

CORE-IBD

A Multidisciplinary International Consensus Initiative to Develop a Core Outcome Set for Randomized Controlled Trials in Inflammatory Bowel Disease

Christopher Ma, MD MPH FRCPC
Division of Gastroenterology & Hepatology
Departments of Medicine & Community Health Sciences

November 5, 2022



UNIVERSITY OF
CALGARY



INFLAMMATORY
BOWEL DISEASE UNIT
UNIVERSITY OF CALGARY



Western

Disclosures & Territorial Acknowledgments

- **Consulting:** AbbVie, Alimentiv, American College of Gastroenterology, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche, Sanofi
- **Speaking:** AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Bristol Myers Squibb, Ferring, Fresenius Kabi, Janssen, Takeda, Pendopharm, and Pfizer
- **Royalties:** Springer Publishing
- **Research Support:** Ferring, Pfizer

We would like to acknowledge the traditional territories of the people of the Treaty 7 region in Southern Alberta, which includes the Blackfoot Confederacy (comprising the Siksika, Piikani, and Kainai First Nations), as well as the Tsuut'ina First Nation, and the Stoney Nakoda (including the Chiniki, Bearspaw, and Wesley First Nations). The City of Calgary is also home to Métis Nation of Alberta, Region 3.



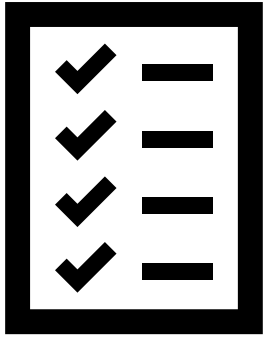
CORE-IBD: A Multidisciplinary International Consensus Initiative to Develop a Core Outcome Set for Randomized Controlled Trials in Inflammatory Bowel Disease

Christopher Ma, Jurij Hanzel, Remo Panaccione, William J. Sandborn, Geert R. D'Haens, Vineet Ahuja, Raja Atreya, Charles N. Bernstein, Peter Bossuyt, Brian Bressler, Robert V. Bryant, Benjamin Cohen, Jean-Frederic Colombel, Silvio Danese, Axel Dignass, Marla C. Dubinsky, Phillip R. Fleshner, Richard B. Gearry, Stephen B. Hanauer, Ailsa Hart, Paulo G. Kotze, Torsten Kucharzik, Peter L. Lakatos, Rupert W. Leong, Fernando Magro, Julian Panes, Laurent Peyrin-Biroulet, Zhihua Ran, Miguel Regueiro, Siddharth Singh, Antonino Spinelli, A. Hillary Steinhart, Simon P. Travis, C. Janneke van der Woude, Bruce Yacyshyn, Takayuki Yamamoto, Matthieu Allez, Willem A. Bemelman, Amy L. Lightner, Edouard Louis, David T. Rubin, Ellen J. Scherl, Corey A. Siegel, Mark S. Silverberg, Severine Vermeire, Claire E. Parker, Stephanie C. McFarlane, Leonardo Guizzetti, Michelle I. Smith, Niels Vande Casteele, Brian G. Feagan, and Vipul Jairath

