IBD in Action
A Clinical Case Presentation

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UNIVERSITY OF TORONTO

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CanMEDS Roles Covered

X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
	Communicator (as *Communicators*, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
X	**Collaborator** (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
X	**Leader** (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
X	**Health Advocate** (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
	Scholar (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Disclosures

Company	Speaking Fees	Advisory Board	Research Support
Janssen	x	x	
Pfizer	x	x	x
Takeda	x	x	
Abbvie	x	x	

A short case introduction

Historical category	Patient details
Identifying data	18 year old South Asian man (on presentation to the adult GI clinic)
Reason for referral	New diagnosis of CD made at OHP by a hepatologist
Past medical history	Ankylosing spondylitis
Past surgical history	Cholecystectomy
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Allergies	NKDA
Social history	Non-smoker, no EtOH, regular cannabis use. Studying mathematics at UofT but unable to attend regularly given symptoms, single, no children, born in India and immigrated to Canada at age 2
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A short case introduction

Does this age of presentation affect your clinical approach

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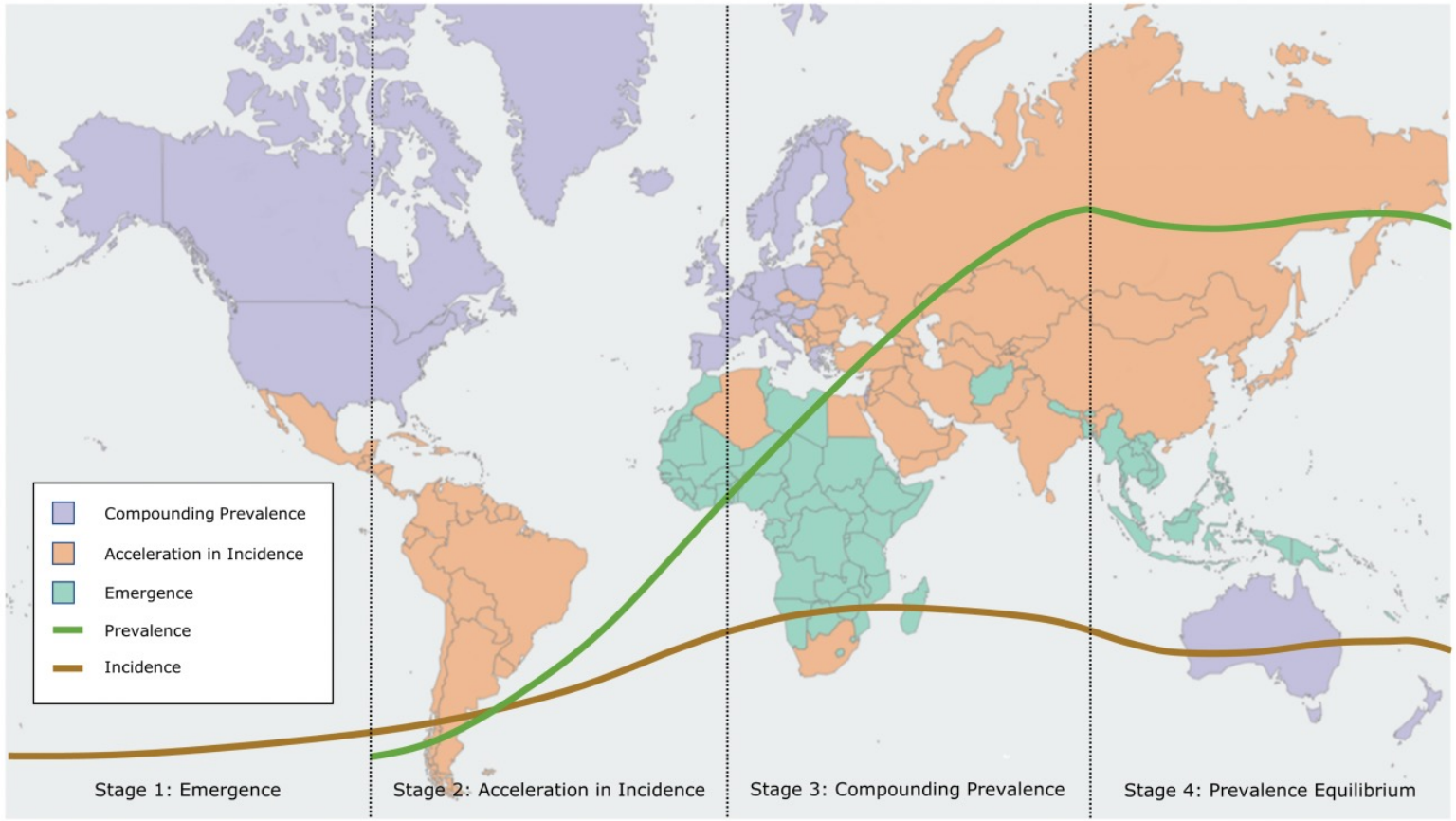
What are the current demographics of IBD in Canada?



- Canada is currently in stage 3 of a 4-stage epidemiologic evolution of IBD. Stage 3 represents Compounding Prevalence. Incidence stabilizes and prevalence continues to climb.
- The prevalence of IBD in 2023 is estimated to be 825 per 100,000 (410 per 100,000 for Crohn's Disease and 414 per 100,000 for ulcerative colitis and IBD-U)
    - 0.82% prevalence represents 322,600 people living with IBD in Canada.
- The incidence of pediatric-onset IBD was 13.9 per 100,000 in 2014 and is forecast to rise by 1.23% per year up to 18.0 per 100,000 in 2035.
    - There has been a similar incidence of IBD among children of South Asian ethnicity living in Canada compared to the general population.

References: Coward et al. The 2023 Impact of IBD in Canada: Epidemiology of IBD. JCAG 2023;6(2):S9-15.

