

## Role of surgery in the modern management of slow-transit constipation

### **Charles Knowles**

Queen Mary University of London Cleveland Clinic London Barts Health NHS Trust, St Mark's Hospital





## Disclosures



Company	Consultancy	Speaker fees	Research funding	Research collaboration	Share holder, director
Medtronic	х	х	х	х	
Amber Therapeutics			х	х	x
Saluda Medical	x		х	x	
Cook Myosite	x			x	
Enterika	x				x
Coloplast	x			x	
Uroplasty	x	х	х	x	
Congentix Med	x	x		х	
Firstkind Med			x	x	
Exero Med	x		x	x	
Ardmore HC, MMS				x	
Motilent				х	
Enteromed	х			х	
JEB Medical				x	
usMIMA	x				





### Overview

Myth busting

The modern role for colectomy

Other options





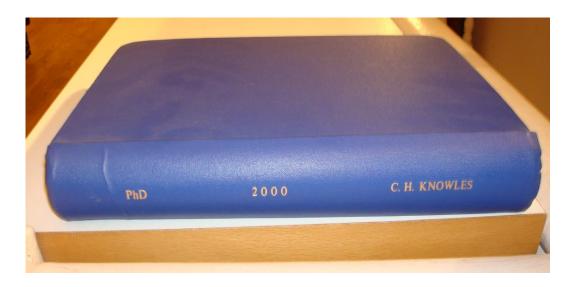


## Myth busting

## STC: myths

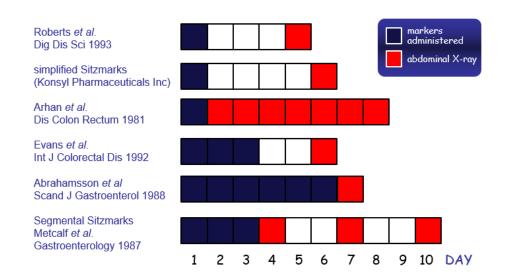


- STC is a disease
- STC is an inertial problem





- STC is only defined by a measurement
- Usually based on WGTT using single radio-opaque marker study
- Multiple methods with poorly defined cut-offs



Gut, 1986, 27, 41-48

## Severe chronic constipation of young women: 'idiopathic slow transit constipation'

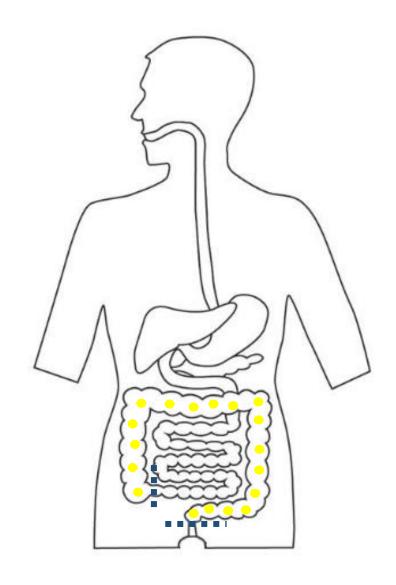
D M PRESTON AND J E LENNARD-JONES

From St Mark's Hospital, London

- N = 64 'white women': 1969-82
- 33 / 64 family history
- Distinct phenotype characterised by infantile or childhood onset and severe bowel infrequency

Table 1 Ages at which patients first experienced symptoms, consulted their doctor and were referred to hospital

	Age (yr)							
	0–5	6–10	11-15	16–2	0 21-25	26–30	31-4	0 >40
Onset of symptoms	15	6	16	16	8	1	2	0
Consulted doctor	6	4	11	22	14	5	2	0
Referred to hospital	0	3	7	16	21	5	7	5



- Defined enteric
  neuropathology leading
  to reduced digestive
  motility
- Heritability +/- genetic
   aetiology ×

### Defining neuropathology



The London Classification of gastrointestinal neuromuscular pathology: report on behalf of the Gastro 2009 International Working Group

Charles H Knowles, Roberto De Giorgio, Raj P Kapur, et al.

Gut 2010 59: 882-887

doi: 10.1136/gut.2009.200444

Acta Neuropathol (2009) 118:271–301 DOI 10.1007/s00401-009-0527-y

#### CONSENSUS PAPER

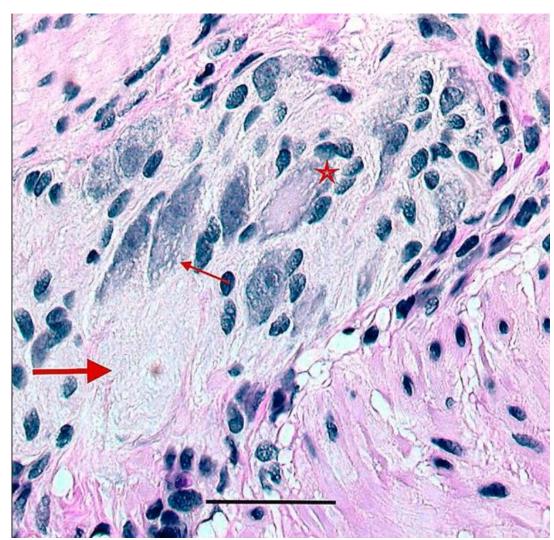
Gastrointestinal neuromuscular pathology: guidelines for histological techniques and reporting on behalf of the Gastro 2009 International Working Group