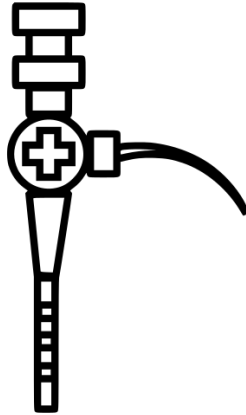
Gastroenterology. 2022;163(4):950-964



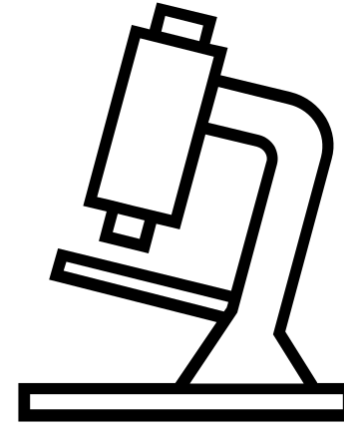
The landscape of IBD trials is changing



**Shifting from
symptom-based to
objective disease
measures**



**Patients are qualified
for trials differently
now**

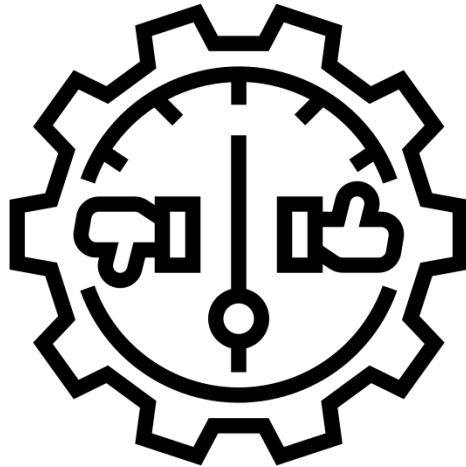


**Targeting deeper
levels of remission**



**Capturing the patient
experience**

Why selecting appropriate outcomes in RCT matters



Operating properties
of outcome
measures influences
trial efficiency

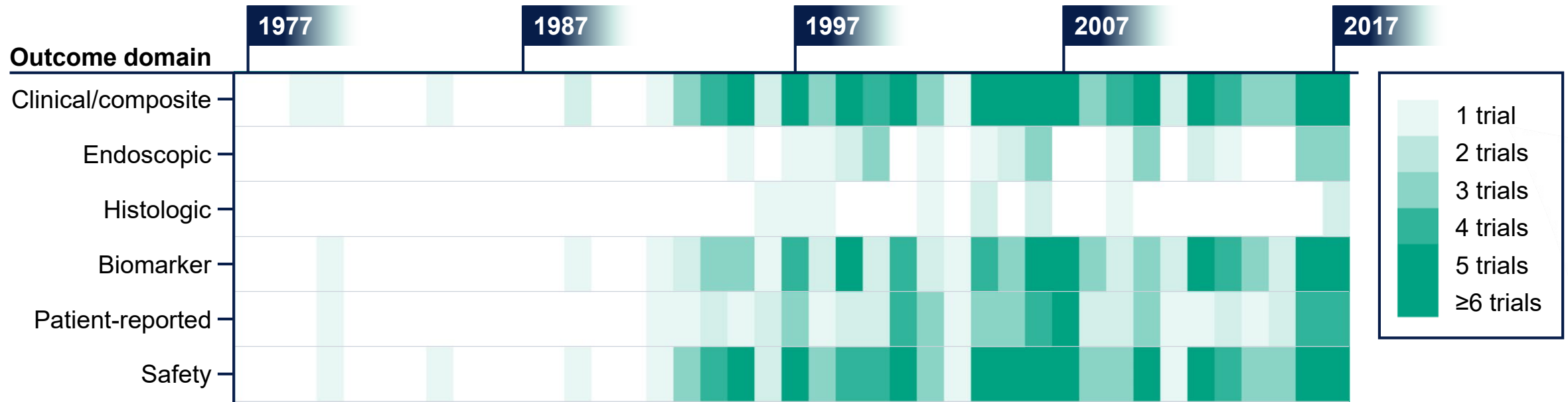


Relevant endpoints
shape clinical
practice



Outcome choices
influence payer and
regulatory policy

Insufficient attention has been paid to standardizing outcome assessments in IBD RCTs

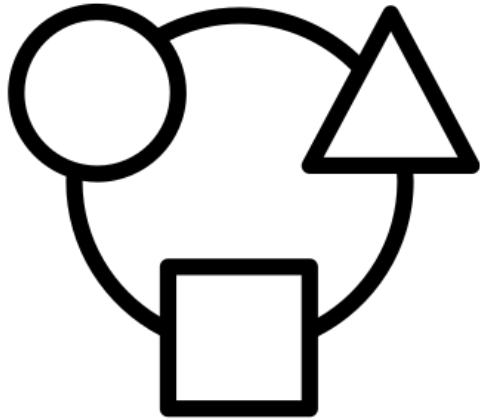


Evolution towards endoscopic, histologic, and biomarker-based endpoints of remission
>30 different definitions of remission in CD trials,¹ >50 different definitions of remission in UC trials²

