 2018 published guidance.

NICE MTG36 (2018) recommends that:

- The case for adopting Peristeen for transanal irrigation in people with bowel dysfunction is supported by the evidence. Peristeen can reduce the severity of constipation and incontinence, improve quality of life and promote dignity and independence.

While acknowledging that Peristeen may not be suitable for all patients and that there is uncertainty in the cost modelling:

- Peristeen may not be suitable for all people with bowel dysfunction. It may take several weeks before a person is comfortable with using Peristeen, and some people may choose to stop using it. Peristeen is therefore most effective when it is offered with specialist training for users, carers and NHS staff, and structured patient support.

- Cost modelling for Peristeen is uncertain, but it is likely that Peristeen provides additional clinical benefits without costing more than standard bowel care.

The purpose of this 2021 report is to investigate changes to the costs in the original model and the potential impact these changes have on the original results to determine whether the current guidance for Peristeen should be reviewed or remain as it is.

8. Published Evidence

In the original economicanalysis there was considerable uncertainty around the findings of the audit data on which the model relied. There was no information on longer term outcomes such as the need for stomas. The model was sensitive to frequency of use, pressure ulcer treatment and faecal incontinence and there was limited clinical evidence around these variables.

The EAC notes that, since the original guidance, there have been a number of clinical studies published across patient groups with the company providing details of 25 potentially relevant publications. Studies include children and adult populations and potentially include long-term follow up. Only one study reports on cost-effectiveness (Sengoku et al. 2018). This study is based on a modified version of the Markov model in a previously published study (Emmanuel et al. 2016), the same model on which the company's submitted model was based. The purpose of the study was to analyse the cost-effectiveness of transanal irrigation using Peristeen for bowel management of patients with neurogenic bowel dysfunction in a Japanese clinical setting and the results of the study found the treatment strategy to be cost-effective in a Japanese setting. This is likely to have limited relevance to any UK based update, due to the difference in health care settings and costs.

The EAC considers that, given the potential volume of new clinical evidence, it may be necessary to conduct a review of this new clinical evidence, the results of which may address some of the uncertainties identified in the original assessment.

9. Current validity of model

Since the development of the guidance in 2018 the Peristeen device has been updated to Peristeen Plus. Information provided by the company indicates that this upgrade does not affect the functionality of Peristeen and that the mode of action of Peristeen Plus remains the same as that of Peristeen. Currently both Peristeen and Peristeen Plus are in use in the NHS, however patients are being transitioned to the upgraded Peristeen Plus. The company states that they will discontinue Peristeen at the end of 2021 and from

January 2022 Peristeen Plus will be the only trans-anal irrigation system marketed by the company.

Peristeen Plus is a CE-marked, non-sterile class 1 device and the company has stated that there are plans to apply for the device to be UK conformity Assessed (UKCA) to meet requirements for use in the UK post 2023.

No new guidance which might potentially impact the use of the device has been published. There have not been any changes to the clinical pathway since publication of the original guidance. One clinical expert noted that there has been an increased frequency of use particularly in patients with neurogenic bowel.

Clinical experts were asked whether they considered that the care pathway or evidence had changed to the extent that an update was warranted. One clinical expert noted that a care pathway which includes Peristeen should consider the setting in which the patient is assessed for use of the system. The expert reported that in settings where training is given and support is available, retention of system use is high. One expert noted that having long-term studies would add to the evidence base and one expert did not think there were any changes that would impact the current recommendations.

The EAC considers that the current model structure remains valid at this time.

10. Updated input parameters

The EAC identified updated costs for all parameters in the model (tables 1 to 4). Where possible, the original source for the cost has been used to identify updated costs and all cost inputs have been kept consistent with the original model. The company submitted updated costs for all parameters and cross-checking indicates that the EAC and company updated costs are in approximate agreement in most cases and that the updated costs are valid.

Peristeen Costs

Costs which have been updated in the economic model include costs associated with the Peristeen device which have been provided by the company and staff costs associated with using the device (Table *1*) which have been taken from PSSRU 2020 (Curtis & Burns 2020).

The EAC note that the cost of Peristeen has increased slightly in line with Prescription Pricing Authority (PPA) Guidelines. Staff costs associated with Peristeen have also increased. Overall there has been a slight increase in the cost of Peristeen.

From the details provided by the company there are two options for purchasing catheters;

- 15 catheters plus water bag at £138.47
- 10 catheters without water bag at £88.53.

The cost included in the original model was for catheters plus water bag and this has been used in the updated model for consistency. However, using the alternative costs for catheters has a small impact on cost savings.

Standard Bowel Care

Costs associated with standard bowel care have been updated using original sources such as BNF, NHS Drug Tariff and PSSRU 2020 (Table *2*). In almost all cases the costs have varied slightly from the original 2018 costs. The EAC note that the cost of the enema (Docusate Sodium) has increased from £0.66 per unit to £4.67 per unit. This is the only enema currently listed on BNF, and the EAC has confirmed with the company that this is the correct cost. The EAC also contacted a clinical expert for input but has not received a response.

Third Line Treatment

Third line treatment costs have increased overall (Table *3*), however none of the individual increase in costs was significant. The EAC note that there was uncertainty around the cost of sacral anterior root stimulation (SARS). The cost included in the original analysis was for the device only and this approach has been maintained in the current review. It should be noted however that the cost for the total procedure may be significantly higher (see Assessment Report).

Adverse Events

There have been some potentially substantial changes to the costs associated with adverse events (Table *4*). Assuming the proportion of patients experiencing adverse events remains the same, the impact of the changing costs is to reduce cost savings associated with Peristeen (table 5). It is unclear whether new clinical evidence would result in any changes to the proportions of patients assumed to experience adverse events.

Table 1: Peristeen Costs

			2018 (Peristeen)	2021 (Peristeen Plus)	
Value	**Source**	**Unit Size**	**Cost Per Unit**	**Cost Per Unit**	**Change**
Peristeen System (with or without toilet bag)	**2018:** NHS Drug Tariff/Company **2021:** NHS Drug Tariff/Company	1	£76.28	£79.45	Increase
Catheters (15 catheters, 1 water bag)	**2018:** NHS Drug Tariff/Company **2021:** NHS Drug Tariff/Company	1	£132.95	£138.47	Increase
Alternative Catheters (10 catheters, no water bag)	**2018:** NHS Drug Tariff/Company **2021:** NHS Drug Tariff/Company	1		£88.53	Not used in model
Initial Consultation	**2018:** PSSRU 2014 (consultant time with patient contact) **2021:** PSSRU 2020 Consultant Medical	1 hour	£142.00	£152.07	Increase
Follow-up Phone Call	**2018:** PSSRU 2014 (nurse (day ward) with patient contact) **2021:** PSSRU 2020 (Hospital based health care staff. Band 5 Nurse including qualification cost using 1.44 ratio from 2013/14 publication)	1 hour	£100.00	£111.16	Increase

Table 2: Standard Bowel Care Costs

Standard Bowel Care		2018		2021		
Value	**Source**	**Unit Size**	**Cost Per Unit**	**Unit Size**	**Cost Per Unit**	**Change**
Bulking agent: Fybogel sachet (3.5g)	BNF Ispaghula Husk: Fybogel 3.5g sachet	30	£2.29	30	£3.24	Increase
Softener: docusate	BNF Docusate Sodium: Dioctyl 100mg	100	£6.98	100	£6.98	No Change
Stimulant: bisacodyl	BNF Bisacodyl 5mg tablets	100	£3.43	100	£4.63	Increase
Osmotic: Macrogol 3350 with Potassium Chloride, Sodium Bicarbonate and Sodium Chloride)	BNF Movicol plain oral powder, (13.7g sachet)	50	£11.13	50	£13.49	Increase
Suppository glycerine	BNF Glycerol 4g **2021**: updated costs using an average of all costs ranging from £1.31 to £1.86	12	£1.94	12	£1.67	Decrease
Suppository bisacodyl	BNF Bisacodyl 10mg suppositories	12	£1.57	12	£2.35	Increase
Enema (Docusate Sodium)	BNF (Norgalax 120mg/10g enema (£28 for 6)	1	£0.66	1	£4.67	Increase
Anal plug	**2018:** NHS Electronic Drug Tariff **2021:** NHS Electronic Drug Tariff, August 2021	20	£44.89	20	£48.69	Increase
Incontinence pad	Tena.co.uk **2021:** Updated costs using: Tena Men Absorbent Protector Level 3	7	£5.95 (£0.85 per pad)	96	£53.88 (0.56 per pad)	Decrease

Table 3: Additional Costs

3rd line treatment	Patients going to 3rd line treatment are given a 33% probability of going to either of the three treatments				
			2018	2021	
	Description	**Source**	**Cost**	**Cost**	**Change**
SNS initial procedure	Procedure cost (per episode)	**2018:** NHS England Clinical Commissioning Policy (2013 inflated) **2021**: Inflated using PSSRU 2020	£9,368.00	£10,343.76	Increase
SNS follow up	Follow up, description not given, occurs once in 7 years (1 hour)	**2018**: NHS England Clinical Commissioning Policy (2013 inflated) **2021:** Inflated using PSSRU 2020	£6,286.00	£6,940.74	Increase
SARS initial procedure	Procedure cost (per episode)	**2018:** Dagenais 2013 (10,500 EUR converted to GBP at 1 EUR=0.74 GBP and inflated) **2021**: Inflated using PSSRU 2020 pay & prices inflation indices.	£7,770.00	£8,579	Increase
SARS outpatient appointment*	Follow up every two months (1 hour)	**2018:** NHS reference costs 2013-14, Colorectal surgery, outpatient attendance **2021:** NHS Reference Costs 2019-20, Colorectal surgery, outpatient attendance	£118.92	£118	Decrease
ACE initial procedure	Procedure cost (per episode)	**2018**: NHS reference costs 2013-14, Major large intestine procedure - Elective **2021**: NHS reference costs 2019-20, Major large intestine procedures - Elective (FF34A-FF34C)	£3,870.33	£5,522.58	Increase

