



Update on the Management of Inflammatory Bowel Diseases

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Faculty Disclosure

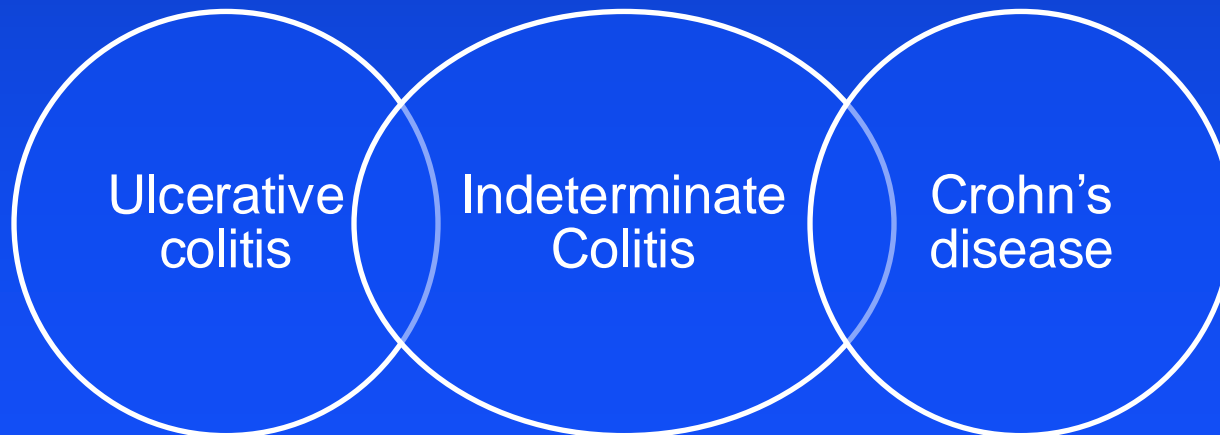
Name of Ineligible Company	Nature of Relevant Financial Relationship
<ul style="list-style-type: none">Prometheus Biosciences	<ul style="list-style-type: none">Research grant
<ul style="list-style-type: none">Gilead	<ul style="list-style-type: none">Research grant
<ul style="list-style-type: none">Bristol Myers Squibb	<ul style="list-style-type: none">Consultant (Institutional Agreement through UCSD)
<ul style="list-style-type: none">Takeda	<ul style="list-style-type: none">Consultant (Institutional Agreement through UCSD)

Overview

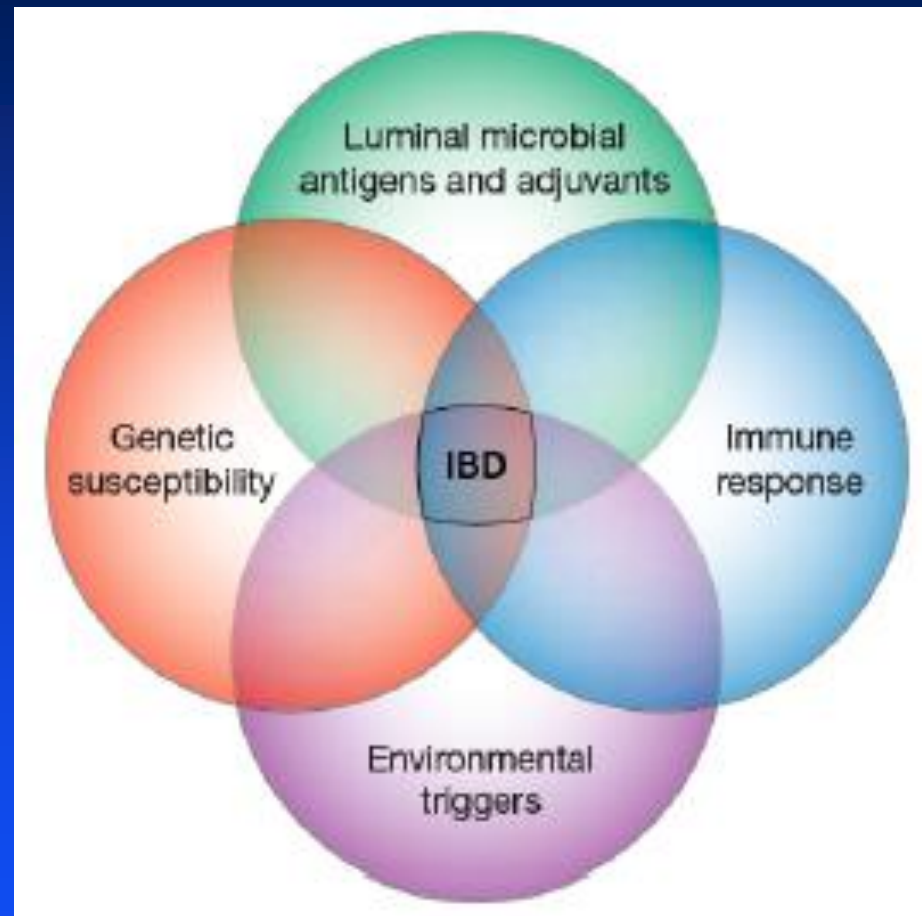
- **Pathogenesis**
- **Ulcerative colitis**
- **Crohn's Disease**
- **Approach to Management**
- **Conventional Therapies**
- **Novel Therapies**

What is Inflammatory Bowel Diseases?

- Aberrant immune response to enteric bacteria in a genetically susceptible host
- Spectrum of disease:

