Treatment Targets in Inflammatory Bowel Disease: Current Status in Daily Practice

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ABSTRACT

Background & Aims: Recently, treatment goals in inflammatory bowel disease (IBD) in clinical trials have shifted from mainly symptom-based to more mucosa-driven. Real world data on treatment priorities are lacking. We aimed to investigate the current practice and most commonly used definitions of IBD treatment targets among Dutch gastroenterologists.
Methods: Dutch gastroenterologists were asked to participate in a computer-based nation-wide survey. We asked questions on demographics, opinion and current practice regarding IBD treatment targets.
Results: Twenty-four percent (134/556) of the respondents completed the survey. For both Crohn's disease (CD) (47.3%, 61/129) and ulcerative colitis (UC)(45%, 58/129) the main treatment goal was to achieve and maintain deep remission, defined as clinical, biochemical and endoscopic remission. Seventy-six percent of the participants use mucosal healing (MH) as a potential treatment target for IBD, whereas 22.6% use histological remission. There is no single definition for MH in IBD. The majority use Mayo score ≤ 1 in UC (52%) and 'macroscopic normal mucosa' in CD (66%).
Conclusion: More stringent and mucosa-driven treatment targets as 'deep remission' and 'mucosal healing' have found traction in clinical practice. The most commonly used definition for MH in routine practice is endoscopic MAYO score ≤ 1 in UC and 'macroscopic normal mucosa' in CD.

Key words: Inflammatory bowel disease – mucosal healing – treatment goals – deep remission – ulcerative colitis – Crohn's disease.

Abbreviations: CD: Crohn's disease; CDEIS: Crohn's Disease Endoscopic Index of Severity; IBD: Inflammatory Bowel Disease; IBDU: IBD unclassified; IOIBD: International Organization for the Study of Inflammatory Bowel Diseases; MH: Mucosal healing; MMH: Microscopic mucosal healing; PROMS: Patient reported outcome measures; SES-CD: Simple endoscopic score for Crohn's disease; UC: ulcerative colitis; UCEIS: Ulcerative Colitis Endoscopic Index of Severity.

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INTRODUCTION

Treatment targets in Inflammatory Bowel Disease (IBD) have shifted over the recent years. Therapeutic strategies focusing on induction and maintenance of clinical remission have no effect on the natural course of the disease [1, 2]. In the late 1990s, the advent of biologic agents for the treatment of IBD has taught us that while patients may be in clinical remission, they may still have ongoing mucosal inflammation resulting in structural damage [3-8]. This has led to the concept of mucosal healing (MH) as a more meaningful therapeutic target in clinical practice. Indeed, emerging data suggest that MH is strongly associated with a reduction in steroid use, complications, hospitalizations, and surgeries. This has fueled a shift in IBD trials and guidelines from mainly symptom-based management of IBD patients to more complex management considerations. Composite treatment targets including both patient reported outcome measures (PROMS) and mucosal healing are promoted [9-15, 34]. Despite the clinical relevance of MH, no standardized definition is available yet. In addition, definitions for newly defined, but not yet widely accepted targets, such as "deep remission" or "histological remission" are emerging in clinical trials. There are a number of endoscopic disease activity scores that assist endoscopists, but few have been properly evaluated and validated in large cohorts.

Good examples are the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) for ulcerative colitis (UC) [16, 17], the Crohn's Disease Endoscopic Index of Severity (CDEIS) and the Simple Endoscopic Score (SES-CD) for Crohn's disease (CD) [18-20]. Practical and commonly used definitions for MH such as "the complete resolution of the visible alteration or lesions" [21], or endoscopic Mayo score ≤ 1 [22] have the disadvantage of higher interobserver variability and limited accuracy [9, 23, 24]. In view of the above, (inter)national guidelines are still unclear which treatment goals we should use in routine clinical practice, and how much efforts, risks and resources we should use to achieve implementation [25-28]. This leads to the question how endoscopic endpoints such as MH are used in real world IBD practices.

Therefore, we conducted a survey to investigate the current practice and used definitions of IBD treatment targets among Dutch gastroenterologists. In addition, we aimed to map factors that influence decision-making in clinical practice.

METHODS

Survey development, testing and distribution

We developed a structured survey on IBD management in daily practice consisting of 23 multiple-choice questions (Q1-23) including 3 clinical cases and 3 endoscopy images (Supplementary Appendix). The cases and images were mainly designed to monitor the internal consistency of the survey. Academic review of important literature and guidelines on this topic, as well as gastroenterologist's interviews guided the survey development. The survey was published at the professional survey website www.surveymonkey.com between June 2015 and October 2015. In accordance with survey design guidelines [29], a pilot questionnaire was pre-tested on 5 dedicated IBD gastroenterologists to examine for questionnaire applicability, clarity, and content validity. As a result of this pilot survey, the initial questionnaire was modified. The questionnaire was shortened, questions asked on treatment targets were made more clear and specific, 'other' response options were included, and the clinical cases were refined. The questionnaire (Supplementary Appendix) led to collection of data on demographics of participants and their institutes (7 questions), their opinion and current clinical practice with respect to IBD treatment targets (13 questions, of which 3 contained endoscopy images) and the most relevant decision-making factors in their clinical IBD practice (3 cases). With respect to IBD treatment targets, we asked both general and more detailed questions. To ensure that participants should only answer for those relevant survey questions, we redirected those that answered negatively on general questions in a specific topic to the next cluster of questions on the subsequent topic.