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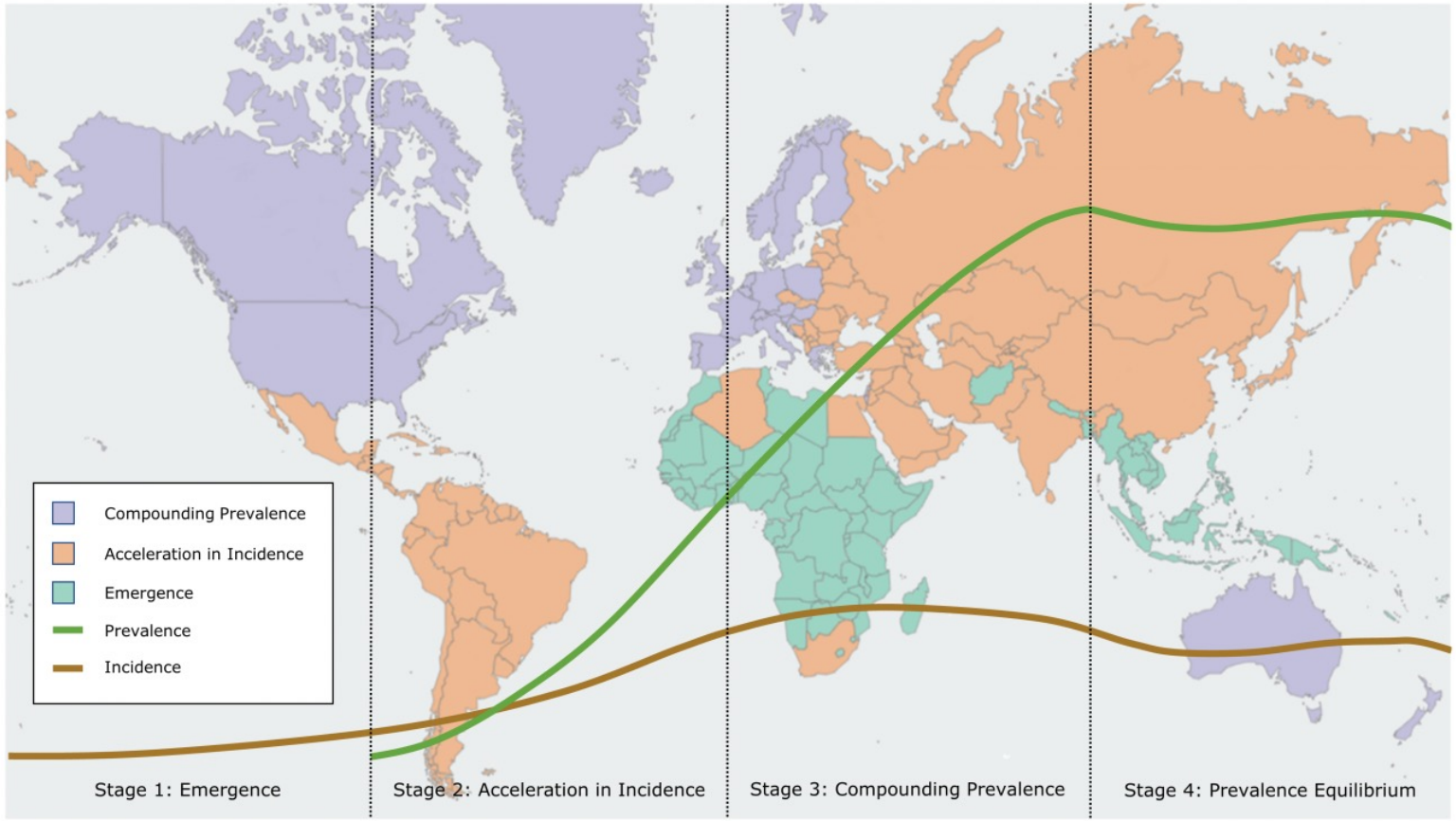

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Journal of the Canadian Association of Gastroenterology, 2022, **5**, 105–115
https://doi.org/10.1093/jcag/gwab050
Advance access publication 26 March 2022
Original Article

Canadian Consensus Statements on the Transition of Adolescents and Young Adults with Inflammatory Bowel Disease from Pediatric to Adult Care: A Collaborative Initiative Between the Canadian IBD Transition Network and Crohn's and Colitis Canada

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A short case introduction

How do you approach EIMs and comorbidities in IBD?

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Extra-intestinal manifestations & Comorbidities of IBD

Table 1 Major extraintestinal immune-related manifestations of IBD

Arthritis
Erythema nodosum
Pyoderma gangrenosum
Aphthous stomatitis
Iritis/uveitis

Table 2 Autoimmune disorders associated to IBD

Alopecia areata
Ankylosing spondylitis
Bronchiolitis obliterans
Cold urticaria
Hemolytic anemia
Henoch-Schoenlein purpura
Insulin-dependent diabetes mellitus
Pancreatitis
Primary biliary cirrhosis
Primary sclerosing cholangitis
Polymyositis
Raynaud phenomenon
Seropositive rheumatoid arthritis
Sjogren syndrome
Thyroid disease
Vitiligo
Wegener's granulomatosis
Takayasu's arteritis

Denese S et al. Extraintestinal manifestations in inflammatory bowel disease. World J Gastroenterol; 2005 Dec 14;11(46):7227-36.

***Panel:* Comorbidities in inflammatory bowel disease**

Classic
- Psoriasis and psoriatic arthritis
- Psychological and psychiatric disorders
- Osteoporosis

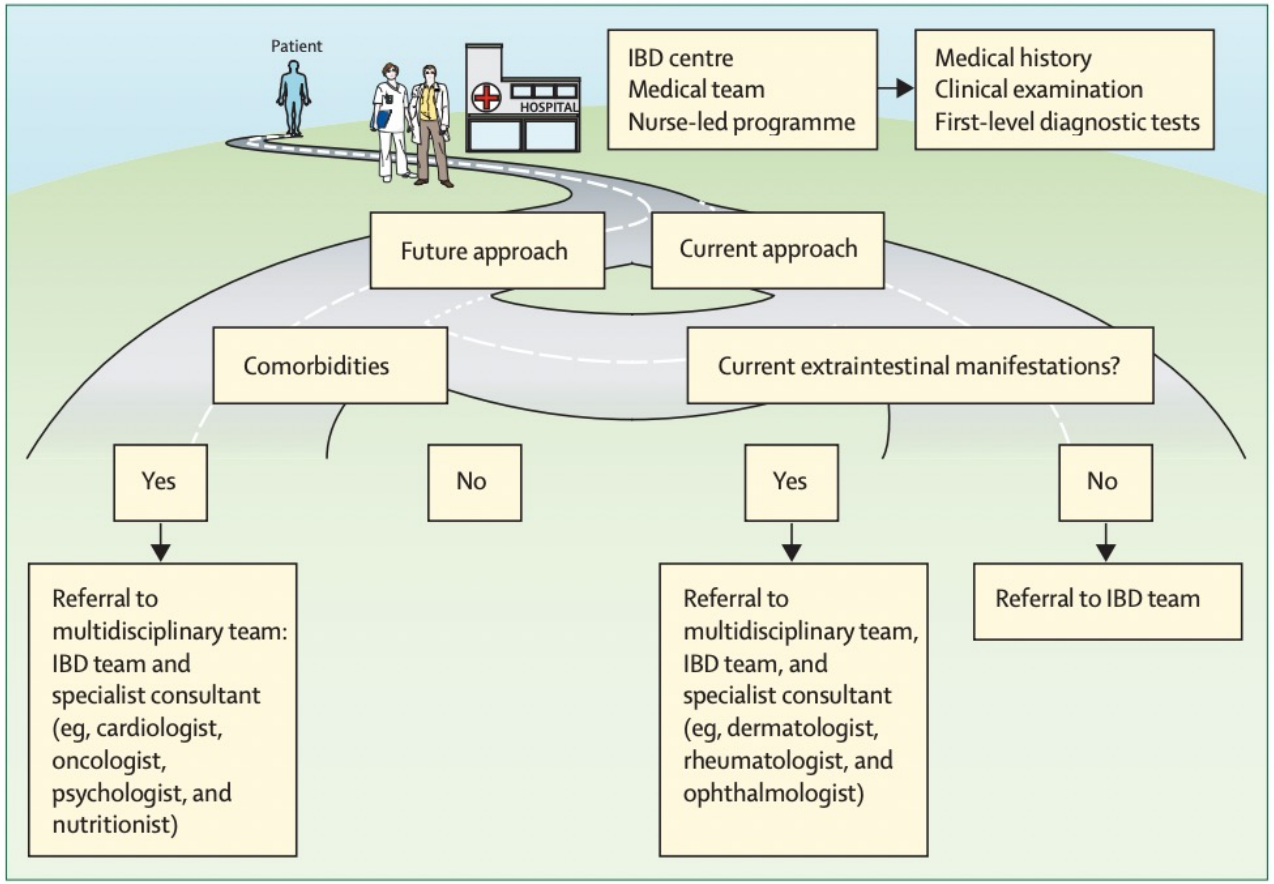
Emerging
- Metabolic syndrome and its components
- Cardiovascular diseases
- Atherosclerosis
- Fatigue
- Chronic obstructive pulmonary disease
- Sexual dysfunction
- Parkinson's disease

