UPMC
LIFE CHANGING MEDICINE

Surgery for IBD: Timing is everything

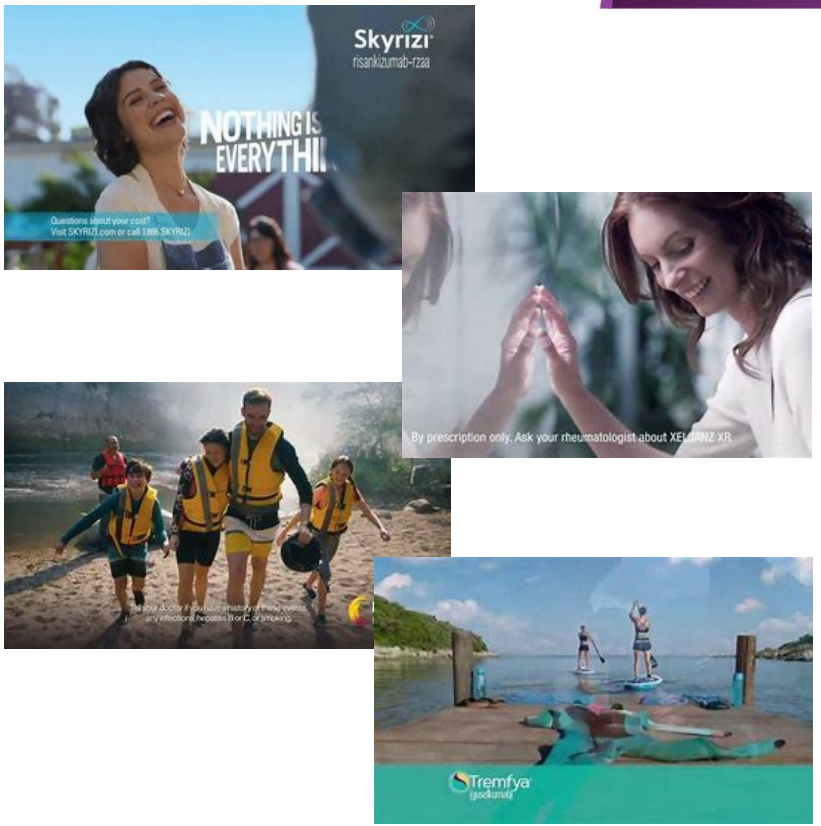
Sean Whelan, MD FACS FASCRS

Associate Professor, Division of Colon and Rectal Surgery

Chair of Surgery, UPMC St Margaret

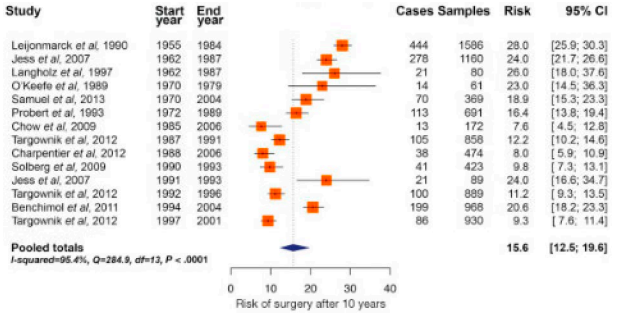
One day...

- Medical treatment will eliminate IBD

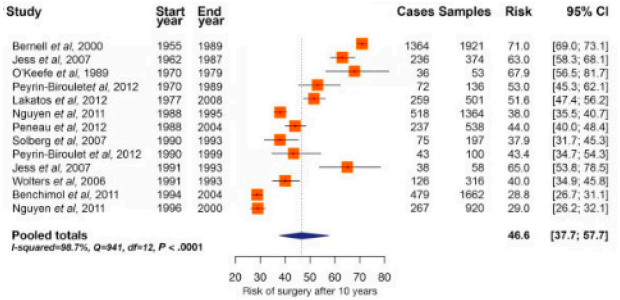


...but that day is not today

- About 20% of UC patients require surgery



- About 70% of CD patients require surgery



...but that day is not today

- About 20% of UC patients require surgery

- About 70% of CD patients require surgery

Challenges in surgical management of IBD

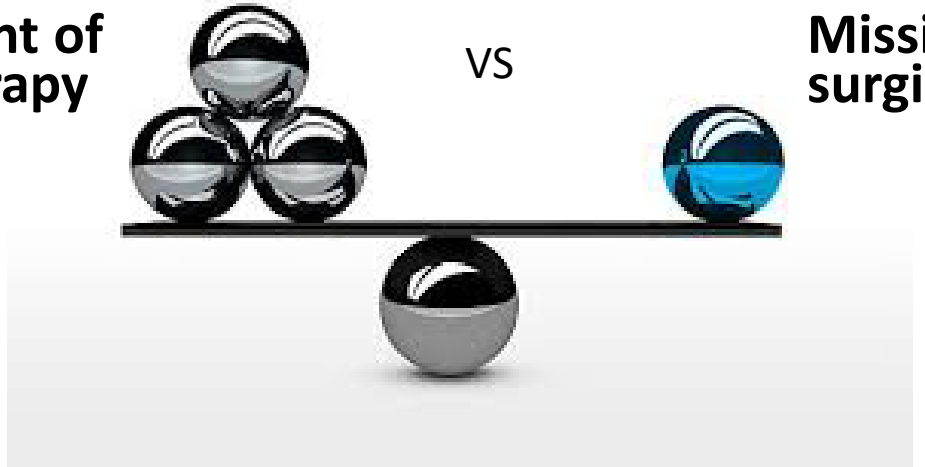
- Complex disease with imperfect prognostic data
- Surgery is often point of no return
- Patient VS physician perspectives
- Multidisciplinary approach