Participants

The survey and two reminders were distributed to potential participants through e-mail. A cover e-mail explained the purpose of the survey and provided a link to the survey. Responses were accepted up to 4 months from the initial survey distribution date. Participants comprised all Dutch gastroenterologists and gastroenterology (GI) fellows, who were members of the Dutch association for gastroenterologists.

As the survey was based on voluntary participation and information disclosure, the study protocol did not need to undergo a formal review by an Ethics Committee. Voluntary survey return was taken as consent.

Data collection and statistics

Data collection was anonymous and treated confidentially. Statistical analyses were performed using descriptive statistics, independent t-tests, and nonparametric tests. We used descriptive statistics to analyze the results using counts and proportions for categorical data and means and standard deviations for continuous variables. Missing values were not imputed. The answers to most questions regarding definition, treatment goals and the case descriptions were tested against the mean number of years of experience (t-test after dichotomization) and type of hospital (chi-square). We assumed a two-tailed $p < 0.05$ as statistically significant. We examined the consistency of the participants' answers by testing associations between theoretical questions and clinical cases or endoscopy images concerning the same subject (chi-square). Interobserver agreement for endoscopy images was tested by kappa statistics. Statistical analysis was performed with IBM SPSS version 22, excel version 2007, and GraphPad Prism (GraphPad Software,version 5.03).

RESULTS

Participants

The survey was sent to 556 eligible e-mail addresses. Overall, 134 physicians participated and completed the survey (24%). The response rate was 25% for gastroenterologists (n=97/396) and 23% for GI fellows (n=37/160). Table I contains the demographic characteristics of the participants and their working environment. Fifty-nine percent of the participants were male (79/134), mean age was 42.1 years and the mean duration of working experience as a gastroenterologist was 8.5 years (fellows reported 0 on this question).

Table I. Demographic characteristics of the participants

Variable	n/N(%)
Response rate GI fellows	37/160 (23%)
Response rate gastroenterologists	97/396 (25%)
Male sex	79/134 (59%)
Age (years) (mean ± SD)	42.1 ± 9.8 (range 28-65)
Type of hospital	
University hospital	44/134 (33%)
Teaching hospital	59/134 (44%)
General hospital	31/134 (23%)
IBD population#	
<400	10/134 (8%)
400-800	44/134 (33%)
800-1200	38/134 (28%)
>1200	42/134 (31%)
Treat IBD in practice	130/134 (97%)

IBD = inflammatory bowel disease; # total number of IBD patients in follow up at the outpatient clinic of the center

Survey topics

Treatment goals (Q8-9)

All selectable treatment goals, and their range are depicted in Fig. 1. The main overall treatment goal was to achieve and maintain deep remission for both CD (47.3%, 61/129) and UC (45%, 58/129). In this survey, this was defined as clinical, biochemical and endoscopic remission. Participants who indicated deep remission as a key treatment goal (N=61 in CD, N= 58 in UC), had fewer years of working experience. This was significant for CD (11.5 ± 9.8 vs 6.0 ± 7.3 years ; p= 0.001); for UC the same trend was seen, but this did not reach the threshold for statistical significance (10.2 ± 9.5 versus 7.2 ± 8.5 years; p= 0.06). We found no association between treatment goals and the type of hospital (Table II).

Mucosal healing and definitions (Q10-13)

Seventy-six percent (98/129) of the participants indicated that they used MH as a potential treatment target for IBD. Years of working experience or type of hospital were independent of the use of MH (Table II). Ninety-four participants (73%) answered more detailed questions on MH. The majority (70%; 66/94) mentioned that they used MH as endpoints for both CD, IBD unclassified (IBDU) and UC.

To define MH in UC, 52% (49/94) used the Mayo score, with 40% (38/94) using 'macroscopic normal mucosa' as a definition for MH (Fig. 2a). For UC, we did not detect an association with the type of definition used for MH and years of working experience (Table II). The majority of respondents (66%; 62/94) used 'macroscopic normal mucosa' to define MH in CD, with almost one-fifth (18.1%; 17/94) using the CDEIS, and 9.6% (9/94) the SES-CD (Fig. 2b). Again, we found no

association with the type of definition used for MH and years of working experience, but in university hospitals the MH definition 'macroscopic normal mucosa' was used significantly more often (p=0.043)(Table II).