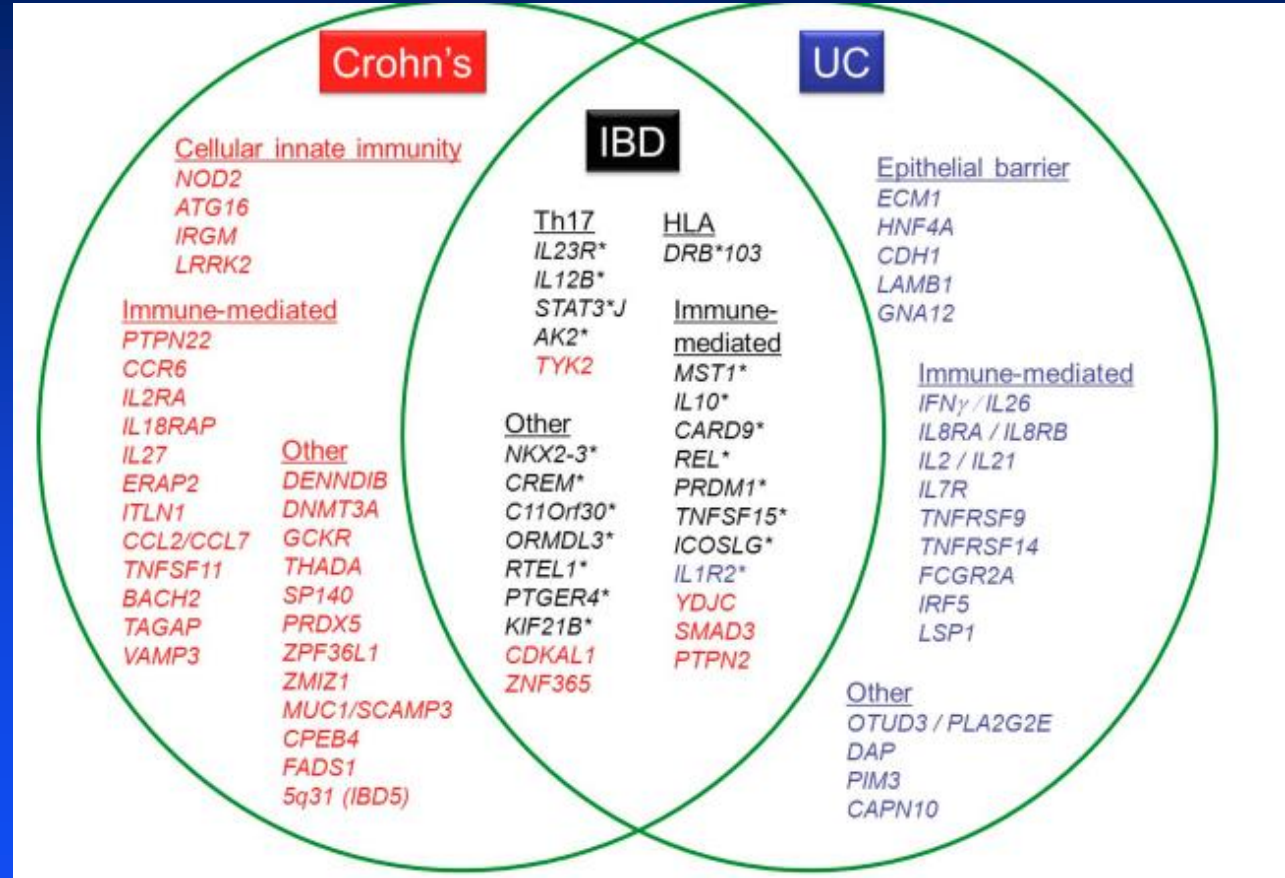


IBD is a multifactorial disease

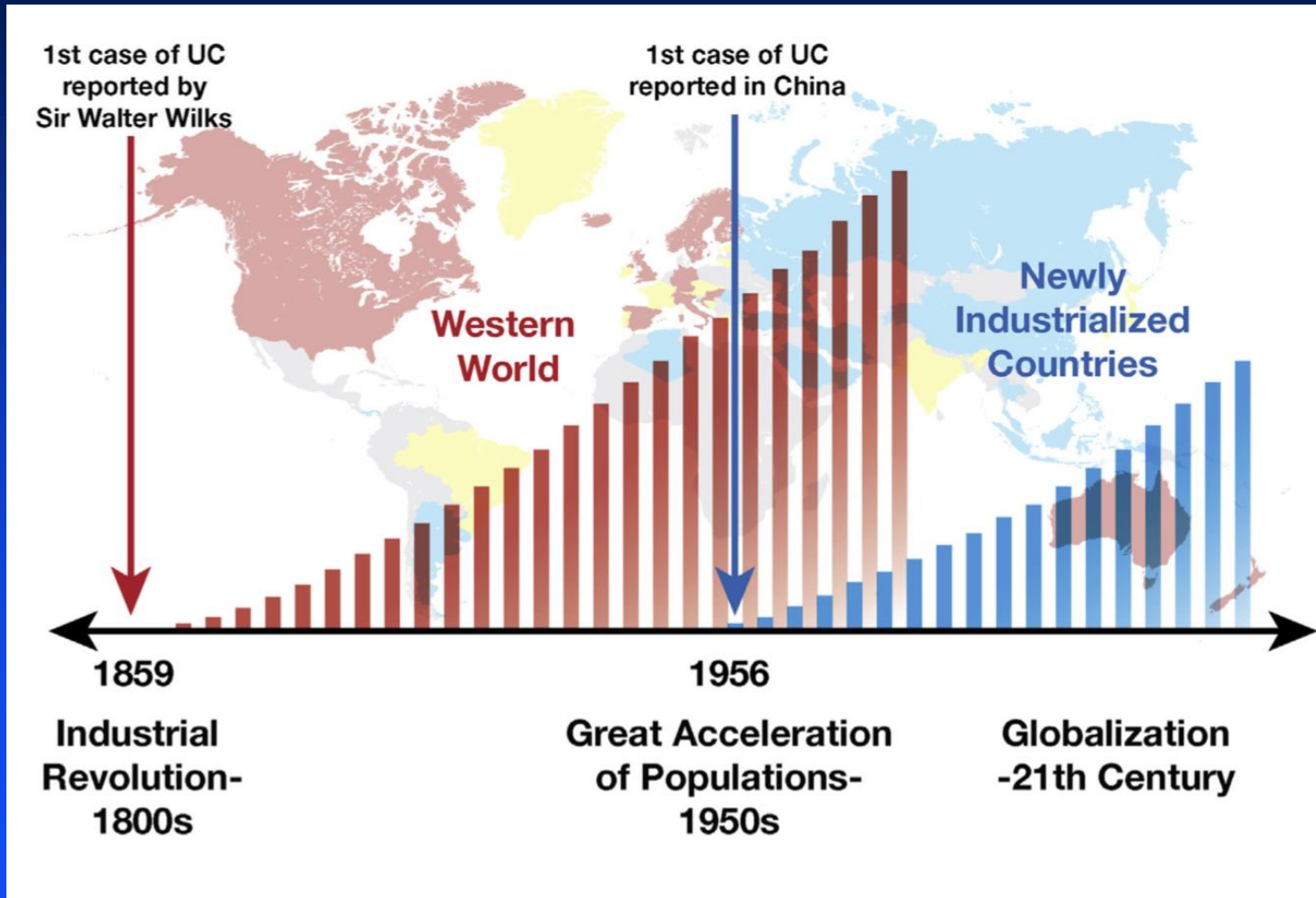


Genetics of Inflammatory Bowel Diseases