Related to lifestyle
- Smoking
- Alcohol consumption
- Anxiety and stress
- Substance misuse

Related to treatment
- Skin cancer
- Lymphoma
- Dyslipidaemia

Argollo, M et al. Comorbidities in inflammatory bowel disease: a call for action. Lancet Gastroenterol Hepatol 2019; 4: 643–54.

Extra-intestinal manifestations & Comorbidities of IBD



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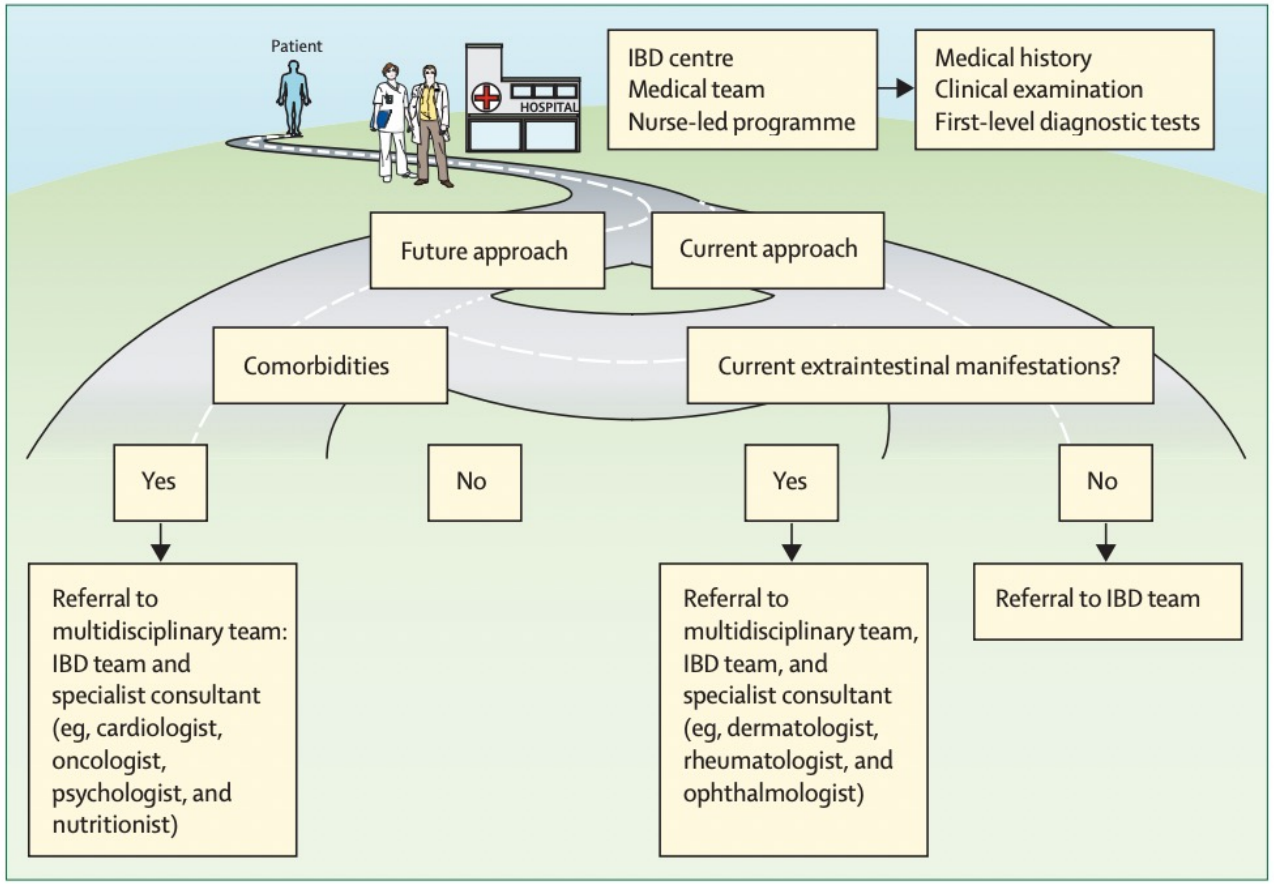
Extra-intestinal manifestations & Comorbidities of IBD

*Psychology & Psychiatry related services

Mental health, diet & nutrition



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A short case introduction

What is your advice to patients using NSAIDs for arthropathy?

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NSAIDs in the management of comorbid arthropathy

ECCO Guidelines on Extraintestinal Manifestations in Inflammatory Bowel Disease

Journal of Crohn's and Colitis, 2023, **XX**, 1–37
https://doi.org/10.1093/ecco-jcc/jjad108

4.2.2 NSAID use in the management of joint disease in IBD

Statement 17

There is no evidence of an association between NSAID use and UC flare [EL1], although there is potentially an association with CD flare [EL2]. We recommend that the decision to use NSAIDs for the management of arthropathy is made on a case-by-case basis [EL3]. Selective COX-2 inhibitors may be used for short periods of time [EL2] [consensus: 91%]

NSAIDs in the management of comorbid arthropathy

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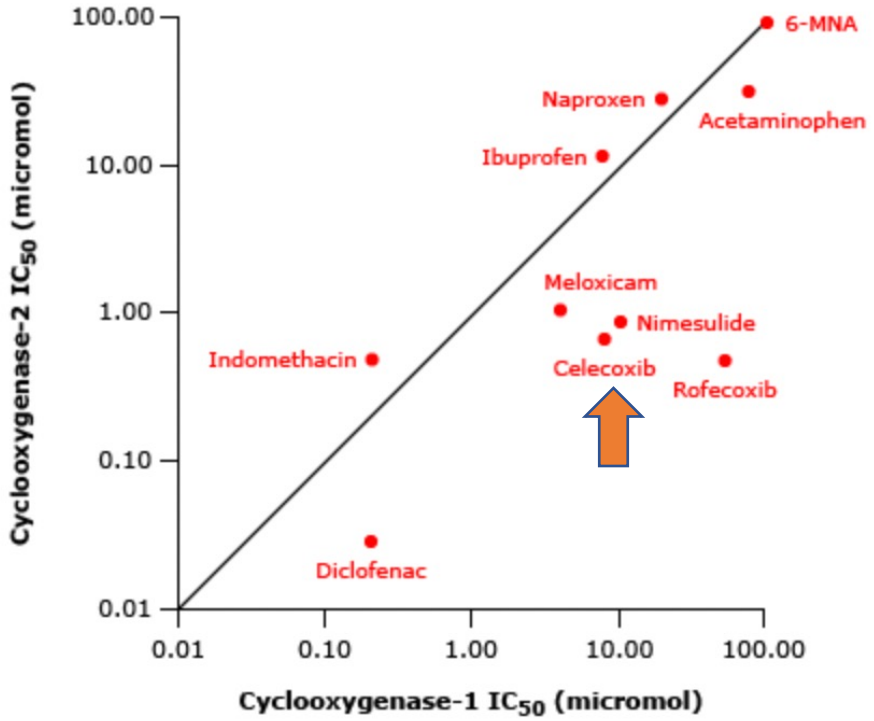

A short case introduction

What is your experience with cannabis in your practice?

