UTSW What's New in GI

Using and Choosing IBD Therapies in 2026

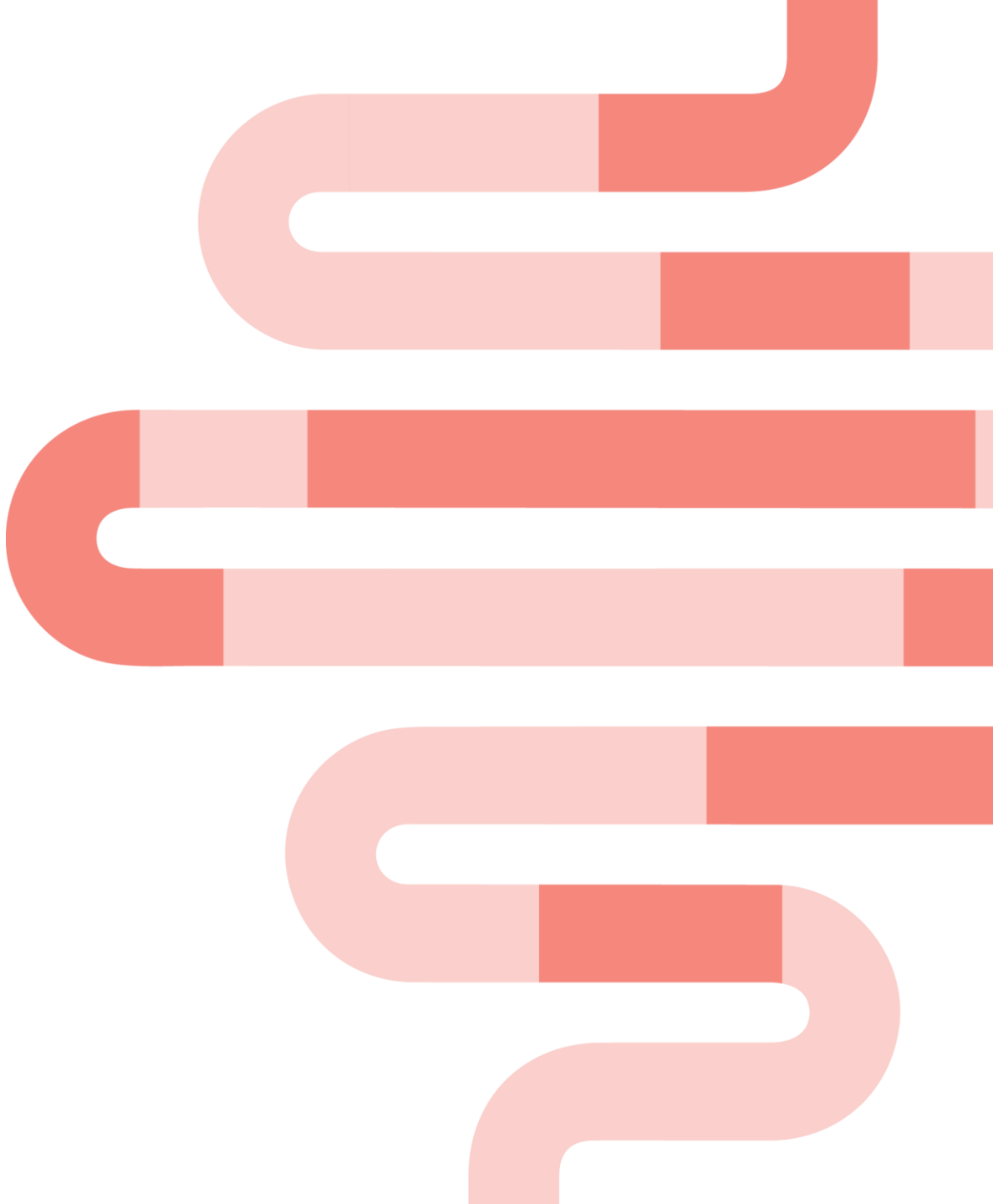
David Fudman, MD

Director, Inflammatory Bowel Disease Clinic

Quality Officer, Division of Digestive and Liver Diseases

Associate Professor, Department of Internal Medicine

University of Texas Southwestern Medical Center



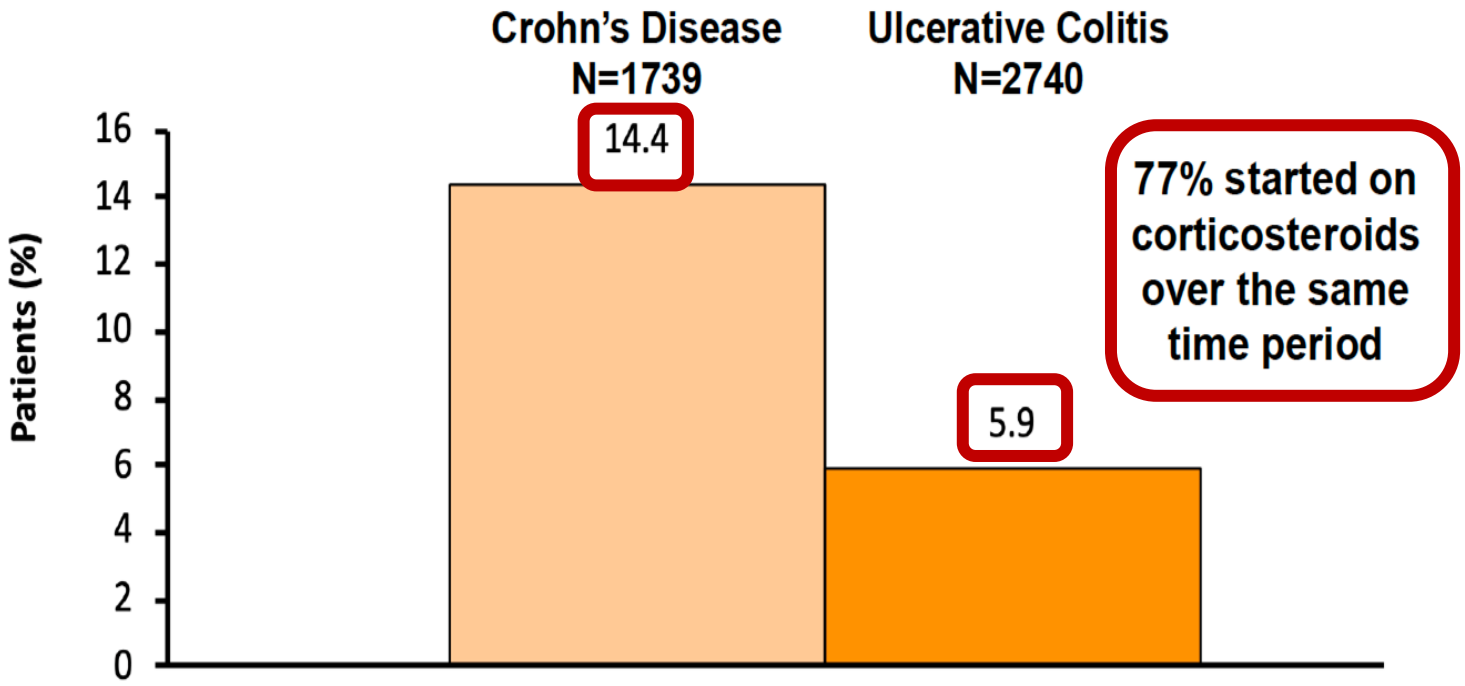
Disclosures

- Consulting/advisory boards for Pfizer, Fresenius Kabi, Janssen, Eli Lilly
- Off-label use will be discussed

Therapy and Positioning in IBD: Challenges and Advances in 2026

- Is looking for the "**perfect**" drug selection an **enemy of good** selection?
- What is our **source of truth**? Incorporating multiple imperfect data sources for comparative effectiveness
- How can we incorporate **patient-specific factors** in selection?
- What can we take into practice from the **updated AGA** (2024, 2025) **and ACG guidelines** (2025)?
- What are **indicators of quality** medical management of IBD in 2026?

