IBDREAM ANNUAL REPORT 2021

Real-Time Registry of Inflammatory Bowel Disease Patients

IBDREAM registry of IBD patients

The IBDREAM registry responds to the call of the Dutch IBD Patients Association (Crohn & Colitis NL) for more personalised patient care to improve quality of life for people suffering this chronic disease. In addition, the IBDREAM registry is designed to monitor and aim for value-based healthcare which is a core item of modern-day healthcare, with the goal to realise optimal health outcomes and patient experiences. Initiated in 2014 and launched online in 2016, the IBDREAM registry is a major step towards meeting the increasing need for country-wide, systematic treatment and management of IBD patients. By using available real-time data on patient care and quality of life, IBDREAM is contributing not only to improving patient wellbeing but also to rationalising the ever-spiralling healthcare costs.

We are pleased to present this report which briefly sets out the IBDREAM activities in 2020 and 2021.

Content

IBDREAM

Organization

IBDREAM steering committee

Chair	Dr. Tessa Römkens, Gastroenterologist, Jeroen Bosch Ziekenhuis, 's-Hertogenbosch
Vice chair	Dr. Rachel West, Gastroenterologist Franciscus Gasthuis & Vlietland, Rotterdam
Secretary	Drs. Jeroen Jansen, Gastroenterologist Onze Lieve Vrouwe Gasthuis, Amsterdam
Treasurer	Dr. Maurice Russel, Gastroenterologist Medisch Spectrum Twente, Enschede
Member	Dr. Peter Mensink, Gastroenterologist, Medisch Spectrum Twente, Enschede
Member	Dr. Marjolijn Duijvestein, Gastroenterologist, Radboud University Medical Centre, Nijmegen
Member	Dr. Pepijn Thomas, Radboud University Medical Centre, Nijmegen

Hospitals participating in IBDREAM

Jeroen Bosch Hospital, Den Bosch; Dr. T. Römkens

Franciscus Gasthuis en Vlietland, Rotterdam: Dr. R. West

Radboudumc, Nijmegen: Dr. M. Duijvestein, Dr. P. Thomas

Medisch Spectrum Twente, Enschede: Dr. M. Russel, Dr. P. Mensink

Onze Lieve Vrouwe Gasthuis, Amsterdam: Drs. J. Jansen.

Financial support

Biogen Netherlands*

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** Support from 2019 onward*

Inflammatory bowel disease

Impacting quality of life

Approximately 90,000 people in the Netherlands have been diagnosed with inflammatory bowel disease (IBD) and the disease prevalence is rising. Often occurring in the second or third decade of life, this chronic disease has considerable impact on patient quality of life, requiring hospitalisation and resulting in work disability. Symptoms are wide ranging and may include diarrhoea, rectal blood loss, abdominal pain, vomiting, weight loss, and anaemia. IBD can lead to complications, such as fistulas, abscesses and even colorectal cancer, as well as extra-intestinal symptoms, such as fatigue, arthritis, and skin disorders.

Although the disease pathogenesis is largely unknown, IBD is considered to originate from an overly aggressive mucosal immune response to luminal bacteria in the genetically susceptible. The disease is diagnosed based on colonoscopy and histology.

IBDREAM: more patient involvement, better healthcare

With the prime goal of improving quality of patient care, IBDREAM is a web-based portal designed specifically for IBD patients to provide two-way feedback between patient and healthcare providers. In addition, data on patient long-term follow-up are used by healthcare providers in assessing and improving the safety and efficacy of IBD treatment.

IBDREAM contains real-time data provided by the patients themselves (via patient-reported outcomes measures (PROMs)) and their healthcare providers, displayed in a comprehensive dashboard layout. These real-time data include disease diagnosis, activity and treatment, laboratory results, co-morbidities, prior surgery, impact on patient-reported quality of life and other outcomes. After initial patient registration, data relating to disease treatment and management are collected and registered during regular patient care and follow-up with healthcare providers.

Since 2015 when the registry was online and open for inclusion, IBDREAM has included real-time data on IBD patients registered in five medical centres in the Netherlands: Radboud University Medical Center, Nijmegen, Medisch Spectrum Twente, Enschede, Onze Lieve Vrouwe Gasthuis, Amsterdam, Franciscus Gasthuis & Vlietland, Rotterdam, and Jeroen Bosch Ziekenhuis, Den Bosch.

Patient involvement

IBDREAM enables patients to participate in their disease management and treatment decision-making. The portal provides easy and direct contact for patients with their healthcare providers to receive answers to specific questions and to provide input for their next consultation.

Patients are encouraged to be pro-active in their disease treatment and management by completing and uploading their responses to especially designed questionnaires known as PROMs, increasing patient involvement and engagement.

Accredited and uniform data collection

In 2018, an audit of IBDREAM in Medisch Spectrum Twente by the *Dutch Healthcare Inspectorate* (*Inspectie voor gezondheidszorg*) confirmed that the registry satisfies the strict legal requirements for patient data. Initially, IBD patients on biologicals were invited to participate in IBDREAM and gradually patients with less complex IBD disease course and patients on other medication (immunomodulators and mesalamines) were included. At the end of 2021, nearly 3,500 patients had given their consent for inclusion in the registry. Our aim is to establish an automatic data transfer system between the electronic patient files in the hospital and the IBDREAM registry and enable single-data entry at the source for IBD patients in hospitals. The data collected in the registry can be used in daily clinical practice to support clinical decision-making, reduce variation, and improve outcomes important to IBD. In addition, the real-life data collected in this registry can be used to answer important research questions.

Data collected in IBDREAM are those recommended by the International Consortium for Health Outcomes Measurement (ICHOM). In 2021, IBDREAM was updated according to the outcomes that have recently been defined by the “uitkomst gerichte zorg” programme of the Dutch ministry of Health. This is in line with the requirement for uniform data collection on IBD in order to compare and improve treatment outcomes country wide.

IBDREAM and the database are fully compatible with other health applications for example electronic patient records, enabling linkage to other systems in primary and secondary medical care in the Netherlands. This is an essential step towards a universal personal health environment (*persoonlijke gezondheidsomgeving*) giving patients access to their complete medical file. Furthermore, integrating patient files in primary and secondary care enables greater patient involvement as well as reducing administrative burdens on healthcare providers. In 2023 patients will also be able to access the registry by using a app, this will make the registry more accessible and easier to use.

Better healthcare

IBDREAM is a vital resource for improving patient empowerment through the use of patient-reported outcomes in daily practice for clinicians and hospital gastroenterology departments. The registry contributes to a greater transparency in IBD treatment and care and to more effectiveness and safety of medical therapies especially biologicals and small molecules, as well as for benchmarking with other hospitals. These are also the main goals set by the Dutch ministry of health in the “uitkomst gerichte zorg” programme.

The information collected in IBDREAM is useful for a wide range of stakeholders with the main goal of improving quality of IBD care and healthcare outcomes. IBD patients can access their complete medical file, this way patients gain greater control over decisions and actions affecting their health. Healthcare providers get a better insight in the overall wellbeing of their patients, and they can use the information for shared decision making and for

benchmarking with other healthcare providers. The information can also be used to provide policy makers and insurance companies insight in quality of care and healthcare costs. IBDREAM is also becoming increasingly important in improving healthcare and research in the Netherlands that is increasingly depending on compatible data for national and international comparison.

Longitudinal data collected in IBDREAM on patients throughout their disease activity and treatment will give insight into direct and indirect costs, and into the short- and long-term effectiveness of treatment strategies and thus to cost-effectiveness of IBD care. These insights are becoming increasingly important as promising new but expensive treatment options are shifting healthcare costs from in-hospital care to medication costs.

Activities report 2020-2021

By the end of 2021, IBDREAM included 2056 patients with Crohn's disease, 1258 patients with ulcerative colitis, and 72 unclassified IBD. In the same period, 126 patients had withdrawn from the registry for various reasons including change of residence, patient decision, or death. In December 2021, 3,386 patients were registered in IBDREAM (Figure 1).