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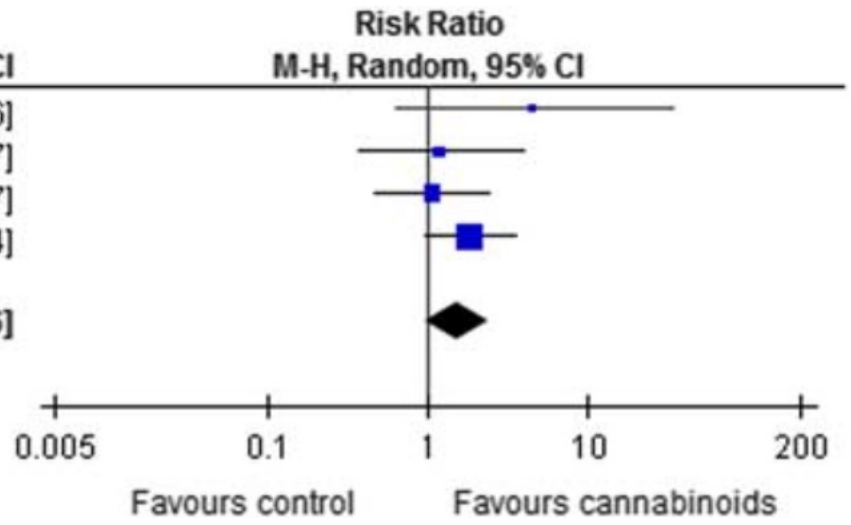
The use of Cannabinoids in IBD: Induction of Remission

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Naftali 2013	5	11	1	10	5.3%	4.55 [0.63, 32.56]
Naftali 2017	4	10	3	9	14.4%	1.20 [0.36, 3.97]
Irving 2018	8	29	8	31	29.2%	1.07 [0.46, 2.47]
Naftali 2018 (UEG)	15	23	8	23	51.1%	1.88 [0.99, 3.54]
Total (95% CI)		**73**		**73**	**100.0%**	**1.56 [0.99, 2.46]**
Total events	32		20			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.43$, df = 3 (P = 0.49); $I^2 = 0\%$

Test for overall effect: Z = 1.93 (P = 0.05)



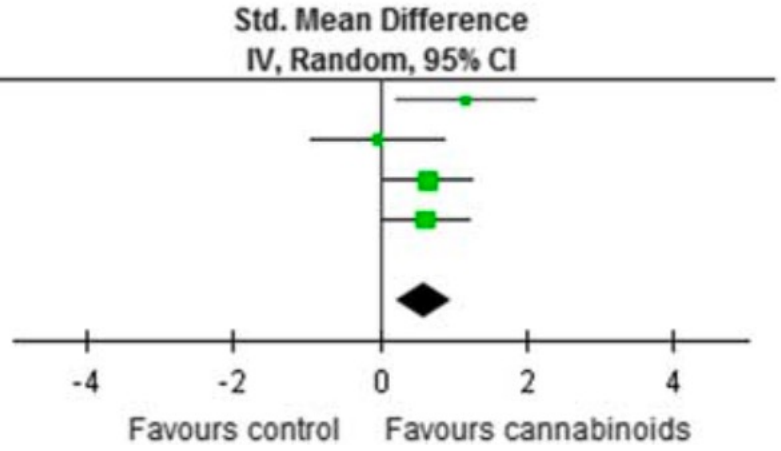
Doeve B et al. A Systematic Review With Meta-Analysis of the Efficacy of Cannabis and Cannabinoids for Inflammatory Bowel Disease. What Can We Learn From Randomized and Nonrandomized Studies? J Clin Gastroenterol;55(9):2021.

The use of Cannabinoids in IBD: Post-treatment disease activity

	Control			Cannabinoids				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Naftali 2013	306	143	10	152	109	11	14.9%	1.17 [0.23, 2.11]
Naftali 2017	216	121	9	220	122	10	16.2%	-0.03 [-0.93, 0.87]
Irving 2018	4.9	3.22	26	3	2.25	21	34.5%	0.66 [0.07, 1.25]
Naftali 2018 (UEG)	209.5	113	23	143.1	96	23	34.4%	0.62 [0.03, 1.22]
Total (95% CI)			**68**			**65**	**100.0%**	**0.61 [0.24, 0.99]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 3.34$, df = 3 (P = 0.34); $I^2 = 10\%$

Test for overall effect: Z = 3.19 (P = 0.001)



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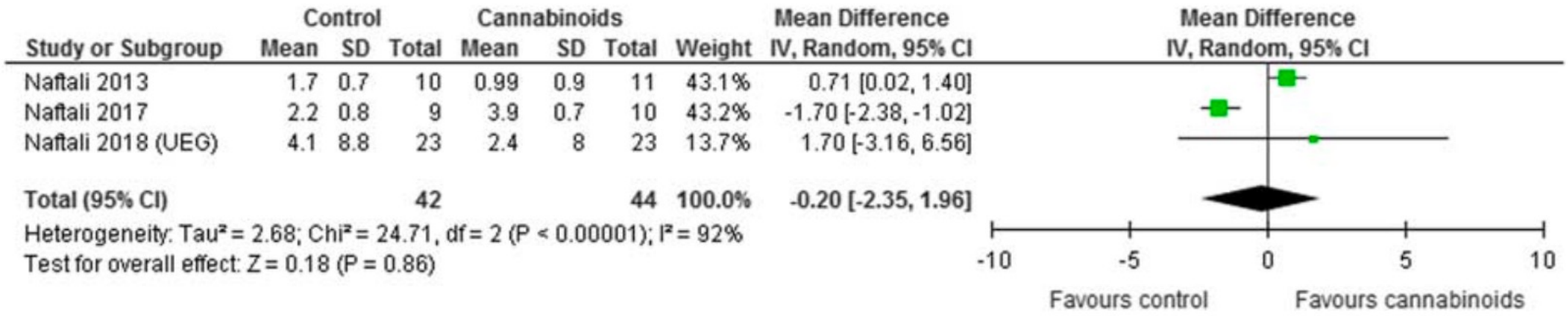
The use of Cannabinoids in IBD: The Effect on biomarkers - CRP



Study or Subgroup	Control Mean	Control SD	Control Total	Cannabinoids Mean	Cannabinoids SD	Cannabinoids Total	Weight	Mean Difference IV, Random, 95% CI
Naftali 2013	1.7	0.7	10	0.99	0.9	11	43.1%	0.71 [0.02, 1.40]
Naftali 2017	2.2	0.8	9	3.9	0.7	10	43.2%	-1.70 [-2.38, -1.02]
Naftali 2018 (UEG)	4.1	8.8	23	2.4	8	23	13.7%	1.70 [-3.16, 6.56]
Total (95% CI)			**42**			**44**	**100.0%**	**-0.20 [-2.35, 1.96]**

Heterogeneity: Tau² = 2.68; Chi² = 24.71, df = 2 (P < 0.00001); I² = 92%
Test for overall effect: Z = 0.18 (P = 0.86)

Doeve B et al. A Systematic Review With Meta-Analysis of the Efficacy of Cannabis and Cannabinoids for Inflammatory Bowel Disease. What Can We Learn From Randomized and Nonrandomized Studies? J Clin Gastroenterol;55(9):2021.

