Common mistakes in the management of Chron's disease

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Common mistakes in the management of Crohn's disease

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ACG guidelines

CME

ACG Clinical Guideline: Management of Crohn's Disease in Adults

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Am J Gastroenterol 2018

AGA key quality indicators

1. Document disease activity and severity
2. Recommend steroid-sparing therapy after 60 days
3. Assess bone health if steroid-exposed
4. Recommend influenza vaccine
5. Recommend pneumococcal vaccine
6. Document recommendation for cessation of smoking
7. Assess for Hepatitis B virus status pre-anti-TNF
8. Assess for latent Tuberculosis pre-anti-TNF

Allen J et al AGA 2011

Common mistakes to be discussed

- Not reviewing the diagnosis
- Not documenting disease activity and severity
- Not having a goal of therapy
  - GI and non GI symptoms
  - Objective measurement of mucosal healing: SES-CD and faecal biomarkers
  - QOL
- Using Mesalazine / 5ASAs
- Excessive steroid use
- *Not discussed: Many mistakes made in use of immunomodulators, biologics (and newer drugs), suboptimal co-management with surgeon, IBD nurse and rest of the MDT*

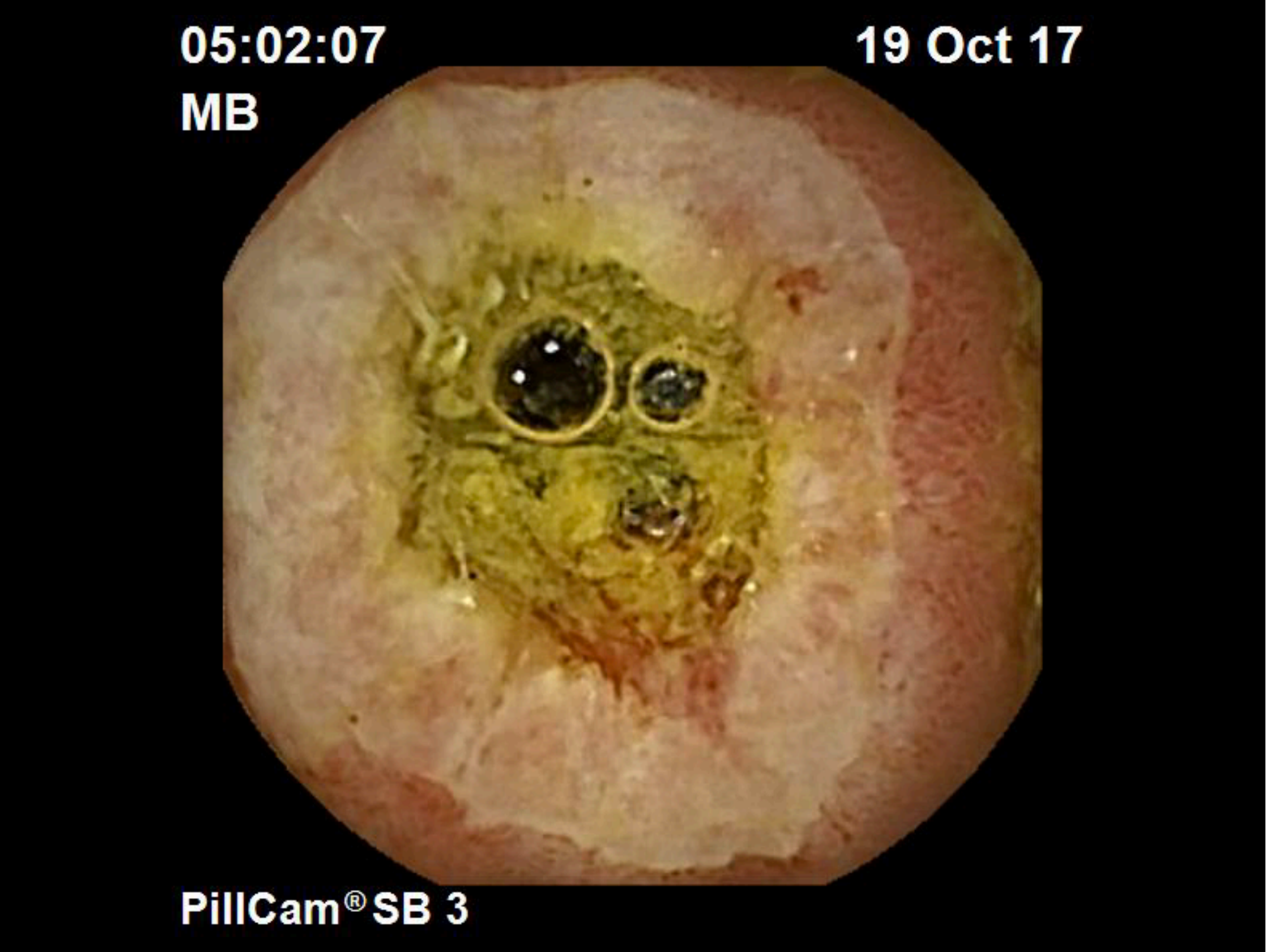
Not reviewing the diagnosis

Not reviewing the diagnosis

- New patient with a previous diagnosis of Crohn's or old patient refractory to therapy
- Especially important in SA private sector?
  - Patient "migration"
  - Fragmentation of care
  - Escalated workup for acute / sub-acute illness GI symptoms
  - Non-GI specialists
  - Over diagnosis is a problem
- Wrong diagnoses typical scenarios
  - Acute ileo-colitis: infective, drugs etc
  - "Over-interpretation" of subtle abnormalities on investigations (usually driven by a lot symptoms)