Histological remission (microscopic mucosal healing) and deep remission (Q14-Q17)

Histological remission (microscopic mucosal healing, MMH) as a possible treatment target for IBD was used by 22.6% (28/124) of the participants. Twenty-seven participants (22%) provided additional details on MMH. Fifty-nine percent (16/27) stated to use MMH for CD, as well as for IBDU and UC, with 22.2% (6/27) using it only in UC. The most frequently used definition of MMH was 'perfectly normal mucosa' (44.4%; 12/27). This was followed by the criteria of Truelove and Richards (29.6%; 8/27) (Fig. 2c). There was no association between the used definition of MMH and years of working experience or type of hospital (Table II).

The participants defined deep remission frequently as 'clinical, biochemical and endoscopic remission' (56.5%; 70/124), with the definition 'clinical, biochemical, endoscopic and histological remission' (39.5%; 49/124) following suit (Fig. 2d). There was no association between the latter (most stringent definition of deep remission) and years of working experience or type of hospital (Table II).

Endoscopy images (Q18-20)

One hundred and twenty-four participants (93%) assessed 3 endoscopy images of the colonic mucosa on MH, to monitor for internal consistency of the survey. The 3 images linked to circle diagrams indicating the opinion of the participants on MH are depicted in Supplementary Fig. 3a-c. The inter
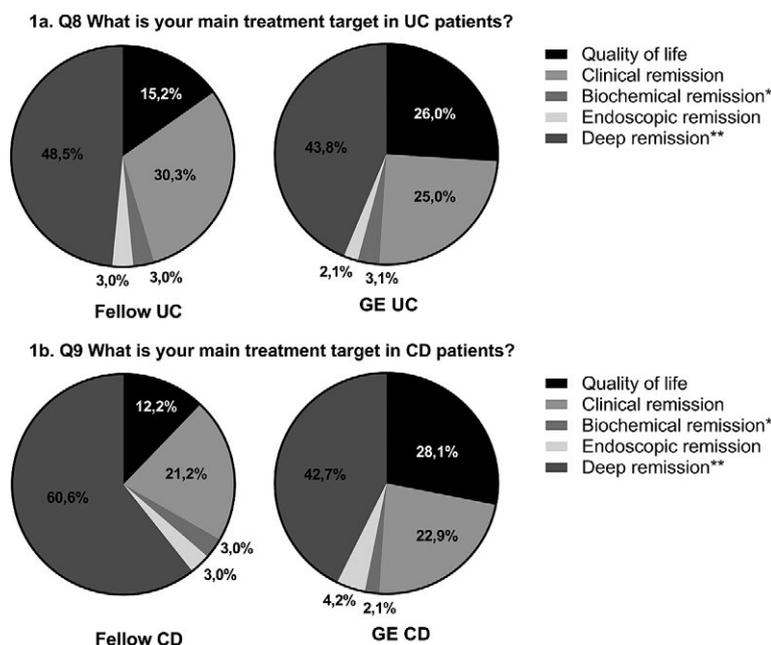

1a. Q8 What is your main treatment target in UC patients?

Quality of life
Clinical remission
Biochemical remission*
Endoscopic remission
Deep remission**

Fellow UC
15,2% · 30,3% · 48,5% · 3,0% · 3,0%

GE UC
26,0% · 25,0% · 43,8% · 2,1% · 3,1%

1b. Q9 What is your main treatment target in CD patients?

Quality of life
Clinical remission
Biochemical remission*
Endoscopic remission
Deep remission**

Fellow CD
12,2% · 21,2% · 60,6% · 3,0% · 3,0%

GE CD
28,1% · 22,9% · 42,7% · 4,2% · 2,1%

Fig. 1. Selectable treatment targets in ulcerative colitis (1a) and Crohn's disease (1b) (*Defined as normal laboratory results and normal fecal calprotectine; **Defined as clinical, biochemical and endoscopic remission; MH = mucosal healing; UC= ulcerative colitis; CD = Crohn's disease; GE= gastroenterologist).

