

Inflammatory Bowel Disease

Management of a Challenging Disease

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Knowledge that will change your world

Disclosures

- I **do not** have any relevant financial relationships with any commercial interest that pertains to the content of my presentation.

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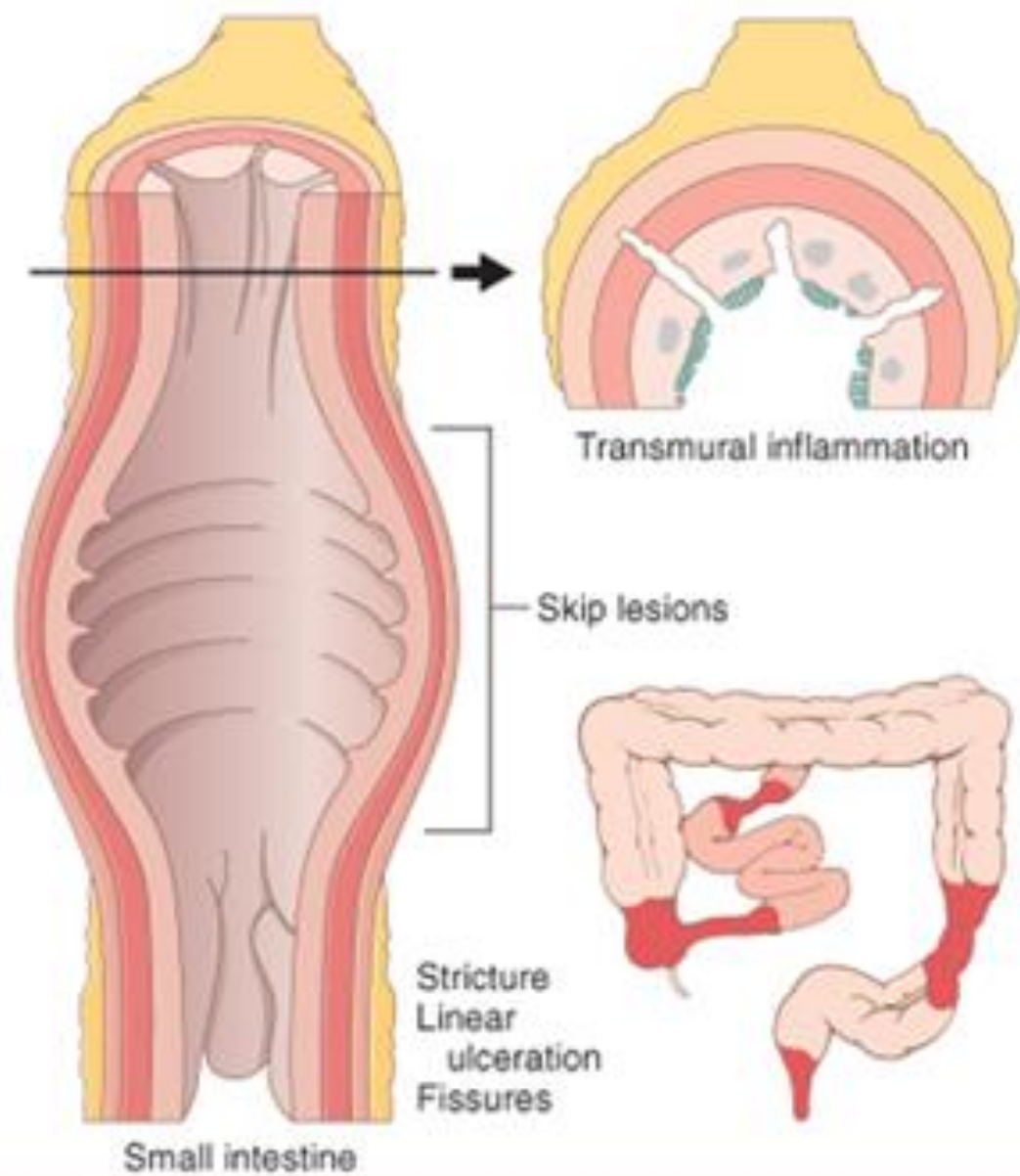
Crohn's Disease



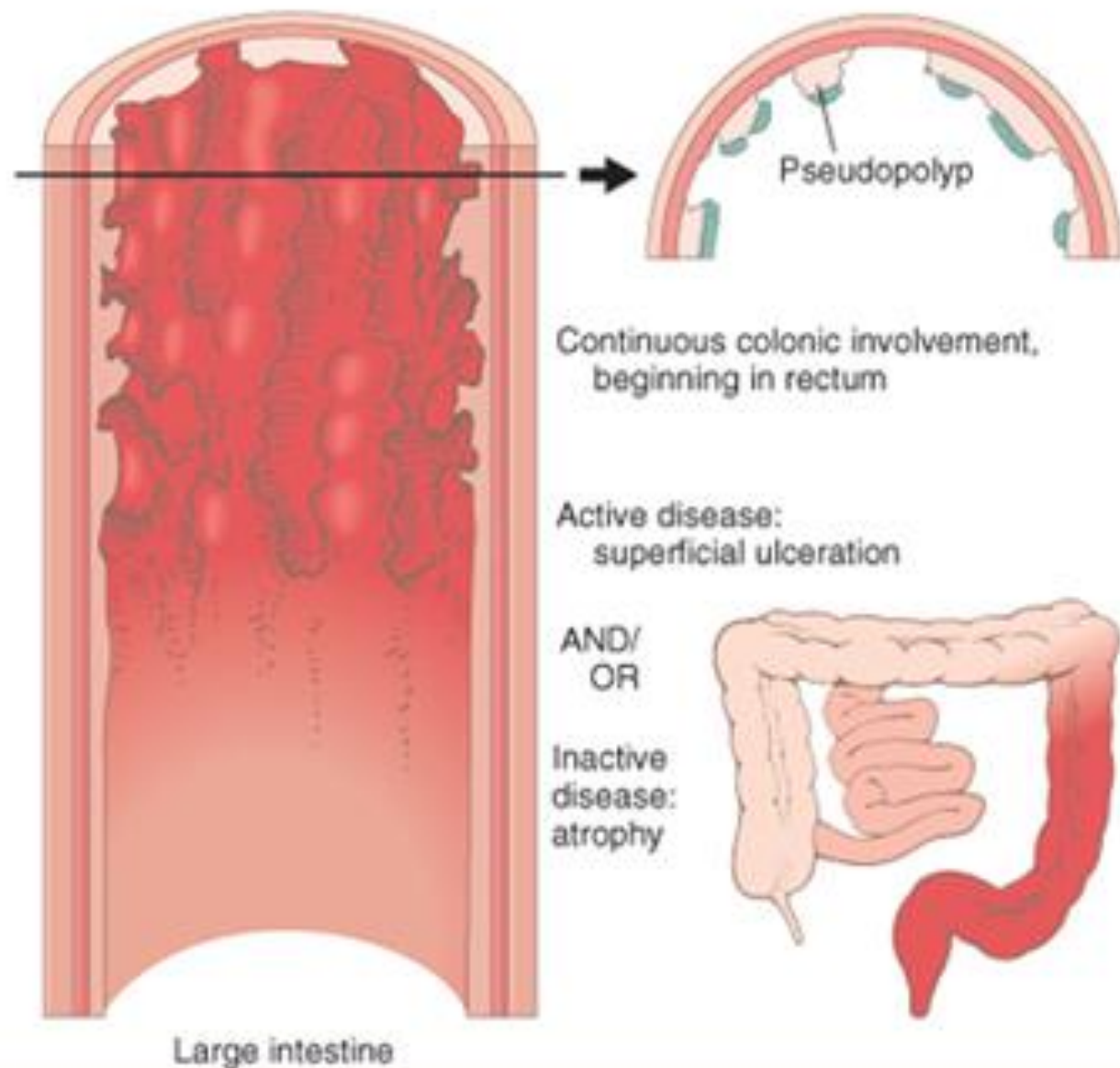
Ulcerative Colitis



CROHN DISEASE



ULCERATIVE COLITIS

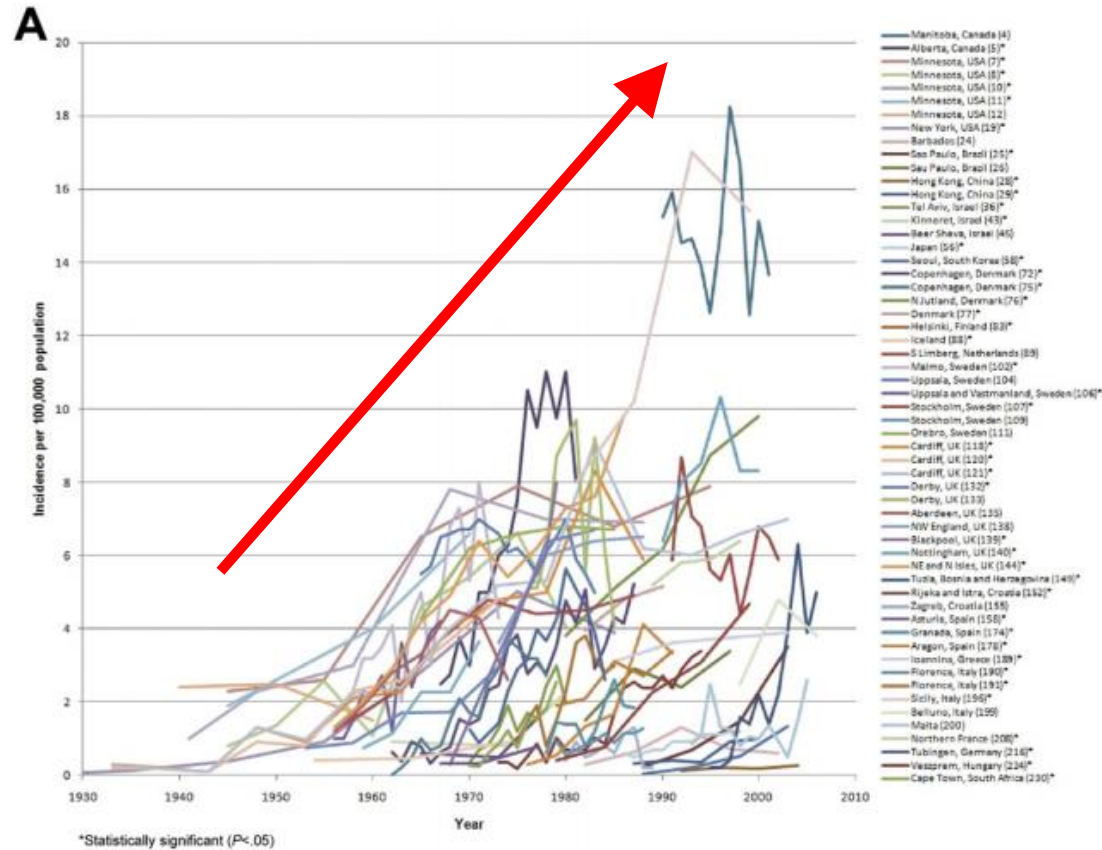


Global Burden of Inflammatory Bowel Disease

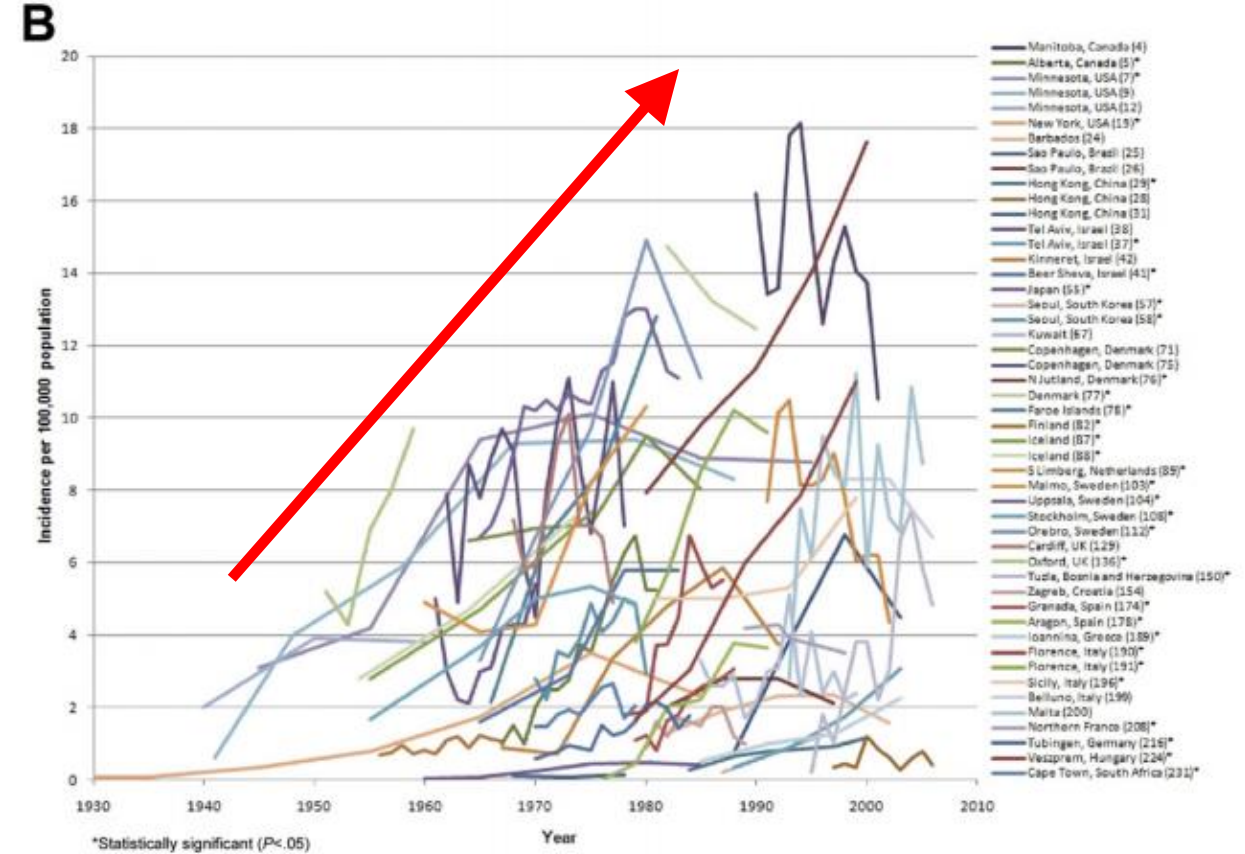


of IBD is increasing: 3.1 million people in US

Crohn's disease



Ulcerative colitis



of IBD is increasing: 3.1 million people in US

- **Incidence** in North America¹⁻²
 - 2.2-19.2 cases per 100,000 person-years for UC
 - 3.1-20.2 cases per 100,000 person-years for CD
- **Prevalence** in U.S.³
 - 238 per 100,000 population for UC
 - 201 per 100,000 population for CD
- **U.S. Population** (2018): 372.2 million
 - Incidence ~148,800/yr, Prevalence of IBD increasing to over 3.1 million
- **Birmingham, AL Metro Population** (2017): 1,149,807
 - Incidence ~ 440/year, Prevalence ~ 5,000 patients

More Epidemiology

- Peak incidence **14-24** years of age and **50-70** years of age
- Both sexes equally affected
- **Most common** in certain populations
 - Northern European
 - Anglo-Saxon
 - Ashkenazi Jews (2-4 times more common)
- BUT... **incidence is increasing** in other populations in N America
 - Latino Americans
 - African Americans
 - Asian Americans

Risk Factors

- **Genetic components**
 - First-degree relatives have a 4-20 fold increased risk of developing IBD
 - Familial tendency higher for Crohn's disease
 - Several gene mutations have been identified conferring higher risk of IBD
- **Cigarette smoking**
 - Associated with development and exacerbation of Crohn's disease
 - Decreased risk seen with CUC
- **Appendix**
 - Lack of appendix (appendectomy) associated with lower risk of CUC
- **NSAIDs** exacerbate IBD

There is no single, absolute diagnostic test

Diagnosis

History & Physical

Symptoms
Family History
Extraintestinal effects



Radiographic

CT scans
MR scans



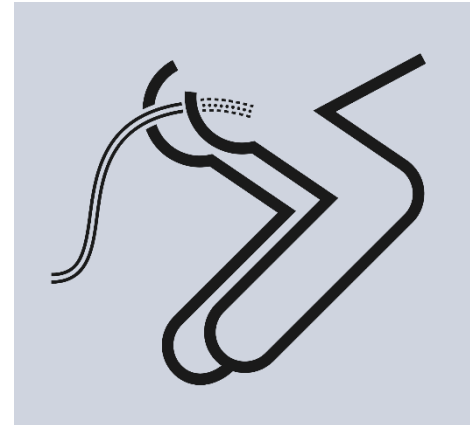
Laboratory

Inflammatory markers
Serological markers
Genetic tests



Endoscopic

Colonoscopy / EGD
Capsule endoscopy

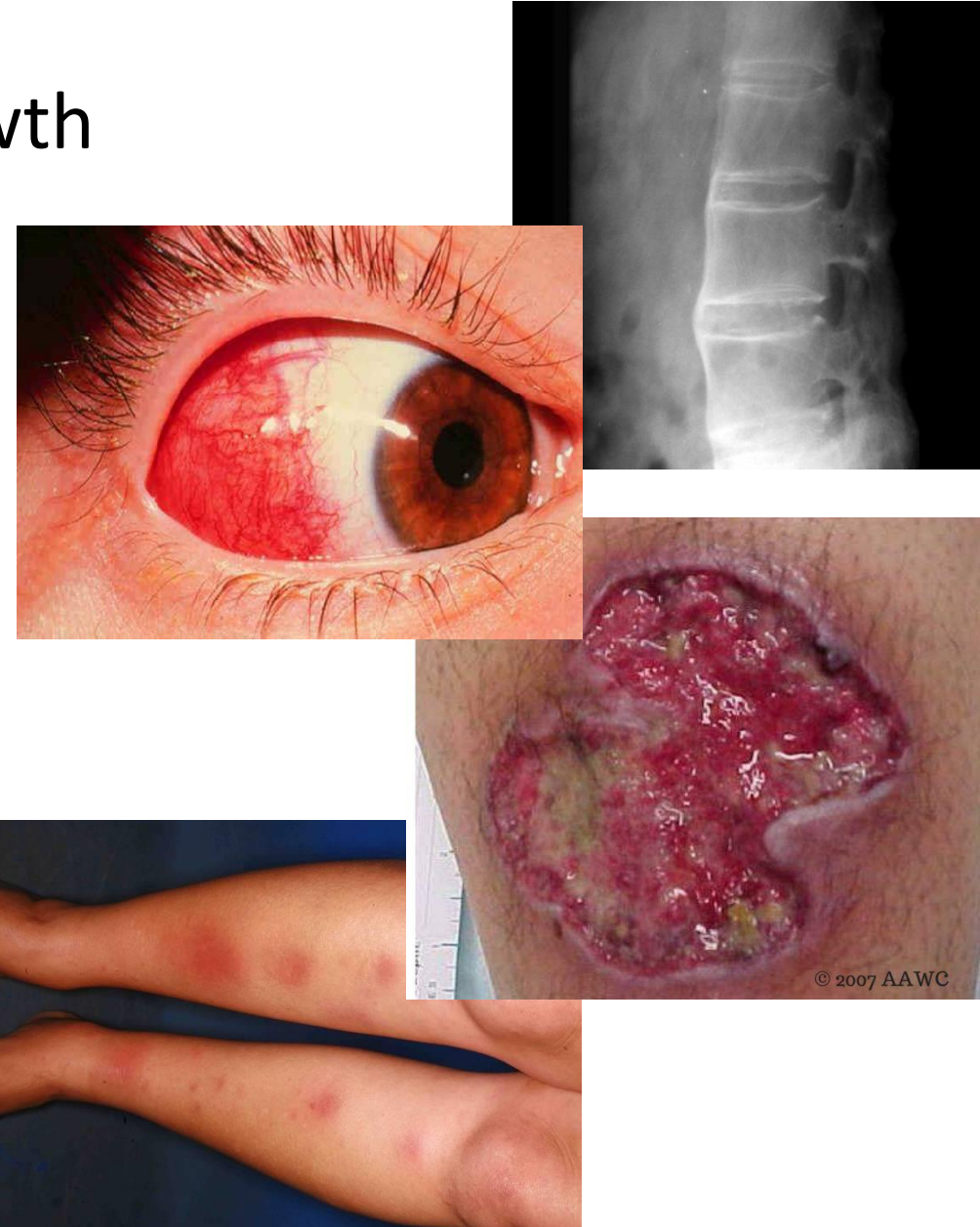


Diagnosis

| Feature | Crohn's Colitis | Ulcerative Colitis |
|-----------------------|---|--|
| Mucosal lesions | Aphthous ulcers are common in early disease; late disease is notable for deeper ulcers and cobblestoning | Micro-ulcers are more common, but larger ulcers are seen Pseudopolyps are more common |
| Distribution | Often discontinuous and asymmetric, with skipped segments of normal intervening mucosa, especially in early disease | Continuous, diffuse, granularity or ulceration found in the entirety of involved segments; cecal patch |
| Rectum | Often spared | Always involved |
| Ileum | Often involved (≈75% of cases) | Not involved, except as backwash ileitis |
| Depth of inflammation | Mucosal, submucosal, and transmural | Mucosal; transmural in fulminant disease |
| Serosal findings | Marked erythema and creeping fat (the latter is virtually pathognomonic) | Absent except in severe colitis or toxic megacolon |
| Strictures | Often present | Rarely present; suggests adenocarcinoma |
| Fistulas | Perianal, enterocutaneous, rectovaginal, enterovesicular, and other fistulas present | Absent, except for the rare occurrence of rectovaginal or perianal fistula |
| Histopathology | Granulomas in 15%-60% of patients | Granulomas should not be present |
| Serology | pANCA in 20%-25%, ASCA in 41%-76% | pANCA in 60%-65%, ASCA in 5% |

Diagnosis | Extraintestinal Manifestations

- **Bone/Joints:** Arthritis, arthropathy, growth delay (children), osteoporosis
- **Eye:** Uveitis, iritis, episcleritis
- **Skin:** Aphthous stomatitis, Erythema nodosum, pyoderma gangrenosum
- **Liver:** Gallstones, Primary sclerosing cholangitis
- **Kidney:** nephrolithiasis
- **Vascular:** thromboembolic events



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Management

Medical

Surgical



Management

Medical

Surgical

*Table 1. Current Status of Drug Therapy for Irritable Bowel Disease**

| Drug | Ulcerative Colitis | | Crohn Disease | |
|---------------------------------|--------------------|-------------|---------------|-------------|
| | Short-Term | Maintenance | Short-Term | Maintenance |
| 5-acetylsalicylic acid | + | + | ± | ± (colon) |
| Steroids | + | — | + | — |
| 6-mercaptopurine or azathiopine | — | + | — | + |
| Methotrexate | — | ? | ± | + |
| Cyclosporine | + | — (bridge) | — | — |
| Anti-tumor necrosis factor | ? | ? | ± | + |
| Probiotics | No data | ± | No data | ± |

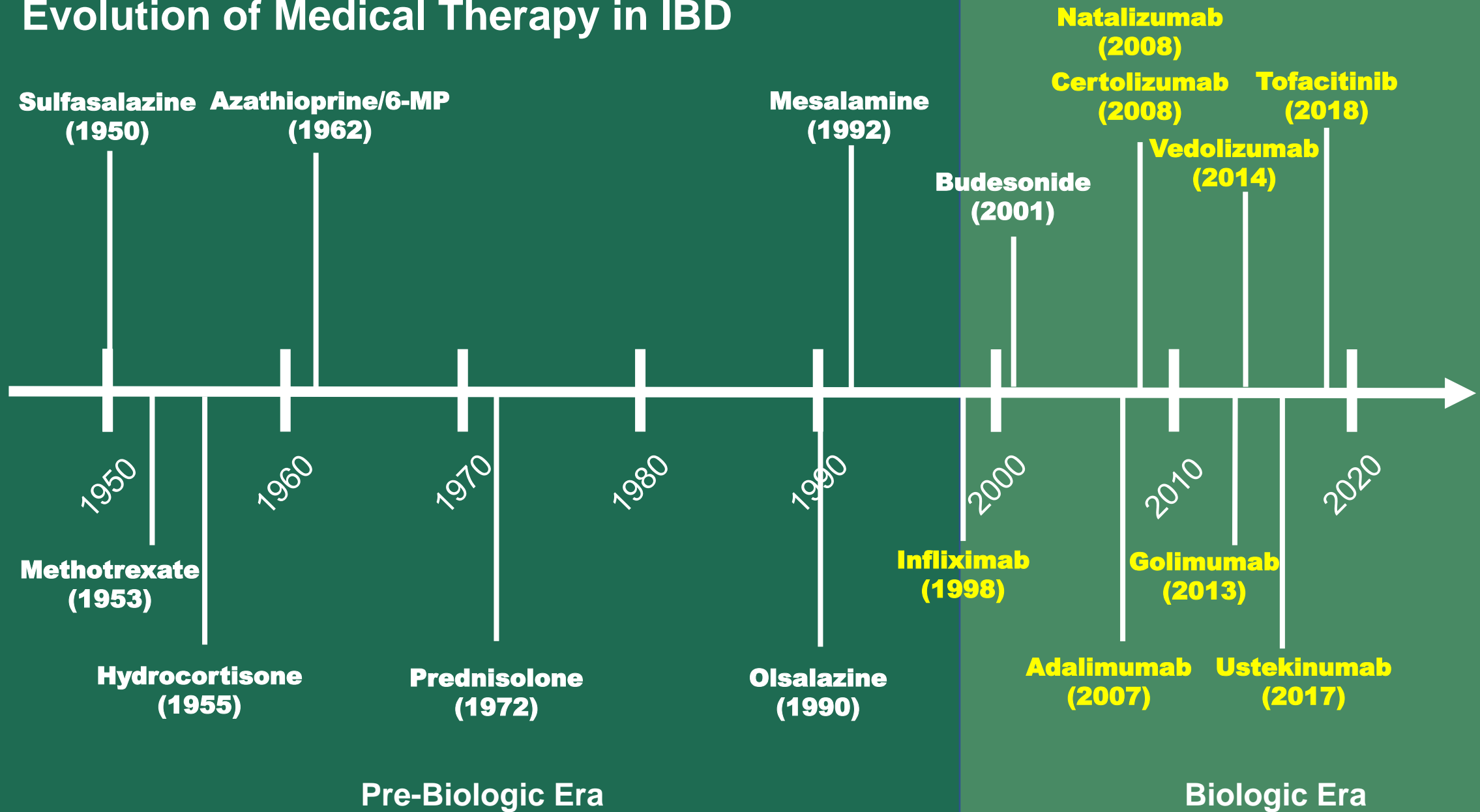
* Plus sign = effective; minus sign = not recommended; plus/minus sign = equivocal data; question mark = only small trials reported.