Decision for surgery

Premature abandonment of medical therapy

VS

Missing optimal surgical timing



Timing is Everything

- Surgery is an **OPTION**, not a last resort

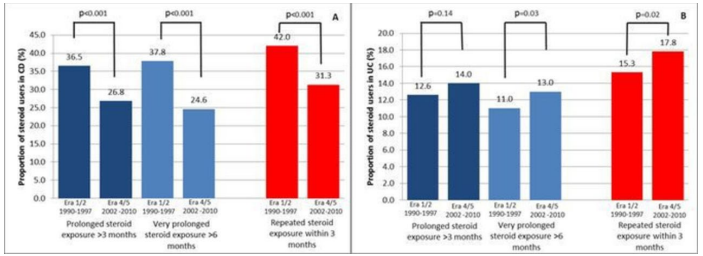
- We are missing optimal surgical timing in both Elective and Emergent settings

Only two things can happen?

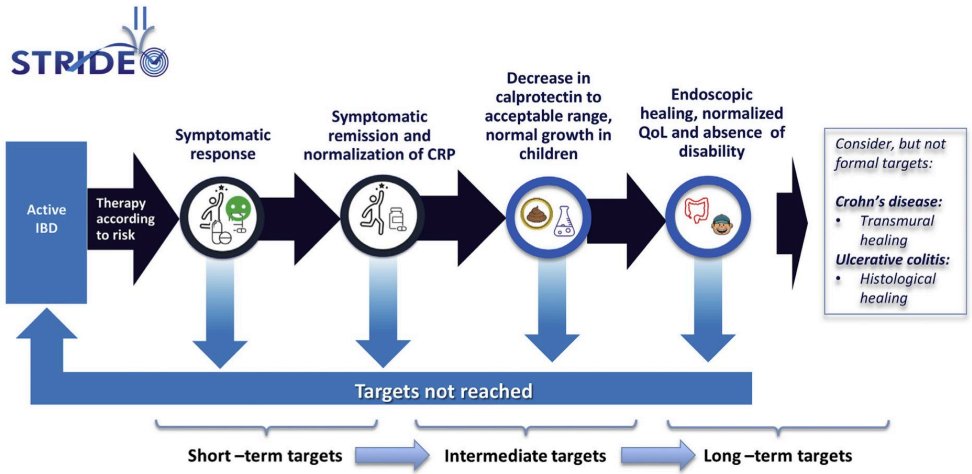
Only two things can happen?

Indications for Surgery

- Failure of medical therapy
  - Lack/Loss of Response
- Steroid dependence
  - Inability to reduce prednisone to 10mg in 3 months or steroid-free interval < 3-6 months
- Anatomic Complication
  - Perforation, Stricture, Fistula
- Dysplasia/Cancer



Defining response



- Variable definitions of endoscopic and clinical remission
- Time to response/remission/healing are long: 4-24wks depending on agent
- No universal definition for lack/loss of response
- LOR can be high
- No standardized guidelines on treatment optimization/monitoring

The case for early surgery

- Elective management of isolated disease
- Emergent management of acute colitis
- System factors
  - Economic impact
  - Recurrent disease/subsequent treatment
- Patient factors
  - Risk of malignancy
  - Perception of surgery / QOL

LIR!C

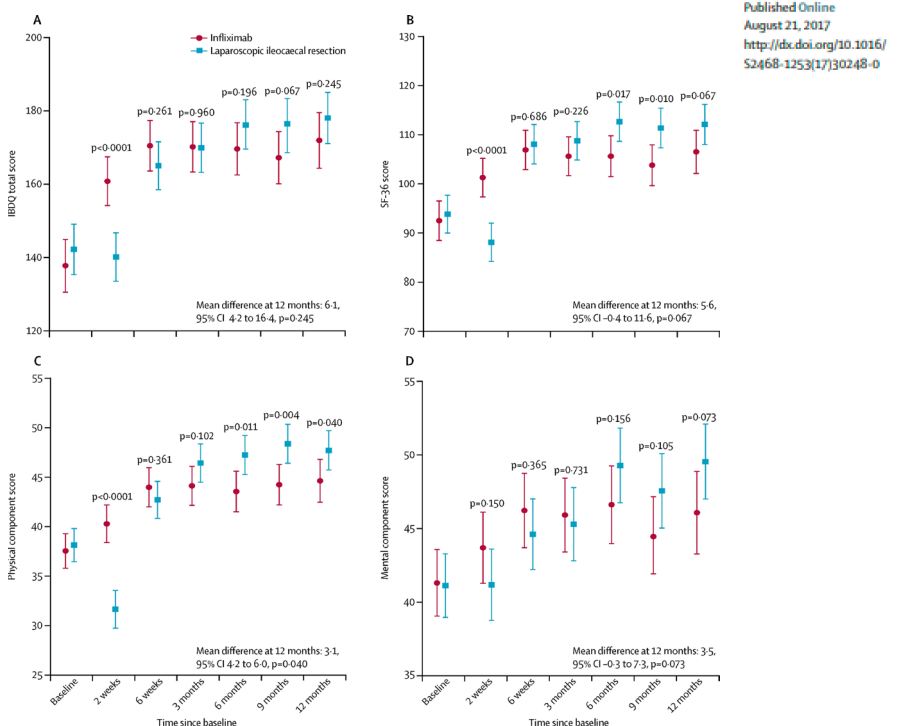
- 143 patients failed 3 months of steroids, thiopurines, methotrexate
  - 73 – Lap IC resection
  - 70 – Infliximab
- 1° outcome – IBDQ 12months
- After 4yrs follow up
  - 19(26%) of surgery had anti-TNF
  - 26(37%) of infliximab had surgery

Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease: a randomised controlled, open-label, multicentre trial