Charles H. Knowles · Roberto De Giorgio · Raj P. Kapur · Elisabeth Bruder · Gianrico Farrugia · Karel Geboes · Michael D. Gershon · John Hutson · Greger Lindberg · Joanne E. Martin · William A. Meier-Ruge · Peter J. Milla · Virpi V. Smith · Jean Marie Vandervinden · Béla Veress · Thilo Wedel

### Myenteric ganglion: lap biopsy: 20F CIPO

Swelling, chromatolysis, vacuolation, marginalisation of NissI granules

Ghost neuron (remnant nucleolus)





Contents lists available at ScienceDirect

### Best Practice & Research Clinical Gastroenterology



### Gastrointestinal neuromuscular pathology in chronic constipation

Charles H. Knowles, PhD, FRCS, Clinical Senior Lecturer and Hon Consultant Surgeon a,\*, Gianrico Farrugia, MD, Professor b,1

Table 1 Controlled studies using immunostaining for neuronal associated antigens in the colon of patients with STC.

Author	Year	N	Immunostain	Number of neurons	Degeneration
Benson et al [48]	1992	12	S100/NSE/NF <sub>2</sub> F <sub>11</sub>	Normal	Not stated
Park et al [49]	1995	14	PGP9.5/S100	Normal	No
Porter et al [44]	1998	15	NSE	Normal	No
Schouten et al [50]	1993	39	$NF_2F_{11}$	Normal	No
Romanska et al [51]	1996	6	NCAM	Normal	No
F-Pellegrini et al [52]	1999	16	NSE/S100	↓ Neurons	No
Wedel et al [43]	2001	10	PGP9.5	↓ Neurons & ganglia	Not stated
Knowles et al [47]	2001	36	NSE, PGP9.5, S100	Normal	No
Wedel et al [42]	2002	11	PGP9.5 <sup>a</sup>	↓ Neurons & ganglia	Not stated
Yu et al [53]	2002	14	NF2F11	↓ Neurons & ganglia	Not stated
Bassotti et al [54]	2006	26	NSE/S100	↓ Neurons	Apoptosis
Wattchow et al [45]	2008	4	Anti-Hu C/D	Normal <sup>b</sup>	No

KEY: PGP9.5 = protein gene product 9.5, NF = neurofilament, NSE = neuron-specific enolase.

#### Neurogastroenterology & Motility

Neurogastroenterol Motil (2011) 23, 115-124



#### **REVIEW ARTICLE**

Quantitation of cellular components of the enteric nervous system in the normal human gastrointestinal tract – report on behalf of the Gastro 2009 International Working Group

C. H. KNOWLES, \* B. VERESS, † R. P. KAPUR, ‡, § T. WEDEL, ¶ G. FARRUGIA, \* \* J.-M. VANDERWINDEN, † † K. GEBOES, ‡‡ V. V. SMITH, §§ J. E. MARTIN, ¶¶ G. LINDBERG, \*\*\* P. J. MILLA††† & R. DE GIORGIO!!!

### Enteric neuropathology

- Small N + selection bias (megacolon)
- Issues of technical validity (silver staining)
- Neuropathology not demonstrated by contemporary methods
- Normal variation too wide

<sup>&</sup>lt;sup>a</sup> Included nine patients from earlier publication (REF 2001).

b Non-significant reductions noted in neurons and ganglia.

Gut, 1986, 27, 41-48

Severe chronic constipation of young women: 'idiopathic slow transit constipation'

D M PRESTON AND J E LENNARD-JONES

From St Mark's Hospital, London

- N = 64 'white women': 1969-82
- 33 / 64 family history
- vs. 23/64 matched community controls
- 2 MZ twins unaffected



- N = 240 (120 + / FDR)
- FHx<sup>+</sup>: present younger due to detection bias (11-20 vs. 21-30 years), but otherwise phenotypically identical





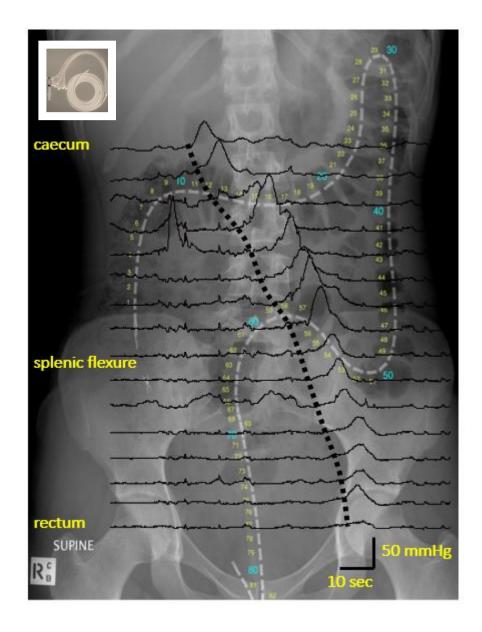
### Hereditary +/- genetic

- No controlled data support
- No mendelian evidence
- No twin studies
- STC not studied by GWAS (but related phenotypes e.g. IBS show low genomic heritability and very low polygenic risk)
- All candidate gene approaches negative