5-ASA
Immunomodulators
Biologics

Steroids

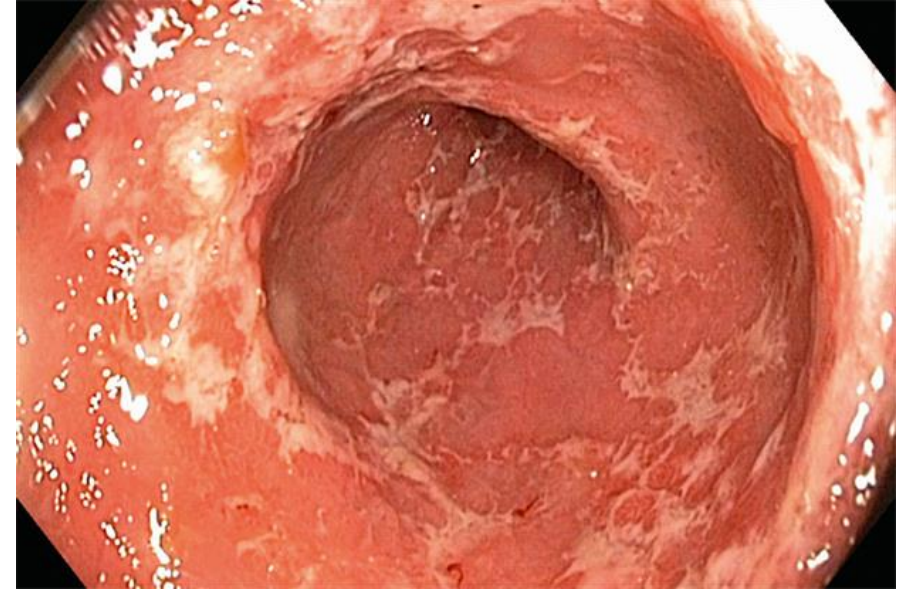
Probiotics

Evolution of Medical Therapy in IBD

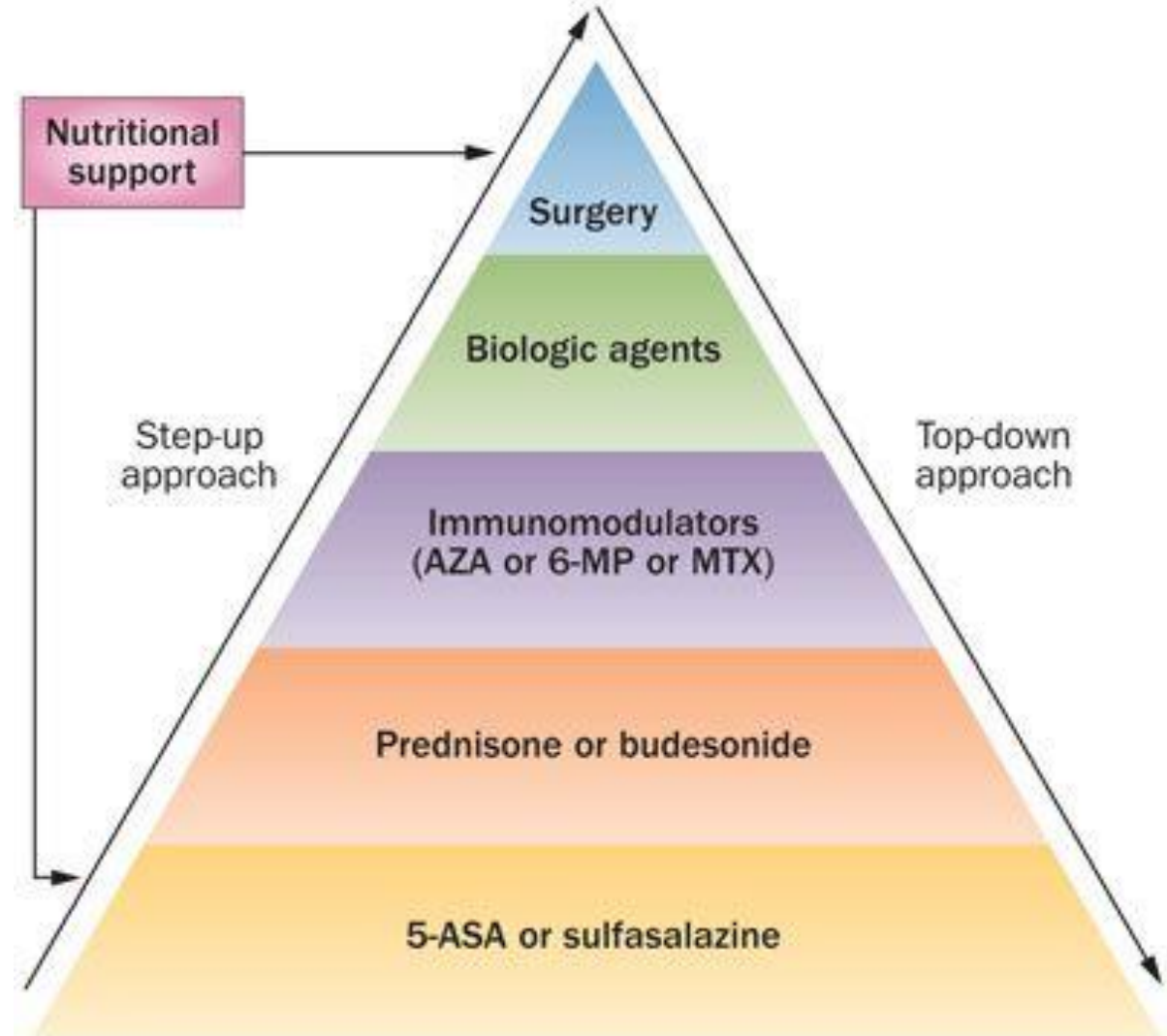


Goals

- Clinical remission
- Mucosal healing
- Prevention of long-term complications
 - Treatment related
 - Medication adverse effects
 - Disease related
 - Structural bowel damage
 - Cancer

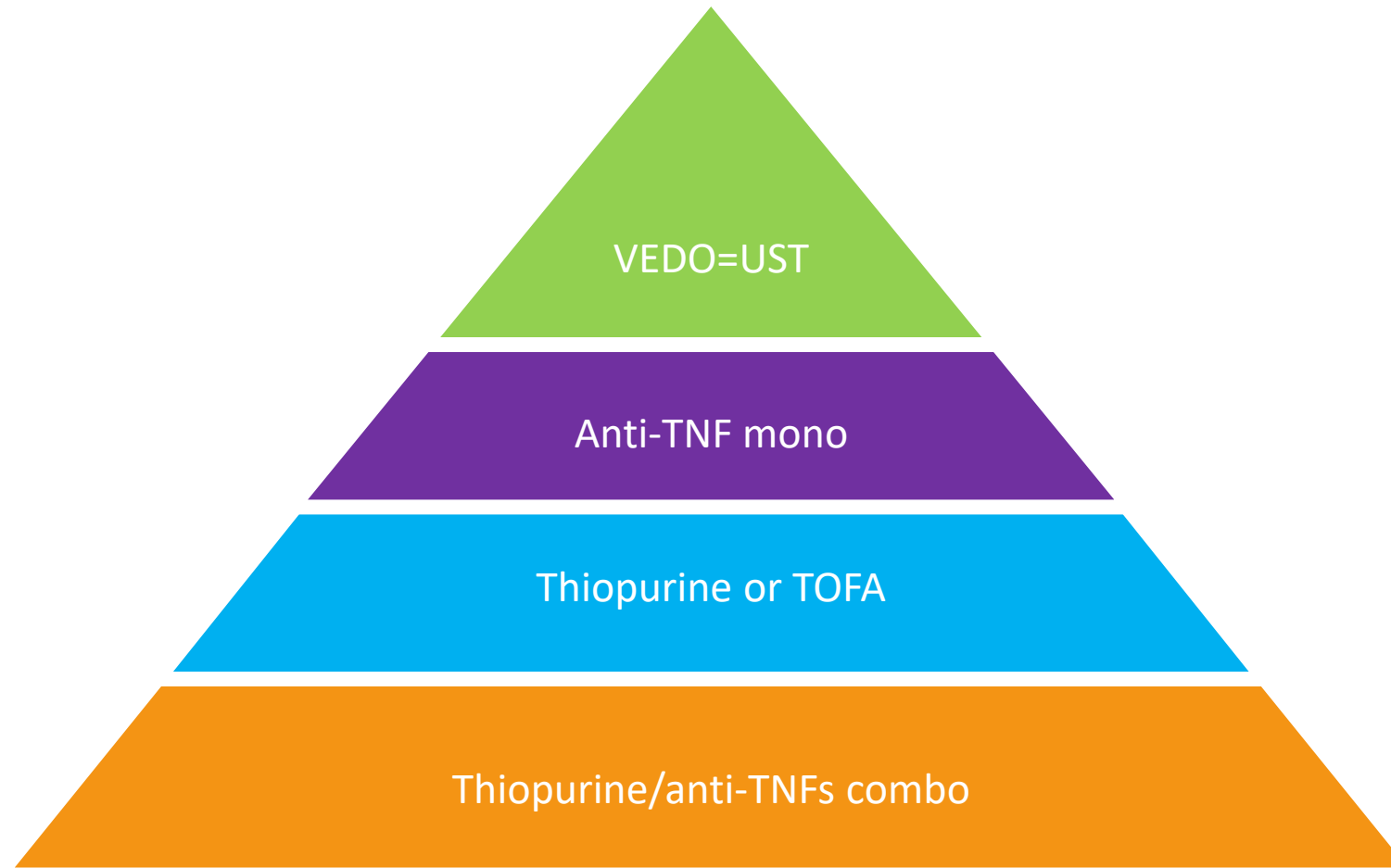


- **Treatment goals:**
 - Achieve clinical & endo remission
 - Prevent disease flares
 - Prevent bowel damage, cancer
 - Minimize steroids
- **Step-Up Approach**
 - UC (Mild-moderate)
- **Top-Down Approach**
 - UC (Severe)
 - Crohn's disease



Safest

Safety pyramid of current IBD meds*



STEROIDS

Management | Medical | Biologics

| Class | Antibody | Name | Tradename | Indication | Admin | Dosing | Half-Life | Year Approved |
|-----------------------|---------------|------------|-----------------|------------|-------|---------|-----------|-----------------------------|
| Anti-TNF-alpha | Chimeric IgG1 | Infliximab | Remicade | Crohn's UC | IV | 8-weeks | 7.7-9.5d | 1998 (Crohn's) 2005 (UC) |

Management | Medical | Biologics

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| | Human IgG1 | Adalimumab | Humira | Crohn's UC | SC | 2-weeks | 14d | 2008 (Crohn's) 2012 (UC) |
| | Humanized anti-TNF Fab' fragment | Certolizumab pegol | Cimzia | Crohn's | SC | 4-weeks | 14d | 2008 (Crohn's) |
| | Human IgG1 | Golimumab | Simponi | UC | SC | 4-weeks | 14d | 2013 (UC) |

Management | Medical | Biologics

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| Anti-integrins | Humanized | Natalizumab | Tysabri | Crohn's | IV | 28-days | 11d | 2008 (Crohn's) |
| | Humanized | Vedolizumab | Entyvio | Crohn's UC | IV, IM | 8-weeks | 15-22d | 2014 (Crohn's) 2014 (UC) |

Management | Medical | Biologics

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| Biosimilars | Inflectra, Remsima, Infimab, Inflectra | | | Biosimilar to Remicade | | | | |
| | Exemptia, Adfrar | | | Biosimilar to Humira | | | | |

Colorectal Cancer Prevention

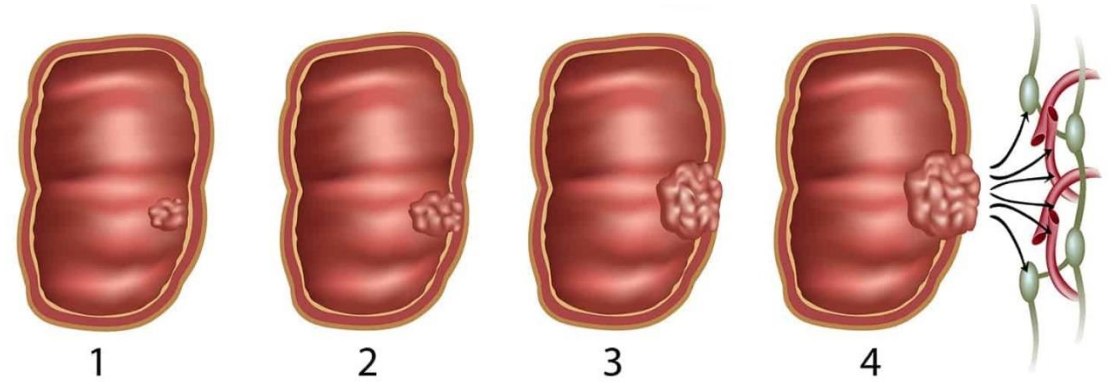
- Surveillance colonoscopy every 1-2 years

- Disease duration ≥ 8 years
- $\geq 30\%$ colonic involvement

- PS + UC = yearly colonoscopy

- Proctitis and isolated ileal CD do not require surveillance

- Earlier surveillance colonoscopy if \uparrow age at index diagnosis



Cervical Dysplasia Prevention

- **Increased risk** of cervical HGD and cancer in patients with IBD on immunosuppressive therapy (HR 1.34, 95% CI 1.23-1.46)¹
- UC: LGD (IRR 1.15), HGD (IRR 1.12)²
- CD: LGD (IRR 1.26), HGD (IRR 1.28), Cancer (IRR 1.53)²

ACOG & CDC Recommendation

- **Yearly pap** for all female patients on chronic immunosuppression

Vaccines

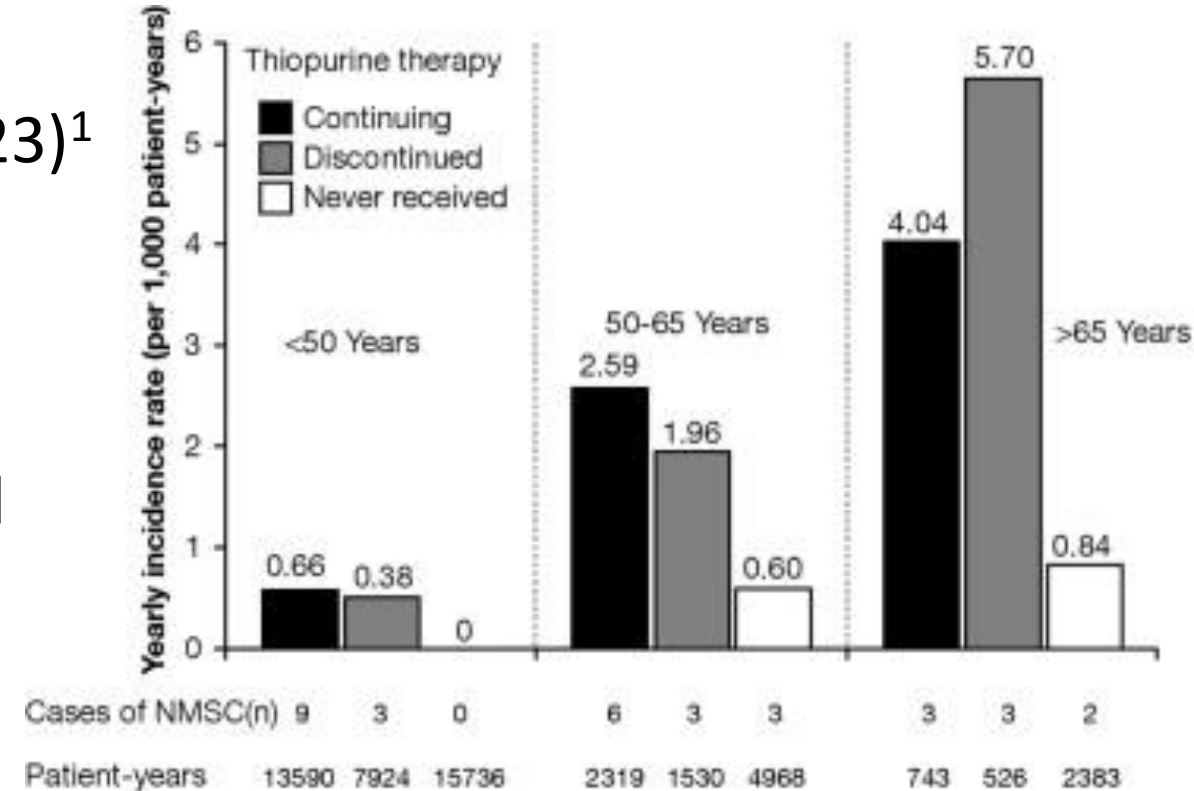
- **Influenza:** All patients & close household contacts: Annual
- **Pneumococcal:** Immunosuppressed patients | Increased risk in IBD (HR 1.54)²
 - PCV13 x 1, PPSV23 6 (2-12) mo later then booster 5 yrs later and at age 65
- **Shingles:** patients ≥ 50 | Increased risk in IBD (HR 1.49, HR 3.49 w/ anti-TNF)³
 - 2 doses at 0 and 2-6 months
- **HPV:** patients 11-26 years old
 - 3 doses at 0, 2, and 6 months
- **Avoid live vaccines*** if on biologic

* MMR, Varicella, Yellow fever, Meningococcal, Zostavax



Skin Cancer Prevention

- Melanoma:
 - IBD (RR 1.37): CD (RR 1.80), UC (RR 1.23)¹
 - Anti-TNF therapy x 1 year (RR 1.88)²
- Non-melanoma skin cancer
 - Azathioprine: active tx vs discontinued
 - (HR 2.1-5.9 vs. 0.7-3.9) prior use³⁻⁴
 - Tofacitinib therapy



Recommendation

Sunscreen use, Dermatologist skin exam

1. Singh S, et. al. Clin Gastroenterol Hepatol. 2014
2. Long MD, et. al. Gastroenterology 2012
3. Abbas AM, et. al. Am J Gastroenterol. 2014.
4. Peyrin-Biroulet L, et. al. Gastroenterology. 2011



Management

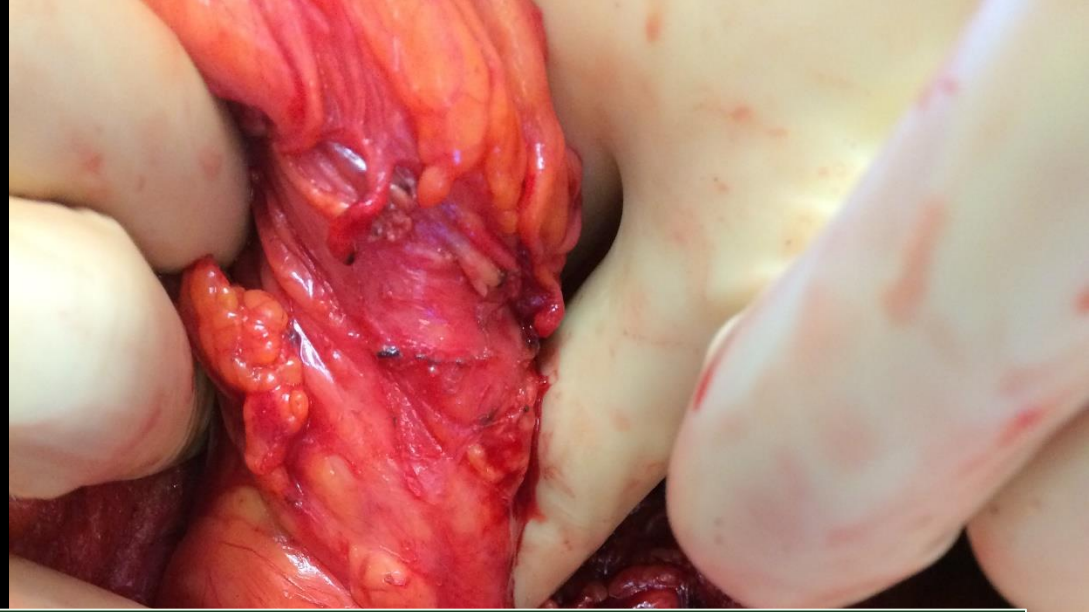
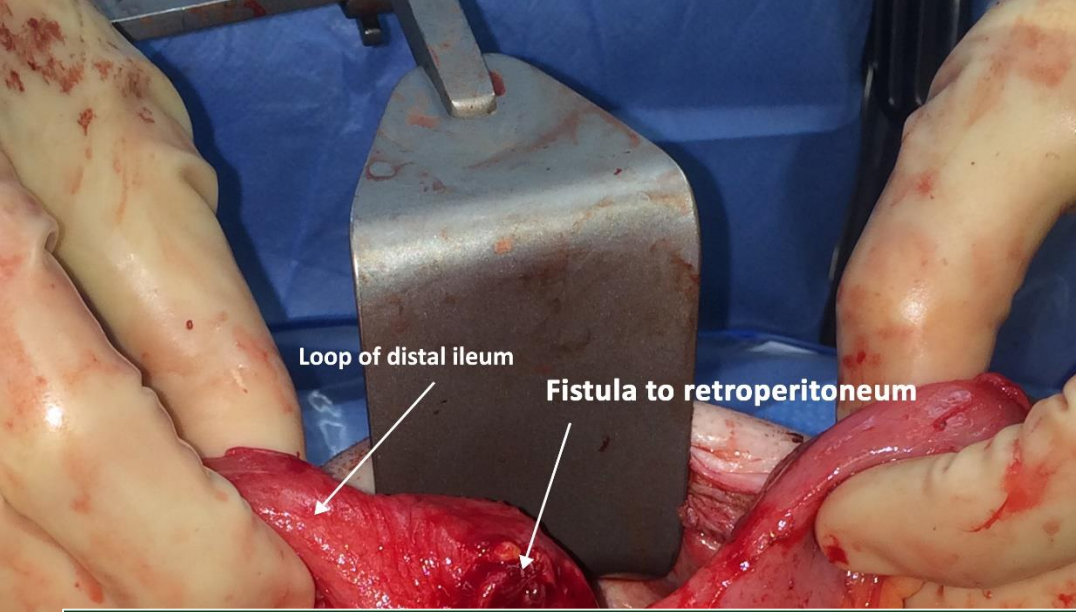
Medical