The use of Cannabinoids in IBD: Perceived symptom improvement

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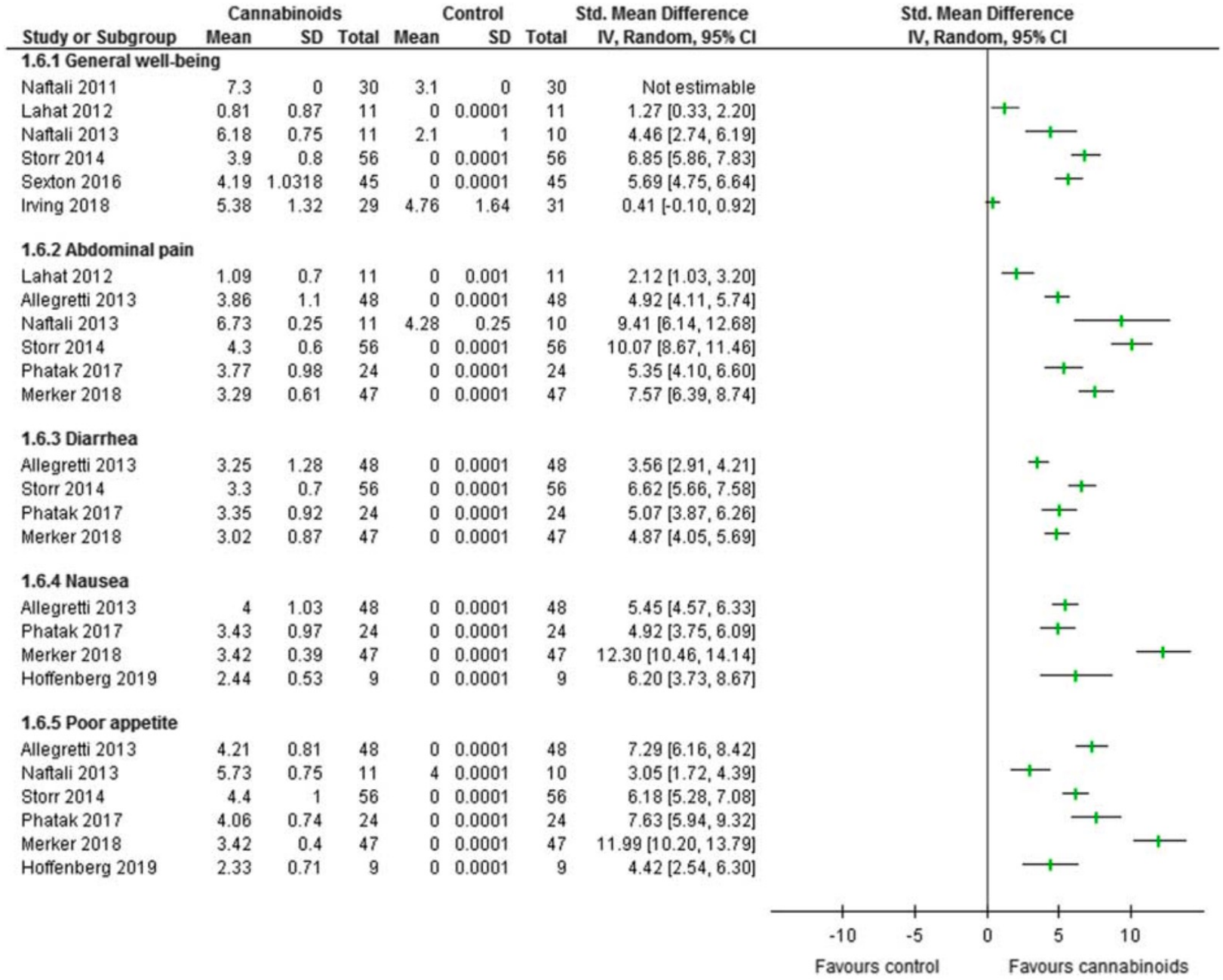


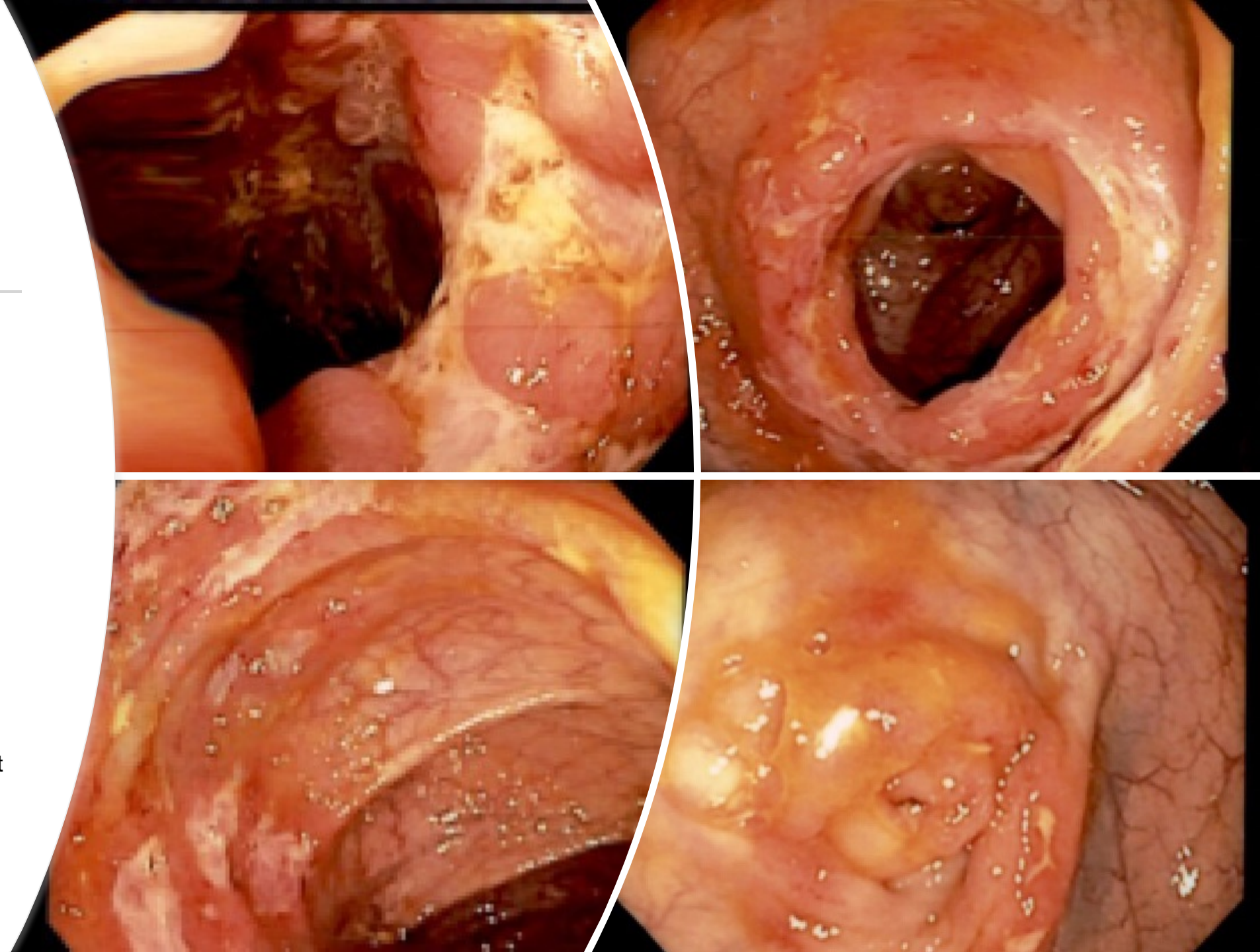
FIGURE 6. Perceived efficacy score for symptoms: "general well-being," "abdominal pain," "diarrhea," "nausea," and "poor appetite" as measured using different forms of Likert-scales for all studies that reported this outcome. CI indicates confidence interval. full color online