*Cyriel Y Ponsioen, E Joline de Graaf, Emma J Eshuis, Tjibbe J Gardenbroek, Patrick M M Bossuyt, Ailsa Hart, Janindra Warusavitarne, Christianne J Buskens, Ad A van Bodegraven, Menno A Brink, Esther C J Consten, Bart A van Wagensveld, Marno C M Rijk, Rogier M P H Crolla, Casper G Noomen, Alexander P J Houdijk, Rosalie C Mallant, Maarten Boom, Willem A Marsman, Hein B Stockmann, Bregje Mol, A Jeroen de Graaf, Pieter C Stokkers, Geert R D'Haens, Willem A Bemelman, on behalf of the LIR!C study group**

Lancet Gastroenterol Hepatol 2017; 2: 785–92

Published Online August 21, 2017 http://dx.doi.org/10.1016/S2468-1253(17)30248-0



- What about the risk of subsequent surgery?

Early surgery in CD

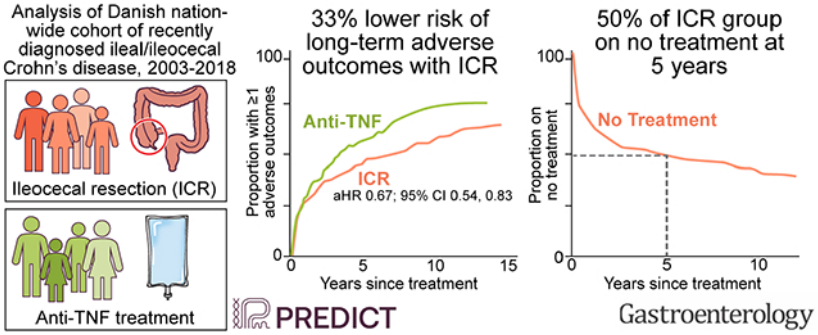
Early ileocecal resection for Crohn's disease is associated with improved long-term outcomes compared to anti-tumor necrosis factor therapy: a population-based cohort study

Manasi Agrawal [1,2,*], Anthony C Ebert [1,*], Gry Poulsen [1], Ryan C Ungaro [2], Adam S Faye [3], Tine Jess [1,4], Jean-Frederic Colombel [2,*], Kristine H Allin [1,4,*]

Author information · Article notes · Copyright and License information

PMCID: PMC10527197 NIHMSID: NIHMS1909225 PMID: 37321356

- 1279 IC Crohn's disease patients
  - 45.4% ICR vs 54.6% anti-TNF within 1yr of dx
  - Composite outcome in
    - 273 of ICR
    - 318 of anti-TNF



Early surgery in CD

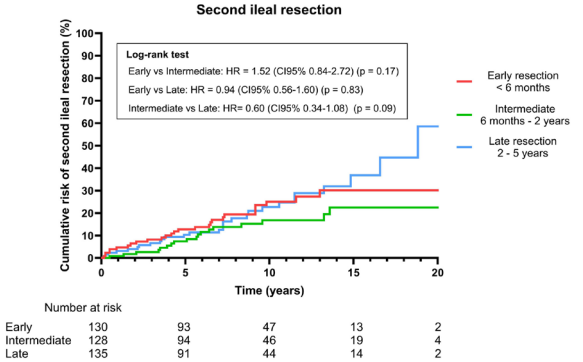
Early ileal resection in Crohn's disease is not associated with severe long-term outcomes: The ERIC study

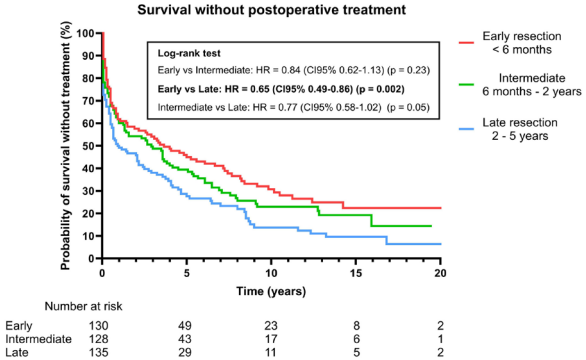
Nathan Grellier, Julien Kirchgesner, Mathieu Uzzan, Paul Mclellan, Carmen Stefanescu, Jérémie H. Lefèvre, Xavier Treton, Yves Panis, Harry Sokol, Laurent Beaugerie, the ERIC Study group, Philippe Seksik

First published: 05 September 2024 | https://doi.org/10.1111/apt.18247 | Citations: 2

- 393 IC resections for CD
  - 130 Early (0-6mo)
  - 128 Intermed (6mo– 2yr)
  - 135 Late (2yr – 5yr)

- Early had no diff in second resection at 10yrs, fewer postop tx's, and less morphologic recurrence





Dangers of Late Surgery

- Inflammatory complications happen in 50% at some point
- Time from surgical indication to surgery increases complications
- Postponing surgery leads to worse outcomes
  - Abscess
  - Malnutrition
  - Immunosuppression
- Postop complications lead to early recurrence

Perforating Crohn's ileitis: Delay of surgery is associated with inferior postoperative outcome

Igors Iesalnieks, MD, Alexandra Kilger, MD, Heidi Glaß, MD, Florian Obermeier, MD, Ayman Agha, MD, Hans J. Schlitt Author Notes

Inflammatory Bowel Diseases, Volume 16, Issue 12, 1 December 2010, Pages 2125–2130,
https://doi.org/10.1002/ibd.21303

- Delay of surgery increases:
  - Inflammatory complications
  - Malnutrition
  - Postop infection

Table 2

Variables Differing Between Patients with Various Duration of Clinical Deterioration

Duration of Clinical Deterioration	Inflammatory Mass Consisting of >3 Structures	Multiple-drug Combination	Patients with Weight Loss of >5 %	Proportion of Patients Taking Immunosuppressive Drugs	Postoperative IASC Rate
<1 month ($n = 21$)	23%	5%	0%	5%	9%
1–5 months ($n = 90$)	20%	19%	41%	17%	14 %
6–12 months ($n = 64$)	34%	27%	33%	20%	36%
>12 months ($n = 41$)	56%	38%	53%	34%	24%

For all variables, statistically significant differences between groups.