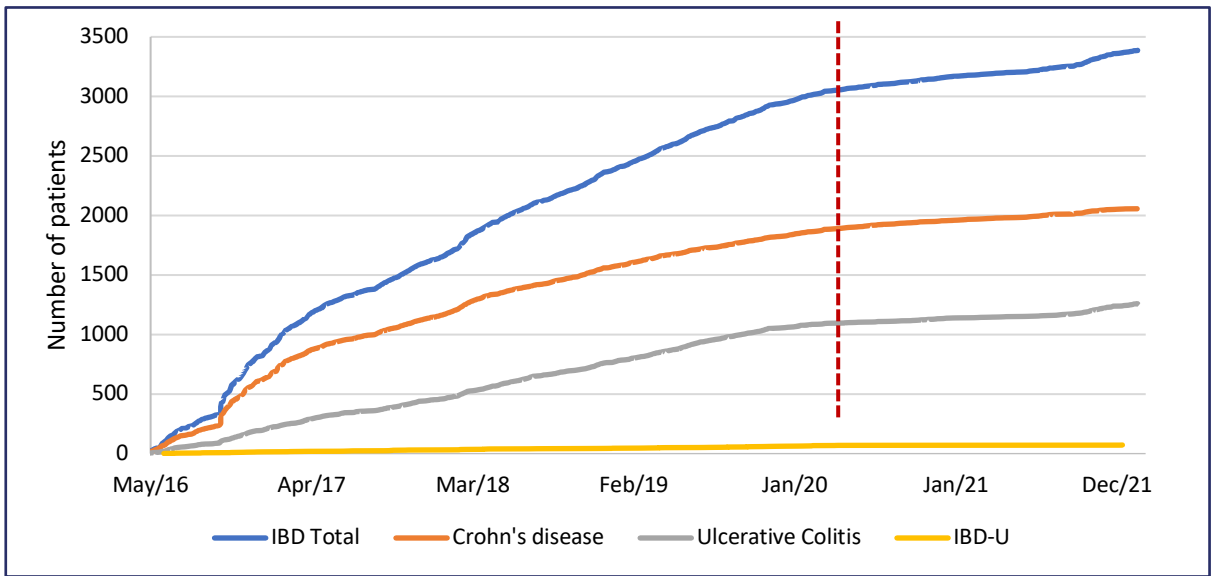

Figure 1. *Number of inflammatory bowel disease patients in the IBDREAM registry. The broken red line indicates the introduction of COVID-19 restrictions in the Netherlands (March 2020). IBD-U = inflammatory bowel disease-unclassified*

In 2021 61% of patients registered in IBDREAM had Crohn's disease (61%). Most IBD patients in IBDREAM (2,095, 62%) had ever been treated with a biological agent, and 1,446 patients (48%) were actively on a biological agent or tofacitinib.

Table 1. Characteristics of the active patients registered in IBDREAM in 2021.

Characteristics	IBDREAM N = 3386
Sex, female N (%)	1893 (56)
Current age in years, mean ± SD	45.7 ± 15.8
Prospective follow-up since IBDREAM inclusion (years, median IQR)	4.0 (2.8 – 5.1)
Disease	
Crohn's disease, n (%)	2056 (61)
Ulcerative colitis, n (%)	1258 (37)
Unclassified IBD, n (%)	72 (2)
Current biological/tofactinib use, total patients	1509
Infliximab, n (%)	660 (44)
Adalimumab, n (%)	425 (28)
Ustekinumab, n (%)	199 (13)
Vedolizumab, n (%)	191 (13)
Tofacitinib, n (%)	24 (2)
Golimumab, n (%)	10 (<1)

N = number; SD = standard deviation; IQR = interquartile range

Clinical assessment

As registered in IBDREAM, 1,028 patients had a documented physician assessment of IBD in 2021. Most of these patients were in remission as assessed by their treating physician (n=782, 76%), 18% had mild disease (n=190), 5% moderate disease activity (n=54), and only 0.1% severe disease (n=2), see Figure 2. However, as physician assessments tend to be subjective making comparing data difficult, clinical disease activity indices are used to standardise these assessments. The Harvey Bradshaw Index (HBI) score is used for Crohn's disease; and simple clinical colitis activity index (SCCAI) score for ulcerative colitis and unclassified IBD. HBI scores <5 and SCCAI scores <3 are considered clinical remission. Based on these scores, 86% of Crohn's disease patients (n=734) and 78% of ulcerative colitis (n=400) were in clinical remission in 2021 (Figure 2).

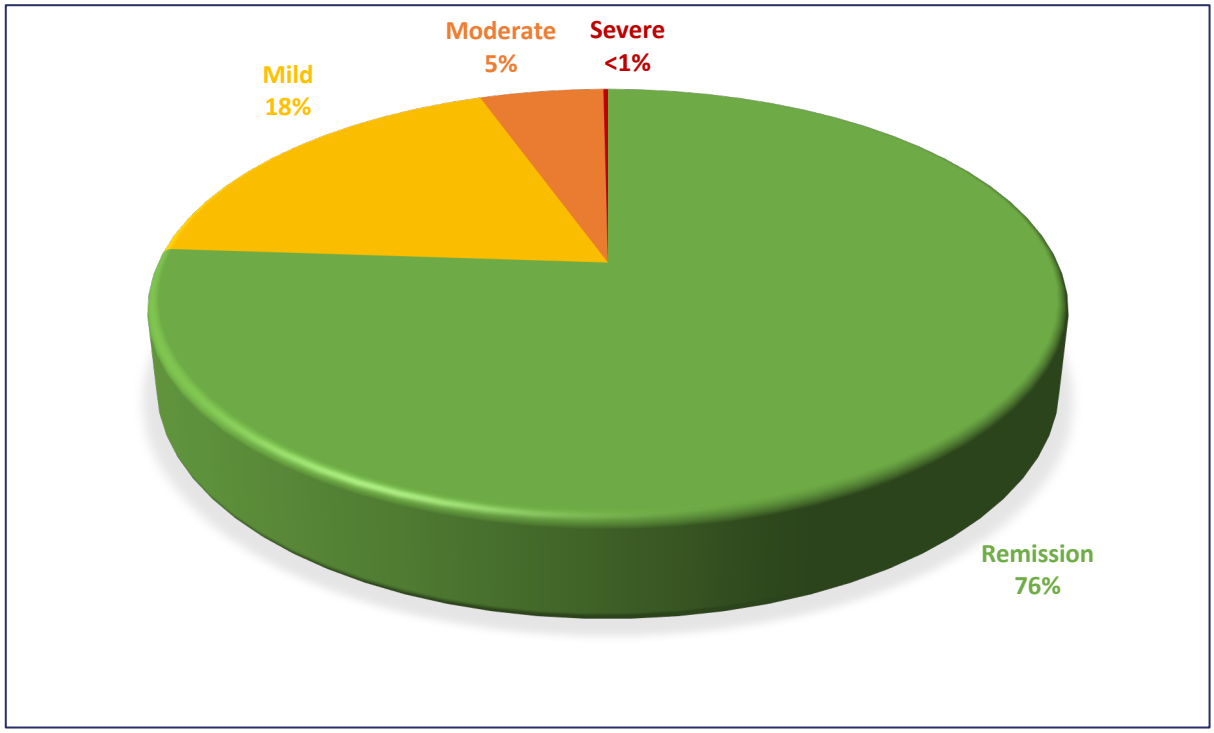

Figure 2. *Disease activity of patients registered in IBDREAM in 2021 based on recent physician assessment.*

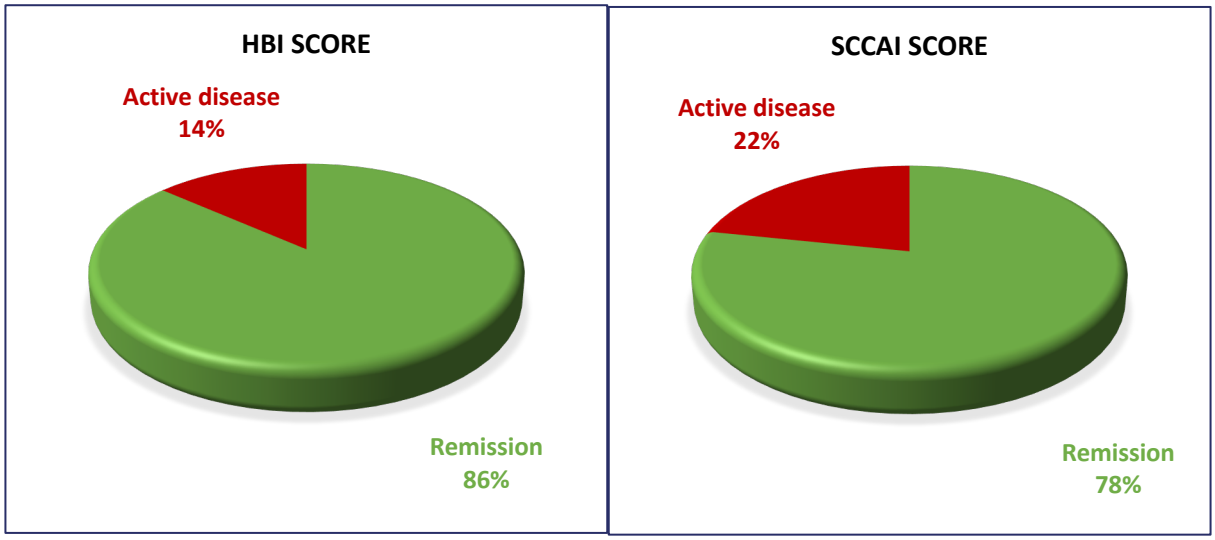

Figure 3. *Clinical disease activity in IBDREAM registered patients in 2021 based on the HBI score and SCCAI score. HBI = Harvey Bradshaw Index; SCCAI = Simple Clinical Colitis Activity Index*

Biological therapies

The cumulative numbers of Crohn's disease, ulcerative colitis and inflammatory bowel disease-unclassified patients on a biological therapy or tofacitinib are shown in Figures 4 and 5, respectively.