Surgical

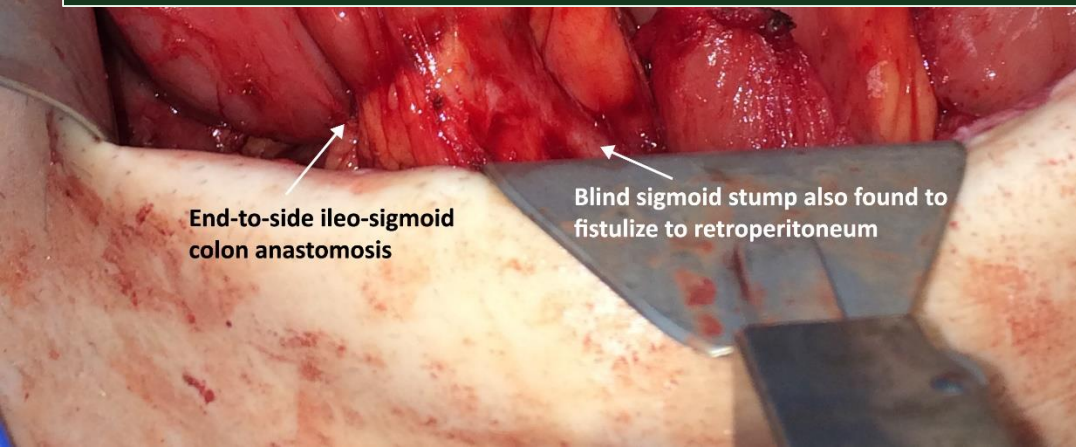
Management

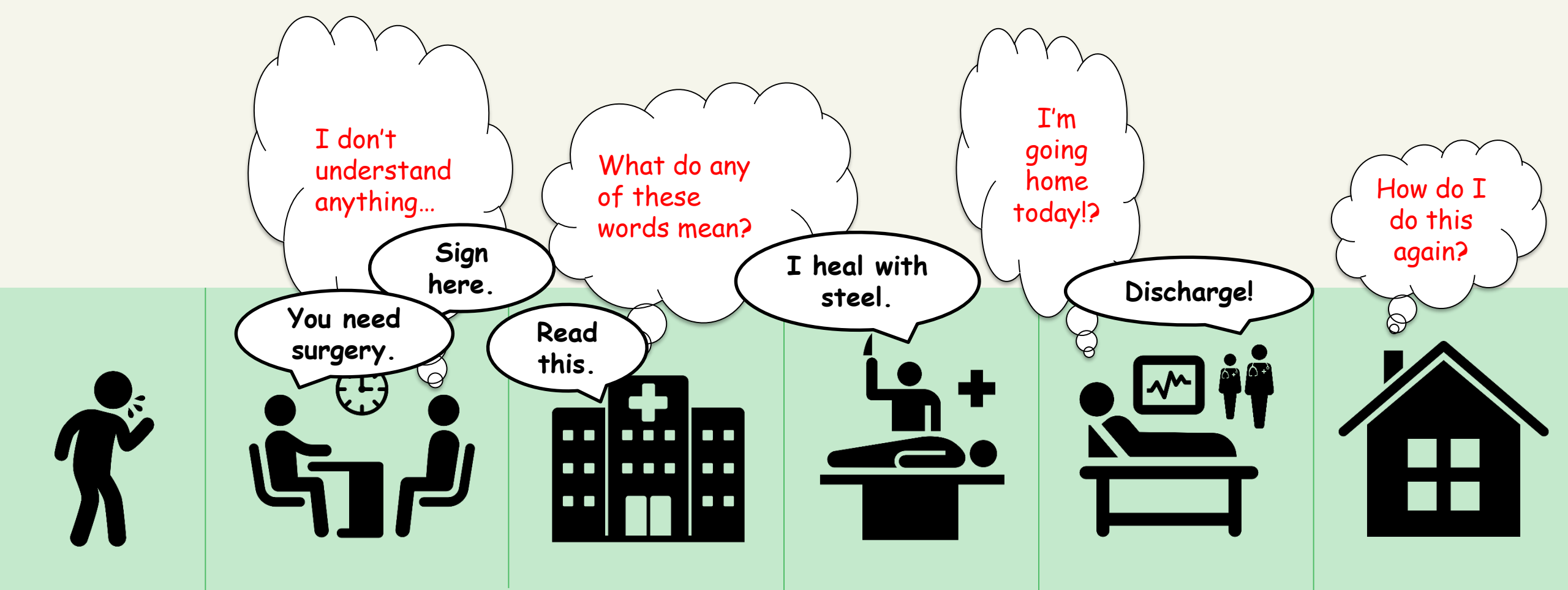
Medical

Surgical



Surgery for IBD is challenging and particularly high-risk for complications





Surgery is very confusing and we need to do a better job helping our patients understand the surgical journey.

Over 3.1 million people in the US have IBD

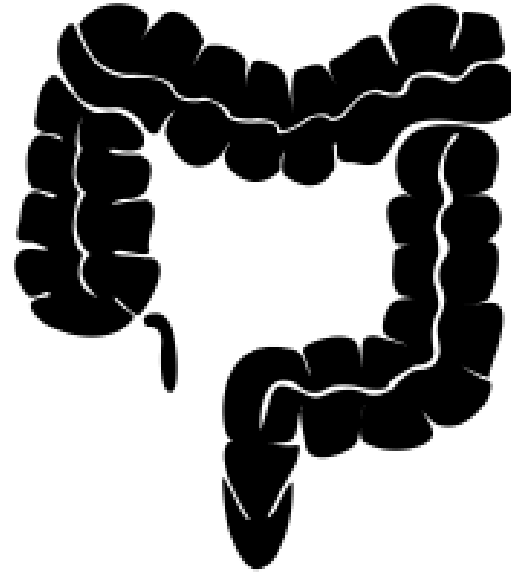
Crohn's: More than **75%** patient have surgery

UC: More than **25%** patient have surgery



1. Indications

— Why? When? —



2. Operation

————— How? —————



3. Complications



1. Indications



Elective

1. “Failure of medical therapy”

Steroid dependency
Complications from biologics
Extraintestinal manifestations

2. Cancer

High-grade dysplasia
“DALM” (non-adenoma-like)

3. Complications

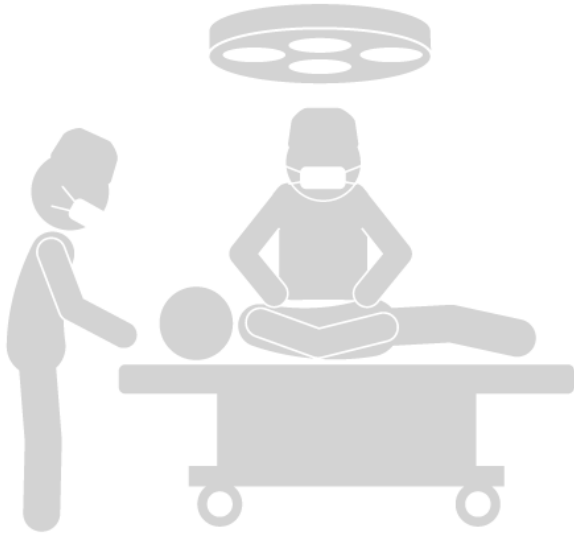
Stricture
Fistula



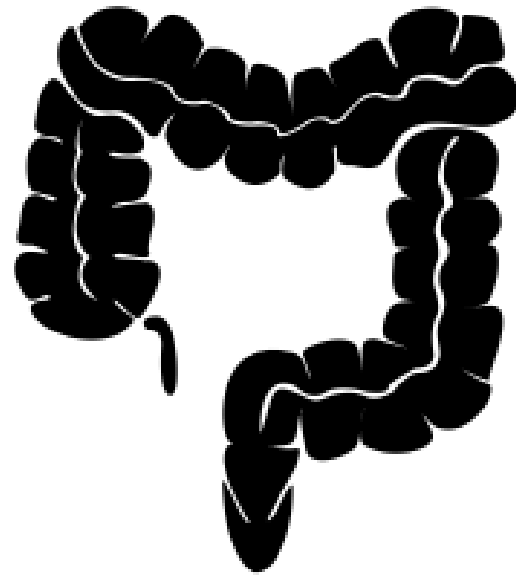
Emergent

1. Hemorrhage
2. Obstruction
3. Perforation





1. Indications



2. Operation

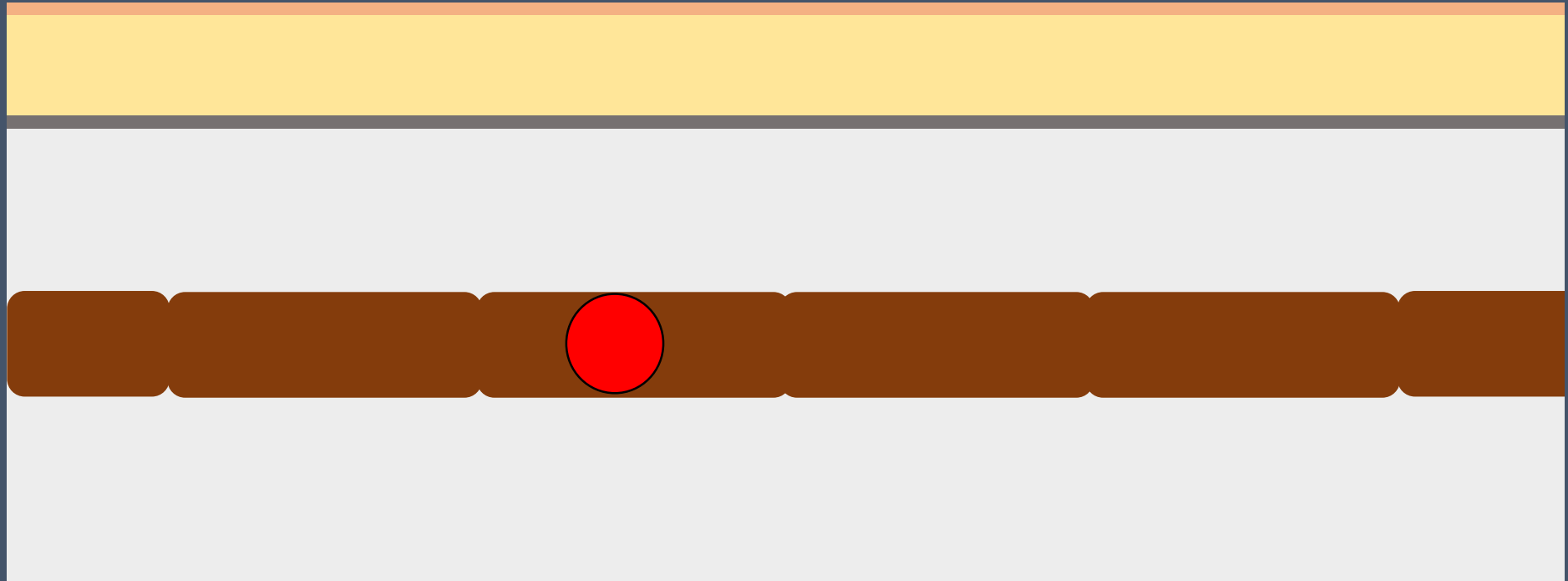
1. Resection

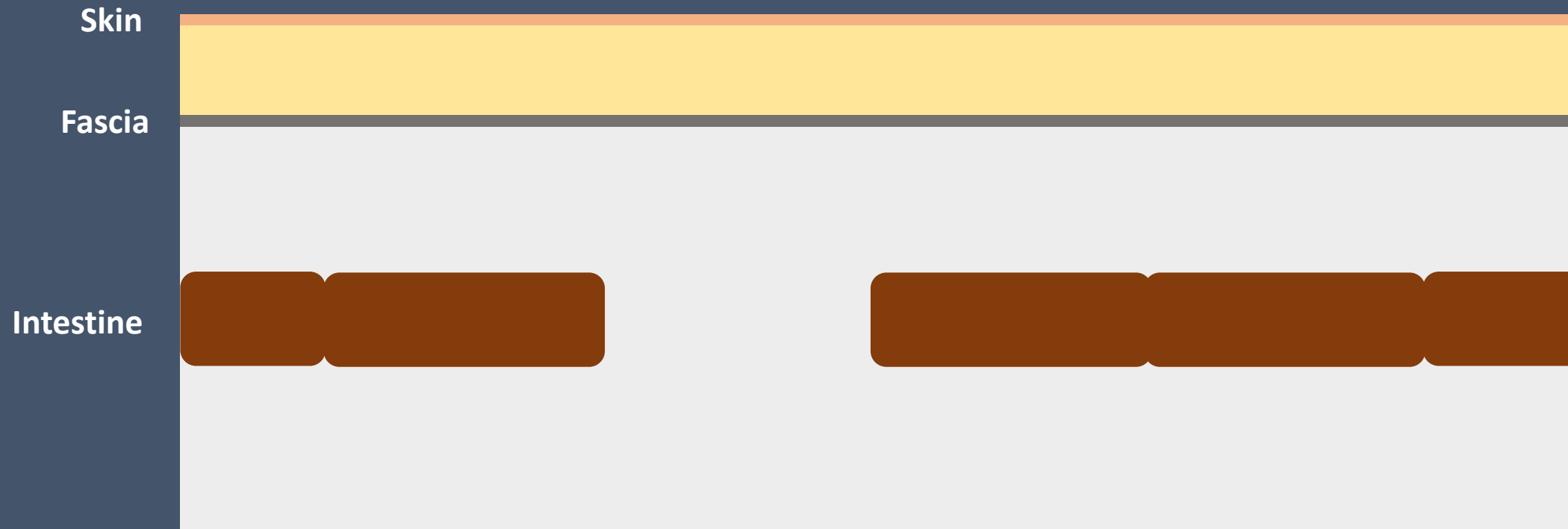
2. Reconstruction ± Stoma

Skin

Fascia

Intestine





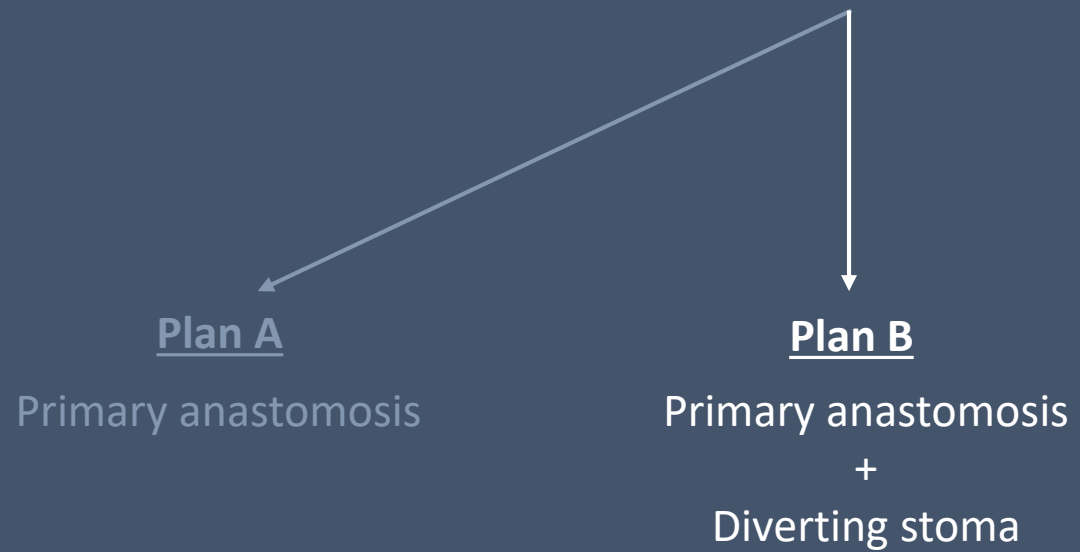
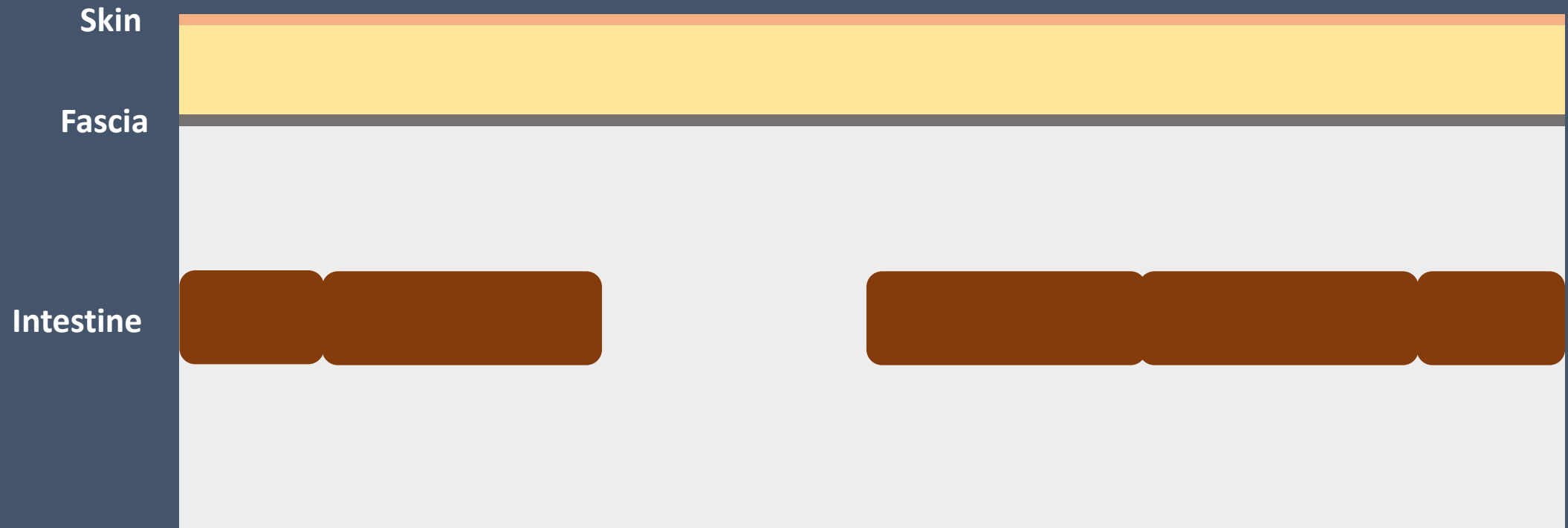
Plan A

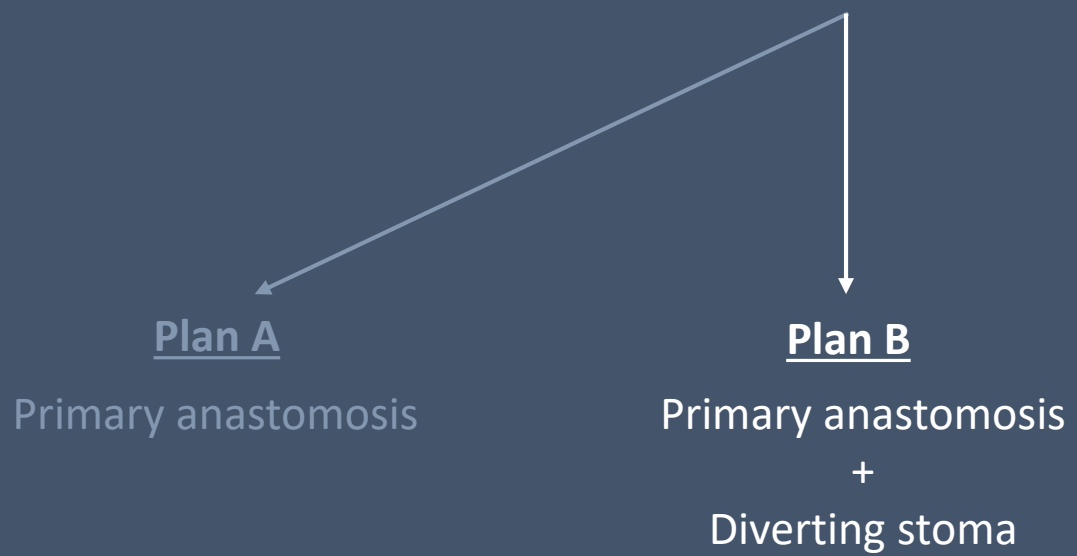
Primary anastomosis

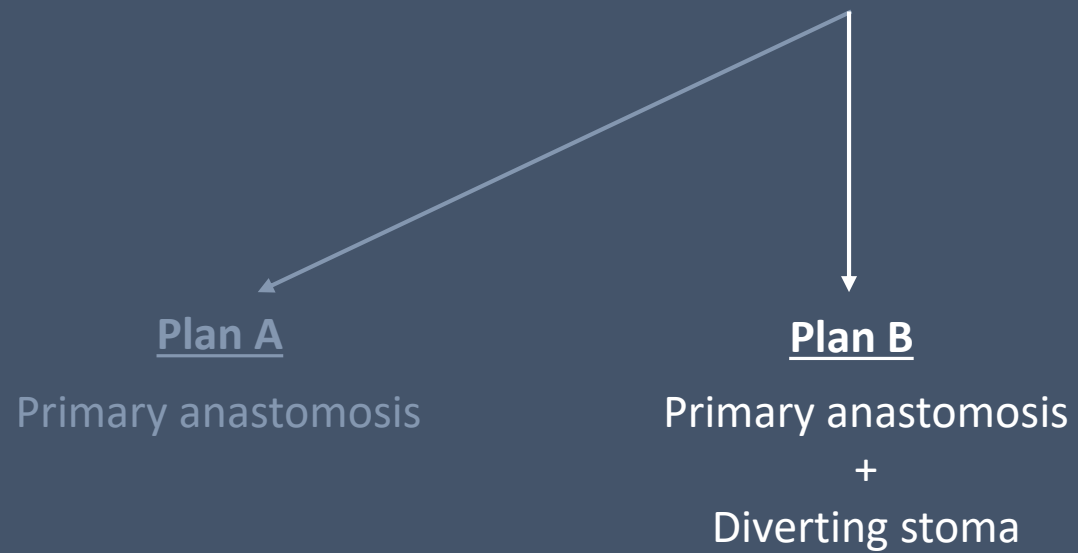
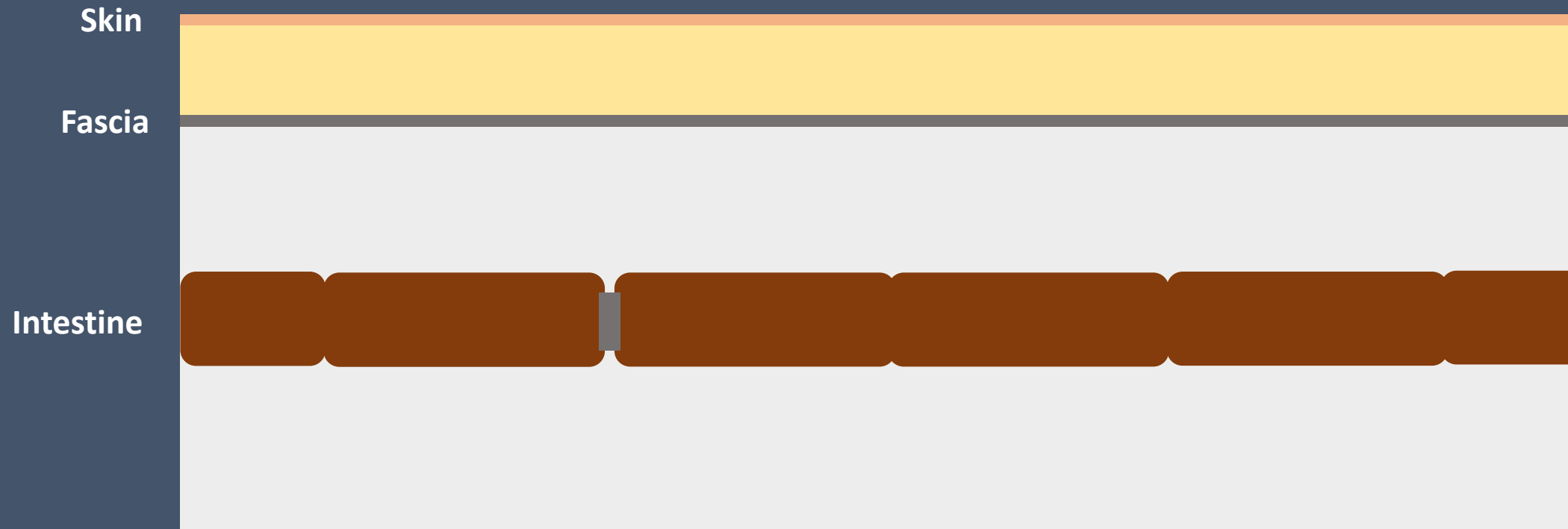


