Common format for Evidence Table – Treatment Primary studies

Headings	Description
I Study ID	
1. Reference	First author; Journal name; Publication Date;
II Method	
1. Study design	Specify the type of study: RCT, CCT, case control, case series
2. Source of funding/conflicts of interest	Specify the source of funding: public research funds, government, not governmental organization, healthcare industry or other (give name of organization or corporation) presence of declaration of interest.
3. Setting	Numbers of centers, countries involved, healthcare setting, urban/rural/mixed.
4. Sample size	Give the calculated number in each group and the actual number of patients in each group.
5. Duration of the Study	Duration in months or years.
III Patient characteristics	
1. Eligibility criteria	State the most relevant inclusion and exclusion criteria for population (patients and pathology).
2. Patient characteristics	Specify a priori characteristics (age, tumor, stage).
3. Group comparability	p for group comparability.
IV Intervention(s)	
1. Intervention(s)	Precise details of the interventions for each group (including dose, length, regimen and timing if relevant).
2. Comparator(s)	Placebo, other treatment (including dose, length, regimen and timing if relevant).
V Results primary outcome	
1. Effect size primary outcome	Summary of the primary outcome in each and between groups: effect size and its precision (p value, CI) Including efficacy: Absolute risk reduction, relative risk (reduction), odds ratios, confidence intervals.
VI Results secondary and all other outcomes	
1. Effect size secondary outcome(s)	Brief description of secondary outcome(s) and p values.
2. Effect size all other outcomes, endpoints	All other outcomes, endpoints, including adverse effects, toxicity, quality of life
VII Critical appraisal of study quality	
1.Level of evidence	Classification of intervention studies.
2. Dropouts	Number of dropouts/withdrawals in each group
3. Results critical appraisal	Summarize internal validity: sample size, randomization and blinding, use of inappropriate statistical analysis, etc

KEY QUESTION 4A

Assessment table relative importance patient important outcomes

Patient-important outcomes	Mean rating	Relative importance
Quality of life	7	Critical

As rated by 5 guideline panel members, none of whom were patients

1.1.1.1 Evidence table observational studies biofeedback therapy

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality

Bartlett 2011	• Observational study
	• Support: James Cook University Program Grant; Cancer Council, Queensland ; CoI: not reported
	• Setting: Australia
	• Sample size: N= 19
	• Duration: July 2003-July 2006
	• Follow-up: post-intervention, 2.4 years
		• Inclusion: patients with symptoms including frequency, urgency, faecal incontinence, incomplete evacuation, failure to respond to dietary, medication or standard pelvic floor exercises (≥6 months) after surgery for colorectal cancer, referred for incontinence treatment
		• Exclusion:
		• Patient characteristics:
		  • Male: 53%
		  • Mean age: 64.1 years
		  • Anterior resection: 3; ultra-low anterior resection : 10; segmental colectomy: 2; and proctocolectomy: 4
		  • Median duration post-surgery: 18 months
			Biofeedback therapy + coping strategy and dietary advice
			
			2 to 4 weekly sessions with suggested coping strategies, including timing and dosage of anti-diarrheal medications; defecation delay strategies; clean-up kits; continence aids/products; access to toilet maps. The therapist also gave dietary advice including the impact of fat, fiber, alcohol, caffeine, chocolate, spicy foods, drinks with a low pH and some chemical additives, as well as avoiding rapidly drinking large volumes of hot or cold fluid, especially with meals, together with possible use of cholestyramine and
				Median FIQL scores before and post-intervention (IQR):
				• Lifestyle: 2.8 (2.1–3.7) and 3.5 (3.0–4.0) (p=0.001)
				• Coping: 2.1 (1.7–3.0) and 2.9 (2.3–3.5) (p=0.001)
				• Depression: 3.4 (2.6–3.7) and 3.3 (3.0–3.6) (p=0.828)
				• Embarrassment: 3.0 (1.7–3.0) and 3.3 (2.7–4.0) (p=0.001)
				
				Median Wexner continence scores before and post-intervention (IQR):
				• Total score: 9.0 (7.0–12.0) and 6.0 (3.0–8.0) (p=0.001)
				• Solid and liquid faecal incontinence score (max 8): 4.0 (1.0–5.0) and 2.0 (1.0–3.0) (p=0.001)
				• Flatus score (max 4): 3.0 (1.0–4.0) and 0.0 (0.0–3.0) (p=0.017)
				
				Median incontinent episodes before and post-intervention (IQR): 1.0 (0.0–6.5) and 0.5 (0.0–3.0) (P=0.183)
					Adverse events not reported on	• No control group
						• 12/19 patients provided data at a follow-up of 2.4 years on average. Not reported on what happened to the other 7 patients