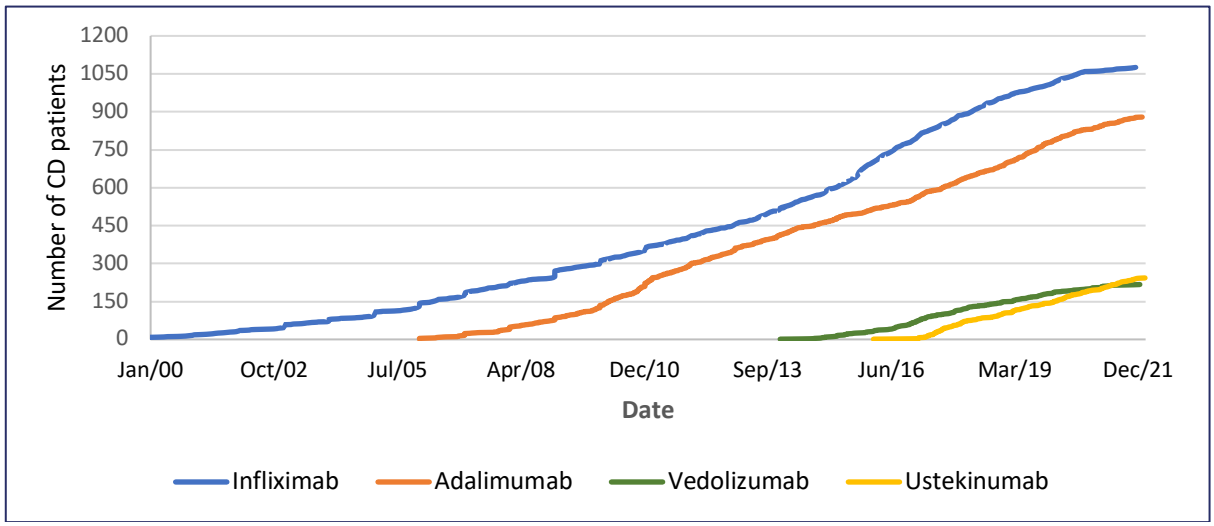

Figure 4. *Cumulative number of Crohn's disease patients in IBDREAM on biological therapies: infliximab, adalimumab, vedolizumab and ustekinumab. In total, 1528 unique Crohn's disease patients have used at least one biological therapy. CD = Crohn's disease*

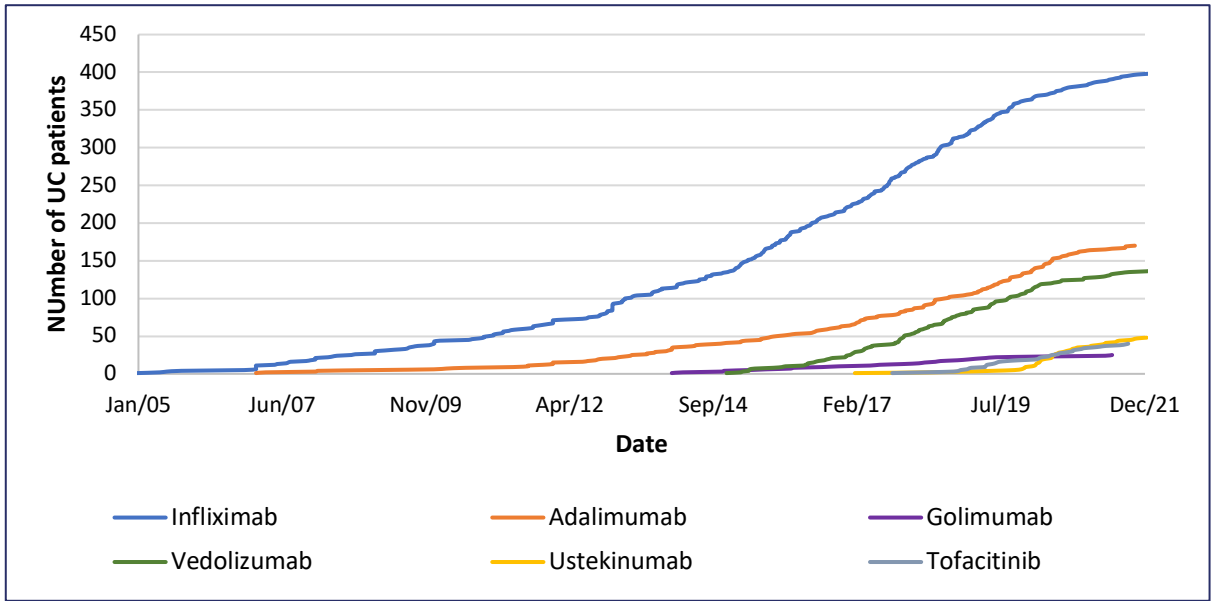

Figure 5. *Cumulative number of ulcerative colitis patients in IBDREAM on biological therapies or small molecule therapy: infliximab, adalimumab, golimumab, vedolizumab, ustekinumab or tofacitinib. In total, 529 unique ulcerative colitis patients have used at least one biological therapy or small molecule therapy. UC = ulcerative colitis*

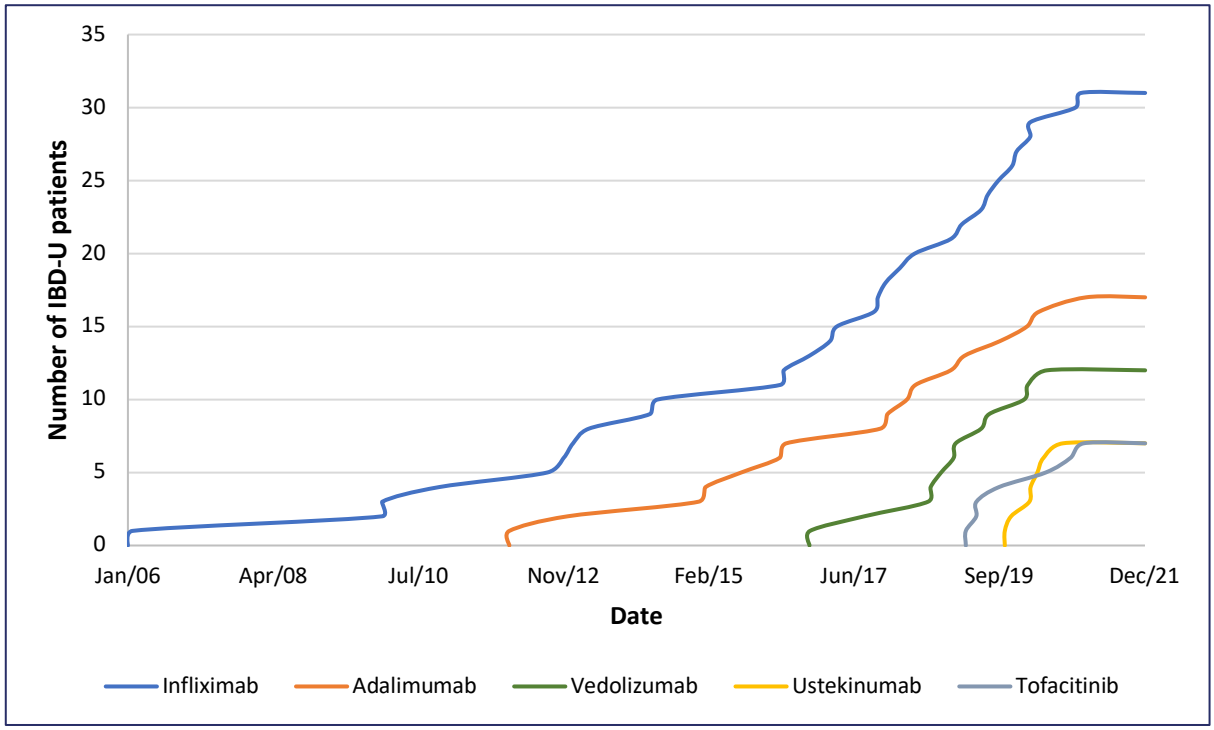

Figure 6. *Cumulative number of inflammatory bowel disease-unclassified patients in IBDREAM on biological therapies or small molecule therapy: infliximab, adalimumab, golimumab, vedolizumab, ustekinumab or tofacitinib. In total, 38 unique inflammatory bowel disease-unclassified patients have used at least one biological therapy or small molecule therapy. IBD-U = inflammatory bowel disease-unclassified.*

Data on medication use is captured both retrospectively and prospectively in IBDREAM. Retrospective data includes all data prior to inclusion in IBDREAM, whereas prospective data are the data that have been recorded since participation in IBDREAM. As registered in IBDREAM in the period between 2016 and 2021, 1,532 patients received at least one dose of infliximab; 1076 patients adalimumab; 367 patients vedolizumab; 298 patients ustekinumab, 48 patients tofacitinib and 31 patients golimumab. Antidrug antibodies were reported as a reason for discontinuing treatment in 71 patients on infliximab (4.6%) and 59 (5.5%) patients on adalimumab. No patients on vedolizumab and ustekinumab reported antidrug antibodies as a reason for discontinuing treatment.