3rd line treatment	Patients going to 3rd line treatment are given a 33% probability of going to either of the three treatments				
			2018	2021	
	Description	**Source**	**Cost**	**Cost**	**Change**
ACE outpatient appointment*	Follow up every two months (1 hour)	**2018:** NHS reference costs 2013-14, Colorectal surgery, outpatient attendance **2021:** NHS Reference Costs 2019-20, Colorectal surgery, outpatient attendance	£118.92	£118	Decrease
*A copy/paste error in the Assessment Report has these listed as SNS outpatients					
Stoma					
Surgery	Procedure cost	**2018**: NHS reference costs 2013-14, Very complex, complex and major large intestine procedure, elective **2021:** NHS reference costs 2019-20, Very Complex, Complex, and major large intestine procedures, elective (Total HRGS, FF30A-FF31D, FF34A-FF34C)	£7,459.76	£10,420.69	Increase
Colostomy bag	two per day (30 units)	**2018:** NHS Electronic Drug Tariff, June 2015 **2021:** NHS Drug tariff 2021	£87.00	£86.00	Decrease
Belt	one per month (1 unit)	**2018:** NHS Electronic Drug Tariff, June 2015 **2021:** NHS Drug Tariff 2021 Coloplast Ltd. Brava Belt,	£6.78	£7.20	Increase
Skin barrier	twice per day (30 applications)	**2018:** NHS Electronic Drug Tariff, June 2015	£22.24	£23.58	Increase

3rd line treatment	Patients going to 3rd line treatment are given a 33% probability of going to either of the three treatments				
			2018	2021	
	Description	Source	Cost	Cost	Change
		2021: NHS Drug Tariff 2021 Coloplast Ltd. Skin barrier wipe x30,			
Adhesive remover	twice per day (30 applications)	**2018:** NHS Electronic Drug Tariff, June 2015 **2021:** NHS Drug Tariff 2021 Coloplast Ltd. Brava adhesive remover wipe x30	£14.96	£15.86	Increase
HCP visits					
Consultant	1 hour (Peristeen 0.88/year SBC: 1.04/year)	**2018:** PSSRU 2014 **2021:** PSSRU 2020, Consultant Medical including qualifications	£142.00	£152.07	Increase
Dietician	1 hour (Peristeen 0.19/year SBC: 0.57/year)	**2018:** PSSRU 2014 **2021:** PSSRU 2020 (Scientific and Professional staff, band 6)	£37.00	£48	Increase
GP	1 hour (Peristeen 2.89/year SBC: 3.75/year)	**2018:** PSSRU 2014 **2021:** PSSRU 2020 (GP Unit costs, including direct care staff cost, per hour of patient contact)	£234.00	£255	Increase
Time spent on bowel management					
Caregiver salary	1 hour (Peristeen: 19 min/day for 30% SBC: 26 min/day for 44%)	**2018:** PSSRU 2014 **2021:** PSSRU 2020 (Homecare worker, cost per weekday hour)	£24.00	£24	No change

Table 4: Adverse Events

Adverse Events					
2nd line	**Description**	**Source**	**2018**	**2021**	**Change**
UTI (responding to initial treatment)	per episode (Peristeen: 0.67/year SBC: 1.37/year)	**2018:** Bermingham 2013 **2021:** Inflated using PSSRU 2020 pay & prices inflation indices.	£52.57	£58.05	Decrease
Overall hospitalisation	Peristeen: 0.28/year SBC: 0.63/year				
Gastrointestinal infection	per episode (20% of hospitalisations)	**2018:** NHS reference costs 2013-14, Gastrointestinal infection, non-elective long and short stay **2021:** NHS reference costs 2019/20, Non-Elective Gastrointestinal Infections with multiple interventions, single interventions, no interventions, non-elective long and short stay (codes FD01A – FD01J)	£1,998.84	£1,379.30	Decrease
Pressure ulcer management	per episode (20% of hospitalisations)	**2018:** Grade 4 pressure ulcer, SCNs High Impact Action Steering Group 2010, inflated **2021:** NICE CG179 (2014) Pressure ulcers: Prevention and Management (See Appendix L, table 5). Inflated using PSSRU 2020 pay & prices inflation indices.	£15,134.84	£15,577.48	Increase
Falls or other trauma	per episode (20% of hospitalisations)	**2018:** NHS reference costs 2013-14, Falls without specific cause, non-elective. **2021:** NHS reference costs 2019/20 Non elective (long and short stay) • Tendency to Fall, Senility or Other Conditions Affecting Cognitive Functions, with Multiple Interventions, Tendency to Fall, Senility or Other	£2,326.32	£2,901.26	Increase

		Conditions Affecting Cognitive Functions (codes WH09A-9G).			
Abdominal pain	per episode (20% of hospitalisations)	**2018:** Abdominal pain with and without interventions, NHS reference costs 2013-14 **2021:** NHS Reference Costs 2019/20 Non-elective (long and short stay) • Abdominal Pain with interventions (FD05A) • Abdominal pain without interventions (FD05B)	£1,432.09	£655.90	Decrease
UTI	per episode (20% of hospitalisations)	**2018:** NHS reference costs 2013-14, Kidney or Urinary Tract Infections **2021:** NHS Reference costs 2019/20 Non-elective (long and short stay) • Kidney or Urinary Tract Infections, with Interventions (codes FD01A-FD01J)	£2,485.03	£1,738.54	Decrease
3rd line	once per two years	**2018**: NHS England Clinical Commissioning Policy (2013 inflated) **2021:** Inflated using PSSRU 2020	£210	£231.87	Increase
Stoma					
Peristomal complications	per episode (61% of patients, Peristeen 7.3/year SBC: 1/ year)	**2018:** Meisner 2012 **2021:** Inflated using PSSRU 2020 inflation indices	£34.89	£38.52	Increase
Hernia complications	per episode (18% of patients, 3/year)	**2018** Hernia procedure, NHS reference costs 2013-14 **2021:** NHS Reference costs 2019/20 Elective • Abdominal Hernia Procedures (FF61A-FF61C)	£3,355.69	£4,688.17	Increase

11. Results from updated model

In 2018, the cost savings reported with Peristeen were an estimated £2,867 per patient over a 37-year time horizon, corrected to £5,627 in 2021. The EAC used the updated costs to assess whether and to what extent these cost savings have changed.

The EAC has not updated the sensitivity analysis at this time as this would require a full update of the economic model, including the clinical parameters which is not within the scope of this review.

Once the updated costs have been incorporated into the model, Peristeen remains cost saving however the savings are reduced from £5,627 to £5,144 per patient (Table *5*).

Table 5: Impact of changes on cost savings over a 37-year time horizon

	Cost saving per patient	Comment
MTG36 (2016)	£2,867	EAC base case result
MTG36 (2021)	£5,627	EAC base case result corrected
Updated Peristeen Costs	£4,961	
Adding in the updated Standard Bowel Care Costs	£3,765	The greatest change in the cost of standard bowel care is the increase in cost of the enema from £0.66 per unit to £4.67 per unit.
Adding in 3rd line Treatment	£4,173	
Adding in the updated Adverse Events Costs 2nd line	£3,770	
Adding in the updated Adverse Events cost 3rd line	£3,771	

Adding in updated stoma costs	£5,144	Peristeen remains cost saving in the base case
Current Estimated Cost Saving	**£5,144**	**Based on updated costs only.**

12. Conclusion

The EAC found nothing to indicate that there have been any changes to the clinical pathway. There have been no new guidelines published and clinical expert input did not indicate any changes.

The clinical inputs were the area of most uncertainty in the original cost modelling and it should be recognised that this uncertainty still remains. Information submitted by the company as part of this review suggest that there is a large volume of potentially relevant clinical evidence published since the guidance development. This was supported by clinical expert input which suggested that there may now be evidence from long-term use – an area which was particularly lacking. If such evidence is now available, this should be reviewed as it may result in changes to the model assumptions and clinical inputs and in turn impact on the cost savings with Peristeen.

Updating the costs in the current model result in a reduction in cost savings from £5,627 to £5,144.

The EAC therefore concludes that the model structure and assumptions remain valid at this time although assumptions may need to be modified based on availability of new clinical evidence. Peristeen remains cost saving with all costs updated.

13. References

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Appendix 1. Background documents for this review

Hyperlinks for the background documents for this review report:

1. Medical technologies guidance document
2. Assessment report
3. Scope of assessment
4. A copy of the company information request regarding the technology
5. A list of expert advisers and their completed questionnaires on the MTG review
6. Executable cost model which aligns with the base case described in the MTG documents
7. If there is new evidence which is relevant to any of the clinical parameters in the model, the analyst should send the updated values.
8. Any relevant other documents which are not available on the NICE website.