			supplements; relaxation breathing; evacuation techniques; anal and pelvic floor muscle exercises using computerized visual feedback; followed by 4 weeks home therapy	Median subjective measure of patient´s bowel control before and post-intervention (IQR): 3.3 (1.3–5) and 7.3 (6–8.8) (p=0.006) Median FIQL scores before and at 2.4 years (IQR): • Lifestyle: 2.8 (2.1–3.7) and 3.3 • Coping: 2.1 (1.7–3.0) and 3.8 • Depression: 3.4 (2.6–3.7) and 3.6 • Embarrassment: 3.0 (1.7–3.0) and 3.7 Median total Wexner continence scores before and at 2.4 years (IQR): 9.0 (7.0–12.0) and 7.0		
Ho 1997	• Observational study • Support: not reported on; CoI: not reported on • Setting: single centre, Singapore • Sample size: N= 6 • Duration: not reported • Follow-up: post-intervention, mean 12.9 months	• Inclusion: faecal incontinence after low anterior resection, not responding to medication; ≥ 6 months after surgery • Exclusion: not reported • Patient characteristics: not reported for six incontinent patients	Biofeedback therapy 4 Sessions of outpatient therapy	Weekly incontinent episodes before and post-intervention (SE): 14.8 (2.1) to 1.8 (0.8) (p<0.05) Number of patients needing anti-diarrheal drugs before and post-intervention: 6 to 0 (p<0.05) Number of patients needing pads before and post-intervention: 5 to 0 (p<0.05)	At a mean follow-up of 12 months there were no complications and no regressions from treatment (unspecified)	• No control group • Study reported on 11 patients of whom 6 had faecal incontinence and 5 had intractable constipation; data for incontinent patients extracted here • 10/11 patients had low anterior resection for rectal cancer; 1/11 patients had low anterior resection for severe radiation proctolitis following radiation for cervical carcinoma. Not reported whether this last patient had incontinence or constipation • 2/11 patients underwent post-operative adjuvant radiotherapy • Unclear what the source population was
Kim 2011	• Observational study • Support: not reported on; CoI: not reported • Setting: single centre,	• Inclusion: patients with intractable faecal incontinence after sphincter-saving surgery for rectal cancer; had normal	Biofeedback therapy Once weekly for 10 weeks	Mean Wexner continence scores before and post-intervention (SD): 13.6 (5.0) to 8.7 (6.0) (p<0.001)	Adverse events not reported on	• Retrospective study without a control group • Out of the larger series of 70 patients, 83% had

	South Korea
	• Sample size: N= 58 (with faecal incontinence out of a series of 70)
	• Duration: January 2003-December 2008
	• Follow-up: post-intervention
		sphincter tone measured by anorectal manometry
		• Exclusion: diverting stoma at the time of biofeedback therapy; evidence of local recurrence or distant metastasis in follow-up colonoscopy, CT or MRI; anal sphincter injury detected by preoperative transrectal ultrasonography analysis; had no other co-morbidities that might alter sensory and motor responses, such as collagen vascular and connective tissue disorders, or neurologic disorders
		• Patient characteristics of all 70 patients:
		  • Male: 70%
		  • Mean age: 58.1 years
		  • 49/70 patients had had radiotherapy
				Number bowel movements/day before and post-intervention (SD): 10.1 (4.4) to 6.3 (3.4) (p<0.001)		faecal incontinence as primary symptom, for whom data were extracted here; 11% had difficult evacuation and 6% frequent defecation
						• No follow-up data available

Abbreviations: FIQL: faecal incontinence quality of life; IQR: inter-quartile range; SE: standard error

1.1.1.2 Grade table 4a biofeedback therapy

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Biofeedback**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
Quality of life: FIQL and Wexner scores post-intervention												
1 (Bartlett 2011) (Kim 2011)	Observational study	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision	No other considerations	19 58	0 0	- -	Significant improvements in FIQL subscales lifestyle, coping and embarrassment. Significant improvement in mean Wexner score Significant improvement in mean Wexner score	Very low ⊕OOO	Critical
Quality of life: incontinent episodes before and post-intervention												
1 (Bartlett 2011)	Observational study	Serious risk of bias[1]	Serious inconsistency [2]	No serious indirectness	Serious imprecision [3]	No other considerations	19 6	0 0	- -	Median (IQR): 1.0 (0.0–6.5) and 0.5 (0.0–3.0) (p=0.183)	Very low ⊕OOO	Critical

(Ho 1997)										Weekly (SE): 14.8 (2.1) to 1.8 (0.8) (p<0.05)		
Overall quality of evidence: very low												

Abbreviations: FIQL: faecal incontinence quality of life; IQR: inter-quartile range; SE: standard error
[1] Uncontrolled studies
[2] One study reporting significant difference; one study reporting non-significant difference
[3] Fragility of results due to very small studies

1.1.1.3 Evidence table studies multimodal rehabilitation

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality
Allgayer 2005	• Observational study • Support: not reported; CoI: not reported • Setting: single centre, Germany • Sample size: N= 95 • Duration: June 2001-January 2004 • Follow-up: post-intervention, 1 year	• Inclusion: patients admitted for faecal incontinence after low anterior surgery for colorectal cancer; UICC II/III tumour stage; macroscopically and histologically tumour-free resection margins; normal laboratory tests including carcinoembryonic antigen and a normal abdominal ultrasound/CT on admission • Exclusion: impaired general health conditions (Karnofsky index <80); age >75 years; a second malignancy or other relevant adverse clinical conditions such as advanced heart failure (NYHA III/IV), pulmonary diseases, metabolic diseases,	Multimodal inpatient programme Three weeks of intensive in-hospital programme: daily pelvic floor exercise under supervision for 30-40 minutes; information, psychological support, light aerobic exercise; daily 1-hour biofeedback training sessions After discharge from the rehabilitation unit, patients were asked to continue combined sphincter training therapy daily for one hour	Mean MCIS before and post-intervention (SD): • irradiated patients: 7.49 (2.2) to 9.49 (2.7) (p<0.0001) • non-irradiated patients: 8.79 (2.7) to 11.49 (2.5) (p<0.0001) Mean MCIS before and 1 year after intervention (SD): • irradiated patients: 7.49 (2.2) to 8.29 (3.8) (p<0.0001) • non-irradiated patients: (2.7) to 10.79 (4.4) (p<0.0001) Nine patients had treatment failure at post-intervention; 14 patients had treatment failure at 1 year follow-up. When the MCIS remained at <6.0 points (corresponding to complete incontinence) after 3 weeks, short-term	Irradiated patients presented with a significantly higher degree of faecal incontinence (lower MCIS incontinence score) compared to non-irradiated patients: 7.49 (2.2) vs. 8.79 (2.7) points (p<0.001). Rectosigmoidal inflammation was more frequent in irradiated than non-irradiated patients (26.9% versus 9.3%) (p<0.03). Sphincter pressure, sensation/pain threshold and the recto anal inhibitory reflex were similar in both groups In patients with short-term treatment failure (16.6%) anal EUS revealed structural defects of the external sphincter in four patients	• No control group • Results not reported for the overall group of patients, only for irradiated and non-irradiated patients separately • Study on inpatients admitted for faecal incontinence • 71 patients provided 1 year follow-up data