Table 2. *Reasons for discontinuing treatment of biological therapies and tofacitinib*

Reason for discontinuation		Infliximab (n=968)	Adalimumab (n=707)	Vedolizumab (n=186)	Ustekinumab (n=102)	Tofacitinib (n=25)	Golimumab (n=19)
Insufficient response	N (%)	326 (34)	293 (41)	126 (68)	68 (67)	16 (64)	13 (68)
Adverse events	N (%)	207 (21)	120 (17)	22 (12))	13 (13)	4 (16)	1 (5)
Insufficient response + adverse events	N (%)	31 (3)	21 (3)	2 (1)	3 (3)	1 (4)	1 (5)
Other⁺	N (%)	291 (30)	215 (30)	32 (17)	18 (18)	4 (16)	4 (21)
Remission	N (%)	113 (12)	58 (8)	4 (2)	0 (0)	0 (0)	0 (0)

⁺Other reasons include pregnancy, patient request, logistical adjustments, travelling, only induction dosing of the therapy and no maintenance dosing and cases in which no stop reason was described.

Technical improvements to IBDREAM

COVID-19 has had a detrimental impact on healthcare worldwide and on the recruitment of new patients to IBDREAM as well as data entry by healthcare providers and patients.

In this period, several technical updates were made to increase IBDREAM effectiveness and efficiency. One of these updates is the introduction of Health Monitor™ which was implemented in daily practice in two participating hospitals, and a third hospital is currently preparing to integrate this tool in IBD care. Heath monitor is a cross-disease segmentation model developed by Bloem & Stalpers that discriminates patients based on disease acceptance and perceived control. Segmentation of patients based on psychological determinants of subjective health may provide new methods for personalized care. In addition, a technical update was added to enable patients and healthcare providers to receive an alert when a message has been posted in IBDREAM. Through this update, two-way communication via IBDREAM is possible which enables both patients and healthcare providers to use one portal for digital communication rather than different communication platforms and unsecured mailing.

In 2018, a link was established between the electronic healthcare records and IBDREAM in the Radboudumc for automatic and safe data sharing. This link automatically transfers data to IBDREAM making our portal more comprehensive and reducing the administrative burden of data input. Currently, similar links between IBDREAM and the electronic healthcare records are been explored in other participating hospitals.

Future plans

Plans for the (near) future are directed to optimising IBDREAM by extending the portal to more hospitals. Currently, collaboration is being explored with other IBD platforms such as Luscii, a digital healthcare platform for monitoring patients remotely. We performed a pilot study in two IBDREAM participating hospitals and more projects will follow. In addition, there is a collaboration with *myIBDcoach*. In 2022 a consortium agreement will be made-up and signed by all involved parties. There are several collaborative projects that were initiated in 2022 and beyond. The first project was in collaboration with Crohn&Colitis.nl concerning lifestyle and IBD. The aim of this project was to find out which lifestyle interventions patients find important using questionnaires and after this a webinar was organised for patients. With the results of these questionnaires and the input of patients after the webinar research questions will be formulated.

A second project is the FRESH (Federated data driven decision support for Crohn's disease). The aim of this project is to create a federated learning network for data of CD patients throughout the Netherlands, enabling us to further build on the knowledge of large IBD registries while ensuring that the outcomes of FRESH will be clinically applicable to all the Netherlands and include the same clinical and patient-reported outcomes so that the outcomes can be used for benchmarking.

In 2022, the final dataset as proposed by a nationwide steering committee coordinated by the ministry of Health, in the "uitkomst gerichte zorg" programme was accomplished, and this dataset will be implemented in IBDREAM. IBDREAM will also participate in a project focusing on the implementation and use of the dataset in daily clinical practice.

IBDREAM will also focus on telemonitoring, monitoring patients remotely. This will provide patients control over their own care and prevent unnecessary check-ups and hospitalisations.

New software partner: Brightfish

As from 2022 IBDREAM will be working with a new software partner, Brightfish (www.brightfish.com). Brightfish is experienced in engaging patients remotely with PROMs and integrating surveys into daily clinic practice. One of the main aims is to integrate IBDREAM and the different electronic patient record systems in the different hospitals. Brightfish will also make the use of the registry more flexible and user friendly on mobile phones and tablets by establishing an IBDREAM application. This will make data registration for patients a lot easier. These changes will reduce the burden of data registration for patients and healthcare providers and ensure that complete and reliable data will be available. The Brightfish Dashboard will illustrate the outcomes clearly and show how the patient is doing compared to the previous measurement(s) in table or graph form. The healthcare provider can review the data before and during a consultation and can look at the values together with the patient.

Appendixes

Appendix I: Overview of IBDREAM

Patient criteria

All patients registered in IBDREAM are 18 years of age or older with a diagnosis of Crohn's disease, ulcerative colitis or IBD-unclassified. The diagnosis is made according to the golden standard of a combination of clinical, endoscopic, histologic and radiological criteria. All patients included in the registry have given written consent for the use of their medical information and health-related quality of life information.

Medication - Treatment

The patients in the registry are being or have been treated with the following medications:

- Biologic agents or small molecule targeting therapy (biological-experienced and biological-naive patients) including Infliximab, Adalimumab, Golimumab, Vedolizumab, Ustekinumab, Tofacitinib, Filgotinib, Upadacitinib, Ozanimod and all new medication that will be registered for IBD;
- Other immunosuppressive therapy, including Azathioprine, 6-Mercaptopurine, 6-Tioguanine, Methotrexate, Corticosteroids or Budesonide;
- Non-immunosuppressive agents including Mesalamines.

Data on patient medication registered in IBDREAM include type of medication, dose, frequency, start date, stop date, change in medication, and reasons for discontinuing medication, and adverse drug reactions.

While the medication and dosage are decided by the attending gastroenterologist, patients start treatment according to national guidelines.

Data input

IBDREAM contains comprehensive, real-time data on each patient registered in the system. These data include input by healthcare providers, gastroenterologists, IBD nurses and physician assistants and patients.

Healthcare input

After initial input of the patient's medical history, including co-morbidities, prior surgery and medication, the patent record is updated after each outpatient visit. Data include clinical assessment by the healthcare provider at each clinical visit, clinician-based outcome, such as laboratory results and endoscopy reports. In addition, diagnostic results, clinical outcomes (Harvey Bradshaw Index (HBI)/ Simple Clinical Colitis Activity Index (SCCAI) and Physician Global Assessment (PGA), and events (adverse drug reactions, hospitalisation, surgery) are regularly updated.

Complications are reported, such as stenosis, perforation, extra-intestinal manifestations, fistulas, osteoporosis and thrombosis. All hospital admissions and visits to the emergency department are documented. The treating physician assesses whether adverse drug reactions reported are related to medication treatment, and also reports adverse drug reactions which may be categorised as minor, mild, major or life threatening.

Patient input

To ensure patient perspective and involvement in their treatment, patients are asked to complete questionnaires at least twice a year which are discussed with their healthcare providers at subsequent outpatient visits. These questionnaires focus on quality of life, experienced disease control and effect of disease on work and daily life. Patient-reported adverse drug reactions are discussed during visits with their healthcare providers.

To capture patient-reported outcomes in 2017-2021, IBD patients were asked to complete the following questionnaires:

- Short Inflammatory Bowel Disease Questionnaire (SIBDQ)
- Inflammatory Bowel Disease control questionnaire (IBD-Control)
- EuroQol 5D-5L (EQ5D-3L)
- Work Productivity and Activity Impairment (WPAI) to assess the impact of IBD on work and daily activities.

