Systematic review

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Surgery for constipation: systematic review and practice recommendations

Graded practice and future research recommendations

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Abstract

Aim This manuscript forms the final of seven that address the surgical management of chronic constipation (CC) in adults. The content coalesces results from the five systematic reviews that precede it and of the European Consensus process to derive graded practice recommendations (GPR).

Methods Summary of review data, development of GPR and future research recommendations as outlined in detail in the 'introduction and methods' paper.

Results The overall quality of data in the five reviews was poor with 113/156(72.4%) of included studies providing only level IV evidence and only four included level I RCTs. Coalescence of data from the five procedural classes revealed that few firm conclusions could be drawn regarding procedural choice or patient selection: no single procedure dominated in addressing dynamic structural abnormalities of the anorectum and pelvic floor with each having similar overall efficacy. Of one hundred 'prototype' GPRs developed by the clinical guideline group, 85/100 were deemed 'appropriate' based on the independent scoring of a panel of 18 European experts and use of RAND-UCLA consensus methodology. The remaining 15 were all deemed uncertain. Future research recommendations included some potential RCTs but also a strong emphasis on delivery of large multinational high-quality prospective cohort studies.

Conclusion While the evidence base for surgery in CC is poor, the widespread European consensus for GPRs is encouraging. Professional bodies have the opportunity to build on this work by supporting the efforts of their membership to help convert the documented recommendations into clinical guidelines.

Keywords Constipation, surgery, obstructed defaecation

Introduction

This manuscript forms the final of seven that address the surgical management of chronic constipation in adults. The content coalesces results from the five systematic reviews that precede it and of the European Consensus process to derive graded practice recommendations.

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[a]European Society of Coloproctology members are listed in Appendix 1.

Methods

These have been fully explained in the 'Introduction and Methods' paper. Procedures have been grouped as:

1 Colonic resection, including total colectomy, subtotal and segmental colectomy (with some anastomotic variations for subtotal colectomy) by open and laparoscopic approaches;
2 Rectal suspension procedures, including forms of open and laparoscopic rectopexy;
3 Rectal excisional procedures, including stapled transanal rectal resection (STARR) and intra-anal Delorme's;

4 Rectovaginal reinforcement procedures, including trans-vaginal and trans-anal approaches with or without mesh;
5 Sacral nerve stimulation.

Results have been presented as follows:
1 Summary tables of results where these could be compared between classes of procedure based on homogeneous outcomes;
2 Graded practice recommendations. All prototype GPRs have been documented with consensus statistics and thence a clear indication of those that were upheld (found to be appropriate) by consensus.

A final section addresses implications for future research. Note: consideration was given to summarizing all summary evidence statements in this manuscript however these are covered in each individual review and were omitted here for brevity.

Results

Study characteristics

Table 1 repeats the information provided in the 'introduction and methods' paper on overall study characteristics by procedure. As previously noted, the overall quality of evidence was poor with 113/156 (72.4%) providing only level IV evidence. The best evidence was extracted for rectal excisional procedures where the majority of studies were level I or II.

Summary of systematic review data

In each of the five reviews, results were presented for perioperative variables, harms (post-operative complications and long-term adverse events), efficacy and prognostic factors. These data have been presented together below.

Perioperative variables

Data were available for nearly all procedure classes (except SNS) on operation duration and length of stay (Table 2, Figure 1). Not unsurprisingly, colectomy had the longest operative duration and length of stay. For the three classes of rectal procedure lengths of stay were similar, however duration of surgery was clearly longer for rectal suspension (rectopexy) and shortest for rectal excision - in effect for forms of stapled trans-anal resection (STARR).

Harms

There were large discrepancies in harm recording with selected outcomes being based on *a priori* knowledge of recognized harms for each class of procedure. Given considerable heterogeneity in reporting (covered in the individual reviews), it was only possible to summarize main harms semi-quantitatively (Table 3). A mortality rate of approximately 1/200 occurred after colectomy. Other procedures had no recorded mortality or a very low rate (rectovaginal reinforcement procedures: 1/1600). Colectomy was associated with substantial risks in the short and long-term, particularly in relation to small bowel obstruction and poor functional outcomes. Other procedures had generally fewer complications, including some where review data reflected concerns expressed widely in the international surgical community, notably mesh complications after rectopexy and chronic pain ± urgency after STARR.