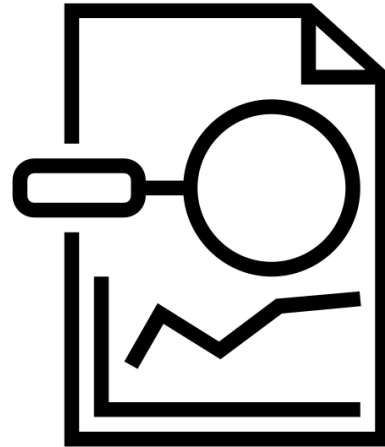
1. Ma C et al. Clin Gastroenterol Hepatol 2018;16(9):1407–1419;

2. Ma C et al. Clin Gastroenterol Hepatol 2018;16(5):637–647.

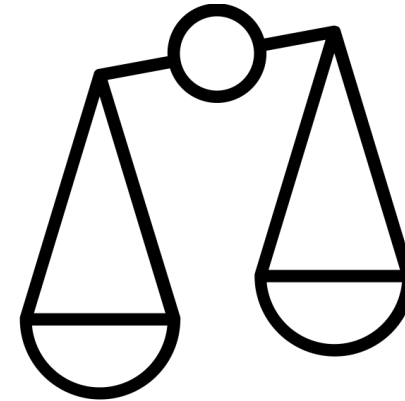
Standardizing outcome measures in a COS



**Reduces
heterogeneity in
outcome reporting**



**Reduces the risk of
reporting bias**



**Increases quality and
validity of evidence
synthesis**