		neurologic diseases and/or language barriers
		• Patient characteristics irradiated patients (n=41):
		  • Male: 68%
		  • Mean age: 58.5 years
		• Patient characteristics non-irradiated patients (n=54):
		  • Male: 61%
		  • Mean age: 67.0 years
				treatment failure was assumed, when this score reached <6.0 points after 1 year, long-term treatment failure was assumed	Patients receiving treatment with loperamide had a slightly inferior training effect than those not taking loperamide
					
					Adverse events not reported on	

Laforest 2012	• Matched case-control study
	• Support: not reported; CoI: not reported
	• Setting: single centre, France
	• Sample size: N= 22 cases, 24 controls
	• Duration: March 2007-February 2009
	• Follow-up: mean 21.2 months
		• Inclusion: patients undergoing a total mesenteric excision with low colorectal or coloanal anastomosis for rectal cancer, no previous history of faecal incontinence, with an anastomosis located at or below 30 mm from the dentate line, and who lived near Beaujon Hospital
		• Exclusion: not reported
		• Patient characteristics:
		  • Male: 50%
		  • Mean age: 55 years
			Biofeedback + pelvic floor exercises vs. no such training
			
			15 Weekly one-hour sessions with a specialised physiotherapist
				Mean Wexner incontinence scores post rehabilitation: 8.3 (range: 2–14) vs. 9.9 (range: 5–17) (p=0.10)
				
				Kirwan incontinence classification post rehabilitation: 18/22 cases and 21/24 controls had some form of continence (p=1.00)
				
				Stool frequency/24 hours: 2.6 (range: 1–6) vs. 4.0 (range: 1–10) (p=0.025)
				
				SF-36: cases scores significantly better on 2/10 SF-36 subscales (vitality and mental functioning subscales)
				
				FIQL: cases scored significantly better on 1/4 FIQL subscales (depression/self perception subscale)
					-	• Not described why cases entered the training programme and controls did not
						• Each patient from the rehabilitation group was manually matched according to the following criteria: age, sex, tumour stage, tumour height from the anal verge, preoperative treatment and postoperative septic complications (anastomotic leakage, pelvic abscess, reoperation)
						• Pre-rehabilitation incontinence scores not reported: were cases and controls comparable?

Pucciani 2008	• Observational study • Support: not reported; CoI: not reported	• Inclusion: faecal incontinence after sphincter saving	Multimodal rehabilitation programme, with a	Mean Wexner incontinence scores (SD) before and after	Adverse events not reported on	• No control group • Consecutive patients • All patients underwent anorectal

	• Setting: single centre, Italy
	• Sample size: N= 88 (69 low anterior resection)
	• Duration: January 2000-June 2007
	• Follow-up: post-intervention
		operations
		• Exclusion: age >75 years, impaired general health status, neurologic disease, physical handicap, general problems (language, distance from the outpatient unit, non-collaboration)
		• Patient characteristics:
		  • Male: 39%
		  • Mean age: 59.6 years
		  • 53 patients were irradiated; 19 had had neoadjuvant radiotherapy
		  • Mean time from operation to presentation: 22.4 months
			combination of:
			• Pelviperineal kinesitherapy: twice weekly in 7 outpatient sessions
			• Biofeedback: customised number of sessions, twice daily for 20 minutes, 1 month long, at home
			• Volumetric rehabilitation: twice daily administration of a tepid water enema, at home
			• Electrostimulation: 3 months of electrostimulation at home
				intervention: 12.28 (5.29) to 4.87 (3.91) (p<0.03)
				• In patients with a low anterior resection: 11.8 (5.09) to 6.4 (3.71) (p<0.05)
				• In patients with a colorectal anastomosis: 12.52 (4.45) to 5.81 (3.6) (p<0.02)
				
				29 Patients (33%) were included as Class I (good results); 21 (24%) patients were symptom-free; 37 (42%) were included as Class III (bad results); these patients had a post-intervention Wexner incontinence score that was not significantly different from their pre-intervention score
						manometry; anal endosonography was used when necessary (open anus, previous anal surgery, adjuvant or neoadjuvant radiotherapy) to identify sphincteric traumatic lesions or scars. 16 Patients had a preliminary neurophysiologic study of the anus (sphincteric EMG, latency of sacral reflex, motor and sensorial evoked potentials) to exclude neurologic diseases
						• 12 Patients underwent all 4 rehabilitative procedures; 41 used three techniques and 35 patients were treated using only biofeedback and volumetric rehabilitation. The mean length of the rehabilitation cycle was 121±34 days
						• Only 66 patients were reported on
						• No follow-up post-intervention