Case: Mrs M

- 50 year old female
  - IBS diagnosed during childhood
  - Multiple gastroscopies and ileocolonoscopies later in life all normal
  - At age 43 right hemicolectomy for diverticulitis with perforation: ++ surgical complications
  - Further abdominal symptoms and repeated investigations at age 48
    - Some calprotectins a bit raised (NSAID use history)
    - Mild non-specific ileocolitis at one of the endoscopies
    - MRE: Mid to distal ileum short segment mural thickening
    - Capsule endoscopy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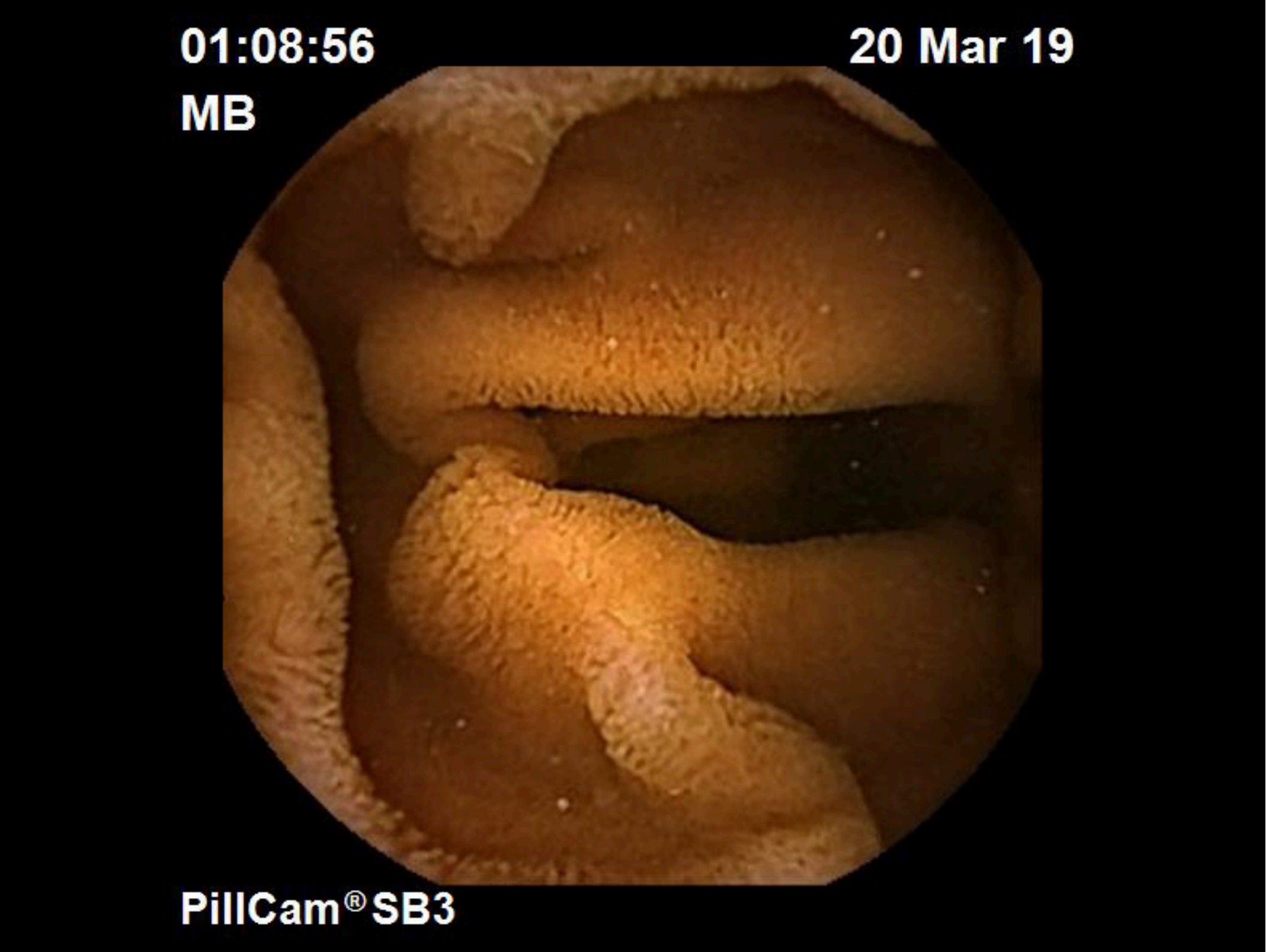
Case: Mrs M

- Diagnosed with isolated mid-small bowel Crohn's disease
  - Steroids followed by Azathioprine
- Ongoing symptoms despite normal calprotectin
- Biological was going to be considered
- Moved down to Cape Town

Case: Mrs M

- Investigations with me:
  - Retrograde double balloon enteroscopy
  - Repeat capsule endoscopy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Case: Mrs M

- Revised diagnosis
  - IBS with NSAID induced small bowel ulcer: resolved
  - Stop NSAIDs
  - Stop Azathioprine and follow-up
  - So far unchanged symptoms and normal faecal calprotectin

Not documenting disease activity and severity

CD severity

- Only 20-30% of CD patients will have indolent course
- The rest will have typical pattern: “CD is a chronic destructive progressive disease”
  - 80% will require hospitalisation
  - 10 year risk of surgery ± 50% (decreasing to 30% in biologic era)
- Therefore important to identify factors predictive of progressive disease

Old definitions

- Old definition of severity
  - Symptoms: CDAI and others: Remission < 150, Severe > 450

Clinical or laboratory variable	Weighting factor
Number of liquid or soft stools each day for seven days	x 2
Abdominal pain (graded from 0-3 on severity) each day for seven days	x 5
General well being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days	x 7
Presence of complications*	x 20
Taking Lomotil or opiates for diarrhea	x 30
Presence of an abdominal mass (0 as none, 2 as questionable, 5 as definite)	x 10
Hematocrit of <0.47 in men and <0.42 in women	x 6
Percentage deviation from standard weight	x 1

*One point each is added for each set of complications:

- the presence of joint pains (arthralgia) or frank arthritis
- inflammation of the iris or uveitis
- presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers
- anal fissures, fistulae or abscesses
- other fistulae
- fever during the previous week.

New definitions

- Symptoms
- Endoscopy
  - Deep ulcerations
  - SES-CD
- Prognostic factors
  - Young age
  - Extensive bowel involvement
  - Perianal disease
  - Penetrating and stenosing phenotype

SES-CD

Simple endoscopic score (SES-CD)

SES Score

Variable	0	1	2	3
Size of ulcers (cm)	None	Aphthous ulcers (diameter 0.1-0.5)	Large ulcers (diameter 0.5-2)	Very large ulcers (diameter > 2)
Ulcerated surface	None	< 10%	10-30%	> 30%
Affected surface	Unaffected segment	< 50%	50-75%	> 75%
Presence of narrowings	None	Single, can be passed	Multiple, can be passed	Cannot be passed