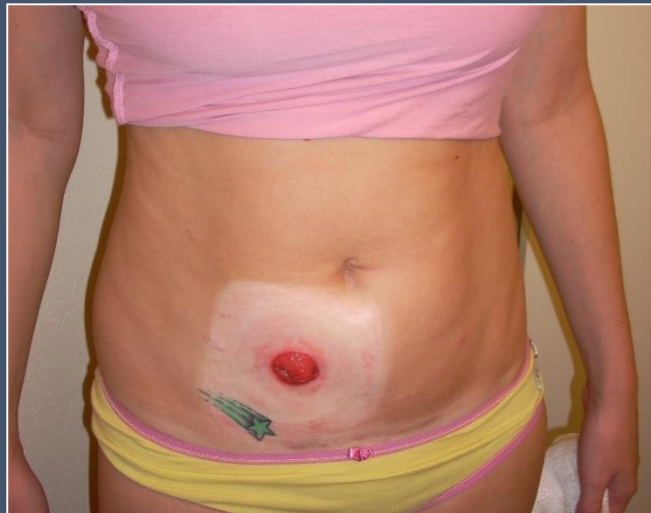
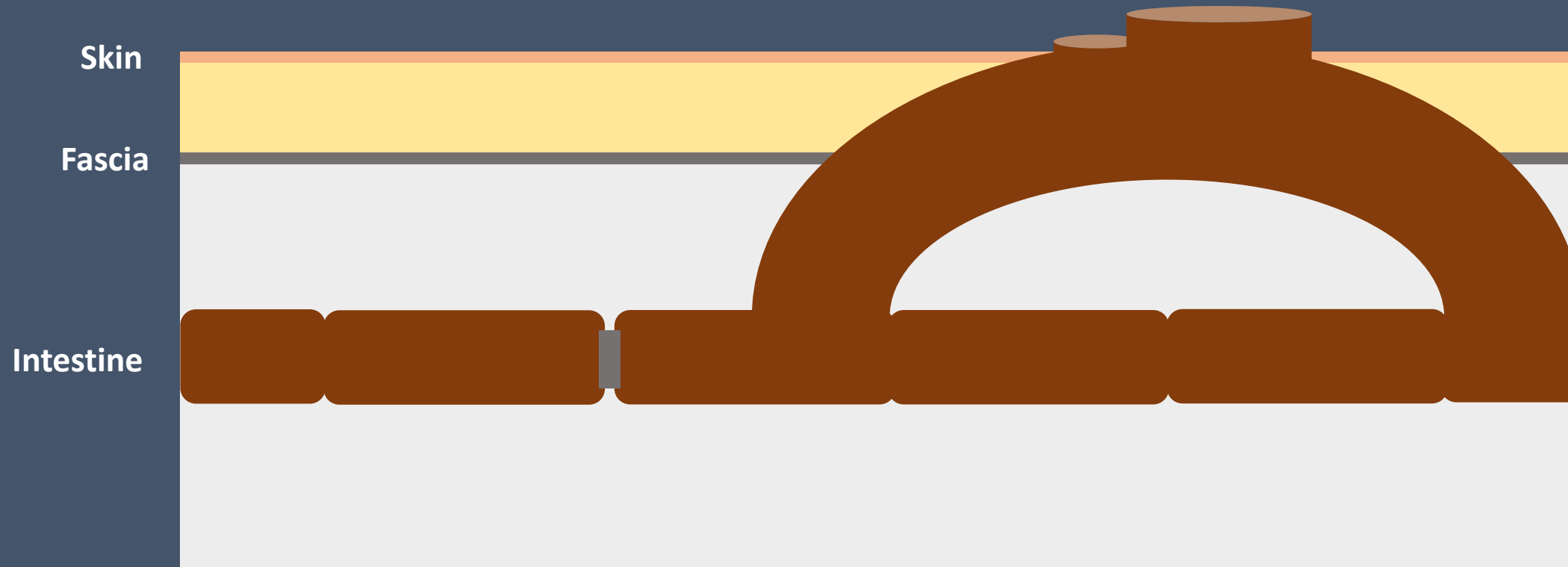
Plan A

Primary anastomosis



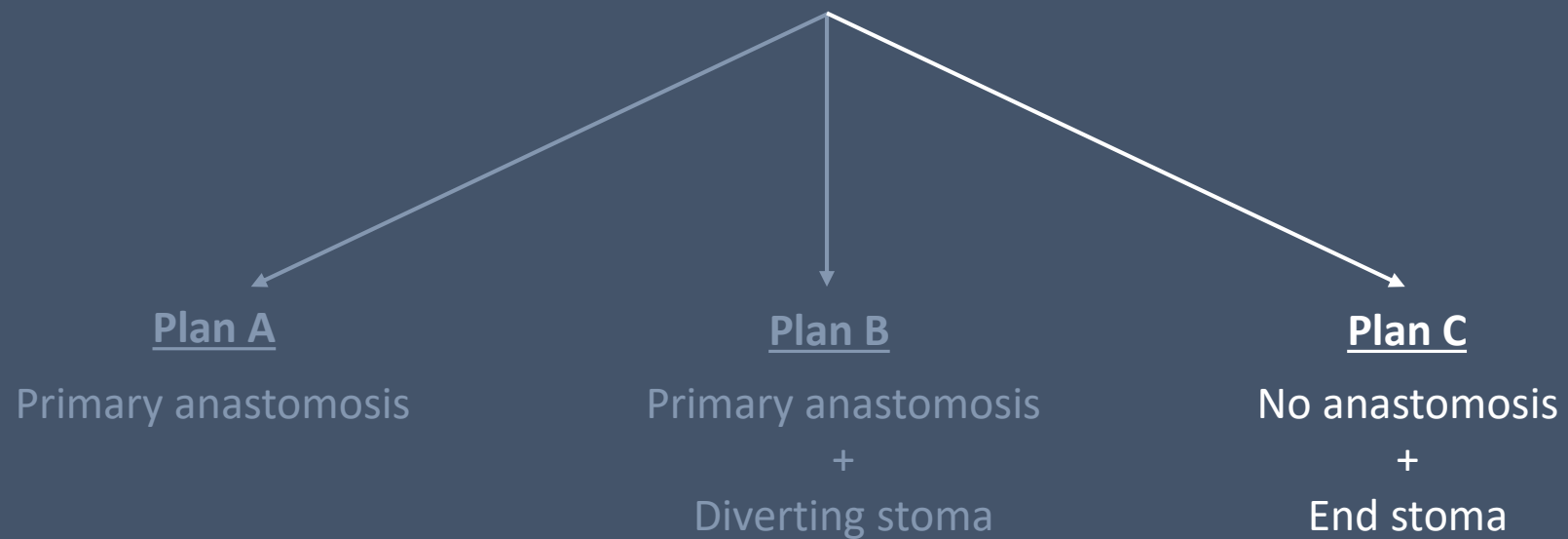
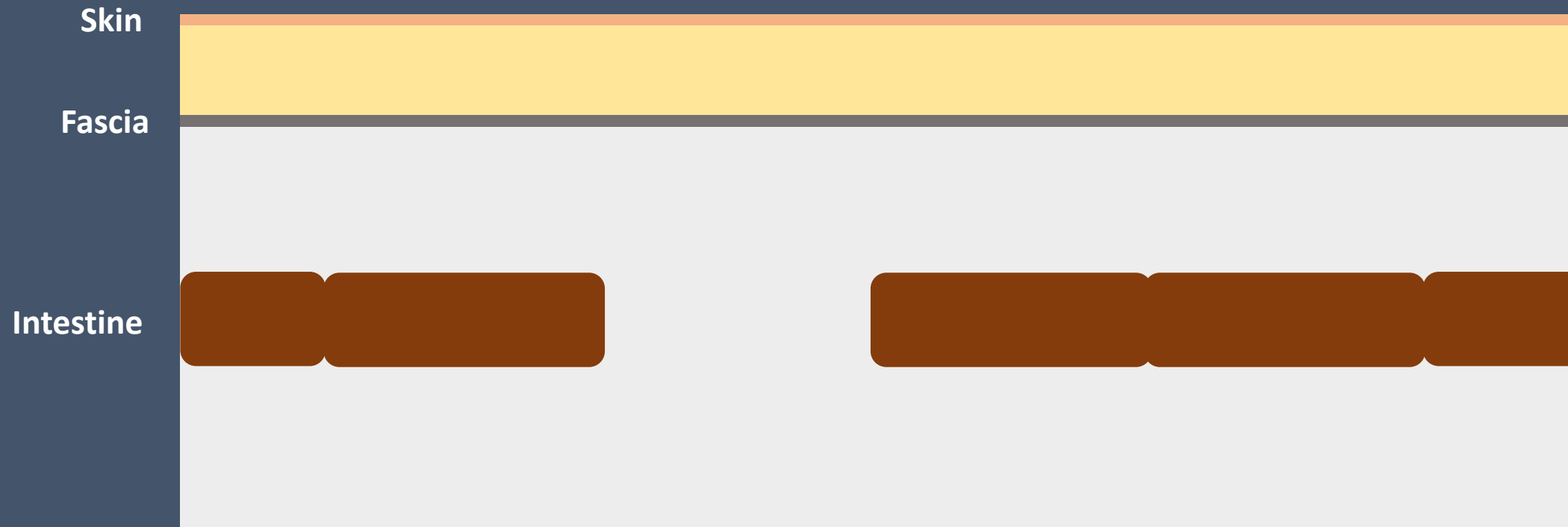


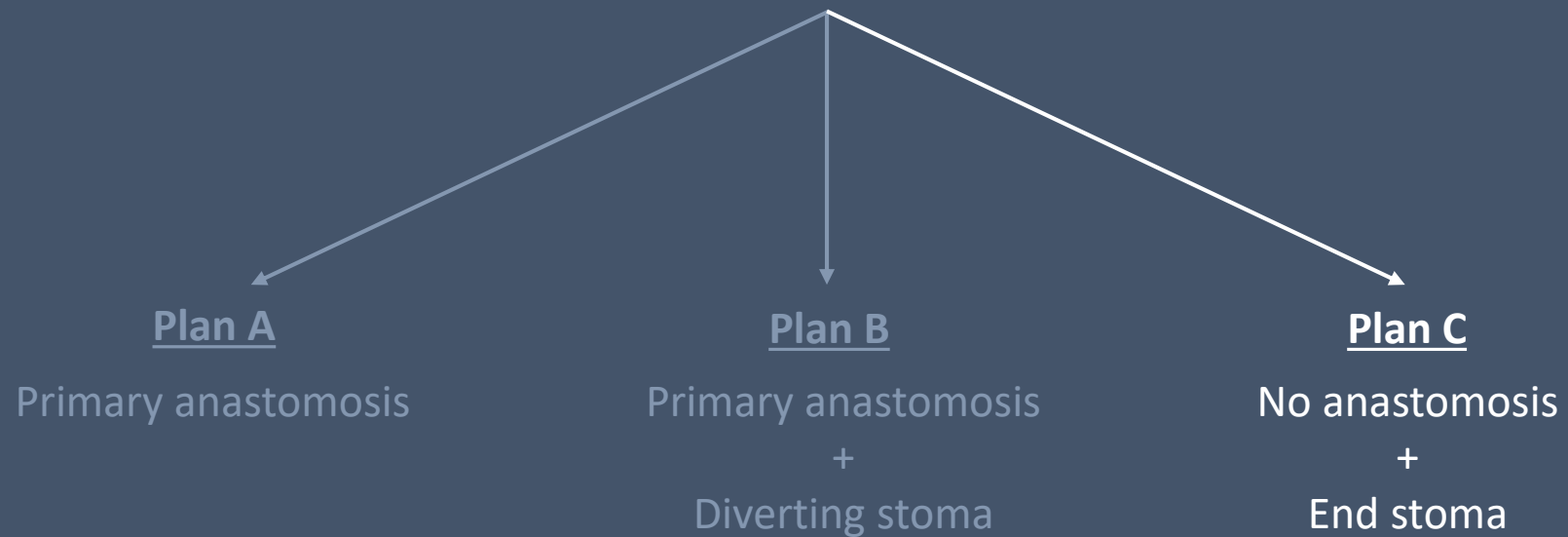
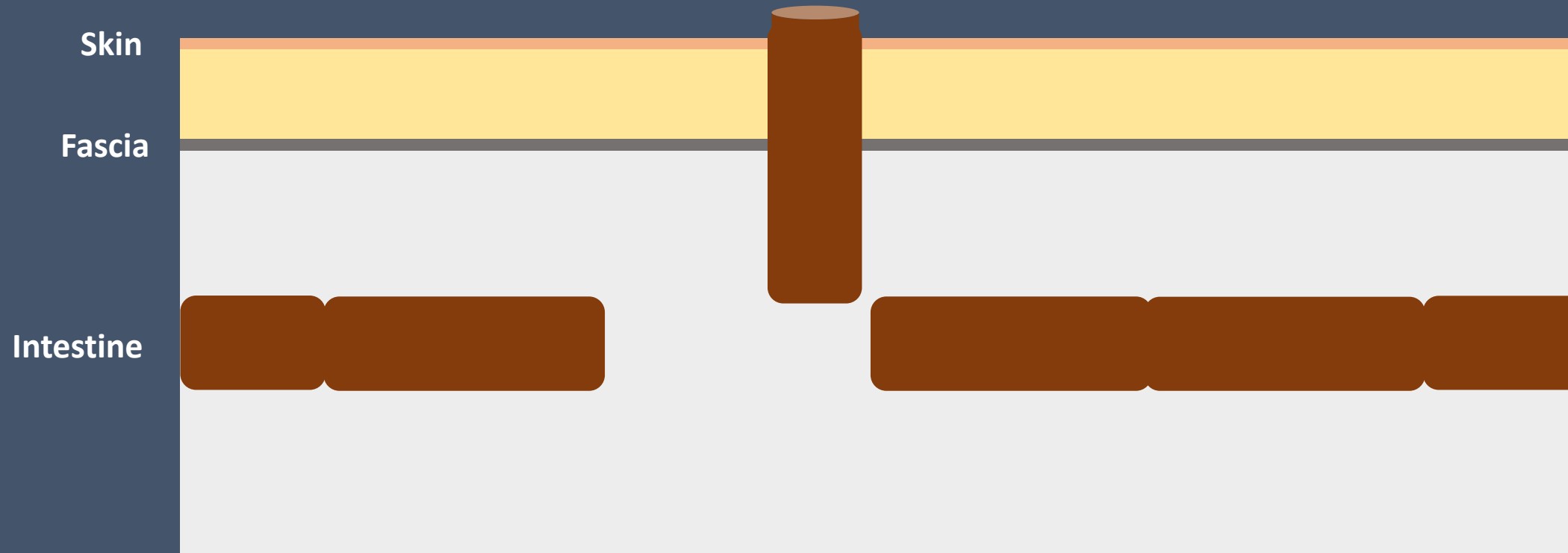


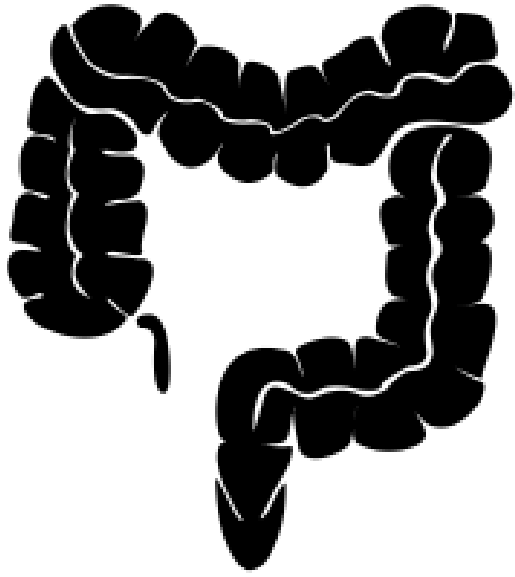


Plan B
Primary anastomosis
+
Diverting stoma





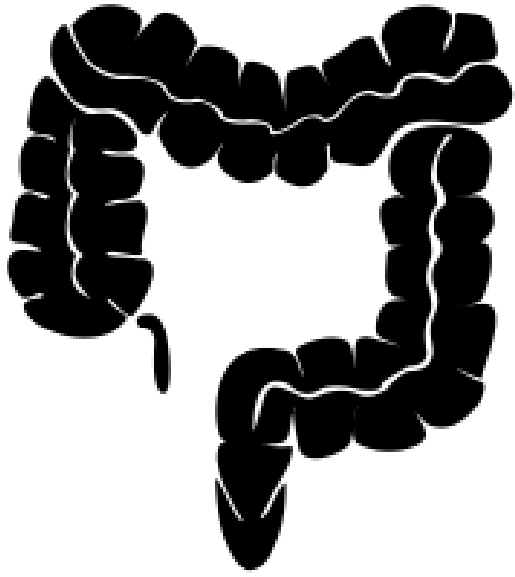




2. Operation

Emergent





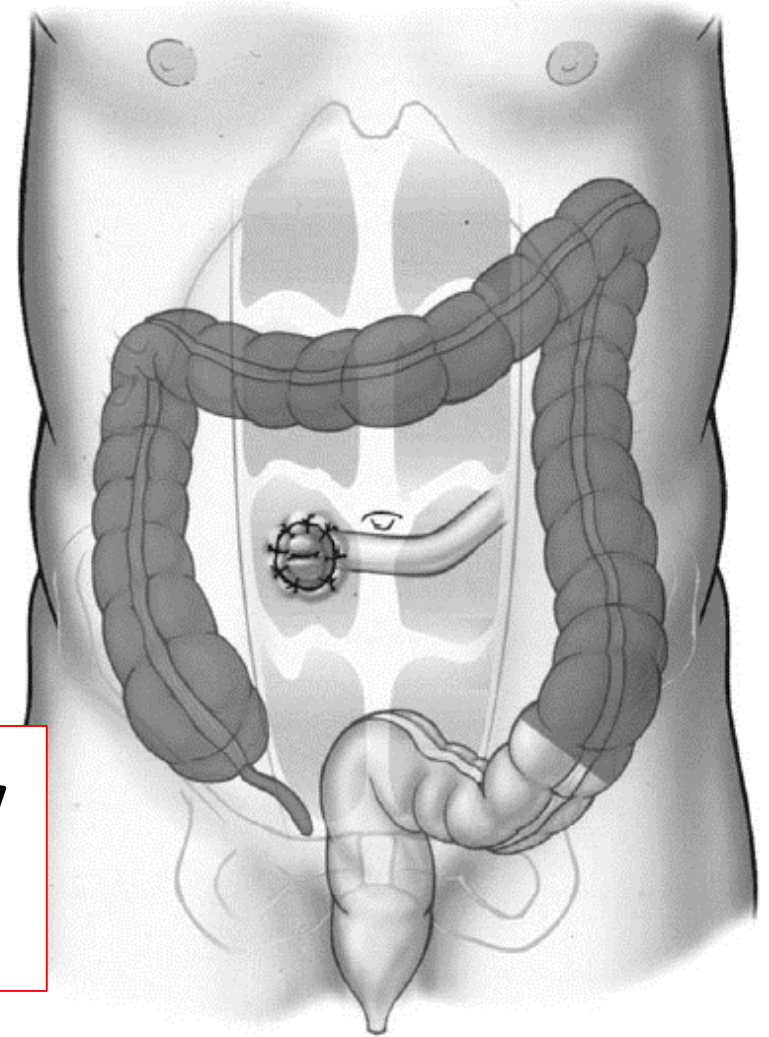
Emergent

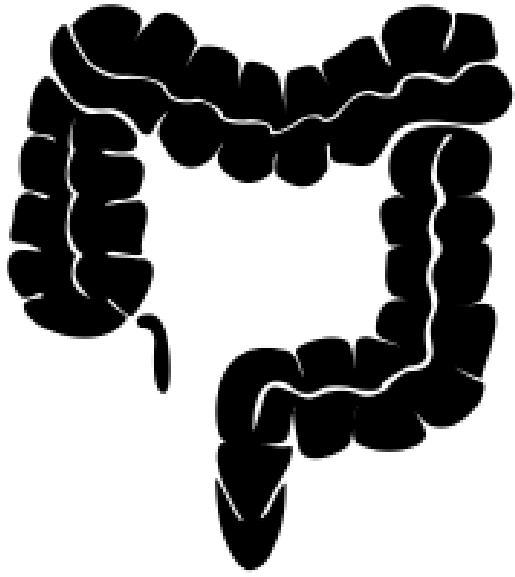


2. Operation



**Subtotal colectomy
w end ileostomy**





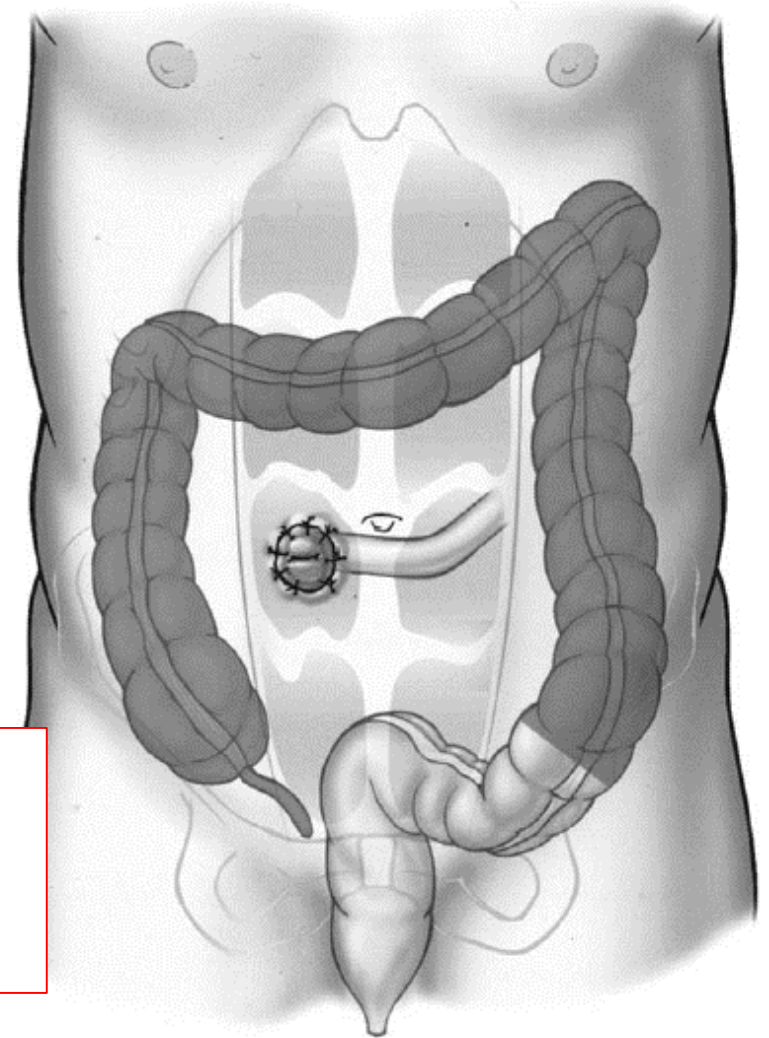
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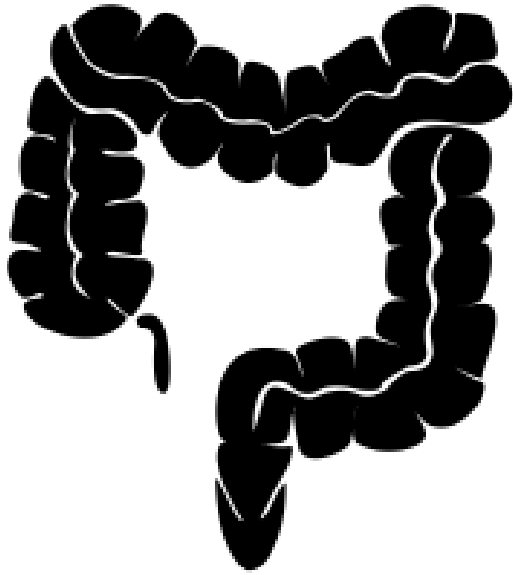


2. Operation



You do what you
have to do....





