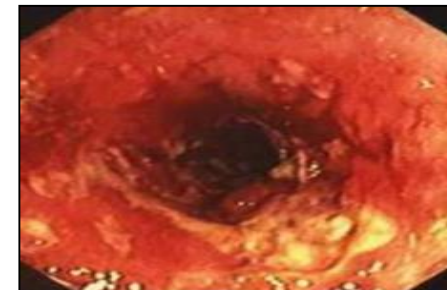




Inflammatory Bowel Disease:

“Clinical updates”

Dr Jeff Chao
Princess Alexandra Hospital

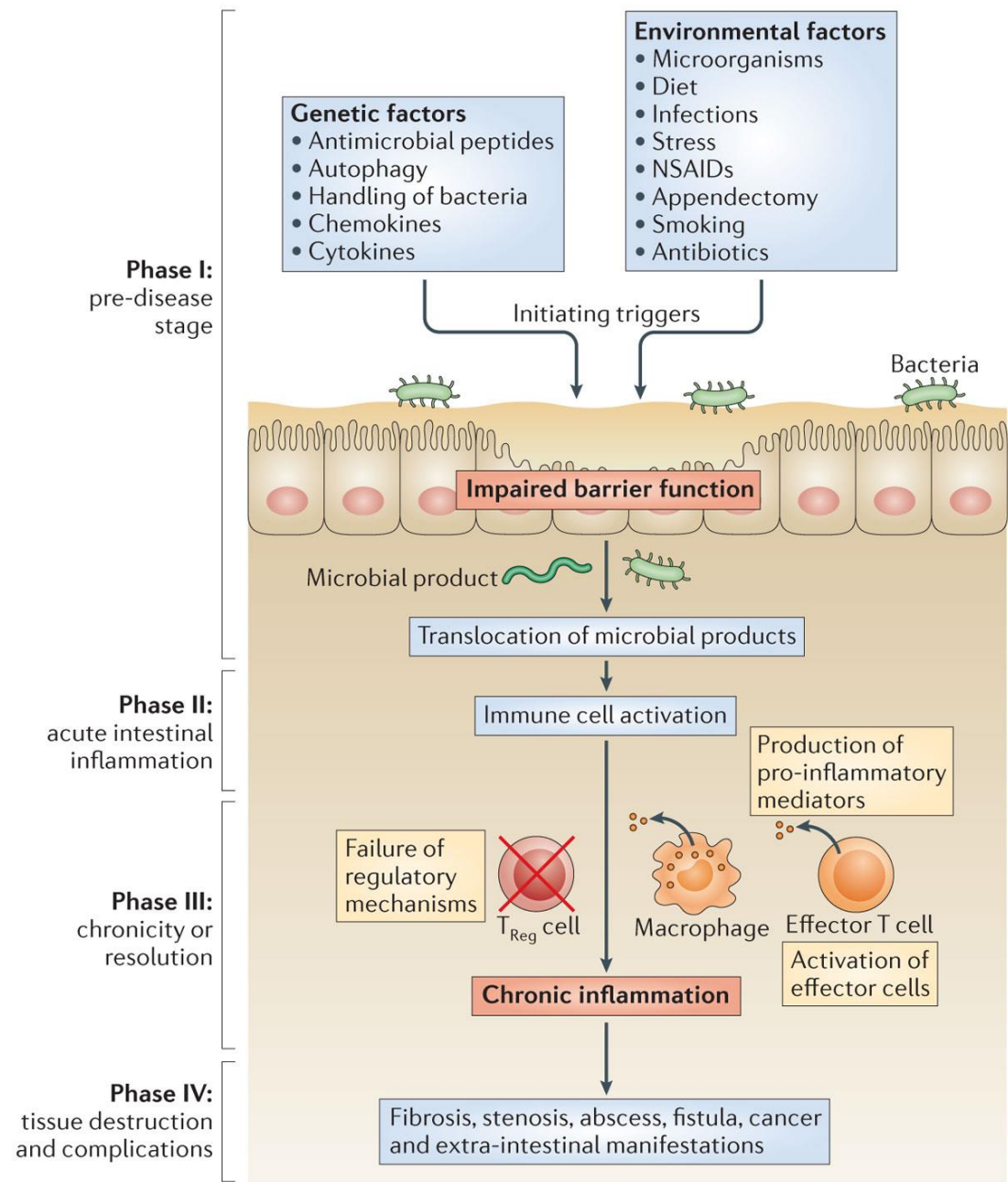


Inflammatory bowel disease 2017

- Clinical updates and future directions
 - Pathogenesis
 - Treatment targets
 - Therapeutic agents
 - Individualized therapy
 - Dysplasia surveillance technology
 - Prevention

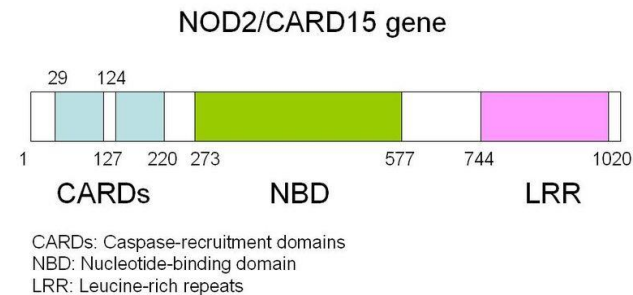
- Clinical dilemma
 - CMV in acute severe UC



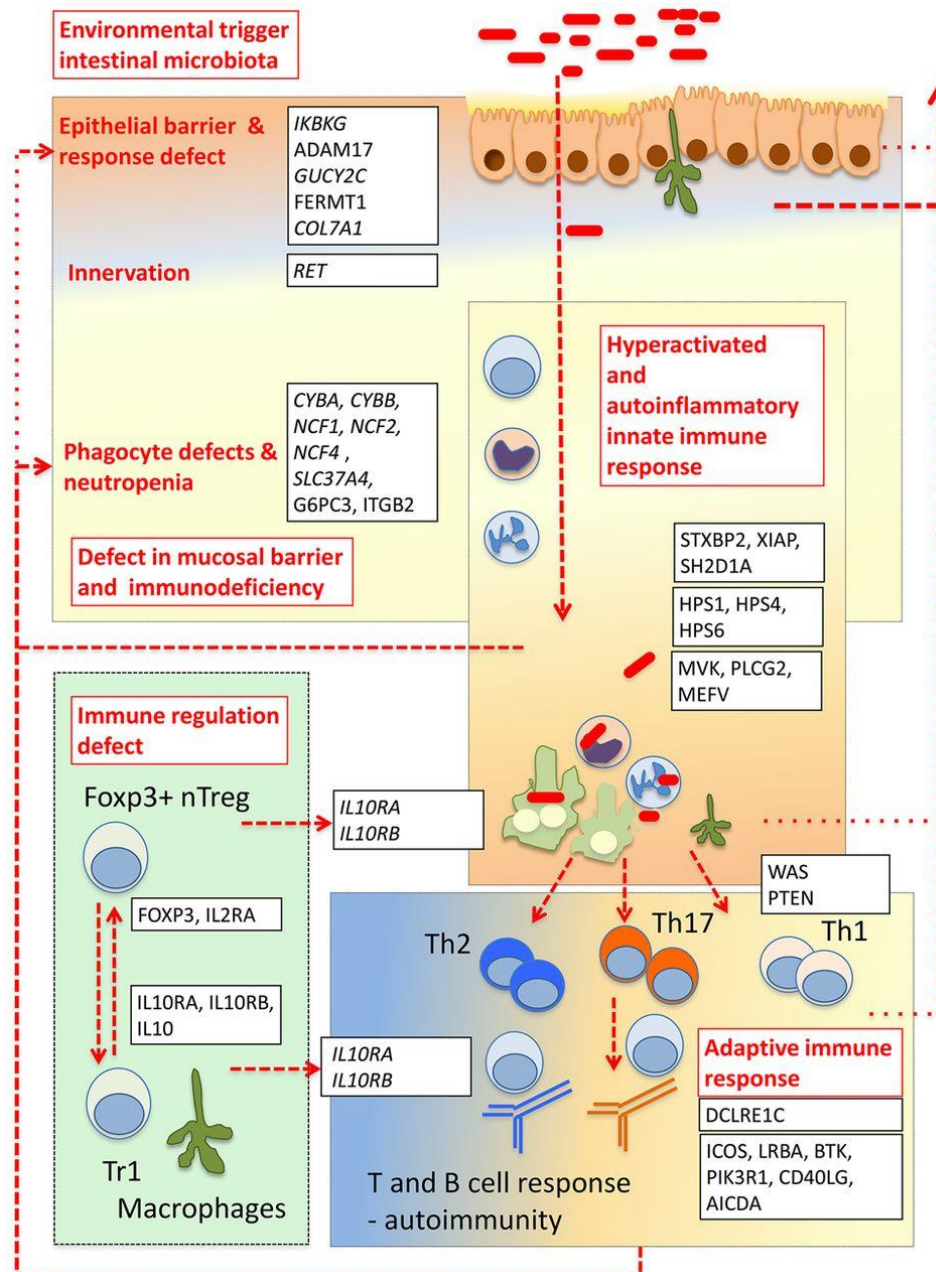


Genetic factors

- Complex polygenic disorder
- >200 susceptibility loci
- NOD2 / CARD15
 - Younger age of onset
 - Small bowel involvement
 - Fibro-stenosing complication
 - Higher risk of surgery
- Limited utility in clinical practice