Table II. Survey answers tested against working experience and type of hospital

Question (Q)	N	Working[a] Experience	P	Type of hospital			P
				University	Teaching	General	
Q8 Treatment goal UC deep remission	58	10.3±9.5	0.06	21 (36%)	20(48%)	17(61%)	
Q8 Treatment goal UC other answers	71	7.22±8.5		38 (64%)	22(52%)	11(39%)	0.08
Q9 Treatment goal CD deep remission	61	6.0±7.3	0.001	25(42%)	21(50%)	15(54%)	
Q9 Treatment goal CD other answers	68	11.5±9.8		34(58%)	21(50%)	13(46%)	0.57
Q10 MH used as treatment goal - yes	98	8.6±9.0	0.57	49(83%)	31(74%)	18(64%)	
Q10 MH used as treatment goal - no	31	9.7±9.6		10(17%)	11(26%)	10(36%)	0.15
Q12 Definition MH in UC- macr.normal	38	10.6±9.7	0.31	24(50%)	9(30%)	5(31%)	
Q12 Definition MH in UC- Mayo	50	7.8±8.8		22(46%)	20(67%)	8(50%)	0.08
Q12 Definition MH in UC- other	6	7.0±5.8		2(4%)	1(3%)	3(19%)	
Q13 Definition MH in CD- macr.normal	63	9.5±8.9	0.34	37(77%)	19(63%)	7(44%)	
Q13 Definition MH in CD- other	31	7.6±9.4		11(23%)	11(37%)	9(56%)	0.04[b]
Q14 Stringent definition deep remission	49	9.0±8.9	0.92	24(42%)	16(39%)	9(35%)	
Q14 Other definition deep remission-	75	9.2±9.4		33(58%)	25(61%)	17(65%)	0.81
Q15 MMH used as treatment goal –yes-	28	11.5±8.1	0.12	14(25%)	9(22%)	5(19%)	
Q15 MMH used as treatment goal –no-	96	8.5±9.4		43(75%)	32(78%)	21(81%)	0.86

[a]years; mean ± SD; [b]P 0.013 University hospital versus General; MH = mucosal healing; UC= ulcerative colitis; CD = Crohn's disease; MMH= histological remission.

observer agreement depicted as Fleiss generalized kappa was almost perfect for respectively image A (0.94) and image B (0.88) and moderate for image C (0.53). To control for internal consistency, we compared answers of Q12 ('which definition do you use for mucosal healing?') with the judgment of the endoscopic image C. For this purpose we created two groups: 1) MH defined as Mayo score 0 (answer Q12b); 2) MH defined as Mayo score ≤ 1 (answer Q12c). Some 68% (43/63) of the

participants in group 1 judged image C as MH, while 48% (10/21) did from group 2 (p=0.09).

Clinical cases (Q21-23)

The survey comprised three clinical cases (Q21-23). The first 2 cases (Q21-22) dealt with the use of deep remission in UC patients (Supplementary Fig. 4a-b), and were used to test internal consistency of the survey. Question 8 (Q8) is
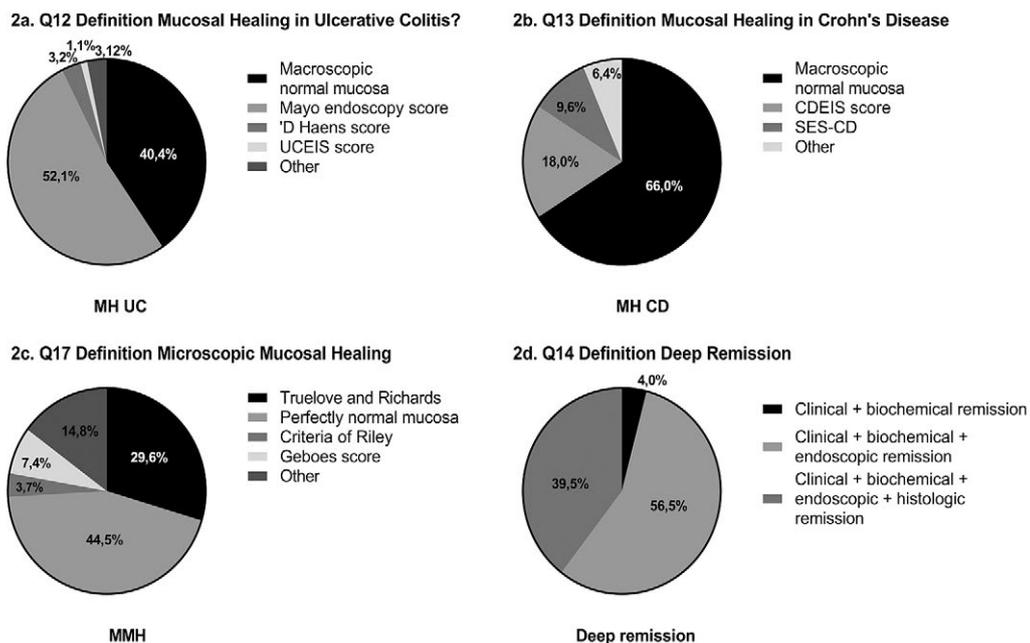

Fig. 2. Definitions used for mucosal healing in ulcerative colitis (2a), in Crohn's disease (2b), for histological remission (2c) and for deep remission in inflammatory bowel disease (2d). (MH = mucosal healing; UC= ulcerative colitis; CD = Crohn's disease; MMH= histological remission)

the theoretical part that complements these 2 cases ('what do you consider the most important treatment target in your patients with UC') and therefore we analyzed the internal consistency of the participants by comparing the answers of Q8 and Q21/22 (n=120). For both cases and Q8, we created two groups of respondents: 1) treatment target is deep remission (answer Q8e) versus 2) all other answers (answer Q8a-d). Most respondents chose to intensify their treatment in both cases (Q21: 75%; 92/124 /Q22: 84%; 103/123), with a significant association with the answer 'deep remission' in Q8 for both Q21 (p=0.026) and Q22 (p=0.03). The third case (Q23) dealt with 'stopping criteria' for IBD medication after one year of deep remission in UC, an issue that is outside the scope of this article. Fifty-three percent (65/122) of the participants were willing to stop the immunosuppressive medication in a young male patient, who was in deep remission for 1.5 years, but was initially treated top-down because of severe pancolitis at presentation.