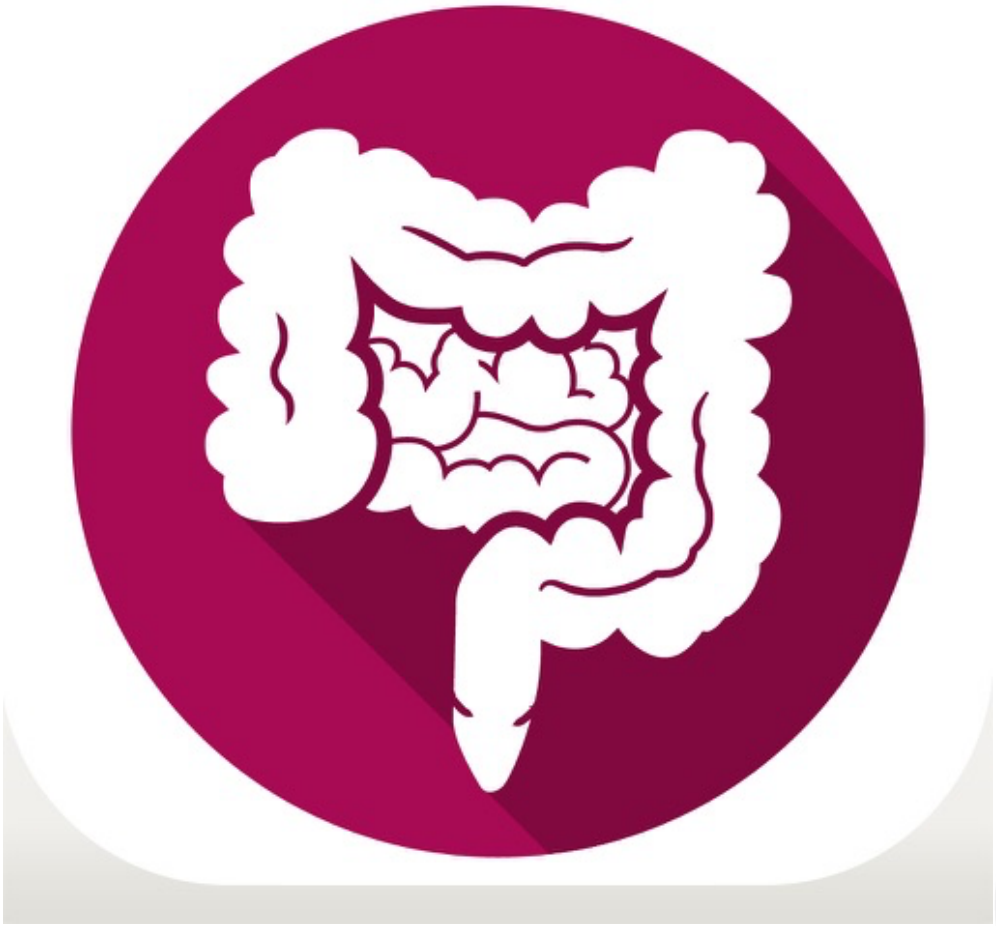
SES-CD = sum of all variables for the 5 bowel segments.
Values are given to each variable for every examined bowel segment

Segments:
Rectum
Left colon
Transverse
Right colon
Ileum

Scoring:
Inactive
Up to 6: mild
7-15 moderate
≥16 severe

Daperno, M et al. Gastrointestin Endosc. 2004

Get the app: IG-IBD



The application

CALCULATORS IN GASTROENTEROLOGY

Has been implemented with the scientific contribution of

IG-IBD
the Italian Group for the study of Inflammatory Bowel Disease

Supported by an unrestricted grant from

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DISCLAIMER

SETTINGS | INFO | SCORE | IG-IBD | ABOUT

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CLINICAL SCORES

- **CDAI** — CROHN'S DISEASE ACTIVITY INDEX
- **HBI** — HARVEY-BRADSHAW INDEX
- **MAYO** — PARTIAL
- **MAYO** — FULL

ENDOSCOPIC SCORES

- **CDEIS** — CROHN'S DISEASE OF SEVERITY
- **SES-CD** — SIMPLE ENDOSCOPIC SCORE FOR CROHN'S DISEASE
- **CDEIS ⟳ SES-CD**
- **MAYO** — ENDOSCOPIC
- **RUTGEERTS**

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SES-CD

SCORE DECODING TABLE

Score	Decoding
0 - 2	remission
3 - 6	mild endoscopic activity
7 - 15	moderate endoscopic activity
> 15	severe endoscopic activity

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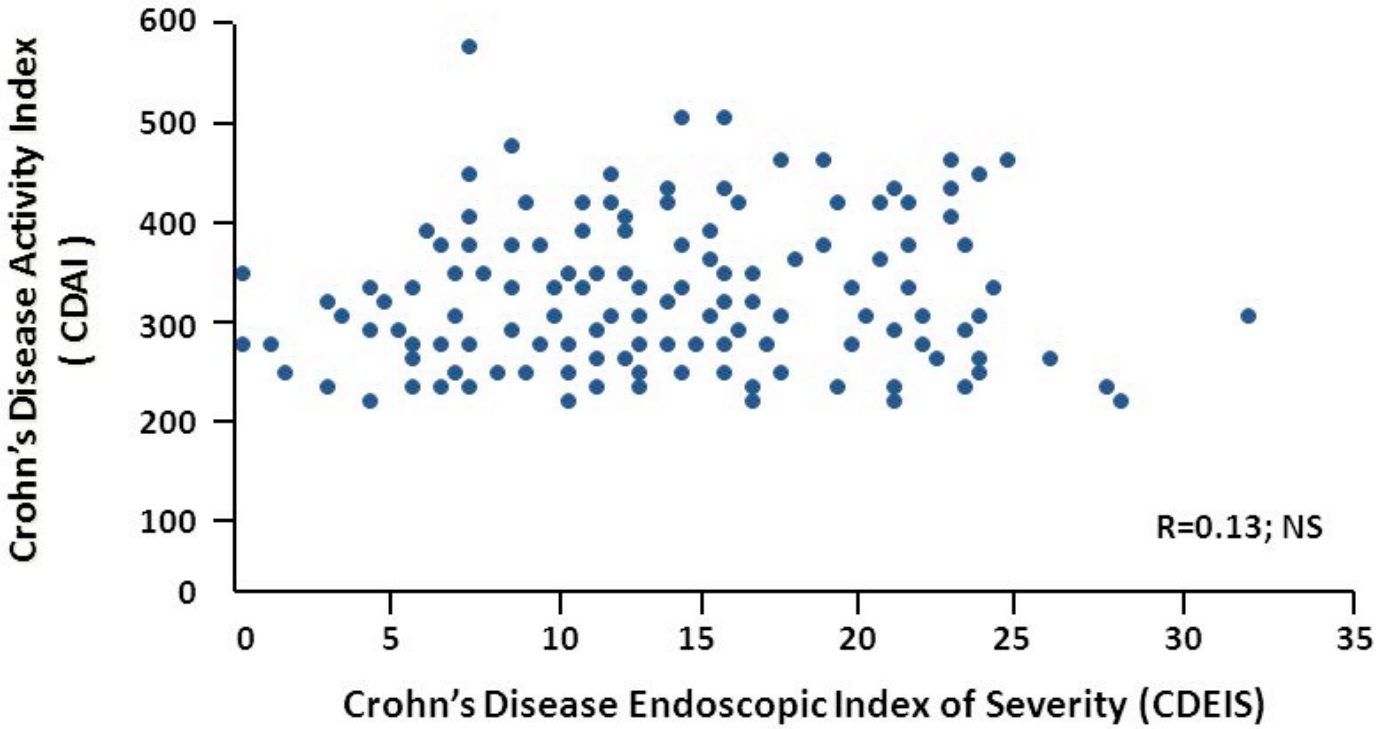
Not having a management goal

What should the goals be?