Monogenic Disorders in very early onset IBD



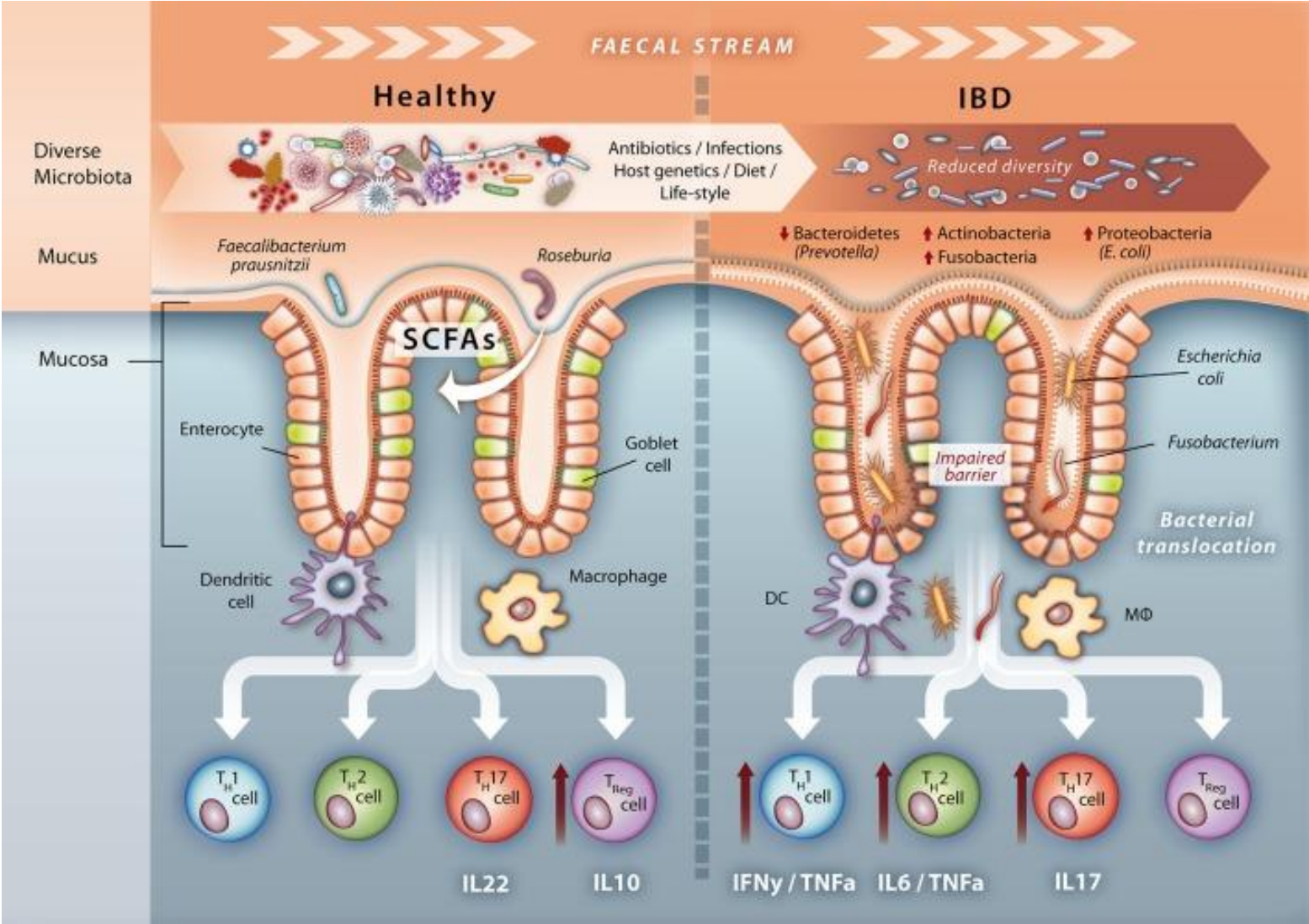
Uhlig HH Gut 2013



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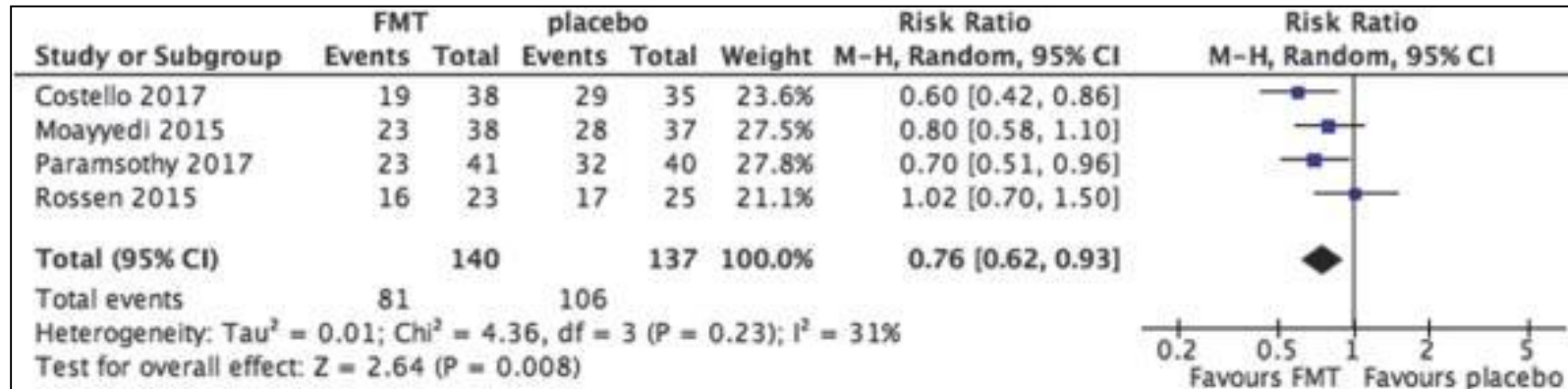
Microbiome in IBD



Reduced diversity

Sommer F Gut 2017

Fecal microbiota transplantation



Neeraj N IBD 2017

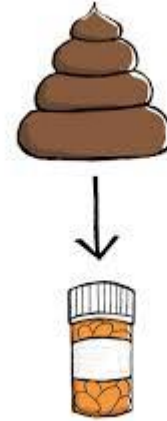


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Fecal microbiota transplantation

 # CRAPSULES

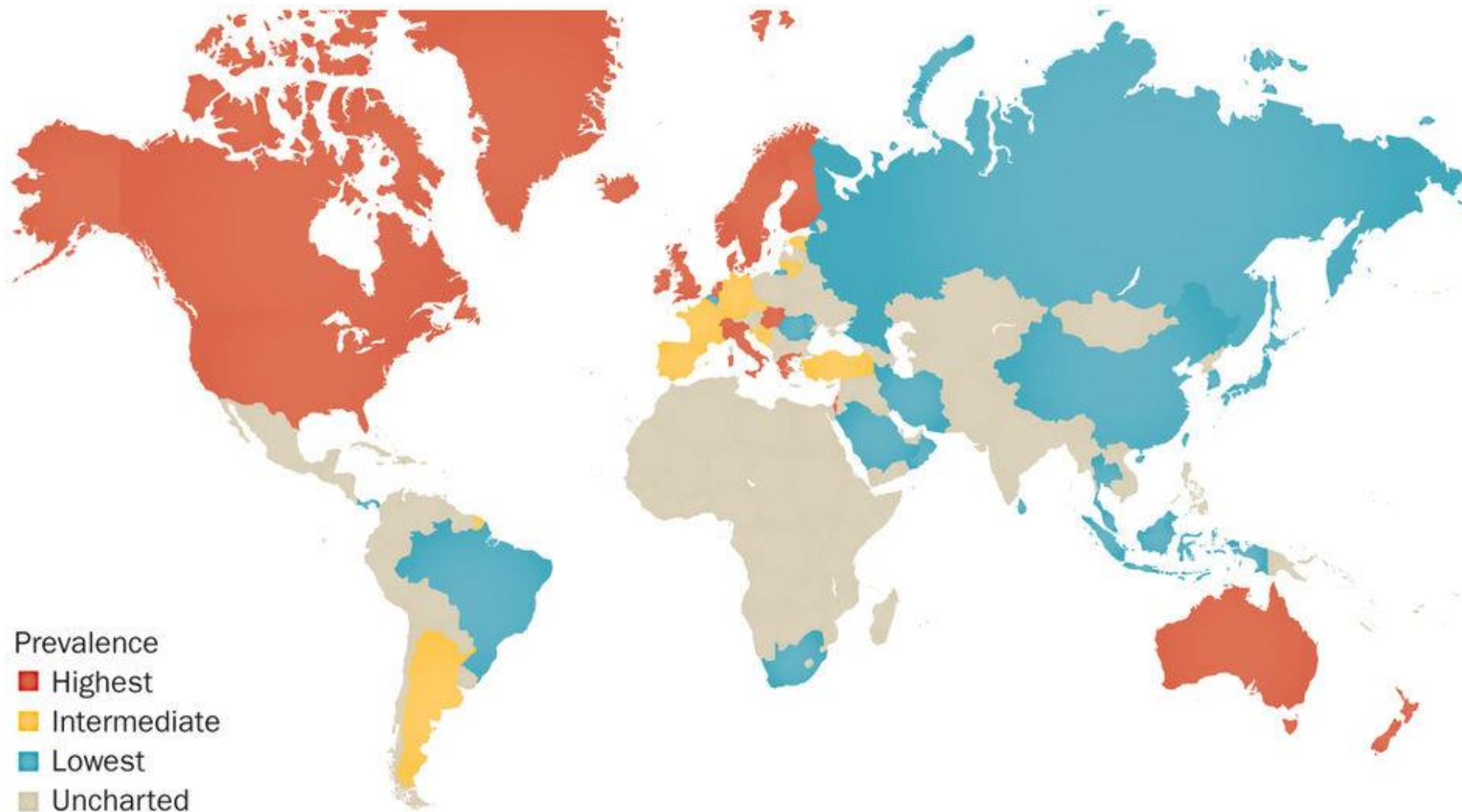


Home DIY FMT Kit
By The Power of Poop



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Prevalence
■ Highest
■ Intermediate
■ Lowest
■ Uncharted

Nature Reviews | **Gastroenterology & Hepatology**



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FIGURE 3-11: INCIDENCE OF CD, 2005