Abbreviations: CoI: conflicts of interest; FIQL: faecal incontinence quality of life; MCIS: Modified Cleveland Incontinence Score; ns: not significant; SD: standard deviation

1.1.1.4 Grade table 4a multimodal rehabilitation

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Multimodal rehabilitation**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
Faecal incontinence quality of life post-intervention												
1 (Allgaye r 2005; Laforest 2012, Puccian i 2008)	1 Matched case-control study, 2 observational studies	Serious risk of bias [1]	Serious inconsistency [2]	No serious indirectness	No serious imprecision	No other considerations	95 22 88	0 24 0	- - -	Mean faecal incontinence quality of life scores improved significantly Wexner incontinence score and Kirwan classification did not differ significantly post-rehabilitation	Very low ⊕OOO	Critical

										21 (24%) patients were symptom-free; 37 (42%) were included as Class III (bad results)		
Overall quality of evidence: very low												

[1] Two uncontrolled studies; 1 matched case-control study with no matching according to outcomes of interest
[2] The uncontrolled studies found an improvement in the treated groups; the matched case-controlled study did not find a significant difference between cases and controls

1.1.1.5 Evidence table observational studies oral diazepam

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality
Maeda 2002	• Observational study • Support: not reported; CoI: not reported • Setting: single centre, Japan • Sample size: N= 5 • Duration: not reported • Follow-up: 3 months	• Inclusion: patients with persistent incontinence after low anterior resection for rectal cancer, not responding to traditional measures including bulk agents and high fiber diet, sphincter exercises and anti diarrheal drugs • Exclusion: • Patient characteristics: • 0% women • Median age: 64 years • 9-90 months post-surgery • None of the patients had had radiation or chemoradiation	Oral diazepam 2 mg/day	Median Cleveland Clinic's continence grading scale (range): 14 (9–16) to 0 (0–12) Continence grading system of Kirwan et and Miller: before diazepam 1 patient with major soiling (grade IV) and 4 patients with minor soiling (grade III). After diazepam, 3 of the 4 grade III patients improved to perfect continence (grade I), the fourth had no change in grade of continence. The patient with grade IV continence improved to grade III	Adverse events not reported on Three patients were always incontinent, one patient was usually incontinent (once per week) and the other patient was sometimes incontinent (once every two weeks) for liquid stool and gas before treatment. Incontinence disappeared in 3 cases after medication. In 2 patients frequency of incontinence for liquid stool and gas decreased from daily to weekly after taking diazepam. While all patients needed to wear a pad night and day before medication, this was the case in only 2 patients after medication. These 2 patients used it only usually or mainly at night for their own security. Lifestyle alteration was always needed in 1 case, sometimes needed in 3 cases and rarely needed in 1 case before treatment. Lifestyle alteration was not need in 3 cases and improved from always to usually in 1 case after medication. Lifestyle did not change in 1 patient, who sometimes needed alteration after medication	• No control group • Unclear what the source population was

Abbreviations: CoI: conflicts of interest

1.1.1.6 Grade table 4a oral diazepam

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Oral diazepam**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
Faecal incontinence related quality of life												
1 (Maeda 2002)	Observational study	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision [2]	No other considerations	5	0	-	Median Cleveland Clinic's continence grading scale (range): 14 (9–16) to 0 (0–12)	Very low ⊕OOO	Critical
Overall quality of evidence: very low												

[1] No control group
[2] Small study (n=5)

1.1.1.7 Evidence table randomised controlled trials phenylephrine

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality
Park 2007	• RCT • Support: not reported; CoI: not reported • Setting: single centre, South Korea • Sample size: N= 35 • Duration: not reported • Follow-up: post-intervention	• Inclusion: patients with anal incontinence after low anterior resection for rectal cancer; symptom duration ≥ 6 m; circumferentially intact sphincter documented on endosonography • Exclusion: pregnancy, ischemic heart disease, uncontrolled hypertension, aortic aneurysm, treatment with monoamine oxidase inhibitors or tricyclic antidepressants, surgically reparable external sphincter injury, inflammatory bowel disease, any other disorder known to cause secondary anal incontinence • Patient characteristics: all experienced the failure of other treatments with anti diarrheal agents or biofeedback; all patients underwent straight type reconstruction, without any pouch after resection • 37% women • Mean age: 60 years	30% phenylephrine vs. placebo gel, applied topically to the anal margin twice daily for 4 weeks	Mean FISI score (SD) post-intervention: 32.3 (14.7) vs. 32.4 (14.4) Mean FIQL scores (SD) post-intervention: • Lifestyle: 2.9 (1.0) vs. 3.0 (0.8) • Coping: 2.8 (0.9) vs. 2.8 (0.5) • Depression: 3.2 (0.8) vs. 3.2 (0.5) • Embarrassment: 3.0 (0.7) vs. 2.6 (0.8) Subjective improvement: 29.4 vs. 33.3% (p=0.57)	Five patients of the phenylephrine group experienced a localized dermatitis consisting of erythema, heat sensation, and pruritis. This dermatitis resolved soon after withdrawal of the drug for 2–3 days. One patient developed dermatitis in response to the placebo gel. Two patients on phenylephrine treatment experienced mild headache, but this did not recur after the dose of phenylephrine drug was reduced. In total, 7 (41.2%) of 17 phenylephrine-treated patients experienced side effects compared with 3 (16.7%) of 12 placebo-treated patients (not statistically significant)	• Computer-generated sequence generation • Adequate allocation concealment procedure, though patients may have guessed allocation as some developed a localised dermatitis • Similar patient characteristics in each group • Six patients were excluded from the analysis because of poor compliance (2 vs. 4 patients)