Efficacy

Few variables could be analysed across procedure classes on the basis that, like harms, outcomes chosen tended to be bespoke to each procedure class. It was however possible to summarise global satisfaction ratings, i.e. the proportion of patients self-reporting a good or excellent outcome. Accepting the considerable limitations of such outcomes, data in Table 4 show that all procedures are almost equally-well received by patients with rates around 70–85% for all.

Table 1 Reviewed studies by main procedure type and evidence level.

	Number of reviewed studies by evidence level				
Procedure	1b	2b	3b	4	Total
Colonic resection	0	1	0	39	40
Rectal suspension procedures	0	2	0	16	18
Rectal excisional procedures	3	26	0	18	47
RV reinforcement procedures	1	10	0	33	44
Sacral nerve stimulation	0	0	0	7	7
ALL	4	39	0	113	156

RV, recto-vaginal.

Table 2 Summary of perioperative data for main classes of procedure.

	Operation Duration, mins		Length of Stay (LOS), days	
Procedure	Mean	Range of study means	Mean	Range of study means
Colonic resection	167	120–248	10.4	7.0–15.5
Rectal suspension	159	75–198	4.6	1.0–7.1
Rectal excision	44	23–95	3.0	1.0–8.0
RV reinforcement	67	20–169	3.9	1.0–9.0
SNS	NK	NK	NK	NK

RV, recto-vaginal; NK, not known.

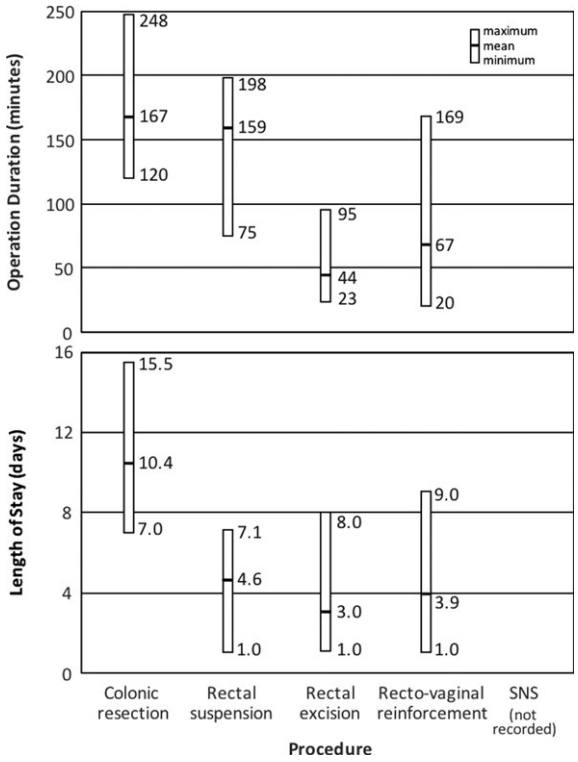

Figure 1 Summary of perioperative data for main classes of procedure, showing range of study means.

Patient selection

For most classes of procedure, some information could be obtained about prognostic baseline characteristics that might guide patient selection. In all instances, the level of evidence was poor with no formal stratified medicine studies and very few (if any) adequately powered *post-hoc* analyses of good quality cohort studies. Table 5 summarizes the broad phenotypes of patients that may most benefit from each procedure and some negative prognostic features.

Graded practice recommendations

A series of tables (Table 6 a-e) show all GPRs proposed by the clinical guideline group by main procedure class. The outcomes of the consensus process have been presented as median score (1–9) and by classification based on RAND-UCLA methodology: appropriate; uncertain and inappropriate. The reader is reminded that appropriateness is not directly extrapolated from the median score but rather the overall data distribution (see introduction and methods).

Discussion

This manuscript summarises the body of data from five systematic reviews and presents new graded practice recommendations.

Table 3 Summary of perioperative complications and long-term adverse events

Procedure	Total perioperative complications*	Mortality†	Specific adverse events*
Colonic resection	24.4% (17.8–31.7%)	6/1568 (0.4%)	Small bowel obstruction: 15.2%, (RE: 10.2% to 20.9%) Re-op: 13.3%, (RE: 8.6% to 18.7%) Poor function: abdominal pain, bloating (20–50%), rec. constipation (10–30%), diarrhea & incontinence (5–15%)
Rectal suspension	9.5% (6.1–13.1%)	0/1044	Minor complications predominate e.g. UTI Some major poorly documented e.g. SBO Mesh complications 0.5% (range 0–3.9%)
Rectal excision	16.9% (12.7–21.5%)	0/5896	PO bleeding: 1.6% (0.9% to 2.5%) Sepsis: 0.2% (0.0% to 0.7%) Anastomotic dehiscence: 0.3% (0.0% to 0.8%) Rectal stenosis: 0.2% (0.0% to 0.6%) Chronic anorectal pain: 0.7% (0.1% to 1.6%) Chronic urgency: 5.2% (2.7% to 8.2%)
RV reinforcement	11.5% (7.2–16.6%)	2/3209(0.06%)	Post-op. bleeding: 2.0% (0.7% to 3.6%) Haematoma or sepsis: 0.9% (0.2% to 2.0%) Dyspareunia: inadequately reported to analyse
SNS	22.7% (12.9–34.1%)	0/375	At least one reportable event: 58% Infection: 0–7% Device removal: 14.4% (7.8% to 22.5%)