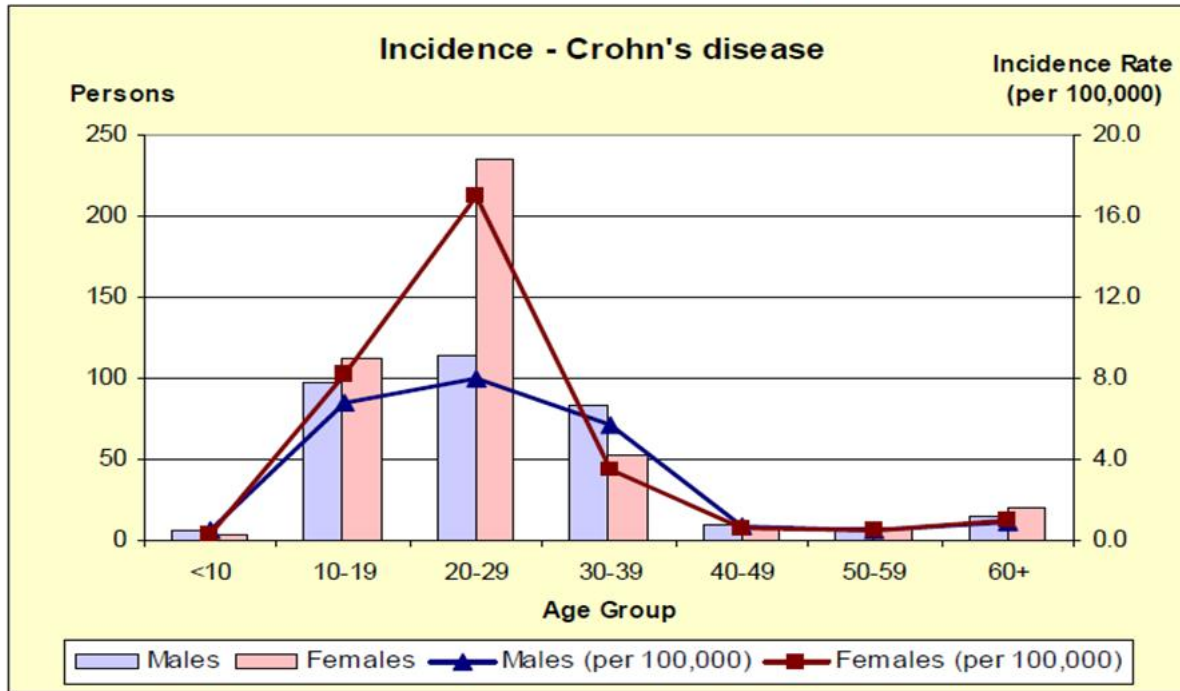
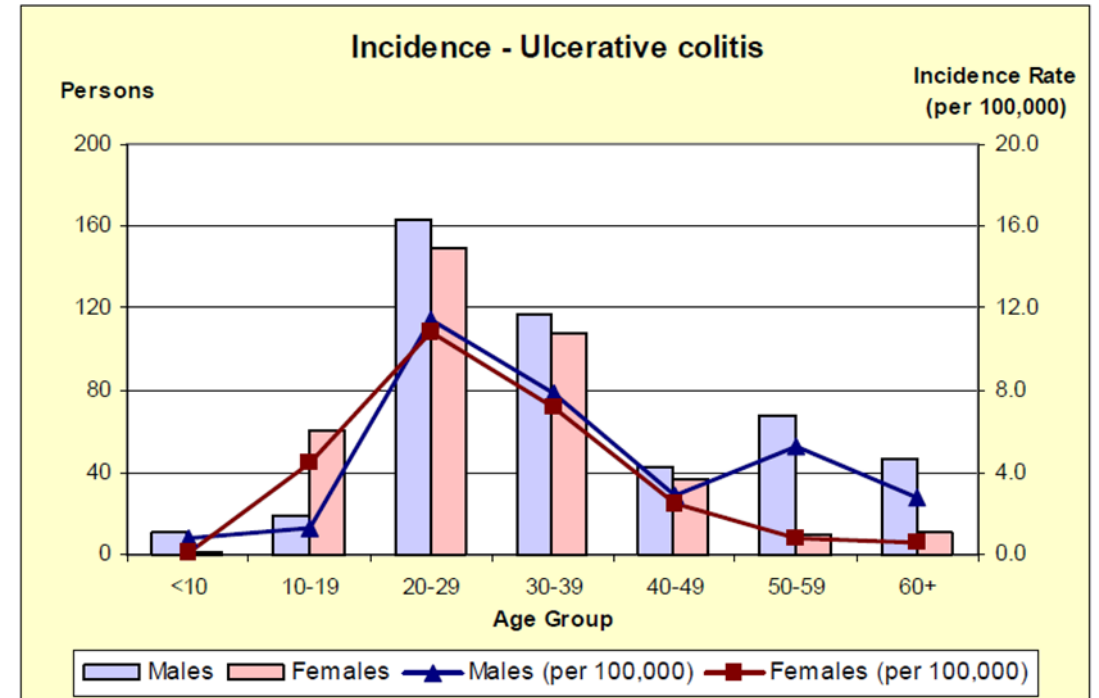


FIGURE 3-12: INCIDENCE OF UC, 2005

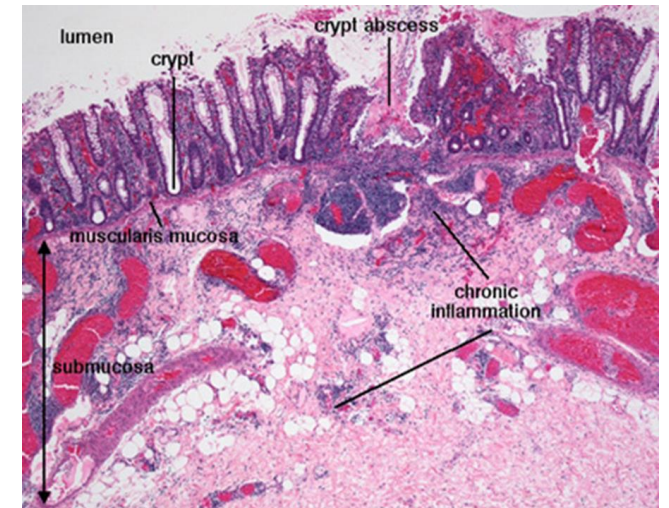
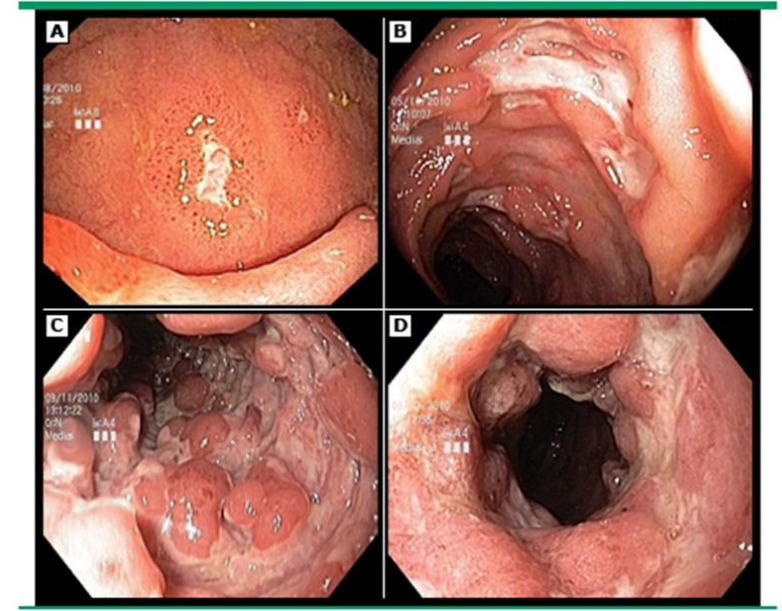
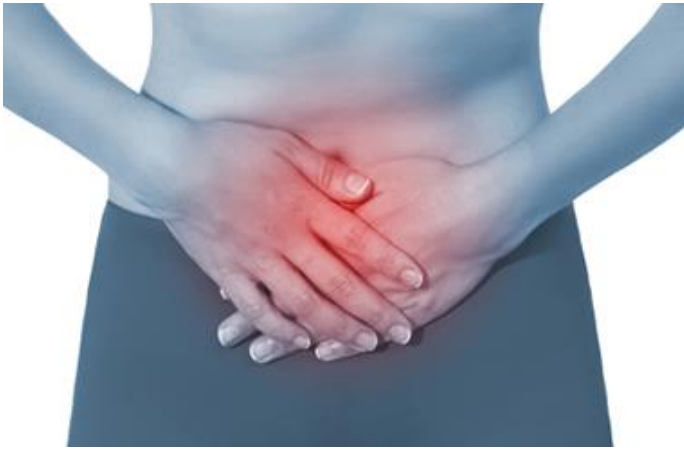


Clinical manifestations

- Abdominal pain
- Altered bowel habits
- GI bleeding
- Peri-anal complications
- Fistulizing / Stenosing complications
- Malnutrition
- Extra-intestinal manifestations