Appendix C – Details of studies and ongoing trials

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr>
<td>Alhamzi 2019

Study type: Retrospective case series

Location: Saudi Arabia

Study period: January 2008 to January 2016

Follow-up: Mean 84.1 ± 32.1 months; median 48 months; range 22-118 months.</td>
<td>n=109

Children (age 5-18 years, median 84 months, range 60-216) with myelomeningocoele (MMC), who had failed to respond to conservative measures for stool incontinence</td>
<td>Patients and families received in-person training from a paediatric urotherapist. Follow-up by telephone was scheduled in the first week, and another follow-up appointment made after 1 month.

Peristeen irrigation was performed 2-3 times per week, using 5ml of tap water per kg body weight. The frequency was reduced to twice per week if the patient showed good response. Water volume was reduced in</td>
<td>• Successful response (freedom from stool soiling; absence of faecal incontinence; minimal or no constipation)

• Diaper dependence

• Dependence on caregivers for bowel management</td>
<td>Patients were initially started on Peristeen TAI 2 times per week (n=104) or 3 times per week (n=5).

<table>
<tr><th></th><th>n (%)</th></tr>
<tr><td>Complete stool continence</td><td>101 (92.6%*)</td></tr>
<tr><td>No longer needed diapers</td><td>26 (23.9%)</td></tr>
<tr><td>Occasional diaper use due to urine incontinence</td><td>48 (44.0%)</td></tr>
<tr><td>Occasional diaper use due to concern about soiling</td><td>27 (24.8%)</td></tr>
<tr><td>Ongoing stool incontinence despite use of Peristeen</td><td>6 (5.5%)</td></tr>
<tr><td>Stool incontinence due to non-compliance</td><td>2 (1.8%)</td></tr>
<tr><td>TOTAL</td><td>109</td></tr>
</table>
*reported as 90.4% in the abstract.

All participants needed help from caregivers to complete the irrigation procedure. Most had motor disabilities and paraplegia, and a large number were wheelchair users.

No serious adverse events were reported by parents.

Parental satisfaction with treatment results was high.</td>
<td>Patients with faecal incontinence and planned bladder augmentation were started on Peristeen TAI 3 months before surgery. Those with successful response to TAI underwent bladder reconstructive surgery and remained on TAI. Others were offered a MACE procedure in addition to bladder reconstructive surgery.

Non-comparative study; descriptive statistics only

The length of follow-up was reported inconsistently in the abstract and main body of the paper.

No data was provided to verify parental satisfaction.</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td></td><td>case of abdominal pain.</td><td></td><td></td><td></td></tr>
<tr><td>Ausili 2018

Study type: Prospective case series

Location: Italy (8 sites)

Recruitment period: January 2014 to September 2016

Follow-up: Minimum 2 years (range 24-32 months)</td><td>n=74

Children (age 6-17 years) with neurogenic bowel dysfunction and unsatisfactory bowel management

Spina bifida (SB) n=36

Anorectal malformations (ARM) n=38</td><td>Intervention: TAI (Peristeen)

Patients were trained by specialised nurses and a medical doctor. Irrigation was performed every day for the first week, then 3 times a week, adjusting water volume as required.</td><td>• Constipation
• Faecal incontinence
• Bristol stool scale
• Symptoms during evacuation
• Assistance by a caregiver
• Time for evacuation
• Quality of life (CHQ-PF50 for ages 6-11; SF-36 for ages 12-17)
• Complications and side effects</td><td><u>Primary outcomes</u>
<table><tr><th></th><th>Baseline</th><th>3 months</th><th>≥2 years</th></tr><tr><td>Constipation</td><td>60/74 (81%)</td><td>24/72 (33%)</td><td>30/67 (45%)</td></tr><tr><td>Faecal incontinence</td><td>33/74 (45%)</td><td>10/72 (14%)</td><td>14/67 (21%)</td></tr></table><u>Bristol stool scale</u>
<table><tr><th></th><th>Baseline</th><th>3 months</th><th>≥2 years</th></tr><tr><td>Type 1 or 2 (hard)</td><td>48% ARM
78% SB</td><td>0% ARM
3% SB</td><td>11% ARM
19% SB</td></tr><tr><td>Type 4 or 5 (soft)</td><td>30% ARM
3% SB</td><td>87% ARM
82% SB</td><td>65% ARM
50% SB</td></tr></table><u>Symptoms during evacuation</u>
<table><tr><th></th><th>Baseline</th><th>3 months</th><th>≥2 years</th></tr><tr><td>No symptoms</td><td>43% ARM
27% AB</td><td>84% ARM
69% SB</td><td>62% ARM
70% SB</td></tr></table><u>Assistance by a caregiver</u>
<table><tr><th></th><th>Baseline</th><th>3 months</th><th>≥2 years</th></tr><tr><td>Need to be assisted</td><td>60% ARM
76% SB</td><td>41% ARM
76% SB</td><td>47% ARM
69% SB</td></tr></table><u>Time for evacuation</u>
<table><tr><th></th><th>Baseline</th><th>3 months</th><th>≥2 years</th></tr><tr><td>Less than 30 minutes</td><td>44% ARM</td><td>73% ARM</td><td>50% ARM</td></tr></table></td><td>Three-month outcomes of this study were included in the previous EAC report and contributed to the original NICE guidance.

The authors also report outcomes separately according to diagnosis (SB or ARM).

Although changes in proportions of patients with constipation and faecal incontinence were reported as statistically significant ($p<0.05$), it is not clear whether this applied to both groups (SB and ARM) between all time points.

The number of quality of life variables showing significant</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td></td><td>7% SB</td><td>45% SB</td><td>39% SB</td></tr>
<tr><td>30-45 minutes</td><td>19% ARM
32% SB</td><td>17% ARM
41% SB</td><td>38% ARM
39% SB</td></tr>
<tr><td>45-60 minutes</td><td>21% ARM
24% SB</td><td>5% ARM
10% SB</td><td>9% ARM
17% SB</td></tr>
<tr><td>More than 60 minutes</td><td>16% ARM
37% SB</td><td>5% ARM
5% SB</td><td>3% ARM
6% SB</td></tr>
</table>
<u>Quality of life</u>
CHQ-PF50 (ages 6-11)
<table>
<tr><th></th><th>Baseline n=39</th><th>3 months n=25</th><th>≥2 years n=35</th></tr>
<tr><td>Number of variables showing significant improvement from baseline</td><td></td><td>8/15 ARM
9/15 SB</td><td>4/15 ARM
5/15 SB</td></tr>
</table>
SF-36 (ages 12-17)
<table>
<tr><th></th><th>Baseline n=35</th><th>3 months n=25</th><th>≥2 years n=32</th></tr>
<tr><td>Number of variables showing significant improvement from baseline</td><td></td><td>2/10 ARM
9/10 SB</td><td>2/10 ARM
6/10 SB</td></tr>
</table>
<u>Complications and side effects</u>
No severe side effects were recorded. There was no evidence of hyponatraemia or perforation.
<table>
<tr><th>Complications</th><th>3 months</th><th>≥2 years</th></tr>
</table>
</td><td>improvement from baseline is not reported consistently in the table and text (for both CHQ-PF50 and SF-36 measures).</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td colspan="2">Bursting of the balloon</td><td>15% ARM
5% SB</td><td>21% ARM
15% SB</td></tr>
<tr><td colspan="2">Faecal leakage during irrigation</td><td>21% ARM
17% SB</td><td>18% ARM
3% SB</td></tr>
<tr><td colspan="2">Balloon expulsion</td><td>21% ARM
10% SB</td><td>24% ARM
3% SB</td></tr>
<tr><td colspan="2">“No useful effect”</td><td>7% ARM
2% SB</td><td>8% ARM
3% SB</td></tr>
<tr><td rowspan="2">Flatus incontinence</td><td>Baseline</td><td>3 months</td><td>≥2 years</td></tr>
<tr><td>21% ARM
32% SB</td><td>10% ARM
10% SB</td><td>10% ARM
10% SB</td></tr>
</table>
</td><td></td></tr>
<tr><td>Bildstein 2017

Study type: Retrospective case series

Location: France

Study period: January 2010 to December 2014

Follow-up: 1 year (median 16 (1-67) months)</td><td>n=108

Adults (median age 55 years range 18-83) with constipation (n=65) or faecal incontinence (n=43) who had not responded to conservative management (education, behavioural therapy, biofeedback,</td><td>Intervention: TAI (Peristeen), n=108

Specialist nurses provided training and supervision. During the first month, patients were instructed to perform irrigation daily or every 2 days. After 1, 3,6 and 12 months, frequency and water volume were discussed.</td><td>• Compliance with TAI one year after training
• Reasons for discontinuing TAI
• Predictive factors for continuing TAI</td><td>
<u>Compliance with TAI</u>
<table>
<tr><th></th><th>Continued using TAI (n, %)</th><th>Exclusions (n)</th></tr>
<tr><td>Baseline</td><td>108 (100%)</td><td></td></tr>
<tr><td>After training</td><td>103 (95%)</td><td>5 training failures</td></tr>
<tr><td>1 month</td><td>92 (85%)</td><td>9 stopped treatment
2 lost to follow-up</td></tr>
<tr><td>3 months</td><td>70 (65%)</td><td>15 stopped treatment
6 lost to follow-up
1 death</td></tr>
<tr><td>6 months</td><td>59 (55%)</td><td>10 stopped treatment
1 lost to follow-up</td></tr>
<tr><td>12 months</td><td>46 (43%)</td><td>10 stopped treatment
3 lost to follow-up</td></tr>
</table>
Outcomes of training
<table>
<tr><th></th><th>n (%)</th></tr>
</table>
</td><td>The population was heterogeneous, with dysfunction attributed to neurological disease (multiple sclerosis, spina bifida, spinal cord injury, or Parkinson’s Disease), slow transit constipation, or obstructed defaecation syndrome.