Advanced therapies broadly underutilized



Low rates of advanced therapy use among newly diagnosed patients, mean follow up 2.3 years (2017-21)

ACG: **We suggest *AGAINST requiring failure of conventional therapy* before initiation of advanced therapy for management of CD**

AGA: **"In adult outpatients with moderate-to-severely active Crohn's disease the AGA suggests *upfront use of advanced therapy* compared with step-up therapy"**

Lichtenstein GR, et al. *Am J Gastroenterol*. 2025;120(6):1225-1264.
Scott et al. Gastroenterology. 2025;169(7):1397-1448.
Siegel CA, et al. *Crohns Colitis 360*. 2024;6(3):otae040.

Advanced therapy: making a choice gets patients off hamster wheel

Patients starting biologic or small molecule 2017-2021

	Crohn's	UC
Years before biologic, mean (SD)	**6 years** (3)	**6 years** (3)
***Steroid episodes* before biologic** (among steroid users), mean (SD)	***5 episodes*** (4)	***6 episodes*** (5)
Days on conventional therapy, mean	420 days	685 days

Siegel et al. Sa1814 DDW 2023

IBD is a progressive disease

Symptoms do not correlate with inflammatory disease activity

Objective assessments are needed to guide and assess response to treatment

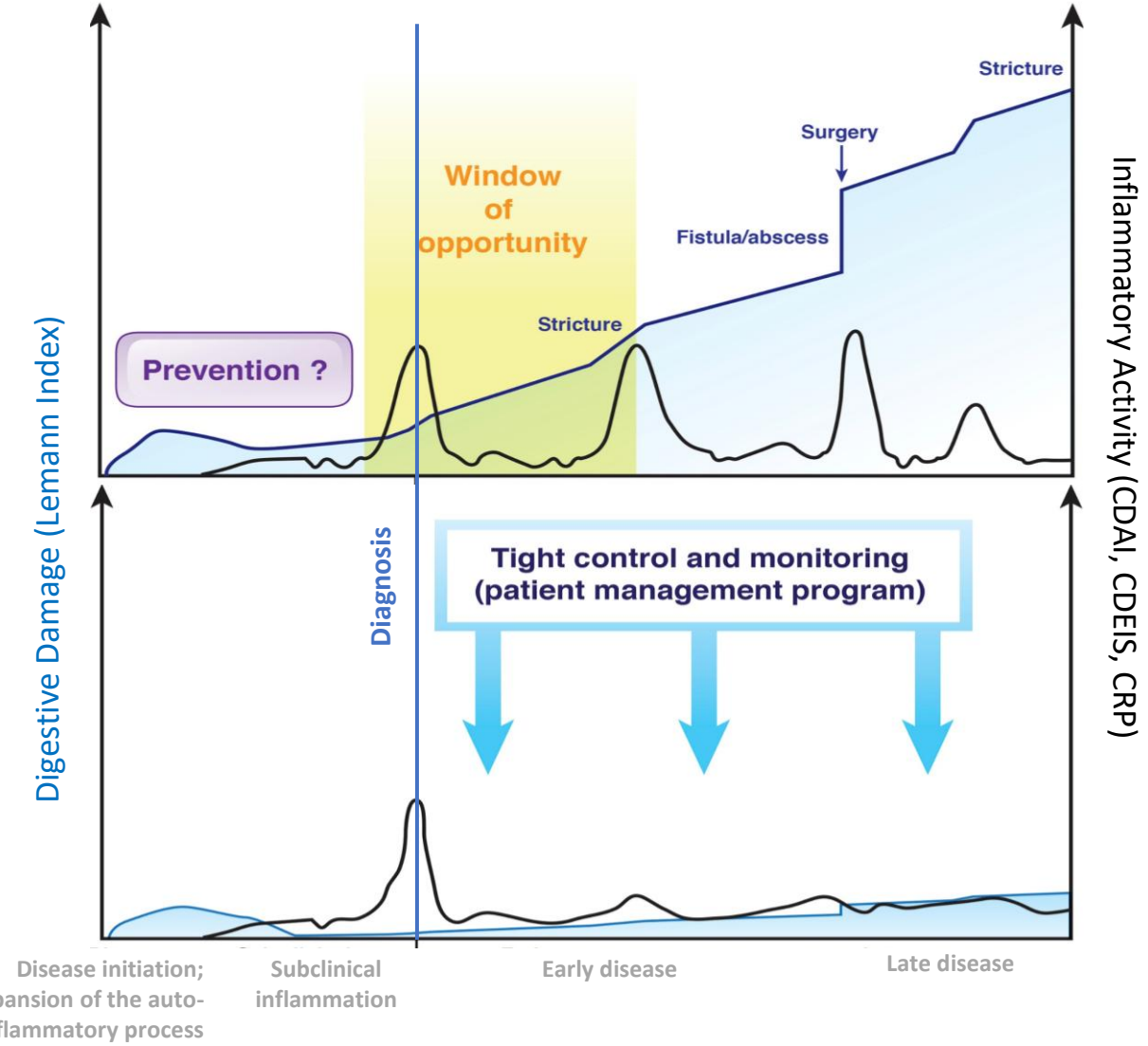


Image source:
Adapted from Colombel et al. *Gastroenterology* (2017)

PROFILE study: Early therapy powerful

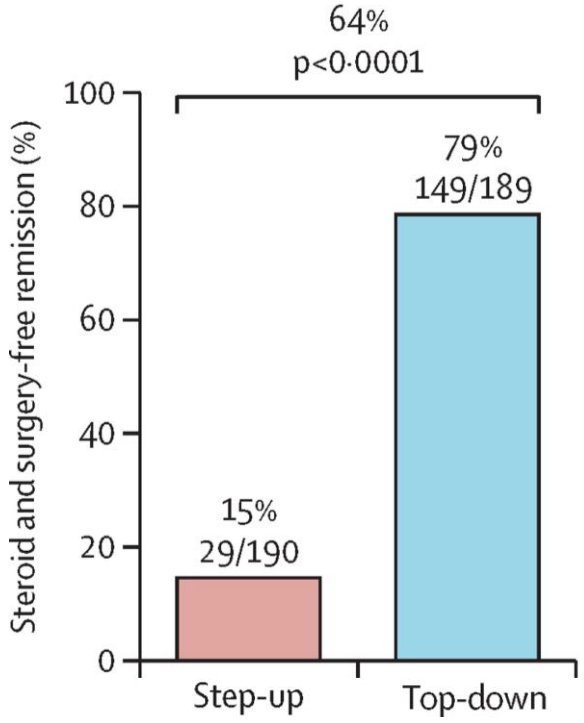
Newly diagnosed CD:

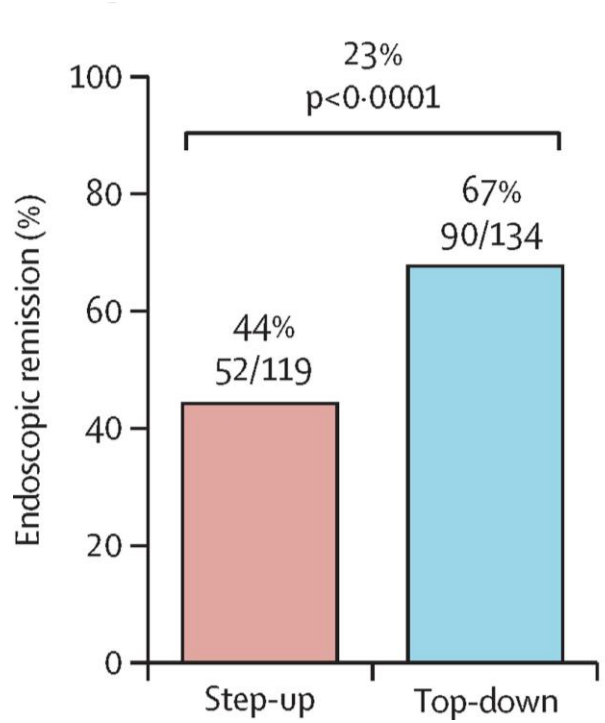
<u>Top-down vs. accelerated step-up</u>

- **Top down:** infliximab plus immunomodulator
- **Accelerated step-up:** Steroids and immunomodulator for 1st flare, add infliximab if 2nd flare

<u>Top-down</u>: Better efficacy AND better safety

- >5x more patients in steroid- and surgery-free remission at 48wk
- Fewer adverse events at 48wk