*Pooled estimates based on random effects (RE) models with (95% CI); RV: recto-vaginal.
†denominator represents only those studies where mortality was recorded and documented.

Table 4 Summary of efficacy data based on global satisfaction ratings.

Procedure	No studies	Total No patients	Follow up (mean and range of means, months)	Global satisfaction*
Colonic resection	40	2045	47 (12–132)	86 (81–89)%
Rectal suspension	18	1238	25 (12–72)	83 (74–91)%
RV reinforcement	44	3499	25 (12–74)	72 (67–77)%
Rectal wall excision	47	8340	23 (12–66)	76 (73–80)%
SNS	7	375	27 (20–51)	73 (57–87)%

*Pooled estimates based on random effects models with (95% CI).

Table 5 Patient characteristics influencing selection for each class of procedure

Procedure	Main positive characteristic	Secondary positive characteristics	Negative characteristics
Colonic resection	Proven slow transit constipation		Proven upper GI dysmotility Proven psychiatric disorder Inconsistent evidence for combined defaecation disorder
Rectal suspension	High grade intussusception (Oxford grade III-V)	Solitary rectal ulcer syndrome (SRUS)Rectocoele	None established
Rectal excision	Minimum of 3 ODS symptoms; Functioning rectocoele	High grade intussusception (Oxford grade III-V)	None established
Rectovaginal reinforcement	Functioning and significantly-sized rectocoele	None established	None established
SNS	Chronic constipation	None established	None established

ODS, obstructed defaecation symptoms.

Summary of systematic review data

The overall quality of data was poor with 113/156 (72.4%) of included studies providing only level IV evidence, thus greatly limiting the number and grade of summary evidence statements. This was a particular problem for colonic resection, rectal suspension procedures and sacral nerve stimulation, where nearly all data were derived from level IV studies. The limitations of such observational data are well acknowledged and are a source of concern when used as a basis for promoting procedures. For instance, colectomy for slow-transit constipation would, based on systematic review of 40 observational studies, appear to be an attractive prospect with 86% global satisfaction rate (the highest of any of the studied classes of procedure). However, recently published US retrospective cohort data on over 2000 patients [1] paint a very different picture of high complication rates and greater long-term post-procedural health utilization (ambulatory care, hospital admissions, radiology etc.) than before surgery. It is difficult to reconcile such disparity [2], and the increasing rates of colectomy for constipation in the US [1] also seem at odds with international opinion (that promotes extreme caution). Sacral nerve stimulation also had generally supportive observational evidence based on seven included studies. However, subsequent randomised studies [3,4] directly contradict these data and most centres no longer offer SNS for the constipation indication.

Perhaps the greatest area of academic contention in the pelvic floor community concerns the choice of procedure to address dynamic structural abnormalities of the pelvic floor that lead to prolapse and obstructed defaecation symptoms. The results presented here do little to help resolve this issue and certainly cannot help underpin a much needed treatment algorithm for such patients. In effect, all have similar global satisfaction ratings, similar lengths of stay and complication profiles that are to some extent procedure-specific. Based on reviewed indications, rectal suspension and excision procedures can be applied to patients with rectal intussusception and/or rectocoele and rectovaginal reinforcement procedures to rectocoele only. Aside from a generally longer operating time for rectopexy (and shorter for STARR), decision making for a patient with one or both of these abnormalities currently rests with personal views about the acceptability of certain complications and (possibly) surgeon enthusiasm for

