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Occurrence of Anaemia in the First Year of Inflammatory Bowel Disease in a European Population-based Inception Cohort—An ECCO-EpiCom Study

Johan Burisch,[a] Zsuzsanna Vegh,[b] Konstantinnos H. Katsanos,[c] Dimitrios K. Christodoulou,[c] Daniela Lazar,[d] Adrian Goldis,[d] Colm O'Morain,[e] Alberto Fernandez,[f] Santos Pereira,[g] Sally Myers,[h] Shaji Sebastian,[h] Natalia Pedersen,[i] Jóngerð Olse,[j] Kári Rubek Nielsen,[j] Doron Schwartz,[k] Selwyn Odes,[k] Sven Almer,[l,m] Jonas Halfvarson,[n] Niksa Turk,[o] Silvja Cukovic-Cavka,[o] Inna Nikulina,[p] Elena Belousova,[p] Dana Duricova,[q] Martin Bortlik,[q,r] Olga Shonová,[s] Riina Salupere,[t] Louisa Barros,[u] Fernando Magro,[v,w,x] Laimas Jonaitis,[y] Limas Kupcinskas,[y] Svetlana Turcan,[z] Ioannis Kaimakliotis,[aa] Karin Ladefoged,[bb] Karen Kudsk,[cc] Vibeke Andersen,[cc,dd,ee] Ida Vind,[ff] Niels Thorsgaard,[gg] Pia Oksanen,[hh] Pekka Collin,[hh] Giulia Dal Piaz,[ii,jj] Alessia Santini,[jj,kk] Ola Niewiadomski,[ll] Sally Bell,[ll] Bjørn Moum,[mm] Naila Arebi,[nn] Jens Kjeldsen,[oo] Katrine Carlsen,[pp] Ebbe Langholz,[qq] Peter Laszlo Lakatos,[b] Pia Munkholm,[a] Lars Ulrik Gerdes,[rr] Jens Frederik Dahlerup[ss]; for the EpiCom study group

[a]Department of Gastroenterology, North Zealand University Hospital, Frederikssund, Denmark [b]1st Department of Medicine, Semmelweis University, Budapest, Hungary [c]1st Division of Internal Medicine and Hepato-Gastroenterology Unit, University Hospital, Ioannina, Greece [d]Clinic of Gastroenterology, University of Medicine 'Victor Babes', Timisoara, Romania [e]Department of Gastroenterology, Adelaide and Meath Hospital, TCD, Dublin, Ireland [f]Department of Gastroenterology. POVISA Hospital, Vigo, Spain [g]Department of Gastroenterology. Instituto de Investigación Sanitaria Galicia Sur, Estrutura Organizativa de Xestión Integrada de Vigo, Vigo, Spain [h]IBD Unit, Hull & East Yorkshire NHS Trust, Hull, UK [i]Gastroenterology Department, Slagelse Hospital, Slagelse, Denmark [j]Medical Department, National Hospital of the Faroe Islands, Torshavn, Faroe Islands [k]Department of Gastroenterology and Hepatology, Soroka Medical Center and Ben Gurion University of the Negev, Beer Sheva, Israel [l]Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden [m]Center for Digestive Diseases, Karolinska University Hospital, Stockholm, Sweden [n]Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden [o]Division of Gastroenterology and Hepatology, University Hospital Center Zagreb, Zagreb, Croatia [p]Department of Gastroenterology, Moscow Regional Research Clinical Institute, Moscow, Russian Federation [q]IBD Clinical and Research Centre ISCARE, Charles University, Prague, Czech Republic [r]Institute of Pharmacology, 1st Medical Faculty, Charles University, Prague, Czech Republic [s]Gastroenterology Department, Hospital České Budějovice, České Budějovice, Czech Republic [t]Division of Gastroenterology, Tartu University Hospital, Tartu, Estonia [u]Department of Medicine, Hospital de Vale de Sousa, Porto, Portugal [v]Department of Gastroenterology, Hospital de São João, Porto, Portugal [w]Institute of Pharmacology and Therapeutics, Oporto Medical School, Porto, Portugal [x]Institute for Molecular and Cell Biology, University of Porto, Porto, Portugal [y]Institute for Digestive