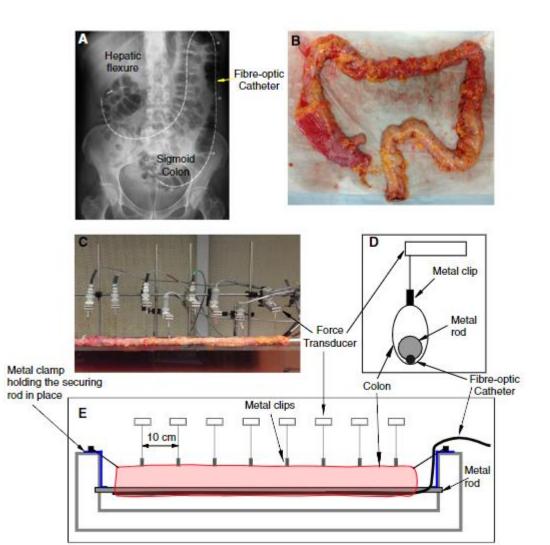


## STC is not an inertial problem



### high-amplitude propagated contractions (HAPCs)

author	year	n	HAPC frequency /24 h
Bassotti	1988	14	Į.
Bassotti	1994	25	į.
Leroi	2000	14	
Hagger	2003	8	
Herve	2004	40	
Ravi	2010	111	
Dinning	2010	16	
			*



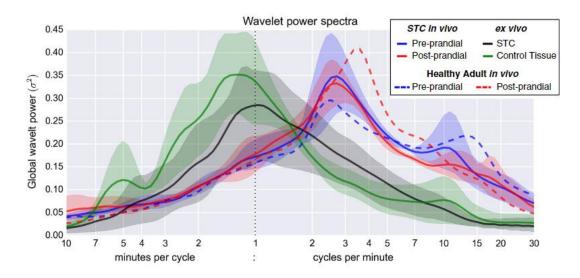
### **Neurogastroenterology & Motility**



Neurogastroenterol Motil (2016) 28, 1824-1835

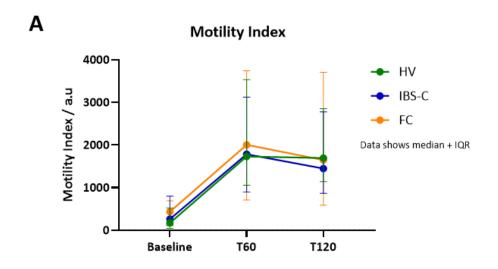
High-resolution colonic motility recordings *in vivo* compared with *ex vivo* recordings after colectomy, in patients with slow transit constipation

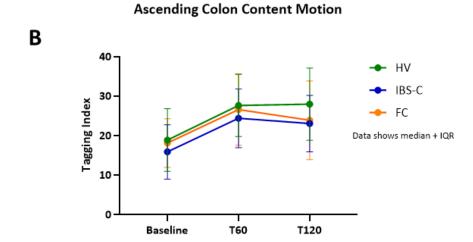
P. G. DINNING, \*,† T. C. SIA, \*,† R. KUMAR, \*,† R. MOHD ROSLI, \*,† M. KYLOH, \* D. A. WATTCHOW, \*,† L. WIKLENDT, \* S. J. H. BROOKES, \* M. COSTA \* & N. J. SPENCER \*



- Not inertia
- Some in vivo differences in propagating activity not evident ex vivo

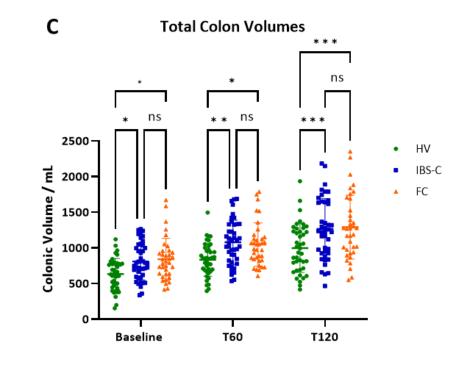
MRI Motility Index, ascending Colon Content Movement and Total Colonic Volumes after Moviprep challenge.

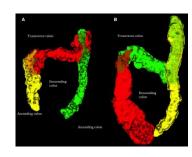






## **RECLAIM** study





Lam et al., NGM 2016; 28: 861-70; Wilkinson Smith et al., NGM 2020; 32: ee13942; Wilkinson Smith et al., Gut (under revision)



## The modern role for colectomy

## "Civilization's curse can be conquered," says England's Great Surgeon Sir W. Arbuthnot Lane, Bart., C. B.



"CONSTIPATION is the curse of evilication, the disease of diseases. There is no doubt that a shortage of the Vitamin B is responsible for and aggravates this complaint. Fresh yeart is perticularly rich in Vitamin B. It stimulates intestinal action and has a most important effect on constipation and its related digestive troubles and diseases. The diet of our community soffers from a shortage of Vitamin B, which deficiency is most readily made up by the addition of a small quantity of fresh yeast."