DISCUSSION

This nationwide survey was designed to determine the current practice of IBD treatment targets among Dutch gastroenterologists and to assess factors that influence decision making. Almost half of all respondents use deep remission as a key treatment goal. Deep remission was mostly defined as 'clinical, biochemical and endoscopic remission'. The majority are willing to intensify treatment to reach deep remission. Over three-quarters of the gastroenterologists use MH as a potential treatment target for IBD, whereas less than a quarter use histological remission. There is no single definition for MH in IBD. The majority use Mayo score ≤ 1 in UC and 'macroscopic normal mucosa' in CD.

Nowadays, MH is an accepted treatment target in clinical IBD trials [9, 15, 21] and has been accepted in the guidelines [25-28]. We found that 75% of the gastroenterologists use MH in daily IBD practice, irrespective of experience or type of hospital. Our data suggest that the concept of MH is embraced by many IBD practices. This indicates a watershed with the situation in 2010 when a Swiss survey found that gastroenterologists judged clinical activity as more relevant than endoscopic severity or biomarkers [30]. Worth noting, and probably partly explaining the discrepancy, is that the Swiss participants were all gastroenterologists, with on average, a longer working experience, with probably less IBD patients in their center. However, it remains important to realise that we cannot achieve MH in all IBD patients with the currently available therapies. In UC, varying data on achieving MH with the use of 5-ASA (36,9%-80%)[31, 32], azathioprine (53%) [33] and biologics 32%-62% [34-37] exist, depending on the used definition of MH and duration of follow up. In the case of CD similar results for budesonide (24%)[38], azathioprine (16.5-73%)[38-40], combinations of azathioprine and biologics (43,9-70.4%) [39, 40], and biologics (20%-63%) [39-42] exist.

Newly defined treatment targets, such as deep or histological remission come from endpoints defined for clinical IBD trials [40, 43-44], but are not widely accepted or integrated in the IBD guidelines [25-28]. Surprisingly, almost half of all respondents used deep remission as a key treatment target in

daily clinical practice, which suggests that practice is being shaped prior to development or revision of guidelines. Most guidelines date from around 2011 and are updated every 3 years [25-27]. Indeed, a recent consensus meeting initiated by the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) did define composite treatment targets for both UC and CD, combining both clinical and endoscopic remission [45]. Also, the majority of these respondents have fewer years of working experience. Possibly, a greater focus on evolving treatment targets in the current training schemes of GI fellows plays a role here. Histological remission appears to be used less often in daily practice, with a preference for UC when used. This is in line with international guidelines that do not advise histological remission as a treatment target [25-27]. Also, IOIBD experts agreed upon histological remission as an adjunctive goal that might come into view in the future, in particular in UC [45]. A unified single definition for MH in IBD is lacking. For UC, several endoscopic scoring systems have been developed but none were validated until recently [46-47]. In 2012, the UCEIS has been developed and validated [16, 17]. UCEIS is rather complex and time consuming, which makes it less attractive for routine use in daily practice [48]. Currently, the IOIBD consensus group recommends the endoscopic Mayo score in UC because of its ease of use and established predictive value [45,49-50]. In line with this recommendation we found that more than half of the participants use the Mayo score (0 or ≤ 1) to define MH in UC. Of these, one-third defined MH as Mayo score 0. In the literature, the debate continues whether Mayo score 0 or 1 qualifies as a definition for MH [45, 51]. Still, in UC 40% of the participants indicated the definition of MH as 'macroscopic normal mucosa', and the same applied for 66% in CD. The latter is in accordance with the IOIBD consensus which agreed on the 'absence of ulceration' as an endoscopic target in CD [45]. Both CDEIS and SES-CD are validated scoring systems for CD. Surprisingly, we found that only one-fifth use the CDEIS, and 9.6% the SES-CD, while the CDEIS is known as time consuming and complex [19, 20, 48].

The participants went through three clinical UC cases dealing with treatment targets and stopping criteria of immunosuppressive medication. In line with their answers on the theoretical questions concerning treatment targets in UC, most respondents chose to intensify the treatment to reach deep remission.