Research, Lithuanian University of Health Sciences, Kaunas, Lithuania [z]Department of Gastroenterology, State University of Medicine and Pharmacy of the Republic of Moldova, Chisinau, Republic of Moldova [aa]Nicosia private practice, Nicosia, Cyprus [bb]Medical Department, Dronning Ingrids Hospital, Nuuk, Greenland [cc]Institute of Molecular Medicine, University of Southern Denmark, Odense, Denmark [dd]Laboratory Center, Hospital of Southern Jutland, Aabenraa, Denmark [ee]Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark [ff]Gastrounit, Medical Division, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark [gg]Department of Medicine, Herning Central Hospital, Herning, Denmark [hh]Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland [ii]Dipartimento Medicina Specialistica Gastroenterologia ed Endoscopia Digestiva, Ospedale Morgagni — Pierantoni, Forlì, Italy [jj]On behalf of the EpiCom Northern Italy centre based in Crema & Cremona, Firenze, Forlì, Padova, and Reggio Emilia, Italy [kk]Gastroenterology Unit, Careggi Hospital, Florence, Italy [ll]Department of Gastroenterology, St Vincent's Hospital, Melbourne, VIC, Australia [mm]Department of Gastroenterology, Oslo University Hospital, Oslo, Norway [nn]St Mark's Hospital, Imperial College London, London, UK [oo]Department of Medical Gastroenterology, Odense University Hospital, Odense, Denmark [pp]Department of Pediatrics, Hvidovre University Hospital, Hvidovre, Denmark [qq]Department of Gastroenterology, Herlev Univerisity Hospital, Herlev, Denmark [rr]Center for Quality, Region of Southern Denmark, Denmark [ss]Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark

Corresponding author: Johan Burisch, MD, PhD, Department of Gastroenterology, North Zealand University Hospital, Frederikssund, Denmark, Frederikssundvej 30, 3600 Frederikssund, Denmark. Email: burisch@dadlnet.dk

Abstract

Background and aims: Anaemia is an important complication of inflammatory bowel disease [IBD]. The aim of this study was to determine the prevalence of anaemia and the practice of anaemia screening during the first year following diagnosis, in a European prospective population-based inception cohort.

Methods: Newly diagnosed IBD patients were included and followed prospectively for 1 year in 29 European and one Australian centre. Clinical data including demographics, medical therapy, surgery and blood samples were collected. Anaemia was defined according to the World Health Organization criteria.

Results: A total of 1871 patients (Crohn's disease [CD]: 686, 88%; ulcerative colitis [UC]: 1,021, 87%; IBD unclassified [IBDU] 164. 81%) were included in the study. The prevalence of anaemia was higher in CD than in UC patients and, overall, 49% of CD and 39% of UC patients experienced at least one instance of anaemia during the first 12 months after diagnosis. UC patients with more extensive disease and those from Eastern European countries, and CD patients with penetrating disease or colonic disease location, had higher risks of anaemia. CD and UC patients in need of none or only mild anti-inflammatory treatment had a lower risk of anaemia. In a significant proportion of patients, anaemia was not assessed until several months after diagnosis, and in almost half of all cases of anaemia a thorough work-up was not performed.

Conclusions: Overall, 42% of patients had at least one instance of anaemia during the first year following diagnosis. Most patients were assessed for anaemia regularly; however, a full anaemia work-up was frequently neglected in this community setting.

Key Words: anaemia, inflammatory bowel disease, prevalence

1. Introduction

Anaemia is a systemic complication considered as an extra-intestinal manifestation of the inflammatory bowel diseases [IBD] Crohn's disease [CD] and ulcerative colitis [UC]. The two most common forms of anaemia in IBD patients are iron deficiency anaemia [IDA] and anaemia of chronic disease [ACD][1,2]; often, however, the two conditions overlap. Approximately one in five IBD patients is anaemic at any given time,[2,3] and anaemia affects patients' perceived health-related quality of life [HRQoL], their ability to work, and cognitive functions,[4,5],as well as increasing their health care costs.[6] Anaemia also provides an indicator of the global quality of care and inflammation control of IBD patients. Accordingly, international guidelines recommend that IBD patients be checked for anaemia at diagnosis.[7,8]

