IBDREAM: A real-time registry for IBD care

Update on a nationwide IBD cohort: report September 2020

IBDREAM committee members and participating hospitals

Dr. Frank Hoentjen, Gastroenterologist Radboudumc Nijmegen
Dr. Maurice Russel, Gastroenterologist MST Enschede
Drs. Jeroen Jansen, Gastroenterologist OLVG Amsterdam
Dr. Rachel West, Gastroenterologist Franciscus Gasthuis en Vlietland Rotterdam
Dr. Tessa Römkens, Gastroenterologist JBZ Den Bosch

Contents

1. Background

In the Netherlands approximately 90.000 patients have been diagnosed with inflammatory bowel disease (IBD) and its incidence appears to be rising. The disease typically manifests in the 2nd or 3rd decade of life with a remarkable impact on health-related quality of life. Although the pathogenesis of IBD is still unclear, it is hypothesized that chronic inflammation originates from an overly aggressive mucosal immune response against luminal bacteria in genetically susceptible subjects. Patients may show symptoms of diarrhea or rectal blood loss, abdominal pain, vomiting and occasionally weight loss or anemia. In combination with elevated inflammatory parameters and colonoscopy combined with histology the diagnosis can be made. Extra-intestinal manifestations such as arthritis, skin disorders and uveitis are common. The disease can lead to several complications like fistulas, abscesses and even colorectal cancer. IBD is a chronic disabling disease, frequently leading to hospitalizations, lower quality of life and work disability.

The Dutch IBD patient organization (Crohn en Colitis Vereniging Nederland, CCUVN) has shown that there is a need for personalized medical care and aims at teaching IBD patients how to take the lead and how to participate and help orchestrating their personal IBD care (CCUVN working plan 2017, http://www.crohn-colitis.nl/). Furthermore, nationwide systematic data on the course, management, quality and costs of IBD therapy are scarce.

2. Vision IBDREAM

IBDREAM follows the philosophy and scope of the other DREAM registries, that are also successfully implemented in clinical practice (www.dreamregistry.nl). The DREAM registry for rheumatoid arthritis is one of the largest disease-specific registries in the Netherlands and has evolved to a national quality management system where benchmarking information improves quality and efficiency of care. Various cohort studies have been performed within the DREAM registry. The organization of IBDREAM resembles the structure of the DREAM registers and promises to be equally successful.

IBDREAM **aims** to be the registry for future-proof IBD care. The core pillars of IBDREAM are:

- Patient empowerment
- Integrated care
- Data-driven IBD care
- Value based IBD healthcare

Patient empowerment

IBDREAM is a registry that was specifically designed for IBD patients and will facilitate this approach through the web-based patient portal, which will provide individual feed-back on treatment, disease activity, and quality of life and long-term follow-up data on safety and efficacy of treatment. The portal also provides a means for addressing the patient's questions before consultation with their health provider, guaranteeing their own input for consultation. IBDREAM improves patient empowerment by getting patients involved in their disease and management.

Integrated care

IBDREAM's Transparency in Healthcare (TiH) Online Monitoring Application (OMA) and database are fully compatible with other health applications and devices. This allows future linkage with systems used in both primary- and secondary medical care. This is crucial for a future universal 'personal health environment' (Dutch: persoonlijke gezondheidsomgeving) where patients can gain access to their complete medical file. Integration of electronical patient files of both primary and secondary care, will lead to a lower registration burden of clinicians and more involvement of the patient.

Data-driven IBD care

The goal is to improve the quality of care for IBD patients in the Netherlands. Through IBDREAM, information is prospectively gathered regarding diagnosis and specific IBD manifestations, clinical, laboratory and PROMs (disease activity, complications of disease, quality of life, work). Results are used to learn as a clinician, as gastroenterology department and for benchmarking with other hospitals. Furthermore, data collection will lead to transparency of IBD care, to establishment of the real-life effectiveness and safety of biological therapies and will eventually lead to optimization of IBD pharmacotherapy.

Value-based IBD care

With all new promising but expensive treatment options the main proportion of healthcare costs shifted from in-hospital care to medication costs. With the rising healthcare costs, value based healthcare is becoming more important for making responsible decisions by decision makers and clinical management. The patient-value (health-outcomes / costs) is the main focus. The IBDREAM registry is the pre-eminent tool to determine both patient value and costs, as it collects longitudinal data 'from the whole patient journey'. Both direct and indirect costs can be obtained from all data

collected. Furthermore, more insight in the short-term and long-term effectiveness of different treatment strategies can be established. By learning from and reacting to these outcomes, a more effective and cost-effective IBD care can be achieved in the future.

$$\text{Patient Value} = \frac{\text{Health Outcomes}}{\text{Cost}}$$

Contents of year report

This document reports the four-year follow-up data of a nationwide IBD cohort in the Netherlands. The following research questions will be addressed in this report.

1. What is the number of patients included in total?
2. What are the baseline characteristics of enrolled patients?
3. What was the most recent reported disease activity?
4. How many patients were treated with biologic agents?
5. What stop reasons are reported at the time of biological discontinuation?

Furthermore, we will provide an update about published and current research projects using IBDREAM data.

3. Methods

3.1 General information IBDREAM

In 2016, IBDREAM started with the prospective real-life data collection of IBD patients in five medical centers in the Netherlands: Radboud University Medical Center, Nijmegen, Medisch Spectrum Twente, Enschede, Onze Lieve Vrouwe Gasthuis, Amsterdam, Franciscus Gasthuis en Vlietland, Rotterdam, and Jeroen Bosch Ziekenhuis, Den Bosch. The registry follows the patient journey and contains integrated information on diagnosis, disease activity, therapy, laboratory results, quality of life and other outcomes over time. Patients are subsequently followed during the course of their chronic disease. This will allow for collection of data on long-term efficacy and safety of medication, with special interest in biologicals. As the regular patient care is followed and no additional treatments take place, there is no burden on the patient. Data collection by the IBDREAM registry is started after informed consent. In 2018 the *Dutch Health Care Inspectorate* (Dutch: *Inspectie voor gezondheidszorg*) reviewed and enthusiastically approved the IBDREAM registry in Medisch Spectrum Twente, underlining that the registry meets all the latest strict legal requirements.