Our study has several strengths and some limitations. Mucosal healing has been a theme in clinical trial design but it was unknown whether this concept had been adopted in clinical practice. Our data suggest that it has. Secondly, this survey has been developed according to survey guidelines [29], and carried high internal consistency when comparing theoretical questions with practical cases. Naturally, the voluntary participation to this survey creates response bias. Since our target population was 'gastroenterologists who treat IBD patients', we chose a purposive sampling design and mentioned this element in the cover e-mail that was sent to possible participants.

The purposive sampling, national design of our survey, and the inclusion of physicians from both general and academic hospitals, were in support of the external generalizability of our findings.

CONCLUSION

We demonstrated that the use of MH, as a marker of treatment efficacy for both UC and CD, has made its way into routine practice. Although there is no single definition for MH, the majority of gastroenterologists use endoscopic MAYO score ≤ 1 in UC or 'macroscopic normal mucosa' in CD. This seems to be the least complex and most pragmatic definition for widespread use in clinical practice.

Conflicts of interest: None to declare.

Authors' contributions: T.E.H.R.: conception and design of the work, data collection, analysis and interpretation, drafting the article; K.G.: Data collection, analysis and interpretation; W.K.: data analysis and interpretation; F. H. and J.P.H.D.: critical revision of the article. All authors gave final approval of the version to be published.

Supplementary material: To access the supplementary material visit the online version of the *J Gastrointestin Liver Dis* at http://www.jgld. ro/wp/archive/ and http://dx.doi.org/10.15403/jgld.2014.1121.254.ken

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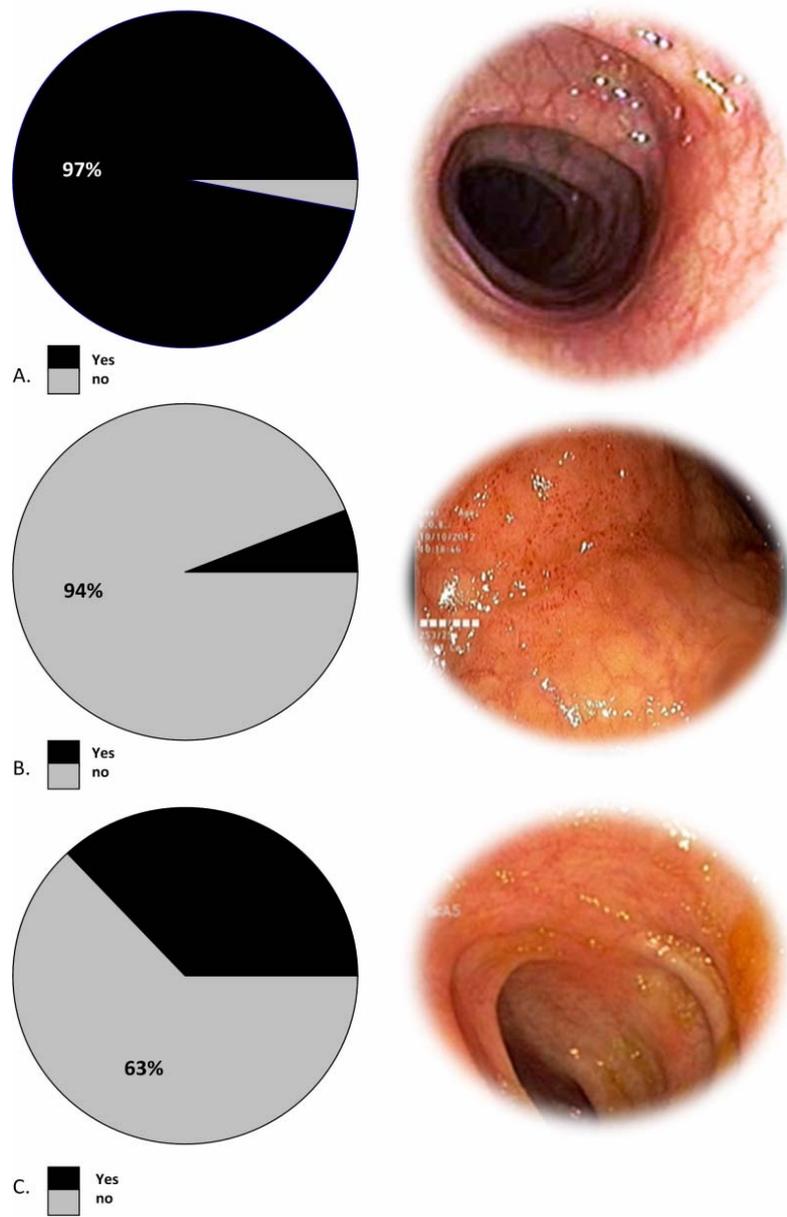
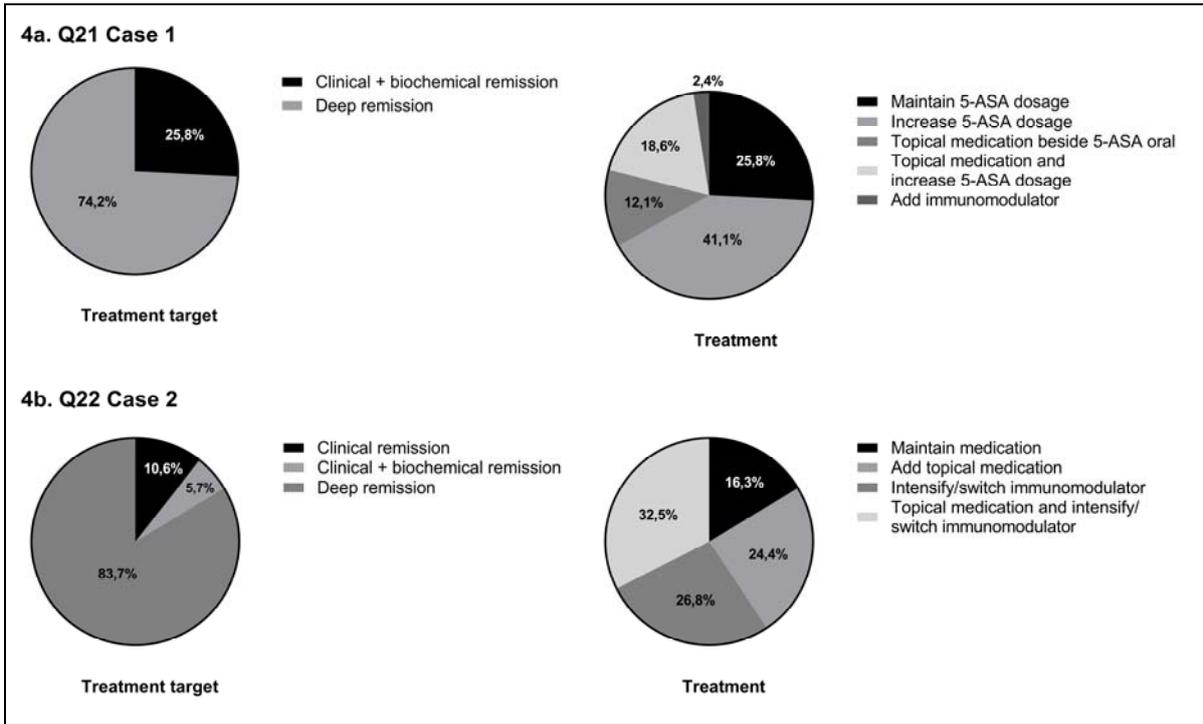**Fig. 3a-c.** Endoscopy images and % participants judging the image as mucosal healing