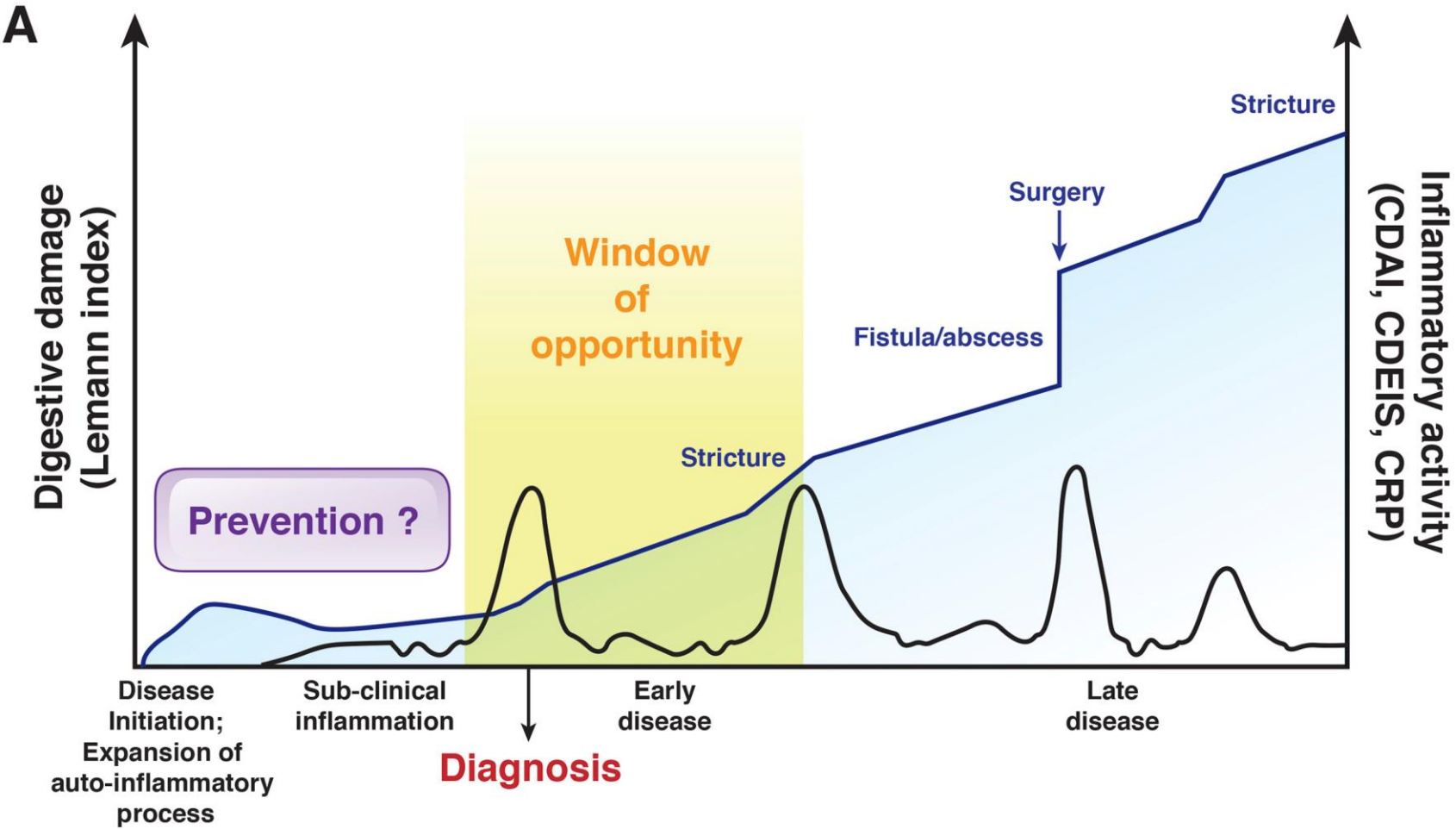
Diagnosis



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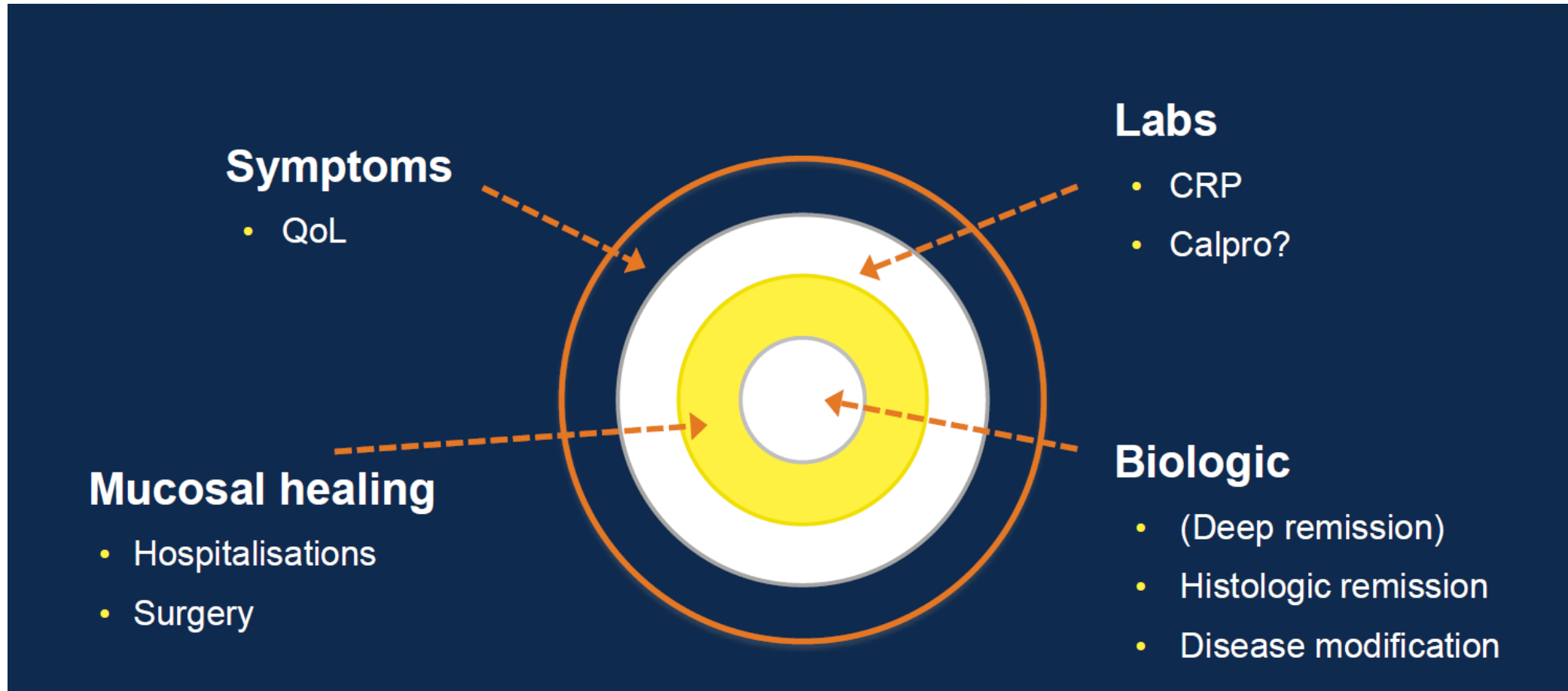
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Natural history