3.2 Patients

The study design is a multi-center, prospective registry. From 2016 on, IBD patients treated with biologicals (such as infliximab, adalimumab, golimumab, ustekinumab, vedolizumab) or small molecule targeting therapies (tofacitinib) were included, and subsequently patients with other immunosuppressive therapies (like thiopurines, methotrexate, and 6-tioguanine) and now also non-immunosuppressives such as mesalamines were asked informed consent by their treating physician. Data collection is continued even after cessation of immunosuppressive or biological therapy. Inclusion started in May 2016 and in 2020, only 4 years later, already 3000 patients provided consent and were included.

3.3 Project group

The following hospitals participate in the IBDREAM project.

1. Radboud University Medical Centre, Nijmegen, Dr. F. Hoentjen
2. Medisch Spectrum Twente, Enschede, Dr. M. Russel
3. Onze Lieve Vrouwe Gasthuis, Amsterdam, Drs. J. Jansen
4. Franciscus Gasthuis en Vlietland, Rotterdam, Dr. R. West
5. Jeroen Bosch hospital, Den Bosch, Dr. T. Römkens

The committee consists of one gastroenterologist from every participating hospital. Furthermore, the daily management is in the hands of the above mentioned project managers, supported by drs. P. Thomas. Prof. Mart van der Laar serves as external advisers on behalf of the DREAM registries.

IBDREAM committee members:

Dr. Frank Hoentjen, Gastroenterologist Radboudumc Nijmegen: Chairman

Dr. Maurice Russel, Gastroenterologist MST Enschede: Treasurer

Drs. Jeroen Jansen, Gastroenterologist OLVG Amsterdam: Secretary

Dr. Rachel West, Gastroenterologist Franciscus Gasthuis en Vlietland Rotterdam: Board member

Dr. Tessa Römkens, Gastroenterologist JBZ Den Bosch: Board member

Drs. Pepijn Thomas, PhD candidate Radboudumc Nijmegen.

3.4 Support

This project is supported by an unrestricted grant from:

The Netherlands Organization for Health Research & Development: **ZonMw**

And is currently supported by:

And supported in the past by:

4. Methodology IBDREAM

4.1 Inclusion criteria

1. Diagnosis of IBD (Crohn's disease, ulcerative colitis or unclassified IBD) (according to the combination of clinical, endoscopic, histologic and radiologic criteria used as a gold standard) (1).
2. 18 years or older
3. Patient treated with biologic agents or small molecule targeting therapy (both biological-experienced and naïve patients):
    - Infliximab
    - Adalimumab
    - Golimumab
    - Vedolizumab
    - Ustekinumab
    - Tofacitinib
4. Patients treated with other immunosuppressive therapy:
    - Azathioprine
    - 6-Mercaptopurine
    - 6-Tioguanine
    - Methotrexate
    - Corticosteroids
5. Patients treatment with non-immunosuppressive agents:
    - Mesalamines
6. Signed informed consent by the patient for the use of medical information and health-related quality of life information.

4.2 Treatment

Although dosing occurs at the discretion of the attending gastroenterologist, in general, patients

start treatment according to national guidelines and label.

- Infliximab: 5 mg/kg every 8 weeks intravenous after loading doses at week 0, week 2 and week 6;
- Adalimumab: 40 mg per two weeks subcutaneous after loading doses at week 0 and week 2;
- Golimumab: 50 mg (< 80 kg) or 100 mg (> 80 kg) every 4 weeks after loading doses at week 0 and week 2;
- Vedolizumab: 300 mg every 8 weeks intravenous after loading doses at week 0, week 2, and week 6;
- Ustekinumab: 90 mg s.c. every 8-12 weeks after loading dose at week 0 (6 mg/kg IV).
- Tofacitinib: 5-10 mg oral twice daily after induction phase of 10 mg oral twice daily during 8 weeks;

All start and stop dates, doses, changes in doses or intervals, and reasons for changes have been registered. Dose escalations or tapering are registered.

4.3 Data management

4.3.1 Data collection

Login in the web-based environment is possible by both caregiver and patient. Consequently, added or updated information by the other party is accessible in real-time. Each caregiver, such as the gastroenterologist, IBD nurse and physician assistant have their own personal passwords to access the electronical system. Physicians and nurses can only access IBDREAM if their identity has been verified using their BIG registration number. Patients are provided their own passwords from their caregiver after signing informed consent.

After uploading the patient medical history, including co-morbidities, prior surgery and medication, follow-up is collected prospectively. Every outpatient visit, newly prescribed medication is updated. In addition, diagnostic results, clinical outcomes (Harvey Bradshaw Index(HBI)/ Simple Clinical Colitis Activity Index (SCCAI) and Physician Global Assessment (PGA)), and past events (adverse events, hospitalization, surgery) are updated. To capture the patient perspective, patients are asked to fill in questionnaires at least twice yearly, the results are discussed during the outpatient visits. These questionnaires capture quality of life, experienced disease control and influence of disease on work

and daily life (*for more details: see paragraph 3.4)*. All outcomes are presented in tables and visualized in graphs. In these graphs, different scores are shown over time, and information about the medication at time of the results is added.

The combination of clinician- and patient reported outcomes provides a perfect overview of the patient's current and past disease. Hospitals use this overview for multidisciplinary meetings.

Quality control

In 2018, a large proportion of the database has been reviewed for quality of data, showing a very high percentage of up-to-date patient files. This quality control is part of a standard check for inconsistencies. We strive to complete the data-sharing with the hospital files in the near future in order to apply single-data entry at the source.

4.3.2 Privacy and security measures

Strong security measures are in place in the Transparency in Healthcare (TiH) Online Monitoring Application (OMA) and database to ensure the safety of patients records. Access to the system is only possible via log-in codes and personal passwords, which must comply with a minimum level of complexity and which must be periodically renewed.