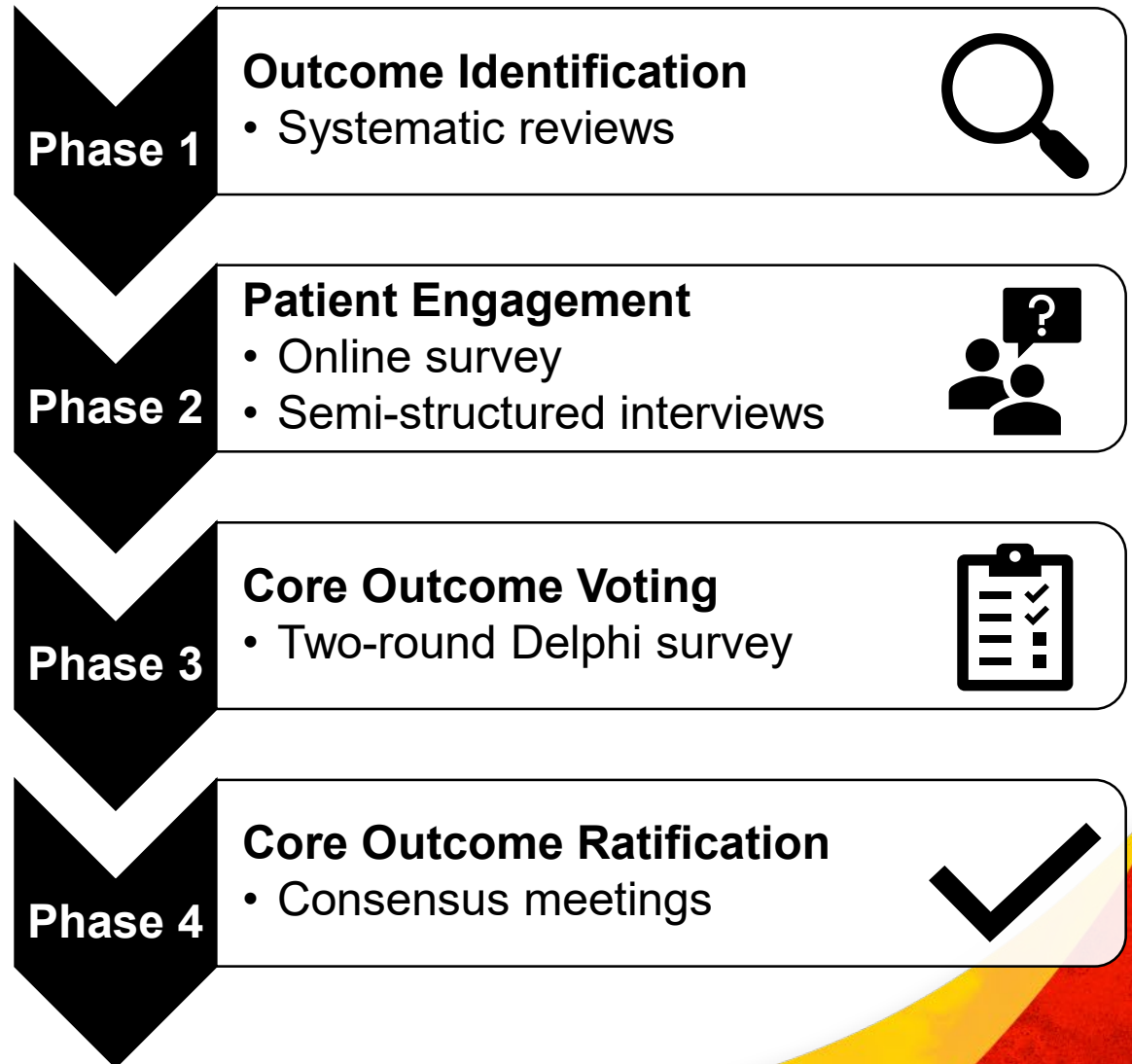
Methods



Scope

Randomized controlled trials
Pharmacologic interventions
Adult patients with CD/UC

Surgical interventions
Pediatric patients
Other phenotypes (e.g. perianal)

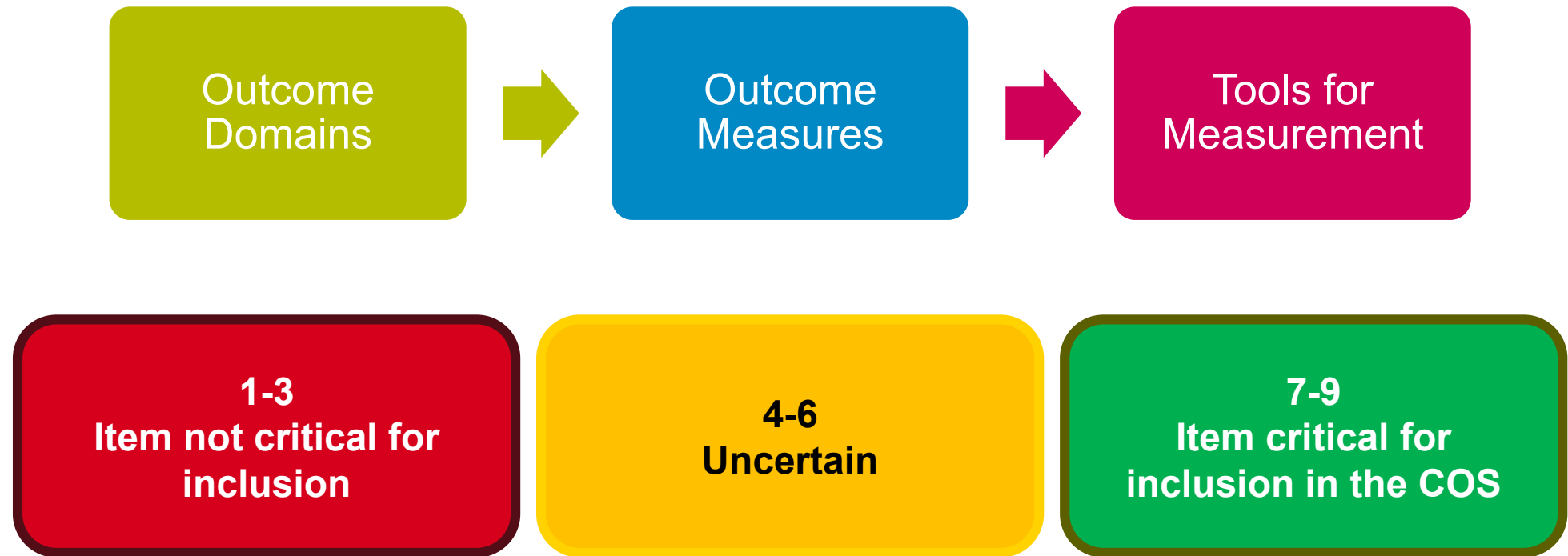


Expert Panel

Expertise in IBD trial conduct,
methods, outcome assessment
Gastroenterologists, colorectal
surgeons, methodologists,
clinical trialists