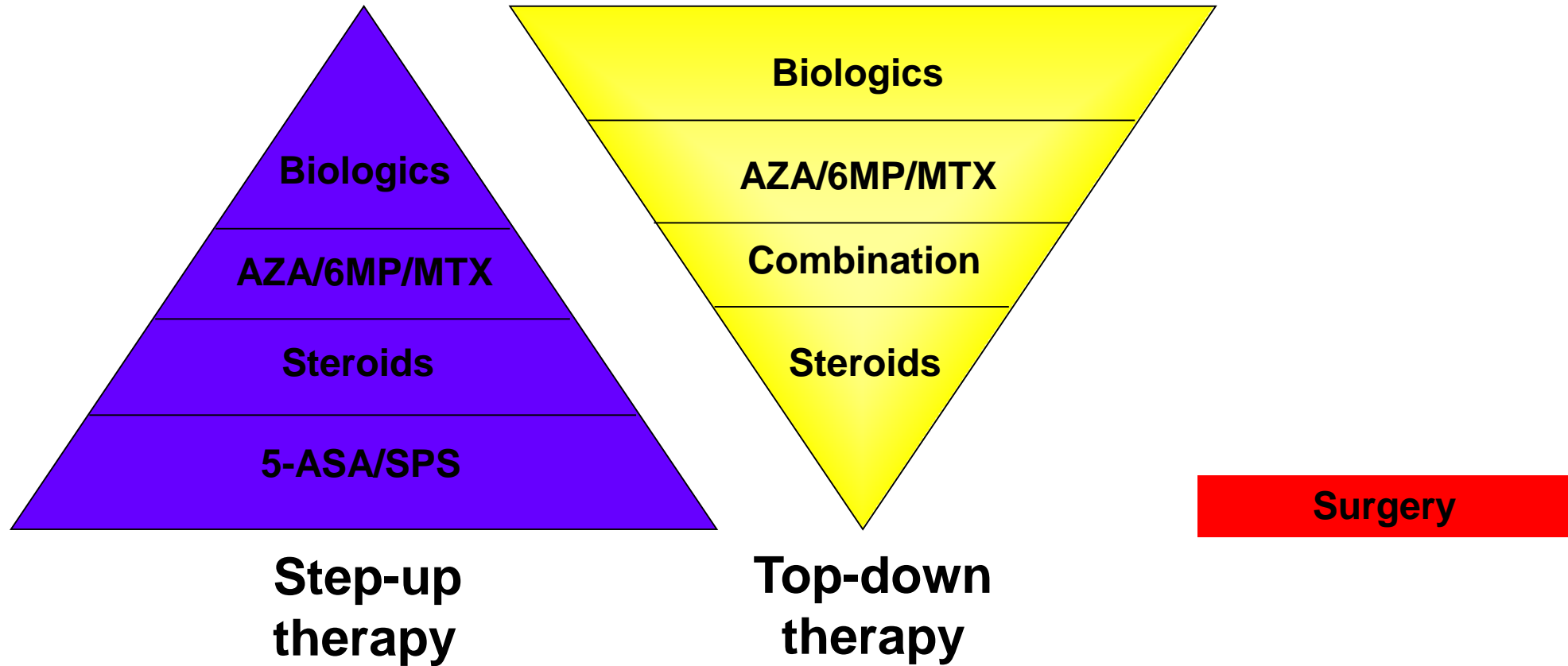


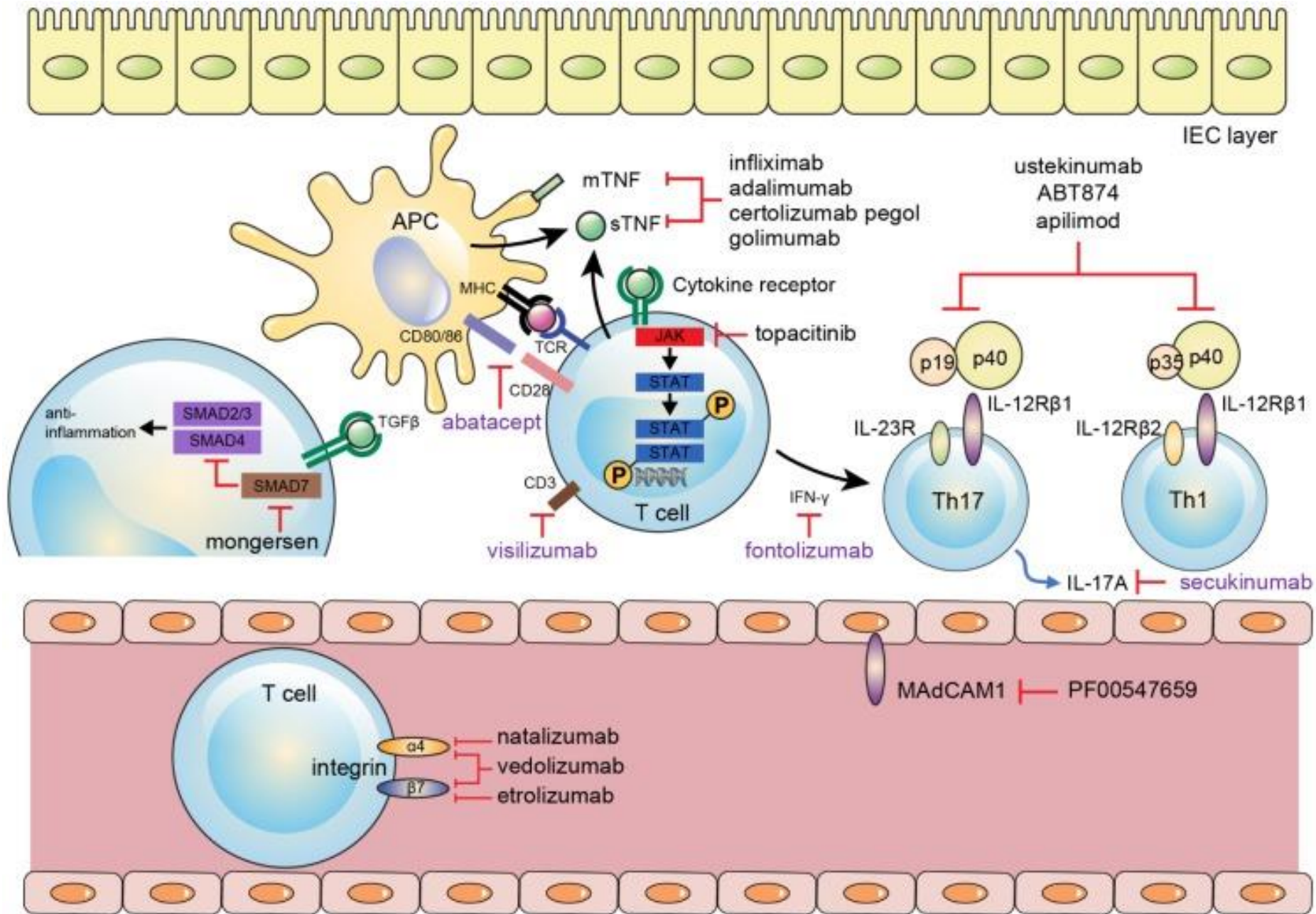
Colombel JF Gastroenterology 2017

Treat to target



Treatment paradigm





Therapeutic drug monitoring

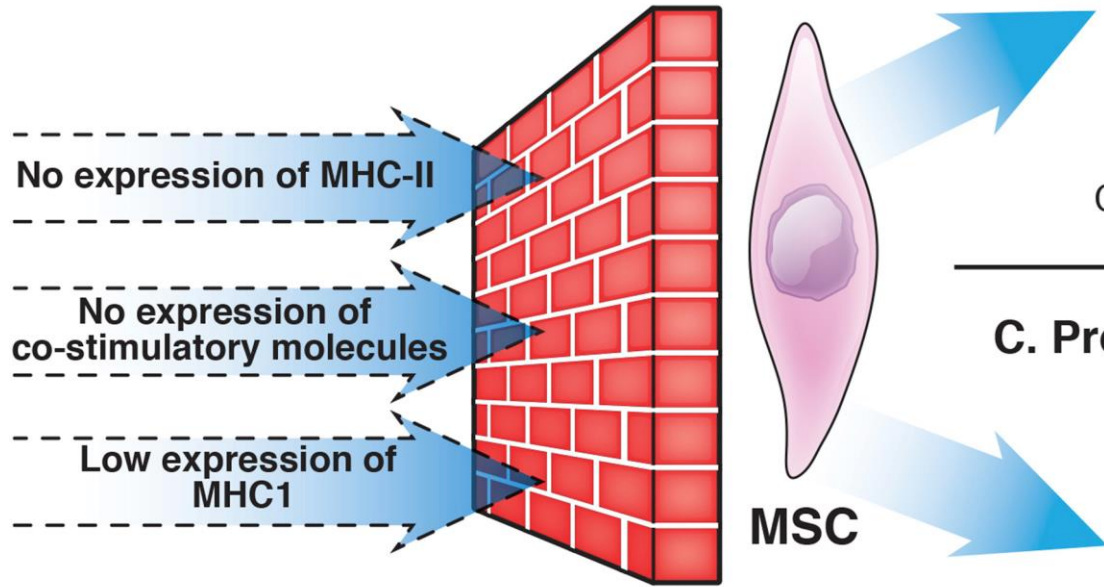
Biosimilars



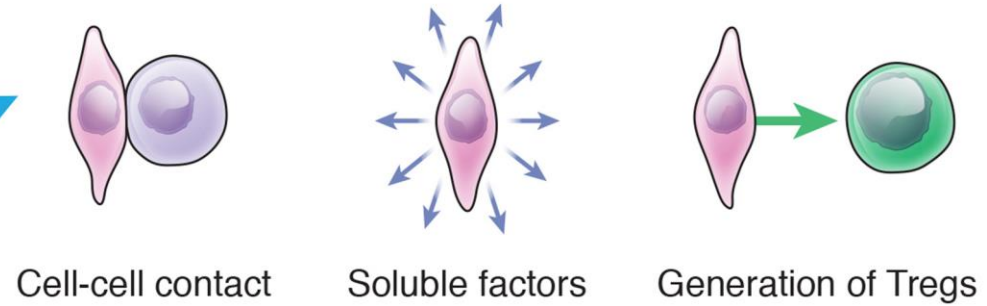
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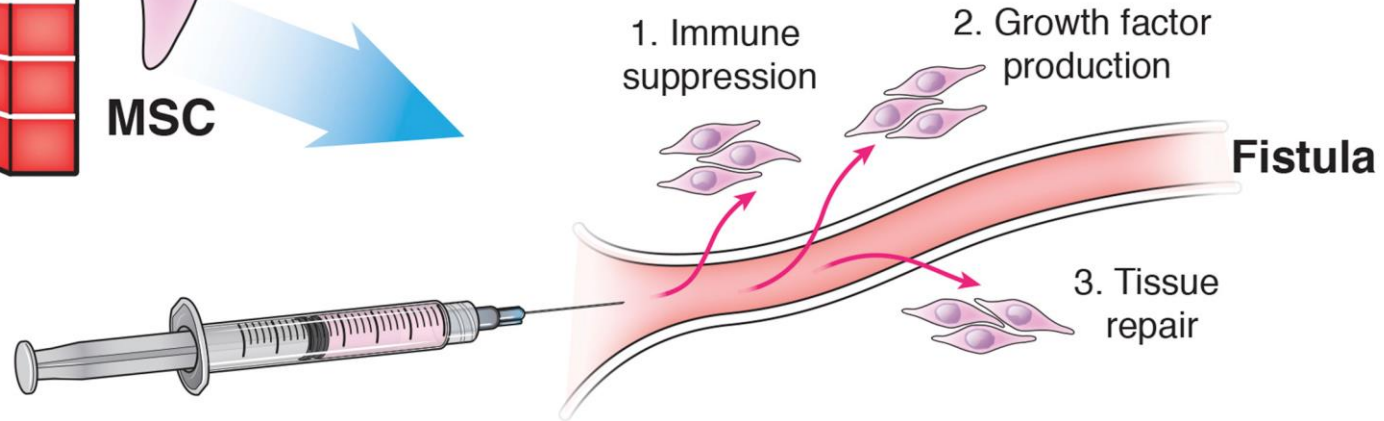
A. MSCs escape immune surveillance