Anonymous patient records are stored in a secured environment that adheres to all available international guidelines, including the new Dutch privacy legislation (May 2018) 'Algemene verordening gegevensbescherming' which is based on security guidelines established by the European Union.

4.3.3 Data extraction

Researchers with specific IBDREAM accounts can download anonymous data to address specific research questions, only after approval by the IBDREAM regulatory board.

4.3.4 Detailed outcome measures

The assessments are performed during every visit. Not only the clinician-based outcomes (laboratory results, endoscopy reports, physician assessment) are reported, but we specifically aimed to capture the patient related outcomes (PROMs) as well. Disease activity is measured by inflammatory parameters, C-reactive protein (CRP) and fecal calprotectin (FCP), HBI/SCCAI and endoscopic mucosal healing rate. For measurement of disease activity, FCP is used. FCP is a granulocyte-derived protein

measured in the stool and is a non-invasive, cheap and extensively studied biomarker used in inflammatory bowel disease (IBD) and correlates with clinical and endoscopic disease activity. The Harvey Bradshaw Index (HBI) is a validated and easy-to-use disease activity index containing 5 items of which 4 items are patient-reported. The Simple Clinical Colitis Activity Index (SCCAI) is the activity index used for ulcerative colitis.

We aimed to incorporate the use of PROMs in daily practice. Therefore we use validated questionnaires in order to evaluate the selected outcome measures. Several questionnaires are filled out by patients to monitor health related quality of life of IBD patients: the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), the Inflammatory Bowel Disease control questionnaire, the EuroQol 5D-3L and Work Productivity and Activity Impairment (WPAI) to assess the impact of IBD on work and daily activities. Recently, we validated the IBD-control using IBDREAM as a reliable tool to capture disease control from a patient's perspective.[1] Data of all participating centers are collected during every patient visit and monitored following the guidelines of the participating hospitals. Furthermore, information about all medication use and adverse events is collected.

Medication:

Type of medication, start date, dose and frequency, stop date, change of dose or change of medication is described. The reason for changing dose or stopping medication is registered. When the stopping reason is classified as side effect, those side effects are described in further detail.

Adverse events:

Patients can report experienced adverse events using their own IBDREAM account. Every visit possible adverse events are discussed with the patient as well. The treating physician assesses the reported adverse events to be either unrelated, possibly, probably has the possibility to or very likely related to the treatment with the medication. All adverse events are categorized as minor, mild, major or life threatening.

Complications and hospital admissions

Complications like stenosis, perforation, extra-intestinal manifestations, fistulas, osteoporosis and thrombosis are reported. Furthermore, all hospital admissions and visits to the emergency

[1] *De Jong, M. et al. Cross-cultural translation and validation of the IBD-control questionnaire in the Netherlands a patient reported outcome measure in Inflammatory Bowel Disease. (Veldhoven 2018) [abstract]*

department are documented.

5. IBDREAM Updates 2019-2020 and new goals

IBDream aims to be further developed every year. Several achievements in the last year have been accomplished:

1) The use of the Health Monitor™ is incorporated in the care for a subset of patients during regular visits to the nurses in two hospitals (MST and JBZ). The health monitor is a tool developed by Professor Sjaak Bloem to assess and quantify the general health as experienced by patients, as well as coping and acceptance of their chronic disease. This tool can determine the personal needs of a patient, and this leads to a recommendation about the most needed intervention to improve the patient's general health. This not only includes medical treatment, but also paramedic professional tools like psychological and dietary consults.

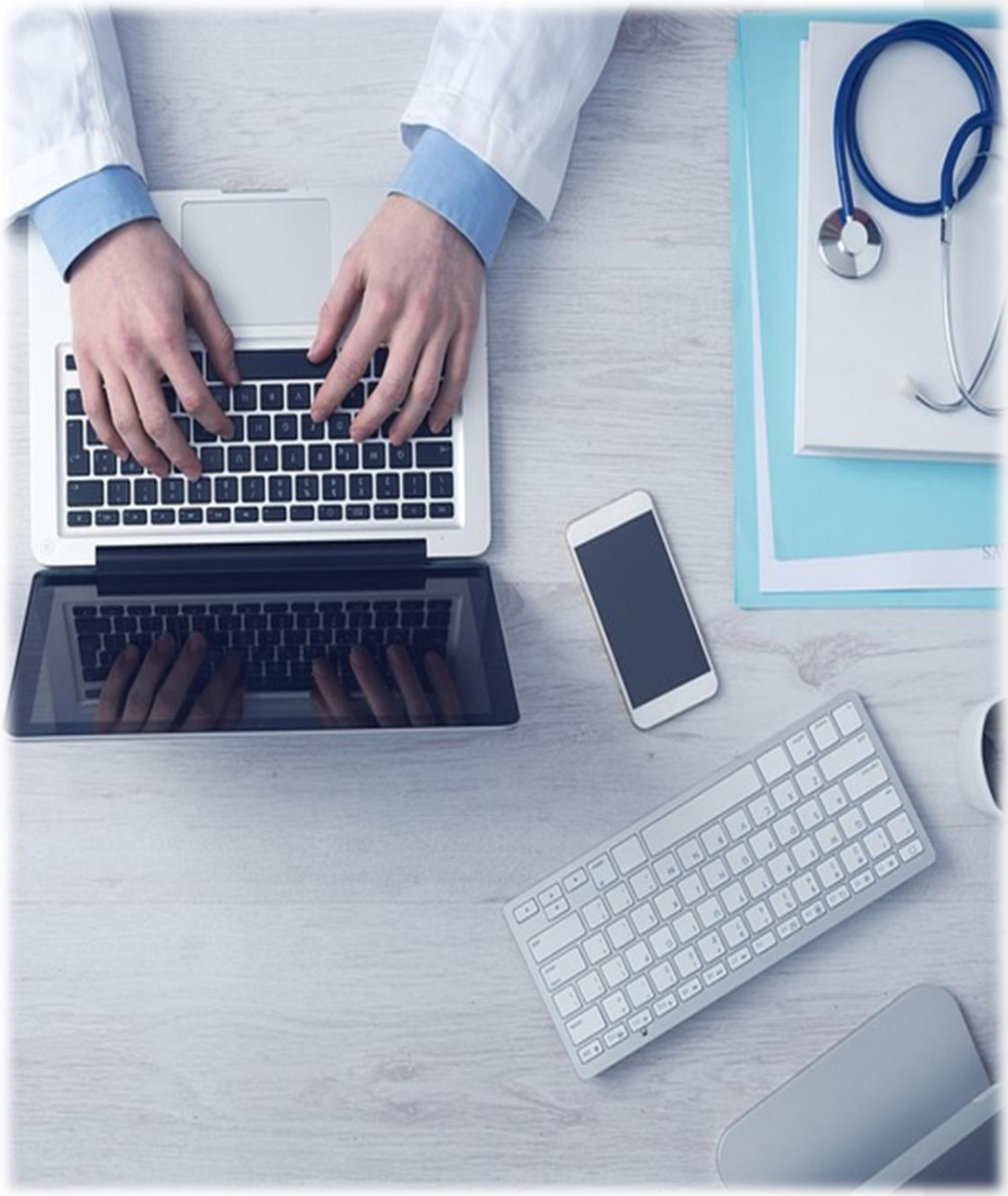
2) The module 'benchmarking' is now available in IBDream. Real-life data is shown for certain characteristics or outcomes that are entered in the IBDREAM database, providing more insight in the IBD population per hospital. These data can be compared between participating hospital and reveal insights in the outcomes of the provided care. For example insight in how many patients use a certain biologic drug, the number of patients in clinical remission, smoking, and corticosteroids use can be compared.