At the end of 2021, a steering committee of public health proposed a new dataset ("uitkomst gerichte zorg") to capture a more complete overview of different patient-reported outcomes including multiple domains on quality of life, health status, disease activity and work. In line with this dataset, we will ask IBD patients to complete the following questionnaires starting in 2023:

- Monitoring IBD At Home (MIAH) questionnaire to assess patient-reported disease activity
- Short Inflammatory Bowel Disease Questionnaire (SIBDQ) to assess disease-specific patient-reported quality of life
- Inflammatory Bowel Disease control (IBD-Control) questionnaire to assess patient-reported disease control
- Hospital Anxiety and Depression Scale (HADS) questionnaire to assess patient-reported scoring on anxiety and depression
- PROMIS Short form for fatigue, social functioning to assess patient-reported social functioning and fatigue
- Separate questions on incontinence, numerical rating scale for fatigue

- Work Productivity and Activity Impairment (WPAI) to assess the impact of IBD on patient-reported working and daily activities
- EuroQoL 5D-5L (EQ5D-5L) to assess generic patient-reported quality of life
- Health-Monitor to assess patient-perceived disease acceptance and disease control

Privacy and security measures

Strict measures on the Transparency in Healthcare (TiH) Online Monitoring Application (OMA) and database ensure the security and safety of patients records. IBDREAM is only accessible with log-in codes and personal passwords based on verified identity, such as their BIG registration (public register for Professions in Individual Health Care). Healthcare providers provide consenting patients with access codes.

Patient records are anonymised and stored in a secure environment in compliance with international guidelines, including the Dutch privacy legislation (May 2018) *Algemene verordening gegevensbescherming* based on EU security guidelines.

In the near future IBDREAM will change to a different software/hosting provider named Brightfish. This company has all the warranted safety certificates to host and secure our database, in compliance with the strict regulations on data storage.

Data extraction

A comprehensive dashboard with relevant data for patient and healthcare providers is displayed after logging in into the web-based portal of IBDREAM. The dashboard includes graphs on the course of disease activity and patient-reported outcomes scores over time, current and previous medical treatment, disease characteristics, adverse events and an easy-to-use communication chat box.

Appendix II: Publications in 2020/2021

The anonymised data in the IBDREAM registry are collected and analysed and used to further develop and validate the IBDREAM registry, specifically with regard to patient-reported outcome measures (PROMs), and safety monitoring and effectiveness of treatment strategies.

Abstracts of papers published in 2020 and 2021 are presented in this appendix.

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

de Jong ME[1], et al. on behalf of the IBDREAM registry. Scand J Gastroenterol. 2021;56:155-161.
[1]Radboud University Medical Centre, Nijmegen, The Netherlands.

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).

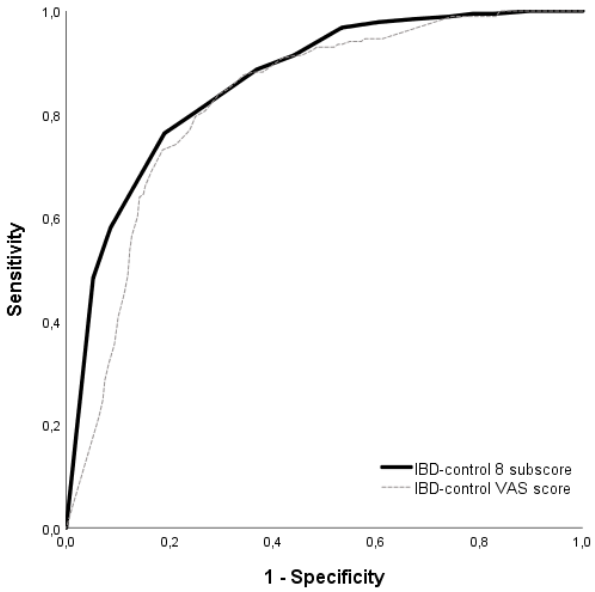

Figure 1. *IBD-control as a screening tool for detecting quiescent patients. Receiver operating characteristics (ROC) curves for the IBD-control-8 subscore and the IBD-control VAS score, using strict pre-specified criteria for the quiescent disease state. AUC for IBD-control-8 subscore was 0.86.*

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.

Increased Discontinuation Rates of Anti-TNF Therapy in Elderly Inflammatory Bowel Disease Patients

de Jong ME[1], et al. on behalf of the IBDREAM registry. J Crohns Colitis. 2020;14:888-895.
[1]Radboud University Medical Centre, Nijmegen, The Netherlands.

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.

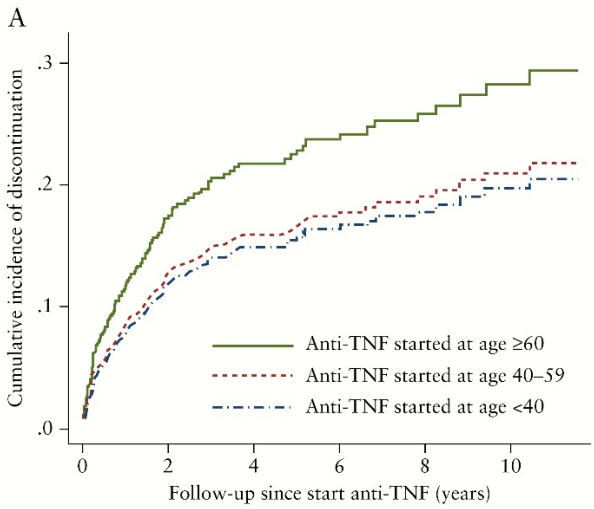

Figure 1. *Cumulative incidence function of discontinuation due to adverse events in patients who started anti- tumour necrosis factor [TNF] at age <40/40–59/≥60 as estimated by the competing risk regression model.*

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.

Impact of biological therapies and tofacitinib on real-world work impairment in Inflammatory Bowel Disease patients: a prospective study

Thomas PWA[1], et al. on behalf of the IBDREAM registry Accepted for publication in Inflammatory Bowel Diseases.
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Background
There are limited real-world data on the change in total work impairment (TWI) in biological-treated inflammatory bowel disease (IBD) patients. This study aimed to evaluate the real-world effects of initiating biological therapy or tofacitinib on change in TWI in IBD patients.

Methods
This multicentre prospective cohort study enrolled IBD patients who started treatment with biological therapy or tofacitinib. Subjects completed the work productivity and activity impairment (WPAI) questionnaire and short inflammatory bowel disease questionnaire at therapy initiation and at week 26. TWI comprises working hours missed due to sick leave and impact of disease during working hours (range 0-100%). Clinical disease activity was assessed using the Harvey Bradshaw Index and Simple Clinical Colitis Activity Index (SCCAI).

Results
We included 137 IBD patients for analyses (median age 38 years, 58% Crohn's disease (CD). The median baseline TWI was 50% and decreased by a median 10%-points after 26 weeks. Patients with continued biological therapy or tofacitinib use, clinical disease activity at baseline and clinical response or remission at week 26 showed a greater median TWI reduction (22%-points) than the remaining study patients (7%-points); p=0.014. Ulcerative colitis (UC) and IBD-unclassified (IBD-U) patients showed a greater median TWI reduction (26%-points) than CD patients (6%-points); p=0.041. Correlations were observed between decrease in TWI and decrease in SCCAI, decrease in fatigue and increase in quality of life.

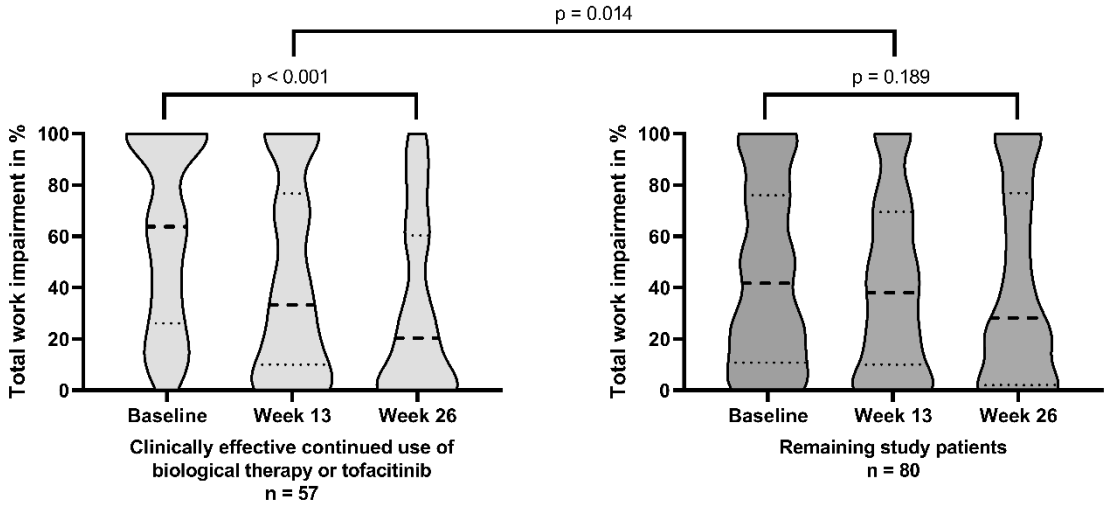

Figure 1. *Violin plots for total work impairment stratified for patients with clinical disease activity at baseline (Harvey Bradshaw Index (HBI) ≥5 or Simple Clinical Colitis Activity Index (SCCAI) ≥3) and clinical response (HBI reduction ≥3 or SCCAI reduction ≥2) or clinical remission (HBI<5 or SCCAI <3) at week 26, and continued use of the of biological therapy or tofacitinib at week 26 (n=57) compared to the remaining patients in the study population (n=80). The thick dotted line represents the median value and the thin dotted lines represent the 25th and 75th percentiles.*