2. Operation

Elective

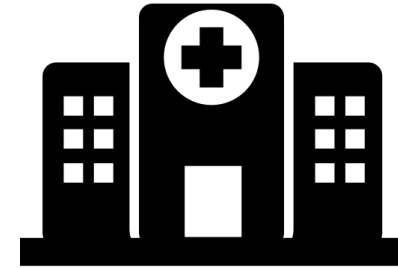


Crohn's



There is no one
operation - you do
what you have to do....

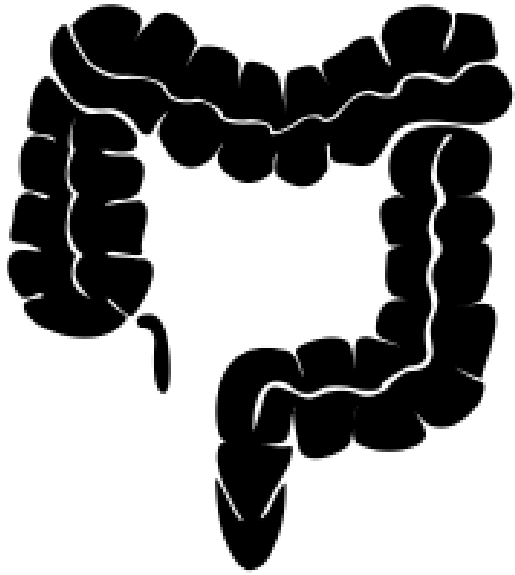
Elective



CUC



You have several
choices of major
operations...



2. Operation

Elective



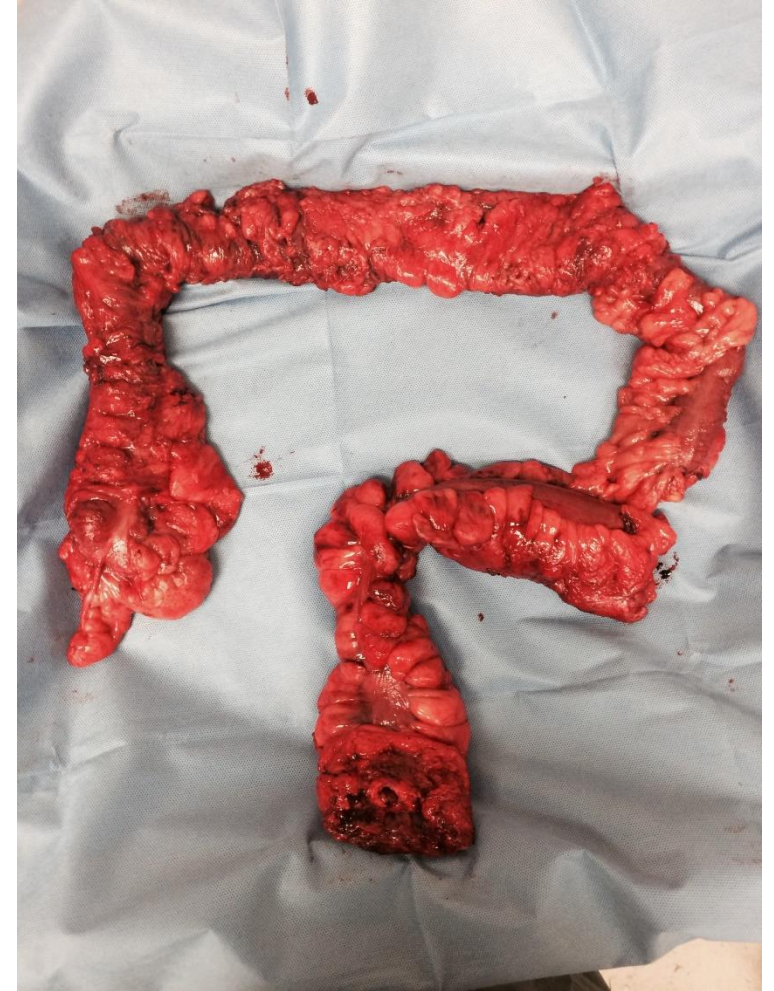
Stage 1 of 2

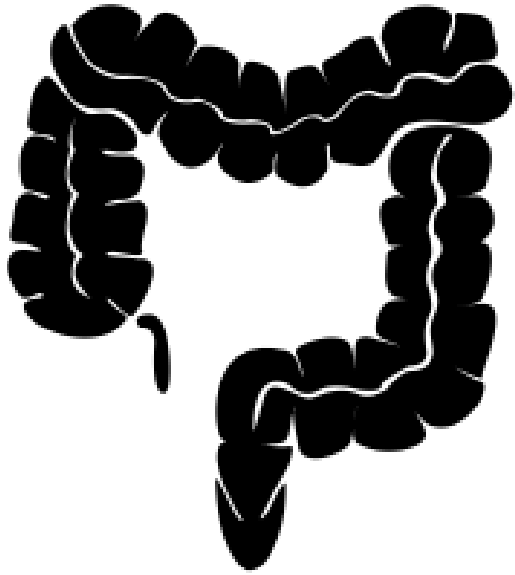
Total proctocolectomy/IPAA/DLI



Stage 2 of 2

DLI stoma reversal





2. Operation

Elective



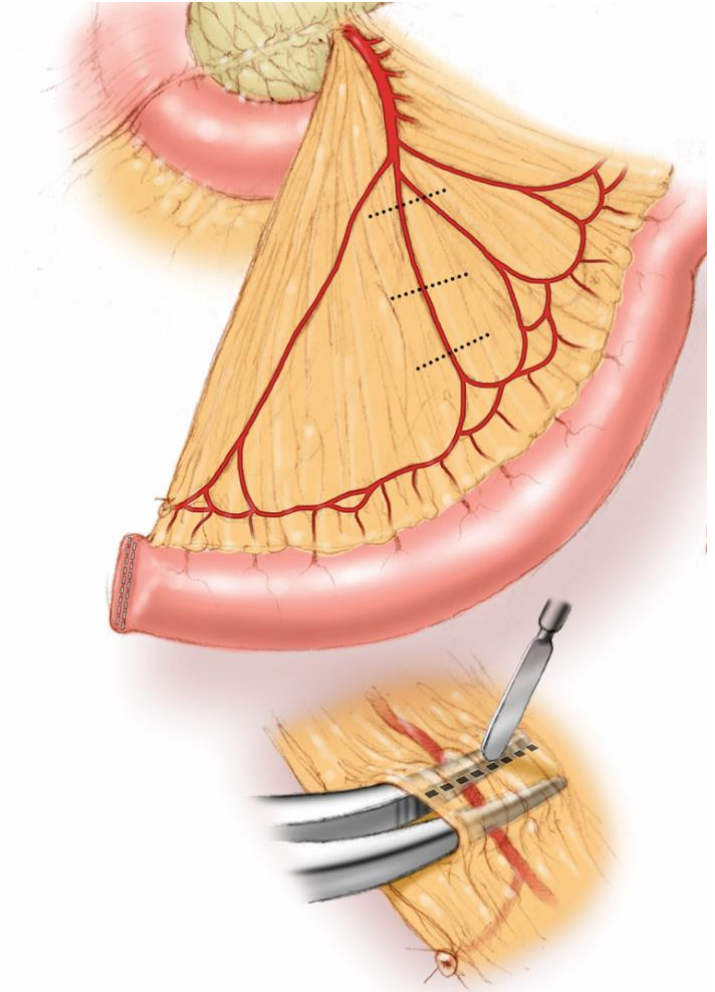
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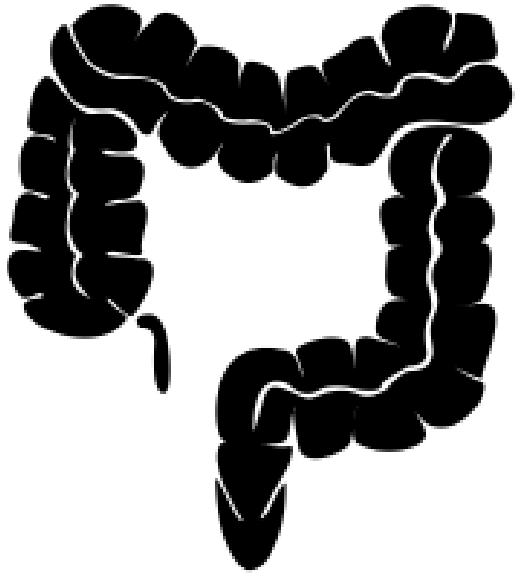
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Stage 2 of 2

DLI stoma reversal





2. Operation

Elective



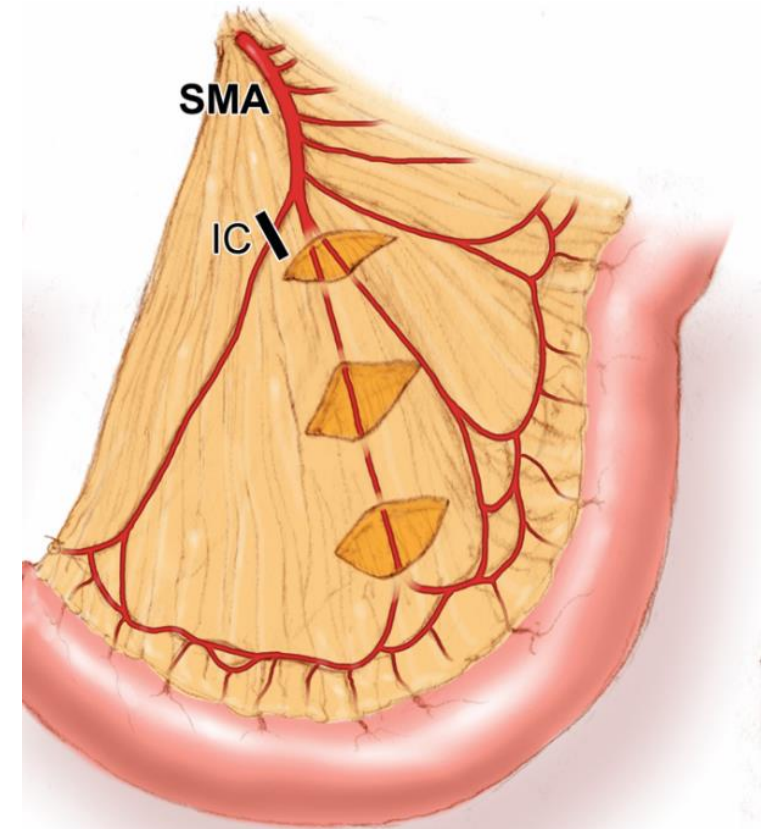
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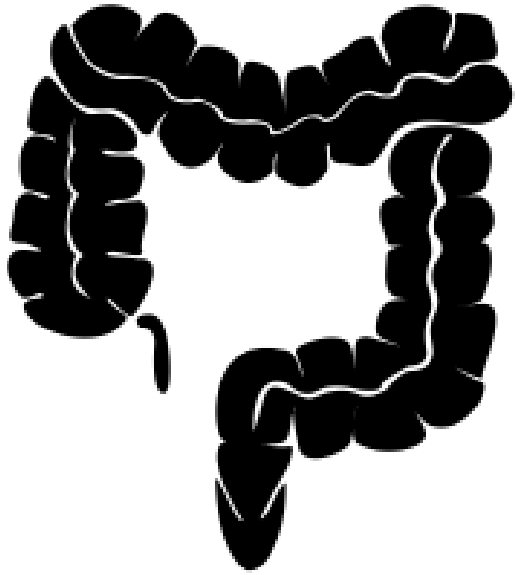
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Stage 2 of 2

DLI stoma reversal





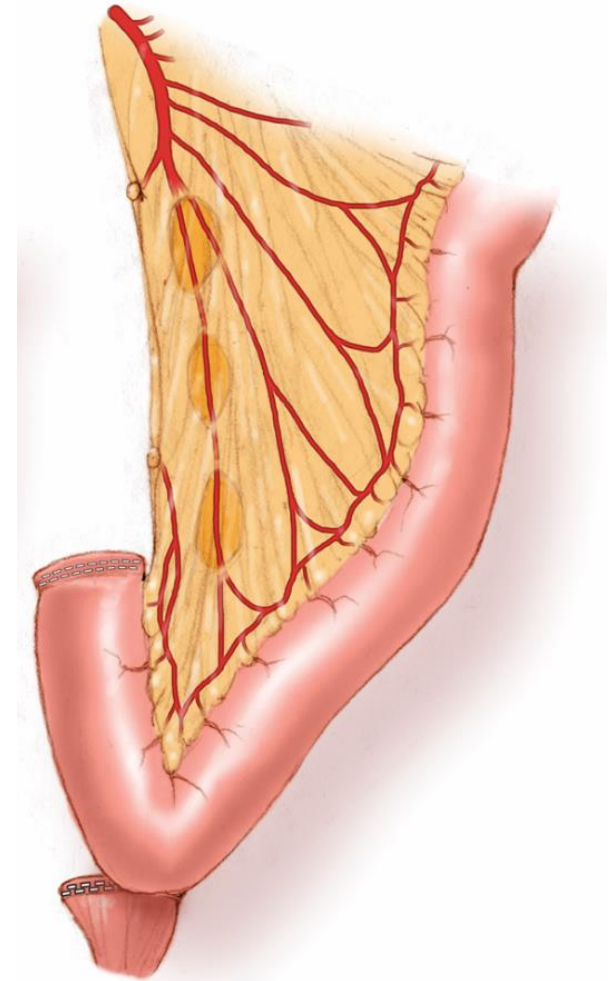
2. Operation

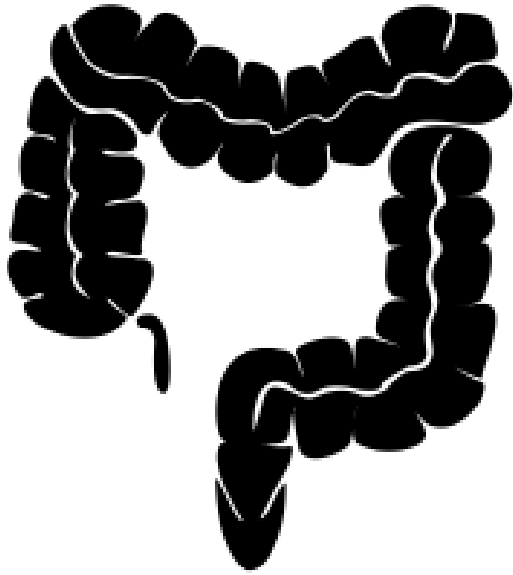


Stage 1 of 2
Total proctocolectomy/IPAA/DLI

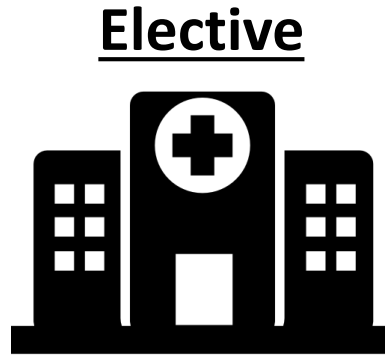


Stage 2 of 2
DLI stoma reversal





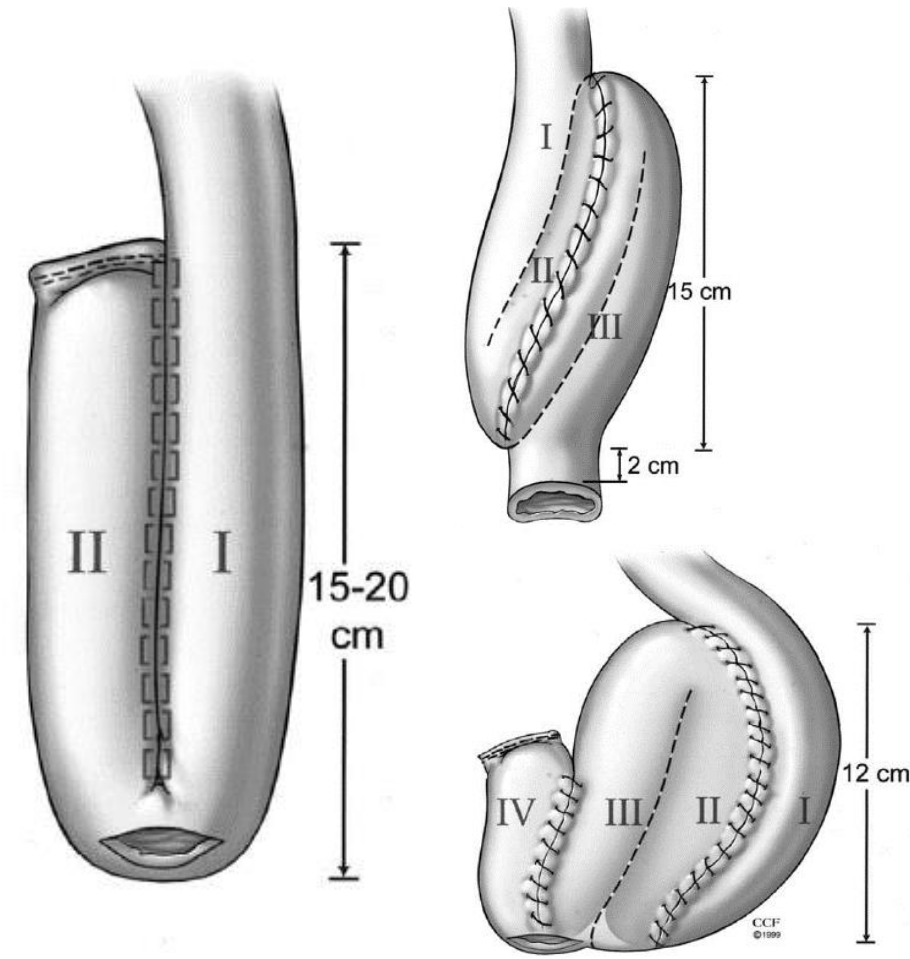
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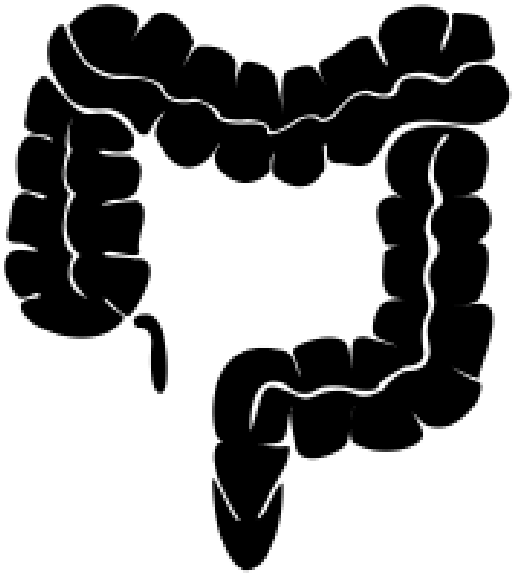