The majority of studies on anaemia in IBD originate from the time before biological therapy was available, and very few population-based inception cohorts have reported on the occurrence of anaemia at diagnosis and during follow-up.[9–11] The European Crohn's and Colitis Organisation's [ECCO] Epidemiological Committee [EpiCom] study is a prospective population-based cohort of unselected IBD patients, for investigating the occurrence, disease course, and prognosis of IBD in Europe.[12] The EpiCom collaboration has

previously documented differences in the incidence of IBD across Europe, and currently unchanged initial disease course when compared with the pre-biological era, despite an earlier and more frequent use of biological agents and immuno-modulating therapy.[13–16]

Using the EpiCom cohort, the aim of the current study was to investigate: [i] the prevalence and course of anaemia during the first year after diagnosis; [ii] the practice of anaemia screening and follow-up; [iii] and any differences between Eastern and Western European centres in terms of screening for and the prevalence of anaemia.

2. Material and Methods

2.1. Study setting

In 2010, the EpiCom study collaboration launched a population-based prospective inception cohort of incident IBD patients diagnosed within a 1-year inclusion period in 31 centres from eight Eastern and 14 Western European countries [hereafter referred to as the EpiCom 2010 cohort; Appendix I].[13] In total, 1560 IBD patients were recruited within well-described geographical areas covering a total background population of 10.1 million [3.3 million in Eastern and 6.8 million in Western Europe]. A total of 1442 IBD patients were followed up prospectively. Of the centres in the EpiCom 2010 cohort, 14 European centres [five from Eastern and nine from Western European countries], along with one centre in Australia, continued to include incident patients in 2011[14] [the EpiCom 2011 cohort]; a total of 709 IBD patients were included. For the purpose of this study, the two cohorts were merged. The Australian centre was grouped with Western European centres. A list of centres in both cohorts is included in Supplementary data, available at *ECCO-JCC* online.

The methodologies of the EpiCom 2010 and EpiCom 2011 cohort studies are identical.[13,14] Participation in the study required a well-defined primary catchment area with up-to-date population data, including age and gender distribution. Similarly, participation required an established network of gastroenterologists, colorectal surgeons, and general practitioners [GPs] within the uptake area, who were contacted twice during the inclusion period to ensure complete coverage and recruitment of patients. Case ascertainment methods, diagnostic criteria for case definition, time period of inclusion, and patient data recorded were all standardised.

2.2. Patient population

Incident patients diagnosed with IBD during the inclusion periods [1 January to 31 December 2010 and 1 January to 31 December 2011], aged 15 years or older, and living in the predefined catchment areas at the time of diagnosis, were prospectively included in the EpiCom cohorts. The diagnosis of CD, UC, or IBDU was based on the *Copenhagen Diagnostic Criteria*[17–19] [see Supplementary data, available at *ECCO-JCC* online]. Fulfilment of these criteria was assessed by the participating physicians and gastroenterologists. The date of inclusion was the date of diagnosis. Disease extent for UC, as well as disease location and behaviour for CD, were defined according to the *Montreal Classification*.[20]

Patients were followed prospectively every third month from diagnosis and throughout the follow-up period. Data regarding demographics, disease activity, blood samples, medical therapy, surgery, hospitalisation, disease classification, cancers, and deaths were collected and entered prospectively in the web-based inception cohort EpiCom database.[21] Blood samples were taken at the treating physician's discretion. Measures for securing data validity have been thoroughly described elsewhere.[12] In short, data validity was secured by built-in control and validation tests, locked diagnostic criteria in the database, manual data standardisation, and random audits of case ascertainment and data quality.

2.3. Classifications and definitions

Anaemia was defined according to the World Health Organization [WHO] criteria as a haemoglobin [HgB] level of less than 13 g/dL in men and an HgB level of less than 12 g/dL in non-pregnant females.[22] Anaemia was classified using both the serum ferritin and the C-reactive protein [CRP] levels, in accordance with the current ECCO guidelines.[23]

- Pure iron deficiency anaemia [IDA] was defined as anaemia with a ferritin level of < 30 µg/L and CRP < the upper limit of normality at each site.
- Pure anaemia of chronic disease [ACD] was defined as anaemia with a ferritin level of > 100 µg/L and CRP > the upper limit of normality at each site.
- Combined anaemia [mixed IDA and ACD] was defined as anaemia with a ferritin level of < 100 µg/L and CRP > the upper limit of normality at each site.