Fig. 4. Treatment targets and treatment options used to achieve treatment goals in case 1 (4a) and case 2 (4b)

1.	Which gender do you have?
A.	Male
B.	Female
2.	What is your age?
3.	What is your profession?
A.	Gastroenterologist
B.	GI Fellow
C.	Internist
D.	Internal medicine fellow
E.	Other (give explanation)
4.	How many years have you been medical specialist? (If fellow fill in 0)
	.. years
5.	In what type of hospital do you work?
A.	University hospital
B.	Teaching hospital
C.	General hospital
D.	Other (give explanation)
6.	How many IBD outpatients are treated in your center?
A.	<400 patients
B.	400-800 patients
C.	800-1200 patients
D.	>1200 patients
7.	Do you treat IBD patients in clinical practice?
A.	Yes
B.	No
8.	What is your most important treatment goal in UC patients?
A.	Induce and maintain a good quality of life
B.	Induce and maintain clinical remission
C.	Induce and maintain biochemical remission (normal laboratory results and feces calprotectine)
D.	Induce and maintain endoscopic remission (MH)
E.	Induce and maintain deep remission (combination of B, C and D)
9.	What is your most important treatment goal in CD patients?
A.	Induce and maintain a good quality of life
B.	Induce and maintain clinical remission
C.	Induce and maintain biochemical remission (normal laboratory results and feces calprotectine)
D.	Induce and maintain endoscopic remission (MH)
E.	Induce and maintain deep remission (combination of B, C and D)
10.	Do you ever use endoscopic remission (MH) as a treatment target in your IBD patients?
A.	Yes
B.	No
11.	In which patients do you use endoscopic remission (MH) as a treatment target?
A.	CD
B.	UC
C.	IBD-U
D.	Answer A and B
E.	Answer A and C
F.	Answer B and C
G.	All of the above answers
12.	Which definition do you use for endoscopic remission (MH) in UC patients?
A.	Macroscopic complete normal mucosa
B.	Mayo endoscopy score 0
C.	Mayo endoscopy score ≤ 1
D.	'D Haens score[A]