Table 6 (a-e) Graded practice recommendations

	Evidence level	Grade	Median score	Decision
(a)				
Colonic resection				
Patient selection				
1. Given uncertainty of outcome and potential for harm, colectomy should only be offered to patients when all other relevant treatments have failed	IV	C	9	Appropriate
2. Given concerns regarding outcome, the following represent absolute or relative contra-indications to colectomy				
a Concomitant upper GI symptoms (relative)	V	N	6	Uncertain
b Proven upper GI dysmotility (absolute)	IV	C	8	Uncertain
c Unproven generalised delay in colon transit (absolute)	IV	C	8	Appropriate
d Concomitant defecation disorder (relative)	IV	D	6	Uncertain
e Significant symptoms of abdominal pain and bloating, including diagnosis of IBS (relative)	IV	D	6	Uncertain
f Faecal incontinence and/or functionally impaired anal sphincter	V	N	9	Appropriate
3. As a consequence of the above, colectomy should not be considered without precision phenotyping (clinical and radio-physiological)	IV	C	9	Appropriate
4. Given concerns regarding outcome, magnitude and irreversibility of colectomy, patients with concomitant defecation disorder should have this treated first including surgery for structural causes where relevant	IV	D	8	Appropriate
5. All patients considered for colectomy should have specialist multidisciplinary discussion	V	N	9	Appropriate
6. Formal psychological evaluation should be undertaken in all patients considered for colectomy for constipation	V	N	7	Appropriate
7. In view of need for specialist investigations and review, patients should only undergo colectomy for constipation in centres with access to appropriate specialist services	V	N	9	Appropriate
Procedural considerations				
1. Colectomy and ileorectal anastomosis (CIRA) should be considered the default option considering weight of evidence compared to other procedures	IV	C	8	Appropriate
2. There are insufficient data to conclude that the following provide certain benefit in terms of clinical outcome in comparison to CIRA				
• Subtotal or segmental resection	IV	C	8	Appropriate
• Subtypes of subtotal resection (caecorectal *vs* ileosigmoid)	IV	D	7	Appropriate
• Variations in anastomotic configuration (iso- or anti-peristaltic)	IV	D	7	Appropriate
• Laparoscopic *vs* open approach	IV	D	5	Uncertain
• Tailoring of segmental resections using specialist regional transit measurements	IV	D	6	Uncertain
3. Laparoscopic surgery should be considered in suitable patients because of:				
• Modest reductions in length of stay	IV	D	8	Appropriate
• Cosmesis and other generally-perceived benefits e.g. reduced incisional hernia	V	N	8	Appropriate
• Possible reduction in long-term small bowel obstruction and re-operation rates	IV	D	8	Appropriate
Patient counselling				
1. Approximately 85% patients report some benefit at follow up greater than 1 year after colectomy	IV	C	8	Appropriate

Table 6 (Continued).

	Evidence level	Grade	Median score	Decision
2. Total perioperative complication rates vary greatly but may occur in approximately 20–30% of colectomy patients regardless of procedure choice, and include serious life-threatening complications such as anastomotic leak (5% risk) and mortality (0.4%)	IV	C	8	Appropriate
3. Rates of post-operative ileus or early post-operative adhesional small bowel obstruction vary greatly but occur in about 5–15% of patients and about one-third of these patients require re-operation regardless of procedure choice	IV	C	8	Appropriate
4. Long-term adverse events characterized by recurrent episodes of small bowel obstruction occur in about 10–20% of patients and may result in a significant burden of re-hospitalization and frequent recourse to surgery	IV	C	8	Appropriate
5. Negative long term functional outcomes persist in a proportion of patients: diarrhoea and incontinence in about 5–15% of patients; abdominal pain in 30–50% of patients; recurrent constipation in 10–30% of patients and bloating in 10–40%	IV	C	8	Appropriate
6. As a result of immediate and long-term complications, approximately 5% patients will have a permanent ileostomy	IV	C	6	Uncertain
(b)				
Rectal suspension procedures				
Patient selection				
1. Rectal suspension procedures should be considered only for patients failing appropriate non-surgical treatments	IV	D	9	Appropriate
2. Rectal suspension procedures should be considered for patients with the following anatomical abnormalities in conjunction with symptoms suggestive of rectal evacuation disorder				
• High grade intussusception (recto-anal e.g. Oxford grade: 3–5)	IV	C	8	Appropriate
• SRUS with associated intussusception	IV	C	8	Appropriate
3. Diagnosis of anatomical abnormalities should be conducted to a standard where agreement exists that observed findings can be deemed pathological based on appropriate normative data (derived within the department or derived elsewhere but using identical methodology e.g. for proctographic imaging)	V	N	8	Appropriate
4. Given concerns regarding outcome, the following should be regarded as relative contraindications to rectal suspension procedures				
• Significant psychiatric disorders	V	N	7	Appropriate
• Significant chronic pain syndromes including IBS	V	N	8	Appropriate
• Morbid obesity	V	N	8	Appropriate
• Known hostile abdomen/pelvis	V	N	8	Appropriate
• Joint hypermobility syndrome (EDS3)/connective tissue disorders	V	N	5	Uncertain
5. Patients considered for rectal suspension procedures should have specialist multidisciplinary discussion	V	N	8	Appropriate
6. In view of need for specialist investigations and review, patients should only undergo rectal suspension procedures for constipation in centres with access to appropriate specialist services	V	N	8	Appropriate
7. Rectal suspension procedures (especially those employing mesh) require special consideration in women who plan to become pregnant	V	N	8	Appropriate