B. Immunomodulatory properties of MSCs



C. Proposed fistula tissue repair properties of MSCs



Hawkey CJ Gastroenterology 2017



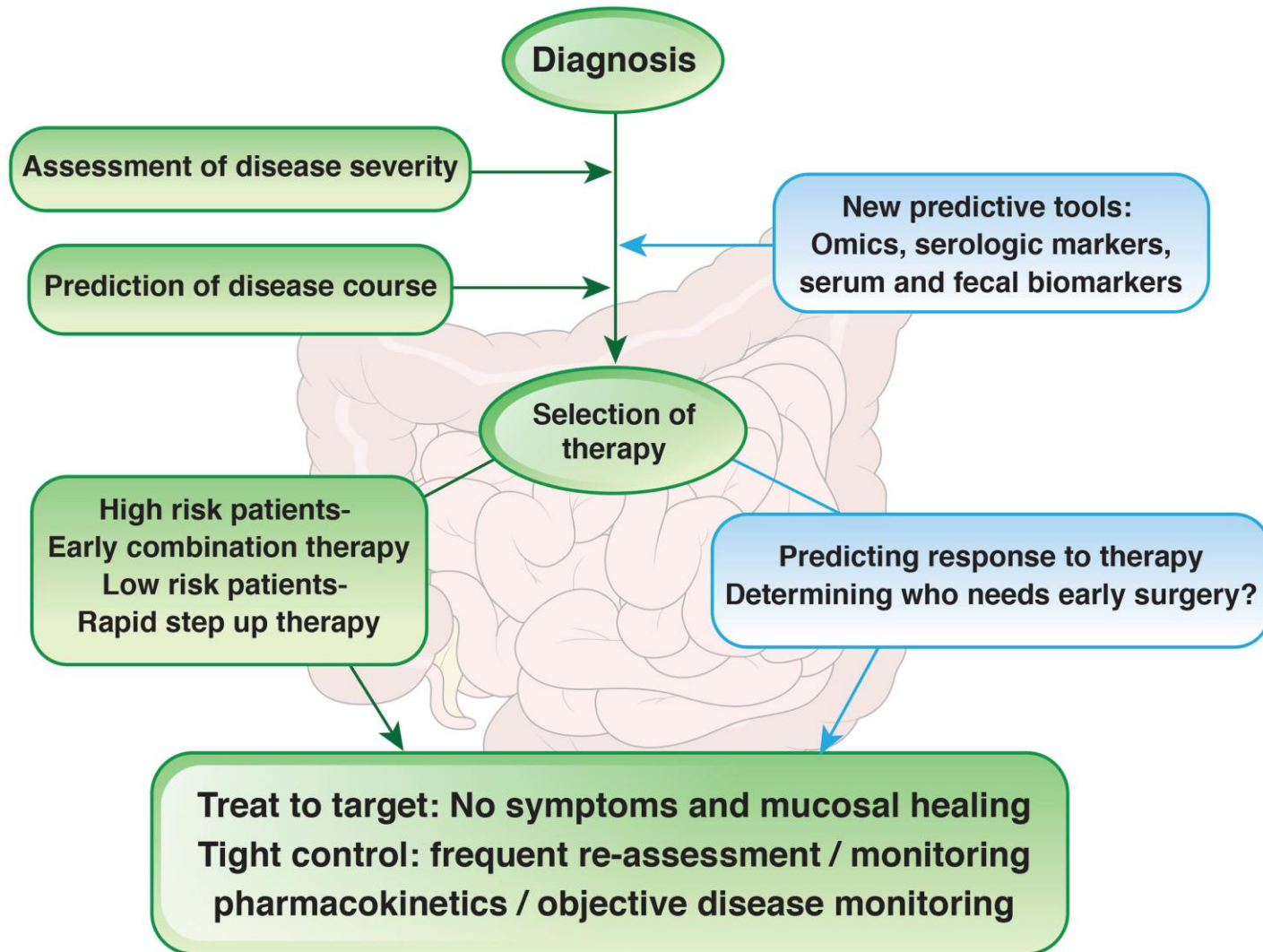
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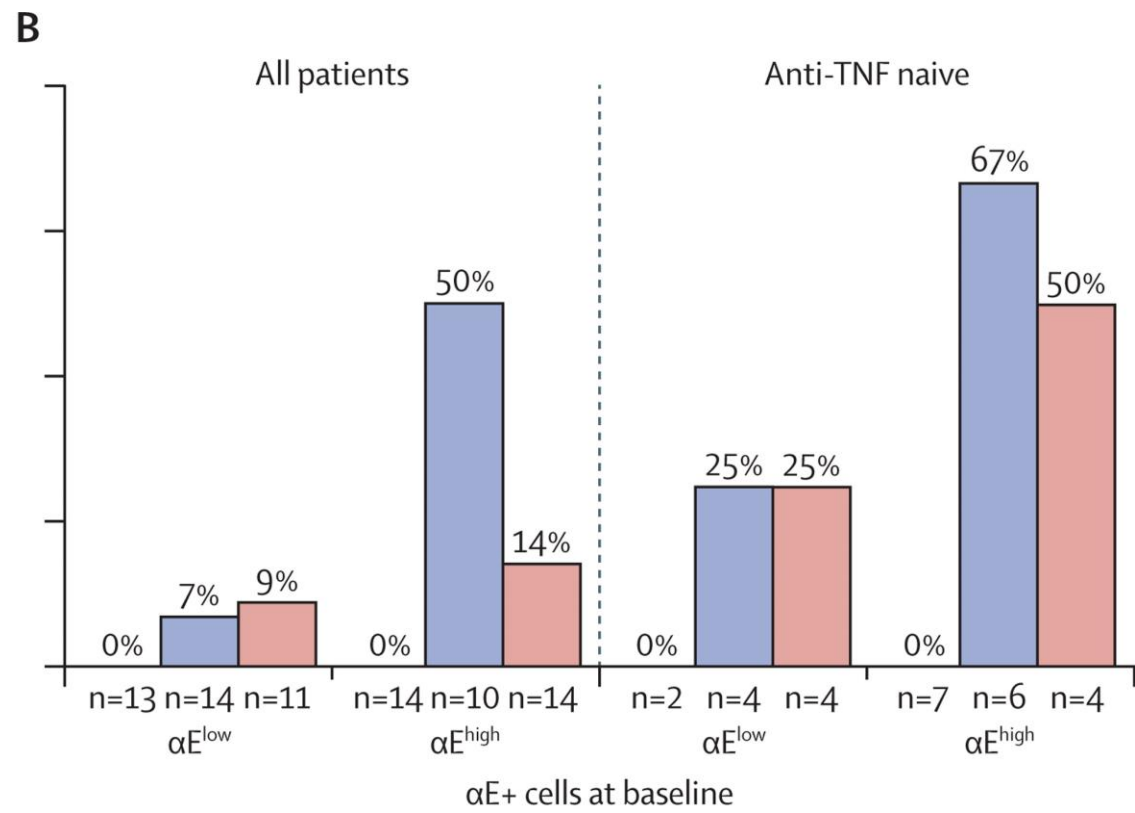
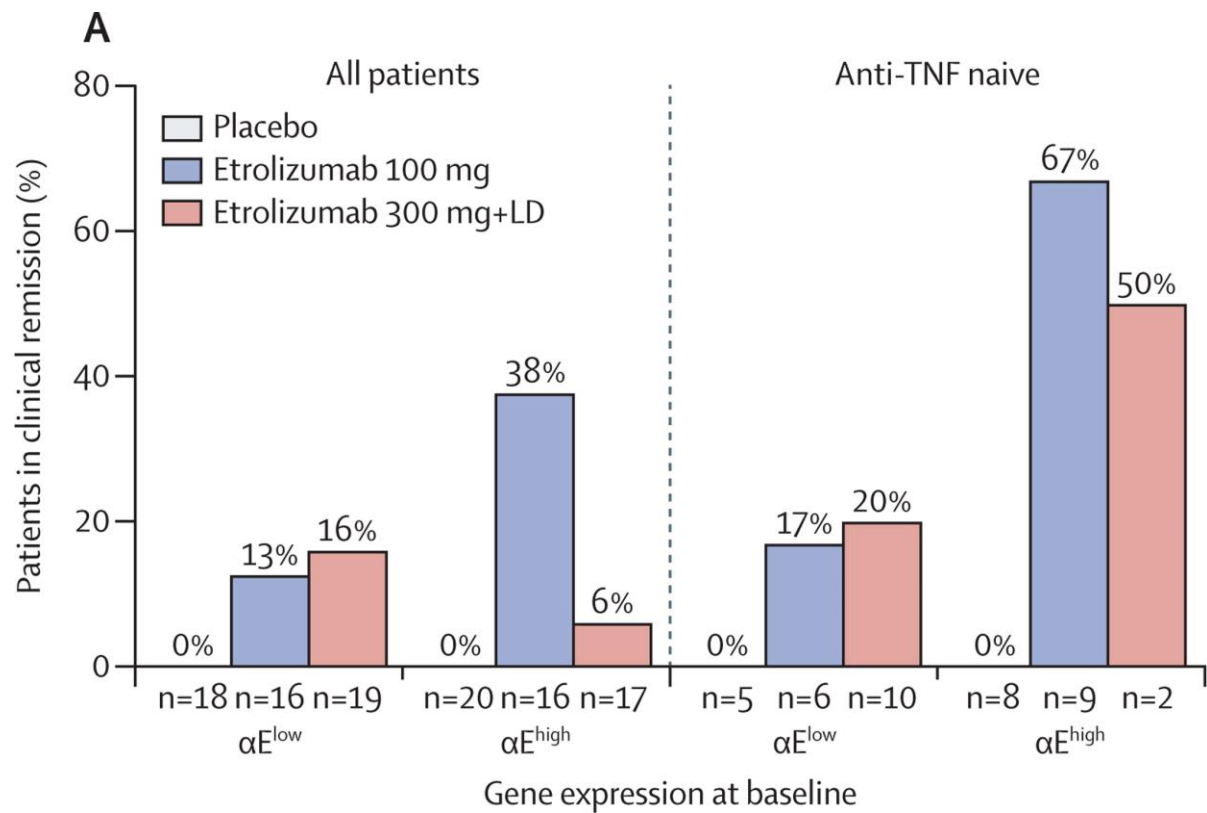
Diet

- Role in disease development and treatment
 - Ongoing investigation
- Exclusive Enteral Nutrition
 - Induction of remission in Pediatrics
- Low FODMAPs
 - For Irritable bowel syndrome overlay





- Currently proposed management strategies
- Potential future personalized management strategies