- Delay is getting worse over time
  - More multidrug combos
  - More staged operations

Table 3

Drug-intake, Duration of Clinical Deterioration, and Morbidity Changes During the Study Period

Study Period	Median Duration of Clinical Deterioration, Months	Multiple-drug Combination	Preoperative Weight Loss of >5%	Inflammatory Mass Consisting of >3 Structures	Resection without an Anastomosis (Ileostomy Rate)	Postoperative IASC Rate
1992–1999 ($n = 72$)	5	15%	30%	28%	1.4%	7%
2000–2004 ($n = 73$)	4	20%	27%	23%	1.4%	18%
2005–2009 ($n = 86$)	6	34%	51%	46%	18.6%	36%

Statistically significant differences between group "2005–2009" compared to two other groups.

UPMC
LIFE CHANGING MEDICINE

Late is too late? Surgical timing and postoperative complications after primary ileocolic resection for Crohn's disease

E. Lavorini[1] · M. E. Allaix[1] · C. A. Ammirati[1] · M. Astegiano[2] · M. Morino[1] · A. Resegotti[1]

Accepted: 2 March 2022 / Published online: 10 March 2022

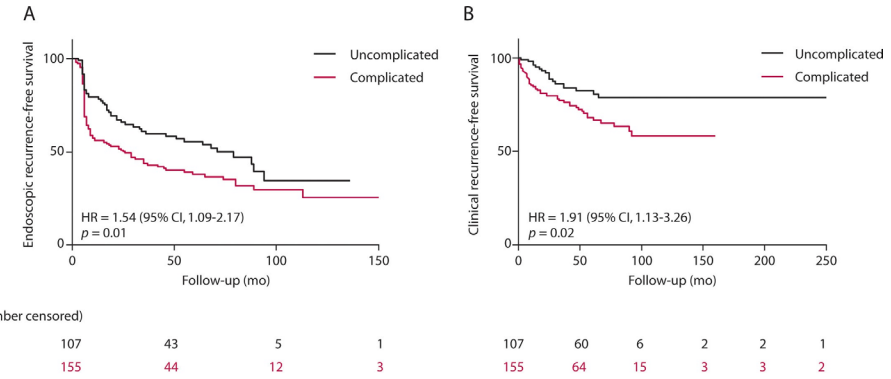
- Increased complications (overall and anastomotic leak)
  - Time from dx to surg
  - Use of steroids

Table 3 Univariate and multivariate analyses of risk factors for major complications

	Surgical complications: major complications					
	Univariate analyses			Multivariate analysis		
	OR	95% Conf.Interval	*p*	OR	95% Conf.Interval	*p*
Males (ref. females)	1.49	(0.67–3.31)	0.333			
Age (yrs)	1.01	(0.99–1.04)	0.408			
Albumin (g/dl)	0.82	(0.39–1.72)	0.608			
Smoking	1.05	(0.47–2.37)	0.904			
Time interval between diagnosis of CD and surgery (yrs)	1.08	(1.02–1.14)	0.007	1.10	(1.03–1.17)	0.002
Steroids	4.49	(2.03–9.95)	<0.001	5.45	(2.39–12.43)	<0.001
Fistulas	1.71	(0.78–3.75)	0.182			
Abscess	0.95	(0.31–2.88)	0.931			
Handsewn anastomosis (ref stapled)	1.40	(0.64–3.04)	0.400			

Complications ↑ Recurrence

- Postop complications are independent risk factors for:
  - Increased rate of recurrence
  - Decreased time to recurrence



Carvello et al. *Dis Colon Rectum* 2023;66(5):691-9

The case for early surgery

- Elective management of isolated disease
- Emergent management of acute colitis
- System factors
  - Economic impact
  - Recurrent disease/subsequent treatment
- Patient factors
  - Risk of malignancy
  - Perception of surgery / QOL

Acute Severe Colitis

- May occur in well-established IBD

OR

- Initial presentation of new IBD
  - Ddx can be broad: infectious/ischemic colitidies
  - Even path can be difficult re: Crohn's vs UC

- 1/3 need colectomy within 6wks of starting therapy

Table 4. Proposed American College of Gastroenterology Ulcerative Colitis Activity Index[a]

	Remission	Mild	Moderate-severe	Fulminant
Stools (no./d)	Formed stools	<4	>6	>10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	<75% of normal	Transfusion required
ESR	<30	<30	>30	>30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
FC (μg/g)	<150–200	>150–200	>150–200	>150–200
Endoscopy (Mayo subscore)	0–1	1	2–3	3
UCEIS	0–1	2–4	5–8	7–8

[a]Modified from reference 44.
The above factors are general guides for disease activity. With the exception of remission, a patient does not need to have all the factors to be considered in a specific category.
CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FC, fecal calprotectin; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

ACG Clinical Guideline: Ulcerative Colitis in Adults Official journal of the American College of Gastroenterology | ACG114(3):384-413, March 2019