Abbreviations: CoI: conflicts of interest; FIQL: faecal incontinence quality of life; FISI: faecal incontinence severity index; RCT: randomised controlled trial; SD: standard deviation

1.1.1.8 Grade table 4a topical phenylephrine

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Phenylephrine**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
Faecal incontinence related quality of life												
1 (Park 2007)	RCT	Serious bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision [2]	No other considerations	19	16	-	No differences between groups in FISI or FIQL scores or subjective improvement	Low ⊕⊕OO	Critical
Overall quality of evidence: low												

Abbreviations: FIQL: faecal incontinence quality of life; FISI: faecal incontinence severity index
[1] Allocation concealment was adequate, but patients may have guessed allocation as 5 vs. 1 patients experienced a localized dermatitis. 2 vs. 4 patients were excluded from analyses because of poor compliance
[2] Small study

1.1.1.9 Evidence table observational studies postanal sphincter repair

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality
Ho 2001	• Case report • Support: not reported; CoI: not reported • Setting: single centre, Singapore • Sample size: N= 3 • Duration: August 1994-April 1996 • Follow-up: mean 3.2 years	• Inclusion: 3 patients with intractable faecal incontinence after ultralow anterior resection for rectal cancer; endoanal ultrasound detected internal sphincter defects; no improvement ≥18 months despite anti diarrhoeal medication and biofeedback treatment • Exclusion: not reported • Patient characteristics: • 2 males, 1 female • Mean age 75.7 years • None received radiation therapy because all cancers	Postanal sphincter repair	Mean stool frequency/day from pre-intervention to follow-up (SD): 5.7 (1.3) to 1.7 (0.3) Incontinence score change from pre-intervention to follow-up: 13.7 (2.2) to 1.3 (0.2) 2 Patients became fully continent; 1 patient was incontinent with regard to gas once a month Perineal pads, anti diarrheal treatment or biofeedback exercises were not required	Adverse events not reported on	• Description of three cases, no control group • Unclear what the source population was

		were early				

Abbreviations: CoI: conflicts of interest; SD: standard deviation

1.1.1.10 Grade table 4a postanal sphincter repair

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Postanal sphincter repair**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
Faecal incontinence at a mean of 3.2 years post-intervention												
1 (Ho 2001)	Case study	Very serious risk of bias [1]	No serious inconsistency	No serious indirectness	Very serious imprecision [2]	No other considerations	3	0	-	2 Patients became fully continent; 1 patient was incontinent with regard to gas once a month	Very low ⊕OOO	Critical
Overall quality of evidence: very low												

[1] Uncontrolled study, single case out of a larger series
[2] Description of three cases

1.1.1.11 Evidence table observational studies retrograde colonic irrigation

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality
Koch 2009	• Observational study • Support: not reported; CoI: not reported • Setting: single centre, the Netherlands • Sample size: N= 26 • Duration: 2005-2008 • Follow-up: mean 1.6 years	• Inclusion: faecal incontinence after a low anterior resection for a rectal carcinoma • Exclusion: not reported • Patient characteristics: • 81% male • Mean age 67.6 years • Mean start with irrigation after low anterior resection: 3.1 years	Retrograde colonic irrigation	12/26 patients (46%) became completely (pseudo)continent; 3/26 patients (12%) were incontinent for flatus; and 6/26 patients (23%) were still incontinent for liquid stool All used pads or a small inlay. 3 Patients used loperamide on occasion	16/26 patients experienced side effects: abdominal cramps 7 patients; 6 leakage after irrigation; 2 too time-consuming; 8 other side effects such as pain on insertion or nausea. Five patients had stopped the treatment due to side effects (irrigation was found to be too time-consuming, not practical or painful).	• No control group • Retrospective data collection of a consecutive series of 30 patients, of which 3 patients had died and 1 patient had cognitive disordered and were excluded. Thus, 26 patients were analysed

Abbreviations: CoI: conflicts of interest

1.1.1.12 Grade table 4a retrograde colonic irrigation

Quality assessment	No of patients	Effect (95%CI)		

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Retrograde colonic irrigation	Placebo	Relative	Absolute	Quality	Importance
(Pseudo)continence												
1 (Koch 2009)	Observational study	Serious risk of bias [1]	No serious inconsistency	No serious indirectness	No serious imprecision	No other considerations	26	0	-	46% of patients became completely (pseudo) continent	Very low ⊕OOO	Critical
Overall quality of evidence: very low												

[1] Uncontrolled study

1.1.1.13 Evidence table observational studies sacral stimulation

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality

De Miguel 2011	• Observational study
	• Support: none; CoI: none
	• Setting: single centre, Spain
	• Sample size: N= 15
	• Duration: 2005-2008
	• Follow-up: median 12 months (range: 1-44)
		• Inclusion: faecal incontinence after low anterior resection for rectal cancer, failed to improve with medical treatment (loperamide medication, dietary counselling) or with biofeedback therapy
		• Exclusion: not reported
		• Patient characteristics:
		  • Male: 80%
		  • Median age: 72 years
		  • All operations R0
		  • 14 patients had had neoadjuvant chemoradiotherapy
		  • At a median postoperative follow-up of 50 months no local or distant recurrence had occurred
			Sacral nerve stimulation	At a median follow-up of 12 months:
				• Mean CCF-FI score was reduced from 19.2 (SD 1.2) to 6.2 (SD 1.7) (p< 0.01)
				• The mean number of days per week with an incontinent episode decreased from 7 (SD 0) to 0.2 (SD 0.3) (p<0.01)
				• Mean number of defecations per week decreased from 42.5 (SD 13.7) to 13.2 (SD 7.4) (p<0.01)
				