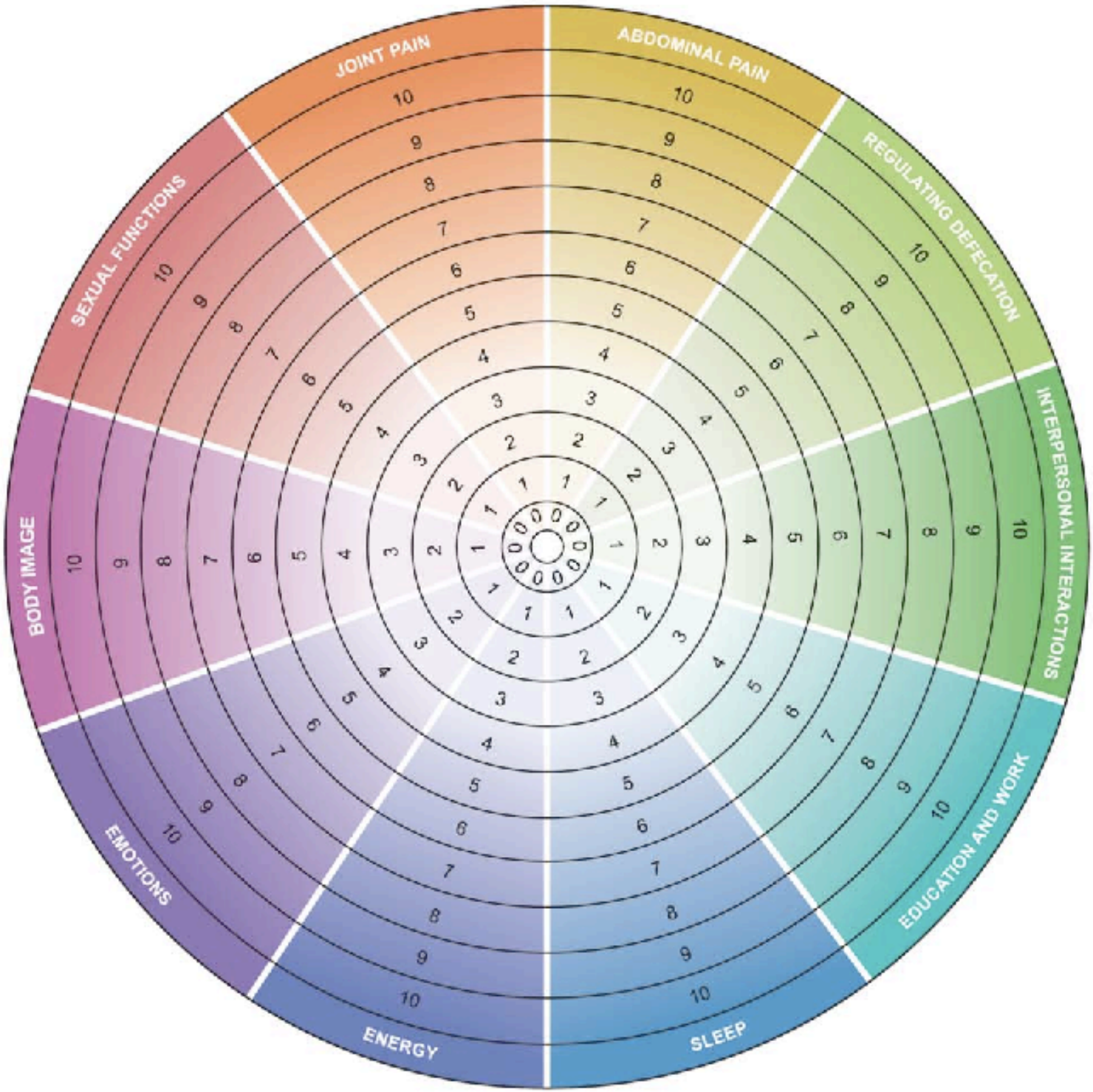
- Symptoms
  - Use of IBD Disk
- Mucosal healing
  - Monitor endoscopic response with endoscopic scores: SES-CD
  - Within 1 year of surgery for POR
  - Faecal biomarkers: calprotectin, lactoferrin
- QOL
  - Attention to management of stress, anxiety and depression

Symptoms correlate very poorly with inflammation and disease activity

Relationship Between Clinical Symptoms and Endoscopic Indices at Presentation of Acute CD



Modigliani R et al. *Gastroenterology*. 1990;98:811.