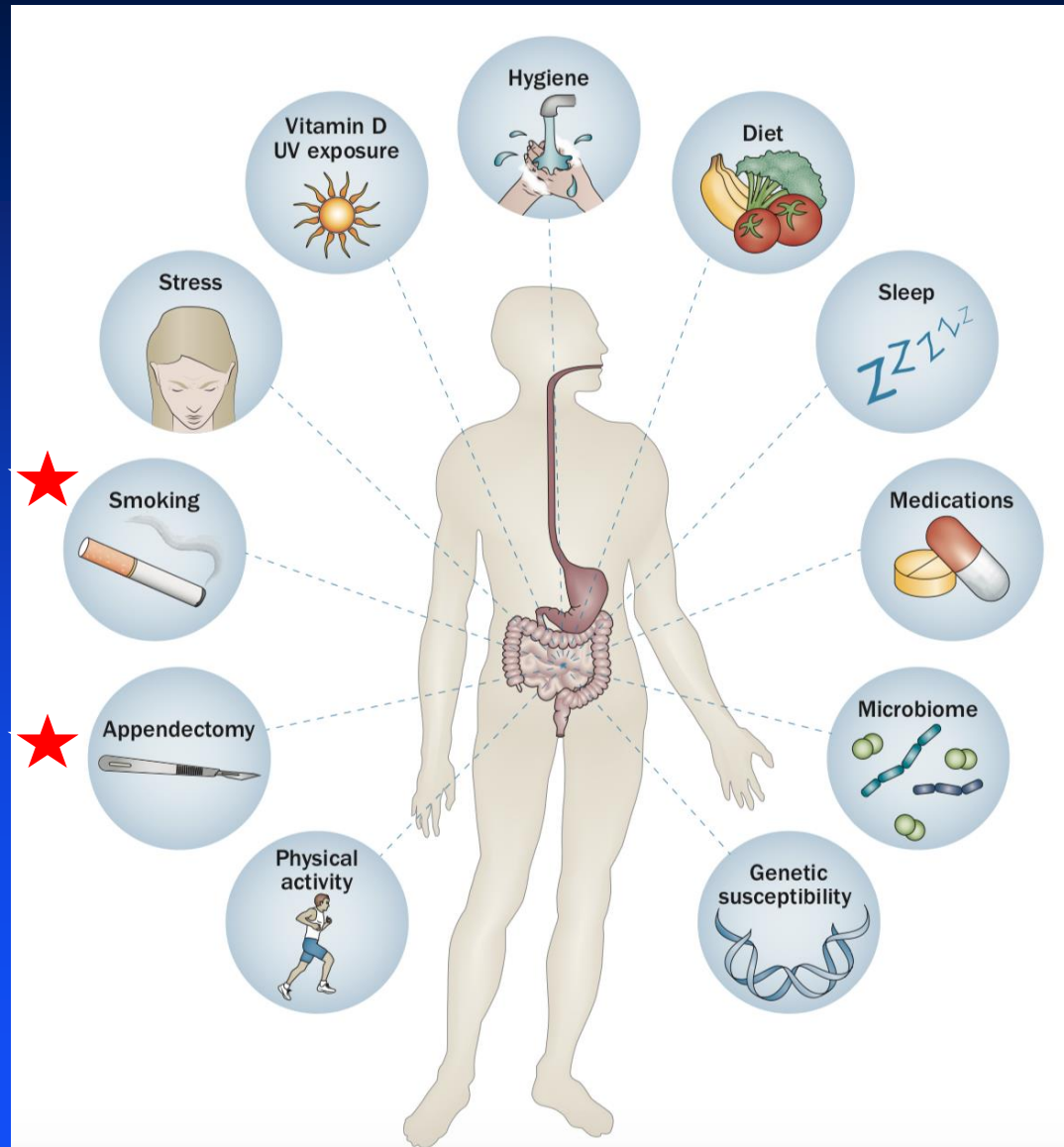
- >200 IBD risk loci
- UC & CD share genes
- “Inheritability”
 - 23% CD
 - 16% UC
- Insight into pathogenesis & treatment