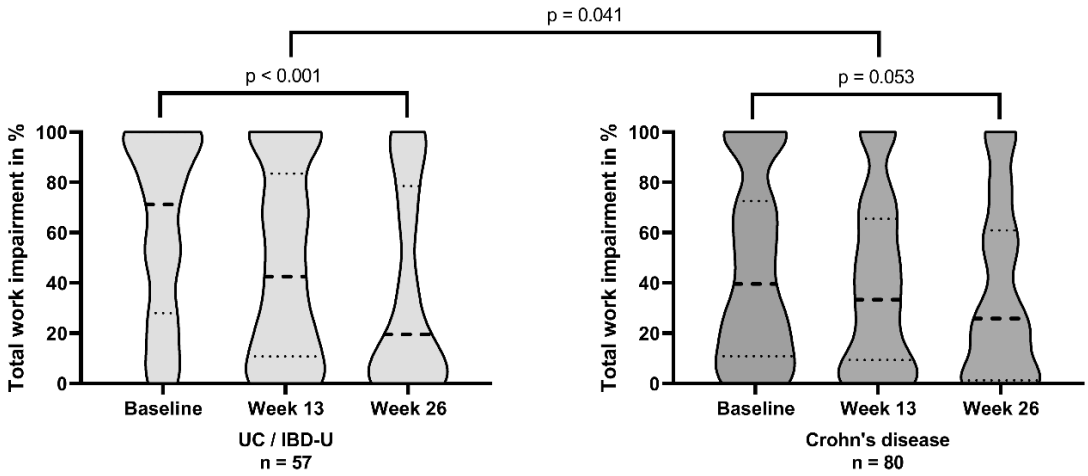

Figure 2. *Violin plots for total work impairment stratified for patients diagnosed with ulcerative colitis and inflammatory bowel disease-unclassified (n=57) versus Crohn's disease (n=80). The thick dotted line represents the median value and the thin dotted lines represent the 25th and 75th percentiles. UC = ulcerative colitis; IBD-U = inflammatory bowel disease-unclassified.*

Conclusion

Work impairment in IBD patients decreased following biological therapy or tofacitinib initiation. Patients achieving clinical remission or response showed the greatest improvement, especially UC and IBD-U patients.

Discrepancy between patient- and healthcare provider-reported adverse drug reactions in inflammatory bowel disease patients on biological therapy

Thomas PWA[1], et al. on behalf of the IBDREAM registry. United European Gastroenterol J. 2021;9:919-928.
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Background
Only limited data is available on the extent and burden of adverse drug reactions (ADRs) to biological therapy in inflammatory bowel disease (IBD) patients in daily practice, especially from a patient's perspective.

Objective
The aim of this study was to systematically assess patient-reported ADRs during biological therapy in IBD patients and compare these with healthcare provider (HCP)-reported ADRs.

Methods
This multicentre, prospective, event monitoring study enrolled biological-treated IBD patients. Patients completed bimonthly comprehensive web-based questionnaires regarding description of biological induced ADRs, follow-up of previous ADRs and experienced burden of the ADR using a five-point Likert scale. The relationship between patient-reported ADRs and biological was assessed. HCP-reported ADRs were extracted from the electronic healthcare records.

Results
In total, 182 patients (female 51%, mean age 42.2 (standard deviation 14.2) years, Crohn's disease 77%) were included and completed 728 questionnaires. At baseline, 60% of patients used infliximab, 30% adalimumab, 9% vedolizumab and 1% ustekinumab. Fifty percent of participants reported at least one ADR with a total of 239 unique ADRs. Fatigue (n=26) and headache (n=20) resulted in the highest burden and a correlation in time with the administration of the biological was described in 56% and 85% respectively. Out of 239 ADRs, 115 were considered biological-related. HCPs reported 119 ADRs. Agreement between patient-reported ADRs and HCP-reported ADRs was only 13%.

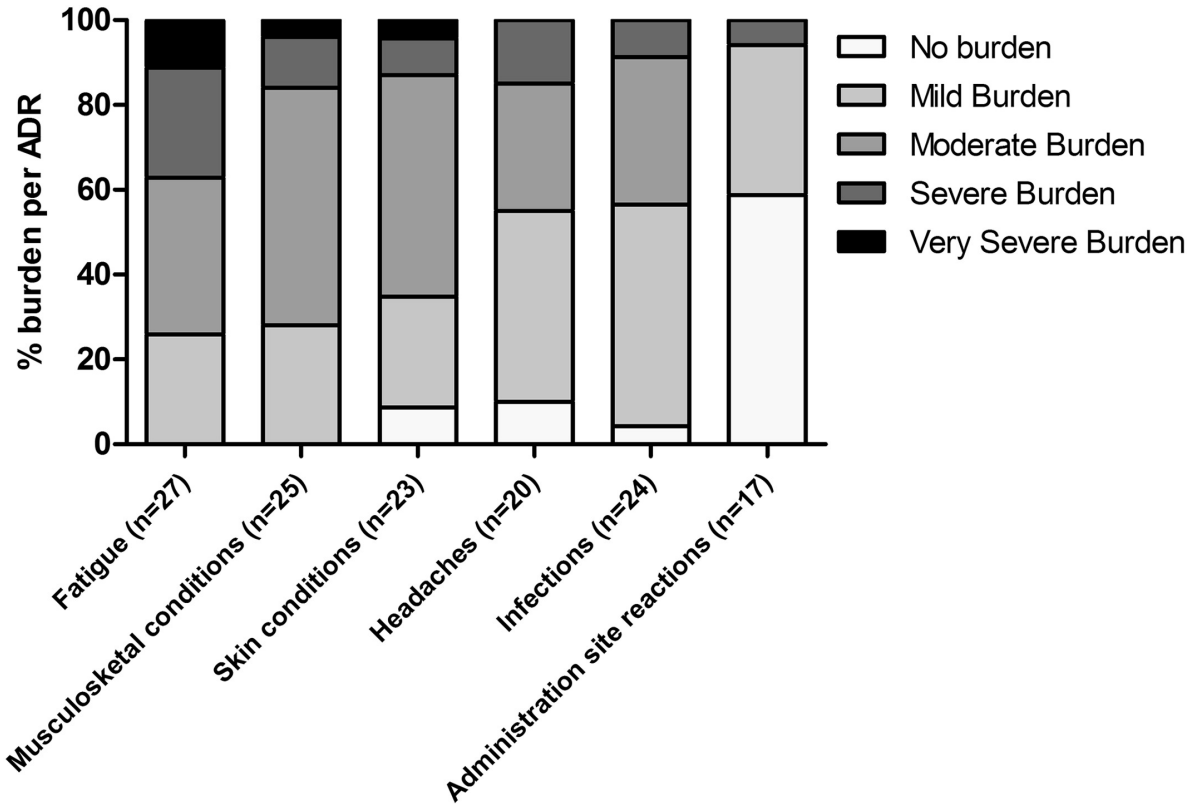

Figure 1. *Top six patient-reported adverse drug reactions with patient-reported burden.*

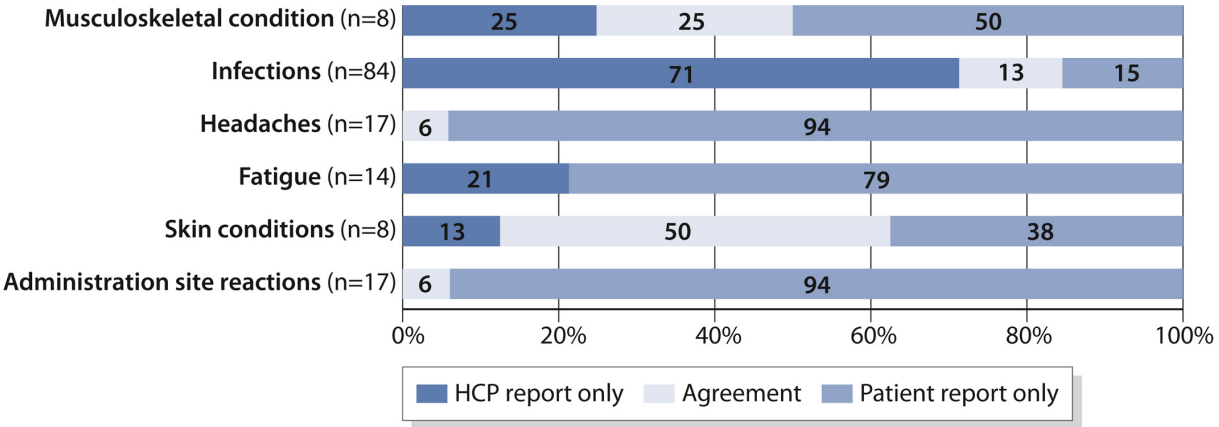

Figure 2. *Agreement between patient- and healthcare provider-reported adverse drug reactions that were related to the biological. HCP = healthcare provider.*

Conclusion

IBD patients often report ADRs during biological treatment. We observed an important significant difference between type and frequency of patient-reported ADRs versus HCP-reported ADRs, leading to an underestimation of more subjective ADRs and patients' ADR-related burden.