IBD Disk. S Ghosh. Inflammatory bowel diseases 2017

IBD Disk

Initial assessment

High scores

High disease burden

Therapeutic goal

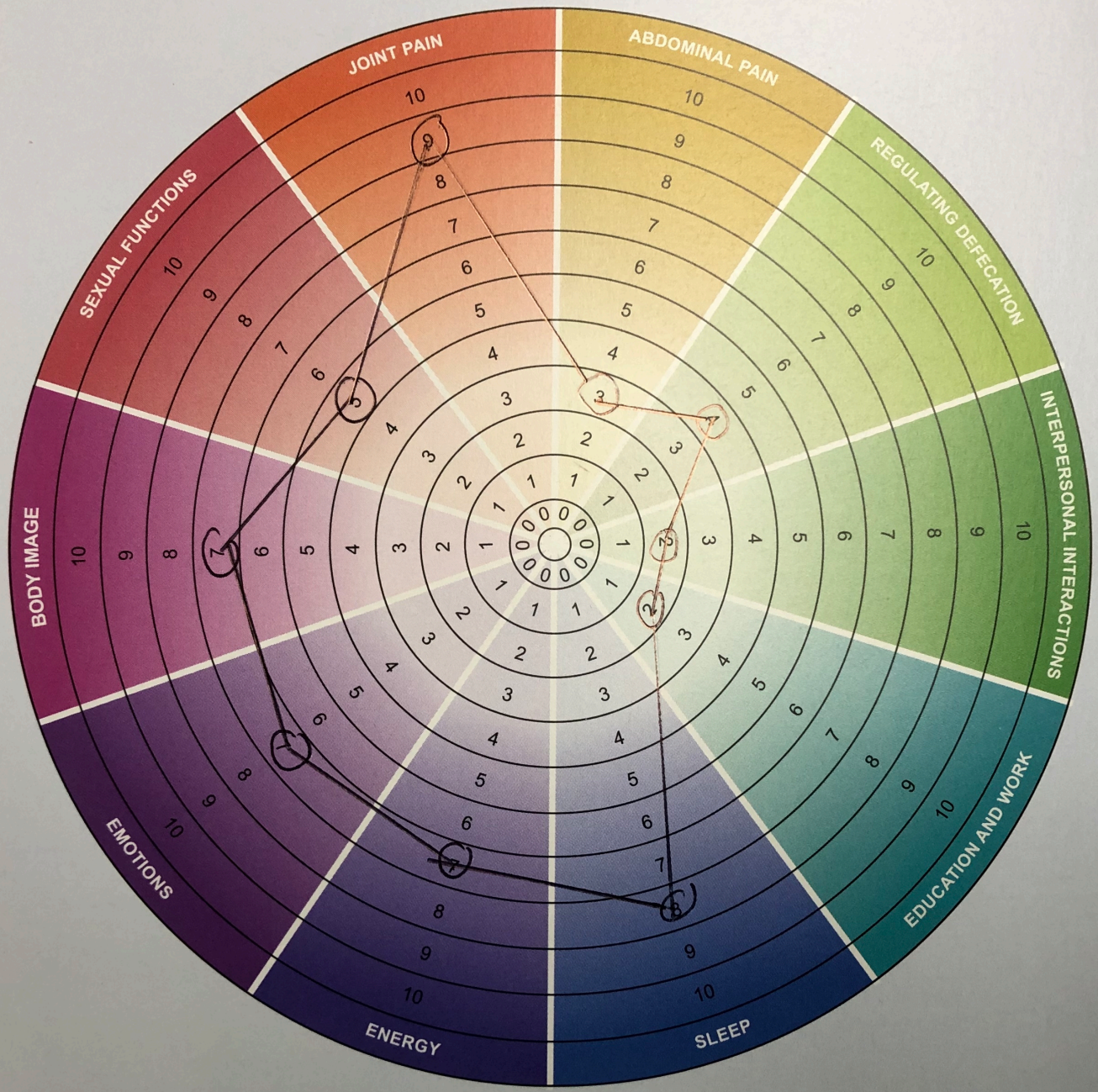
Low scores

Low disease burden

IBD Disk

- “Ms L’s symptoms seem to be in remission and she will continue on her chronic medication”

…… but that is not the full story



SCORE EACH STATEMENT ON A SCALE OF 0 TO 10 AND CIRCLE YOUR SCORE ON THE COLORED DISK

0 1 2 3 4 5 6 7 8 9 10

ABSOLUTELY DISAGREE — NEITHER AGREE OR DISAGREE — ABSOLUTELY AGREE

TOTAL SCORE: 54

Add the scores here for all 10 categories

What should the goals be?

- Symptoms
  - Use of IBD Disk
- Mucosal healing
  - Monitor endoscopic response with endoscopic scores: SES-CD
    - Within 1 year of surgery for post operative recurrence (POR)
  - Faecal biomarkers: calprotectin (lactoferrin)
- QOL
  - Attention to management of stress, anxiety and depression

Role of faecal biomarkers

- Calprotectin (and lactoferrin) correlated with SES-CD
- Specific defined uses
  - Differentiated IBS from IBD
  - Monitor post operative recurrence
    - > 100ug/g: show endoscopic recurrence with sensitivity 89%
  - In patients with anti-TNF-induced remission
    - > 160ug/g: sensitivity of 91.7% and specificity of 82.9% to predict relapse

What should the goals be?

- Symptoms
  - Use of IBD Disk
- Mucosal healing
  - Monitor endoscopic response with endoscopic scores: SES-CD
  - Within 1 year of surgery for POR
  - Faecal biomarkers: calprotectin, lactoferrin
- QOL
  - Attention to management of stress, anxiety and depression

QOL

- Strong association between depression and flares of CD
- Pts with major depression and anxiety have a greater risk of surgery and higher degree of health-care utilisation
- "Assessment and management of stress, depression and anxiety should be included as part of the comprehensive care of the Crohn's disease patient"
- Identify the go to person in your MDT for these issues

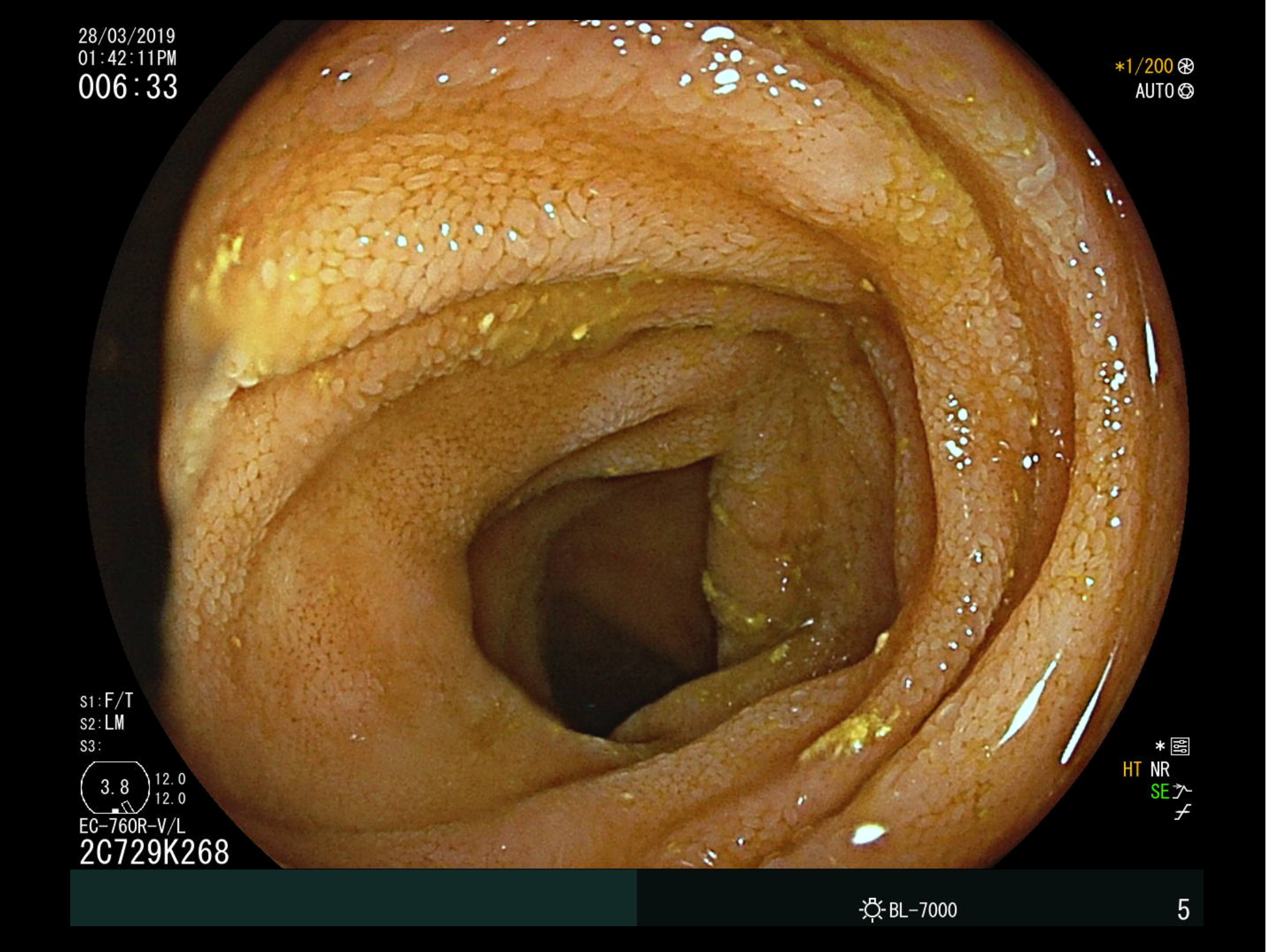
Using Mesalazine in CD

Case: Mrs K

- 47 year old female
- Many years of IBS-type symptoms and heartburn
- Investigated at age 39
  - GORD B
  - Normal ileo-colonoscopy
- Age 40: Gallstone pancreatitis and lap cholecystectomy
- Age 45
  - 3 week spell of diarrhoea an re-investigated
  - GORD C
  - Normal ileo-colonoscopy
  - However CT enterography: suggestive of a colitis of the ascending colon
  - Commenced on Pentasa for suspected Crohn's and has remained on it ever since