Acute Severe Colitis

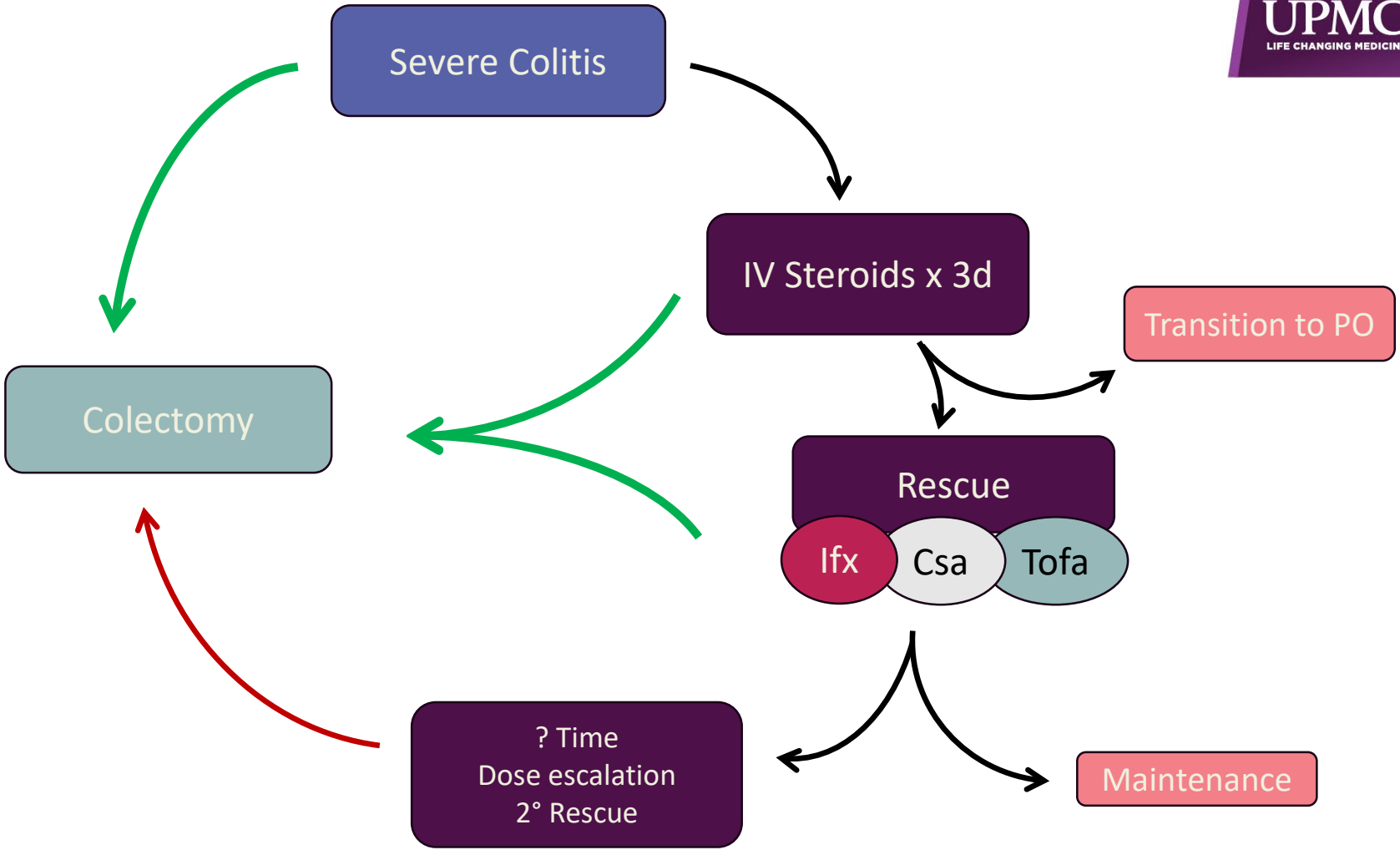
Clinical
- Ho-index
- Travis score

Lab
- CAR
- FC

Endoscopic
- UCEIS
- MES

- Rescue
- Surgery

- Perforation
- Toxic megacolon
- Complication


Severe Colitis
IV Steroids x 3d
Transition to PO
Colectomy
Rescue
Ifx
Csa
Tofa
? Time
Dose escalation
2° Rescue
Maintenance

Emergent colectomy – time is of the essence

- Overall mortality of colectomy
  - Elective – 0.7%
  - Emergent – 5.4%

- Mortality in emergent TAC/EI – 7.4%

Table 3 Mortality Rate by Type of Colectomy Performed Among Patients With Ulcerative Colitis Who Were Admitted Emergently and Electively

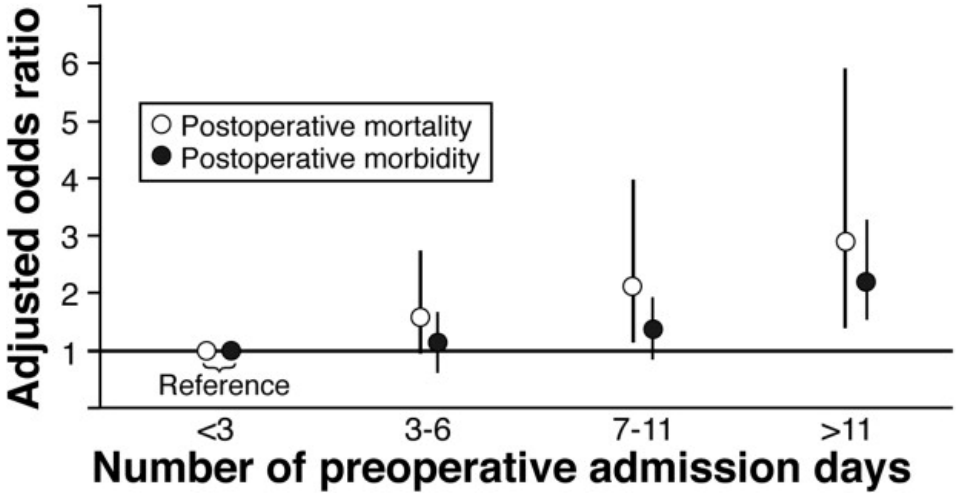
Colectomy type	Mortality, % (95% CI)		
	Total, n = 7108	Emergent or urgent, n = 2186[a]	Elective, n = 4060[a]
Pouch	0.15 (0.05–0.45), n = 2144	0.0 (0.0–0.0), n = 384	0.2 (0.1–0.6), n = 1475
Permanent ileostomy	3.6 (2.9–4.4), n = 2370	6.8 (5.3–8.6), n = 917	1.0 (0.5–1.8), n = 1150
Proctocolectomy and temporary ileostomy	0.3 (0.1–1.1), n = 1010	1.6 (0.5–4.9), n = 220	0.0 (0.0–0.0), n = 684
Ileorectal anastomosis	1.6 (0.6–4.0), n = 246	5.7 (2.2–14.2), n = 67	0.0 (0.0–0.0) n = 147
Total abdominal colectomy, ileostomy, and rectal stump	5.5 (4.1–7.4), n = 975	7.4 (5.2–10.4), n = 483	2.8 (1.5–5.0), n = 406
Nonclassified	4.7 (2.9–7.6), n = 358	10.6 (6.2–17.8), n = 115	1.5 (0.5–4.8), n = 198
All surgeries	2.3 (2.0–2.8)	5.4 (4.4–6.5)	0.7 (0.5–1.0)