Rising Incidence of Global IBD

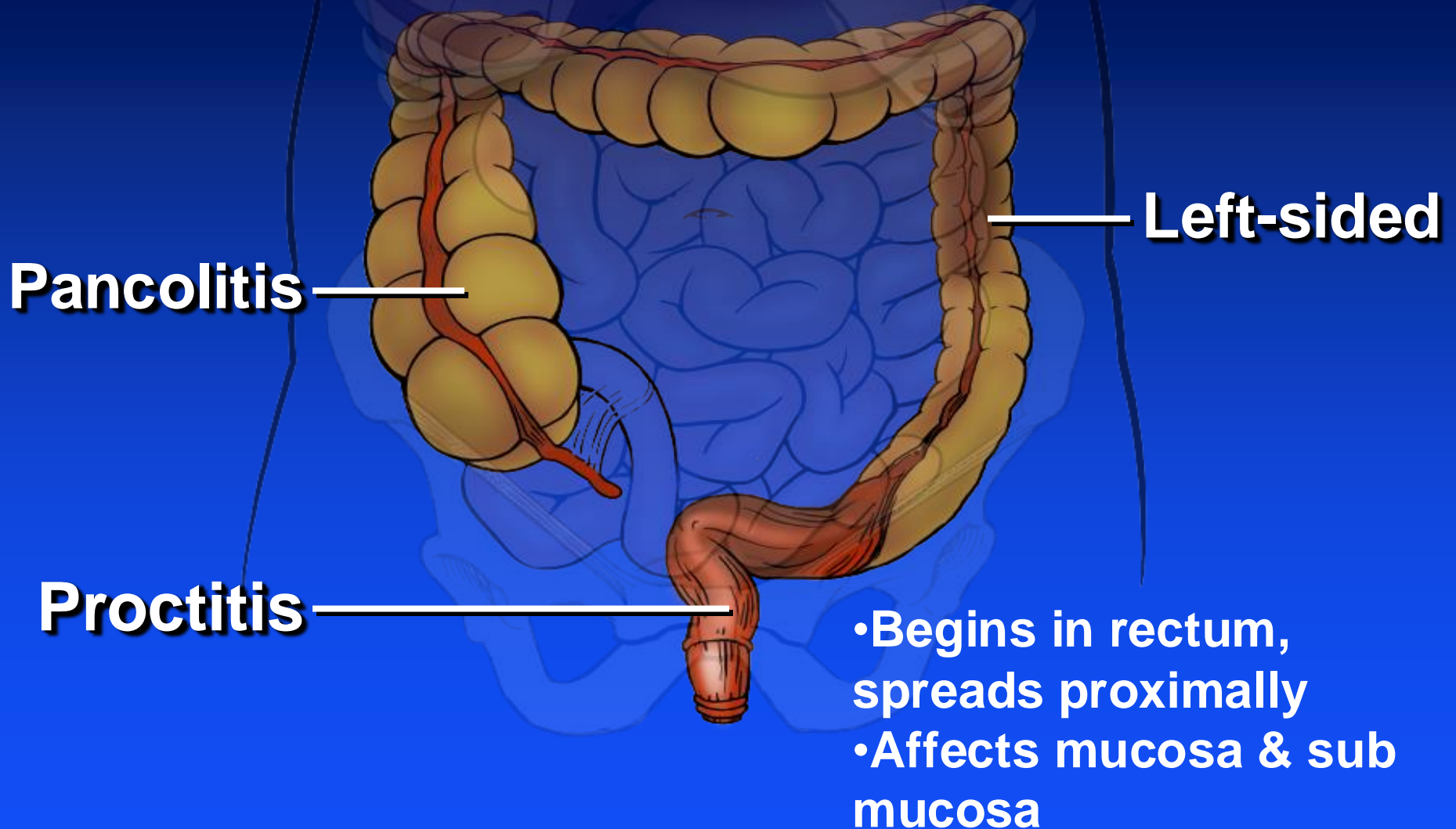


Risk Factors for IBD

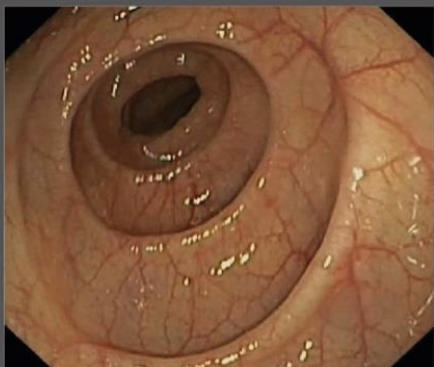
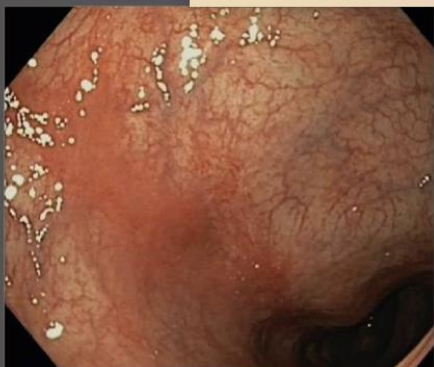





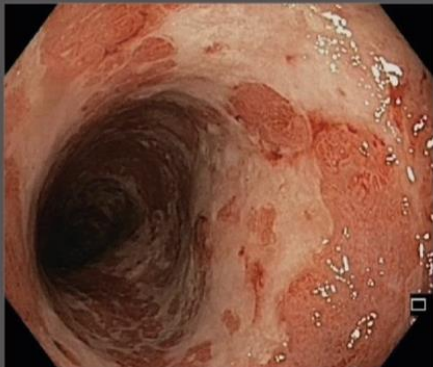


- Smoking increases risk of CD but protective against UC
- Appendectomy increases risk of CD but protective against UC

Defining Ulcerative Colitis: Extent of Disease



Ulcerative Colitis: Endoscopic Disease Severity

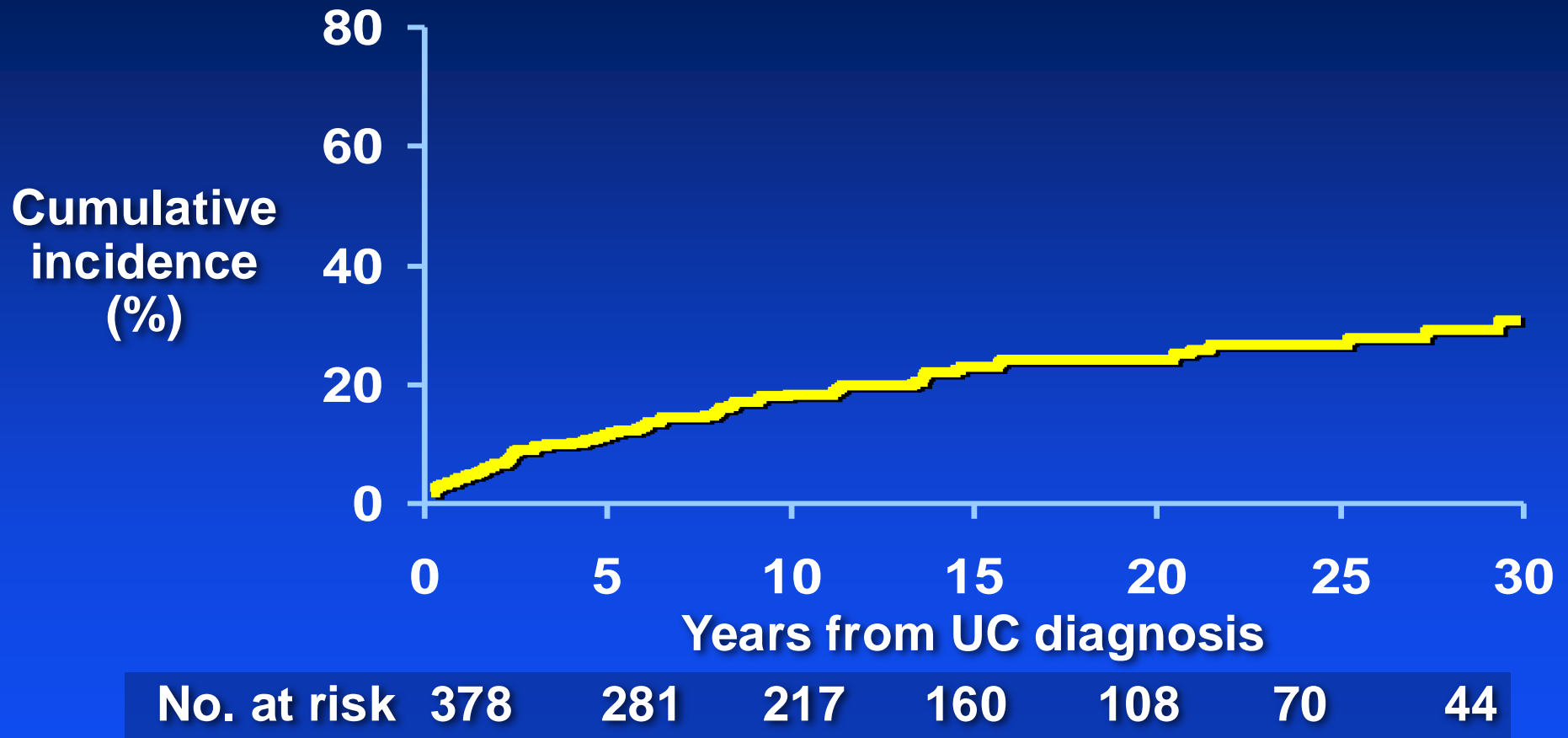
Mayo UC Endoscopic Score = 0 (normal or inactive disease)	Mayo UC Endoscopic Score = 1 (mild disease)	Mayo UC Endoscopic Score = 2 (moderate disease)	Mayo UC Endoscopic Score = 3 (severe disease)
			