Although validated symptom severity scores were collected at baseline, they were not used to evaluate outcome effectiveness.</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td>oral and rectal laxatives)</td><td></td><td></td><td>
<table>
<tr><td>Withdrew from study because of repeated expulsion of the rectal catheter during irrigation and water leakage around the rectal catheter</td><td>4 (4%)</td></tr>
<tr><td>Withdrew from study due to difficulty emptying instilled water</td><td>1 (1%)</td></tr>
<tr><td>Needed 2 training sessions</td><td>8/108 (7%)</td></tr>
<tr><td>Needed 3 training sessions</td><td>1/108 (1%)</td></tr>
<tr><td>Able to self-administer TAI after training</td><td>92/108 (85%)</td></tr>
<tr><td>Required assistance from a nurse</td><td>7/108 (7%)</td></tr>
<tr><td>Required assistance from a family member</td><td>4/108 (4%)</td></tr>
<tr><td>Performed TAI at least 2 to 3 times per week</td><td>70% (denominator not reported)</td></tr>
</table>
<u>Reasons for discontinuing TAI (following training success)</u>
<table>
<tr><td></td><td>n (%)</td></tr>
<tr><td>Technical problems (catheter expulsion, rectal balloon bursting, water leakage or retention, pain during irrigation, anal bleeding, anal fissure)</td><td>16 (36%)</td></tr>
<tr><td>Inefficacy</td><td>18 (41%)</td></tr>
<tr><td>Too many constraints (mainly related to time spent performing irrigation)</td><td>10 (23%)</td></tr>
</table>
Median time using TAI before discontinuation = 3 months (range 0.2-11 months).

At final follow-up, discontinuation of TAI had led to resumption of medical treatment for 21 patients (43%), and an invasive surgical procedure for 18 patients (37%): Malone antegrade</td><td></td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>continence enema (n=6); sigmoid colostomy (n=4); ileostomy (n=1); coloproctectomy (n=1); rectopexy (n=2); sacral nerve stimulation (n=3); artificial bowel sphincter (n=1). 8 patients preferred resuming traditional enemas.

<u>Adverse effects in “adopters” (those continuing TAI at 12 months)</u>
<table><tr><td></td><td>n (%)</td></tr><tr><td>Complaints about time spent on bowel management</td><td>13 (28%)</td></tr><tr><td>Minor/self-limiting adverse events (total of 47)</td><td>25 (54%)</td></tr><tr><td>Leakage of irrigation fluid around the catheter</td><td>16 events</td></tr><tr><td>Pain on catheter insertion or water instillation</td><td>14 events</td></tr><tr><td>Catheter expulsion</td><td>9 events</td></tr><tr><td>Rectal balloon bursting</td><td>5 events</td></tr><tr><td>Instilled water retention</td><td>3 events</td></tr><tr><td>Bowel perforation</td><td>0 events</td></tr></table>
<u>Predictive factors</u>

Technical problems that occurred during the first training session were the only predictive factor for TAI discontinuation within the first 12 months.</td><td></td></tr>
<tr><td>Enriquez-Navascues 2019

Study type: RCT</td><td>n=27

People with major LARS (score >29), at least 1 year</td><td>Intervention: TAI (Peristeen), n=13

Irrigation procedures were initially carried out once a day, then 3 or 4 times a</td><td>Scores on the following scales at baseline, 12, 18 and 24 weeks:

• LARS (anterior resection syndrome) –</td><td>Discontinued intervention: TAI=3; PTNS=1

No significant differences between groups in potentially confounding factors at baseline.

<u>Change in median LARS score (per-protocol analysis)</u>
<table><tr><th>Group</th><th>Baseline</th><th>6 months</th><th>p-value</th></tr><tr><td>TAI</td><td>35 (IQR 32-39)</td><td>12 (IQR 12-26)</td><td>0.021</td></tr></table></td><td>Not UK based

The authors considered this to be an exploratory pilot study (sample size was not estimated a priori). Results were</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr>
<td>Location: Spain

Recruitment period: May 2017 to February 2018

Follow-up:
6 months</td>
<td>after rectal surgery

Mean age TAI group 68 years (range 48-71); PTNS group 68 years (range 56-76)

Setting: Outpatient follow-up</td>
<td>week for a period of up to 6 months.

Before using the system at home, patients were taught how to use it and supervised for 3–4 weeks by trained gastroenterology nurses.

Comparator:
PTNS (Urgent PC device, Uroplasty), n=14

Programme included 20 sessions of 30 minutes each: once a week for 12 weeks; then 4 sessions once a fortnight for 2 months; then 4 sessions once a month.</td>
<td>primary outcome measure
• Vaizey (faecal incontinence)
• Altomare (obstructed defaecation)
• EORTC QLQ-C30 (quality of life)
• Visual Analogue Scale (overall satisfaction with treatment)

Potential confounding factors (sex; age; diverting stoma; previous chemotherapy/radiotherapy; type and level of anastamosis; anastomotic complications; time between surgery and start of intervention/ comparator; astringent medication).</td>
<td>
<table>
<tr><td>PTNS</td><td>35 (IQR 34-37)</td><td>30 (IQR 25-33)</td><td>0.045</td></tr>
</table>
Both groups saw a statistically significant reduction in LARS score. Only the TAI group met the criteria for a clinically significant change in LARS category.

<u>Proportion of people with reduction in LARS category after 6 months</u>
<table>
<tr><th>Group</th><th>ITT analysis</th><th>Per-protocol</th></tr>
<tr><td>TAI</td><td>8/13 (62%)</td><td>8/10 (80%)</td></tr>
<tr><td>PTNS</td><td>4/14 (29%)</td><td>3/13 (23%)</td></tr>
</table>
<u>Faecal incontinence (Vaizey scale, per-protocol)</u>
<table>
<tr><th>Group</th><th>Baseline</th><th>6 months</th><th>p-value</th></tr>
<tr><td>TAI</td><td>15 (IQR 11-18)</td><td>6 (IQR 4-7)</td><td>0.037</td></tr>
<tr><td>PTNS</td><td>14.5 (IQR 13-17)</td><td>9 (IQR 7-10)</td><td>0.007</td></tr>
</table>
<u>Obstructed defaecation (Altomare scale, per-protocol)</u>
<table>
<tr><th>Group</th><th>Baseline</th><th>6 months</th><th>p-value</th></tr>
<tr><td>TAI</td><td>10 (IQR 7-14)</td><td>8 (IQR 6-9)</td><td>0.083</td></tr>
<tr><td>PTNS</td><td>9 (IQR 7-12)</td><td>8 (IQR 4-9)</td><td>0.554</td></tr>
</table>
<u>Quality of Life (EORTC QLQ-C30, per protocol)</u>
<table>
<tr><th>Group</th><th>Measure</th><th>Baseline</th><th>6 months</th><th>p-value</th></tr>
<tr><td rowspan="2">TAI</td><td>Global health status</td><td>8 (IQR 8-9)</td><td>12 (IQR 9-12)</td><td>0.020</td></tr>
<tr><td>Physical functioning</td><td>35 (IQR 28-43)</td><td>28 (IQR 26-34)</td><td>0.071</td></tr>
</table>
</td>
<td>compared before and after treatment within each group, rather than as a direct comparison between groups.

A reduction in LARS category (from ‘major LARS’ to ‘minor LARS’ or ‘no LARS’) for at least 50% of patients was considered to be clinically significant.

A 50% reduction in Vaizey or Altomare scores was considered to be clinically significant.

The authors stated that they “encountered no significant treatment-associated unintended adverse events with either treatment modality”.

*The p-value for change in Global health status in the</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td></td><td>Role functioning</td><td>8 (IQR 7-8)</td><td>7 (IQR 7-7)</td><td>0.058</td></tr>
<tr><td></td><td>VAS</td><td>2 (IQR 0-3)</td><td>7.5 (IQR 6-9)</td><td>0.008</td></tr>
<tr><td>PTNS</td><td>Global health status</td><td>9 (IQR 7-10)</td><td>12 (IQR 9-12)</td><td>0.45*</td></tr>
<tr><td></td><td>Physical functioning</td><td>33 (IQR 27-40)</td><td>28 (IQR 23-31)</td><td>0.092</td></tr>
<tr><td></td><td>Role functioning</td><td>7 (IQR 7-8)</td><td>7 (IQR 7-8)</td><td>0.179</td></tr>
<tr><td></td><td>VAS</td><td>3 (IQR 0.5-4)</td><td>7 (IQR 6-8)</td><td>0.003</td></tr>
</table>
</td><td>PTNS group have may been incorrectly reported. The accompanying text indicates that “quality of life improved overall in both groups”.</td></tr>
<tr><td>Furuta (2021)

Study type: Prospective case series

Location: Japan

Study period: July 2018 to June 2019

Follow-up:3 months</td><td>n=11

Children (aged 6-17 years; mean 10.8 ± 3.3 years) with spina bifida and intractable constipation. All had moderate to severe NBDS scores at baseline.</td><td>Intervention: TAI (Peristeen), n=11

Irrigation was performed every 2 days.</td><td>• NBDS, including frequency of faecal incontinence, use of tablets against constipation, and perianal skin problems
• Bristol stool scale
• Number of urinary tract infections (UTIs)</td><td>
<u>NBDS (mean ± SD)</u>
<table>
<tr><th></th><th>Baseline</th><th>3 months</th><th>p-value</th></tr>
<tr><td>Total NBDS</td><td>15.6 ± 4.1</td><td>11.1 ± 4.6</td><td>0.009</td></tr>
<tr><td>Frequency of faecal incontinence</td><td>5.0 ± 3.7</td><td>3.7 ± 3.4</td><td>0.108</td></tr>
<tr><td>Use of tablets against constipation</td><td>1.1 ± 1.0</td><td>0.4 ± 0.9</td><td>0.019</td></tr>
<tr><td>Perianal skin problems</td><td>0.9 ± 1.4</td><td>0.2 ± 0.8</td><td>0.083</td></tr>
</table>
Bristol stool scale

<u>Mean (</u>± SD) scores changed significantly ($p < 0.001$) between baseline (1.9 ± 1.2) and follow-up (3.6 ± 1.2).