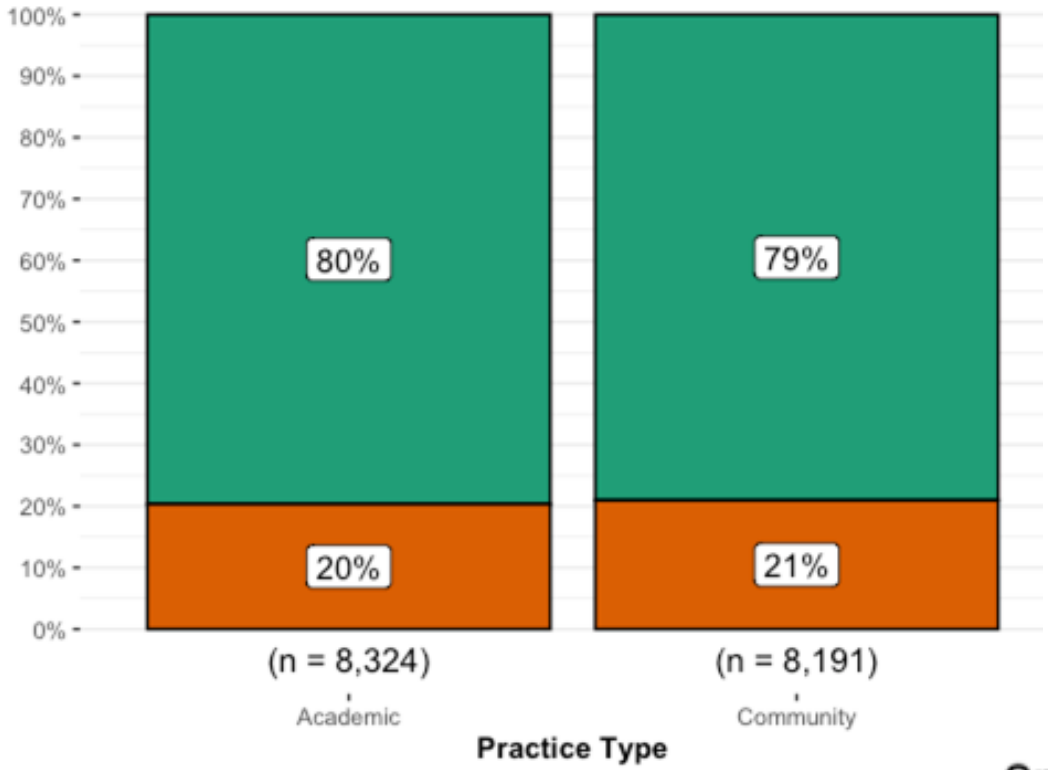




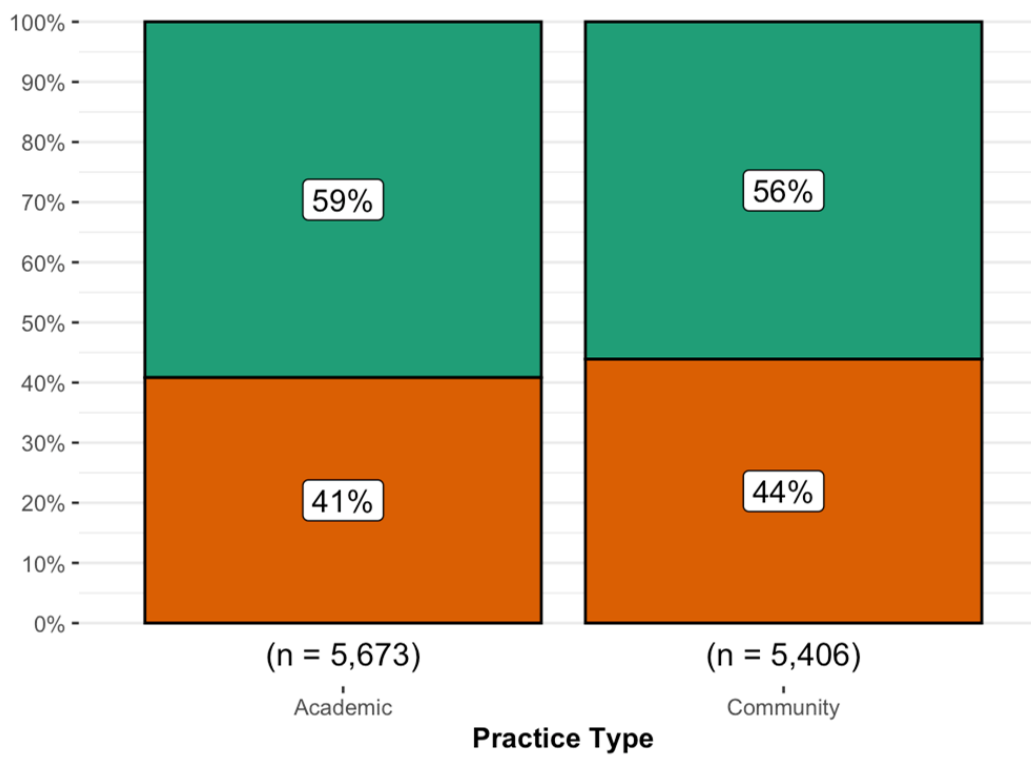
The Lancet Gastroenterology & Hepatology 2024 9415-427DOI: (10.1016/S2468-1253(24)00034-7)

Mission possible:
Broader use of advanced therapies (IBD Qorus, 2020-2025)

Crohn's: 16,515 patient visits



Ulcerative colitis: 11079 patient visits



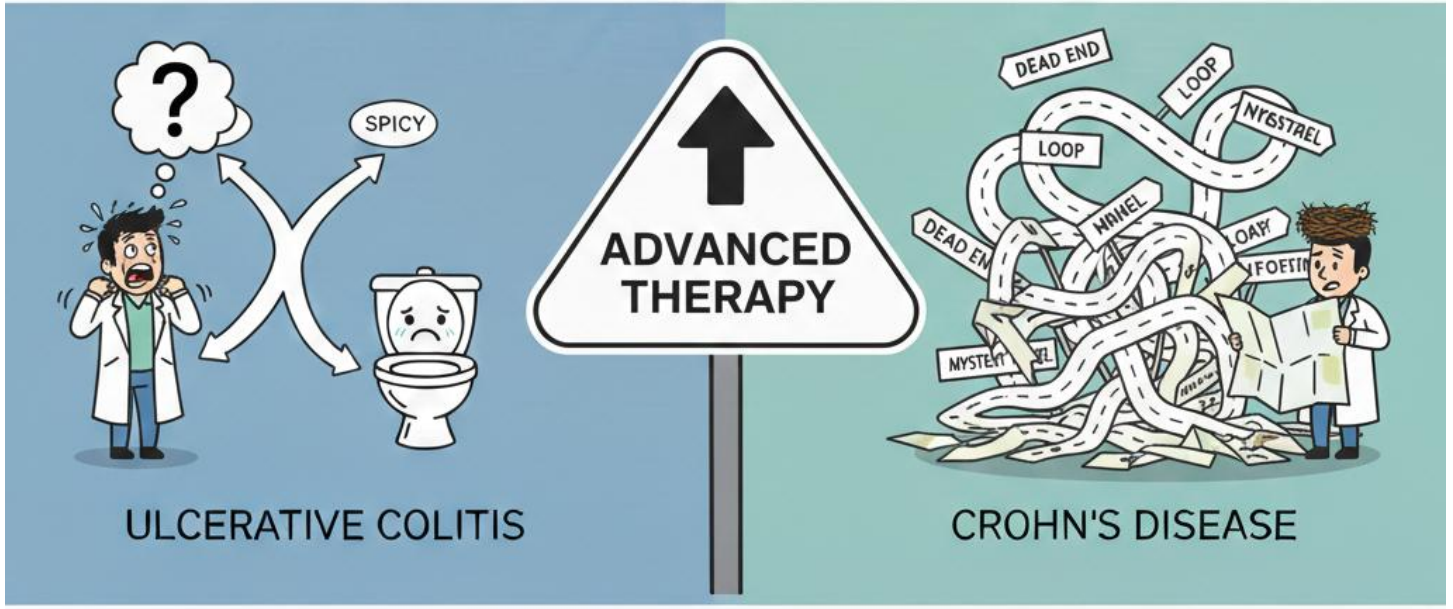
On advanced therapy?