			
Normal vascular pattern	Erythema, decreased vascular pattern, mild friability	Marked erythema, absent vascular pattern, friability, spontaneous bleeding	Spontaneous bleeding, ulcerations

Mayo UC Endoscopic Classification
 • Score = 0 (normal ...)

Patient Stratification: Risk Factors for Severe UC

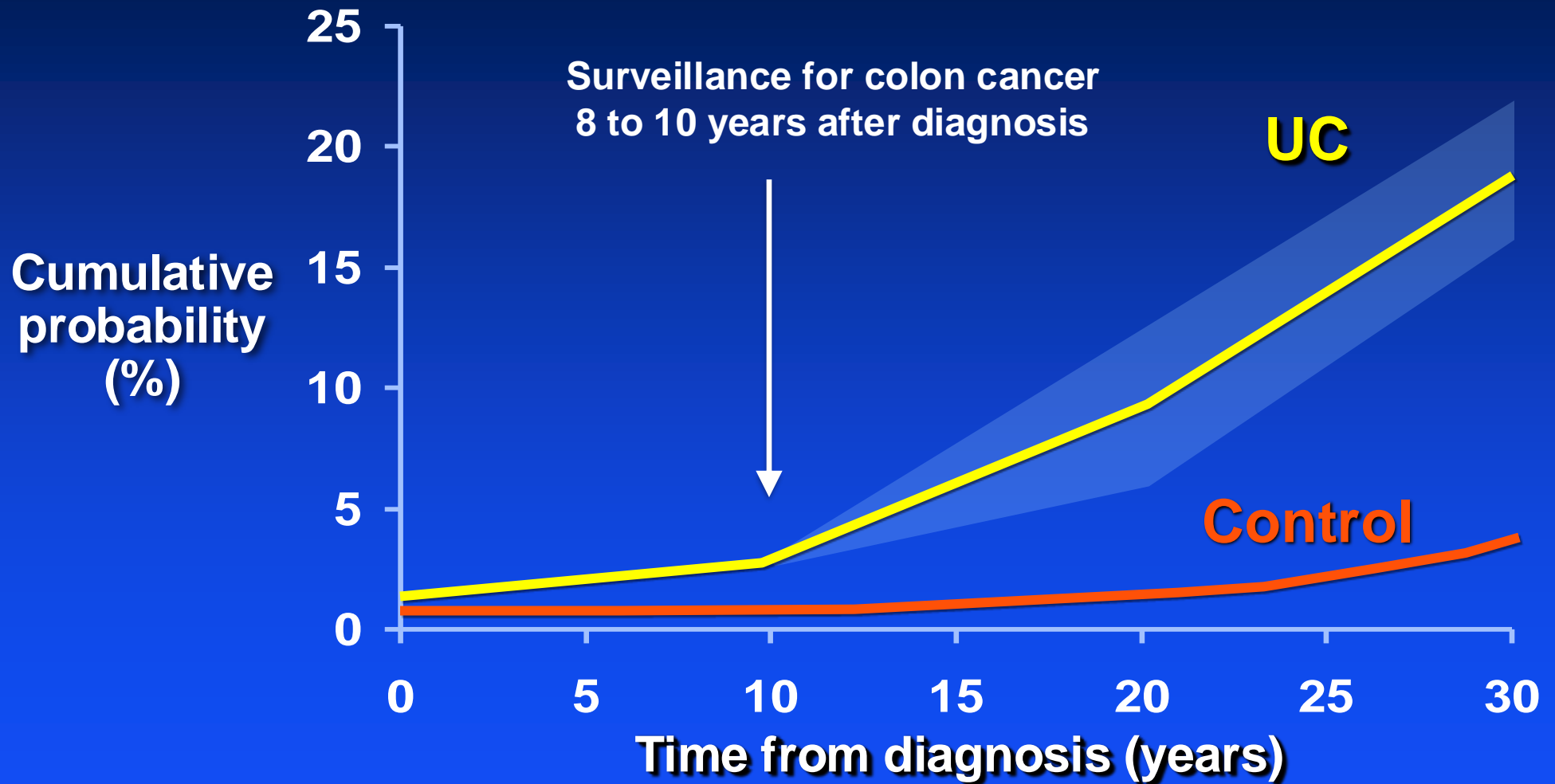
- Age of diagnosis
 <40 years
- Extensive disease
- Severe endoscopic disease activity
 Large +/- deep ulcers
- Extra-intestinal manifestations
- Early need for steroids
- Elevated inflammatory markers