3) Regarding patient empowerment: Communication in IBDream between patients and healthcare providers is possible through a question and answer. This is still in the early phases of the use. The goal is to further develop the communication options and improve effectiveness of communication and completely replace the use of regular mailing.

4) A reminder service has been implemented in IBDream which sends patients a reminder to complete questionnaires before outpatient visits. This will improve the use of PROMs in daily care and provide more insight on patients' perspective on disease control and other subjective matters that would normally not be addressed.

5) The link between the hospital electronical patient files and IBDREAM have been established at the Radboudumc (2018) allowing automatic and safe data sharing. This reduces the administrative burden and realizes an completeness of the IBDREAM database. Currently, we are evaluating the possibilities to establish a similar link between IBDREAM and the electronic healthcare records in the other participating hospitals.

Future plans include optimization of these new features in IBDREAM, minimizing the administrative burden, stimulating communication through IBDREAM and improve the user friendliness. Currently, we are focussed on further improving patient engagement and empowerment. We are constructing an option for communication between caregiver and patients through the use of a chat function. Furthermore, we want optimise user-friendliness on short term by redefining the lay out for better use on phone and tablets. Long term goals are the development of an app. Moreover, we want to establish a feedback system that will provide patients information about their current disease status and what actions should be taken. Ultimately, this should lead to reduction of outpatients visits.



6. Results

6.1 Number of patients in the IBDREAM register

6.1.1 Inclusion

In August 2020, 1878 patients with Crohn's disease, 1060 patients with ulcerative colitis, and 64 IBD-unclassified were included in the IBDREAM registry. After inclusion 76 patients stopped participation due to several reasons including relocation, patient's decision and death. Figure 1 shows the total number of included IBD patients, 3002 patients in total analyzed at 19 August 2020.

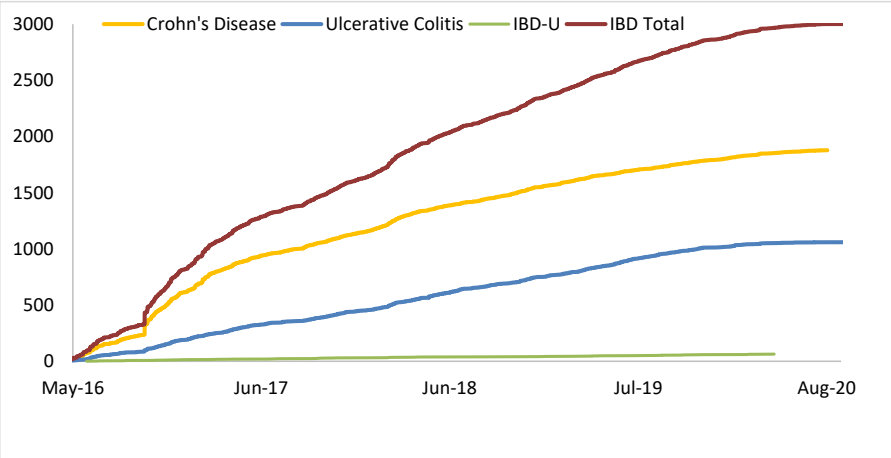


Figure 1. Inclusion patients per IBD diagnosis

6.1.2 Baseline characteristics

Table 2 shows the baseline characteristics of the 3002 enrolled patients. The majority of patients has Crohn's Disease. A total of 1880 (63%) patients ever used a biological and at the time of data extraction 1446 (48%) patients used a biological or small molecule therapy.

Characteristic	IBDREAM N = 3002
Sex, Female N (%)	1687 (56)
Current age in years, mean ± SD	45.3 ± 15.7
Disease	
Crohn's disease, n (%)	1878 (63)
Ulcerative colitis, n (%)	1060 (35)
Unclassified IBD, n (%)	64 (2)
Current biological use, total patients	1446 (100)
Infliximab, n (%)	685 (47)
Adalimumab, n (%)	413 (29)
Vedolizumab, n (%)	191 (13)
Ustekinumab, n (%)	129 (9)
Tofacitinib, n (%)	19 (1)
Golimumab, n (%)	9 (<1)

Table 1. Baseline characteristics

6.1.3 Clinical assessments

Overall, the majority of patients included in IBDREAM were in remission (n=1071, 72%) according to the physician global assessment reported during the most recent visit in the past year ranging from August 2019 to August 2020. Eighteen percent of the IBD patients showed mild disease activity (n=270) and 6% moderate disease activity (n=132). Only 1% of the patients (n=18) were assessed as severe disease activity during their last hospital contact (figure 4). The disease activity was estimated by the physician global assessment, which is measured during every visit to outpatient clinics.