Inflammatory bowel disease patients provide reliable self-reported medical information: A multicentre prospective pharmacovigilance monitoring system

Thomas PWA[1], et al. on behalf of the IBDREAM registry. Pharmacoepidemiology and Drug Safety 2021;30:520-524.
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Purpose

To assess the agreement between patient-reported and health care provider-reported medical information in inflammatory bowel disease (IBD).

Methods

This multicentre, prospective, event monitoring study enrolled adult Crohn's disease (CD) and ulcerative colitis (UC) patients treated with a biological in four medical centers in the Netherlands. At two-monthly intervals, patients completed questionnaires on biological use, combination therapy and indication. The patient-reported information was compared with their electronic health records (EHRs) and analysed for percentage agreement and Cohen's kappa. A reference population from a prospective IBD registry was used to assess the representativeness of the study population.

Results

In total, 182 patients (female 50.5%, mean age 42.2 years, CD 76.9%) were included in the analysis. At baseline, 51.0% of the patients were prescribed an immunomodulator (43.9% thiopurines, 7.1% methotrexate), and patients were prescribed biologicals as follows: 59.3% infliximab, 30.2% adalimumab, 9.3% vedolizumab, and 1.1% ustekinumab. Agreement on patient-reported indication and biological use was almost perfect (κ = 0.878 and κ = 1.000, respectively); substantial for combination therapy (κ = 0.672). Gender, age, type of IBD, biological use and combination therapy were comparable with the reference population.

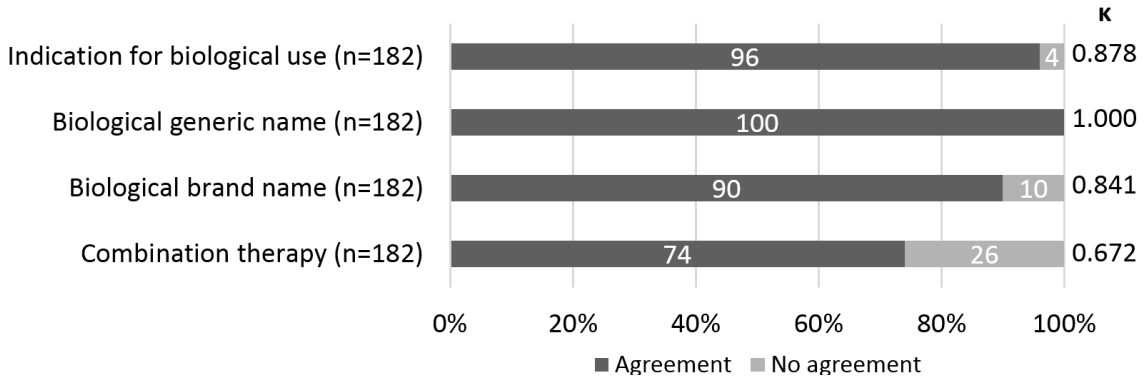

Figure 1. *Agreement between patient-reported and clinician-reported information in electronic health records. κ = level of interrater agreement.*

Conclusion

Systematic patient-reporting by questionnaires was reliable in retrieving indication and treatment specific information from IBD patients. These results indicate that the use of patient-reporting outcomes in daily IBD practice can ensure reliable information collection.

Adverse Drug Reactions from Real-World Data in Inflammatory Bowel Disease Patients in the IBDREAM Registry

Giraud E[1], et al. on behalf of the IBDREAM registry. Drug Safety 2021;44:581-588.
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Introduction
Inflammatory bowel disease (IBD) frequently requires chronic immunosuppressive treatment and active involvement from patients during treatment decision making. Information about the risk of developing adverse drug reactions (ADRs) to IBD therapies is required in this process.

Objective
The aim of this study was to describe the ADRs reported in IBD patients from real-world data, using the Dutch nationwide IBDREAM registry, and compare the occurrence and cumulative incidences with the Summary of Product Characteristics (SmPC) of the associated drugs.

Methods
In this retrospective multicentre study, ADRs related to IBD medication were assessed. Only reports associated with the use of drugs used for the maintenance treatment of IBD were included. All ADRs were verified by healthcare professionals and coded by trained pharmacovigilance assessors.

Results
In total, 3080 ADRs were reported in 1179 patients. Twenty-three new drug-ADR associations related to the use of azathioprine, mercaptopurine, infliximab, oral mesalamine and thioguanine were reported in the IBDREAM registry that were not mentioned in the corresponding SmPCs. The most frequently reported new association was pyrexia for azathioprine (3.1%) and mercaptopurine (4.9%). In addition, there were seven ADRs with a higher cumulative incidence in IBDREAM compared with the SmPC, and included, among others, arthralgia during mercaptopurine use (2.5%), and diarrhoea (1.4%), alopecia (1.2%) and infections (1.6%) during azathioprine use.

Conclusions
Based on real-world data, ADR reporting demonstrated new ADRs and higher incidences of ADRs to IBD therapies. This information will contribute to drug safety by updating the SmPCs, allowing better risk assessment and communication towards patients.

De-escalation of biological therapy in inflammatory bowel disease patients following prior dose escalation

Thomas PWA[1], et al. on behalf of the IBDREAM registry. Eur J Gastrenterol Hepatol. 2021. (Online ahead of print)
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Background
Limited data are available on biological therapy de-escalation after prior escalation in inflammatory bowel disease (IBD) patients. This study aimed to assess the frequency and success rate of de-escalation of biological therapy in IBD patients after prior dose escalation and evaluate which measures are used to guide de-escalation.

Methods
This multicentre retrospective cohort study enrolled IBD patients treated with infliximab (IFX), adalimumab (ADA) or vedolizumab (VEDO) in whom therapy was de-escalated after prior biological escalation. De-escalations were considered pharmacokinetic-driven if based on clinical symptoms combined with therapeutic or supratherapeutic trough levels, and disease-activity driven if based on faecal calprotectin ≤ 200 µg/g and/or resolution of peri-anal fistula drainage or closure and/or endoscopic remission. Successful de-escalation was defined as remaining on the same or lower biological dose for ≥6 months after de-escalation without the need for corticosteroids.

Results
In total, 206 IFX users, 85 ADA users and 55 VEDO users underwent therapy escalation. Of these patients, 34 (17%) on IFX, 18 (21%) on ADA and 8 (15%) on VEDO underwent therapy de-escalation. De-escalation was successful in 88% of IFX patients, 89% of ADA and 100% of VEDO. The probability of remaining on the de-escalated regimen or further de-escalation after 1 year was 85% for IFX, 62% for ADA and 100% for VEDO. Disease activity-driven de-escalations were more often successful (97%) than pharmacokinetic- and no marker-driven de-escalations (76%); p=0.017.