[a] Eight hundred sixty-two observations were missing data on admission type. Percentages and 95% confidence intervals were weighted to reflect national estimates.

Kaplan GG, McCarthy EP, Ayanian JZ, Korzenik J, Hodin R, Sands BE. Impact of hospital volume on postoperative morbidity and mortality following a colectomy for ulcerative colitis. *Gastroenterology*. 2008; **134**(3): 680–687.e1

Emergent colectomy – time is of the essence

- Delay = Complications
- Preop LOS >6d
  - Odds ratio of >2 for in-hospital mortality



Kaplan GG, McCarthy EP, Ayanian JZ, Korzenik J, Hodin R, Sands BE. Impact of hospital volume on postoperative morbidity and mortality following a colectomy for ulcerative colitis. *Gastroenterology*. 2008; **134**(3): 680–687.e1

↑ Preop LOS ↑ Complications

- 80 patients
  - Emergent colectomy after failing IV steroids
  - 60% had one complication
  - Patients w maj complications had sig ↑preop LOS

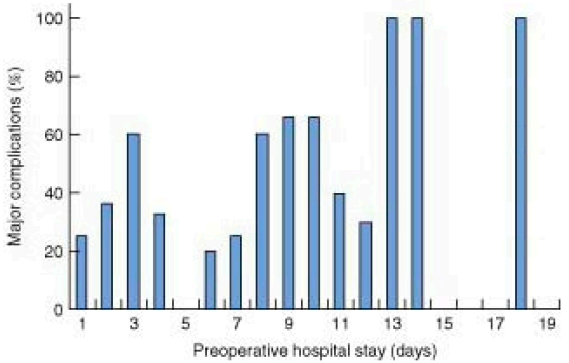
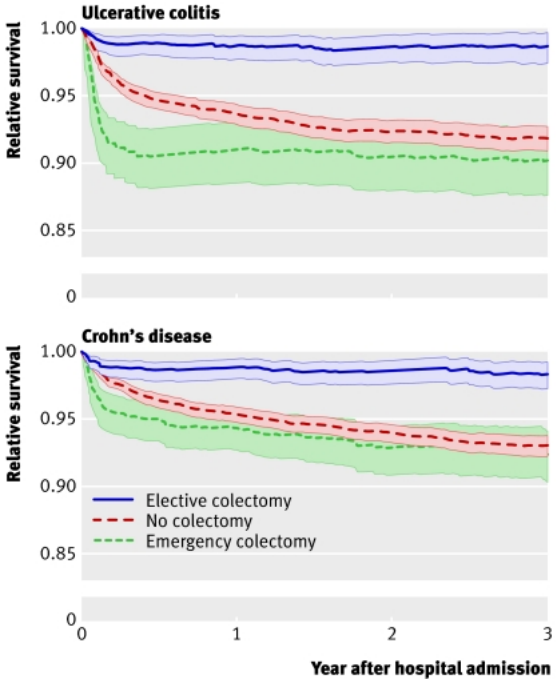


Fig. 1 Rate of major complications in relation to preoperative hospital stay

Randall J, Singh B, Warren BF, Travis SPL, Mortensen NJ, George BD. Delayed surgery for acute severe colitis is associated with increased risk of postoperative complications. *Br J Surg*. 2010; **97**(3): 404–409.

Ounce of prevention or Pound of Flesh?

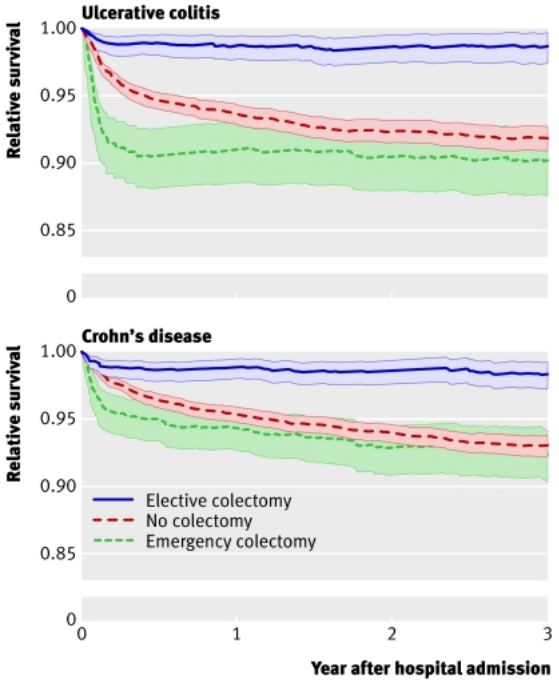
- Threshold for elective colectomy too high?
  - 3-yr survival improved in elective colectomy vs emergent or no colectomy
  - Short-term risks confined to first 2 months and then returns to gen-pop



Roberts SE, Williams JG, Yeates D, Goldacre MJ. Mortality in patients with and without colectomy admitted to hospital for ulcerative colitis and Crohn's disease: record linkage studies. BMJ. 2007;335(7628):1033

Ounce of prevention or Pound of Flesh?