Mouthwothave

WHEN Sir William Arbuthnot Lane speaks the world listens!

Long famous as a brilliant surgeon, Sir Arbuthnot is today recognized as one of the greatest exponents of preventive medicine, health education and dietetic reform that England has ever known. He has devoted his life to the study of the intestinal tract.

In a recent interview Sir Arbuthnot made the characteristically forceful statement that constipation is "civilization's greatest curse." In his opinion constipation can be overcome through the important corrective food—fresh yeast.

In this he reflects the view of enlightened medical opinion everywhere.

Fleischmann's Yeast is as fresh as any garden vegetable. Unlike dangerous cathartic drugs, which "sour out" only the lower intestine, yeast keeps the entire digestive tract naturally clean, active—healthy.

When constipation goes, digestion has a clear track ahead! Appetite picks up. Your skin clears. Your whole being awakens to new vigor and alertness!

In a recent survey covering every state in the United States half the doctors reporting said they prescribed this remarkable food for health.

Eat 3 cakes of Fleischmann's Yeast daily, a cake before each meal or between meals. To get full benefit eat it regularly and over a sufficient period of time. Sold wherever food is sold.

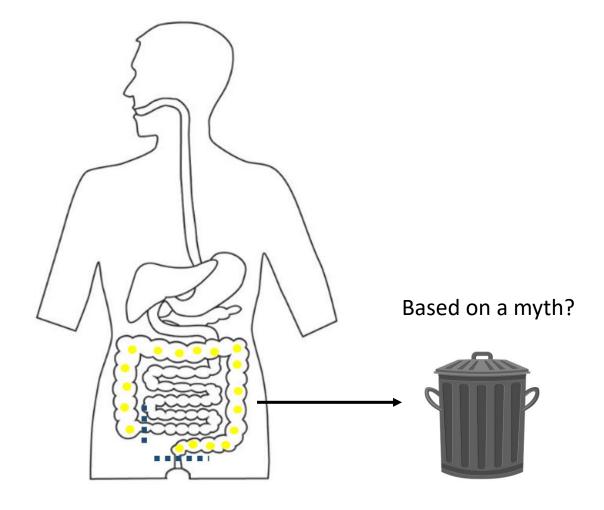


Three years ago Six W. Armuttunfor LASE founded with the late Earl of Oxford and Aquith and other prominent Britons the now famous New Health Society, which it teachers Companion of the Bath and Chewiler of the Legion of Home, Sir Arbathans las won the following distinctions in his field: Fellow, Royal College of Surgeons; President, Fellowing of Medicine; Consulting Surgeon Guy; Hoppital and Hospital for Sick Children; creator of modern methods of surgery copied throughout the world.



THEOAT, stomach, intestines form one continuous tube. When the colon is dogged poisons spread quickly throughout the system. Colds, beadaches, "nerves," skin and stomach disorders develop. To be radiantly well and happy keep the entire intestinal tract always clean, active and shealthy with Fleichmann's Yeast. Start today.

1908.....

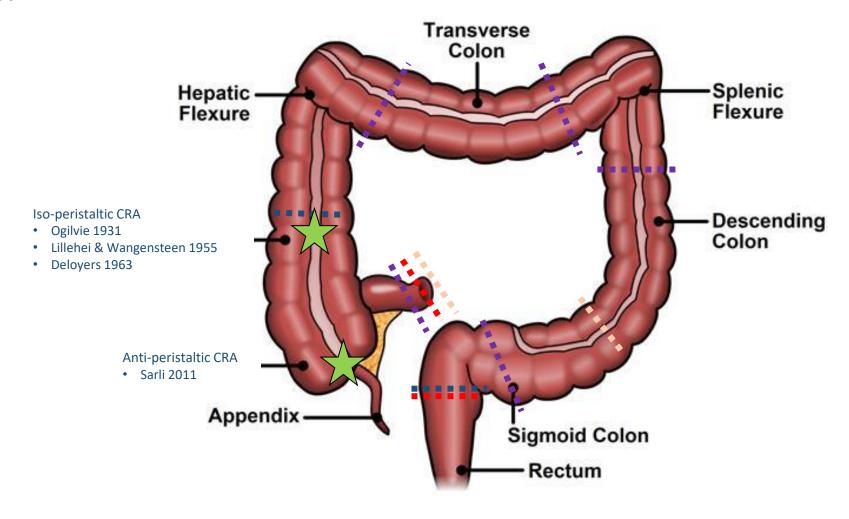


FLEISCHMANNS YEAST

Arbuthnot-Lane W. BMJ 1908: I: 126-30 Arbuthnot-Lane W. BMJ 1909: I: 1408-11

## Colectomy: procedural variation





### Colectomy: procedural variation

Table 1   Types of colonic resection for chronic constipation and access*					
Operation	Access and number of studies				
	Open	Laparoscopic			
Colectomy and ileorectal anastomosis	55	7			
Subtotal colectomy and ileosigmoid anastomosis	7	0			
Subtotal colectomy and isoperistaltic caecorectal anastomosis	9	0			
Subtotal colectomy and antiperistaltic caecorectal anastomosis	7	2			
Segmental resections (right and left hemicolectomy)	6	0			
*Studies report outcomes in >10 patients.					