<u>Urinary tract infections</u>
<table>
<tr><th></th><th>Baseline</th><th>3 months</th><th>p-value</th></tr>
<tr><td>UTIs (number, %)</td><td>9 (82%)</td><td>6 (55%)</td><td>0.082</td></tr>
</table>
</td><td>The main aim of this study was to investigate the impact of TAI on gut microbiota. Samples were also compared with matched healthy controls.</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr>
<td>Gordon 2019

Study type: Prospective case series

Location: USA

Recruitment period: Not reported

Follow-up: 1 year</td>
<td>n=70

Children (aged 3-17 years, mean 8.75 years) with neurogenic bowel who had failed other treatment modalities.

Primary diagnoses varied, but included spina bifida, cerebral palsy, and spinal cord injury).</td>
<td>Intervention: TAI (Peristeen) n=70

Irrigation was carried out daily for 2 weeks, or until only liquid flow results were obtained. Then patients/families were instructed to use Peristeen every other day, but to revert back to daily use if preferred.</td>
<td>• Neurogenic bowel dysfunction score (NBDS)
• Patient/family satisfaction with treatment (Likert scale 0-10, 10 being completely satisfied)
• Complications of treatment</td>
<td><u>Main outcomes after 1 year (mean ± SD)</u>
<table><tr><th>Outcome</th><th>Baseline</th><th>1 year</th><th>p-value</th></tr><tr><td>NBDS (n=24)</td><td>19.3 ± 6.7</td><td>12.5 ± 5.7</td><td><0.001</td></tr><tr><td>Satisfaction (n=22)</td><td>3.9 ± 2.0</td><td>8.6 ± 1.3</td><td><0.001</td></tr></table>There were no complications directly attributed to treatment. Two patients had exacerbation of baseline rectal prolapse.

The authors reported that “a small number of patients were found to have stopped using Peristeen” - this was most commonly attributed to parental preference for other bowel management programmes.</td>
<td>Baseline bowel management methods varied.

The investigators did not collect data about whether the patients were able to perform enemas independently or with assistance.

Response rates, losses to follow-up and reasons for treatment discontinuation were not clearly reported, so there is a relatively high risk of bias.</td>
</tr>
<tr>
<td>Lallemant-Dudek 2020

Study type: Retrospective case series</td>
<td>n=149

Children (aged 2-20 at follow-up, mean 10.6 ± 4.1 years) with faecal incontinence or constipation who had not responded to</td>
<td>Intervention: TAI (Peristeen) n=70

Children/families were trained in use of Peristeen for self-administration or with assistance. Irrigation volume/frequency</td>
<td>• Bowel symptoms
• Adherence to treatment with TAI
• Reasons for discontinuing TAI
• Training time
• Frequency of TAI</td>
<td><u>Bowel symptoms (n, %)</u>
<table><tr><th></th><th>Baseline</th><th>≥9 months</th></tr><tr><td>Constipation</td><td>122/149 (82%)</td><td>40/129 (31%)</td></tr><tr><td>Faecal incontinence</td><td>130/149 (87%)</td><td>50/129 (39%)</td></tr><tr><td>Daily incontinence</td><td>97/149 (65%)</td><td>6/129 (5%)</td></tr></table><u>Adherence and discontinuation rate</u>

129/149 (87%) were still using Peristeen at least 9 months after training. Those who had stopped using it (n=20) had done so at a mean of 16 ± 8.4 months. 25% of discontinuations</td>
<td>The main focus of this study was on adherence to treatment.

Questionnaires were not validated.

Only descriptive statistics are reported.</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr>
<td>Location: France (5 sites)

Study period: October 2009 to May 2012

Follow-up: Minimum 9 months; mean duration of TAI = 14 ± 7.4 months</td>
<td>conservative treatments.

Diagnoses included myelomeningocoele, anorectal malformation, Hirschsprung's disease, and closed spinal dysraphism.</td>
<td>was not standardised.</td>
<td>• Time to perform TAI
• Technical problems
• Adverse events</td>
<td>occurred during the first 3 months; the remaining 75% occurred during the second year of use.

<u>Reasons for discontinuation</u>
<table>
<tr><td>Lack of motivation</td><td>45%</td></tr>
<tr><td>Poor tolerance (including 4 instances of pain)</td><td>35%</td></tr>
<tr><td>Difficulties performing the procedure
- balloon burst
- catheter expulsion</td><td>35%
4 events
1 event</td></tr>
<tr><td>Inefficacy</td><td>30%</td></tr>
<tr><td>Not meeting expectations</td><td>25%</td></tr>
<tr><td>Dependence on carer</td><td>10%</td></tr>
<tr><td>Resolution of disorders</td><td>10%</td></tr>
</table>
Factors associated with continued use of Peristeen: resolution of symptoms/continence (77.3%); other reasons such as social wellbeing, comfort, self-sufficiency at care, and resolution of pain (22.7%). Adherence was also improved when at least one TAI procedure was performed under nurse supervision during training (p=0.014), and when TAI was initially prescribed on a daily basis (p=0.04)

<u>Training time, frequency of TAI, and time to perform TAI</u>

Median training time: 1.5 hours (median 1.5 sessions)

Estimated mean time to perform TAI: 30 ± 19 minutes
<table>
<tr><th>Prescribed frequency of TAI</th><th>n (%)</th></tr>
<tr><td>Daily or every 2 days</td><td>104/149 (70%)</td></tr>
<tr><td>Every 3 days</td><td>30/149 (20%)</td></tr>
<tr><td>Once a week</td><td>9/149 (6%)</td></tr>
<tr><td>Unspecified</td><td>5/149 (3%)</td></tr>
</table>
</td>
<td></td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td><u>Technical problems and adverse events</u>
Technical problems were experienced by n=78 (61%) adherent children, including burst balloon (46%); leakage of irrigation fluid (20%), and catheter expulsion (19%). No adverse events were reported. Within the study follow-up period, no children underwent the Malone procedure (antegrade enema).</td><td></td></tr>
<tr><td>Martellucci 2018

Study type: Prospective case series

Location: Italy

Recruitment period: April 2015 to May 2016

Follow-up: 9 months</td><td>n=33
People who had significant LARS symptoms (score >30) after rectal cancer surgery.
Median age of people with chronic LARS = 64 years (range 42-79)
Of the 27 patients who completed the study,19 were excluded due to the possibility of</td><td>Intervention: TAI (Peristeen), within the “Chronic LARS” subgroup, n=8
All patients were instructed by a specially trained stoma/ rehabilitative nurse, who assisted until they could independently perform the irrigation at home.
Peristeen was used on alternate days (3-4 times per week) for 6 months, followed</td><td>• LARS score</td><td>There were 8 people in the “Chronic LARS” group, who had a mean duration of functional impairment of 21 months (range 6-102 months).
<u>Change in LARS score (median, range)</u>
<table><tr><th></th><th>Baseline</th><th>“During TAI”</th></tr><tr><td>LARS score</td><td>36.5 (31-42)</td><td>12.6 (0-21)</td></tr></table></td><td>Some patients started TAI within the postoperative period. Only the results from those with a time between surgery and TAI of > 6 months are included in this review.
The authors did not specify the outcome measure in Table 3, but summary scores match those in Table 2 and are therefore assumed to represent LARS scores.</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td>having started TAI within the postoperative period (“Early LARS”).</td><td>by 3 months of enema therapy.

The median volume of water used for irrigation was 450ml (range 300-1000ml).</td><td></td><td></td><td></td></tr>
<tr><td>McCarthy 2020

Study type: Prospective case series

Location: UK

Recruitment period: October 2018 to July 2019

Follow-up: 8 weeks</td><td>n=50

People with spinal cord injury reporting neurogenic bowel dysfunction</td><td>Peristeen TAI was prescribed.

Neither frequency of use nor irrigation volumes were reported.</td><td>• Bespoke questionnaire with multiple choice questions

• 10 questions related to symptoms or treatments. The weighted scores combined to generate a total bowel dysfunction score (0-55), where ≥14 indicated severe dysfunction.