Table 6 (Continued).

	Evidence level	Grade	Median score	Decision
Procedural considerations				
1. There is insufficient current evidence to conclude that any one rectal suspension procedure is clearly superior to another	IV	C	7	Appropriate
2. Laparoscopic surgery should be considered in suitable patients because of:				
• Cosmesis and other generally perceived benefits such as reduced incisional hernia	V	N	8	Appropriate
• Possible reduction in adhesion formation	V	N	8	Appropriate
• Superior access to the deep pelvis	V	N	7	Appropriate
3. There is no current evidence to suggest superiority of robotic surgery over a standard laparoscopic approach	IV	D	8	Appropriate
4. Careful consideration should be given to the type of mesh and fixation	V	N	8	Appropriate
Patient counselling				
1. Approximately 83% (73–91%) patients report some benefit at follow up greater than 1 year after rectal suspension procedures	IV	C	8	Appropriate
2. Total perioperative complication rates vary greatly but may occur in approximately 5–15% of patients regardless of procedure choice	IV	C	8	Appropriate
3. Serious complications such as mesh erosion occur in 0–4% of patients however no mortality has not been reported	IV	C	8	Appropriate
4. The effect on constipation symptoms is highly variable and data are only available for lap VMR after which most patients (86%) report an improvement in constipation symptoms	IV	C	7	Appropriate
5. In patients with SRUS, ulcer healing is observed in 78% of patients	IV	C	8	Appropriate
(c)				
Rectal excisional procedures				
Patient selection				
1. Rectal excisional procedures should be considered only for patients failing appropriate non-surgical treatments	II	B	9	Appropriate
2. Rectal excisional procedures should be considered for patients with the following anatomical abnormalities in conjunction with symptoms suggestive of rectal evacuation disorder				
• Minimum of 3 ODS symptoms	II	B	7	Appropriate
• Rectorectal or rectoanal intussusception only	IV	D	5	Uncertain
• Rectocele only	II	B	5	Uncertain
• Rectocele and intussusception	II	B	7	Appropriate
3. Diagnosis of anatomical abnormalities should be conducted to a standard where agreement exists that observed findings can be deemed pathological based on appropriate normative data (derived within the department or derived elsewhere but using identical methodology e.g. for proctographic imaging for grade of intussusception and size/functionality of rectocele)	V	N	8	Appropriate
4. Given concerns regarding outcome, the following should be regarded as relative contraindications to rectal excisional procedures although none were supported by evidence in the systematic review				
• Significant psychiatric disorders	V	N	8	Appropriate
• Significant chronic pain syndromes (including IBS) or perceived susceptibility to chronic post-surgical pain	V	N	8	Appropriate
• Concomitant enterocele (because of perceived risk of bowel injury	V	N	9	Appropriate

Table 6 (Continued).