## Colectomy: evidence

CapaCiTY surgical interventions for chronic constipation: systematic review and practice recommendations







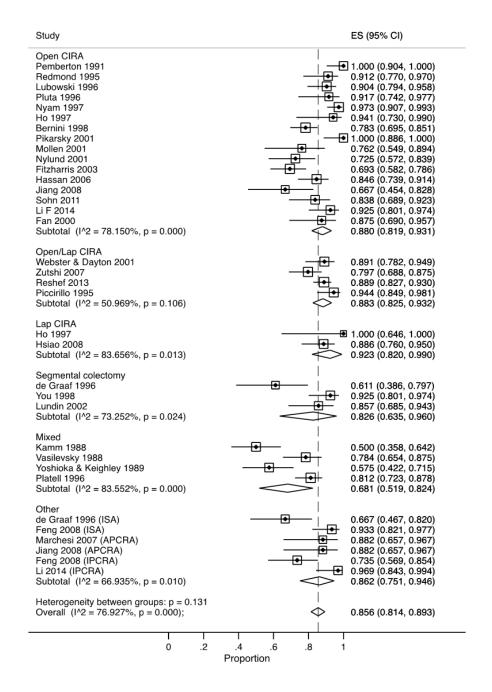




Pro	cedure	Number of reviewed studies by evidence level					
		1b	<u>2</u> b	3b	4	Total	
Cold	onic	0	1	0	39	40	
rese	ection						
Sus	pension	0	2	0	16	18	
prod	cedures						
Exc	isional	3	26	0	18	47	
prod	cedures						
Reir	nforcement	2	9	0	35	46	
prod	cedures						
Sac	ral	0	0	0	8	8	
neu	romodulation						
ALL	-	5	38	0	115	148	

### Colectomy: benefits

- Based on colectomy and ileorectal anastomosis
- Global rating scales (benefit)
  - Median 89% satisfied / very satisfied
  - Range 60-100% (based on 1233 patients reported)
- Mean weekly bowel
   frequency: pre = 1; post = 19
- Symptom scores: Cleveland Clinic score: pre: 22/24 vs. post 2/24





## Colectomy for constipation: time trends and impact based on the Nationwide Inpatient Sample, 1998–2011

A. Dudekula\*, S. Huftless<sup>‡</sup> & K. Bielefeldt\*-<sup>†</sup>

### **NEWS & VIEWS**

#### DEFECATION

## Colectomy for constipation —a time for renewed caution?

Charles H. Knowles

Refers to Dudekula, A. et al.. Colectomy for constipation: time trends and impact based on the nationwide inpatient sample. Aliment. Pharmacol. Ther. http://dx.doi.org/10.1111/apt.13415

Colectomy is rightly viewed as a last resort in selected patients with slow-transit constipation. A new study presents US national data that raises new concerns regarding the outcome of this procedure and perhaps questions whether it should be offered at all.

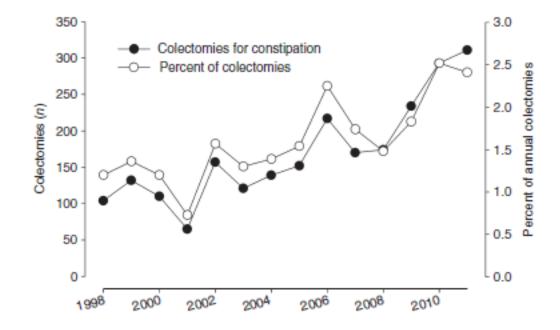
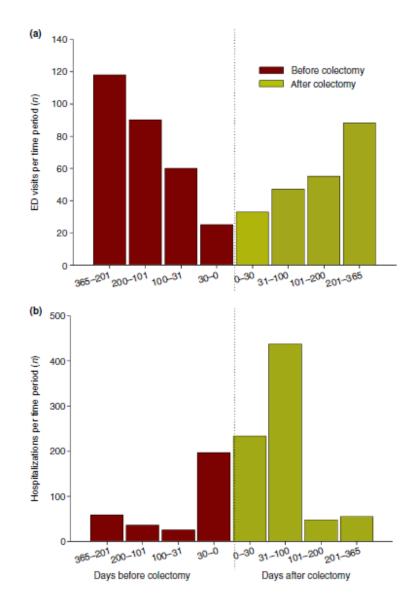


Table 2 | Post-operative complications after colectomy for constipation

Complication type	National
Hospitalisations (n)	1017
Any complication (%)	42.7
Wound complications (%)	
Post-operative haematoma	1
Post-operative seroma and wound dehiscence	0.6
Persistent post-operative fistula	1.5
Post-operative infection (%)	
Post-operative wound infection or abscess	2.8
Urinary tract (%)	
Urinary retention	2
Urinary tract infection	5.8
Acute renal failure	0.8
Pulmonary (%)	
Post-operative pneumonia, atelectasis or	3.2
aspiration	
Respiratory failure	2.5
ARDS, pneumothorax	1
Gastrointestinal tract (%)	
Intestinal obstruction, ileus, nausea/vomiting/	27
haemorrhage	
Cardiovascular (%)	
Cardiac arrest, phlebitis, deep venous thrombosis	0.6
Systemic (%)	
Post-operative fever, electrolyte abnormality	17.5
Mechanical (%)	
Accidental perforation	3.3
Bile duct injury	15
Intraoperative bleeding	2.3
Reopening of the surgical site	0.7

Incidence and type of perioperative complications based on diagnostic codes included in the discharge record associated with the index hospitalisation for colectomy.