Cumulative Risk of Colectomy in UC in Olmsted County, 1940-2001



Dhillon S, Sandborn WJ: Am J Gastroenterol, 2005

Risk of Colorectal Cancer in UC: Meta-Analysis



Eaden: Gut, 2001

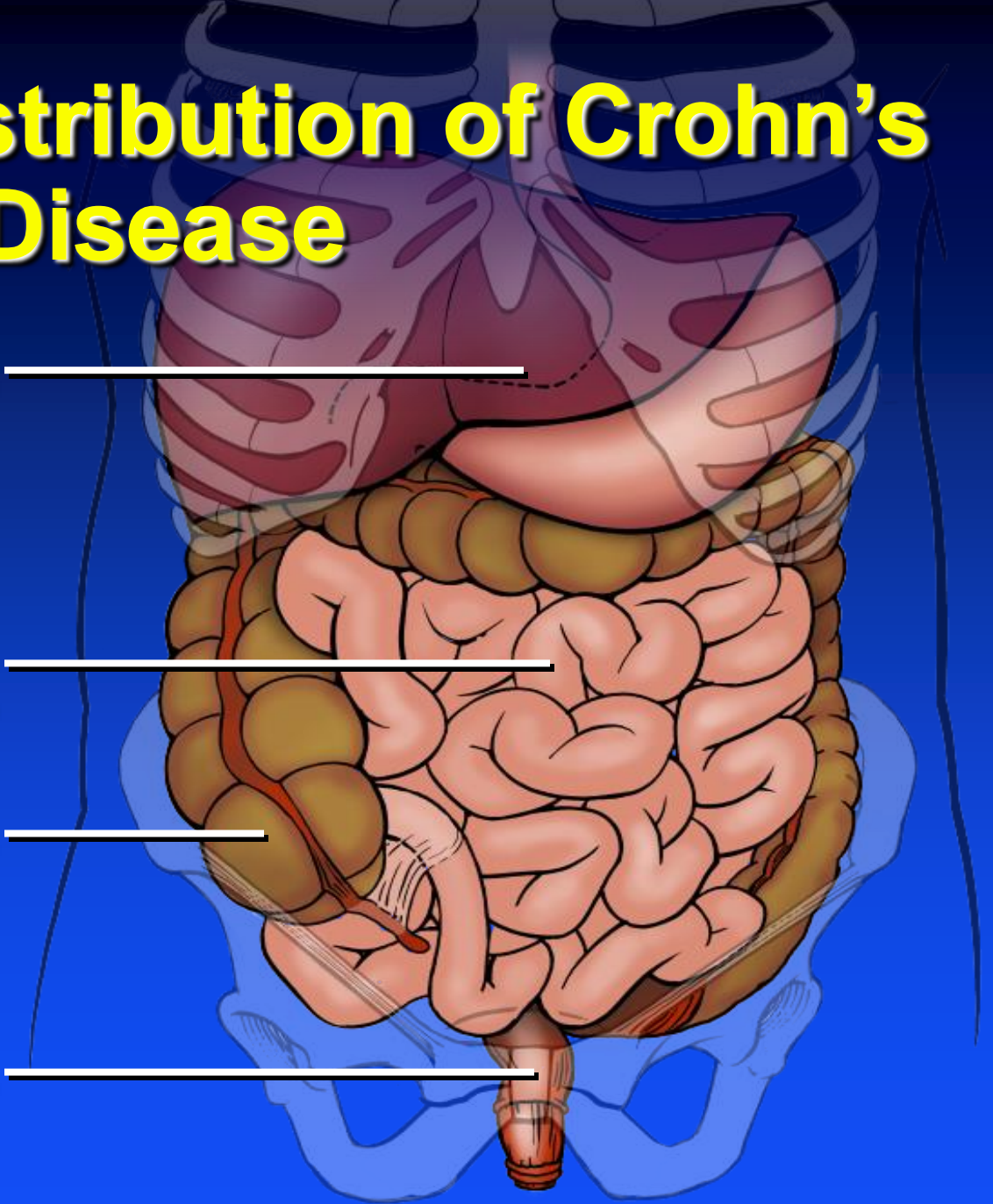
Anatomic Distribution of Crohn's Disease