Clinical disease activity for CD is documented by using the HBI score and for UC and IBD-U the SCCAI score are used. HBI scores <5 and SCCAI scores <2 are considered clinical remission. For CD patients 83% (n=892) were in remission and for UC patients 74% (n=448) were in remission based on the most recent reported score between August 2019 and August 2020 (Figure 5).

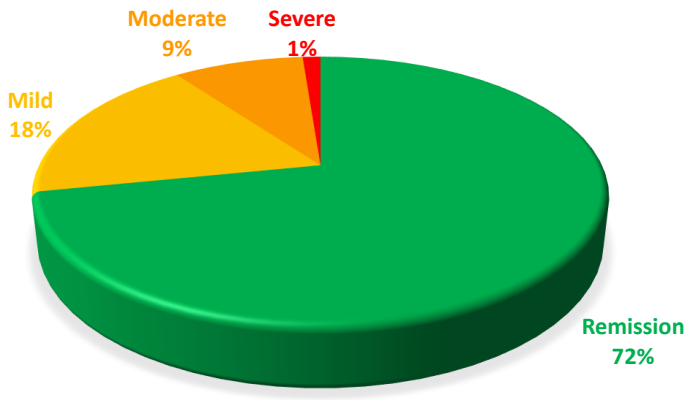


Figure 2. *Disease activity of the IBDREAM IBD population in 2019-2020 according to the most recent physician global assessment.*

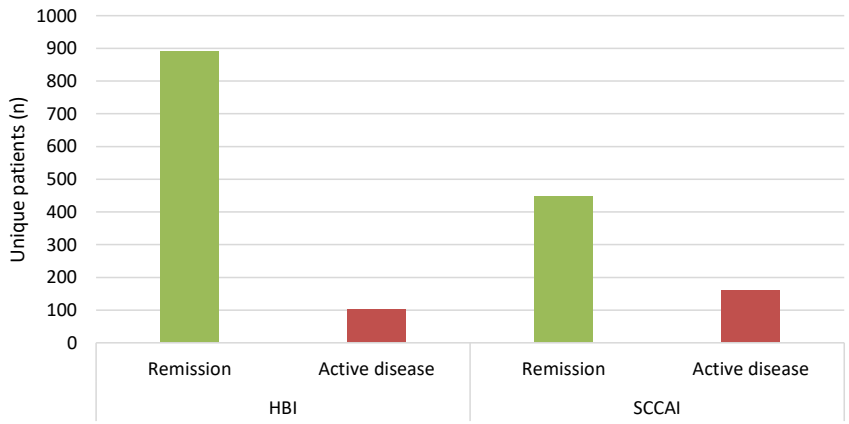


Figure 3. *Most recent clinical disease activity between august 2019 and august 2020 based on the HBI score (total unique patients n=1069) and the SCCAI score (total unique patients n=608).*

6.1.4 Biologic agents use

Figures 7 and 8 show the cumulative number of patients that ever started on a biological stratified for Crohn's disease and ulcerative colitis, respectively.

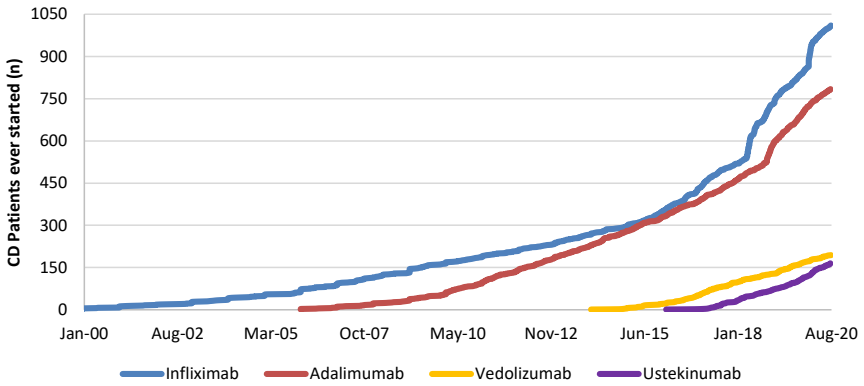


Figure 7. Timeline showing the cumulative number of patients with Crohn's disease included in IBDREAM who ever started with different medication (infliximab, adalimumab, vedolizumab, ustekinumab).

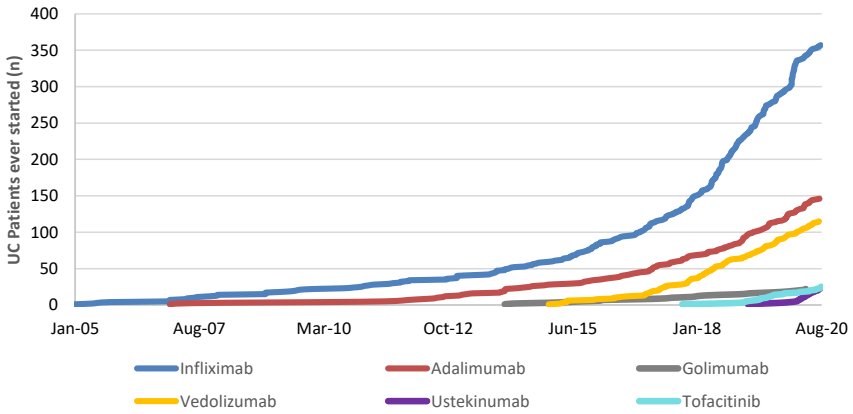


Figure 8. Timeline showing the cumulative number of patients with ulcerative colitis included in IBDREAM who ever started with different medication (infliximab, adalimumab, golimumab, vedolizumab, ustekinumab and tofacitinib).