• Likert scales were used to rate emotional wellbeing (0=best; 5=worst), and</td><td><u>Total bowel dysfunction score category (proportion of respondents)</u>
<table><tr><th></th><th>Baseline</th><th>8 weeks</th></tr><tr><td>No-to-minor</td><td>2%</td><td>46%</td></tr><tr><td>Minor</td><td>8%</td><td>16%</td></tr><tr><td>Moderate</td><td>10%</td><td>22%</td></tr><tr><td>Severe</td><td>80%</td><td>16%</td></tr></table>Average total bowel dysfunction score (range): 20.1 (3-38 at baseline; 8.8 (0-22) at 8 weeks

<u>Involuntary defaecation (proportion of respondents)</u>
<table><tr><th></th><th>Baseline</th><th>8 weeks</th></tr><tr><td>A few times a year or less</td><td>40%</td><td>86%</td></tr><tr><td>3-4 times a month</td><td>26%</td><td>4%</td></tr><tr><td>1-6 times per week</td><td>26%</td><td>10%</td></tr><tr><td>Daily</td><td>8%</td><td>0%</td></tr></table><u>Frequency of defaecation (proportion of respondents)</u>
<table><tr><th></th><th>Baseline</th><th>8 weeks</th></tr><tr><td>Daily</td><td>36%</td><td>30%</td></tr><tr><td>2-6 per week</td><td>58%</td><td>70%</td></tr></table></td><td>UK study

It is not clear whether all (consecutive) eligible patients were invited to participate.

No validated measures used. Poor questionnaire design, with considerable limitations to quality of reported data.

Only descriptive statistics are reported. Those with missing data were excluded from the denominator, but reported only as a proportion (%). For bowel dysfunction</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td></td><td></td><td></td><td>satisfaction with bowel management (0=worst; 10=best).</td><td>
<table>
<tr><td>Less than once a week</td><td>6%</td><td>0%</td></tr>
</table>
<u>Quality of life</u>
<table>
<tr><th></th><th>Baseline</th><th>8 weeks</th></tr>
<tr><td>Emotional wellbeing score (mean)</td><td>4.0</td><td>1.2</td></tr>
<tr><td>Satisfaction with bowel management (mean)</td><td>3.2</td><td>7.3</td></tr>
</table>
The proportion of people with perianal skin problems at baseline and 8 weeks were 15% and 5%, respectively.</td><td>scores, blank entries were counted as 0.</td></tr>
<tr><td>McCutchan 2018

Study type: Comparative observational using mixed methods (mainly qualitative)

Location: UK

Recruitment period: Underwent surgery between January 2009</td><td>n=21

Adults with LARS score of >20, who had restoration of bowel continuity (after anterior resection for bowel cancer) for a minimum of 12 weeks.</td><td>Intervention: TAI (Peristeen) n=15

Comparator: Usual care n=6

Interviews were carried out at baseline with 12 people who accepted the offer of TAI, and 5 people who had declined treatment. Follow-up interviews were carried out after 6 months with those who had accepted treatment (n=11);</td><td>• LARS score
• Faecal incontinence (St Mark’s questionnaire)
• Factors influencing decision to accept or decline treatment
• Quality of life
• Treatment acceptability, usability, and impact on symptoms</td><td><u>LARS score (mean, range)</u>
<table>
<tr><th></th><th>Baseline</th><th>6 months</th></tr>
<tr><td>Intervention group (n=15)</td><td>35.9 (21-42)</td><td>17.7 (0-41)</td></tr>
<tr><td>Comparator group (n=6)</td><td>34.2 (32-37)</td><td>32.4 (26-37)</td></tr>
</table>
<u>Faecal incontinence (mean, range)</u>
<table>
<tr><th></th><th>Baseline</th><th>6 months</th></tr>
<tr><td>Intervention group (n=15)</td><td>9.7 (2-15)</td><td>3.2 (0-9)</td></tr>
<tr><td>Comparator group (n=6)</td><td>9.3 (4-13)</td><td>5.4 (0-9)</td></tr>
</table>
<u>Baseline interviews</u>

Participants described the impact of LARS symptoms on quality of life. When considering TAI, symptom severity and the practicalities of performing the procedure influenced decisions. Some were “willing to try anything”, whereas others declined treatment as they were not comfortable with the concept of daily self-catheterisation, or felt their symptoms were manageable or improving.</td><td>UK study

Focus is on qualitative outcomes. There was no intention to undertake statistical analysis on the quantitative data, and the sample was not sufficiently powered for that purpose.

The authors acknowledge that the sample may not be representative of a larger group.

It was not possible to collect data on reasons for drop out from treatment – only</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr><td>and January 2014

Follow-up:
6 months</td><td></td><td>1 person in this group declined an interview.</td><td>• Frequency and duration of use of TAI</td><td><u>Follow-up interviews</u>

Participants initially experienced problems with using the equipment properly, but gained confidence after a few attempts. One patient required additional telephone support from a nurse outside of their allocated outpatient appointment.

Most participants used TAI daily. The time required ranged from 30-45 minutes.

Patients who completed treatment often described TAI as “life changing”, and felt confident in their ability to pursue activities they had previously avoided, as their symptoms had resolved. These benefits extended to spouses, who had previously forfeited social activities.</td><td>1 person withdrew from treatment and they declined an interview.</td></tr>
<tr><td>Patel 2020

Study type: Retrospective case series

Location: US

Study period: January 2014 to January 2020

Follow-up: Median =</td><td>n=147

Children (aged 2-21 years; average age at initiation was 9 ± 4.6 years) with bowel dysfunction that had failed to respond to conservative management.

<u>Subgroups</u>

Neurogenic bowel</td><td>Intervention: TAI (Peristeen) n=147

Irrigation was recommended once daily, but allowed for adjustments.

A nurse specialist and a paediatric gastroenterologist provided initial training and supervision, with sessions typically</td><td>• Symptoms (stool frequency, incontinence, abdominal pain)
• NBDS scores
• Independence with bowel management
• Irrigation frequency
• Adverse events
• Satisfaction with treatment (score 0-</td><td><u>114/147 (77.6%) patients continued to use TAI at follow-up. 13 were lost to follow-up, and 20 discontinued use:</u>

<table><tr><th>Reasons for discontinuation</th><th>n (%)</th></tr><tr><td>Personal decision</td><td>8 (5.4%)</td></tr><tr><td>Pain with use of device</td><td>2 (1.4%)</td></tr><tr><td>Mechanical problems with catheter</td><td>2 (1.4%)</td></tr><tr><td>Surgical intervention</td><td>3 (2.0%)</td></tr><tr><td>Insurance issues</td><td>4 (2.7%)</td></tr><tr><td>Symptom improvement/resolution</td><td>1 (0.7%)</td></tr></table>
3 patients underwent surgical intervention after starting TAI. 1 did not like using Peristeen; 1 lost insurance coverage; both chose caecostomy. 1 had failure of both prior caecostomy and TAI, and elected for colectomy with diverting ileostomy.

Independence with bowel management</td><td>Follow-up duration varies.

NBDS scores were depicted graphically; precise numbers were not reported.</td></tr>
</table>

<table>
<tr><th>Study</th><th>Population</th><th>Intervention/ Comparator</th><th>Outcomes</th><th>Results</th><th>EAC Comments</th></tr>
<tr>
<td>3 months; mean = 4.5 months. Average duration of usage = 14.4 months.</td>
<td>dysfunction (NBD, n=85)
Refractory constipation (RC, n=43)
Anorectal malformations (ARM, n=19)</td>
<td>lasting 1 to 2 hours.
Follow-up appointments occurred at an average frequency of 4.6 ± 3.2 months.</td>
<td>10, with 10 being perfect satisfaction)
• Reasons for discontinuation</td>
<td>
<table>
<tr><th></th><th>n (%)</th><th>Mean age (years)</th></tr>
<tr><td>Achieved full independence</td><td>23/106 (22%)</td><td>14 ± 4.6</td></tr>
<tr><td>Required some assistance from caregiver</td><td>34/106 (32%)</td><td>10.2 ± 4.6</td></tr>
<tr><td>Required full assistance</td><td>49/106 (46%)</td><td>7 ± 4.5</td></tr>
</table>
<u>The majority of patients performed irrigation daily; 6 (4%) performed irrigations every other day.</u>

<u>Symptoms (n, %)</u>
<table>
<tr><th>Outcome</th><th>Baseline</th><th>Follow-up</th><th>p-value</th></tr>
<tr><td>Faecal incontinence</td><td>82 (96%) NBD;
31 (72%) RC;
18 (95%) ARM</td><td>10 (24%) NBD;
2 (5%) RC;
2 (11%) ARM</td><td><0.001
<0.001
≤0.001</td></tr>
<tr><td>Constipation</td><td>52 (61%) NBD;
43 (100%) RC;
12 (63%) ARM</td><td>7 (8%) NBD;
6 (14%) RC;
1 (5%) ARM</td><td><0.001
<0.001
<0.001</td></tr>
<tr><td>Abdominal pain</td><td>20 (24%) NBD;
25 (58%) RC;
6 (32%) ARM</td><td>4 (5%) NBD;
4 (9%) RC;
1 (5%) ARM</td><td><0.001
≤0.001
=0.219</td></tr>
</table>
In the NBD group, NBDS decreased, indicating improvement in bowel function with TAI use.

<u>Satisfaction with treatment</u>

Mean patient/caregiver satisfaction was rated 8.75 ± 1.97 overall.