				Mean FIQL scores change:
				• Behaviour : 0.92
				• Depression : 0.72
				• Embarrassment : 0.86
				• Lifestyle : 0.94
					Adverse events were not reported on	• Prospective study, no control group
						• 7/15 patients showed a good response during an 18 days screening period and received a permanent implant
						• Changes in FIQL scores were only reported for 5 patients with a follow-up of ≥6 months

Holzer 2008	• Observational study • Support: not reported ; CoI: not reported • Setting: 3 centres, Austria • Sample size: N= 7 • Duration: 2002-2005	• Inclusion: patients with sacral nerve stimulation implanted for faecal incontinence after low anterior resection, failed to improve with medical treatment (loperamide medication, dietary counselling) or with biofeedback	Sacral nerve stimulation	Median within-group change FIQL from baseline to 12 months: • Behaviour 2.0 (1.3–2.5) to 3.6 (3.2–4.4) (p<0.01) • Depression: 2.2 (1.5–3.1) to 3.7 (3.1–4.2) (p<0.01)	One patient developed postoperative hematoma and underwent hematoma evacuation under	• No control group • 6/7 patient underwent a low anterior resection because of rectal cancer; 1 patient because of Crohn´s disease

	• Follow-up: median 32 months (range: 17-46)	therapy
		• Exclusion: not reported
		• Patient characteristics:
		  • Male: 71%
		  • Median age: 57 years
		  • All had normal anal sphincter function
		  • All patients with rectal cancer had had neoadjuvant chemoradiotherapy
		  • Median history of faecal incontinence following rectal resection or closure of the protective stoma was 23 months
				• Embarrassment: 1.5 (1.0–2.4) to 3.8 (3.3–4.7) (p<0.01)
				• Lifestyle: 2.0 (1.0–2.5) to 4.0 (2.7–4.5) (p<0.01)
				
				At a median follow-up of 32 months: 6 patients reported a marked improvement compared to baseline; 3 patients had no further incontinence episodes following the permanent implant. Their incontinence score improved from grade 4 to grade 0–1 according to the Williams classification. 3 patients reported "rare events" (1–2 incontinence episodes/month. In this group, 1 patient with a Cleveland score of 13 at baseline improved to 5. The other 2 patients had preoperatively reported about incontinence episodes of at least 1/week in their diaries. 1 patient who had previously reported an improvement of his continence function during his test stimulation complained about repeated urgency problems as well as incontinence episodes. The patient has changed to retrograde colonic irrigation, thus, reaching an acceptable (pseudo) continence and explant of the stimulation system is presently discussed
					local anaesthesia. One patient needed an explant of the pulse generator due to infection 1 month after the implant procedure. He was successfully re-implanted 3 months later after resolution of the infectious situation	• Unclear what the source population was

Jarrett 2005	• Observational study • Support: Medtronic; CoI: not reported • Setting: multicentre, Denmark; German-speaking countries, United Kingdom • Sample size: N= 3 • Duration: January 1999-June 2001 • Follow-up: 12 months	• Inclusion: ≥4 days of faecal incontinence for solid or liquid stools over a 21-day period following recto-sigmoid resection for colorectal carcinoma; operation had to have been deemed curative; failed pharmacological and biofeedback treatment; age 18-75 years • Exclusion: anorectal malformations; rectal surgery ≤12 months ; rectal prolapse ; chronic bowel disease ; chronic diarrhoea ; stoma; neurological	Sacral nerve stimulation	Two patients had a successful temporary stimulation period and proceeded to permanent implantation Ability to defer was improved in both patients from 0–5 min to 5–15 min Change in mean faecally incontinent episodes/week from before stimulation to 12 months: 10 to 1 The FIQL improved in all 4 subcategories (actual data not given)	The temporary lead broke in the patient whom did not proceed to a permanent implant	• Description of 3 cases • Patients were tested for a minimum of 10 days and proceeded to permanent implantation of a neurostimulation device if there was at least a 50% improvement in continence (i.e. at least a 50% reduction in the number of incontinent episodes per week or a 50% reduction in the number of days with

		disease; bleeding disorder • Patient characteristics: 3 males; 1 colo-anal and 2 colo-rectal anastomosis; intact internal and external anal sphincters; symptom duration in implanted patients 1 year; 2 patients had had radiation treatment		SF-36 scores improved in all subsets except bodily pain (actual data in figure, not reported)		incontinence per week) and no serious complications
Matzel 2002	• Case description • Support: not reported; CoI: not reported • Setting: single centre, Germany • Sample size: N= 1 • Duration: 1996 • Follow-up: 18 months	• Inclusion: a patient with faecal incontinence after surgery for rectal carcinoma; unresponsive to conservative treatment, including medical treatment, biofeedback, dietary manipulation, and anal irrigation. Morphology internal sphincter intact • Exclusion: not reported • Patient characteristics: 48 year old male	Sacral nerve stimulation	The percentage of incontinent bowel movements decreased from 37% to 1% at 12 months and 0% at 18 months The Cleveland Clinic Continence Score declined from 17 before stimulation to 4 after 12 months, and 2 after 18 months Within-patient change FIQL from baseline to 12 months (SD not available): • Behaviour: 0.9 • Depression: 1.0 • Embarrassment: 1.6 • Lifestyle: 1.5 Within-patient change FIQL from baseline to 18 months (SD not available): • Behaviour: 1.6 • Depression: 1.7 • Embarrassment: 2.0 • Lifestyle: 1.9	No complications or side effects of sacral nerve stimulation occurred	• Description of a single case • Unclear what the source population was • Within patient change reported in a figure, actual data not reported. Data extracted here were read from figure 4