Upper gut 10-15%

Small bowel
alone 33%

Ileocolonic 45%

Colon alone 20%



Crohn's Disease – Progression from Inflammation to Complications

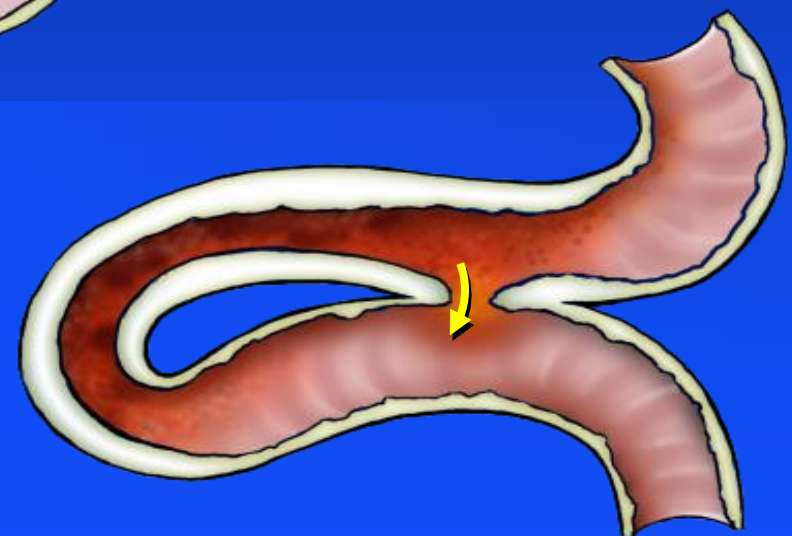
Inflammatory



Fibrostenotic

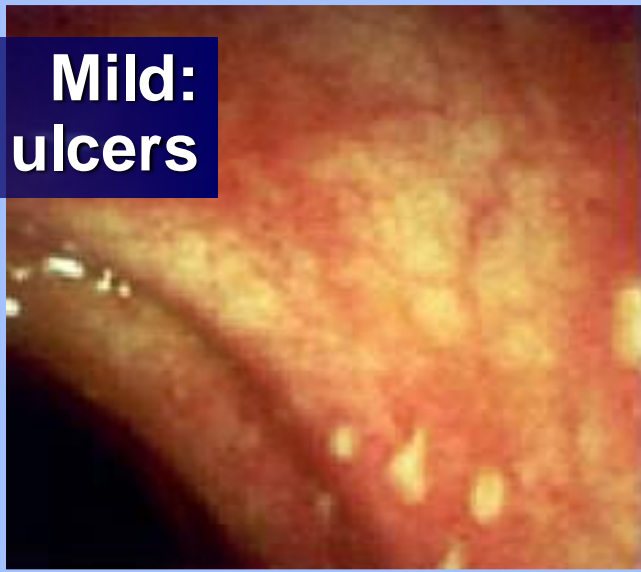


Fistulizing



Crohn's Disease Endoscopic Spectrum

**Mild:
Apthous ulcers**



**Moderate to severe:
Stellate ulcers**



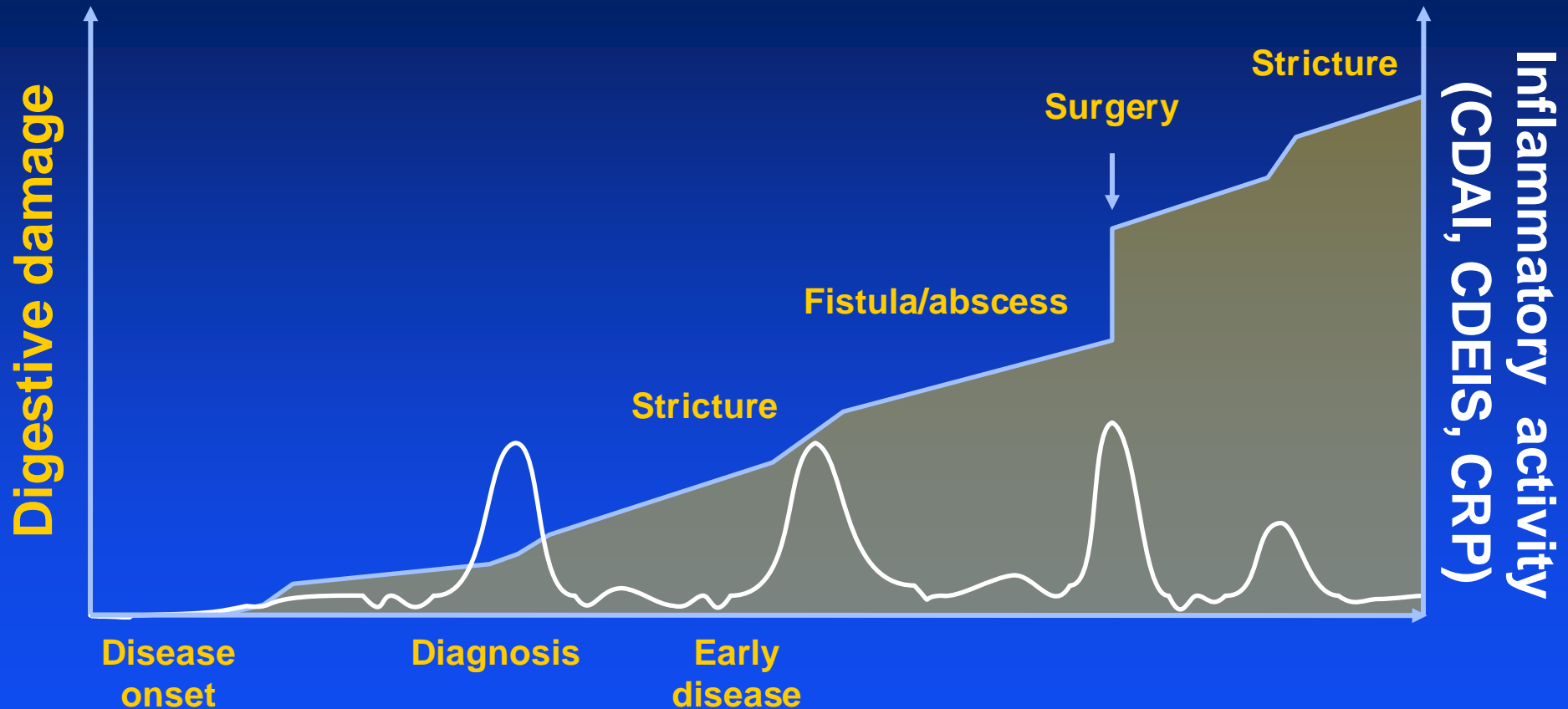
**Severe:
Longitudinal
or serpiginous
ulcers**