Stage 1 of 2
Total proctocolectomy/IPAA/DLI



Stage 2 of 2
DLI stoma reversal





2. Operation

Elective



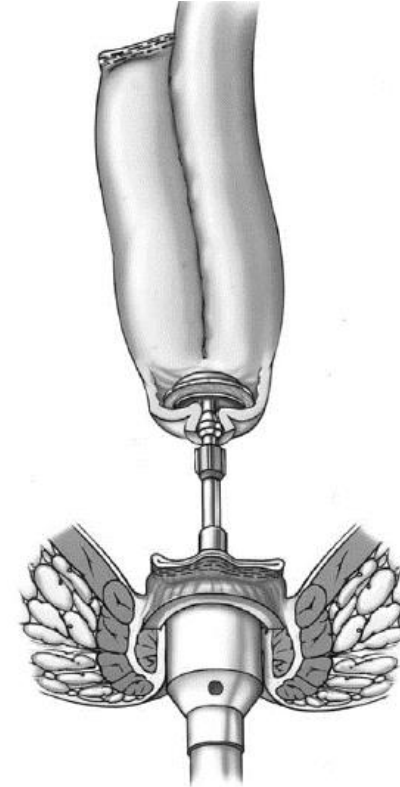
Stage 1 of 2

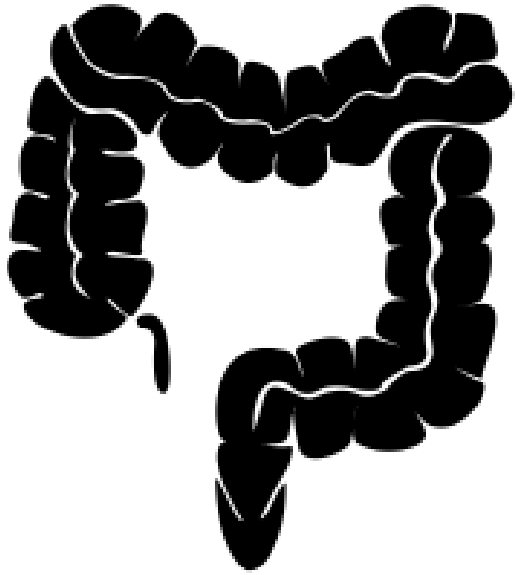
Total proctocolectomy/IPAA/DLI



Stage 2 of 2

DLI stoma reversal





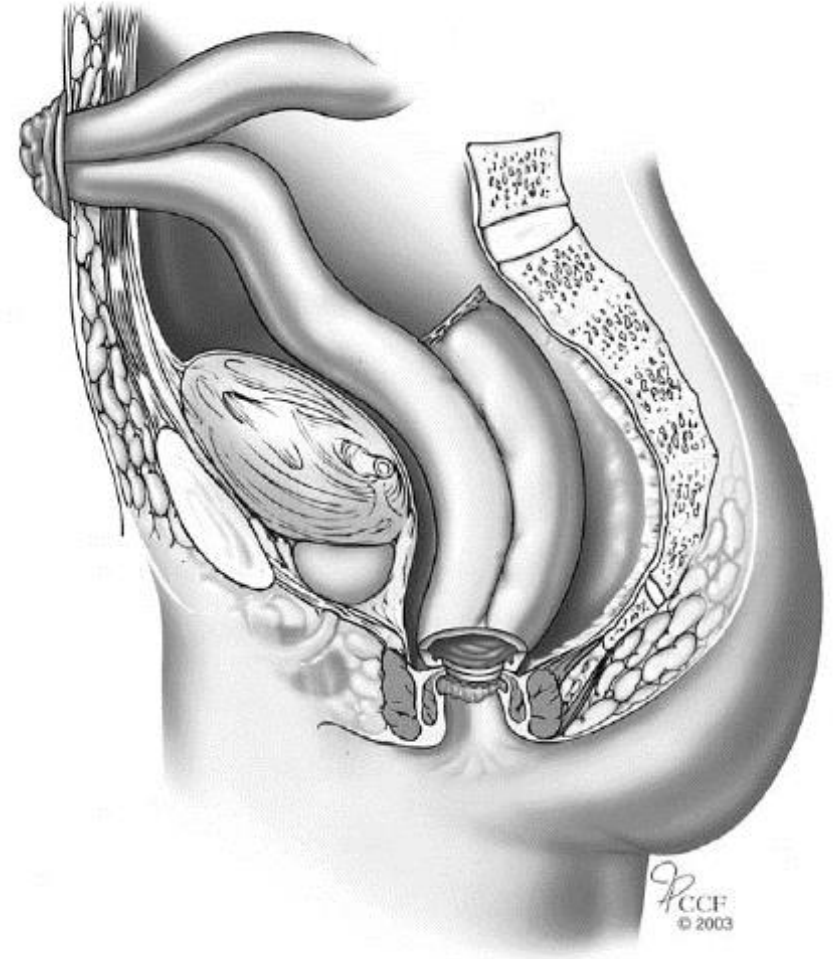
2. Operation

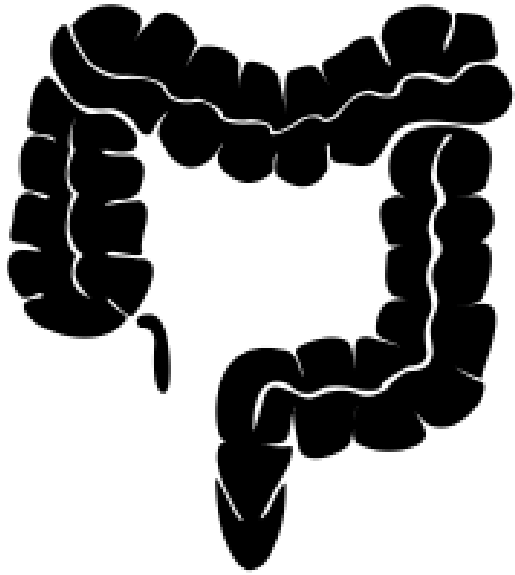


Stage 1 of 2
Total proctocolectomy/IPAA/DLI



Stage 2 of 2
DLI stoma reversal





2. Operation

Elective



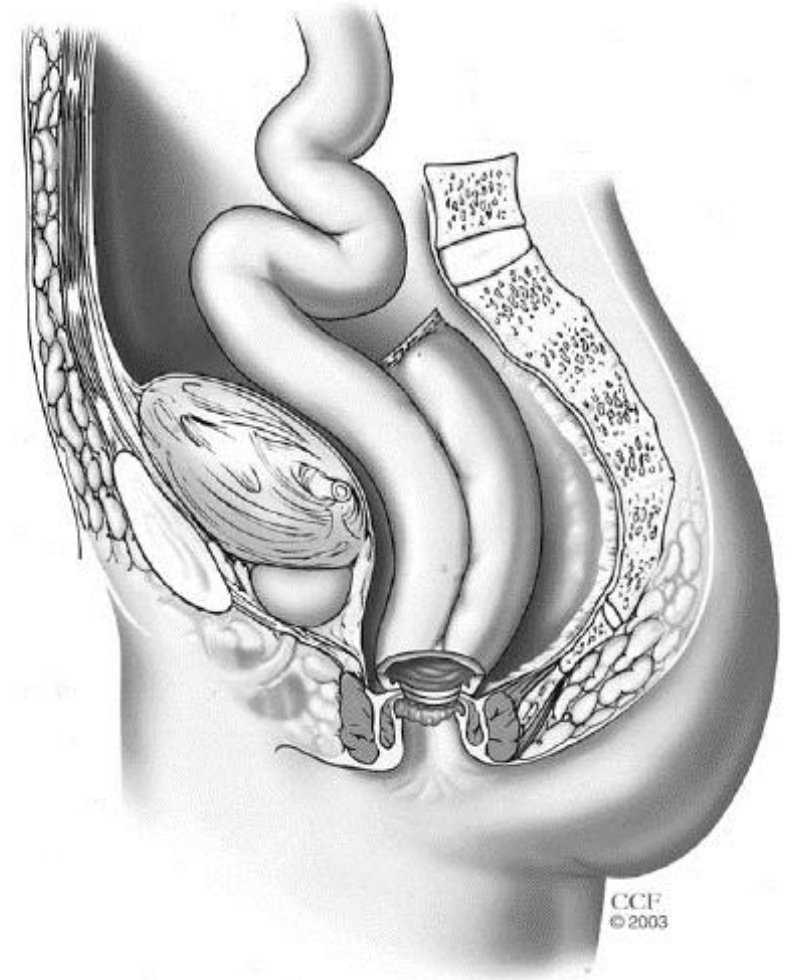
Stage 1 of 2

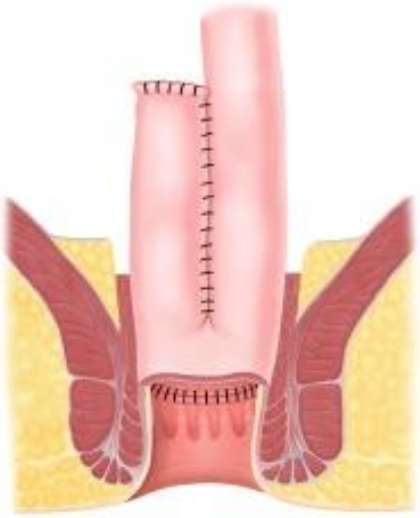
Total proctocolectomy/IPAA/DLI



Stage 2 of 2

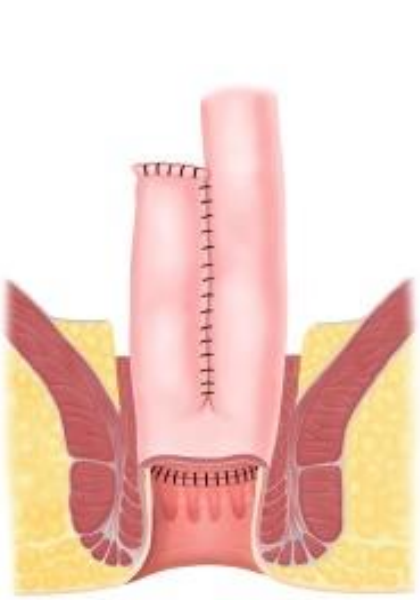
DLI stoma reversal



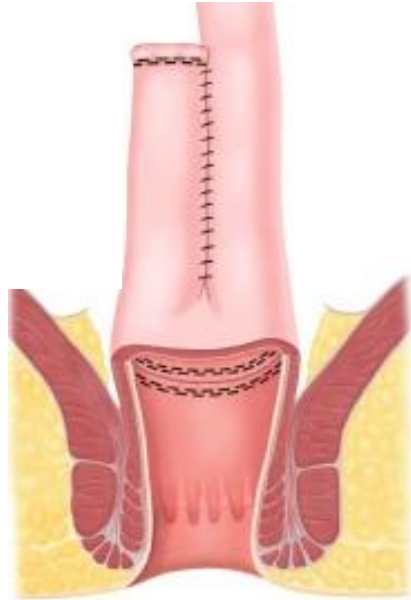


IPAA

Management | Surgical | Operation | CUC

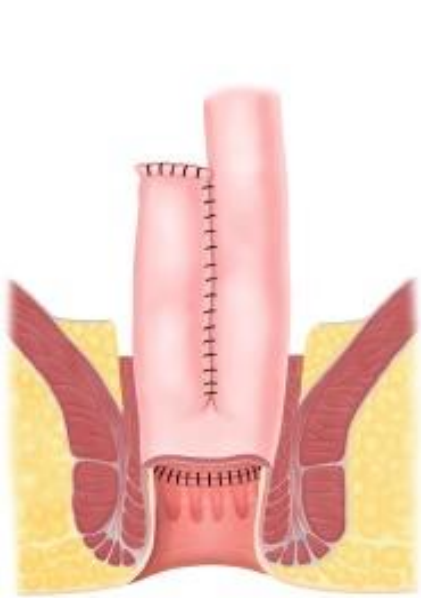


IPAA

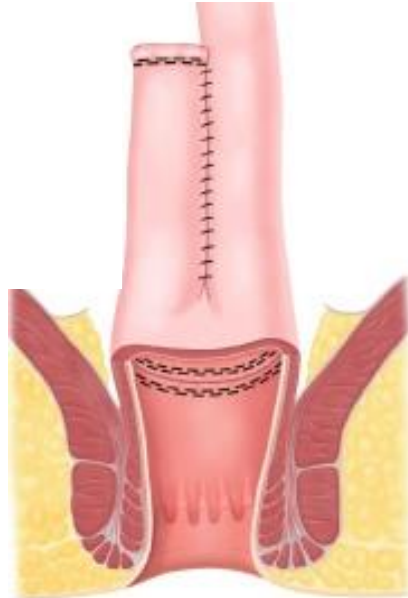


Stapled IPAA

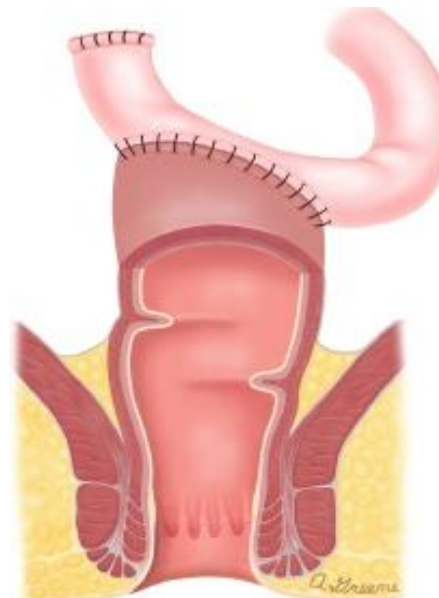
Management | Surgical | Operation | CUC



IPAA

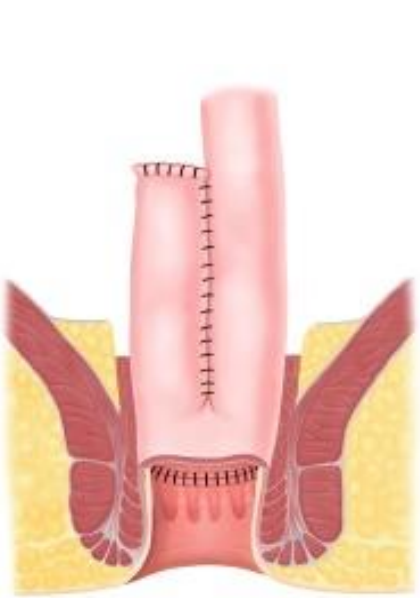


Stapled IPAA

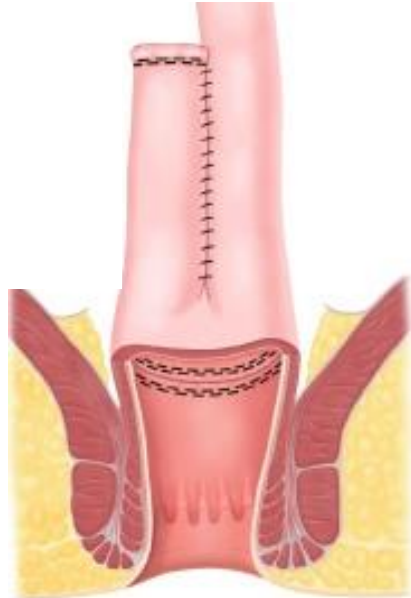


IRA

Management | Surgical | Operation | CUC



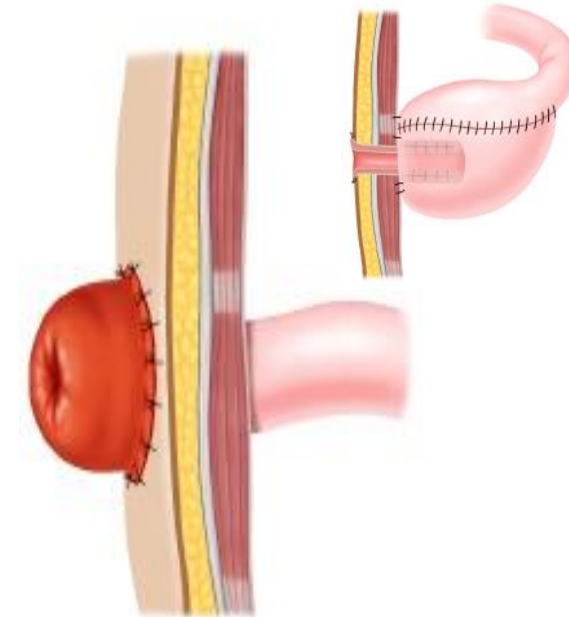
IPAA



Stapled IPAA

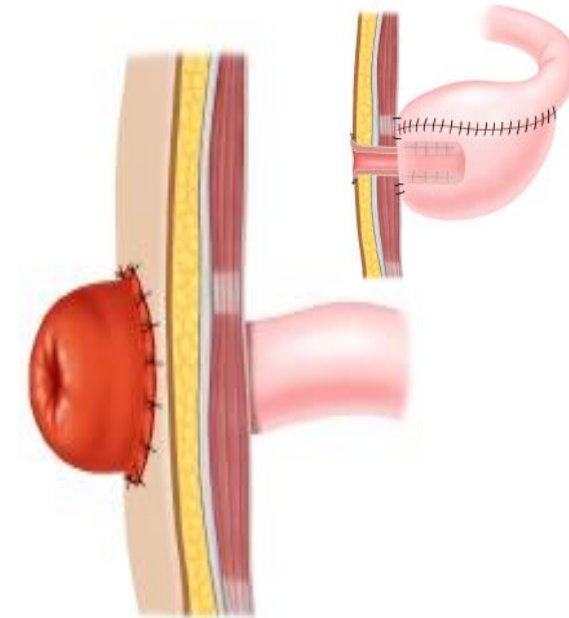
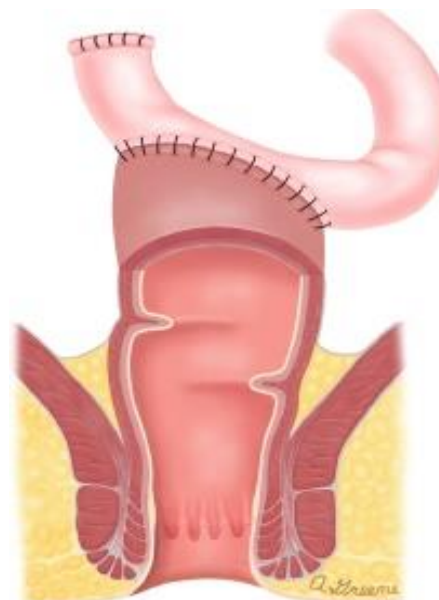
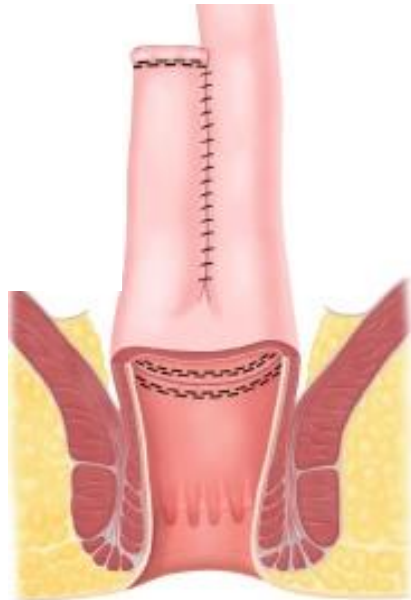
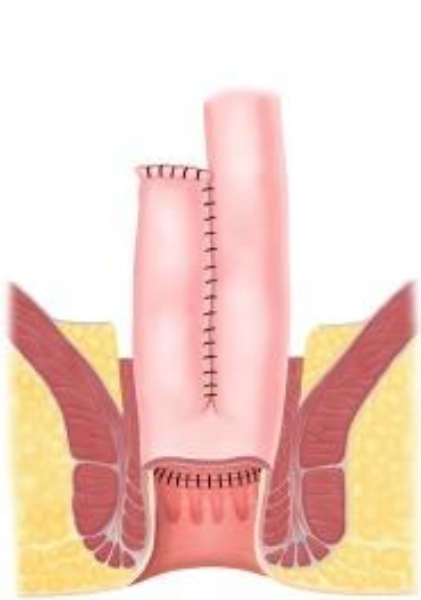


IRA



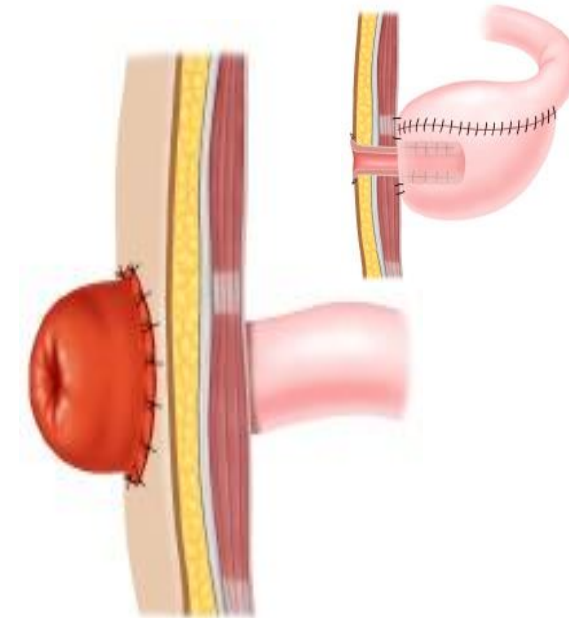
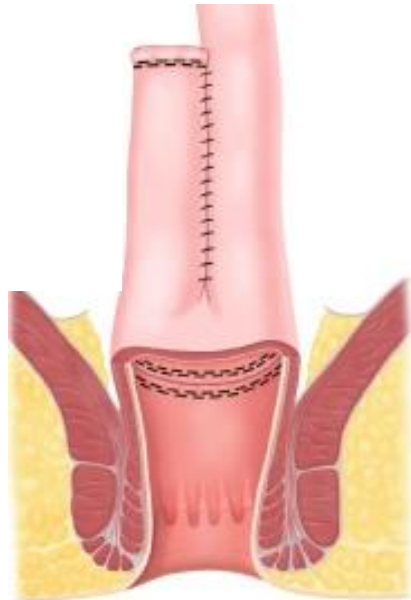
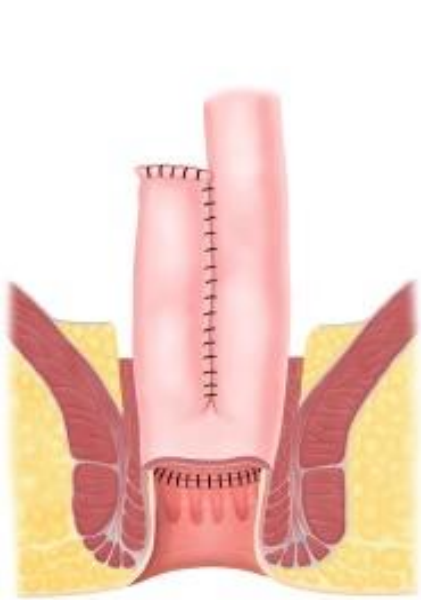
TPC/end ileostomy

Management | Surgical | Operation | CUC

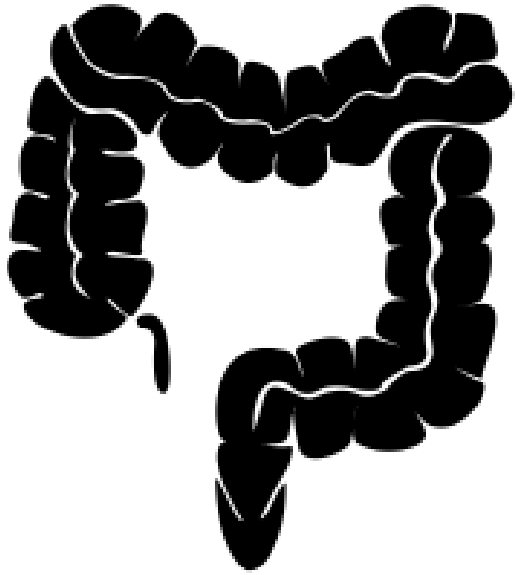


| IPAA | | Stapled IPAA | IRA | TPC/end ileostomy |
|-------------------------------|-------------------------|----------------------------|---------------------------------|-------------------------------|
| Multiple surgeries | | | One surgery | |
| Restorative continuity | | | No continuity | |
| Some fecal incontinence | Better fecal continence | Preserved fecal continence | No continence | |
| ↓↓ cancer risk | ↓ cancer risk | + Risk for cancer | No cancer risk for cancer | |
| Risk of sexual/urinary dysfxn | | | ↓ risk of sexual/urinary dysfxn | Risk of sexual/urinary dysfxn |
| ↓ fertility | | | Fertility preserved | ↓ fertility |
| Pouchitis | Pouchitis + Cuffitis | Rectal stump inflammation | Parastomal hernia | |

Management | Surgical | Operation | CUC



| IPAA | Stapled IPAA | IRA | TPC/end ileostomy |
|-------------------------------|-------------------------|---------------------------------|-------------------------------|
| Multiple surgeries | | One surgery | |
| Restorative continuity | | | No continuity |
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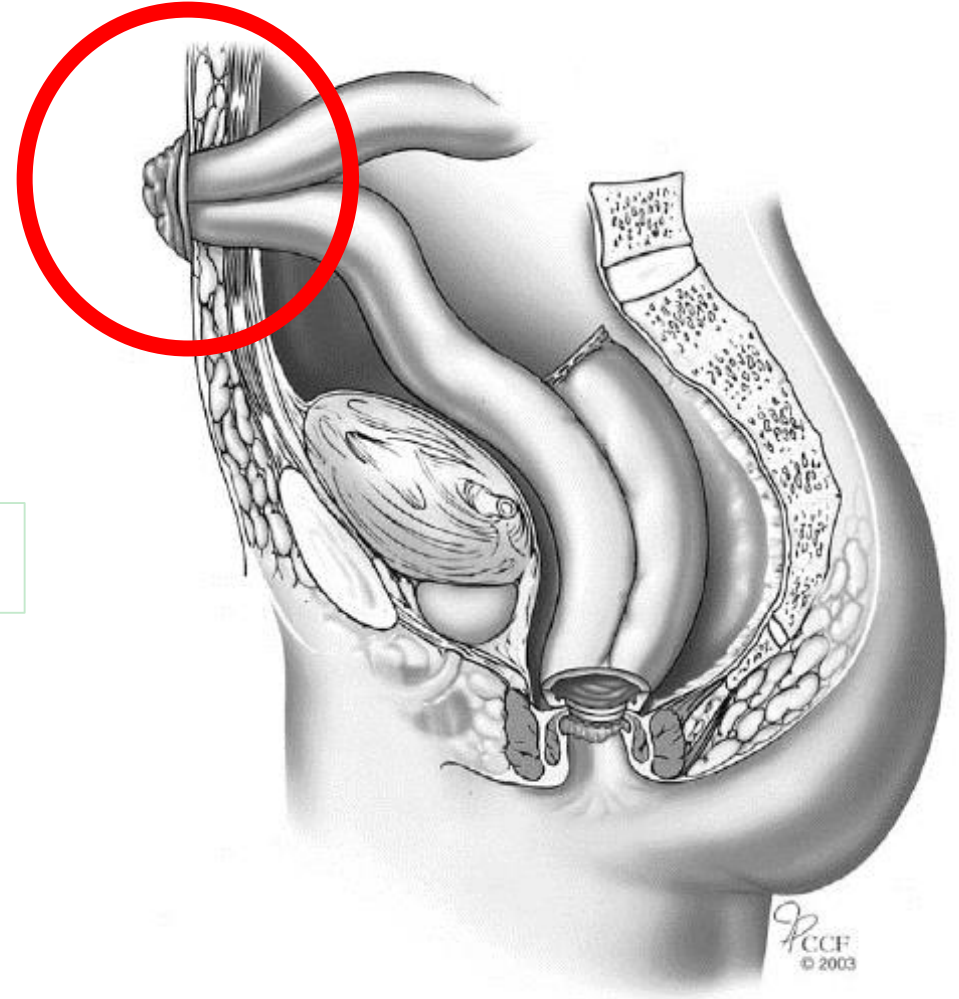