Case: Mrs K

- Persistent symptoms and came to see me for enrolment into a drug trial
- Investigations with me
  - Faecal calprotectin: 664 (But a history of NSAID abuse)
  - Repeat ileocolonoscopy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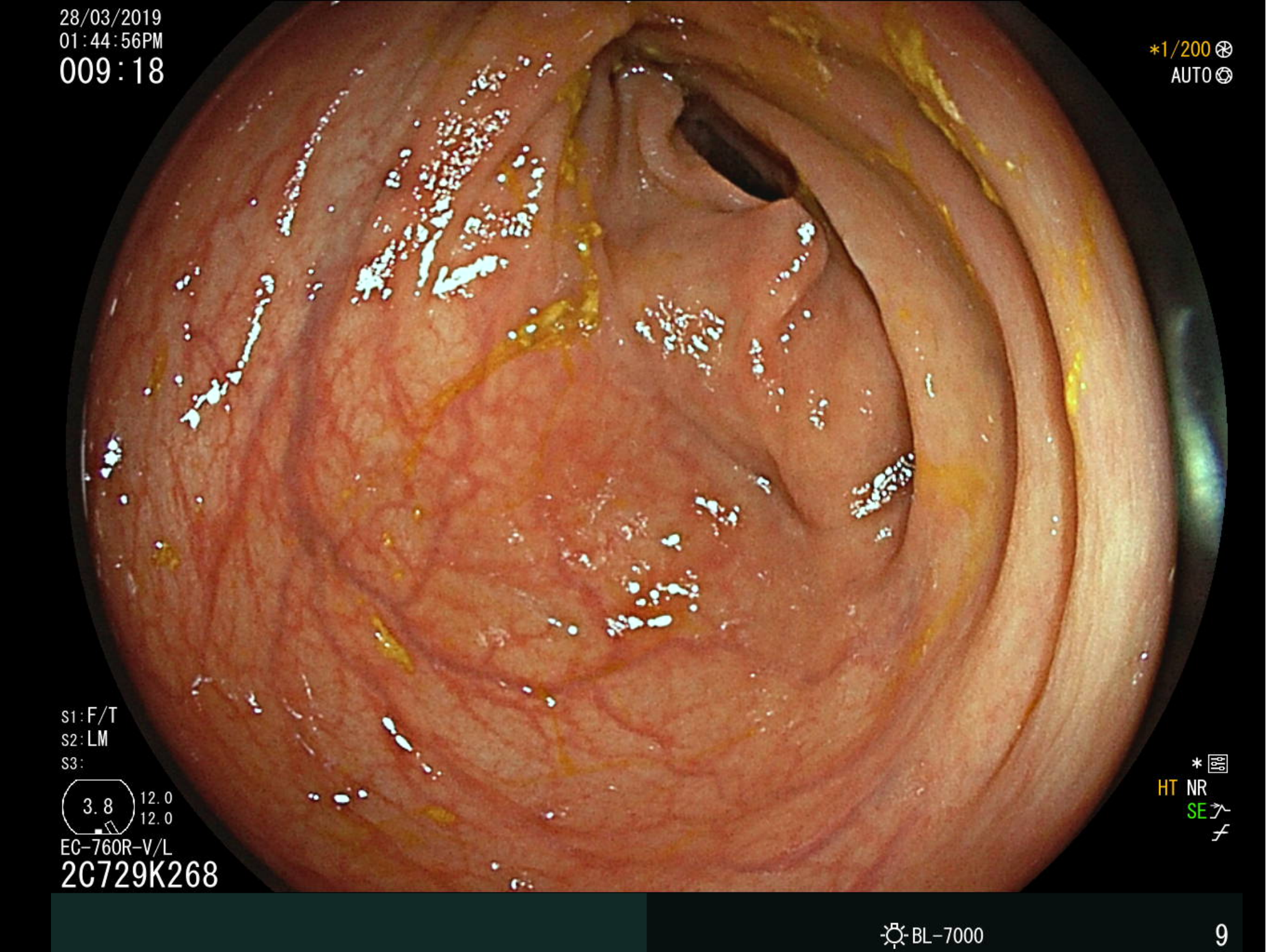
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Case: Mrs K

- Stopped her Pentasa and commenced treatment for IBS
- She was very happy …. has been paying her Pentasa out of pocket!
- I was pretty confident she won't be worse off as Mesalazine doesn't work in Crohn's…

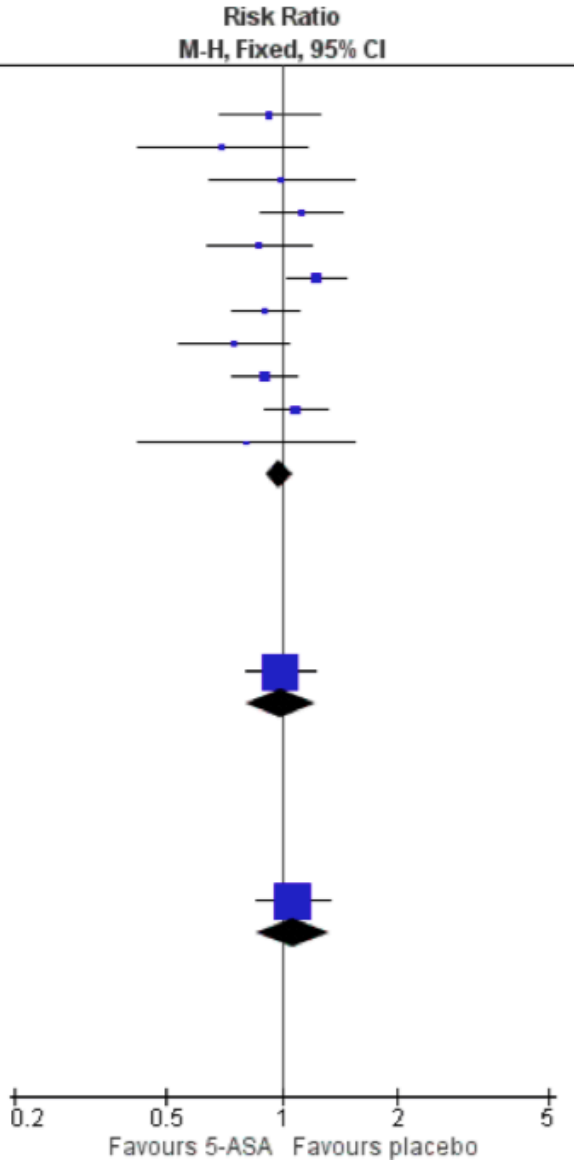
5 ASAs in Crohns

- No role for Mesalazine in induction or maintenance of Crohn's
- Some evidence of Sulphasalazine for mild colonic Crohn's