### Florida & California



## Colectomy harms

Peri-operative morbidity (risk)

Small bowel obstruction: 14% (range 0-50%) ↓ **by lap** 10% (range 0-50%) **approach?** 

Re-operation (30 days): 10% (range 0-50%) approa

Anastomotic leak rate: 0% (range 0-11%)

Mortality rate: 0% (range 0-6%)

Eventual ileostomy: 5% (range 0-25%)

Post-operative function

Diarrhoea:  $14\% (0-35\%) \downarrow \text{by subtotal}$ Incontinence: 11% (0-47%) colectomy

• Abdominal pain: 37% (5-86%)

• Bloating: 26% (8-90%)

• Recurrent constipation: 14% (0-76%) ↑ by subtotal

• Ongoing laxative use: 17% (0-62%) colectomy

Adhesions
Opioids
New diagnostic
uncertainty



Systematic review doi:10.1111/codi.13775

## Surgery for constipation: systematic review and practice recommendations

#### Graded practice and future research recommendations

C. H. Knowles\*, U. Grossi\*, E. J. Horrocks\*, D. Pares†, P. F. Vollebregt\*, M. Chapman‡, S. Brown§, M. Mercer-Jones¶, A. B. Williams\*\*, Y. Yiannakou††, R. J. Hooper‡‡, N. Stevens‡‡ and J. Mason§§, on behalf of the NIHR CapaCiTY working group¶¶, The Pelvic floor Society\*\*\* and European Society of Coloproctology†††



## The Association of Coloproctology of Great Britain and Ireland





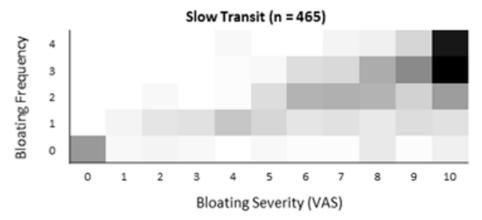




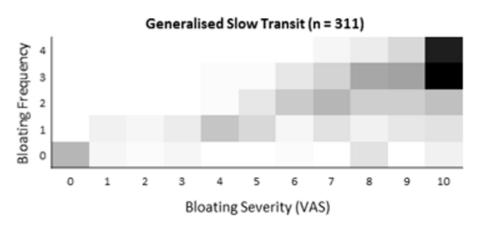
Colonic resection		
Patient selection		
1. Given uncertainty of outcome and potential for harm, colectomy	IV	C
should only be offered to patients when all other relevant		
treatments have failed		
2. Given concerns regarding outcome, the following represent		
absolute or relative contra-indications to colectomy		
a Concomitant upper GI symptoms (relative)	V	N
b Proven upper GI dysmotility (absolute)	IV	C
c Unproven generalised delay in colon transit (absolute)	IV	C
d Concomitant defecation disorder (relative)	IV	D
e Significant symptoms of abdominal pain and bloating, including diag-	IV	D
nosis of IBS (relative)		
f Faecal incontinence and/or functionally impaired anal sphincter	V	N
3. As a consequence of the above, colectomy should not be	IV	C
considered without precision phenotyping (clinical and radio-		
physiological)		
4. Given concerns regarding outcome, magnitude and irreversibility	IV	D
of colectomy, patients with concomitant defecation disorder		
should have this treated first including surgery for structural		
causes where relevant		
5. All patients considered for colectomy should have specialist	V	N
multidisciplinary discussion		
6. Formal psychological evaluation should be undertaken in all	V	N
patients considered for colectomy for constipation		
7. In view of need for specialist investigations and review, patients	V	N
should only undergo colectomy for constipation in centres with		
access to appropriate specialist services		

### STC: symptoms overlap with other phenotypes









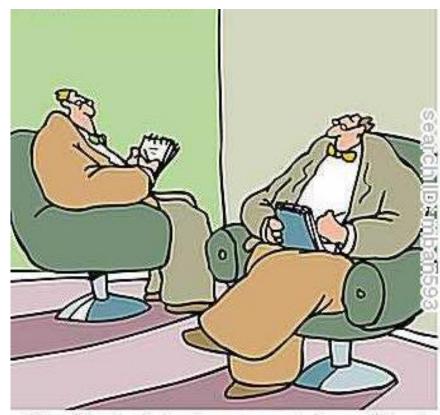
## The impact of laxative use upon symptoms in patients with proven slow transit constipation

Phil G Dinning<sup>1,2\*</sup>, Linda Hunt<sup>2</sup>, David Z Lubowski<sup>3</sup>, Jamshid S Kalantar<sup>4</sup>, Ian J Cook<sup>5</sup> and Mike P Jones<sup>6</sup>

### Laxatives modify stool form and frequency but not pain and bloating

Characteristics	Odds ratio	95% CI	P - value
Stool form	1.64	1.13, 2.40	0.009
Stool frequency	2.23	1.57, 3.17	< 0.001
FOCE	2.01	0.95, 4.22	0.06
Straining	1.10	0.50, 2.45	0.8
Abdominal pain	1.00	0.77, 1.30	>0.9
Abdominal bloating	1.04	0.78, 1.38	0.8

## Formal psychological examination



Won't admit he has a problem. Won't even admit he's the patient.