6.1.5 Stopping reasons biologic agents

Of all patients who started infliximab and are included in IBDREAM, 836 patients discontinued infliximab. The number of patients that stopped adalimumab, vedolizumab and ustekinumab are 602, 137 and 67 respectively. Of note, presence of antidrug antibodies were documented in the stop reason for 64 (4.5%) patients that used infliximab, 48 (5.0%) patients that used adalimumab and 1 (0.3%) patient that used vedolizumab.

Stop reason		Infliximab (n=836)	Adalimumab (n=602)	Vedolizumab (n=137)	Ustekinumab (n=67)
Insufficient response	N (%)	296 (35)	254 (42)	94 (69)	45 (67)
Adverse events	N (%)	200 (24)	118 (20)	19 (14)	14 (21)
Insufficient response + adverse events	N (%)	31 (4)	19 (3)	2 (3)	2 (3)
Other[+]	N (%)	199 (22)	154 (26)	19 (14)	5 (8)
Remission	N (%)	109 (13)	56 (9)	1 (<1)	0

Table 2. *Stopping reasons for several biologic drugs.*
[+]*Other reasons include: pregnancy, patient request, logistical adjustments, travelling, only induction therapy, unknown.*

6.1.6 Current and recent research projects

The first publication regarding the use and safety of biologicals in elderly IBD patients was published in 2020 and a second research project involving patient-reported disease control is now under review. In addition several research projects are being conducted. Below we will discuss some of these projects.

Cross-cultural translation and validation of the IBD-control questionnaire in the Netherlands: a patient-reported outcome measure in Inflammatory Bowel Disease.

Background

Patient Reported Outcome Measures (PROMs) are promising tools in inflammatory bowel disease (IBD) care. The 'IBD-control' is a short IBD-specific questionnaire measuring disease control from the patient's perspective. It was successfully validated and implemented in clinical practice in the United Kingdom and its use is recommended by the International Consortium for Health Outcomes Measurement (ICHOM) even though this questionnaire has not yet been validated in other countries or languages. To this end we aimed to cross-culturally translate and adapt the IBD-control for use in Dutch patients and assess its reliability, validity and responsiveness in a multicentre prospective IBD cohort.

IBD-Control

The IBD-control is a short disease-specific questionnaire for patients with CD and UC [1]. It measures the overall disease control during the last two weeks and consists of five sections, including 13 categorical items and a visual analogue scale (VAS) ranging from 0 (worst possible disease control) to 100 (best possible disease control). Sections 1 and 3 are related to disease control during the past 2 weeks and consist of 8 questions: the IBD-control-8. The IBD-Control-8-subscore ranges from 0 points (worst control) to 16 (best control).

Results

The main finding in our cohort including 998 IBD patients is that the translated version of the IBD-control had a good internal consistency, reliability, construct validity, responsiveness, and discriminant ability. In addition, the questionnaire was able to identify IBD patients with quiescent disease.

The ROC showed an optimal cut-off point of IBD-control-8 subscore of 14 points (UC: sensitivity 77.1%, specificity 83.1%; CD sensitivity 76.1% specificity 80.4%). The AUC was 0.86 for both UC and CD (Figure 2). Of the 37 patients who scored 14 or higher but did not meet our 'quiescent' criteria, no patient needed treatment escalation (i.e. prednisone, start of new medication, surgery) or was hospitalised. Reasons for not meeting the quiescent criteria while scoring >14 on the IBD-control included mild disease according to the PGA (n=28), a HBI>4 (n=5), a short IBDQ score <53 (n=3), or reporting of worsening of bowel symptoms in the past 2 weeks (n=1).

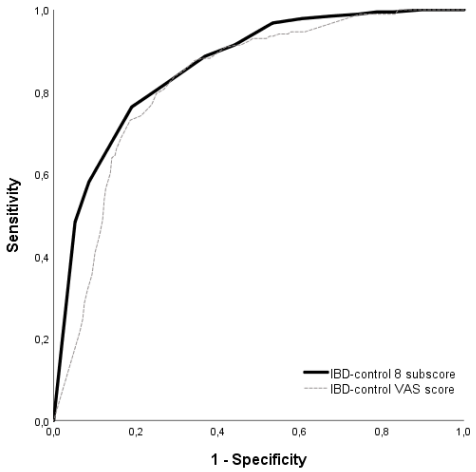


Figure 2. IBD-control as a screening tool for detecting quiescent patients.
Receiver operating characteristics (ROC) curves for the IBD-control-8 subscore and the IBD-control VAS score, using strict pre-specified criteria for the quiescent disease state. AUC for IBD-control-8 subscore was 0.86.

Conclusion

In conclusion, in a large prospective multicentre cohort, the Dutch version of the IBD-control showed to be a reliable and valid tool to capture the patient's perspective on disease control. Moreover, using a cut-off value of 14 points on the IBD-control-8 subscore, the questionnaire was able to identify patients with quiescent disease, allowing it to be a potential and rapid tool for identifying IBD patients with good disease control in regular IBD care in the Netherlands.

de Jong ME, et al (2020) Increased Discontinuation Rates of Anti-TNF Therapy in Elderly Inflammatory Bowel Disease Patients. JCC. 2020. 14 (7): 888-895. *doi.org/10.1093/ecco-jcc/jjaa012*

Background

Since the general risk of infections and malignancies increases with age, the safety of anti-TNF therapy in elderly IBD patients is debated and may affect treatment choices in this specific age group. The aim of this study was to compare the safety and the treatment failure rates of the first anti-TNF therapy in IBD patients between specific age groups [<40, 40–59, and ≥60 years]. Second, we aimed to identify baseline variables associated with anti-TNF treatment failure due to AEs or lack of effectiveness.

Methods

We compared the treatment failure rates of the first treatment with anti-TNF therapy between different age groups in a large multicentre IBD cohort. Risk factors for discontinuation due to AEs or lack of effectiveness were identified.

For this study, data on demographics, medical history, concomitant IBD medication use at start of anti-TNF, reasons for discontinuation, and serious adverse events [SAEs] were extracted from IBDREAM. SAEs included hospital admission due to disease activity or side effects, infections, allergic reactions, IBD-related surgery, or malignancies. Data were retrieved from IBDREAM on August 1, 2018. Follow-up was defined as years from start of first anti-TNF agent until date of data extraction.