	Evidence level	Grade	Median score	Decision
• Reduced anal sphincter function (because of risk of urgency and incontinence)	V	N	7	Appropriate
• Solitary rectal ulcer syndrome	V	N	7	Appropriate
• Clear evidence of anal sphincter dyssynergia	V	N	7	Appropriate
• External rectal prolapse or other significant pelvic organ prolapse syndrome	V	N	9	Appropriate
5. Patients considered for rectal excisional procedures should have specialist multidisciplinary discussion	V	N	9	Appropriate
6. In view of need for specialist investigations and review, patients should only undergo rectal excisional procedures for constipation in centres with access to appropriate specialist services	V	N	8	Appropriate
Procedural consideration				
1. The evidence base of procedural choice is dominated by studies of STARR procedures and all higher quality studies report STARR outcomes; on this basis, it is reasonable to recommend STARR as the default excisional procedure	II	B	8	Appropriate
2. There is insufficient current evidence to conclude that any one rectal excisional procedure is clearly superior to another in terms of efficacy or complications	IV	D	7	Appropriate
Patient counselling				
1. Approximately 76% (73–80%) patients report some benefit at follow up greater than 1 year after rectal excisional procedures	II	B	7	Appropriate
2. Total perioperative complication rates vary greatly but may occur in approximately 13–22% of patients regardless of procedure choice	II	B	7	Appropriate
3. Significant complications such as sepsis, anastomotic dehiscence and bleeding occur in in approximately 2% (1–4%) of patients	II	B	6	Uncertain
4. Life-threatening complications occur in in approximately 1: 1000 patients however no mortality was reported in recent review of almost 6000 patients	II	B	8	Appropriate
5. The effect on constipation symptoms is highly variable although approximately 70% patients will obtain a significant reduction in burden of obstructed defaecation symptoms	II	B	7	Appropriate
6. Patients should be warned of long-term adverse functional outcomes; rates of urgency (10%) and of chronic pain (2%) should be cited	II	B	8	Appropriate
7. Other long-term complications e.g. stenosis (< 1%)and fistula (1 in 1600) are rare	II	B	7	Appropriate
(d)				
Rectovaginal reinforcement				
Patient selection				
1. Rectovaginal reinforcement procedures should be considered for patients with the following anatomical abnormalities in conjunction with typical symptoms (vaginal bulging or prolapse and problematic rectal evacuation)				
• Significant dimensions (depth) based on clinical ± imaging assessment	IV	C	7	Appropriate
• Evidence of functionality (trapping) on dynamic assessment	IV	C	8	Appropriate

Table 6 (Continued).

	Evidence level	Grade	Median score	Decision
2. Diagnosis of the above should be conducted to a standard where agreement exists that observed findings can be deemed pathological based on appropriate normative data (derived within the department or derived elsewhere but using identical methodology e.g. for imaging)	V	N	8	Appropriate
3. Given concerns regarding outcome the following should be regarded as relative contraindications to all forms of rectovaginal reinforcement procedures				
• Diagnosis of major psychiatric disorders	V	N	7	Appropriate
• Significant chronic pain syndromes including IBS	V	N	7	Appropriate
• Morbid obesity	V	N	7	Appropriate
• High grade recto-anal intussusception	V	N	8	Uncertain
4. Procedure-specific relative contraindications should include:				
• Vaginal repairs: smoking	V	N	5	Uncertain
• Transanal repairs: sphincter incompetence, rectal inflammation or anorectal stenosis	V	N	8	Appropriate
5. Patients considered for rectovaginal reinforcement procedures should have specialist multidisciplinary discussion	V	N	9	Appropriate
6. In view of need for specialist investigations and review, patients should only undergo rectovaginal reinforcement procedures for constipation in centres with access to appropriate specialist services	V	N	8	Appropriate
7. Rectovaginal reinforcement procedures require special consideration in women who plan to become pregnant	V	N	8	Appropriate
Procedural considerations				
1. There is insufficient evidence to conclude that any one rectovaginal reinforcement procedure is clearly superior to another for the treatment of constipation	IV	C	8	Appropriate
2. Evidence derived from other indications for rectovaginal reinforcement procedures e.g. pelvic organ prolapse syndromes suggests superiority of vaginal repair (although this has not been demonstrated in the treatment of constipation)	V	N	5	Uncertain
3. Limited evidence suggests that a site specific vaginal repair may lead to a higher recurrence rate than other surgical approaches	IV	C	5	Uncertain
4. There is no evidence that the use of mesh reinforcement in vaginal or perineal surgery leads to net benefit	IV	C	7	Appropriate
Patient counselling				
1. Approximately 73% (67–78%) patients report some benefit at follow up after 1 year after rectovaginal reinforcement procedures	IV	C	7	Appropriate
2. Total perioperative complication rates vary greatly but may occur in approximately 7–17% of patients regardless of procedural choice	IV	C	8	Appropriate
3. Serious complications such as rectovaginal fistula occur rarely (< 1 in 1000 patients); mortality has been reported in 1 in 1600 patients	IV	C	8	Appropriate
4. While dyspareunia may occur with any of the surgical procedures, the particular risks of a vaginal approach should be discussed with the patient	IV	D	9	Appropriate
5. Evidence derived from other indications for rectovaginal reinforcement procedures e.g. pelvic organ prolapse syndromes suggests an increased risk of dyspareunia with a vaginal repair in conjunction with levatorplasty	V	N	7	Appropriate

Table 6 (Continued).