Clinical Case Continued…

- Well until age 16.
- Underwent cholecystectomy in 2016 – details unclear
- Experienced post-operative diarrhea
- Diagnosed with AS in December 2016 after presenting to GP with symptoms of back and shoulder pain. Followed by a community rheumatologist. No original documentation received.
- Prescribed NSAIDs which worsened his diarrhea and caused abdominal pain.
- March 2017: He presented to the ED and received a CT abdomen which revealed 20cm of terminal ileum inflammation and surrounding reactive lymph node enlargement. He was discharged from hospital with a Rx for antibiotics and morphine.

Clinical Case Continued…

- Referred to OHP by GP where EGD and colonoscopy were performed for symptoms of “black tarry stools and weight loss.”
  - EGD: antral erosions, gastric erythema, gastric fundal nodularity, duodenal nodularity.
  - Colonoscopy revealed ulcers, erythema, friability from the HF to cecum. TI revealed serpiginous severe ulceration to at least 10cm
- The patient was started on Entocort and transferred to GI at WCH



Clinical Case Continued…

- Seen at WCH GI March 2017
  - Started on prednisone taper as complete staging of disease performed
    - CT enteroclysis shows *"prominent mucosal hyperenhancement and wall thickening of the distal 50-60cm of ileum, up to the level of the ICV, consistent with moderately active Crohn's disease. There is a prominent "comb sign" associated with a high level of inflammatory activity….Numerous prominent lymph nodes…mild mucosal hyperenhancement and wall thickening of the cecum, ascending colon and the very proximal transverse colon, in keeping with active disease."*
    - Repeat EGD and colonoscopy confirm the diagnosis
  - Re-hospitalized in the community and given solumedrol induction and prednisone taper resumed. Also treated with dilaudid in hospital. Started on IFX 5mg/kg + MTX and B12 supplementation

What is your approach to the medical management of axial arthropathies in IBD?

Treatment of Spondyloarthropathy in IBD

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4.2.3 Management of axial spondyloarthropathy

Statement 18

TNFα antagonists are recommended for treatment of axial spondyloarthropathy associated with IBD. Vedolizumab and ustekinumab are not recommended in axial spondyloarthropathy associated with IBD [EL2] [consensus: 96%]

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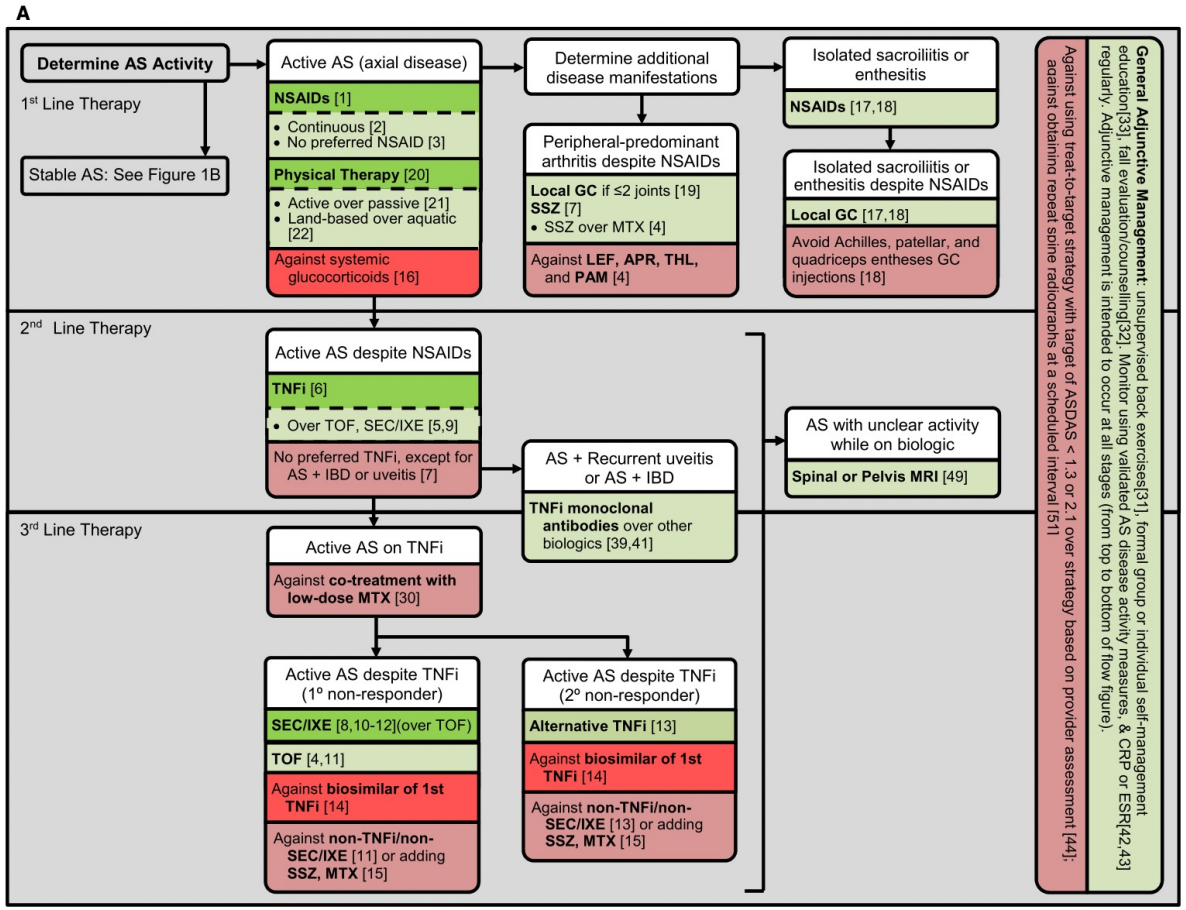
Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS 1): a multicentre, randomised, double-blind, placebo-controlled, phase 2/3 trial