Results

A total of 895 IBD patients with a history of at least one anti-TNF agent were identified. We analysed the probability of treatment failure by a competing-risks regression analysis, with discontinuation due to AEs or lack of effectiveness as the outcome of interest and discontinuation due to remission as a competing event. Overall, age was associated with a higher discontinuation rate [**p** = 0.03 Figure 1], with a subhazard rate [SHR] for discontinuation of 1.23 (95% confidence interval [CI] 0.96–1.56) in the 40–59 group and 1.46 [95% CI 0.94–2.20] in the ≥60 group, both compared with the <40 group.

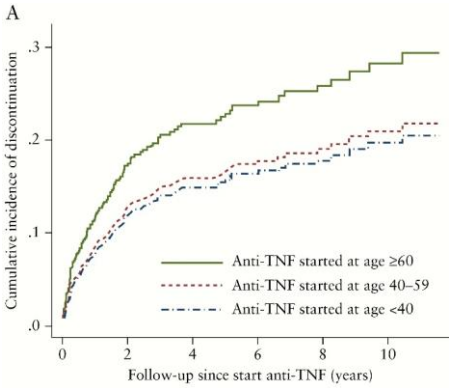


Figure 1. Cumulative incidence function of discontinuation due to adverse events in patients who started anti- tumour necrosis factor [TNF] at age <40/40–59/≥60 as estimated by the competing risk regression model.

Conclusion

In this large multicentre cohort, we found that patients aged ≥60 years starting a first anti-TNF agent are at increased risk of stopping anti-TNF due to AEs or lack of effectiveness, compared with patients <60 years. Elderly IBD patients had a higher SAE and serious infection rate. These findings support tight monitoring and timely management of [S]AEs when starting anti-TNF in elderly IBD patients.

Work productivity and activity impairment in IBD patients starting a biological.

Background

Inflammatory bowel disease (IBD) is a chronic and debilitating disease of the intestines, and typically occurs during the young adulthood. Work disability rates among Dutch patients with Crohn's disease and ulcerative colitis are higher than among the general population, 18.3% and 9.5% versus 6.6% respectively, reflecting the impact of IBD on work. Treatment of IBD is aimed at inducing clinical remission and mucosal healing, and increasing the quality of life of patients. Several phase III studies showed that starting adalimumab resulted in improvement of work productivity and activity impairment (WPAI) as assessed by the WPAI questionnaire. Improvements of absenteeism and presenteeism in these studies ranged from 5% to 9.8% and 19% to 25.7%, respectively. However, due to the strict selection criteria for these studies, we do not know if this reflects the effect in patients in daily practice.

Aim: The primary aim of this study was to evaluate the effect of introduction of biological treatment on the work productivity and activity impairment using the WPAI questionnaire, in patients with active inflammatory bowel disease.

Definitions

Absenteeism = percentage of hours absent from work due to IBD.

Presenteeism = percentage of impact of IBD during worked hours.

Total work productivity impairment (TWPI) = combination of absenteeism and presenteeism.

Total activity impairment (TAI)= percentage of impact of IBD on daily activities.

Preliminary results

In total 199 patients were included in the study (53% male, 57% Crohn's disease, median age 39 years [IQR 27 – 51]. Of these patients, 89% completed the baseline questionnaire and 6% was aged ≥67 years. For patients that completed the baseline questionnaire and were aged <67 years, 123 (70%) patients were employed.

Regarding all patients at baseline, median absenteeism was 0% [IQR 0 - 40] and the median TWPI was 50% [IQR 20-80]. In 47.5% of patients, work productivity impairment was experienced for more than 1 month. If work productivity impairment was experienced, 69% of patients reported IBD to be the main cause.

Met opmerkingen [HF1]: Klopt dit wel??

Met opmerkingen [TP2]: Eens dat dit een vreemd getal lijkt maar gaat om de mediaan. Een groot deel (dus minstens 50%) mist geen uren vanwege IBD klachten bij baseline; hier zitten ook patiënten zonder klinische klachten bij. Het grootste deel ervaart echter wel hinder op werk zoals weerspiegelt door de Total Work Productivity Impairment (TWPI)
Ik heb niet direct gekeken hoeveel % ten minste 1 uur werk per week mist.

Employed patients that completed both baseline questionnaire and at week 13 (n=78), median TWPI decreased from 50% [IQR 12-85] to 30% [IQR 10-60] (p=0.005). When comparing baseline questionnaire and week 26 (n=63), median TWPI decreased from 50% [IQR 20-80] to 20% [IQR 0-67] (p=0.017). Grouped percentages for the TWPI are shown in Figure 1.