5-ASA vs placebo

Outcome: Relapse of CD

Study or Subgroup	5-ASA Events	5-ASA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 12 months						
Anonymous 1990	49	125	52	123	9.7%	0.93 [0.69, 1.25]
Arber 1995	12	28	19	31	3.3%	0.70 [0.42, 1.17]
Bondesen 1991	29	101	29	101	5.4%	1.00 [0.65, 1.54]
De Franchis 1997	42	58	38	59	7.0%	1.12 [0.88, 1.44]
Gendre 1993	37	80	43	81	7.9%	0.87 [0.64, 1.19]
Mahmud 2001	110	167	86	161	16.3%	1.23 [1.03, 1.48]
Modigliani 1996	46	65	50	64	9.4%	0.91 [0.74, 1.11]
Prantera 1992	29	64	37	61	7.0%	0.75 [0.53, 1.05]
Sutherland 1997	77	141	92	152	16.4%	0.90 [0.74, 1.10]
Thomson 1995	85	138	84	148	15.1%	1.09 [0.90, 1.32]
Wellman 1988	10	31	14	35	2.4%	0.81 [0.42, 1.55]
Subtotal (95% CI)		**998**		**1016**	**100.0%**	**0.98 [0.91, 1.07]**
Total events	526		544			
Heterogeneity: Chi² = 14.84, df = 10 (P = 0.14); I² = 33%						
Test for overall effect: Z = 0.38 (P = 0.70)						
1.1.2 24 months						
Gendre 1993	54	80	55	81	100.0%	0.99 [0.80, 1.23]
Subtotal (95% CI)		**80**		**81**	**100.0%**	**0.99 [0.80, 1.23]**
Total events	54		55			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.05 (P = 0.96)						
1.1.3 Pediatric						
Cezard 2009	50	68	44	64	100.0%	1.07 [0.86, 1.33]
Subtotal (95% CI)		**68**		**64**	**100.0%**	**1.07 [0.86, 1.33]**
Total events	50		44			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.60 (P = 0.55)						

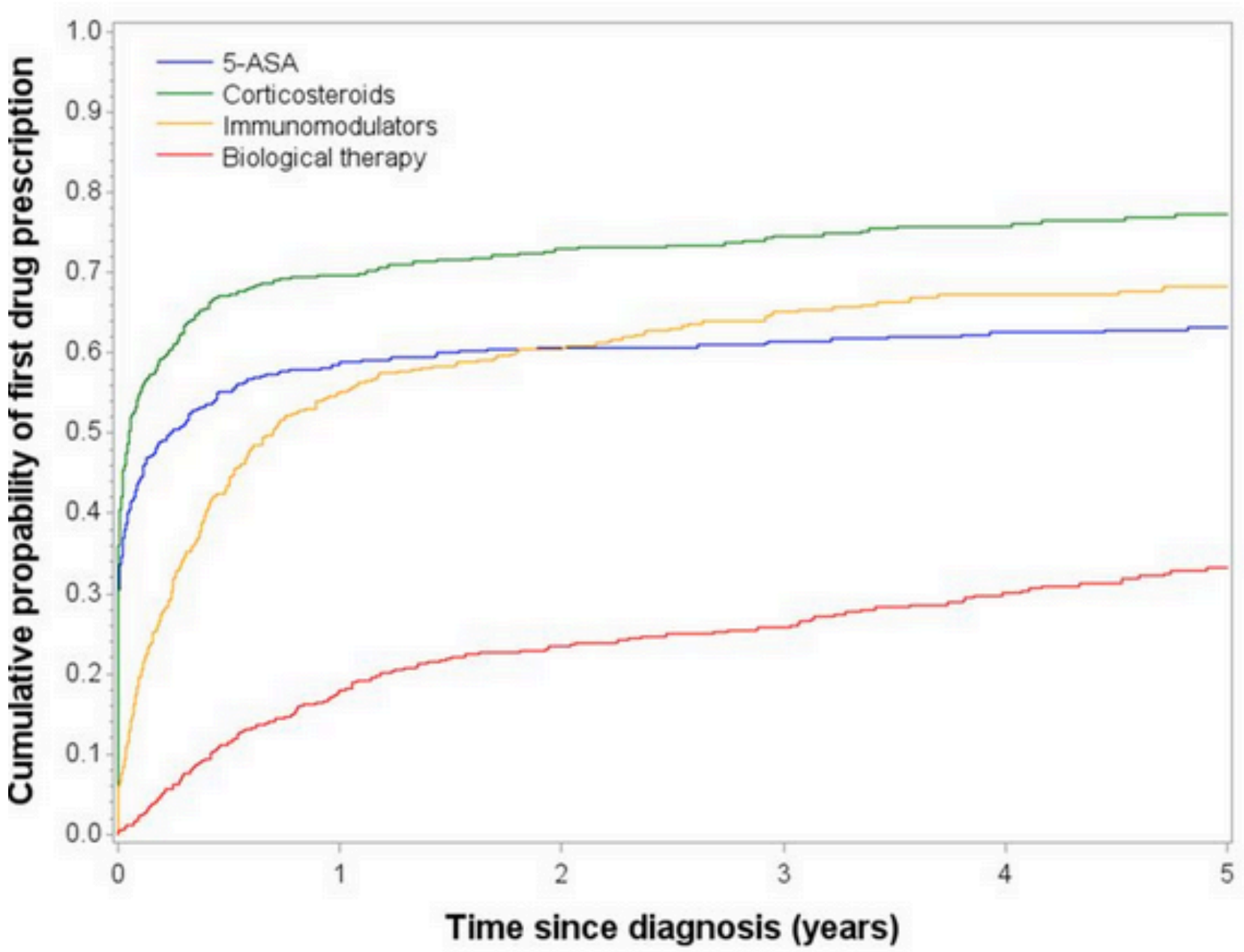


Akobeng AK et al. Cochrane Database of Systemic Reviews 2016

5-ASAs for maintenance of medical remission in Crohn's

- No RCT to show that these drugs are useful in this situation
- Cochrane meta-analysis: "No further evidence is needed" "Further RCT in this area might be unethical"
- We are however all still using it…..

> 50% exposed to 5ASA's in the first year after dx



Burisch J et al. Gut 2018

How we rationalise using 5 ASAs

Possible justification	Reality
Colonic disease	No evidence
Cheap	R1400/month for Asacol 2.4g daily
Few side effects	Not completely true – renal toxicity etc
No alternatives	Not true
Worth a try	Opportunity cost / delay in effective treatment
Personal experience	This is not evidence / placebo etc

Excessive steroid use

Quiz

How many courses of steroids in 12 months are excessive?

- 1
- 2
- 3
- Any amount

Quiz

How many courses of steroids in 12 months are excessive?