Désirée van der Heijde, In-Ho Song, Aileen L Pangan, Atul Deodhar, Filip van den Bosch, Walter P Maksymowych, Tae-Hwan Kim, Mitsumasa Kishimoto, Andrea Everding, Yunxia Sui, Xin Wang, Alvina D Chu, Joachim Sieper

Lancet 2019; 394: 2108–17

2019 Update of the American College of Rheumatology/ Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis

Arthritis & Rheumatology
Vol. 71, No. 10, October 2019, pp 1599–1613



Upadacitinib for the treatment of active non-radiographic axial spondyloarthritis (SELECT-AXIS 2): a randomised, double-blind, placebo-controlled, phase 3 trial

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***Lancet* 2022; 400: 369–79**

Treatment of Spondyloarthropathy in IBD

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4.2.4 Management of non-axial spondyloarthropathy

Statement 19

TNFα antagonists are recommended for treatment of IBD-associated non-axial spondyloarthropathy [EL2]. There are also data to support use of methotrexate, sulfasalazine, and ustekinumab [EL3] [consensus: 100%].

Clinical Case Continued…

- Ongoing GI FU
  - Improved clinically and normalization of CRP by November 2017
    - 2 additional ED visits triggered by anxiety/panic resulting in 2 additional CT abdomen.
    - Referred to psychiatry and started on Venlafaxine.

Clinical Case Continued…

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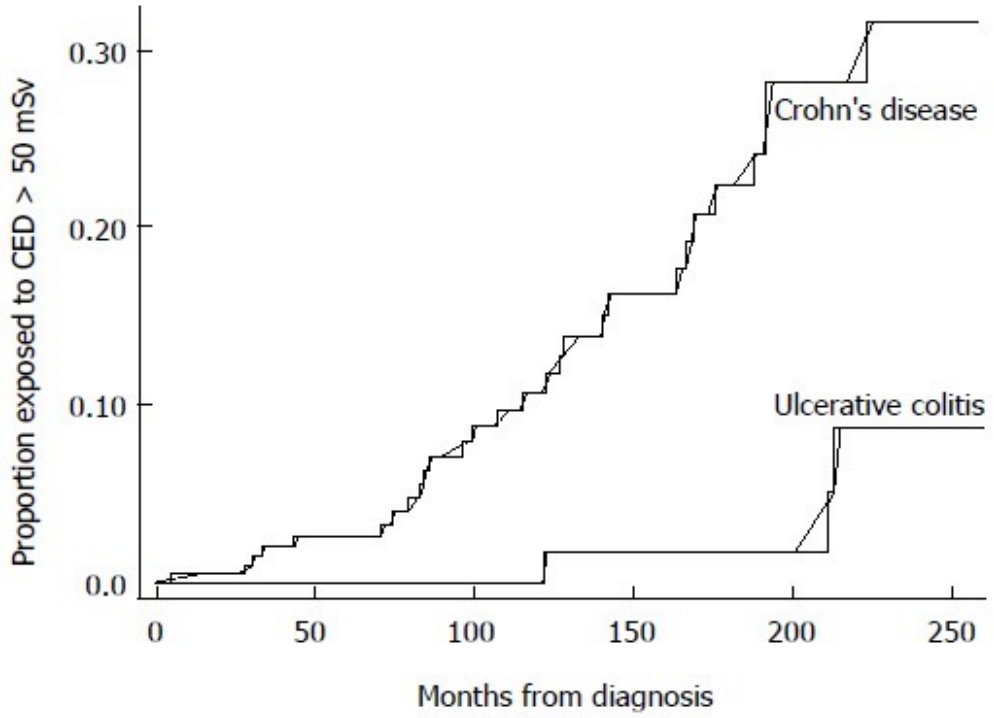
Table 1

Radiation doses from gastrointestinal imaging studies in comparison to background radiation, condensed from RadiologyInfo.org[9] and Mettler et al[10]

Imaging procedure	Average effective dose (mSv)	Time period for equivalent effective dose from natural background radiation[1]
Multiphase CT abdomen and pelvis	31	10.3 yr
PET/CT	25	8.3 yr
CT Abdomen and Pelvis	10	3.3 yr
CT Colonography	10	3.3 yr
CT Abdomen	8	2.7 yr
Barium Enema	8	2.7 yr
Small bowel follow-through	5	1.7 yr
X-ray abdomen	0.7	2.8 mo

[1]Based on the assumption of an average effective dose of 3 mSv per year from natural background radiation. CT: Computed tomography; PET: Positron emission tomography.

Zakeri N et al. Diagnostic imaging and radiation exposure in inflammatory bowel disease. WJG 2016;22(7):2165-2178.