	Evidence level	Grade	Median score	Decision
(e)				
Sacral nerve stimulation				
Patient selection				
1. Recent trial data (from 2 independent RCTs) suggest no overall benefit of SNS for chronic constipation regardless of type of constipation; on this basis, the procedure cannot be recommended for this indication	II	B	7	Appropriate
Procedural considerations				
1. Not applicable (follow manufacturer's instructions and specific training)	NA	NA	NA	NA
Patient counselling				
1. Patients should be counselled that the evidence base does not support the use of SNS for chronic constipation	II	B	9	Appropriate
2. If performed, patients should be warned of:				
• Highly variable rates of device removal for adverse effects or lack of efficacy	IV	D	8	Appropriate
• Very high rates of reprogramming	IV	D	8	Appropriate
• Low eventual success rates	II	B	9	Appropriate

type of approach and surgical instruments (flippantly whether the surgeon prefers basic surgical instruments, laparoscopy or staplers). With respect to complications, limited reporting prevented much discussion beyond the importance of counselling patients about established complications (covered in GPRs). However, it is tempting to speculate that future stratification might provide the opportunity to select patients for one or other procedure e.g. avoiding patients with certain prior phenotypic features or modifying risk. An example would be chronic pain development, where perhaps STARR should be relatively contra-indicated in patients with preceding evidence of pain syndromes (e.g. migraine, fibromyalgia or chronic back pain) or modified using one of a number of available agents to prevent sensitization during surgery e.g. pre-operative gabapentin or intra-operative ketamine [5]. At the very least the data provide the opportunity to appraise patients with the options and their complication profiles where more than one surgical option exists.

Another difficulty with interpretation was that inclusion (in the review) necessarily reflected the availability of studies, in turn reflecting the tendency to publish studies of new techniques rather than well-established ones. Higher quality data were available for rectal excisional procedures due to several prospective cohort studies and small RCTs of the STARR procedure (and variations). It is well acknowledged that this body of data, including over 8000 patients, reflects a period of intense popularity for this procedure (nearly all published in the decade 2004–14) with (interestingly) no included papers arising from the final 18 months of the review period. The large numbers are also known to reflect industry investment in several data registries, two of which included over 2000 patients. Anecdotal evidence and expert opinion from international meetings is that the popularity for this procedure has waned (even in Italy – the origin of the procedure and its main proponents). Such a peak and decline in popularity was not present for other procedures that were more evenly spread across the review period.

Graded practice recommendations

The clinical guidelines group developed a total of 100 'prototype' graded practice recommendations by taking forward summary evidence statements from the five reviews and combining these with expert opinion and a small number of RCTs (SNS only) published after the extraction data (22/02/2016). These statements covered patient selection, procedural considerations and patient counselling. The limitations in review evidence meant that only 59/100 prototype GPRs were directly derived from summary evidence (level II-IV; grades B-D) with the remainder, 41/100 derived by expert opinion only (level V; grade N). Of the 100 total, 85 were deemed 'appropriate' based on the independent scoring of 18 European experts and the remaining 15 were all

deemed uncertain, i.e. none was considered inappropriate by the panel. This is a high level of consensus for a single round of questioning and suggests that there is reasonable European agreement as to selection of patients for each class of procedure, which procedure to perform and how to counsel the patient (often related to outlining potential harms). However, this does not signify unequivocal evidence of value for these recommendations and they do not represent minimum standards, but can act as a basis for further research and guideline development.

The 15 'uncertain' GPRs were spread across procedures with most in colectomy ($n = 7$) and least for rectal suspension (1) and SNS (0). The majority concerned patient selection ($n = 8$). Interestingly, only 5/15 (33.3%) related to prototype GPRs based only on expert opinion (level V, grade N). The remaining 10 included five where uncertainty by consensus accurately reflected uncertainty by grade (D) (33.3%), three with grade C summary evidence from the systematic reviews (20.0%) and two with grade B evidence (13.3%). There was thus no strong suggestion that grade weighed panelist opinion. The two grade B statements deemed uncertain both concerned rectal excision: first that 'rectocoele only' was an indication in terms of benefiting the patient; and secondly that significant complications such as sepsis, anastomotic dehiscence and bleeding can occur post-procedure in approximately 2% (1–4%) of patients. The panelist consensus on these two GPRs is surprising since both would seem to reflect widespread practice and knowledge, respectively. Overall, while it would be possible to have further rounds of consensus building among the European panel, the GPRs as stands are a good start to develop future clinical guidelines.