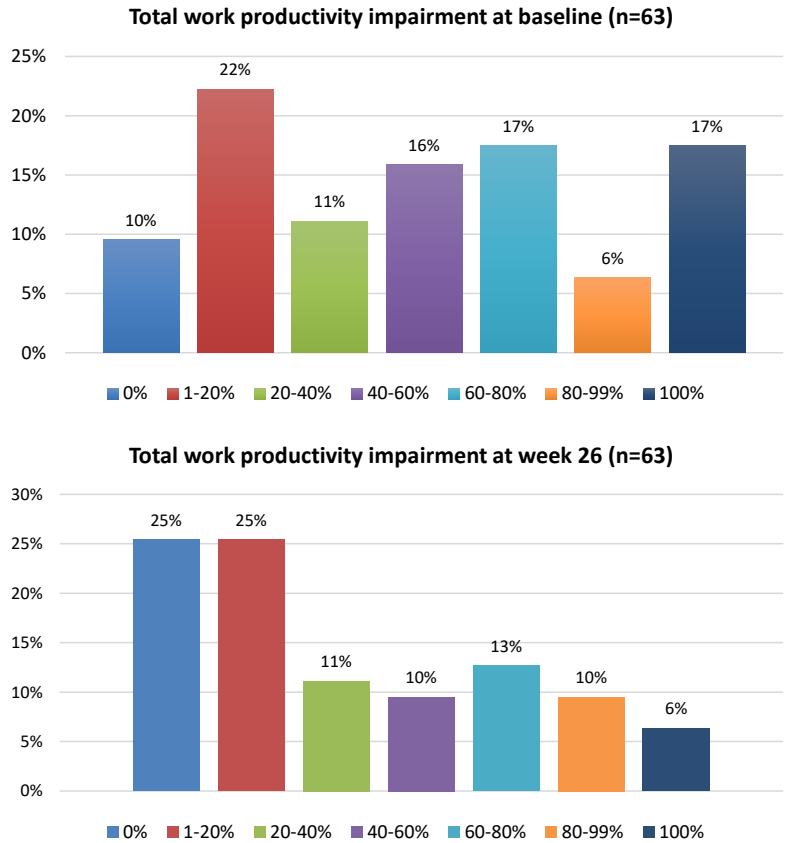


Figure 1. Grouped total work productivity impairment at baseline and week 26 for employed patients that completed questionnaires at both time points.

Table 1. Domains of the Work Productivity and Activity Impairment Questionnaires. TWPI = total work productivity impairment. TAI = total activity impairment.

	Baseline		Week 13		Week 26		Week 39	
	Median (IQR)	N	Median (IQR)	N	Median (IQR)	N	Median (IQR)	N
Absenteeism, in %	0 (0 – 40)	120	0 (0 – 17)	82	0 (0 – 24)	67	0 (0 – 0)	37
Presenteesim, in %	30 (10 -60)	100	20 (10 – 40)	74	20 (0 – 50)	64	20 (0 – 20)	35
TWPI, in %	50 (20 - 80)	120	30 (10 – 65)	82	28 (0 – 67)	67	20 (0 - 45)	37
TAI, in %	60 (30 – 80)	187	30 (12.5 – 60)	140	40 (10 -60)	128	25 (0 – 60)	62

Inflammatory bowel disease (IBD) patients frequently report adverse events during biologic therapy: a multicentre, prospective, patient-reported pharmacovigilance monitoring system.

Background

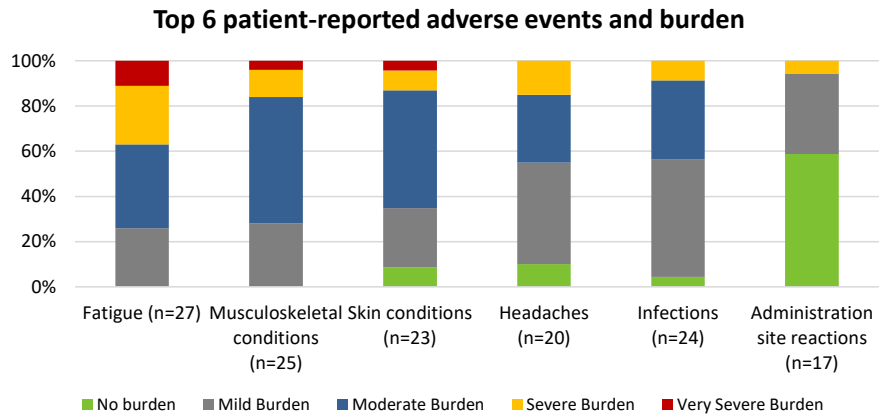
The use of biologicals has improved the treatment of inflammatory bowel disease but only limited data is available on the extent and burden of ADRs in daily practice, especially from a patient's perspective.

Aim: This study aimed to systematically assess patient-reported adverse events (prAEs) during biological therapy in IBD patients.

Methods This multicentre, prospective, event monitoring study enrolled adult Crohn's disease (CD) and ulcerative colitis (UC) patients treated with a biological between 1 January 2017 and 31 December 2018. Patients completed bimonthly comprehensive web-based questionnaires regarding description of biological induced prAEs, follow-up of previous prAEs, experienced burden of the prAE using a five-point Likert scale, contact with a healthcare provider and therapeutic consequences due to the AE. The author assessed the relationship between prAE and biological based on the description. Subsequently, healthcare provider(HCP)-reported ADRs (hcpADR) were extracted from the electronic healthcare for the participants. All prAEs, prADRs and hcpADRs were MedDRA coded.

Results

In total, 182 patients in 4 centres (female 51%, mean (standard deviation) age 42.2 (14.2) years, CD 77%) were included and completed 728 questionnaires. At baseline, 59% of patients used infliximab, 30% adalimumab, 9% vedolizumab and 1% ustekinumab, while 49% used combination therapy with an immunomodulator. Fifty percent of participants reported at least one AE with a total of 239 unique AEs. Fatigue (n=26) and headache (n=20) resulted in the highest burden and a correlation in time with the administration of the biologic was described in 56% and 85% respectively. In four cases changes in biological prescription were made. Out of 239 prAEs, 115 were considered possibly related to the biological. For these patients, HCPs reported 119 hcpADRs. Agreement between patient- and HCP-reported ADRs was 13% for the six most frequent reported ADRs.



Conclusion

IBD patients often reported AEs during the use of a biological in which fatigue and arthralgia resulted in the highest burden. For specific prAEs, patients were able relate this to the biological to a good degree. However, many prAEs were not considered related to the biological which may affect the compliance. In addition, the gap between HCP- and patient-reported ADRs shows that more awareness of the patient's ADR perception is needed during outpatient visits. This may ultimately lead to increased adherence and improve quality of life.

Dr. Frank Hoentjen, Gastroenterologist, Radboudumc Nijmegen
Dr. Maurice Russel, Gastroenterologist, Medisch Spectrum Twente Enschede
Drs. Jeroen Jansen, Gastroenterologist, Onze Lieve Vrouwe Gasthuis Amsterdam
Dr. Rachel West, Gastroenterologist, Franciscus Gasthuis en Vlietland Rotterdam
Dr. Tessa Römkens, Gastroenterologist, Jeroen Bosch Ziekenhuis, Den Bosch

www.ibdream.nl
www.dreamregistry.nl