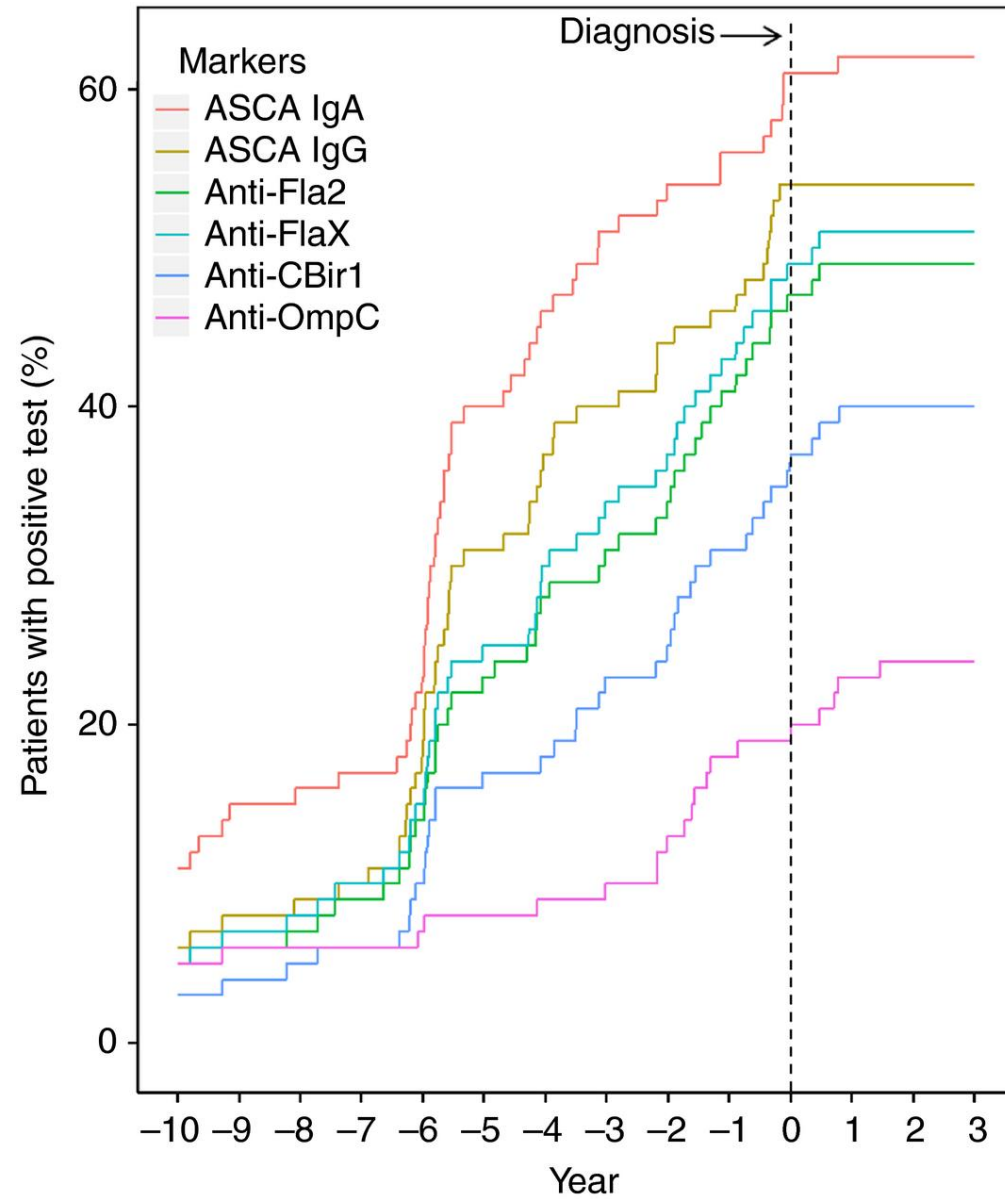


Vermeire S. Lancet 2014



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Choung RS. Aliment Pharmacol Ther 2016



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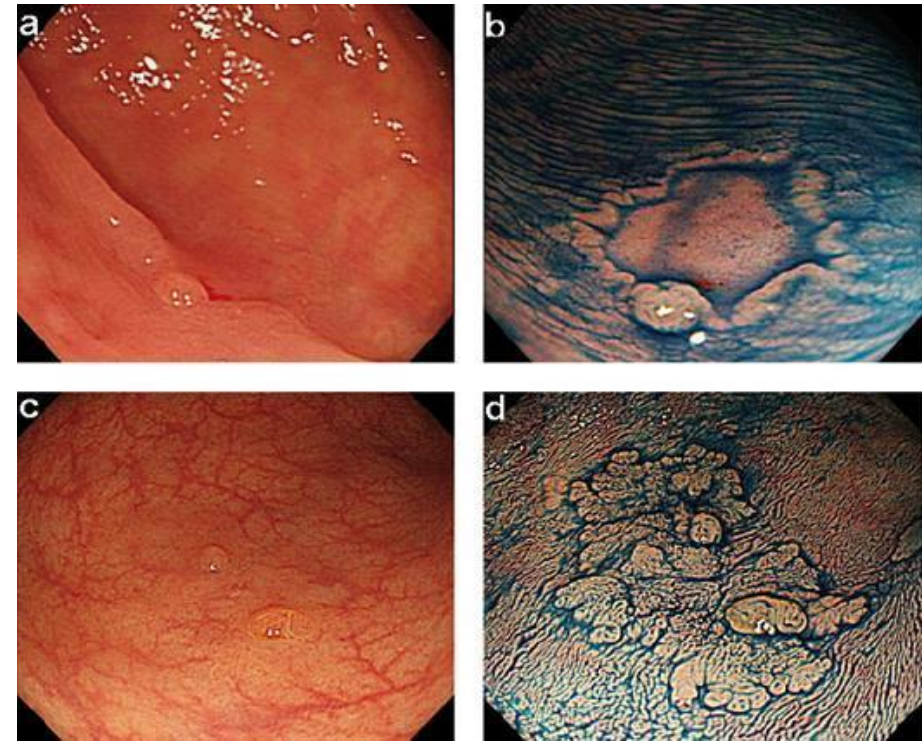
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Dysplasia surveillance



Polypoid lesion
Adenomatous
Inflammatory

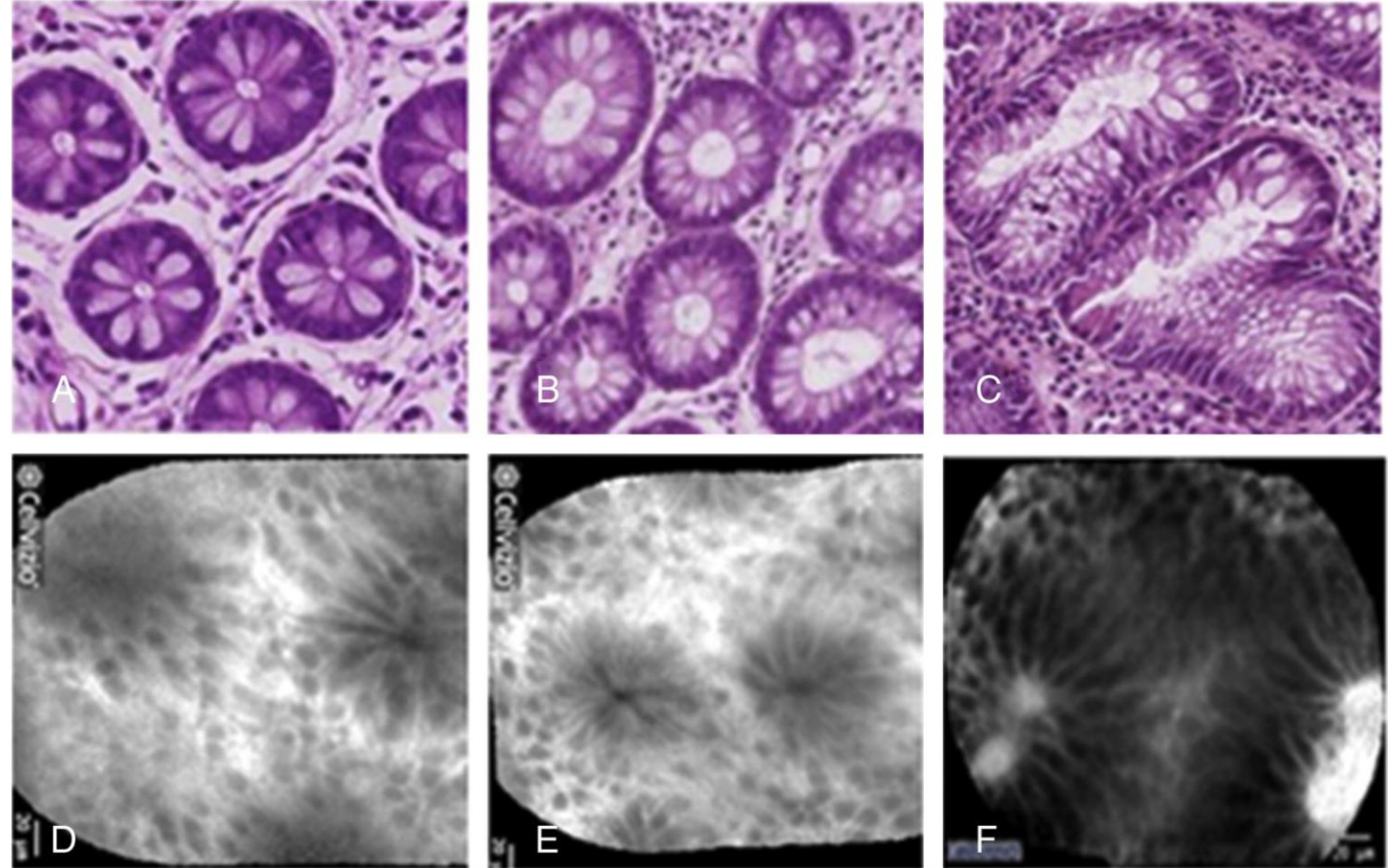
Targeted biopsy
Quadratic random biopsy



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Confocal laser endomicroscopy



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Acute severe ulcerative colitis