Yes

No

Saleh A et al and Sapana G et al. Presented DDW 2025

So, who needs an advanced therapy?

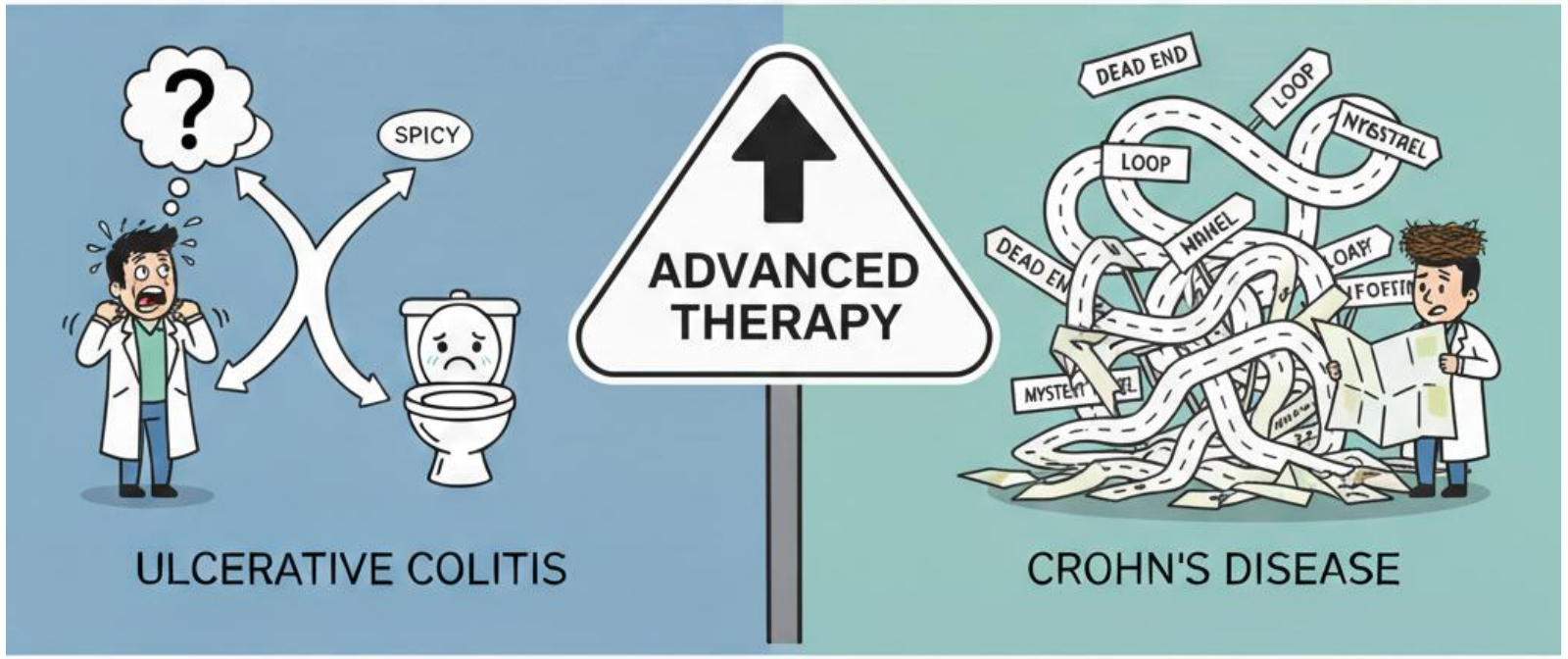


- **Moderate/severe activity**: nearly all
- **Mild/moderate activity**: if not healing on 5ASA or high-risk factors (high disease severity)

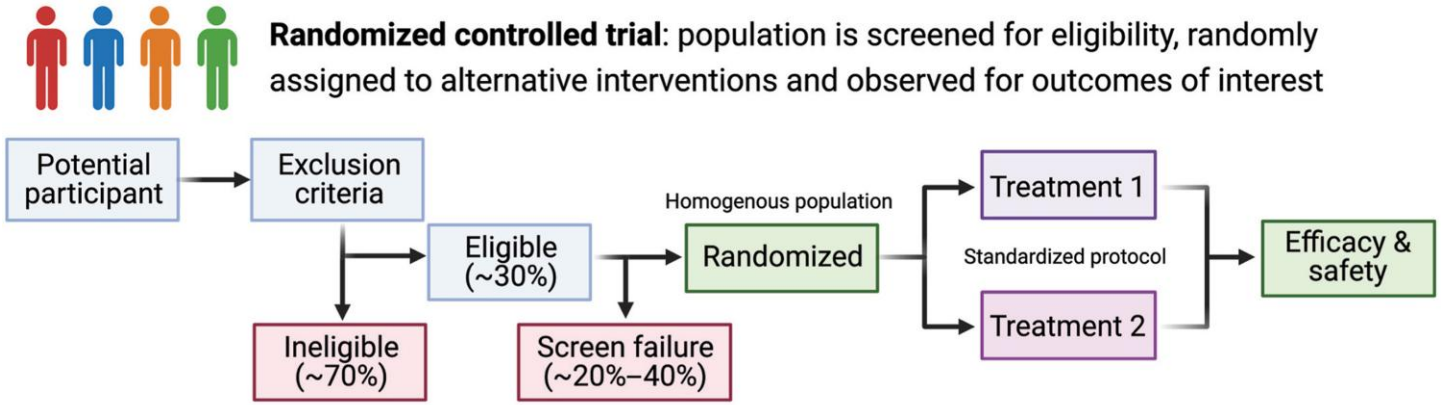
- **Most patients** (~80%) – unless mild disease activity and severity and confident in mild disease course