- Threshold for elective colectomy too high?
  - Mortality for emergency UC surgery is initially high but returns to gen pop. NOT seen in CD
  - 3-yr mortality after NO surgery almost as high as emergency surgery
    - If operated patients were sicker, does this make NON-OP the more dangerous option?



Roberts SE, Williams JG, Yeates D, Goldacre MJ. Mortality in patients with and without colectomy admitted to hospital for ulcerative colitis and Crohn's disease: record linkage studies. BMJ. 2007;335(7628):1033

System burden of NOM

- Medications account for a largest portion of healthcare expenditure in IBD
- Many require injections
- Infection risk
- High utilization for LOR and secondary treatments
- Malignancy risk (conflicting data)

Malignant potential

Gut 2001;**48**:526–535

The risk of colorectal cancer in ulcerative colitis: a meta-analysis

J A Eaden, K R Abrams, J F Mayberry

- Meta-analysis
- 116 studies (41 reported colitis duration)
- Overall incidence of cancer: 3.7%
- Cancer incidence
  - 10yrs: 2%
  - 20yrs: 8%
  - 30yrs: 18%

Forty-Year Analysis of Colonoscopic Surveillance Program for Neoplasia in Ulcerative Colitis: An Updated Overview

Chang-Ho Ryan Choi, MBBS, MSc[1,2], Matthew D. Rutter, MBBS, MD, FRCP[3], Alan Askari, MBChB, MRCS[4], Gui Han Lee, MBBS, MRCS[4], Janindra Warusavitarne, BMed, FRACS, PhD[4], Morgan Moorghen, MBChB, MD, FRCPath[5], Siwan Thomas-Gibson, MBBS, MRCP, MD[6], Brian P. Saunders, MBBS, MD, FRCP[6], Trevor A. Graham, PhD[2,7] and Ailsa L. Hart, BMBCh, PhD, FRCP[1,7]

Time since UC symptom onset (year)

Duration of UC (up to *n* years)	10	20	30	40	50
Number at risk	1,345	1,086.5	635.5	290.5	99.5
Censored	60	455	385	255	107
CRC incidence	1	31	25	10	4
Cumulative incidence of CRC	0.07%	2.9%	6.7%	10.0%	13.6%
s.e.	0.001	0.005	0.009	0.013	0.022
Hazard rate	0.007%	0.29%	0.40%	0.35%	0.41%
s.e. of hazard rate	<0.001	<0.001	<0.001	0.001	0.002

UPMC
LIFE CHANGING MEDICINE

Forty-Year Analysis of Colonoscopic Surveillance Program for Neoplasia in Ulcerative Colitis: An Updated Overview

Chang-Ho Ryan Choi, MBBS, MSc[1,2], Matthew D. Rutter, MBBS, MD, FRCP[3], Alan Askari, MBChB, MRCS[4], Gui Han Lee, MBBS, MRCS[4], Janindra Warusavitarne, BMed, FRACS, PhD[4], Morgan Moorghen, MBChB, MD, FRCPath[5], Siwan Thomas-Gibson, MBBS, MRCP, MD[6], Brian P. Saunders, MBBS, MD, FRCP[6], Trevor A. Graham, PhD[2,7] and Ailsa L. Hart, BMBCh, PhD, FRCP[1,7]

Time since neoplasia diagnosis or index colonoscopy if patient had no neoplasia (year)

	Cumulative incidence of CRC (%)									
Years from dysplasia diagnosis	1	2	3	4	5	6	7	8	9	10
No dysplasia	0.1	0.2	0.4	0.6	0.7	0.9	1.1	1.1	1.4	1.5
Adenoma	1.4	1.4	1.4	1.4	3.2	3.2	3.2	3.2	6.5	6.5
Indefinite for dysplasia	6.3	10.7	10.7	18.8	24.9	24.9	24.9	24.9	28.9	28.9
LGD	9.9	11.8	18.4	19.7	21.2	24.7	29.0	29.0	29.0	32.8
HGD	41	44.7	54.3	54.3	–	–	–	–	–	–

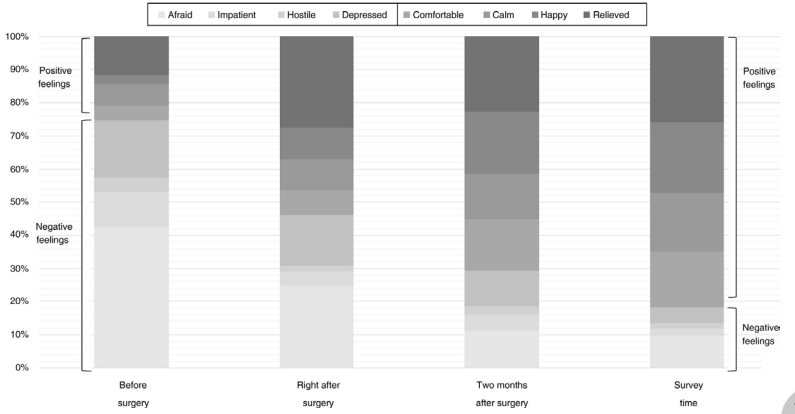
Reasons to avoid surgery

- Operative and perioperative morbidity
- Possible stoma
- Risk of needing future surgery/SGS
- Medications work!