Moya 2012	• Observational study
	• Support: not reported; CoI: none
	• Setting: single centre, Spain
	• Sample size: N= 4
	• Duration: 2006-2009
	• Follow-up: not reported
		• Inclusion: severe fecal incontinence following neoadjuvant therapy and anterior resection performed for rectal cancer; all patients were treated with conservative treatment, including drugs, constipating diet and biofeedback physiotherapy for 2 years
		• Exclusion: not reported
		• Patient characteristics:
		  • Male: 25%
		  • Mean age: 65.5 years
			Sacral nerve stimulation	Median Wexner score fell from 15.5 to 5.5 ($p<0.005$)	No complications were observed	• Reported in a letter
						• No control group
						• Unclear what the source population was
						• 4/4 patients tested were implanted

Ortega 2012	• Observational study
	• Support: not reported; CoI: not reported
	• Setting: not reported
	• Sample size: N= 6
	• Duration: 2010-2011
	• Follow-up: 12 months
		• Inclusion: severe incontinence after total mesorectal excision
		• Exclusion: not reported
		• Patient characteristics:
		  • Male: 33%
		  • Median age: 69 years
			Sacral nerve stimulation	The mean CCF-FI score was reduced from 18.5 (SD 1.2) to 6 (SD 1.7) (p< 0.01)
				
				The mean number of incontinence episodes per week decreased from 14 (SD 2) to 4 (SD 1.3) (p< 0.01)
				
				The mean number of defecations per week decreased from 42.5 (SD 13.7) to 13.2 (SD 7.4) (p< 0.01)
				
				All FIQL scores improved (data or statistical significance not reported)
					Complications not reported on	• Reported in abstract only
						• No control group
						• Unclear what the source population was
						• 6/6 patients tested were implanted

Ratto 2005	• Observational study
	• Support: not reported; CoI: not reported
	• Setting: single centre, Italy
	• Sample size: N= 4
	• Duration: May 2001-February 2003
	• Follow-up: 2 months
		• Inclusion: faecal incontinence following preoperative chemoradiation and anterior resection for rectal cancer ≥2 years prior
		• Exclusion:
		• Patient characteristics:
		  • Male: 75%
		  • Mean age: 61.7 years
			Sacral nerve stimulation	Mean change in Pescatori faecal incontinence score: -3
				
				Mean change in Wexner faecal incontinence score: -11.8
				
				Mean change in number of faecal incontinence episodes per week: -9.5
				
				Mean number of faecal incontinence episodes/week at 2 months: 2.5
				
				Mean change SF-36 QoL:
				• Physical activities: 10.8
				• Role limitations caused by physical health: 17.8
				• Emotional state: 20.5
				• Body pain: 4.8
				• Perception of general health state: 18.5
				• Vitality: 7.5
				• Social activity: 13.8
				• Mental health: 18.8
					Adverse events not reported on	• No control group
						• 2/4 patients also complained of urinary stress incontinence, which commenced following treatment for rectal cancer and resolved completely in 1 patient following neuromodulation and diminished in the other patient
						• Unclear what the source population was
						• Short follow-up

Ratto 2009	• Observational study • Support: not reported; CoI: not reported • Setting: not reported • Sample size: N= 14 • Duration: not reported • Follow-up: mean 47.8 months	• Inclusion: faecal incontinence following anterior resection • Exclusion: not reported • Patient characteristics: not reported	Sacral nerve stimulation Patients with a positive response (at least 70% improvement of incontinence episodes/week)	Mean Wexner score decreased from 18.2 (SD: 1.9) to 9.1 (SD: 4.6) (p< 0.05) Mean number of incontinence episodes decreased: • gas: from 54.0 (SD:43.3) to 13.6 (SD: 16.2) (p<0.05)	1 patient was shortly explanted for device infection	• Reported in abstract form • No control group • Unclear what the source population was • 10/14 tested patients were implanted

			were implanted	• liquid faeces: from 36.3 (SD: 41.7) to 3.4 (SD: 2.9) (p<0.05) • solid faeces: from 10.3 (SD: 8.6) to 0.2 (SD: 0.6) (p< 0.05) Quality of life improved significantly (data not reported)		

Abbreviations: ASCRS: American Society of Colon and Rectal Surgery; CCF-FI: Cleveland Clinic Florida Faecal Incontinence; CoI: conflicts of interest; FIQL: Faecal Incontinence Quality of Life; SD: standard deviation

1.1.1.14 Grade table 4a sacral stimulation

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other considerations**	**Sacral stimulation**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
Faecal incontinence quality of life at 12 months												
4 (de Miguel 2011; Holzer 2008; Jarrett 2005; Matzel 2002; Ortega 2012)	Observational studies	Very serious [1]	No serious inconsistency	No serious indirectness	Very serious imprecision [2]	No other considerations	32	0	-	Mean/median FIQL scores improved in all 4 subcategories in all studies	Very low ⊕OOO	Critical
Overall quality of evidence: very low												

Abbreviations: FIQL: Faecal Incontinence Quality of Life
[1] Uncontrolled studies, for 2 out of 4 studies unclear what the source population was
[2] Very small series