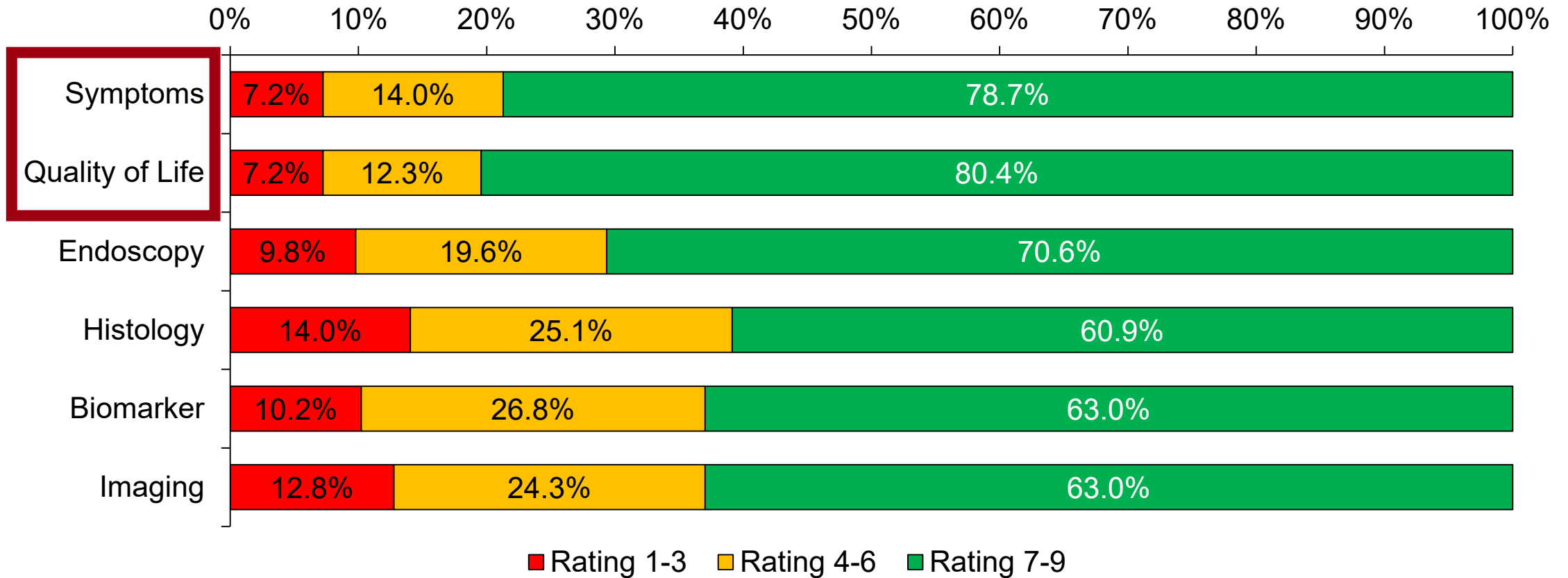
Core Outcome Voting