<u>Adverse events</u>
</td>
<td></td>
</tr>
</table>

Study	Population	Intervention/ Comparator	Outcomes	Results	EAC Comments

	n (%)
Pain with insertion	3 (2%)
Abdominal cramping during irrigation	3 (2%)
Difficulty with catheter retention	3 (2%)
Perianal irritation	1 (0.7%)
Rectal prolapse (reduced with no recurrence)	1 (0.7%)
Colonic perforation	0 (0%)
Fluid/electrolyte abnormalities	0 (0%)
Mortality	0 (0%)

Abbreviations: ARM = anorectal malformation; LARS = low anterior resection syndrome; MMC = myelomeningocoele; MSKCC BFI = Memorial Sloan-Kettering Cancer Center Bowel Function Instrument; NBD = neurogenic bowel dysfunction; NBDS = neurogenic bowel dysfunction score; PTNS = posterior tibial nerve stimulation; RC = refractory constipation; SB = spina bifida; SF-36 = 36-item short form health survey; TAI = transanal irrigation; VAS = Visual Analogue Scale

Ongoing Studies

Study	Population	Intervention/Comparator	Inclusion Criteria	Outcomes	EAC Comments
Effect of Treatment of Low Anterior Resection Syndrome After Rectal Cancer Surgery Trial registration reference; NCT03215017 Design: RCT Location: Sweden	People with LARS after rectal cancer surgery Estimated sample size = 100 Interim analysis to be carried out after the first 40 participants.	**Intervention:** TAI (Peristeen) **Comparator:** Medication (One or a combination of Loperamide, Sorbitol, Sterculia gum)	Adults that have undergone surgery for rectal cancer (sphincter saving surgery, low anterior resection) with major LARS	After 1 year: • Bowel function (Cleveland incontinence questionnaire) • LARS score • Quality of life (EORTC QLQ-C30)	Last update posted August 2021 indicating a status of 'active, not recruiting'. Estimated study completion date is December 2022.
Characteristics of intestinal dysfunction in patients with multiple sclerosis. Effectiveness of the transanal irrigation procedure with the Peristeen device in the treatment of constipation and disease-related anal incontinence.	People with multiple sclerosis. Estimated sample size = 50	**Intervention:** TAI (Peristeen)	People with multiple sclerosis and severe intestinal dysfunction impairment (PAC QoL score ≥ 32).	After 2 years: • Incidence and prevalence of intestinal dysfunction (% people with a PACQoL score ≥ 32 for items B.1 to B.6 and/or a score ≤ 11 for item B.7 of the questionnaire) • % people with a slowed Intestinal	Last update posted October 2020 with a 'completed' recruitment status. This may refer to the selection phase of the study, in which the first 50 consecutive people with a PACQoL score ≥ 32 will be invited to

Study	Population	Intervention/Comparator	Inclusion Criteria	Outcomes	EAC Comments
Trial registration reference: NCT04599595 Design: Prospective cohort study Location: Italy				Transit Time (≥ 60 hours for females and 55 hours for men) Before and after TAI: • Composition of the intestinal microbiota	participate in the next phase. The microbiota profile is expected to be compared with that of a healthy population within the same geographical region.
Randomized Clinical Trial Assessing the Effect of Transanal Irrigation With Cone Catheter Versus Conservative Bowel Management on Symptoms of Low Anterior Resection Syndrome After Rectal Resection Trial registration reference; NCT04586634 Design: RCT	People with LARS after rectal cancer surgery Estimated sample size = 32	**Intervention:** TAI (Peristeen cone catheter) **Comparator:** Standard of care (conservative bowel management) - defined as supportive therapy according to the individual treatment protocols available at each participating site	Adults with LARS score ≥30 at least 3 months after rectal surgery, able to perform TAI using a cone catheter	After 12 weeks: • LARS score • FIQL (Faecal Incontinence Quality of Life) score • Quality of life (EQ-5D-5L) • Satisfaction with treatment • Adverse events	The cone catheter is a recent addition to the Peristeen Plus range; it was not assessed when developing either the original NICE guidance or as part of the current evidence review. Last update posted February 2022, indicating recruitment is complete. The company anticipates publication of results later this year (2022).

Study	Population	Intervention/Comparator	Inclusion Criteria	Outcomes	EAC Comments
Location: France					

Abbreviations: FIQL = Faecal Incontinence Quality of Life; LARS = low anterior resection syndrome; RCT = randomised clinical trial; TAI = transanal irrigation; VAS = Visual Analogue Scale

Appendix D – Literature search strategy

Conducted by NICE gIS

Database searches:

Databases*	**Date searched**	**No retrieved**	**Version/files**
MEDLINE (Ovid)	23/06/2021	124	1946 to June 22, 2021
MEDLINE In-Process (Ovid)	23/06/2021	15	1946 to June 22, 2021
MEDLINE ePub ahead of print (Ovid)	23/06/2021	7	June 22, 2021
EMBASE (Ovid)	23/06/2021	184	1974 to 2021 June 22
Embase conferences (Ovid)	23/06/2021	158	1974 to 2021 June 22
CDSR (Wiley)	23/06/2021	0	Issue 6 of 12, June 2021
CENTRAL (Wiley)	23/06/2021	78	Issue 6 of 12, June 2021
HTA database (INAHTA)	23/06/2021	0	n/a
HTA database (CRD)	23/06/2021	0	n/a
Total		566	
Total after de-duplication		428	

Search strategies

Database: Medline
Strategy used:

Ovid MEDLINE(R) <1996 to June 22, 2021>

1 Peristeen*.tw. 29
2 Coloplast.tw. 164
3 retrograde continence enema*.tw. 1
4 Therapeutic Irrigation/ 8260
5 ((transanal* or anal* or anus* or rectal* or rectum* or bowel* or therapeutic*) adj2 (irrigation* or evacuation*)).tw. 768
6 (douching* or lavage*).tw. 35242
7 or/2-6 42434
8 Constipation/ 10210
9 (constipation* or colonic inertia* or dyschezia*).tw. 17769
10 Fecal Incontinence/ 7400
11 ((fecal* or faecal* or feces* or faeces* or anal* or anus* or rectal* or rectum* or bowel* or intestin*) adj2 (incontinence* or soiling*)).tw. 6724
12 Neurogenic Bowel/ 151
13 (neuro* adj2 bowel*).tw. 453
14 Intestinal Diseases/ 8420
15 ((neuro* or non-neuro* or bowel* or intestin*) adj2 (dysfunct* or disorder*)).tw. 100162
16 Spinal Cord Injuries/ 29220
17 (spin* cord adj2 (injur* or contusion* or compressio* or laceration* or transection* or trauma*)).tw. 34368
18 ((post-traumatic* or traumatic*) adj2 myelopath*).tw. 63
19 or/8-18 172917
20 7 and 19 572
21 (NCT04815226 or NCT01784328 or NCT04586634 or NCT04599595 or NCT04246775 or NCT00286520 or NCT01059370 or NCT03215017 or NCT01313026 or ISRCTN18237643).af. 0
22 1 or 20 or 21 577
23 Animals/ not Humans/ 2630607
24 22 not 23 547
25 limit 24 to ed=20170301-20210623 124

Database: Medline in process

Strategy used:

Ovid MEDLINE(R) In-Process & In-Data-Review Citations <1946 to June 22, 2021>

1 Peristeen*.tw. 0
2 Coloplast.tw. 4
3 retrograde continence enema*.tw. 0
4 Therapeutic Irrigation/ 0
5 ((transanal* or anal* or anus* or rectal* or rectum* or bowel* or therapeutic*) adj2 (irrigation* or evacuation*)).tw. 25
6 (douching* or lavage*).tw. 763
7 or/2-6 792
8 Constipation/ 0
9 (constipation* or colonic inertia* or dyschezia*).tw. 618
10 Fecal Incontinence/ 0
11 ((fecal* or faecal* or feces* or faeces* or anal* or anus* or rectal* or rectum* or bowel* or intestin*) adj2 (incontinence* or soiling*)).tw. 225
12 Neurogenic Bowel/ 0
13 (neuro* adj2 bowel*).tw. 44
14 Intestinal Diseases/ 0
15 ((neuro* or non-neuro* or bowel* or intestin*) adj2 (dysfunct* or disorder*)).tw. 4879
16 Spinal Cord Injuries/ 0
17 (spin* cord adj2 (injur* or contusion* or compressio* or laceration* or transection* or trauma*)).tw. 1332
18 ((post-traumatic* or traumatic*) adj2 myelopath*).tw. 0
19 or/8-18 6902
20 7 and 19 15
21 (NCT04815226 or NCT01784328 or NCT04586634 or NCT04599595 or NCT04246775 or NCT00286520 or NCT01059370 or NCT03215017 or NCT01313026 or ISRCTN18237643).af. 0

22 1 or 20 or 21 15
23 Animals/ not Humans/ 0
24 22 not 23 15

Database: MEDLINE ePub ahead of print

Strategy used:

Ovid MEDLINE(R) Epub Ahead of Print <June 22, 2021>

1 Peristeen*.tw. 0
2 Coloplast.tw. 7
3 retrograde continence enema*.tw. 0
4 Therapeutic Irrigation/ 0
5 ((transanal* or anal* or anus* or rectal* or rectum* or bowel* or therapeutic*) adj2 (irrigation* or evacuation*)).tw. 19
6 (douching* or lavage*).tw. 396
7 or/2-6 421
8 Constipation/ 0
9 (constipation* or colonic inertia* or dyschezia*).tw. 510
10 Fecal Incontinence/ 0
11 ((fecal* or faecal* or feces* or faeces* or anal* or anus* or rectal* or rectum* or bowel* or intestin*) adj2 (incontinence* or soiling*)).tw. 165
12 Neurogenic Bowel/ 0
13 (neuro* adj2 bowel*).tw. 26
14 Intestinal Diseases/ 0
15 ((neuro* or non-neuro* or bowel* or intestin*) adj2 (dysfunct* or disorder*)).tw. 2887
16 Spinal Cord Injuries/ 0
17 (spin* cord adj2 (injur* or contusion* or compressio* or laceration* or transection* or trauma*)).tw. 954
18 ((post-traumatic* or traumatic*) adj2 myelopath*).tw. 1