Future research recommendations

With the exception of rectal excision, there are clear deficiencies in the current evidence base for all surgical procedures directed at the management of chronic constipation in adults. This was particularly true in terms of availability of randomized controlled trials, where only four reviewed studies met criteria for level I evidence. The difficulties in conducting randomized trials for complex interventions such as surgery are well rehearsed [6], but their importance is exemplified by recent SNS RCTs [3,4] that directly contradict observational data. While it can be argued that sham surgery would be difficult to justify for patients with a chronic debilitating condition, it is disappointing that no level I evidence has been produced to compare classes of procedure where more than one is appropriate. Such comparison trials of different techniques may face problems of equipoise and interventional fidelity, and might need to overcome a speciality divide e.g. posterior repair *vs* transanal repair of rectocoele (the former performed largely by gynaecologists or urologists specializing in female patients and the latter by colorectal surgeons). An alternative is waiting-list designs where the wait time for surgery can be randomized and analysis-based on longitudinal outcomes before and after intervention [7]. An example of such a study is the CapaCiTY03 stepped-wedge randomised controlled study of laparoscopic ventral mesh rectopexy in adults with chronic constipation [8].

Accepting the difficulty in performing RCTs, there is still much opportunity to improve the evidence base by encouraging high quality observational studies. Prospective cohort studies could benefit from incorporating some of the scientific rigor of RCTs to limit obvious sources of bias e.g. by multicentre recruitment and use of blinded observers to collect outcomes. Awareness of reporting standards by authors and journals may in turn feed better protocol-driven research [9]. They should incorporate the few validated patient-reported outcome measures (PROMS) that are available e.g. PAC-QoL and PAC-SYM, internationally-accepted HR-QoL measures e.g. EQ-5D-5L and monitor harms in a systematic manner using established systems e.g. Clavien-Dindo [6]. They should also consider collecting health utilization data from patient information systems, the importance of which is illustrated by the Dudekula study [1] of colectomy.

The CCG make the following recommendations as research priorities:

1. Colonic resection: there is a need to determine prospectively and robustly the risks and benefits of this procedure. Considering its low incidence, a prospective cohort study across Europe (or internationally) is recommended. Observer-blinded outcomes (above) should be systematically recorded at regular intervals to 5 years. Standardised baseline phenotyping may permit determination of outcome predictors if numbers are large enough. Consideration could be given to a control group not undergoing surgery (although selection bias is acknowledged). All procedural variations could be evaluated although the main comparison of interest is now considered to be between more (total colectomy) and less radical (subtotal) laparoscopic resections. A double-blind RCT of this latter comparison might also be possible with international effort.
2. Rectal procedures for dynamic structural abnormalities of the pelvic floor. A UK RCT is underway to evaluate laparoscopic ventral mesh rectopexy [8]. A

further RCT is however recommended to determine outcomes of repair of large rectocoele (in isolation), comparing posterior repair of the vagina *vs* transanal repair. It is acknowledged that this might require an expertise-based design [6,10] but it is an unanswered question for the indication of chronic constipation or obstructed defaecation. Systematic review data would also support a randomized comparison of STARR with rectopexy for patients with high-grade intussusception and rectocoele. However, expert opinion suggests that STARR is no longer popular. An alternative would be to perform a prospective cohort study (akin to colectomy) capturing all current practice. This could be performed internationally but might also be possible in a single country where all three main classes of procedure are still commonly utilized.

Conclusions

This manuscript concludes the series of seven, systematically detailing the outcomes of the main surgical procedures directed toward patients with chronic constipation. The current evidence base is poor and heavily reliant on low-quality observational data. On this basis, all procedures reviewed had generally positive (supportive) data. Several authors expressed concern that such data might not reflect the reality of clinical practice. While bias in such observational study designs is well recognized, it is possible that in surgical studies (usually performed by the proponents of the surgery) bias is both unidirectional (favouring the intervention) and powerful. Not only should this lead to a greater willingness to design and deliver high quality controlled trials, but also to an essential understanding that retrospective observational studies should be interpreted with caution. However the finding of widespread consensus for graded practice recommendations is encouraging. The stage is now set for recognised professional bodies worldwide e.g. Societies of Coloproctology/Colorectal surgery to build on this work by supporting the efforts of their membership to address future research recommendations and/or to help convert the recommendations documented in this series of papers into their clinical guidelines.

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Appendix I

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