- 1
- 2
- 3
- Any amount

Steroids

- Effective for induction
- No evidence that steroids are effective maintenance therapies

Adverse effects

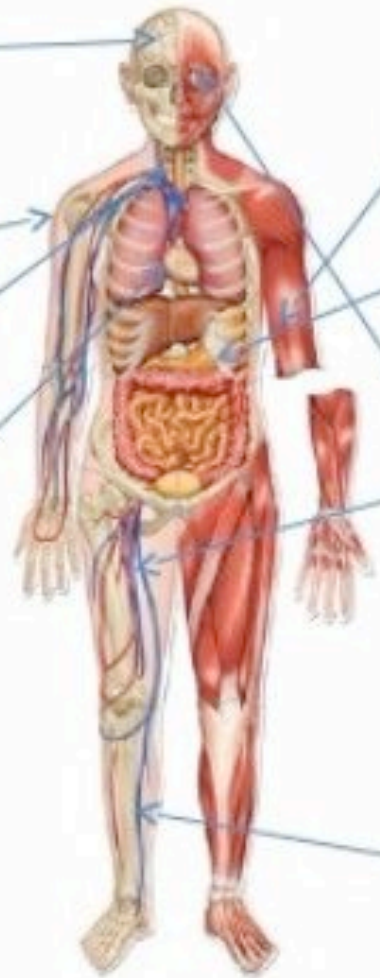
- Occur with prolonged use of high doses
- Cushing's disease

Psychiatric
- Sleep disturbance/activation
- Mood disturbance
- Psychosis

Skin/soft tissue
- Cushingoid appearance
- Abdominal striae
- Acne
- Hirsutism
- Oedema

Neurologic
- Neuropathy
- Pseudomotor cerebri

Cardiovascular
- Hypertension



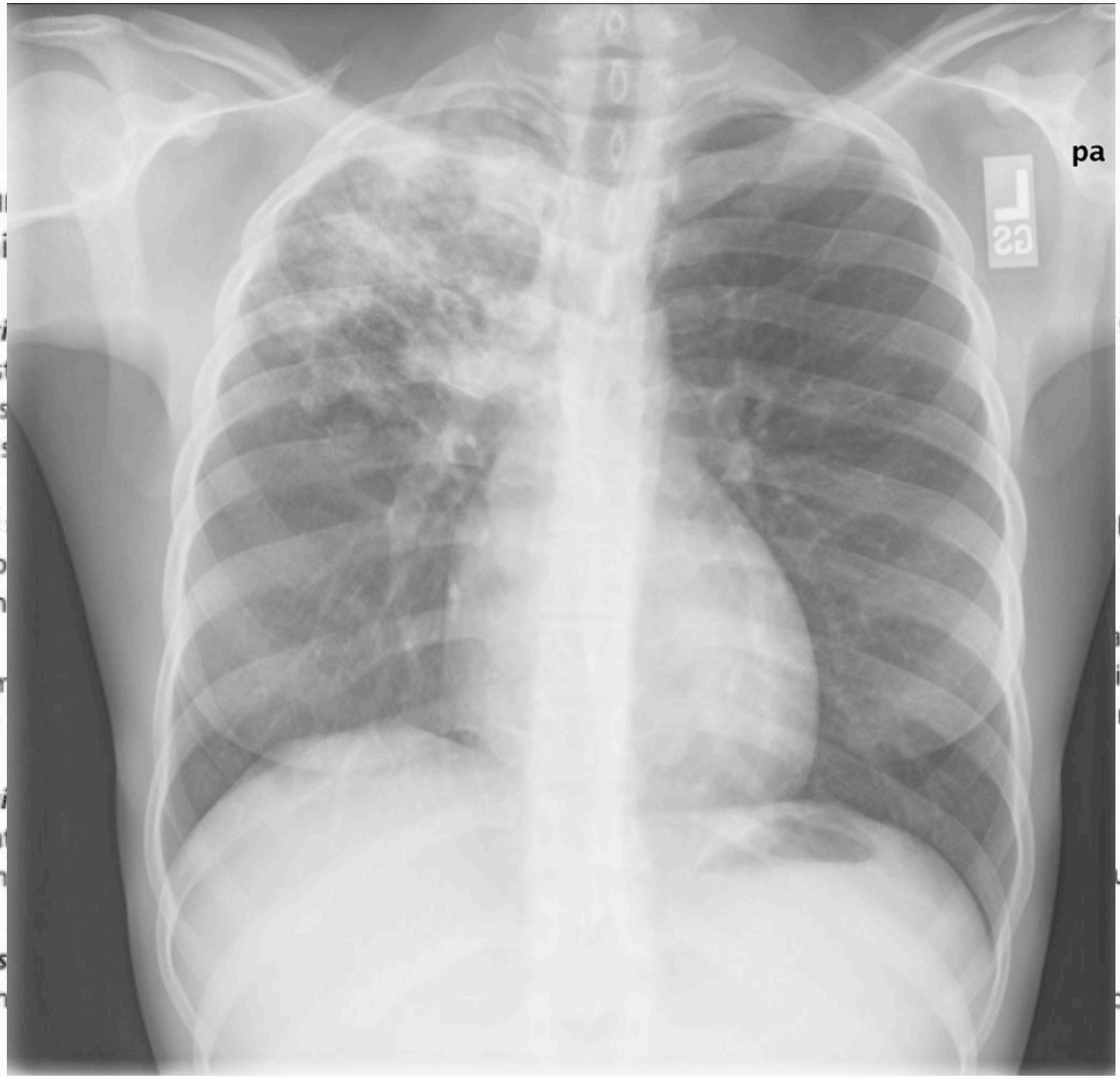
MSK
- Osteoporosis
- Asceptic necrosis of bone
- Myopathy

Endocrine
- Diabetes mellitus
- Adrenal cortex suppression

Immunologic
- Lymphocytopenia
- Immunosuppression
- False-negative skin test

Opthalmic
- Cataract
- Narrow-angle glaucoma

Developmental
- Growth retardation



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- Cushi

Psychiatri
•Sleep dis
•Mood dis
•Psychosis

Skin/soft
•Cushingo
•Abdomin
•Acne
•Hirsutism
•Oedema

Neurologi
•Neuropat
•Pseudom

Cardiovas
•Hyperten

of bone

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Definitions (ECCO)

Steroid refractory disease: active disease despite Prednisolone up to 1mg/kg/day for a period of 4 weeks

Steroid dependent disease:

- Unable to reduce steroids below 10mg/d (or Budesonide 3mg/d) within 3 months of starting steroids, without recurrent active disease
- or who have a relapse within 3 months of stopping steroids

"The aim should be to withdraw steroids completely…more than one full course of systemic steroids per year may be considered as the threshold for induction of steroid sparing agents"

Comollon et al JCC 2017

Summary

- Always consider reviewing the diagnosis
- Disease activity and severity definitions include symptoms, endoscopy and prognostic factors
- Goals of therapy are symptom and endoscopy based (mucosal healing) with role for biomarkers
- No role for the use of Mesalazine in CD
- Guard against excessive steroid use and delaying steroid sparing therapy


Thank you