2. Operation

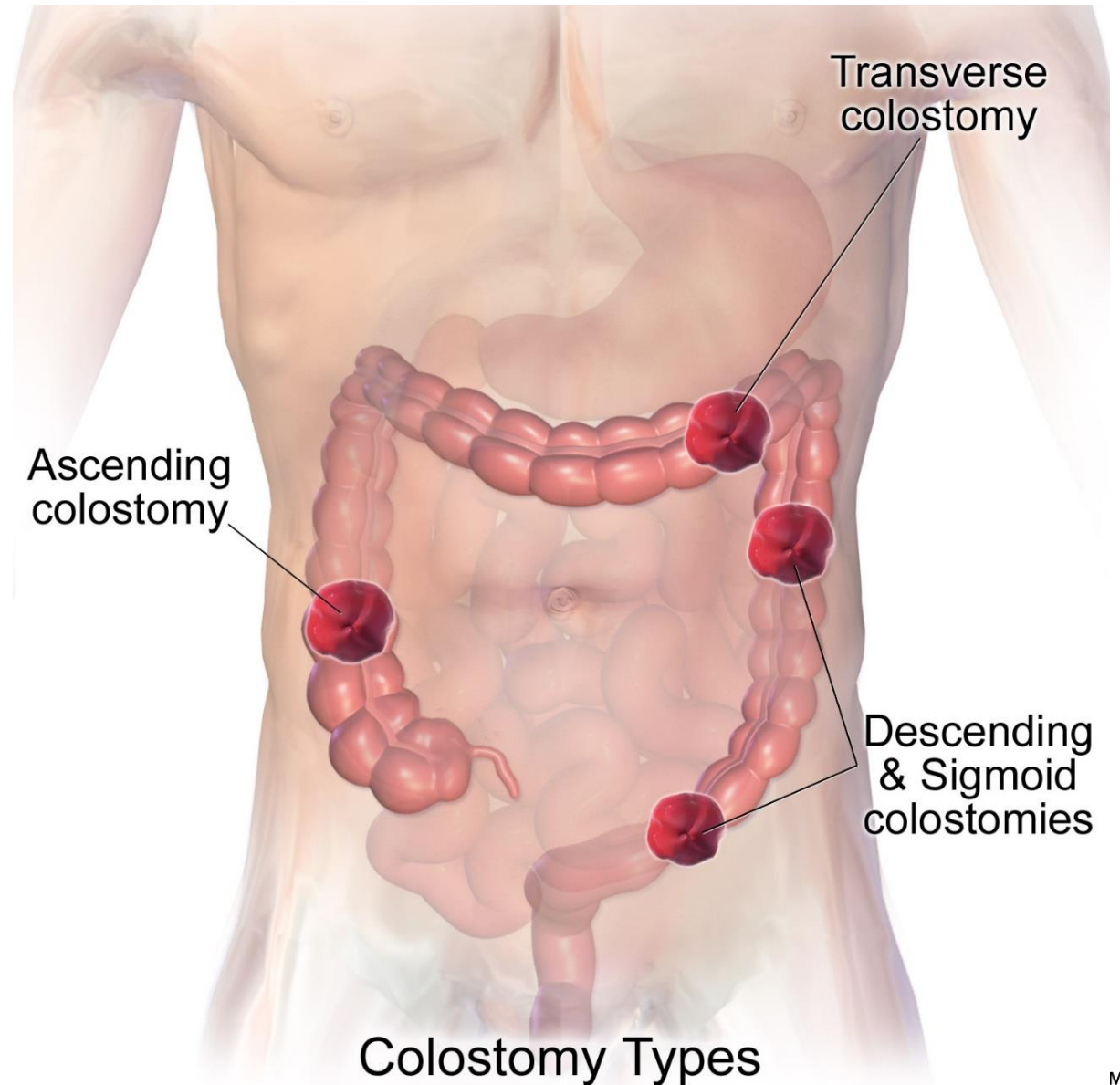
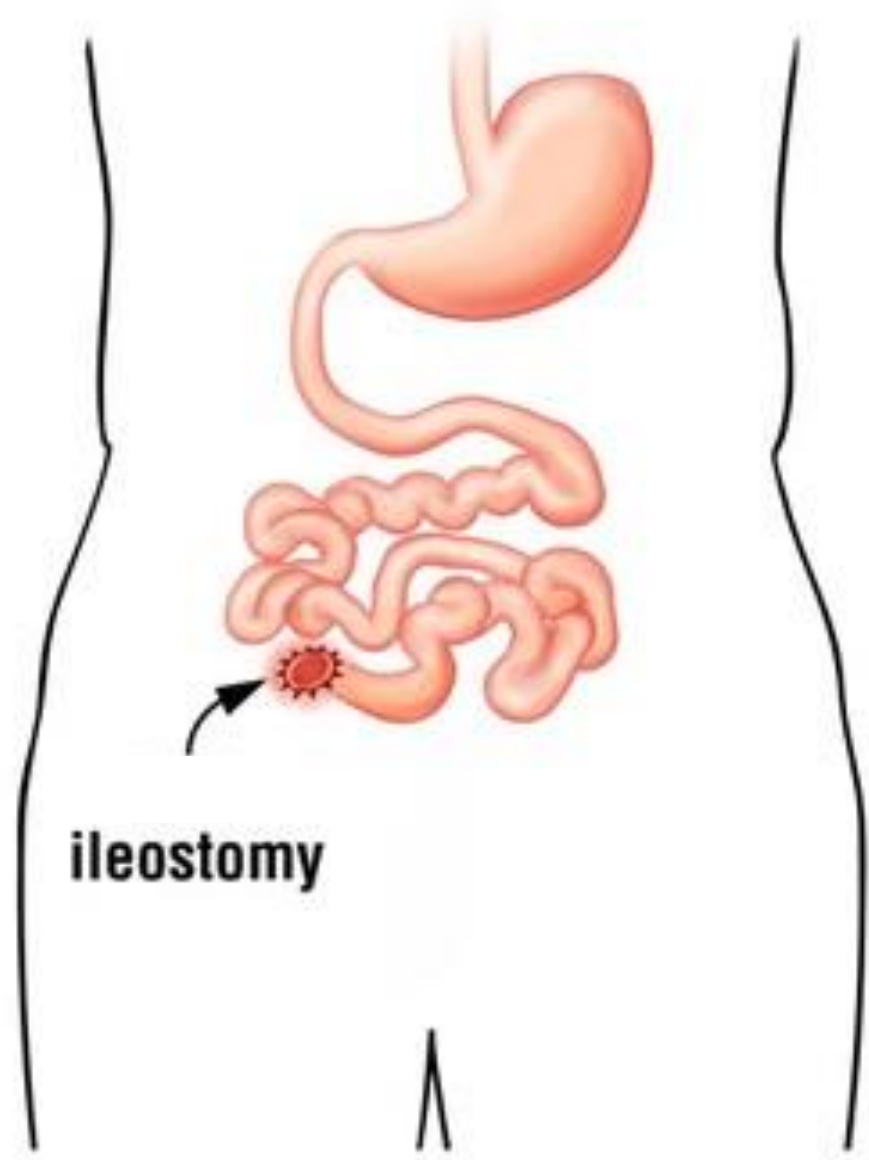
Elective



Ostomies



Management | Surgical | Operation | Ostomies



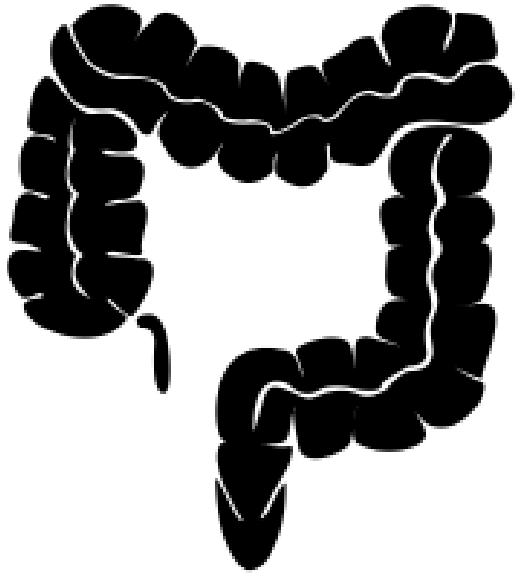
Management | Surgical | Operation | Ostomies



End Ostomy



Loop Ostomy



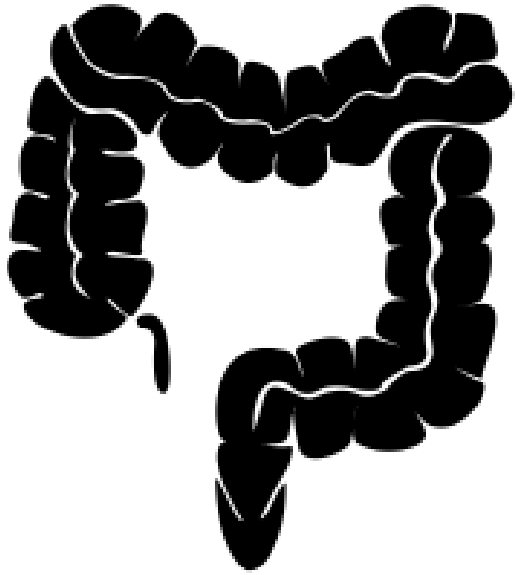
2. Operation

Elective



Ostomies





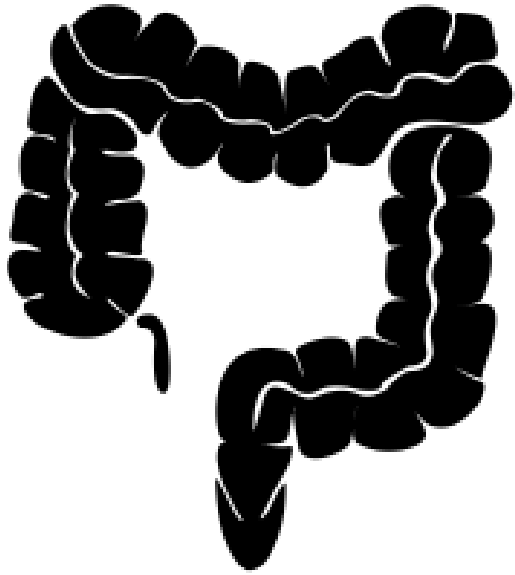
2. Operation

Elective



Ostomies





2. Operation

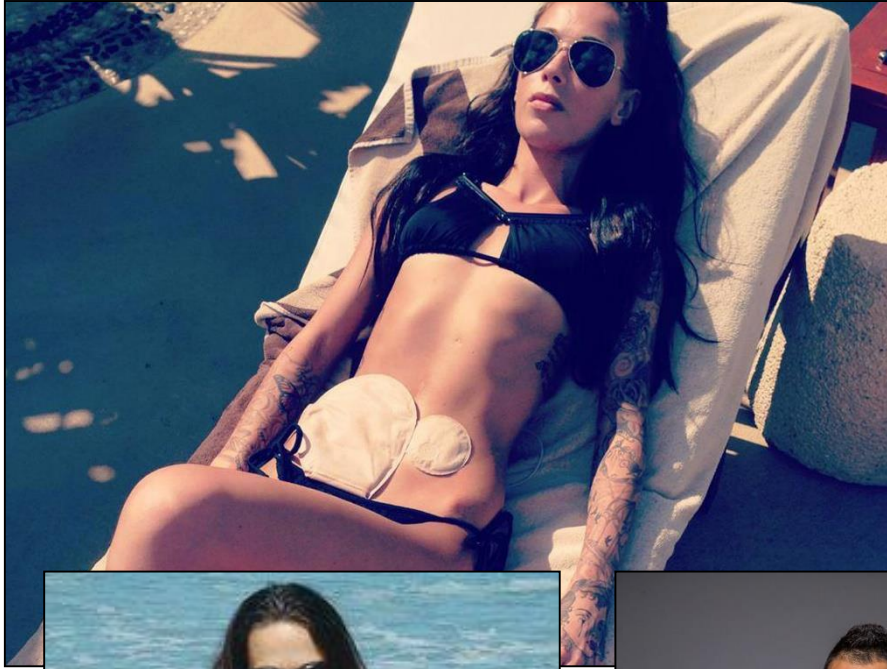
Elective



Ostomies

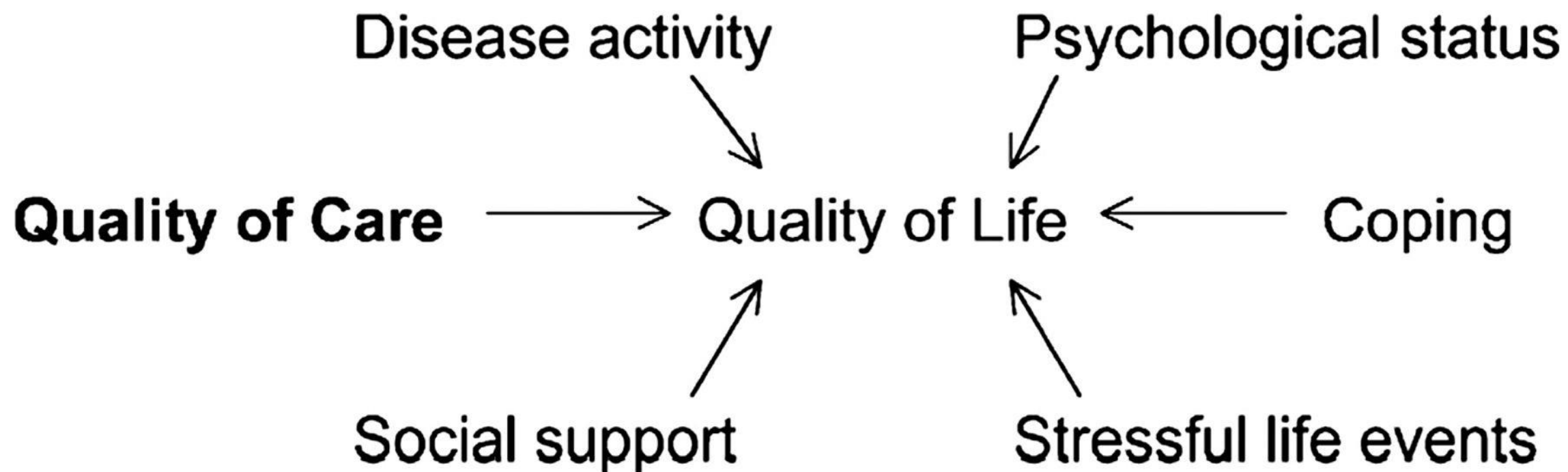


Management | Surgical | Operation

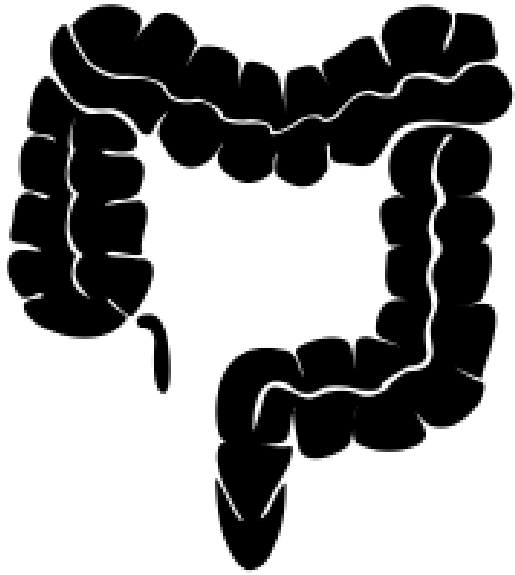


Management | Surgical | Operation

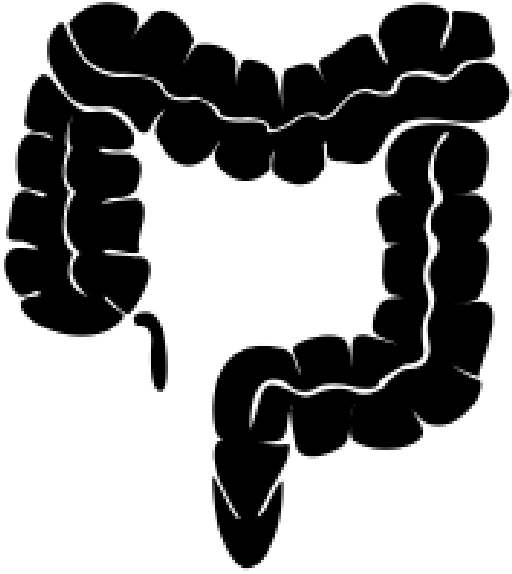
| | | |
|------------|-----------------------|-----------------------------|
| Procedure: | Approach | 56% minimally-invasive |
| | Stoma | 38% |
| Outcomes: | Mortality | <1% |
| | Post-Op Comp | 9% surgical site infections |
| | | 7% organ-space infections |
| | | 10% bleeding |
| | Length-of-Stay | 5 days |
| | Readmission | 15% |



Important Points to Consider



2. Operation



Important Points to Consider

1. Poor pelvic floor function

Elderly patient

2. Operation



STOP

No to IPAA



Important Points to Consider

1. Poor pelvic floor function

Elderly patient

Options:

- (a) End ileostomy
- (b) Ileorectal anastomosis



Important Points to Consider

1. Poor pelvic floor function

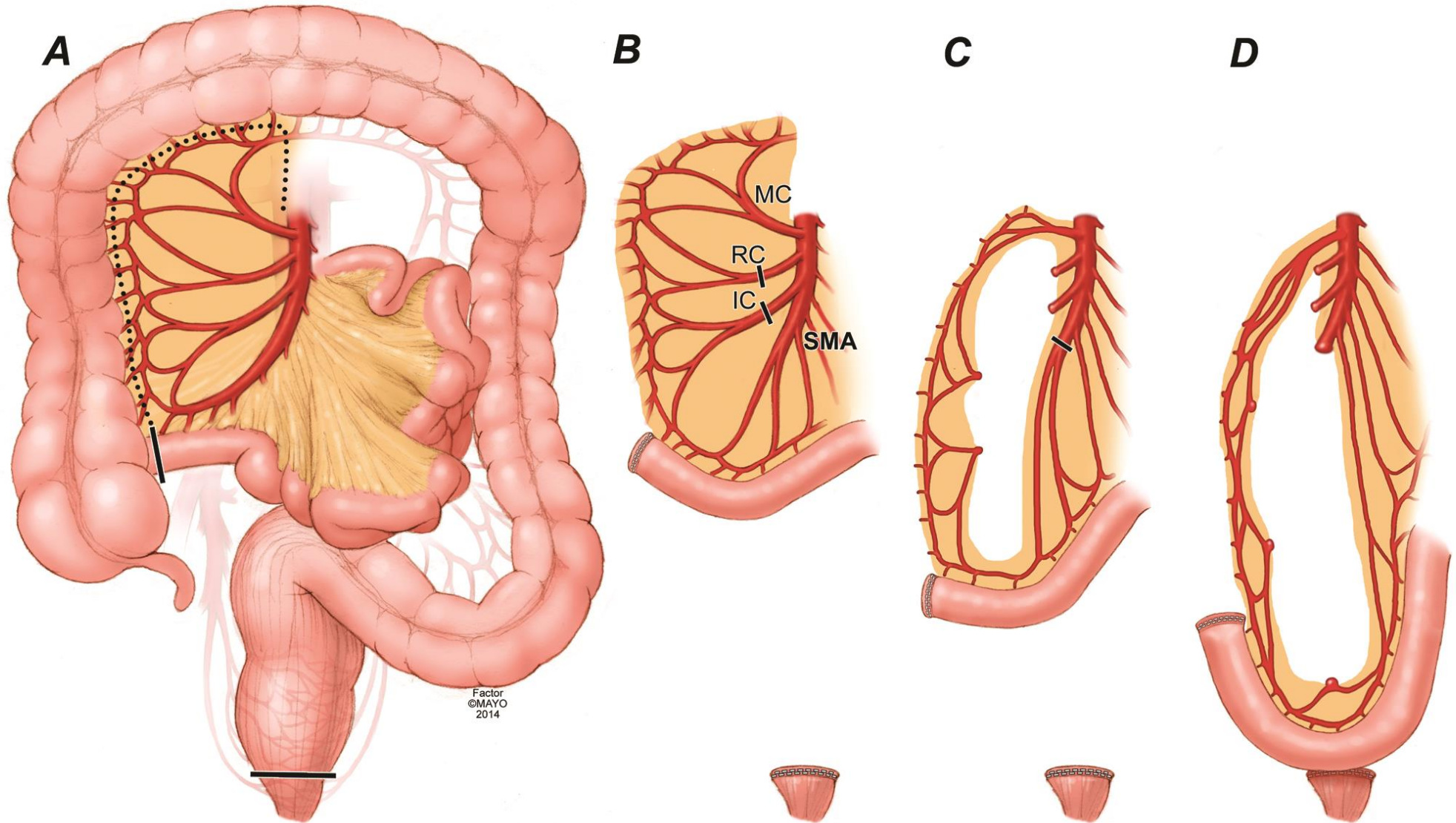
Elderly patient

2. Shortened mesentery

Obese patient



Management | Surgical | Operation





Important Points to Consider

1. Poor pelvic floor function

Elderly patient

2. Shortened mesentery

Obese patient



Important Points to Consider

1. Poor pelvic floor function

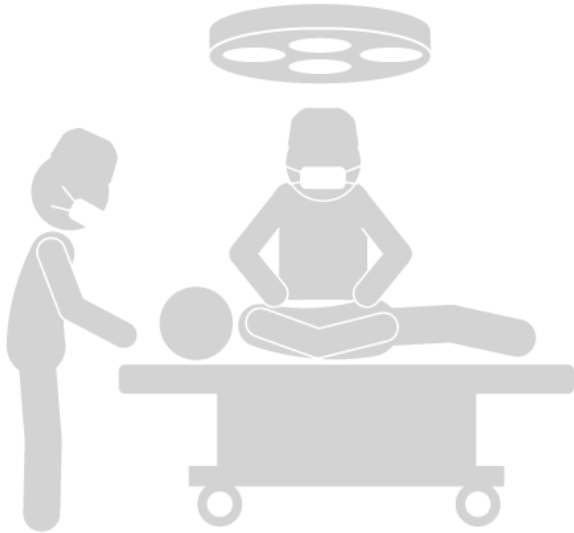
Elderly patient

2. Shortened mesentery

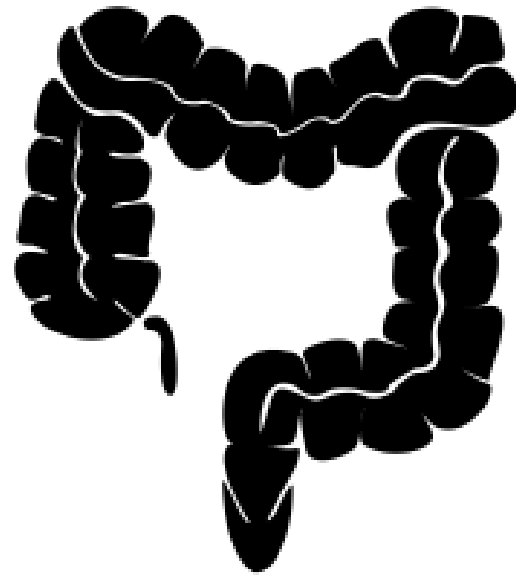
Obese patient

3. Crohn's disease

Don't do a pouch!!!



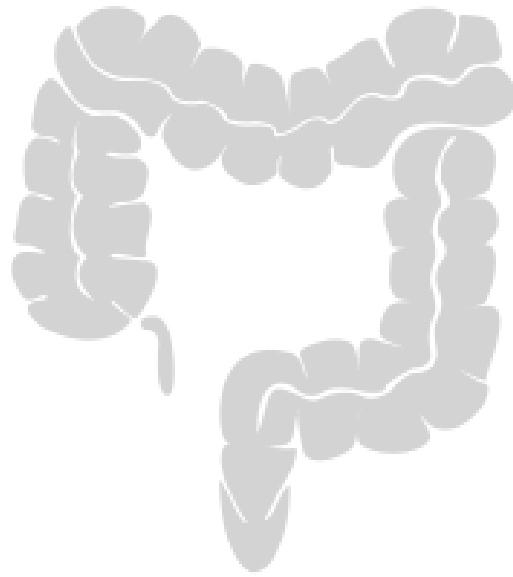
1. Indications



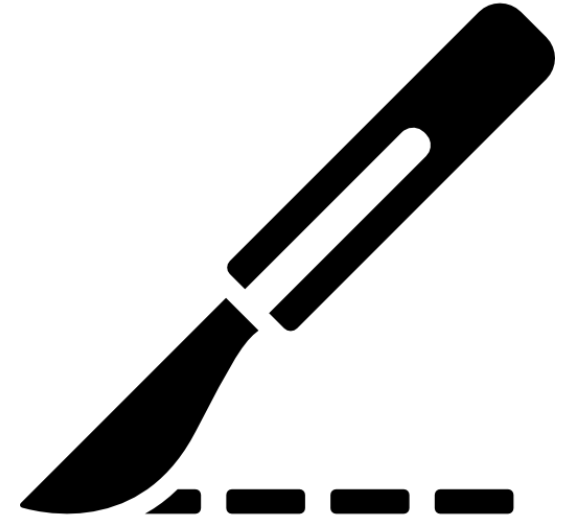
2. Operation



1. Indications

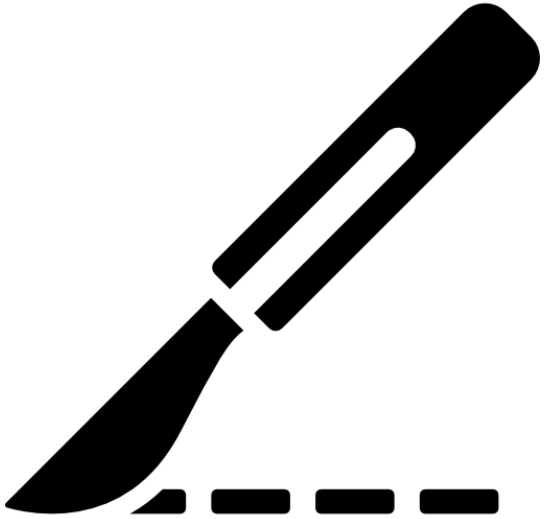


2. Operation



3. Complications

What are complications to consider?