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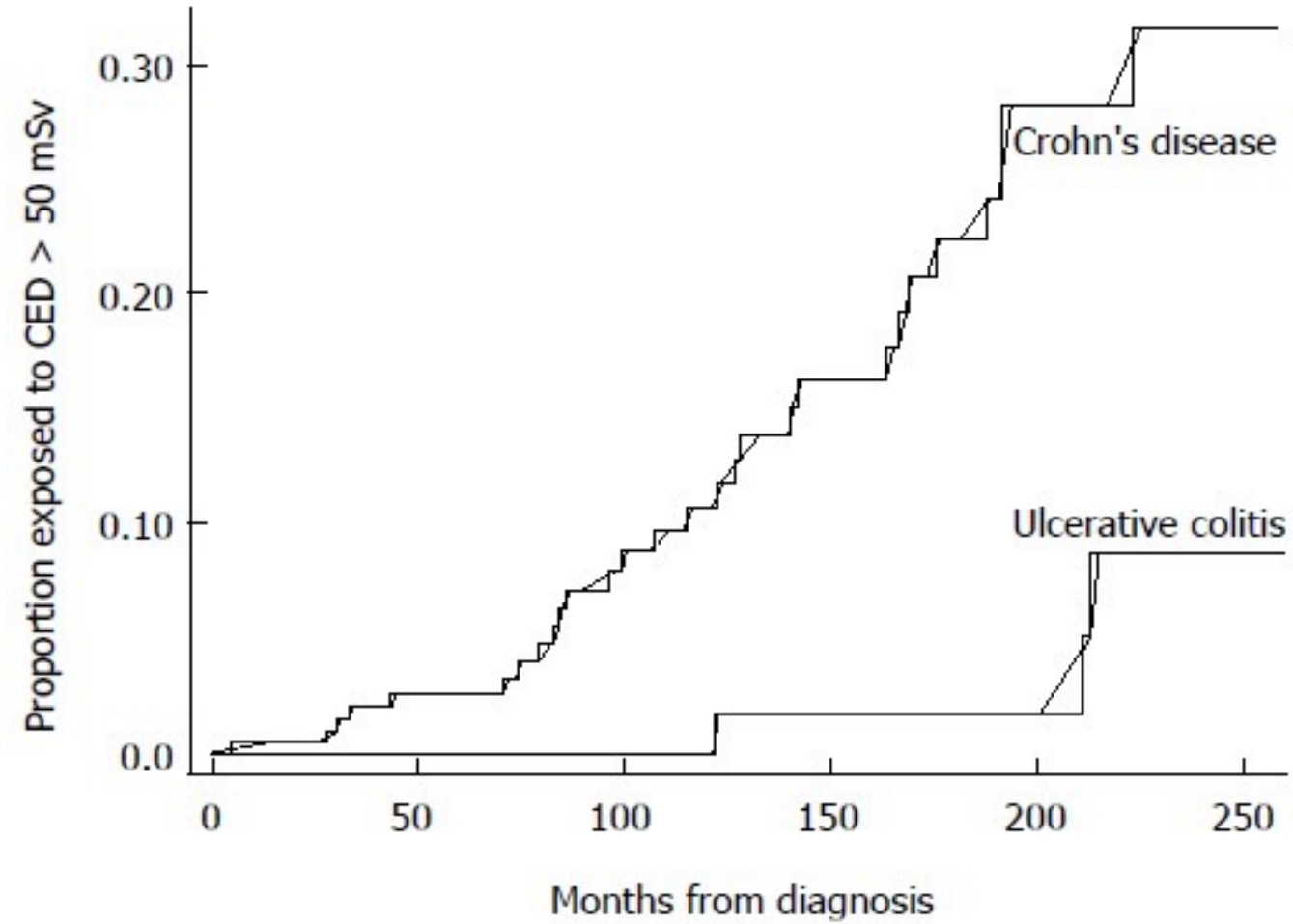
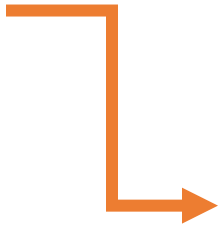


Clinical Case Continued…

- Ongoing GI FU
  - MTX stopped because of nausea
  - Jan 2018: IFX trough level before 1st maintenance dose was 4. Patient had ongoing symptoms leading up to infusion. Increased IFX to 10mg/kg q8 weeks and then eventually q6 weeks to achieve clinical remission
    - Colonoscopy delayed until dose optimization achieved
    - March 2018 colonoscopy: Thickened AC fold otherwise endoscopic remission
    - August 2019 MRE: No active disease
  - No active communication with rheumatologist, who the patient has failed to follow-up with regularly. Multiple no-shows to IBD clinic.



What is your experience with non-compliance in your clinic and how do you manage this?

Treatment Adherence in IBD

Prevalence, predictors, and clinical consequences of medical adherence in IBD: How to improve it?

Peter Laszlo Lakatos

World J Gastroenterol 2009 September 14; 15(34): 4234-4239
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- Adult IBD studies have revealed a medication non-adherence prevalence rate ranging from 35-72%.
- Significant risk factors for poor adherence include:
  - Younger patients tend to be less adherent than older patients
  - In UC, Kane et al[3] reported by means of univariate analysis, that male gender, being without a relationship partner, left-sided disease, and a history of more than four concomitant medications, were negatively associated with adherence
  - Most studies are consistent in finding that topical therapy with enemas, suppositories or foams is more likely to be associated with non-adherence than oral therapy
  - Quality of the patient-physician relationship
    - Sewitch et al[10] found an increased risk of intentional non-adherence to be associated with being treated by the same physician for more than one year, not scheduling another appointment, and greater total discordance between the patient and the physician

Characterizing the Posttransfer Period Among Patients with Pediatric Onset IBD: The Impact of Academic Versus Community Adult Care on Emergent Health Resource Utilization

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TABLE 4. Univariable Analyses of the Secondary Outcomes Evaluating Health Resource Utilization in the Posttransfer Period According to Exposure Group

Univariable Analysis: Secondary Outcomes in the Posttransfer Period		Community (n = 639)	Academic (n = 1057)	Lost to Adult GI Follow-up (n = 347)	*P*
Ambulatory visits					
GI ambulatory visits	Mean (SD)	5.1 (3.8)	5.9 (3.9)	0 (0)	**<0.0001**[a]
GIM ambulatory visits	Mean (SD)	0.3 (1.4)	0.4 (1.7)	0.9 (2.4)	**<0.0001**[a]
GP ambulatory visits	Mean (SD)	10.3 (13.4)	10.3 (9.5)	7.8 (6.9)	**<0.0001**[a]
Total ambulatory visits	Mean (SD)	15.7 (14.3)	16.5 (10.9)	8.7 (7.3)	**<0.0001**[a]
Difference in GI ambulatory visits (posttransfer − pretransfer)	Mean (SD)	1.2 (6.1)	0.8 (8.0)	−6.0 (6.8)	**<0.0001**[a]
Difference in total ambulatory visits (posttransfer − pretransfer)	Mean (SD)	11.8 (14.0)	11.5 (12.5)	2.7 (10.3)	**<0.0001**[a]
Hospitalizations					
Admissions	Mean (SD)	1.4 (0.8)	2.2 (2.2)	1.7 (0.6)	0.09
Length of stay	Mean (SD)	6.9 (13.3)	9.1 (14.8)	2.7 (1.5)	0.05
Difference in admissions (posttransfer—pretransfer)	Mean (SD)	1.4 (0.8)	2.2 (2.2)	1.7 (0.6)	0.09
Surgery					
No admissions in the pretransfer period					
Endoscopy					
Colonoscopy	Mean (SD)	1.4 (0.8)	1.4 (0.7)	1.5 (0.6)	0.3
Flexible sigmoidoscopy	Mean (SD)	1.1 (0.2)	1.2 (0.5)	1.0 (0)	0.3
Total endoscopic procedures	Mean (SD)	1.6 (1.0)	1.6 (1.3)	1.5 (0.6)	0.8
Radiology					
CT	Mean (SD)	1.4 (0.9)	1.6 (1.1)	1.8 (1.1)	0.6
MRI	Mean (SD)	1.3 (0.5)	1.2 (0.4)	1.5 (0.7)	0.3
US	Mean (SD)	1.4 (0.8)	1.6 (1.2)	1.2 (0.6)	0.4
Total endoscopy	Mean (SD)	3.0 (2.5)	3.6 (3.1)	3.5 (3.3)	0.1

[a]$P < 0.05$ considered significant.

CT, computed tomography; GIM, general internal medicine; GP, general practitioner (aka family physician); MRI, magnetic resonance imaging; SD, standard deviation; US, ultrasound.

Summary

Current approaches to the clinical care of IBD continue to focus primarily on medical therapy.

However, the practical reality of providing IBD care demands that we acknowledge and actively manage high risk populations, active comorbidities and adherence challenges in order to achieve our best treatment outcomes.

A multi-disciplinary team can be a significant asset in achieving comprehensive management goals. However, achieving this reality in our current healthcare environment is challenging.