E.	UCEIS^B score 0
F.	UCEIS^B score < 4
G.	Other (give explanation)
13.	Which definition do you use for endoscopic remission (MH) in CD patients?
A.	Macroscopic complete normal mucosa
B.	CDEIS^C score 0
C.	CDEIS^C score < 4
D.	SES-CD^D
E.	Other (give explanation)
14.	How do you define deep remission in your IBD patients?
A.	Clinical remission
B.	Clinical and biochemical remission
C.	Clinical, biochemical and endoscopic remission
D.	Clinical, biochemical endoscopic and histological remission
15.	Do you ever use histological remission/microscopic mucosal healing (MMH) as a treatment target in your IBD patients?
A.	Yes
B.	No
16.	In which patient group do you use MMH as a treatment target?
A.	CD
B.	UC
C.	IBD-U
D.	Answer A and B
E.	Answer A and C
F.	Answer B and C
G.	All of the above answers
17.	Which definition for MMH do you use?
A.	Truelove and Richards^E
B.	Perfectly normal mucosa
C.	Riley criteria^F
D.	Geboes score^G
E.	Other (give explanation)
18.	Do you think this image shows endoscopic remission?
A.	Yes
B.	No
19.	Do you think this image shows endoscopic remission?
A.	Yes
B.	No
20.	Do you think this image shows endoscopic remission?
A.	Yes
B.	No
21.	(1/3) Case: 45 year old female; pancolitis ulcerosa since 1994, is on 2 grams mesalazine/day maintenance dose; no symptoms, normal laboratory results, feces calprotectine 200µg/g. At surveillance colonoscopy: sigmoiditis MAYO I. What is your treatment?
A.	Maintain 5-ASA dose (patient is in clinical and biochemical remission)
B.	Increase 5-ASA dose to achieve deep remission
C.	Add topical medication to oral 5-ASA to achieve deep remission
D.	Combination of B. and C. to achieve deep remission
E.	Add an immunomodulator to achieve deep remission
22.	(2/3) Case: 22 year old male, pancolitis ulcerosa since 2011; Severe disease course at presentation: top down treatment with infliximab 5mg/kg induction scheme followed by maintenance therapy 1x/8 weeks combined with 6-mercaptopurine. Now: no symptoms, laboratory results: CRP 10, feces calprotectine 250 µg/g and at colonoscopy rectosigmoiditis MAYO II. What is your treatment?
A.	Maintain current medication (patient is in clinical remission)
B.	Maintain current medication (patient is in clinical and biochemical remission)
C.	Add topical medication to current medication to achieve deep remission

D.	*Intensify/switch current immunomodulators (after control levels) to achieve deep remission*
E.	*Combination of C. and D.*
23.	*(3/3) Case: 22 year old male, pancolitis ulcerosa since 2011; Severe disease course at presentation: top down treatment with infliximab 5mg/kg induction scheme followed by maintainance therapy 1x/8 weeks combined with 6-mercaptopurine. Since 1,5 years no symptoms, laboratory results: normal, CRP<5, feces calprotectine 250µg/g and normal mucosa at colonoscopy What is your treatment?*
A.	*Maintain current medication because of to "prognostic poor" ulcerative colitis*
B.	*Stop anti-TNF therapy because of >1 year clinical, biochemical and endoscopic remission*
C.	*Stop 6-mercaptopurine because of >1 year clinical, biochemical and endoscopic remission*

[A] 'D Haens score = normaal ogende mucosa <u>zonder</u>: 1) toegenomen kwetsbaarheid, 2) bloedingen, 3) erosies, 4) zweren.

 (*'D Haens score = normal-looking mucosa <u>without:</u> 1) increased vulnerability, 2) haemorrhages, 3) erosions, 4)ulcers*)

[B] UCEIS = Ulcerative Colitis Endoscopy Index of Severity

[C] CDEIS = Crohn's Disease Endoscopy Index of Severity

[D] SES-CD = Simple Endoscopic Score for Crohn's Disease

[E] Truelove and Richards: graad 1: geen significante ontsteking, graad 2: mild-gemiddelde ontsteking, graad 3: ernstige ontsteking

(Truelove and Richards: grade 1: no significant inflammation, grade 2: mild-moderate inflammation, grade 3: severe inflammation)

[F] Riley: score van 6 kenmerken: acuut ontstekingsinfiltraat, crypt abcessen, mucus depletie, epitheliale integriteit, chronisch inflammatoir infiltraat, abnormaliteiten in crypte architectuur

(*Riley: score of 6 features: acute inflammatory cell infiltrate, crypt abscesses, mucine depletion, surface epithelial integrity, chronic inflammatory cell infiltrate, crypt architectural irregularities)*

[G] Geboes: score van 6 kenmerken: architecturele veranderingen, chronisch inflammatoir infiltraat, neutrofielen en eosinofielen in lamina propria, neutrofielen in epitheel, crypt destructie, erosie of ulceratie.

 (*Geboes: score of 6 features: architectural changes, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction, erosion or ulceration).*