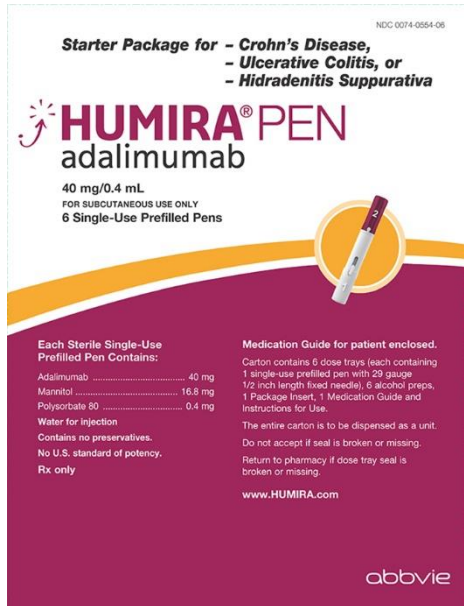


3. Complications

Management | Surgical | Complications

What are complications to consider?

1. Effect of biologics



Management | Surgical | Complications: **Biologics**



Biologics Do they cause complications?

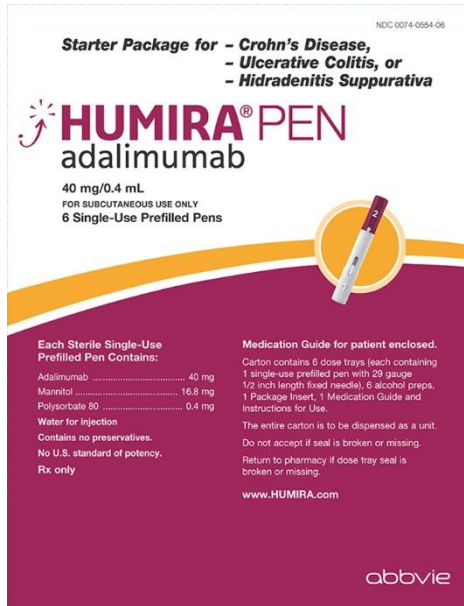
Studies limited by:

Heterogeneous patients

Differences in timing of biologics

Variations in definition of complications

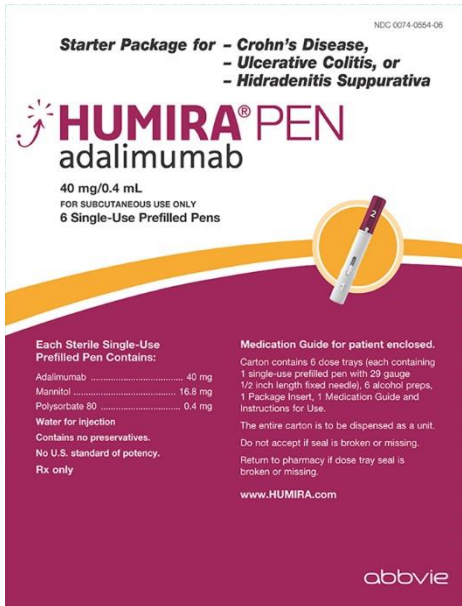
Small, underpowered populations (type 2 errors)



Management | Surgical | Complications: **Biologics**



Biologics Do they cause complications?

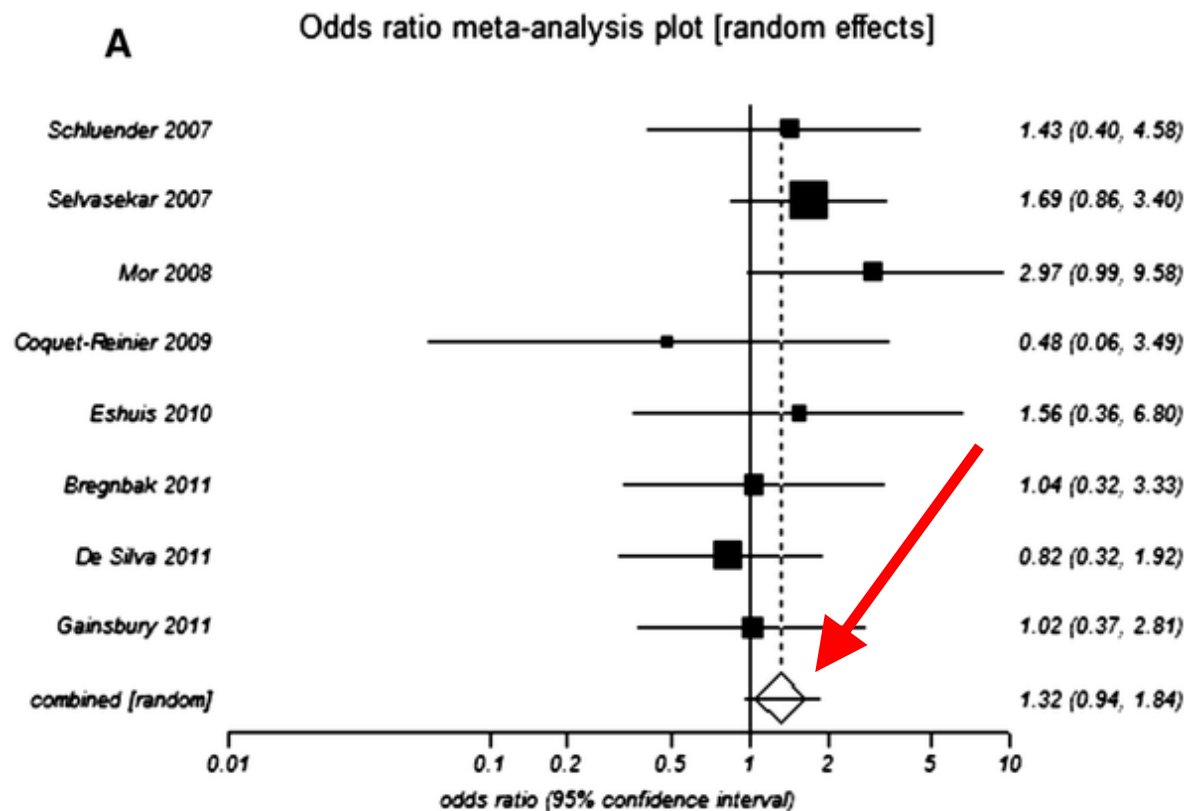


Crohn's
Heck yeah.

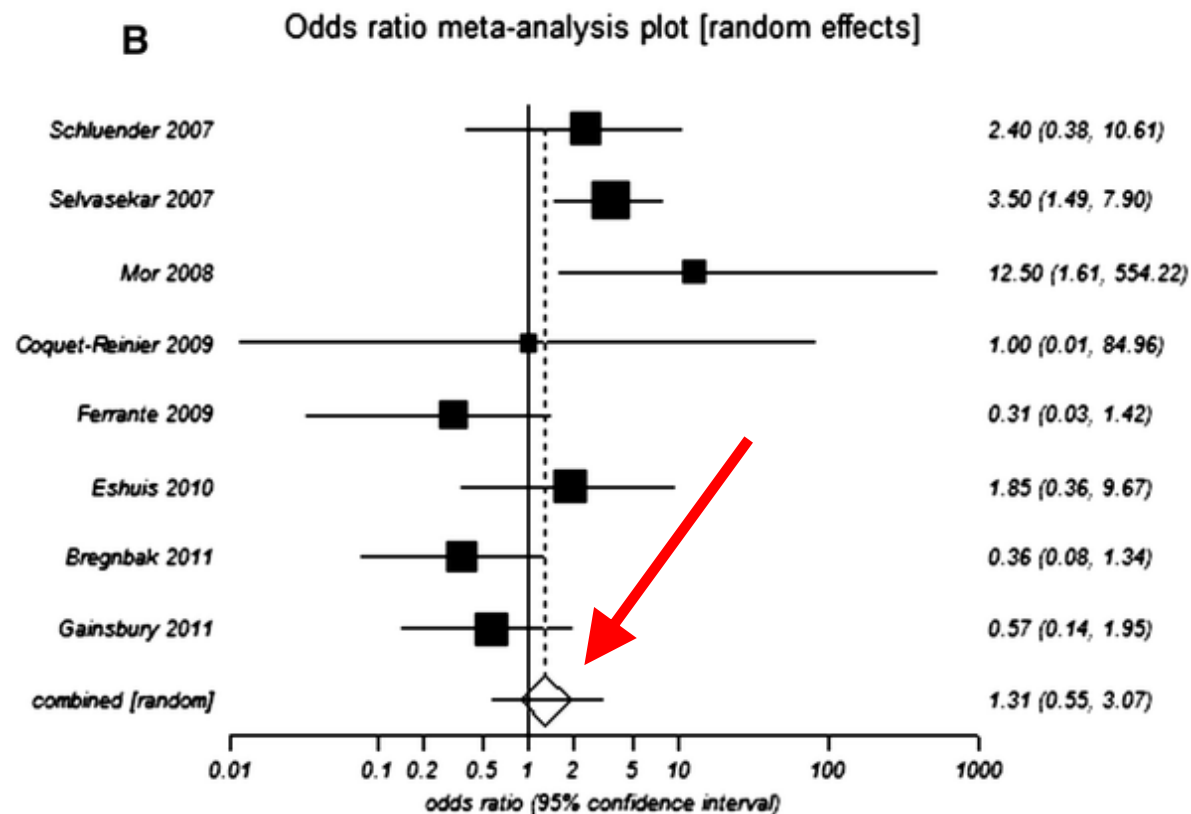
Ulcerative colitis
Maaaybe.

2013 Meta-analysis of Overall Complications

Crohn's: Worse overall complications



Ulcerative Colitis: No difference



Entyvio – Newest 2016 data (Mayo Clinic)

- Compared 3 groups: Entyvio vs TNF vs no therapy (2014-15)
- In Entyvio group, 53% complication rate of which 36% SSI
- Infections: 53 vs. 33 (TNF) vs. 28% (control) ($p<0.05$)
- SSI: 37 vs. 10 vs. 13% ($p<0.05$)

Entyvio within 12-weeks associated with higher complications

- In ideal world, no biologics before surgery – but likely impossible

Crohn's

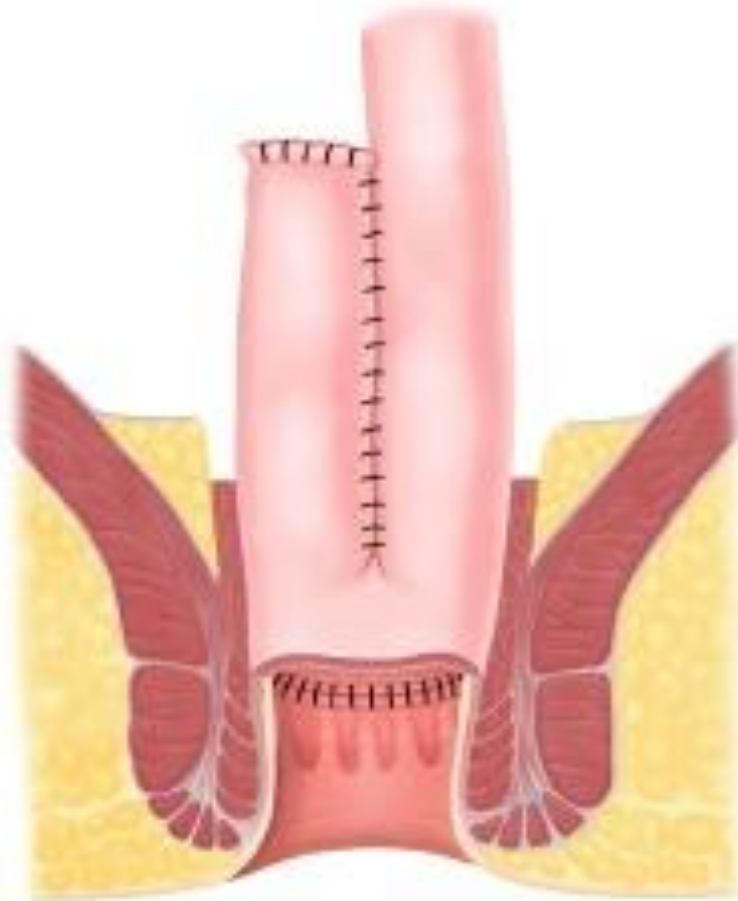
- If biologic present, consider use of diversion (end or loop)

Ulcerative colitis

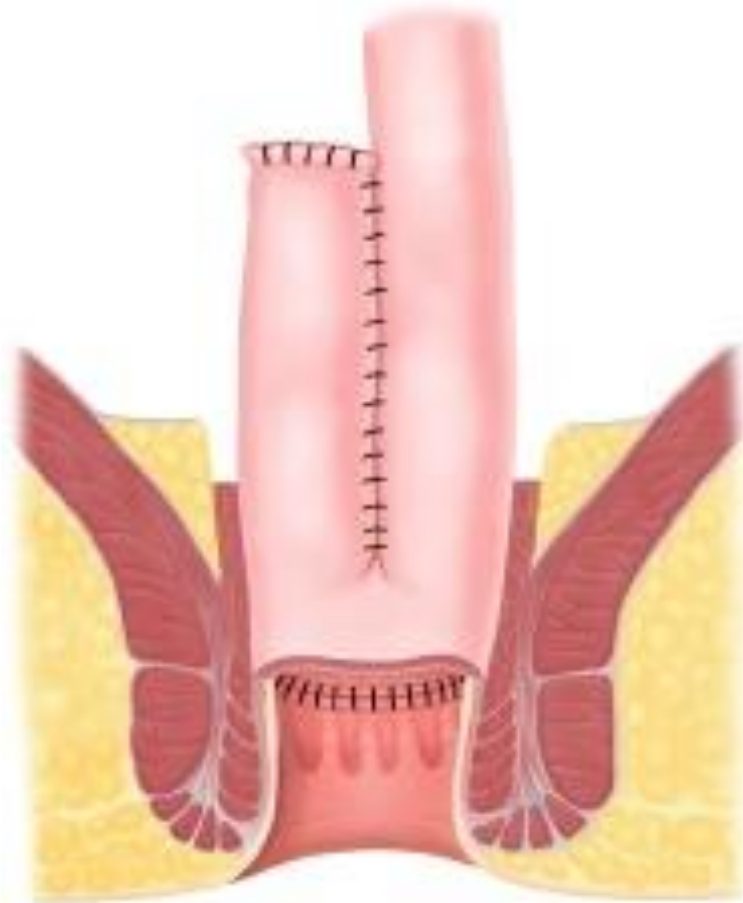
- If biologic present, but no other risk factor, can proceed with 2-stage
- If other risk factor (e.g., **steroids, poor nutrition**), be conservative!!!

What are complications to consider?

1. Effect of biologics
- 2. Pouch dysfunction**



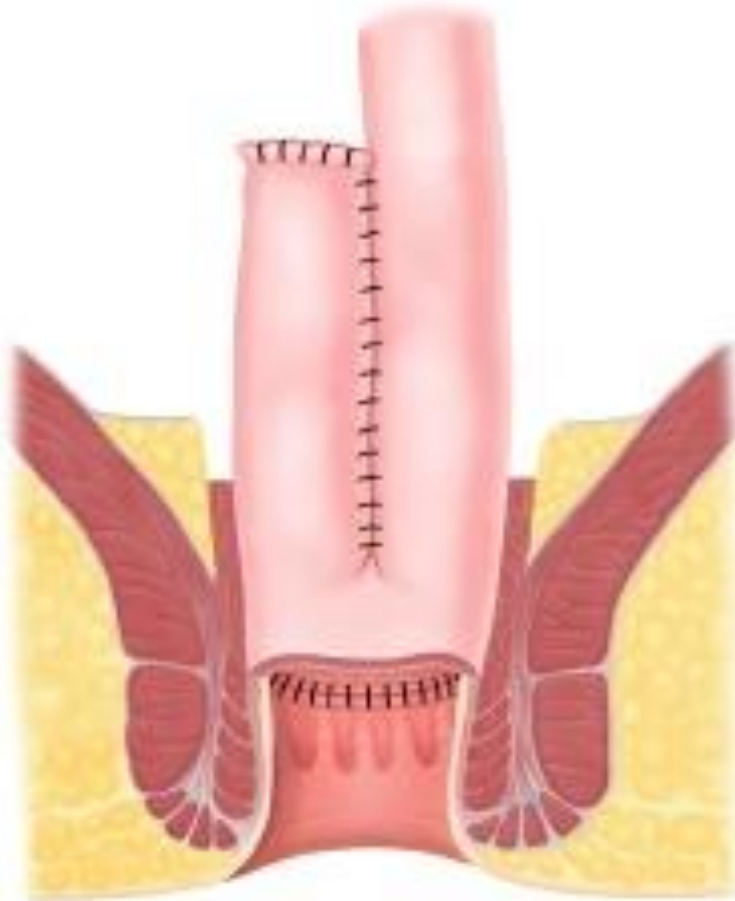
Management | Surgical | Complications: Pouch

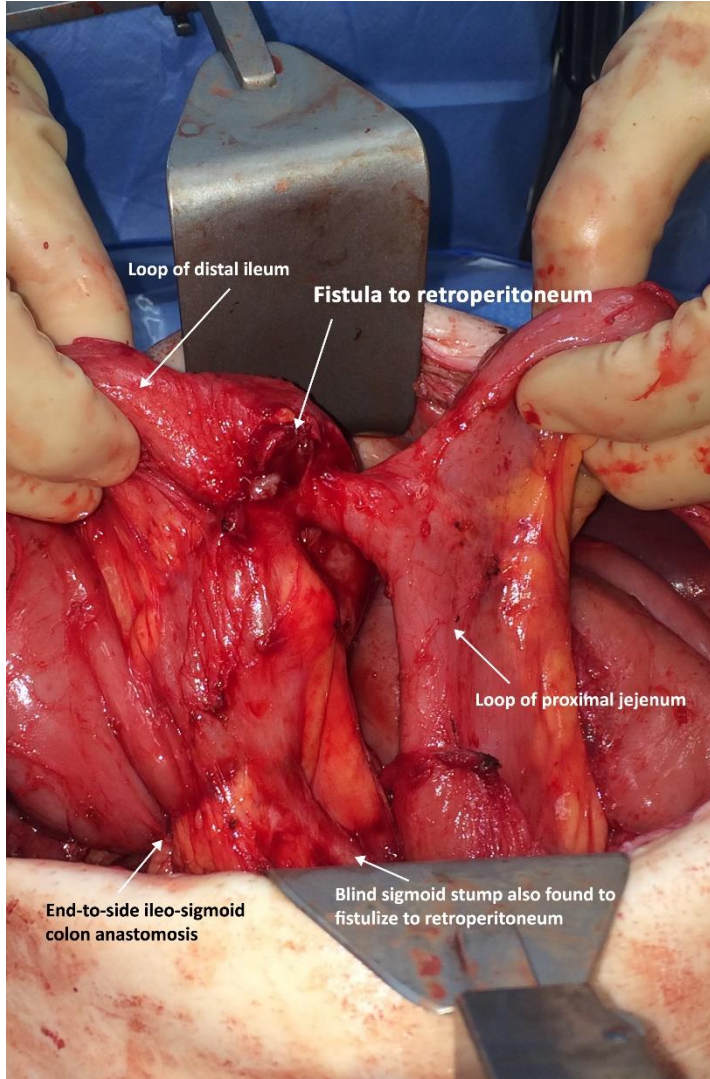


- **Pouchitis** -- **#1 long-term complication**
Tx: Antibiotics
- **Cuffitis** ----- “CUC” of the rectal cuff
Tx: Medical → Surgical (pouch advancement)
- **Stricture** --- Ischemia
Tx: Serial dilations → Surgical (anoplasties)
- **Fistulas** ---- Need to r/o Crohn’s
Tx: Setons, promote drainage

What are complications to consider?

1. Effect of biologics
- 2. Pouch dysfunction**

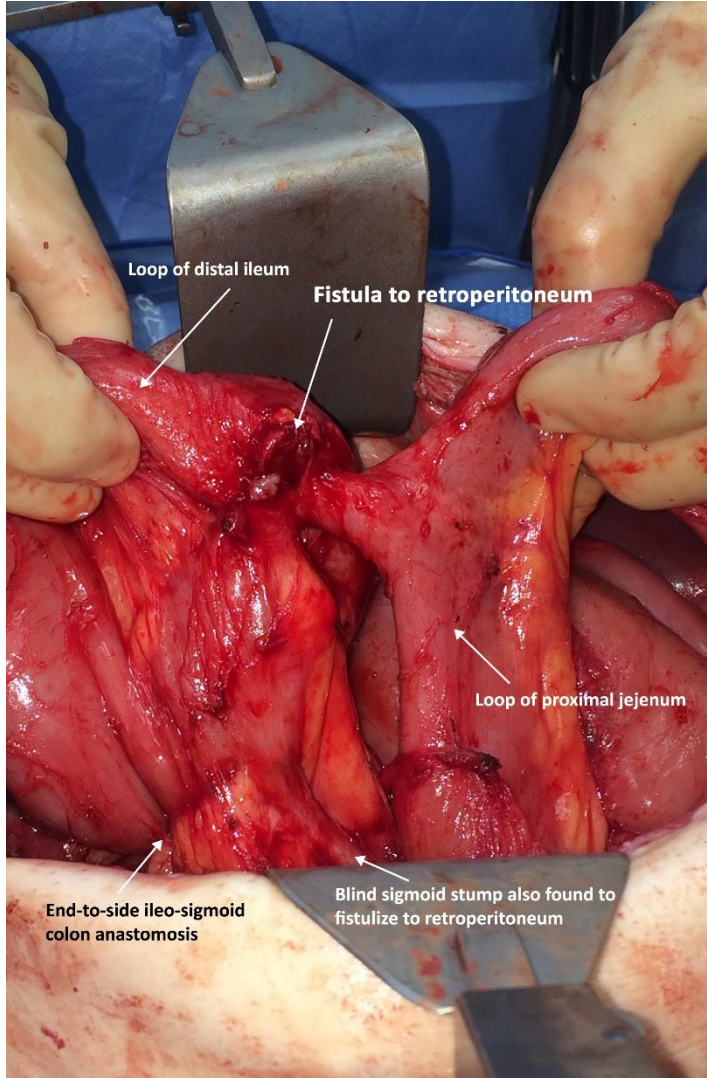




What are complications to consider?

1. Effect of biologics
2. Pouch dysfunction
- 3. Crohn's disease**

Management | Surgical | Complications: Crohn's



- 10-15% rate of Crohn's dx in IPAAAs

- **Worry if:**

- Fistulas
- Strictures
- Other unusual symptoms/findings

- **Treatment options**

Pouch — DLI —→ Pouch excision

Summary



- **IBD** includes both Crohn's and Ulcerative Colitis
- Incidence and prevalence of IBD is increasing
- Diagnosis is challenging - no one way and must know >1 approach
- Management involves both medical *and* surgical strategies
 - Medical strategies follow a spectrum of treatment options
 - Surgical strategies focus on key indications, operations and complications

Bottom Line

IBD is challenging but is quite treatable through a team effort involving best-practices in **medicine** and **surgery**.



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Questions?



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