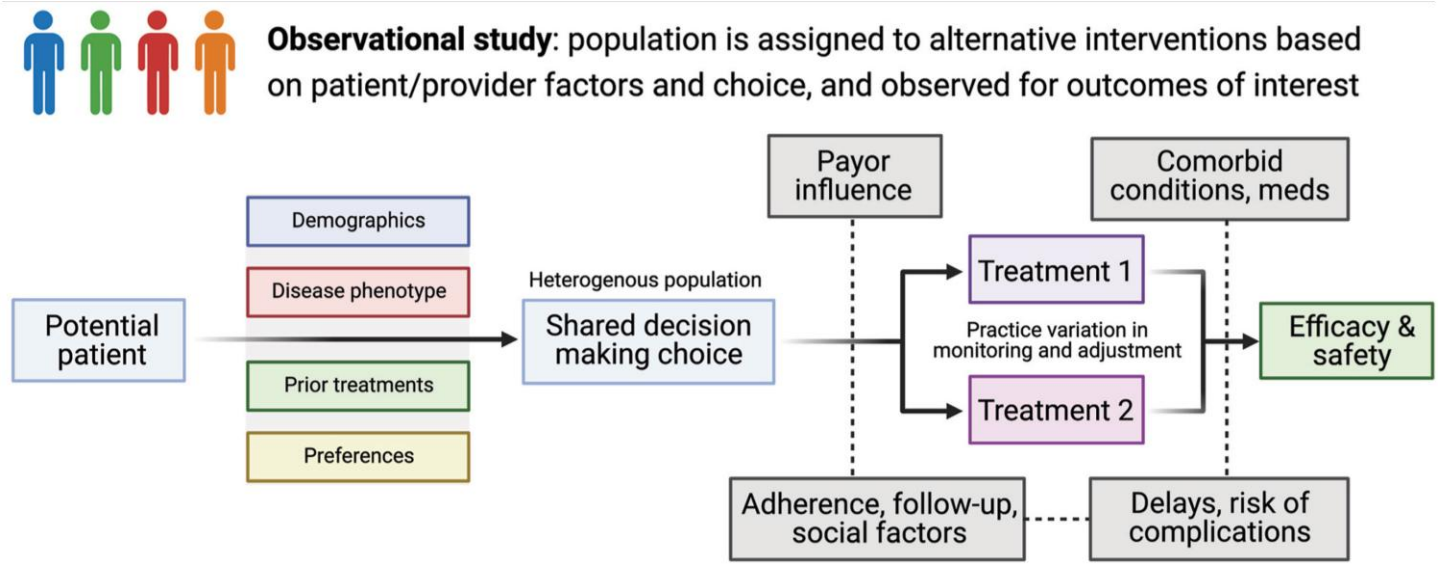
Image: Nano Banana

Which Therapy? Not as Simple



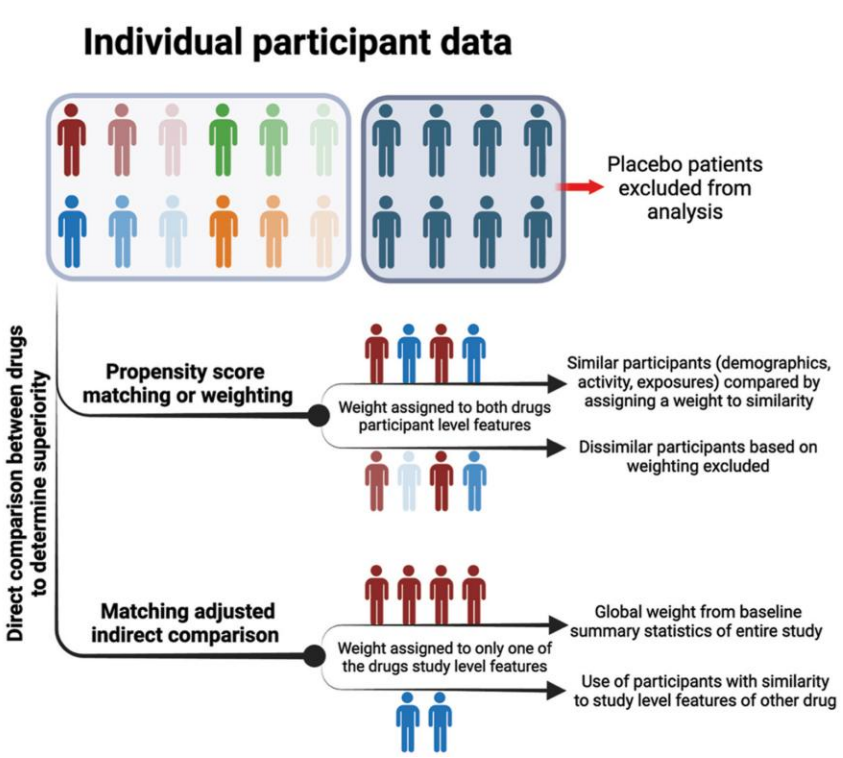
Multiple imperfect data streams inform selection

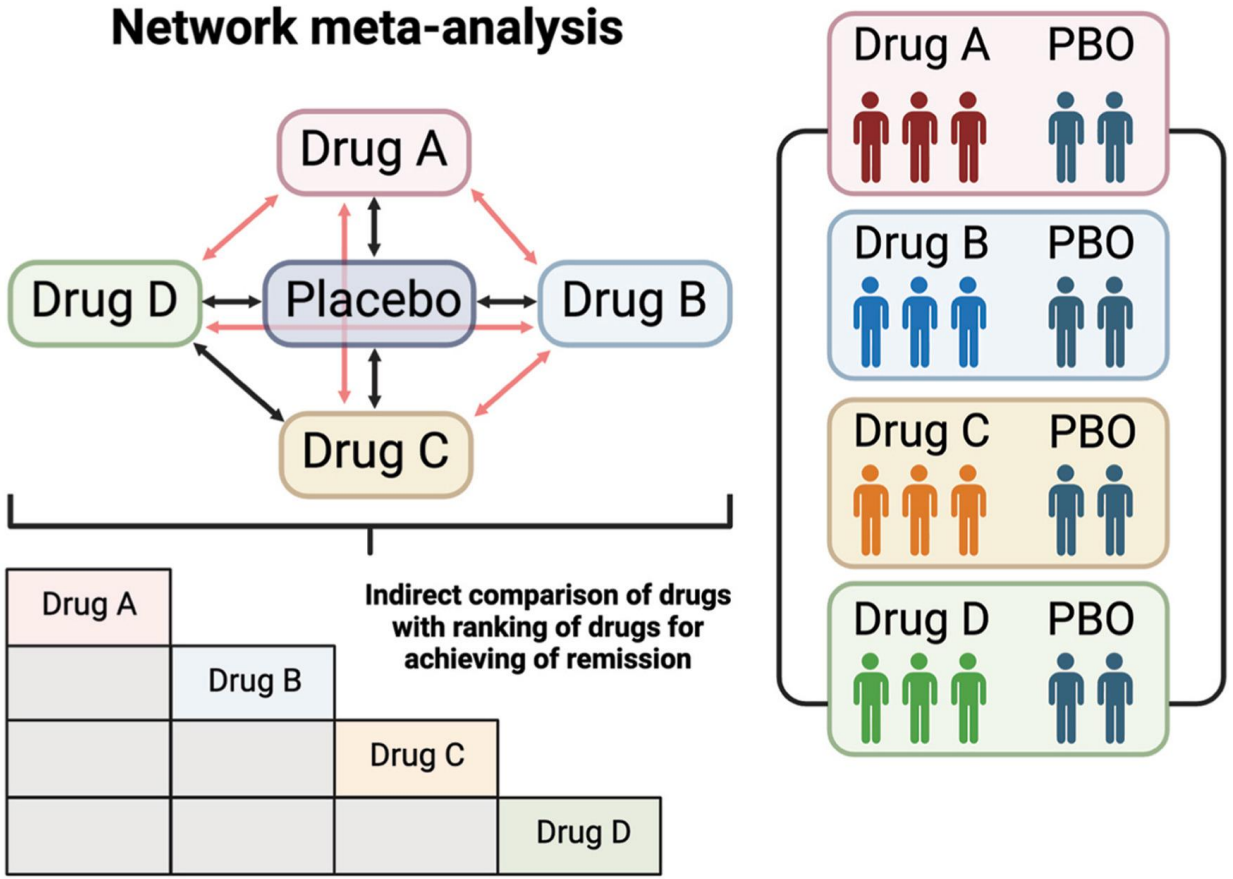




Dalal et al. Gastroenterology. 2024 Mar;166(3):396-408

Multiple imperfect data streams inform selection





Dalal et al. Gastroenterology. 2024 Mar;166(3):396-408

Network meta-analysis: AGA guidelines

AGA Pharmacological Management of Moderate-to-Severe Ulcerative Colitis (2024)

	Higher efficacy	Intermediate efficacy	Lower efficacy
Bio-naïve	• Infliximab • Vedolizumab • Ozanimod, etrasimod • Upadacitinib • Risankizumab	• Ustekinumab • Mirikizumab • Tofacitiinib* • Golimumab	• **Adalimumab**
aTNF/bio-exposed	• Upadacitinib, tofacitinib • Ustekinumab	• Mirikizumab • Risankizumab	• **Adalimumab** • **Vedolizumab** • **Ozanimod, etrasimod**

AGA Pharmacological Management of Moderate-to-Severe Crohn's (2025)

Adult outpatients with moderate-to-severely active Crohn's disease

Moderate-to-severely active Crohn's disease defined as:

- Moderate-to-severe abdominal pain and/or diarrhea due to inflammation
- Mild symptoms, with high burden of inflammation
- Patients with corticosteroid-dependence, or refractory to oral corticosteroids
- Significant extent of disease or upper GI involvement

SUGGEST upfront use of advanced therapies, rather than step-up therapy after corticosteroids and/or immunomodulator monotherapy

(Conditional recommendation, very low certainty of evidence)

Scott et al. Gastroenterology. 2025;169(7):1397-1448.

AGA Pharmacological Management of Moderate-to-Severe Crohn's (2025)

	Higher efficacy	Intermediate efficacy	Lower efficacy
Bio-naïve	• Infliximab • Adalimumab • Vedolizumab • Ustekinumab • Risankizumab • Mirikizumab • Guselkumab		• **Certolizumab** • **Upadacitinib**
aTNF/bio-exposed	• Adalimumab • Risankizumab • Guselkumab • Upadacitinib	• Ustekinumab • Mirikizumab	• **Certolizumab** • **Vedolizumab**

Scott et al. Gastroenterology. 2025;169(7):1397-1448.