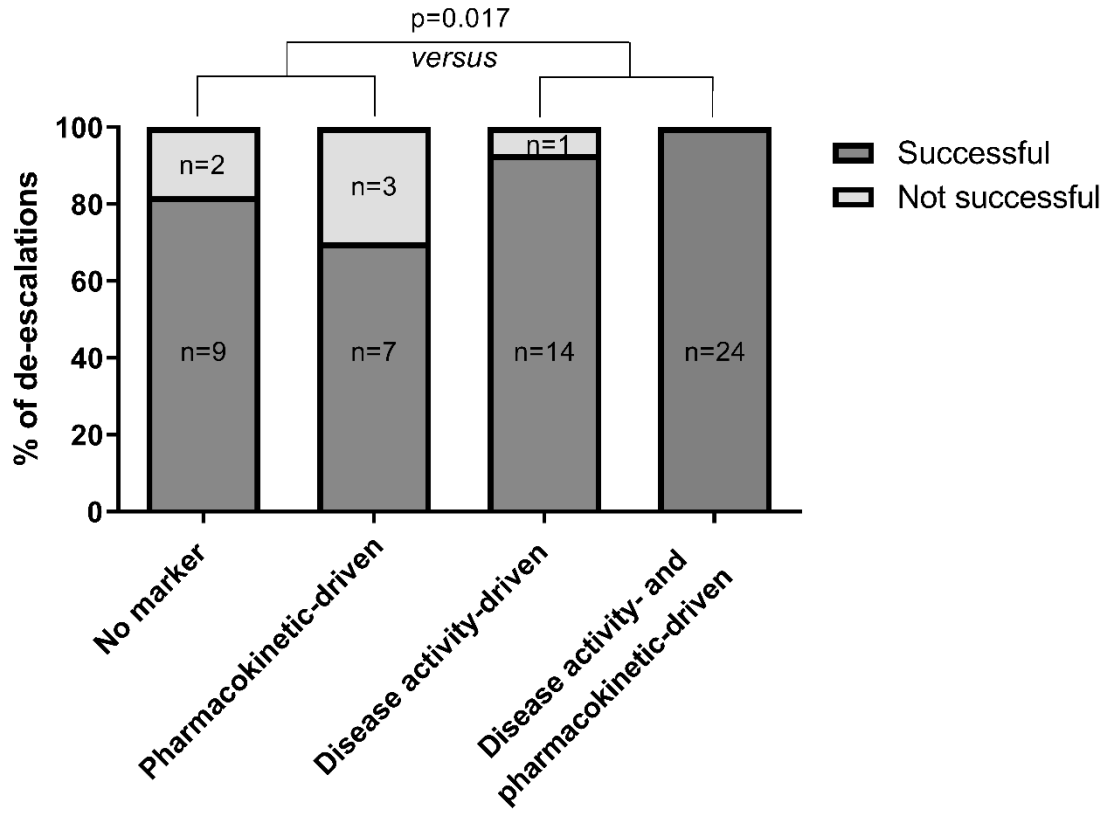

Figure 1. *De-escalation outcomes stratified per diagnostic measure used prior to de-escalation. Pharmacokinetic-driven = de-escalation based on clinical symptoms and therapeutic or supratherapeutic trough levels. Disease activity-driven = de-escalation based on faecal calprotectin ≤ 200 µg/g, resolution of peri-anal fistula drainage or closure or endoscopic remission based on the absence of ulcers. Both = de-escalation based on a combination of pharmacokinetic-driven and disease activity-driven. No marker = de-escalation based on only clinical symptoms.*

Conclusion

De-escalation after biological dose escalation was successful in the majority of carefully selected IBD patients. Objective assessment of remission increased the likelihood of successful de-escalation. Future studies are warranted to assess the outcomes of a standardized de-escalation strategy**.**

Long-term Effectiveness and Safety of Ustekinumab in Crohn's disease: a prospective cohort study

Thomas PWA[1], et al. on behalf of the IBDREAM registry. *Preliminary results*
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Background
Real-world data showed that ustekinumab is an effective treatment for Crohn's disease (CD) up to 52 weeks but data on long-term effectiveness and safety outcomes beyond 52 weeks are limited. This study aimed to evaluate the corticosteroid-free clinical remission up to 104 weeks. Secondary outcomes included biochemical disease activity, dosing adjustments and safety outcomes.

Methods
This multicentre prospective cohort study enrolled CD patients who started ustekinumab between May 2016 and September 2019. Participants had scheduled outpatient visits at week 0, 13, 26, 52 and 104. Data on clinical disease (Harvey Bradshaw Index ≤4 points = remission), biochemical disease (faecal calprotectin ≤ 200 µg/g and/or C-reactive protein ≤ 10 mg/L = remission), dose adjustments and adverse drug reactions (ADRs) were recorded.

Results
We included 106 CD patients. The proportion of patients in corticosteroid-free clinical remission was 45%, 42%, 34% and 35% at weeks 13, 26, 52 and 104 respectively. Of patients achieving corticosteroid-free remission at week 52, 54% maintained corticosteroid-free remission throughout week 104. Biochemical remission rates were 33%, 33%, 24% and 30% at weeks 13, 26, 52 and 104 respectively. In the first year of treatment, 36% required a first dose escalation and 9% in the second year. Overall, 8% of patients discontinued ustekinumab due to ADRs. Ustekinumab persistency rates were 68% at week 52 and 58% at week 104.

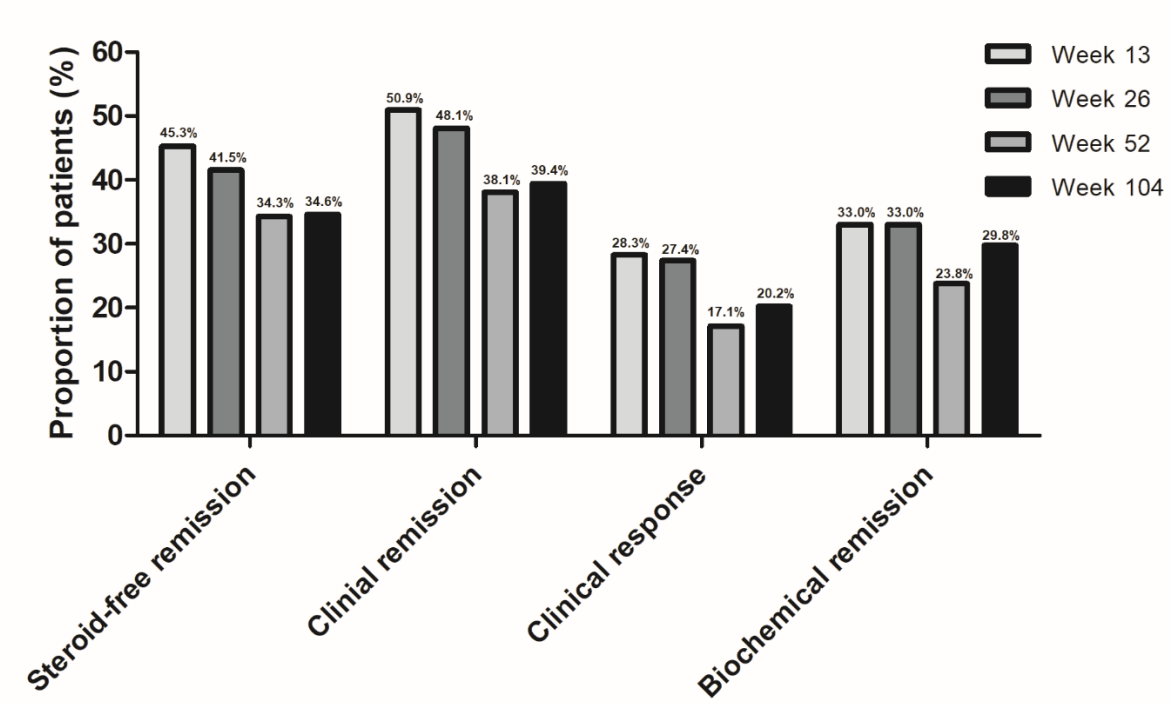

Figure 1. Clinical outcomes in all ustekinumab-treated patients. Proportion of patients with steroid-free remission, clinical remission, clinical response and biochemical remission at weeks 13, 26, 52 and 104. Clinical remission was defined as an Harvey Bradshaw Index score ≤4. Clinical response was defined as least 3 points reduction in the Harvey Bradshaw Index score compared to baseline.

Conclusion

Ustekinumab is an effective and well-tolerated treatment for CD. More than half of all patients continued UST treatment at week 104 while one third achieved corticosteroid-free remission.

External validation and consistency in time of patient segmentation based on disease acceptance and perceived control in Inflammatory Bowel Disease

Van Erp L[1], et al. in collaboration with the IBDREAM registry. Submitted.
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Background
The patient segmentation model based on disease acceptance and perceived control may guide personalized care in inflammatory bowel disease (IBD). We aimed to investigate the external validity of the segmentation model and its consistency in course of time.

Methods
This is a multicentre longitudinal study of adult IBD patients with questionnaires on disease acceptance and perceived control (6-items, 7-point Likert scale) and health-related quality of life (HRQoL) (Short IBD Questionnaire, range 10-70). Segments were created based on mean scores (cut-off>5): (I) high acceptance, high control; (II) high acceptance, low control; (III) low acceptance, high control and; (IV) low acceptance, low control.

Results
The external validation cohort included 921 IBD patients. The acceptance and control scale were unidimensional and internally consistent. Segments differed significantly in gender, disease duration, IBD medication and clinical disease activity. High acceptance and/or high control were significantly associated with a higher HRQoL compared with low acceptance and low control (i.e., segment IV) (Beta (95%CI) segment I = 11.7 (10.4-13.1), segment II = 9.3 (7.7-10.9) and segment III = 3.8 (1.6-6.0), p≤0.001). The follow-up cohort included 783 patients: 58% remained in the same segment while 42% differed in segment over time. Changes in segment were positively correlated with changes in HRQoL over time (Spearman rho 0.38, p<0.001).

Conclusion
The patient segmentation model based on disease acceptance and perceived control was externally valid and showed consistency over time. The different segments were independently associated with HRQoL. Future interventions should aim at improving disease acceptance and perceived control of IBD patients.