- Eating disorders
- Abuse: post-traumatic symptoms
- Opioid use / misuse
- Psychiatric disease
- Understanding of surgery and irreversibility

**Original Article** 

DOI: 10.1093/bjsopen/zrab049

## Slow-transit constipation and criteria for colectomy: a cross-sectional study of 1568 patients

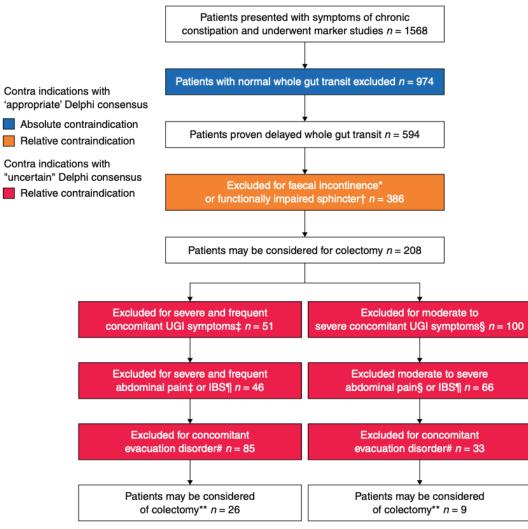
P. Chaichanavichkij (D 1,\*, P. F. Vollebregt (D 1, S. Z. Y. Tee<sup>2</sup>, S. M. Scott<sup>1</sup> and C. H. Knowles<sup>1</sup>

<sup>1</sup>National Bowel Research Centre and GI Physiology Unit, Blizard Institute, Centre for Neuroscience, Surgery & Trauma, Queen Mary University of London, London, UK

\*Correspondence to: 1st Floor, Abernathy Building, 2 Newark Street, London E1 2AT, UK (e-mail: p.chaichanavichkij@qmul.ac.uk)

1.7%

## Meet selection criteria for colectomy



<sup>&</sup>lt;sup>2</sup>Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

## If you do decide to do a colectomy

- MDT ratification [always]
- Consent in great detail
- Colectomy and IRA is the standard (removes rectosigmoid brake)
- Pre-test loop ileostomy advised for effect on symptoms (form high enough to use for second procedure)
- Covering ileostomy for colectomy (reverse after 3 months)
- Laparoscopic probably benefits [surgical skill]







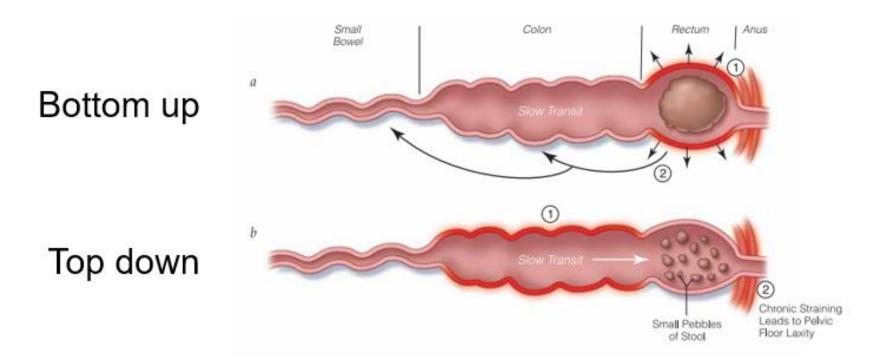
## Other options



# Chronic constipation in adults: Contemporary perspectives and clinical challenges. 2: Conservative, behavioural, medical and surgical treatment

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Maura Corsetti<sup>1,2</sup> | Steven Brown<sup>3</sup> | Giuseppe Chiarioni<sup>4,5</sup> | Eirini Dimidi<sup>6</sup> |
Thomas Dudding<sup>7</sup> | Anton Emmanuel<sup>8</sup> | Mark Fox<sup>9,10</sup> | Alexander C. Ford<sup>11,12</sup> | Pasquale Giordano<sup>13</sup> | Ugo Grossi<sup>14</sup> | Michelle Henderson<sup>15</sup> | Charles H. Knowles<sup>16</sup> |
P. Ronan O'Connell<sup>17</sup> | Eamonn M. M. Quigley<sup>18</sup> | Magnus Simren<sup>5,19</sup> | Robin Spiller<sup>1,2</sup> | Kevin Whelan<sup>6</sup> | William E. Whitehead<sup>5</sup> | Andrew B. Williams<sup>20</sup> | S. Mark Scott<sup>16</sup>
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### Concomitant obstructed defaecation