	Mild	Moderate 'in between mild and severe'	Severe
Bloody stools/day	<4	4 or more if	≥ 6 and
Pulse	<90 bpm	≤ 90 bpm	>90 bpm or
Temperature	<37.5 °C	≤ 37.8 °C	>37.8 °C or
Haemoglobin	>11.5 g/dL	≥ 10.5 g/dL	<10.5 g/dL or
ESR or CRP	<20 mm/h Normal	≤ 30 mm/h ≤ 30 mg/L	>30 mm/h or >30 mg/L

- Overall risk colectomy:
 - 19.9% on first admission
 - 29.0% on second admission
 - 36.6% on third admission
 - 38.2 on subsequent admission

Number of criteria in addition to a bloody stool frequency >6 /day	Colectomy risk
1	9%
2	31%
3	48%
4	45%

- Colectomy rate has not changed in 40 years despite advancement in therapies



**Day 1-3:
Steroids iv**

Methylprednisone iv 60 mg/d or hydrocortisone 100 mg every 6 hours iv

Systematic review 1991 patients:

- Response rate to steroids in ASC of 67%

Turner D et al. Clin Gastroenterol Hepatol. 2007

Endoscopic assessment and exclusion of CMV

**Day 3:
salvage therapy needed?**

Predicting outcome: day 3 Oxford criteria

> 8 stools/day	> 2 stools/day + CRP > 45 mg/l
----------------	--------------------------------

85% chance of emergency colectomy

Travis et al 1996

**Day 4-7:
Incomplete responders**

Medical rescue therapy or colectomy

**Infliximab
Vs.
Cyclosporin
Vs.
Surgery**

*CYSIF: Laharie D et al. Lancet 2012
CONSTRUCT: Williams J.G. et al. Lancet 2016*

Cytomegalovirus

- Herpesviridae family
- Primary versus reactivation
- Immunocompromised
- CMV infection versus disease
- UC >> CD



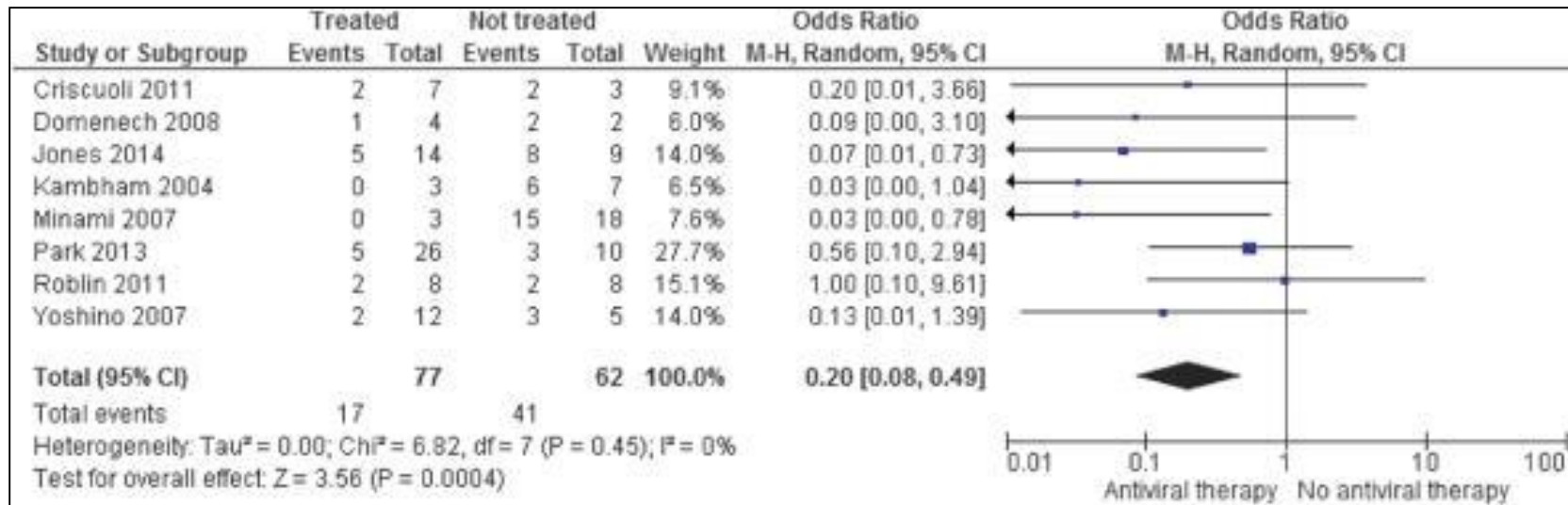
Detection methods

Method	Sensitivity	Specificity	Implications
Serology	-	-	Time delay with seroconversion
Peripheral pp65 antigenemia	60-100%	83-100%	Does not differentiate latent infection versus active disease / intestinal involvement
PCR DNA - blood	65-100	45-92%	Better viral quantification Monitor treatment response ? Better correlation with active disease
H&E	10-87%	92-100%	Gold standard for active disease
IHC	78-93%	92-100%	Gold standard for active disease
PCR DNA – tissue	92-96.7%	93-98.7%	Poor correlation with active disease / histology
Viral culture	45-78%	89-100%	Time delay



Cytomegalovirus in Ulcerative colitis

- Increased hospitalization
- Reduced response to infliximab therapy
- Higher cumulative colectomy rates



Pillet S World J Gastroenterol 2016
Tushar S Inflamm Bowel Dis 2015



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Conflicting data

- Detection of CMV in blood and tissue not necessarily result in poor outcome
- Treatment with infliximab not necessarily associated with poor outcome
- Innocent bystander
 - Reflection of severity of disease and immunotherapy
- Data limited by quality / detection method and classification

Lawlor G Inflamm Bowel Dis 2010



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Predictors of unfavorable outcome

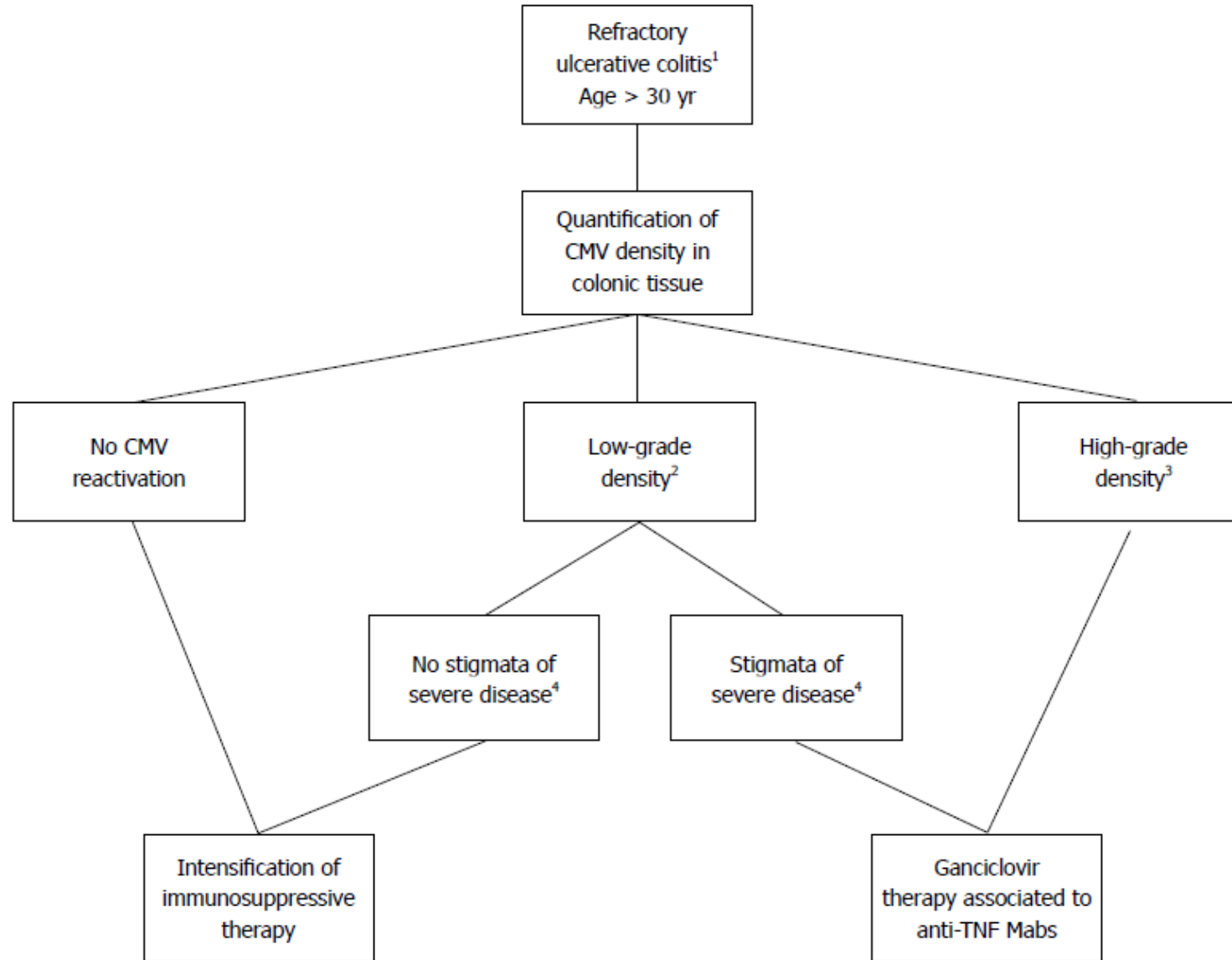
- Age > 30
- Resistance to steroid / immunosuppressive therapy
- Acute severe ulcerative colitis
- +/- endoscopic severity
- Density of viral infection
 - H&E versus IHC
 - 4 – 10 viral inclusions
 - >250 copies / mg of tissue
 - ? Blood PCR DNA level

Park SC Korean J Intern Med 2017



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Summary

- Promising developments
 - Elucidation of pathogenesis
 - Treatment targets and therapeutic options
 - Individualization of therapy
 - Early detection
- Management of CMV in ASUC remains challenging
 - Viral burden may provide guidance to therapy