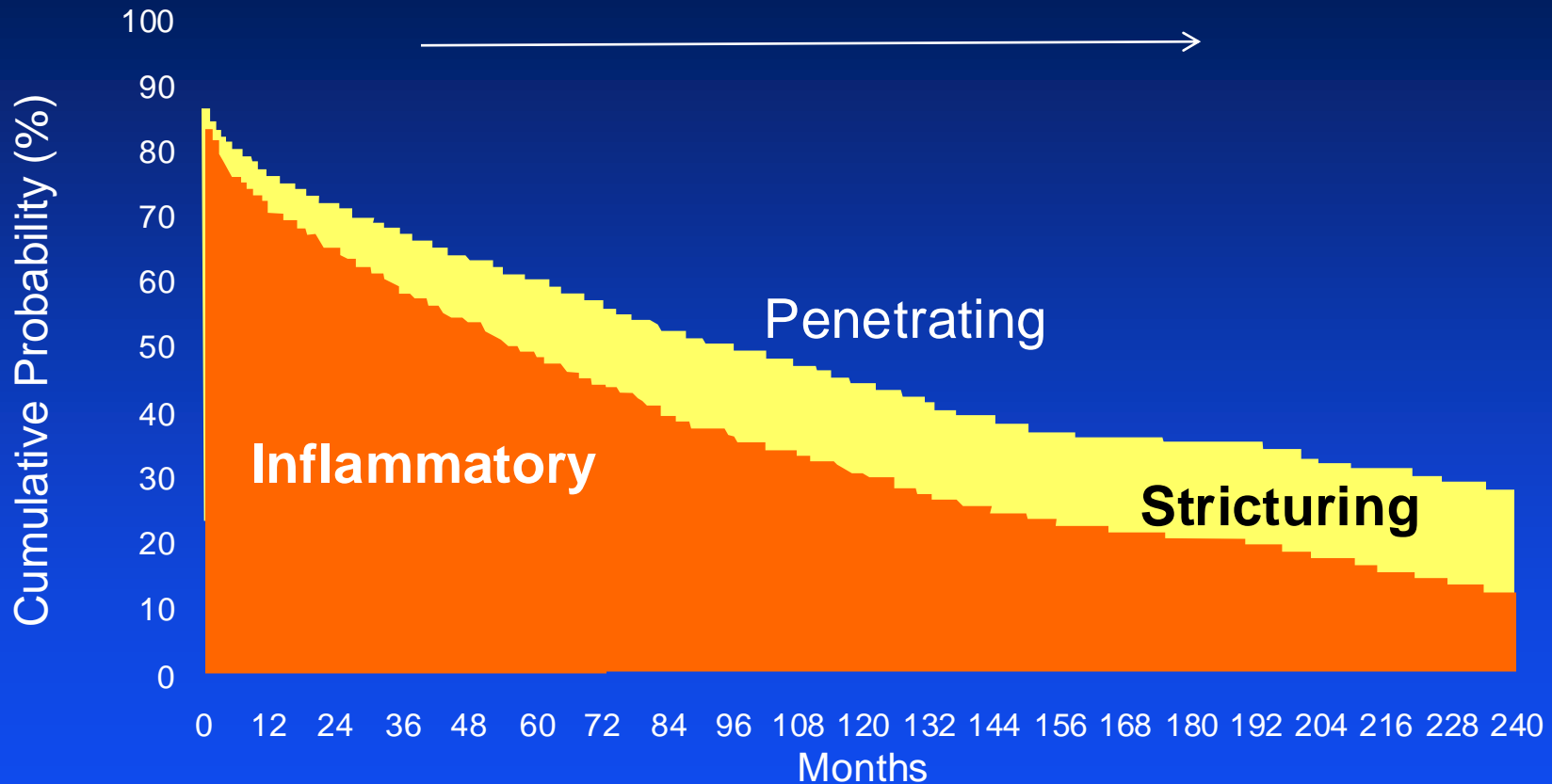
**Severe:
Cobble-stoning of
mucosa**



Inflammatory Activity and Progression of Damage in Crohn's Disease



Natural History of Crohn's Disease



Patients at risk:
N = 2002

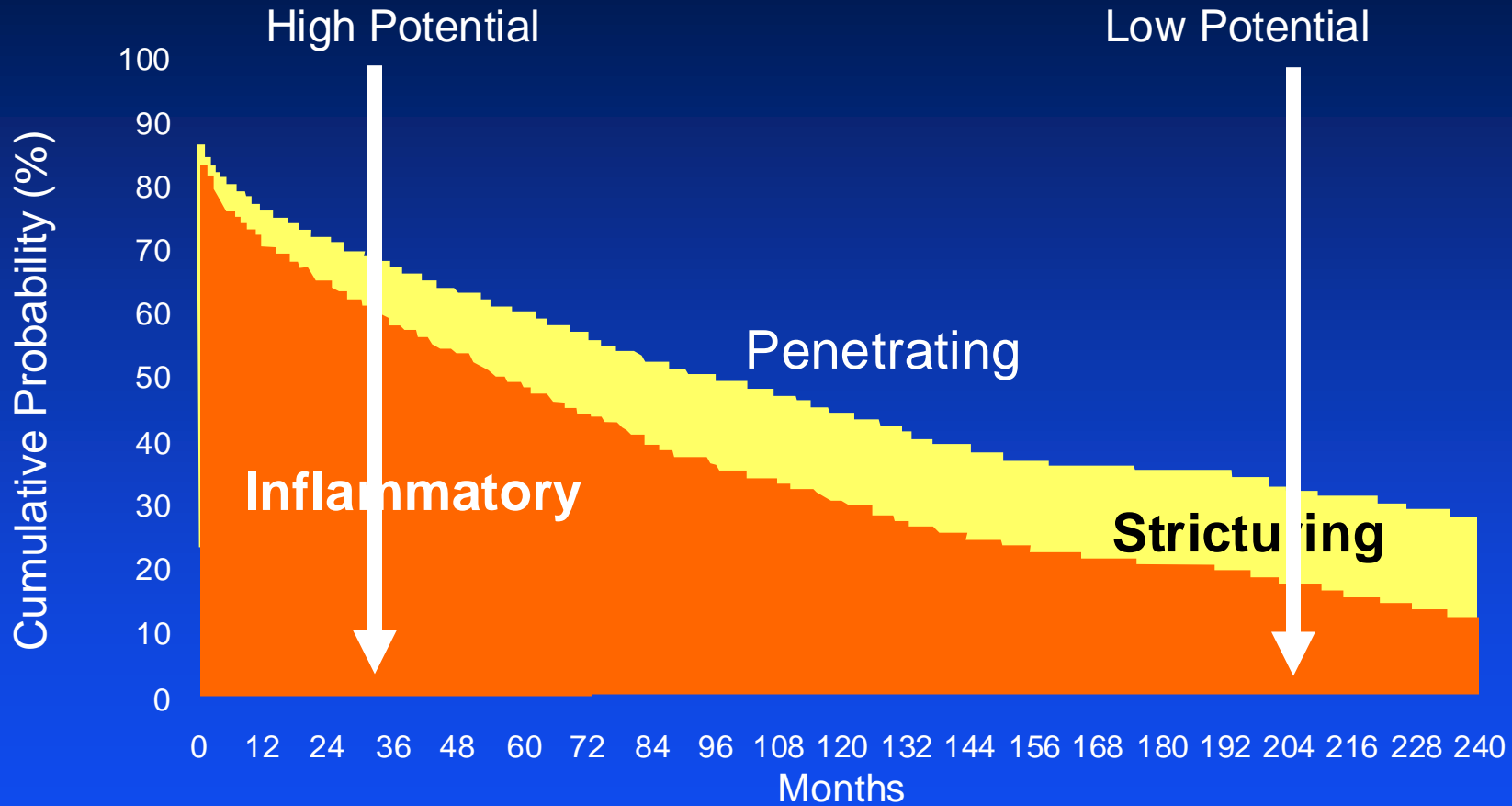
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229

95

37

Impact of Therapy Depends on Degree of Structural Damage & Velocity of Progression



Patients at risk:
N = 2002

552

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