CHRONIC CONSTIPATION IN
ADULTS: CONTEMPORARY
PERSPECTIVES AND CLINICAL
CHALLENGES. 2. CONSERVATIVE,
BEHAVIOURAL, MEDICAL AND
SURGICAL TREATMENT

MDT to discuss surgical options and alternative management strategies



No surgical target defined



Generalised slow transit constipation without absolute and relative contraindications to surgical intervention





Discuss alternatives after refocussed discussion including transanal irrigation, untried behavioural interventions and pharmacology





Relief of symptoms with ileostomy but does not want permanent stoma

Colectomy and ileo-rectal anastomosis

Posterior compartment prolapse syndrome with high grade intussusception +/- rectocoele



Consider laparoscopic ventral mesh rectopexy or alternative e.g. STARR +/- adjuncts 1

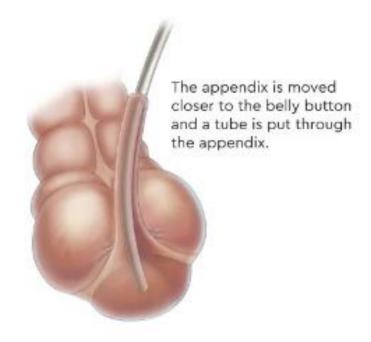
Posterior compartment prolapse syndrome with dominant rectocele +/- intussusception



Rectocele repair via transvaginal or transanal route +/- adjuncts 1

Neurogastroenterology & Motility. 2021;33:e14070. https://doi.org/10.1111/nmo.14070

## Anterograde colonic enema



### KEY:

- Thin
- Native appendix present

- Alternative to stoma
- Well established in paediatric practice
- Several variations
  - Appendicostomy (best)
  - Tunnel
    - Caecal button
    - Chait tube
  - Left colonic
    - Various inc. percutaneous endoscopic colostomy
- Outcomes variable in adults
  - 50% at 3 years
  - Stenosis / leakage / failure to work
  - Caecal volvulus (1%)

### Sacral neuromodulation

### SNM: Observational data 2010

**Neurogastroenterology** 



### Sacral nerve stimulation for intractable constipation

Michael A Kamm, <sup>1,2</sup> Thomas C Dudding, <sup>2</sup> Jarno Melenhorst, <sup>3</sup> Michael Jarrett, <sup>2</sup> Zengri Wang, <sup>4</sup> Steen Buntzen, <sup>5</sup> Claes Johansson, <sup>6</sup> Søren Laurberg, <sup>5</sup> Harald Rosen, <sup>7</sup> Carolynne J Vaizey, <sup>2</sup> Klaus Matzel, <sup>8</sup> Cor Baeten <sup>3</sup>

**Conclusion** SNS is effective in the treatment of idiopathic slow and normal transit constipation resistant to conservative treatment.

Clinical Trial Number NCT00200005.

Gut 2010;59:333-340. doi:10.1136/gut.2009.187989



A randomized double-blinded sham-controlled cross-over trial of tined-lead sacral nerve stimulation testing for chronic constipation

Yan Yiannakou<sup>a</sup>, Kevin Etherson<sup>d</sup>, Helen Close<sup>e</sup>, Adetayo Kasim<sup>e</sup>, Mark Mercer-Jones<sup>h</sup>, Stefan Plusa<sup>g</sup>, Rebecca Maier<sup>l</sup>, Susan Green<sup>b</sup>, Jeremy Cundall<sup>b</sup>, Charles Knowles<sup>l</sup> and James Mason<sup>l</sup>

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### RCTs 2015 & 2017

Treatment Efficacy of Sacral Nerve Stimulation in Slow Transit Constipation: A Two-Phase, Double-Blind Randomized Controlled Crossover Study

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Am J Gastroenterol 2015; 110:733-740;

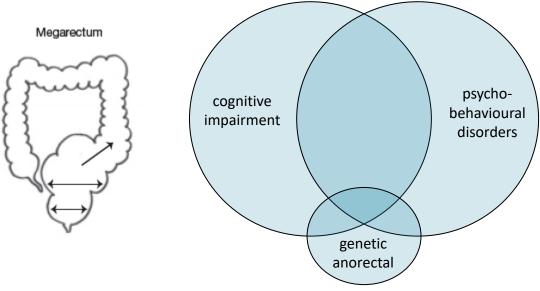
Randomized clinical trial

## Randomized clinical trial of sacral nerve stimulation for refractory constipation

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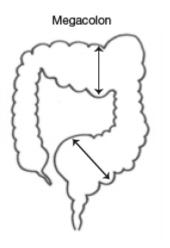
B7S 2017; 104: 205-213

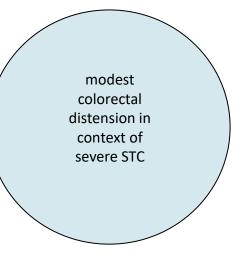
## A slide on megarectum & megacolon





- Full bowel prep
- Loop ileostomy (6 months)
- Low anterior resection
- Reverse ileostomy





- Manage as STC
- Usually require colectomy or ileostomy

### Summary





STC is a non-specific measurement not a disease



The concept of removing a "diseased" colon is flawed



Colectomy has few indications in modern era and should be used with caution



Of other options, ileostomy and ACE have a role