19 or/8-18 4409
20 7 and 19 7
21 (NCT04815226 or NCT01784328 or NCT04586634 or NCT04599595 or NCT04246775 or NCT00286520 or NCT01059370 or NCT03215017 or NCT01313026 or ISRCTN18237643).af. 0
22 1 or 20 or 21 7
23 Animals/ not Humans/ 0
24 22 not 23 7

Database: EMBASE

Strategy used:

Embase <1974 to 2021 June 22>

1 Peristeen*.tw,dv. 86
2 Coloplast.tw,dm. 1172
3 retrograde continence enema*.tw. 1
4 lavage/ 15912
5 ((transanal* or anal* or anus* or rectal* or rectum* or bowel* or therapeutic*) adj2 (irrigation* or evacuation*)).tw. 1697
6 (douching* or lavage*).tw. 74852
7 or/2-6 86076
8 constipation/ or chronic constipation/ 96272
9 (constipation* or colonic inertia* or dyschezia*).tw. 45926
10 feces incontinence/ 21701
11 ((fecal* or faecal* or feces* or faeces* or anal* or anus* or rectal* or rectum* or bowel* or intestin*) adj2 (incontinence* or soiling*)).tw. 14973
12 neurogenic bowel/ 806
13 (neuro* adj2 bowel*).tw. 1093
14 enteropathy/ 18379

15 ((neuro* or non-neuro* or bowel* or intestin*) adj2 (dysfunct* or disorder*)).tw. 186986
16 spinal cord injury/ 57611
17 (spin* cord adj2 (injur* or contusion* or compressio* or laceration* or transection* or trauma*)).tw. 63664
18 ((post-traumatic* or traumatic*) adj2 myelopath*).tw. 143
19 or/8-18 396454
20 7 and 19 1230
21 (NCT04815226 or NCT01784328 or NCT04586634 or NCT04599595 or NCT04246775 or NCT00286520 or NCT01059370 or NCT03215017 or NCT01313026 or ISRCTN18237643).af. 1
22 1 or 20 or 21 1247
23 Nonhuman/ not Human/ 4826277
24 22 not 23 1210
25 limit 24 to dc=20170301-20210623 342
26 limit 25 to (conference abstract or conference paper or "conference review") 158
27 25 not 26 184

Database: CDSR and CENTRAL

Strategy used:

#1 Peristeen*:ti,ab,kw 5
#2 Coloplast:ti,ab,kw 74
#3 retrograde continence enema*:ti,ab,kw 0
#4 MeSH descriptor: [Therapeutic Irrigation] explode all trees 2337
#5 ((transanal* or anal* or anus* or rectal* or rectum* or bowel* or therapeutic*) near/2 (irrigation* or evacuation*)):ti,ab,kw 1569
#6 (douching* or lavage*):ti,ab,kw 4209
#7 {or #2-#6} 5441
#8 MeSH descriptor: [Constipation] explode all trees 1779
#9 (constipation* or colonic inertia* or dyschezia*):ti,ab,kw 13095
#10 MeSH descriptor: [Fecal Incontinence] explode all trees 507

#11 ((fecal* or faecal* or feces* or faeces* or anal* or anus* or rectal* or rectum* or bowel* or intestin*) near/2 (incontinence* or soiling*)):ti,ab,kw 1989
#12 MeSH descriptor: [Neurogenic Bowel] explode all trees 19
#13 (neuro* near/2 bowel*):ti,ab,kw 69
#14 MeSH descriptor: [Intestinal Diseases] explode all trees 22920
#15 ((neuro* or non-neuro* or bowel* or intestin*) near/2 (dysfunct* or disorder*)):ti,ab,kw 7441
#16 MeSH descriptor: [Spinal Cord Injuries] explode all trees 1744
#17 (spin* cord near/2 (injur* or contusion* or compressio* or laceration* or transection* or trauma*)):ti,ab,kw 4003
#18 ((post-traumatic* or traumatic*) near/2 myelopath*):ti,ab,kw 2
#19 {or #8-#18} 47021
#20 #7 and #19 349
#21 (NCT04815226 or NCT01784328 or NCT04586634 or NCT04599595 or NCT04246775 or NCT00286520 or NCT01059370 or NCT03215017 or NCT01313026 or ISRCTN18237643):ti,ab,kw 0
#22 #1 or #20 or #21 with Publication Year from 2017 to 2021, with Cochrane Library publication date Between Mar 2017 and Jun 2021, in Trials 78

Database: HTA database (INAHTA)

Strategy used:

Note: The 5 results retrieved where pre 2017 so therefore not downloaded to EPPI.

	Line	Query	Hits
☐	22	#21 OR #20 OR #1	5

☐	21	(NCT04815226) OR (NCT01784328) OR (NCT04586634) OR (NCT04599595) OR (NCT04246775) OR (NCT00286520) OR (NCT01059370) OR (NCT03215017) OR (NCT01313026) OR (ISRCTN18237643)	0
☐	20	#19 AND #7	5
☐	19	#18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8	1044
☐	18	(post-traumatic* or traumatic*)	596
☐	17	(spin* cord) AND (injur* or contusion* or compressio* or laceration* or transection* or trauma*)	48
☐	16	"Spinal Cord Injuries"[mh]	17
☐	15	(neuro* or non-neuro* or bowel* or intestin*) AND (dysfunct* or disorder*)	302
☐	14	"Intestinal Diseases"[mh]	17
☐	13	(neuro*) AND (bowel*)	6
☐	12	"Neurogenic Bowel"[mh]	0
☐	11	(fecal* or faecal* or feces* or faeces* or anal* or anus* or rectal* or rectum* or bowel* or intestin*) AND (incontinence* or soiling*)	70
☐	10	"Fecal Incontinence"[mh]	35
☐	9	(constipation* or colonic inertia* or dyschezia*)	62
☐	8	"Constipation"[mh]	25
☐	7	#6 OR #5 OR #4 OR #3 OR #2	25
☐	6	(douching* or lavage*)	18
☐	5	(transanal* or anal* or anus* or rectal* or rectum* or bowel* or therapeutic*) AND (irrigation* or evacuation*)	7
☐	4	"Therapeutic Irrigation"[mh]	2

☐	3	(retrograde continence enema*)	0
☐	2	(Coloplast)	1
☐	1	(Peristeen*)	1

Database: HTA database (HTA)

Strategy used:

Line	Search	Hits		
☐	1	(Peristeen)	1	Delete
☐	2	(Coloplast)	6	Delete
☐	3	(retrograde continence enema*)	0	Delete
☐	4	MeSH DESCRIPTOR Therapeutic Irrigation EXPLODE ALL TREES	111	Delete
☐	5	(transanal* or anal* or anus* or rectal* or rectum* or bowel* or therapeutic*) AND (irrigation* or evacuation*)	171	Delete
☐	6	(douching* or lavage*)	122	Delete

	7	#2 OR #3 OR #4 OR #5 OR #6	285	Delete
	8	MeSH DESCRIPTOR Constipation EXPLODE ALL TREES	130	Delete
	9	(constipation* or colonic inertia* or dyschezia*)	345	Delete
	10	MeSH DESCRIPTOR Fecal Incontinence EXPLODE ALL TREES	107	Delete
	11	(fecal* or faecal* or feces* or faeces* or anal* or anus* or rectal* or rectum* or bowel* or intestin*) AND (incontinence* or soiling*)	513	Delete
	12	MeSH DESCRIPTOR Neurogenic Bowel EXPLODE ALL TREES	2	Delete
	13	(neuro*) AND (bowel*)	41	Delete
	14	MeSH DESCRIPTOR Intestinal Diseases EXPLODE ALL TREES	2960	Delete
	15	(neuro* or non-neuro* or bowel* or intestin*) AND (dysfunct* or disorder*)	1496	Delete
	16	MeSH DESCRIPTOR Spinal Cord Injuries EXPLODE ALL TREES	160	Delete
	17	(spin* cord) AND (injur* or contusion* or compressio* or laceration* or transection* or trauma*)	290	Delete
	18	(post-traumatic* or traumatic*) AND (myelopath*)	2	Delete
	19	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18	5265	Delete
	20	#7 AND #19	46	Delete

☐	21	(NCT04815226 or NCT01784328 or NCT04586634 or NCT04599595 or NCT04246775 or NCT00286520 or NCT01059370 or NCT03215017 or NCT01313026 or ISRCTN18237643)	0	Delete
☐	22	#1 OR #20 OR #21	46	Delete
☐	23	* FROM 2017 TO 2021	506	Delete
☐	24	#22 AND #23	0	Delete

Notes:

Record any important decisions on how the strategy was developed.

DARE (CRD) has not been searched as a date limit was required from 2017 and no new records/commentaries have been added to DARE since January 2015.

Appendix E – References

Alhazmi H, Trbay M, Alqarni N, et al. (2019) Long-term results using a transanal irrigation system (Peristeen R) for treatment of stool incontinence in children with myelomeningocele. Journal of Pediatric Urology 15:34.e31-34.e35 doi:10.1016/j.jpurol.2018.08.013

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