Patient perceptions of surgery

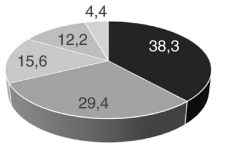
- Before Surgery
  - One of the biggest fears of managing the disease
  - Possible complications
  - Possible permanent stoma
  - “last resort”
    - Sometimes not even aware it is an option
  - 16% get Primary info from internet
    - 82% get some info from internet
- After Surgery
  - High level of satisfaction
  - Many (35%) regret delay in surgery
  - Many would want earlier consultation with a surgeon
  - High stoma acceptance rate

Patient perceptions of surgery



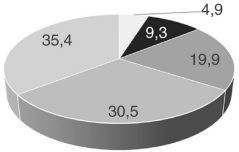
Patients' predominant feelings before and after surgery

Preoperative concerns and postoperative acceptance of stoma



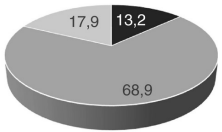
Preoperative concerns about stoma

- It could be permanent
- Leak
- Other
- Cosmetic issues
- Odor



Acceptance of stoma

- Other
- strongly adversed, never accept it anymore
- useful in some situation
- strongly adversed to it, but accept it if needed



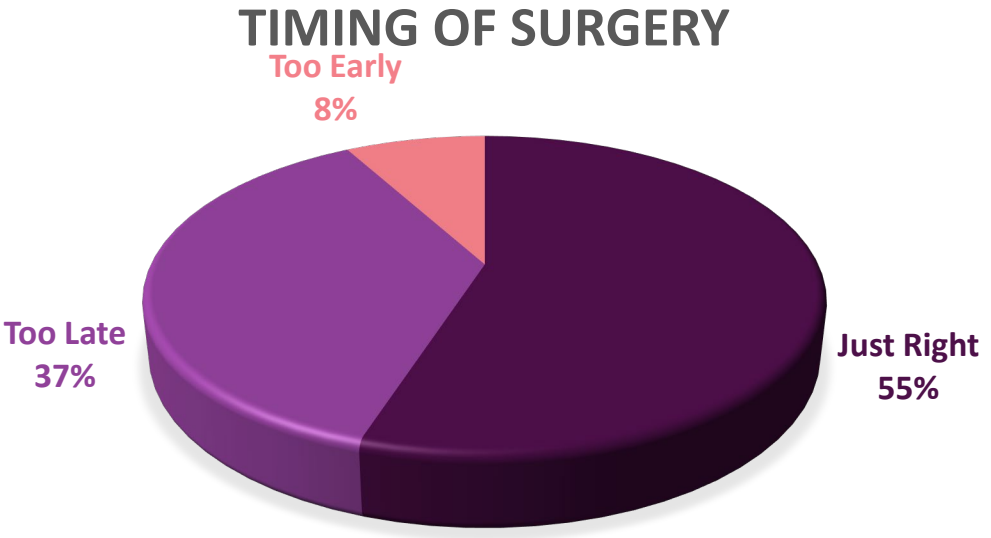
Living with a stoma

- living with the stoma was worse than expected
- living with the stoma was better than expected
- as expected

Colorectal Disease, Volume: 23, Issue: 10, Pages: 2690-2698, First published: 16 July 2021, DOI: (10.1111/codi.15813)

Perception of timing

- In 76%, the rec for surgery was shared decision with GI and surgeon
  - 35% regretted surgery was not proposed sooner
  - 31% considered duration of medial therapy too long



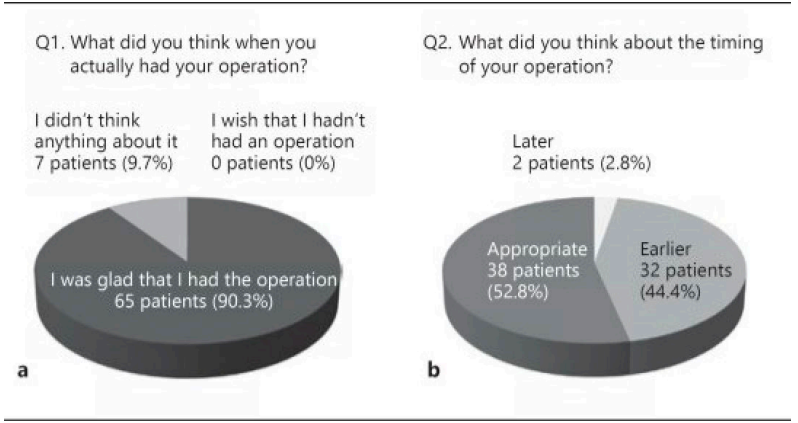
Perception of timing

Timing of Surgery to Treat Ulcerative Colitis: An Investigation Focused on Japanese Adults

Saki Yamada [1], Hitoshi Kameyama [1], Kaoru Abe [1], Kana Tanaka [1], Hidehito Oyanagi [1], Yosuke Tajima [1], Masato Nakano [1], Yoshifumi Shimada [1], Jun Sakata [1], Toshifumi Wakai [1]

Inflamm Intest Dis. 2020 Feb;5(1):20-26. doi: 10.1159/000504885. Epub 2020 Jan 28.

- 72 underwent IPAA
  - 65 (90.3%) were happy they had surgery
  - 0 wished they had not had surgery
    - 52.8% though timing was appropriate
    - 44.4% thought timing was too late



Summary

- Surgery is common in management of IBD
- Early surgery may be helpful
- Late surgery may be harmful
- Surgery is an option, not a last resort

UPMC
LIFE CHANGING MEDICINE

Thank you!