2025 ACG Crohn's Guidelines: Drug Statements

		Induction	Maintenance	Comments
Mild to moderate disease	**Oral mesalamine**	X	X	
	Ileal release budesonide	✓	X	
Moderate to severe	**Oral corticosteroids** (Prednisone 40 mg daily for 1-2 weeks, with subsequent tapering)	✓	X	Think early advanced therapy for these patients
	Thiopurines (Azathioprine 2-2.5 mg/kg/day, Mercaptopurine 1-1.5 mg/kg/day)	X	✓	• TPMT testing before start • Given the adverse effect profile of thiopurine monotherapy (eg, lymphoma, skin cancer), consider newer, safer agents for maintenance
	Methotrexate (up to 25 mg 1×/week IM/SC)	X	✓	• ↓ to 15 mg/wk @ 4 mo if steroid-free remission
	Anti-TNF agents (IV infliximab; SC adalimumab; SC certolizumab pegol)	✓	✓	• SC infliximab for maintenance only • Check TB, hepatitis B testing pre-treatment
	IV vedolizumab	✓	✓	SC vedolizumab for maintenance only
	Anti-IL 12/23 agents (Ustekinumab)	✓	✓	• RISA>> UST for anti-TNF experienced pt • GUS → SC or IV induction • MIRI, RISA, UST → IV induction
	Anti-IL 23 agents (Guselkumab; Mirikizumab; Risankizumab)	✓	✓	
	Upadacitinib	✓	✓	

Sulfasalazine should be considered only for those with symptomatic mild colonic Crohn's disease

Lichenstein et al. Am J Gastroenterol. 2025
Slide: Maia Kayal

2025 ACG Ulcerative Colitis Guidelines: Positioning statements

Comparative efficacy

1. Vedolizumab over adalimumab
2. “Infliximab is the preferred anti-TNF therapy”

Which patients with mildly-to-moderately active UC should be treated as moderate-to-severe?

1. Patients **not responsive** (or are intolerant) **to 5-ASA** therapies
2. Patients with a number of **prognostic factors associated with an increased risk** of hospitalization or surgery

Step therapy and payers

- “Patients with UC should have all medical options available as recommended by their doctor and healthcare team. **Third-party payers and requirements for step therapy should not come between the patient and their healthcare team** in making decisions about treatment for UC”

- **Balance speed of access with getting the right drug**

Rubin et al. American Journal of Gastroenterology 120(6):p 1187-1224, June 2025.

Comparative effectiveness in UC: RCTs and Observational Data

Question	Result	Data source
Vedolizumab vs **adalimumab**	**Vedolizumab superior**	**RCT** (VARSITY)
Ustekinumab or **tofacitnib** vs **vedolizumab** after aTNF	**Vedolizumab inferior**	*Observational* data
Upadacitinib vs **tofacitinib**	**Upadacitinib** superior	*Observational* data

Comparative effectiveness in Crohn's: RCTs and observational data

Drug	Question	Result	Data source
Adalimumab	vs **ustekinumab** in bionaive	**Comparable**	**RCT** (SEAVUE)
Risankizumab	vs **ustekinumab** in aTNF-exposed	**Risankizumab** superior	**RCT** (SEQUENCE)
Guselkumab	vs **ustekinumab**	**Guselkumab** superior	**RCT** (GALAXI2/3)
Mirikizumab	vs **ustekinumab**	Mirikizumab non-inferior	**RCT** (VIVID1)
Risankizumab	after failure of ustekinumab q8w	**Risankizumab** effective	*Observational* data
Vedolizumab	vs **ustekinumab** in aTNF failure	**Ustekinumab** superior	*Observational* data

Not just efficacy

Patient preferences	Safety in select populations	Coexisting IMIDs	Speed, clearance	Insurance barriers
• **Mode and frequency of delivery** • Perceptions of disease-related vs medication-related risks	• **Pregnancy** (avoid JAKi/S1P) • Cardiovascular disease, specifically **atherosclerotic disease** • **Malignancy**	• **Arthritis, especially axial:** aTNF or JAKi • **Psoriasis/PsA**: aTNF or IL23 • **MS**: Ozanimod (and natalizumab)	• **Fastest acting**: aTNF and JAKi • **Most immunogenic:** aTNF (IFX>ADA) • **Clearance:** favors small molecules (ie JAKi)	• Medical (IV) or pharmacy (SC, oral) benefit, or both • **Commercial vs governmental insurance** (assistance programs) • **On vs off-label dosing**

Efficacy not one-size-fits-all

Efficacy of advanced therapies by DISEASE LOCATION in Crohn's disease

Greater benefit with all advanced therapies in patients with colonic disease vs. ileal disease

Anti-interleukins (9 RCTs)

Drug vs. Placebo: OR (95% CI)	
COLONIC disease	4.29 (2.77-6.44)
ILEAL disease	2.31 (1.44-3.70)

JAK inhibitors (3 RCTs)

Drug vs. Placebo: OR (95% CI)	
COLONIC disease	4.37 (2.67-7.15)
ILEAL disease	1.01 (0.54-1.89)

Anti-integrins (2 RCTs)

Drug vs. Placebo: OR (95% CI)	
COLONIC disease	1.79 (0.55-5.87)
ILEAL disease	2.10 (0.80-5.53)

Lee HL et al Clin Gastro Hep 2025

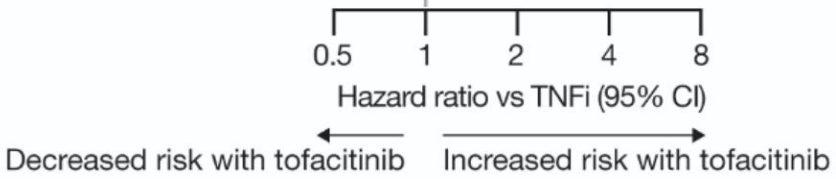
Upadacitinib: 2025 FDA label update

“RINVOQ is indicated for the treatment of adults with moderately to severely active [UC/CD] who have had an inadequate response or intolerance to one or more TNF blockers.

If TNF blockers are clinically inadvisable, patients should have received at least one approved systemic therapy prior to use of RINVOQ.”

ORAL surveillance: Risk of MACE by h/o ASCVD

		n/N (%)	HR vs TNFi (95% CI)	IR per 100 PY (95% CI) [PY]	IRD vs TNFi per 100 PY (95% CI)	NNH (PY) vs TNFi‡	NNH (5-yr) vs TNFi‡
Overall population† N=4362	Tofacitinib 5 mg BID	47/1455 (3.2%)	1.24 (0.81, 1.91)	0.91 (0.67, 1.21) [5166.3]	0.18 (–0.18, 0.53)	567	113
	Tofacitinib 10 mg BID	51/1456 (3.5%)	1.43 (0.94, 2.18)	1.05 (0.78, 1.38) [4872.0]	0.31 (–0.06, 0.69)	319	64
	Combined tofacitinib doses	98/2911 (3.4%)	1.33 (0.91, 1.94)	0.98 (0.79, 1.19) [10038.3]	0.24 (–0.06, 0.55)	412	82
	TNFi	37/1451 (2.5%)		0.73 (0.52, 1.01) [5045.3]			
HxASCVD N=640 (14.7%)	Tofacitinib 5 mg BID	17/204 (8.3%)	1.96 (0.87, 4.40)	2.53 (1.47, 4.05) [672.7]	1.24 (–0.22, 2.71)	80	16
	Tofacitinib 10 mg BID	17/222 (7.7%)	2.01 (0.89, 4.50)	2.61 (1.52, 4.18) [651.7]	1.33 (–0.17, 2.82)	75	15
	Combined tofacitinib doses	34/426 (8.0%)	1.98 (0.95, 4.14)	2.57 (1.78, 3.59) [1324.4]	1.28 (0.08, 2.49)*	78	16
	TNFi	9/214 (4.2%)		1.28 (0.59, 2.44) [701.4]			
No HxASCVD (CV RFs only) N=3722 (85.3%)	Tofacitinib 5 mg BID	30/1251 (2.4%)	1.03 (0.62, 1.73)	0.67 (0.45, 0.95) [4493.6]	0.02 (–0.31, 0.36)	4344	869
	Tofacitinib 10 mg BID	34/1234 (2.8%)	1.25 (0.76, 2.07)	0.81 (0.56, 1.13) [4220.2]	0.16 (–0.20, 0.52)	621	124
	Combined tofacitinib doses	64/2485 (2.6%)	1.14 (0.73, 1.78)	0.73 (0.57, 0.94) [8713.9]	0.09 (–0.21, 0.39)	1113	223
	TNFi	28/1237 (2.3%)		0.64 (0.43, 0.93) [4343.9]			