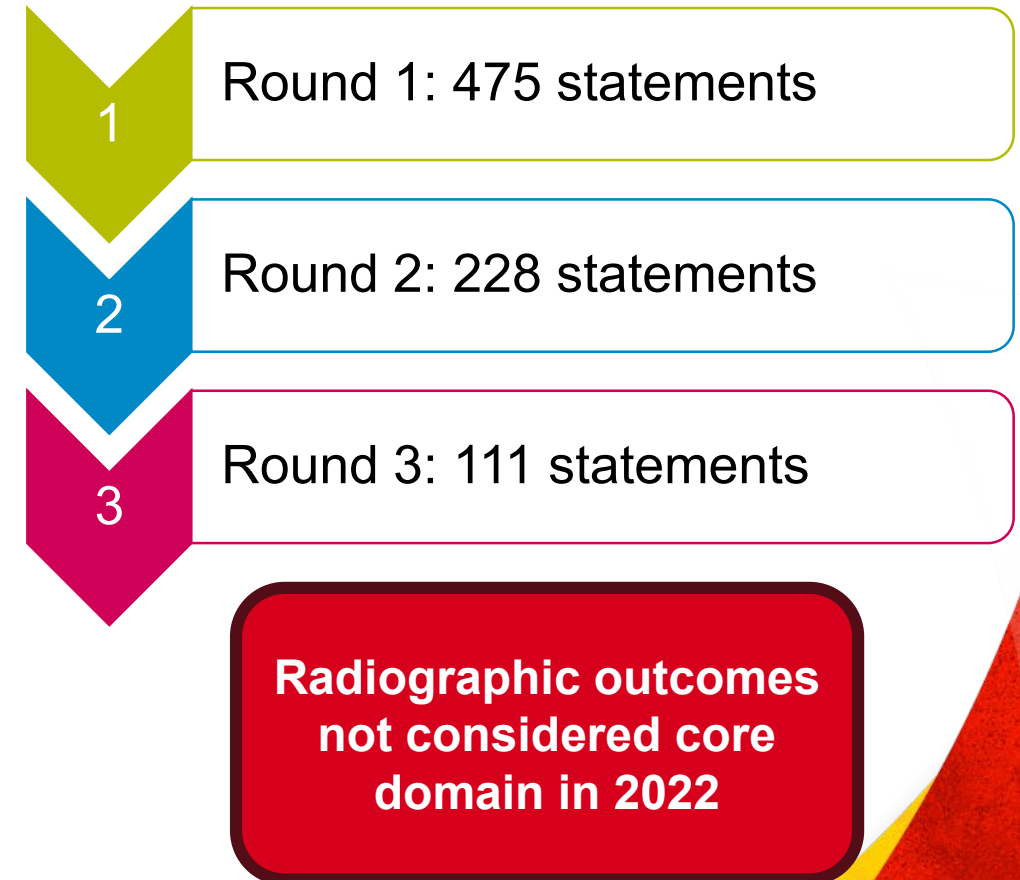
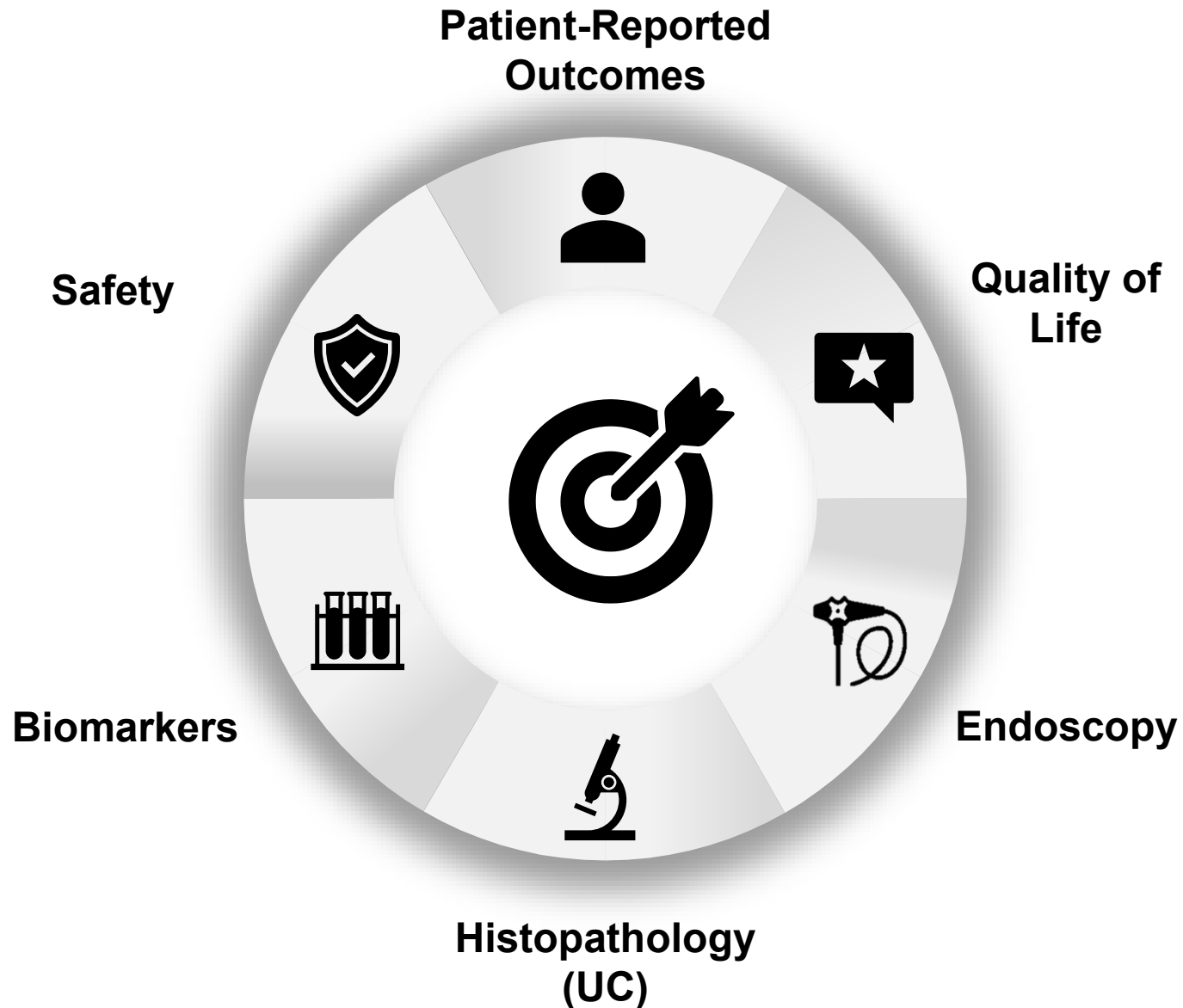