KEY QUESTION 4B

Assessment table relative importance patient important outcomes

Patient-important outcomes	Mean rating	Relative importance
Quality of life	7	Critical

As rated by 5 guideline panel members, none of whom were patients

1.1.1.15 Evidence table observational studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality
Gillespie 1985	• Case study • Support: Not reported • Setting: single centre, United States • Sample size: N= 1 • Duration: 1974-1980 • Follow-up: not reported	• Inclusion: patients that underwent abdominal resection • Exclusion: not described • Patient characteristics: the single case was a 60-year old woman who underwent abdominoperineal resection for a non-invasive rectal carcinoma with complete post-operative incontinence, not responding to unspecified pharmacological treatment. A cystourethrogram revealed a bladder and urethral prolapse with funnelling of the bladder neck	Pereyra suspension	This case achieved complete urinary retention and had no need for external protection with intermittent self-catheterisation	Adverse events not reported on	• Single case from a series of 110 patients that underwent abdominal resection, of whom 17 had urinary dysfunction

Abbreviations: RCT: randomised controlled trial

1.1.1.16 Grade table 4b

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pereyra suspension**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
(Pseudo)continence												
1	Case study	Very serious [1]	No serious inconsistency	No serious indirectness	Very serious imprecision [2]	No other considerations	1	0	Complete urinary retention, no need for external protection with intermittent self-catheterisation		Very low ⊕OOO	Critical
Overall quality of evidence: very low												

[1] Uncontrolled study, single case out of a larger series
[2] Single case description

KEY QUESTION 4C

Assessment table relative importance patient important outcomes

Patient-important outcomes	Mean rating	Relative importance
Quality of life	7	Critical

As rated by 5 guideline panel members, none of whom were patients

1.1.1.17 Evidence table randomised controlled trials sildenafil

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality

Lindsey 2002	• RCT
	• Support: Colorectal Research Fund; sildenafil and placebo were supplied by Pfizer Ltd.; CoI: not reported
	• Setting: single centre, United Kingdom
	• Sample size: N= 32
	• Duration: not reported
	• Follow-up: not reported
		• Inclusion: erectile dysfunction after rectal excision
		• Exclusion: preoperative erectile dysfunction and medical contraindications to sildenafil
		• Patient characteristics:
		  • Male: 100%
		  • Median age: 58.7 years
		  • 12 patients proctectomy for rectal cancer (5 abdominoperineal resection, 7 low anterior resection)
		  • 20 proctectomy for inflammatory bowel disease
			Sildenafil (14) vs. placebo 18)
			
			4 weeks, either 25 mg for patients aged 65 and older or 50 mg for those younger than 65
				11/14 (79%) responded to sildenafil, on global efficacy assessment, compared with 3/18 (17%) taking placebo (mean difference: 61.9%; 95%CI: 34.4 to 89.4%; p=0.0009)
				
				Erectile function score: 23.6 vs. 10.6 (p=0.005)
				
				Total International Index of Erectile Function score: 57.4 vs. 34.5 (p=0.007)
					Seven (50%) of 14 patients on sildenafil compared with 4 (22%) of 18 on placebo experienced side effects (difference: 28; 95%CI: -4.4 to 60.4%; p=0.14), 91% of which were mild and well tolerated	• Computer-generated random sequence
						• Central randomisation
						• Double blinded study
						• ITT analysis
						• The trial was stopped after interim analysis of 32 patients because of the highly significant difference in the response rate between active medication and placebo (more than 3 standard deviations, p<0.0009); it was considered unethical to continue randomizing patients
						• Results not reported separately for cancer patients

Abbreviations: CI: confidence interval; CoI: conflicts of interest; ITT: intention to treat; RCT: randomised controlled trial

1.1.1.18 Grade table 4c sildenafil

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sildenafil	Placebo	Relative	Absolute	Quality	Importance

1	RCT	No serious risk	No serious inconsistency	Serious indirectness [1]	No serious imprecision	Other considerations [2]	14	18	-	79 vs. 17% responded to treatment (mean difference 62%; 95%CI: 34 to 89%)	Low ⊕⊕OO	Critical
Overall quality of evidence: low												

[1] 12/32 patients had had rectal cancer, results not reported separately for these patients
[2] Trial stopped early because of positive results; small trial with few events leading to fragility of results

1.1.1.19 Evidence table randomised controlled trials cavernous auto injection therapy (SKAT)

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results primary outcome	VI Results secondary and other outcome(s)	VII Critical appraisal of study quality

Sterk 2005	• Observational study
	• Support: not reported; CoI: not reported
	• Setting: Germany
	• Sample size: N= 5
	• Duration: not reported
	• Follow-up: not reported
		• Inclusion: no erections 3 months postoperatively, rectal carcinoma
		• Exclusion: not reported
		• Patient characteristics:
		  • Male: 100%
		  • Median age: not reported
			Cavernous auto injection therapy (SKAT)	With SKAT, a good erection (sufficient for intercourse) could be reached in all five men	Adverse events not reported on	• No control group

Abbreviations: CoI: conflicts of interest

1.1.1.20 Grade table 4c cavernous auto injection therapy (SKAT)

Quality assessment							No of patients		Effect (95%CI)			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SKAT**	**Placebo**	**Relative**	**Absolute**	**Quality**	**Importance**
1	Observational study	Serious risk of bias [1]	No serious inconsistency	No serious indirectness	No serious imprecision	No other considerations	5	-	-	With SKAT, a good erection (sufficient for intercourse) could be reached in all five men	Very low ⊕⊕⊕O	Critical
Overall quality of evidence: very low												

[1] No control group