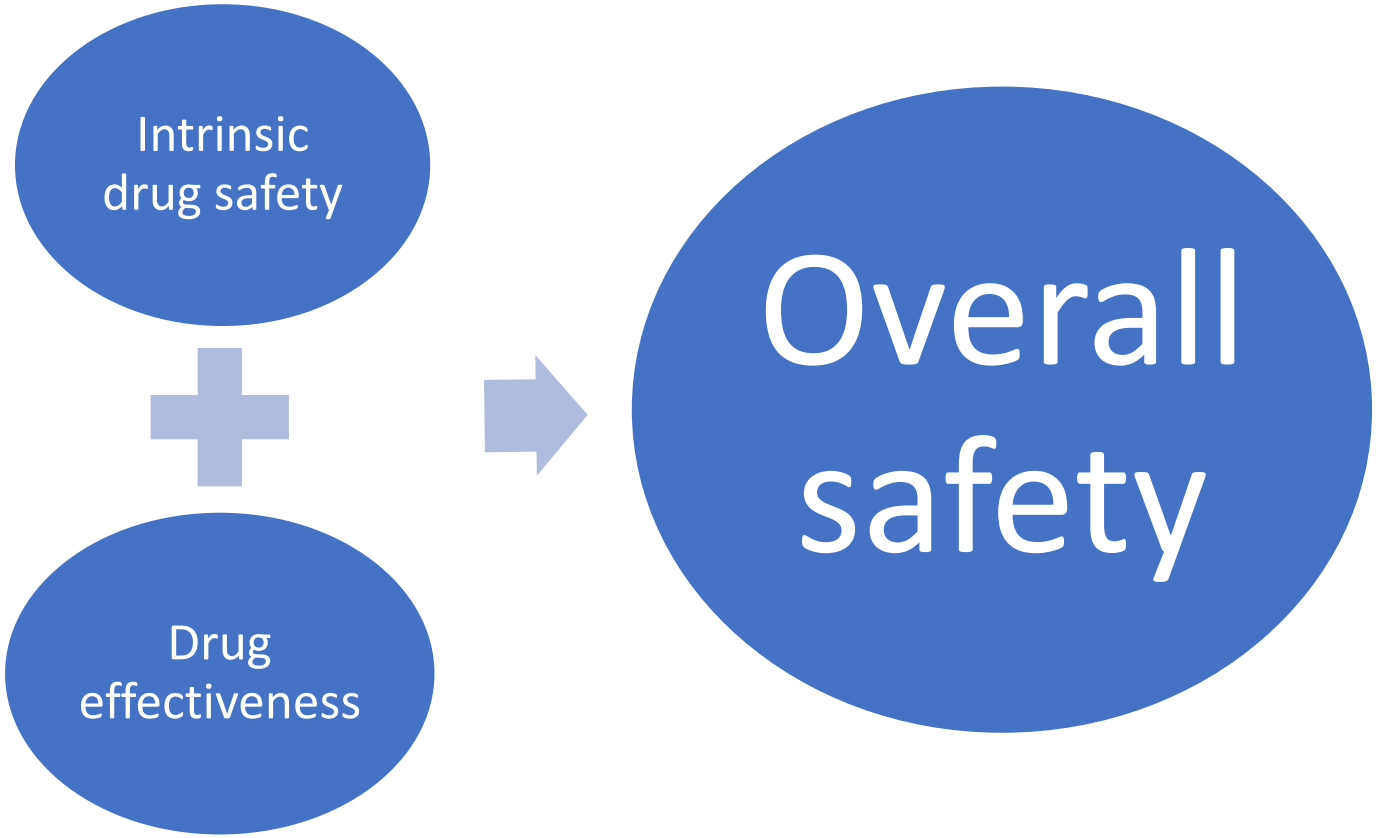


- Study included patients with RA, >=50y, >=1 CV risk factor
- ASCVD = atherosclerotic cardiovascular disease: cerebrovascular disease (TIA or CVA), PAD, or CAD (MI, stable/unstable angina, history of PCI, other coronary heart disease)

Charles-Schoeman C et al. Ann Rheum Dis. 2023;82:119–129.

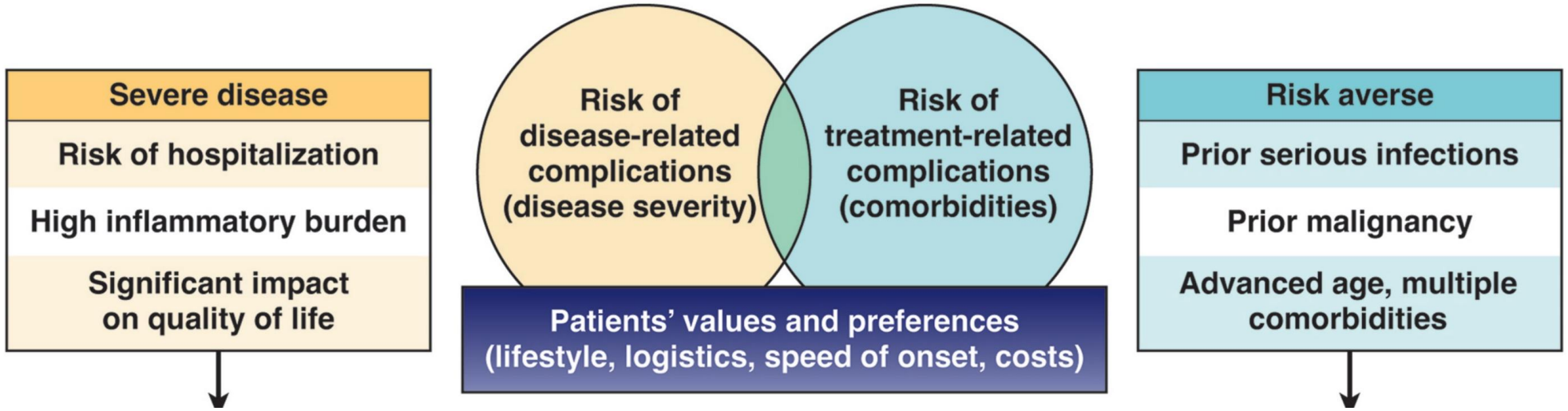
Drug safety is two-pronged

- **"Intrinsic" safety** of medication
  - Most influential on long-term risks
- **Effectiveness in controlling disease**
  - Most influential on short-term risks
  - More effective med generally safer than less effective