$\geq 70\%$ voting in the 7-9 range and $< 15\%$ voting in the 1-3 range



What matters to patients?





Configuration of Outcomes in Crohn's Disease

Outcome Domain	Outcome Measures
PROs	PRO2: stool frequency + abdominal pain CDAI
Endoscopy	SES-CD Endoscopic remission, defined by absence of ulcers
Biomarkers	CRP & FCAL Biomarker remission and response
Overall Configuration	<u>Coprimary</u> outcome of symptomatic remission + endoscopic response Secondary outcome of corticosteroid-free remission in <u>both</u> induction and maintenance

Controversies and Future Directions in Crohn's Disease



- Validation of PRO
 - Liquid stool frequency, anxiety, fatigue, sleep quality, sexual dysfunction, dietary modifications



- Ulcer-free endoscopy
 - Is it attainable?
 - Should we differentiate endoscopic healing by anatomy



- Histopathology in CD
 - Appropriate definitions and sampling protocol



- Configuration in CD
 - What is steroid-free responsiveness?



Configuration of Outcomes in Ulcerative Colitis

Outcome Domain	Outcomes
PROs	Adapted 9-point Mayo Clinic Score Remission requiring rectal bleeding = 0, stool frequency ≤ 1 Fecal urgency
Endoscopy	Flexible sigmoidoscopy Endoscopic remission, modified Mayo Endoscopy Subscore = 0
Biomarkers	FCAL < 150 ug/g
Histopathology	RHI or Geboes Score RHI < 3 or GS < 3.0 (absence of neutrophils in lamina propria)
Overall Configuration	<u>Composite</u> primary outcome defined by PROs and endoscopy

Controversies and Future Directions in Ulcerative Colitis



- Validation of PRO
 - Role of fecal urgency and measuring urgency symptoms



- Endoscopic evaluation
 - Is sigmoidoscopy sufficient?
 - MES vs. UCEIS, paradigms for central reading



- Histopathology in UC
 - RHI or Geboes score included over NHI, histopathology reading paradigms
 - Defined by absence of neutrophils



- Configuration in CD
 - Defining steroid-free remission



Final Thoughts

Funding Sources



UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE



ROYAL COLLEGE
OF PHYSICIANS AND SURGEONS OF CANADA
COLLÈGE ROYAL
DES MÉDECINS ET CHIRURGIENS DU CANADA



HARVARD
T.H. CHAN
SCHOOL OF PUBLIC HEALTH



CALGARY DIVISION OF
GASTROENTEROLOGY & HEPATOLOGY



INFLAMMATORY
BOWEL DISEASE UNIT
UNIVERSITY OF CALGARY

DOM