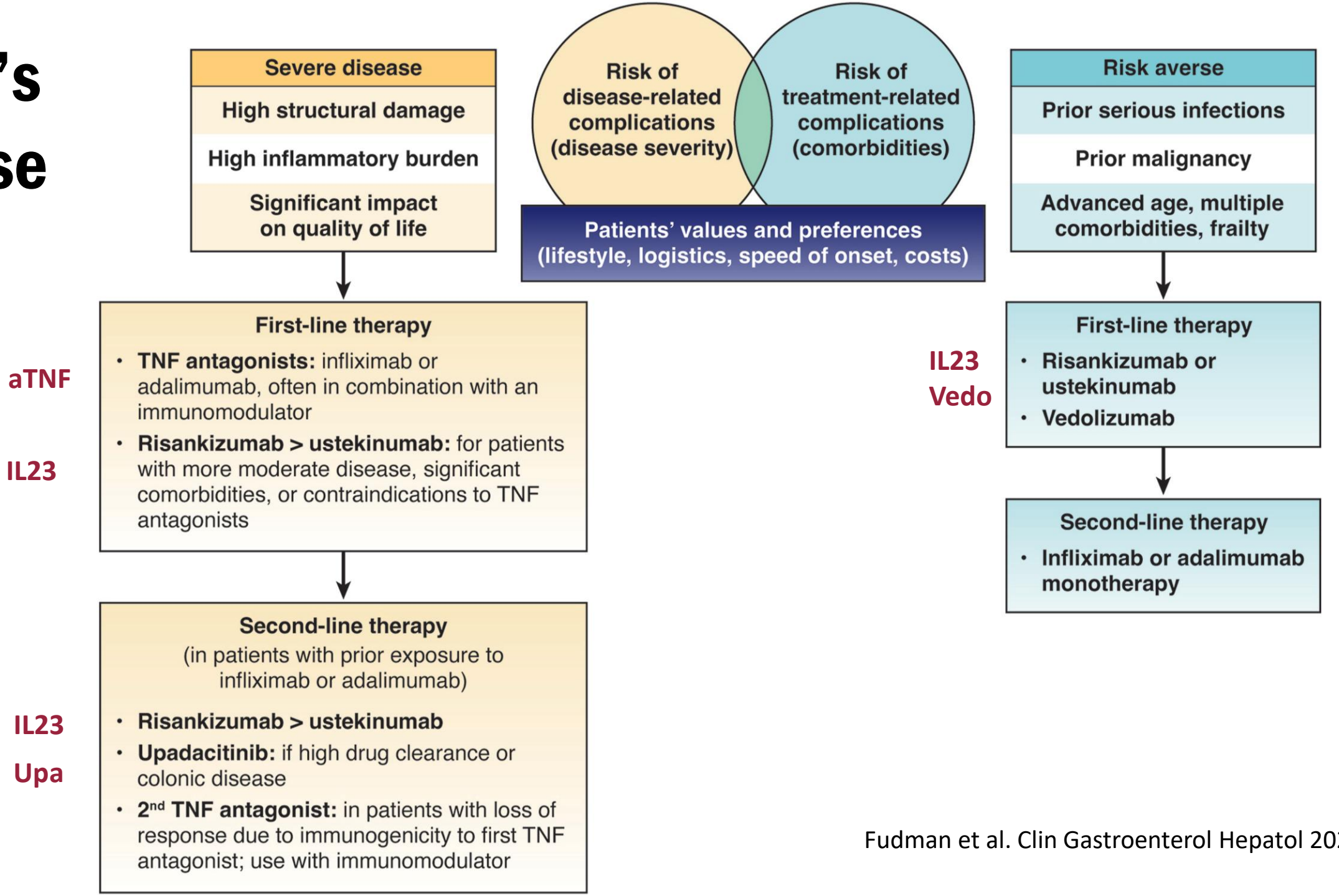
Sick patients don't need to "earn" aTNF or JAKi by failing (multiple) other drugs first

Two sides of risk: disease and drug



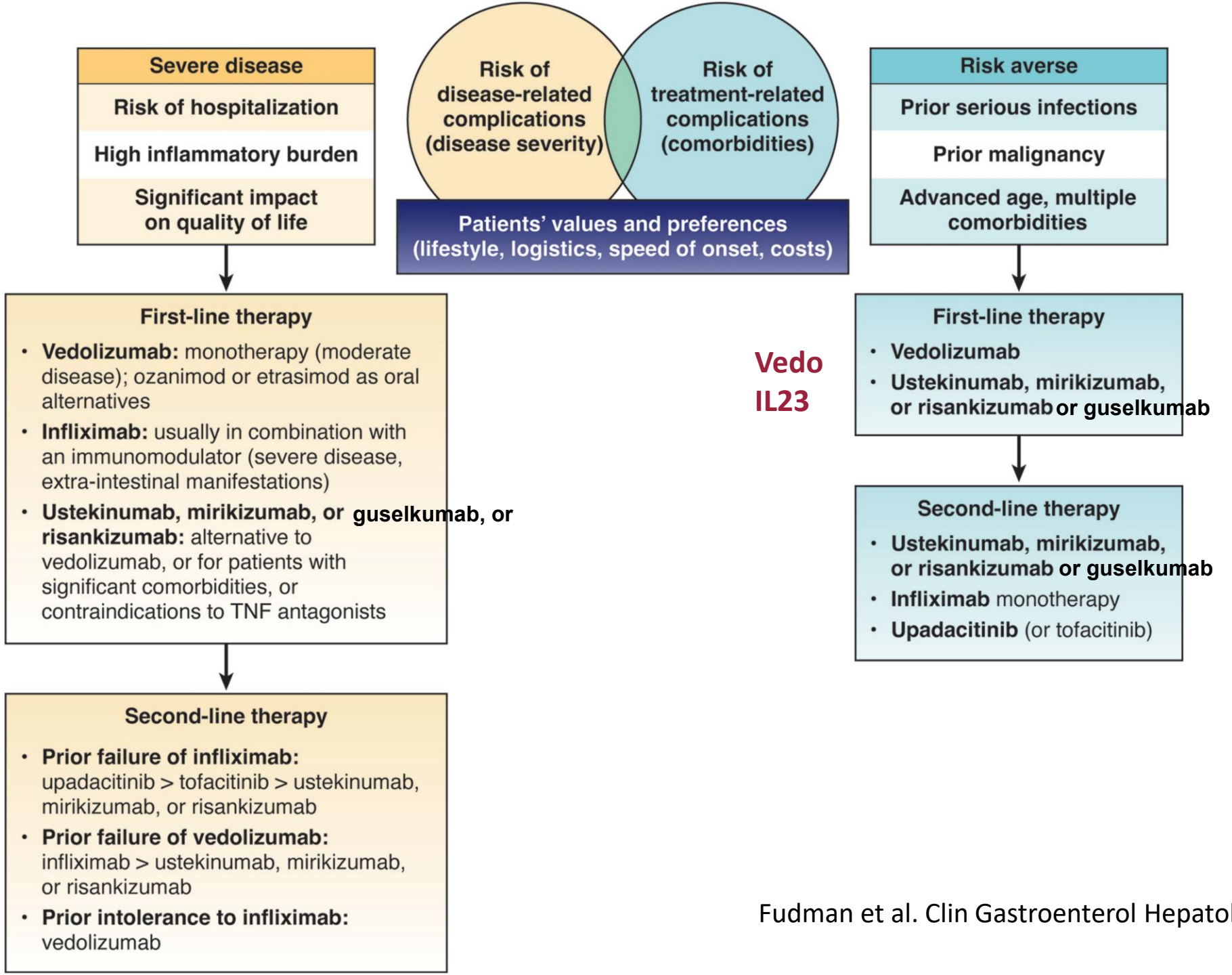
Fudman et al. Clin Gastroenterol Hepatol 2024

Crohn's Disease



Fudman et al. Clin Gastroenterol Hepatol 2024

Ulcerative Colitis



IFX (sick, EIMs)

Vedo
IL23
S1P

Vedo
IL23

After infliximab, upa > IL23

After vedo, infliximab > IL23

Fudman et al. Clin Gastroenterol Hepatol 2024

How does positioning fit into quality of care?

AGA Quality Indicators for Medical Management and Disease Monitoring of IBD

- Focus on **common instances of under-, over- and misuse** of medical therapies and monitoring
- Quality indicators:
  - Evidence standard is short of that required for formal quality metrics
  - Intended to be deployed in quality improvement efforts to narrow care gaps and reduce care variation

Fudman et al. Overuse and Misuse in Inflammatory Bowel Disease: AGA Quality Indicators for Medical Management and Disease Monitoring of IBD. Released for Public Comment 10/2025

AGA Quality Indicators: Selected Statements

Steroids and advanced therapies

- Corticosteroids should not be used for maintenance of remission
- **Patients treated with systemic corticosteroids should be transitioned to a steroid-sparing biologic, targeted small molecule, or immunomodulator**
- Patients with moderate to severe UC or CD should be started on biologic/targeted small molecule therapy based on disease severity and the **practice of step-up therapy should not be used**

Monitoring

- **Routine care for all patients** with asymptomatic UC or CD **should include at least yearly objective monitoring for inflammation** rather than monitoring of symptoms alone

Fudman et al. Released for Public Comment 10/2025

Putting it together

- **Candidates for advanced therapy**:
  - Most with Crohn's
  - Mild/moderately active UC not healing with 5ASA or with risk factors for severe course
  - Moderate/severely active UC

- **Picking pearls**:
  - Don't let picking (or getting) the "right" drug prevent or delay from choosing any drug. Early therapy makes big difference
  - Consider risks of disease alongside those of therapy
    - Vedolizumab, IL(12/)23 ~equally "safe"
  - Sick patients don't need to "earn" most effective therapies (aTNF or JAKi) by failing others

- **Quality care**:
  - Avoid overuse: steroids, step therapy
  - Avoid underuse: advanced therapies, objective disease monitoring

Thank you!