Treatment options were grouped into five levels of ascending therapeutic potency: 5-aminosalicylates [5-ASA] [oral and/or topical 5-ASA treatment ± topical steroids], glucocorticosteroids [GCS] [oral steroids ± 5-ASA or topical steroids], immunomodulators [azathioprine, 6-mercaptopurine, cyclosporine or methotrexate ± steroids], biologics [infliximab or adalimumab in combination with any of the above], and surgery [regardless of medical treatment preceding surgery]. Surgery was defined as total or subtotal colectomy for UC and small or large bowel resections for CD due to IBD, and perianal surgery was excluded.

2.4. Statistical analysis

Statistical analyses were performed using SAS software v. 9.4. Demographics and disease classification between groups were compared with a chi-square test. Results for continuous variables are expressed as the median [interquartile range] unless otherwise stated. Blood samples taken between 30 days before and after the time of diagnosis were used in order to assess anaemia status at the time of diagnosis. Similarly, a window of 30 days before and 3 months after 1 year since the date of diagnosis was used in order to assess anaemia status after 1 year, to account for variations in the 12-month period. If there was more than one set of blood samples within any period of the aforementioned time windows, the samples closest to the date of diagnosis and its 12-month follow-up were used.

Predictors of anaemia were analysed using a logistic regression model including age, gender, geographical region, smoking status at diagnosis, disease extent in UC, disease location and behaviour in CD, extra-intestinal manifestations at diagnosis, and highest treatment level reached during follow-up, all as independent variables.

In patients with HgB measurements at diagnosis and 1-year follow-up, the association of the aforementioned covariates with the relative change [%] in HgB was analysed using linear normal analysis of covariance [ANCOVA]. In patients with HgB measurements available after more than 6 months of follow-up, the final HgB value during follow-up was analysed using ANCOVA, while controlling for the aforementioned covariates. Finally, we included all available HgB measures in a repeated measures analysis of variance [ANOVA] of the final HgB value, again while controlling for the covariates. A p-value < 0.05 was considered statistically significant.

2.5. Ethical considerations

The study was approved by the local ethical committees according to local regulations.

3. Results

3.1. Patient population

Of 2151 incident IBD patients, 157 [7%] were lost to follow-up immediately after diagnosis and 123 [6%] patients did not have blood samples available for analysis. Thus, a total of 1871 [87%] patients had HgB levels measured during the follow-up period and were eligible for inclusion Figure 1. These patients submitted a total of 6895 blood samples for analysis. The proportion of Eastern European patients from the total cohort with HgB measurements available for analysis was higher than that of Western European patients [East: 417 [96%]; West: 1454 [85%], $p < 0.05$]. Patient characteristics are shown in Table 1. Only the disease location in CD differed significantly between Eastern and Western European patients [$p < 0.05$].

3.2. Measurements of haemoglobin during follow-up

Overall, IBD patients had a median of three HgB measurements taken (interquartile range [IQR]: 2–5) during follow-up (CD 4 [IRQ: 2–5]; UC 3 [IQR 2–5]; IBDU 3 [IQR 2–5]). These frequencies did not differ between Eastern and Western European patients. A total of 1086 [58%] (Eastern Europe: 307 [74%]; Western Europe: 779 [54%]) patients had HgB measured at the time of diagnosis, and this proportion increased to 1703 [91%] (Eastern Europe: 403 [97%]; Western Europe: 1300 [89%] [p = nonsignificant]) within 6 months of diagnosis. No difference was found between CD and UC patients ([p = nonsignificant [NS]). In total, 1109 [59%] patients had HgB measured at the 1-year follow-up, and 601 [32%] patients had HgB measured both at diagnosis and at 1e-year follow-up [Figure 1].

3.3. Frequency and type of anaemia

Overall during the follow-up period, 794 [42%] had at least one instance of anaemia (Eastern Europe: 201 [48%]; Western Europe 593 [41%]). Specifically, this was the case in 332 [49%] CD patients (Eastern Europe: 78 [47%]; Western Europe 254 [49%]) and 402 [39%] UC patients (Eastern Europe: 123 [50%]; Western Europe 279 [36%]). In 1791 [26%] of 6895 HgB measurements anaemia was found, and of those 194 [11%] were iron deficiency anaemia [IDA], 203 [11%] were anaemia of chronic disease [ACD], and 925 [52%] did not have results sufficient to define their anaemia subtype.

The prevalence of anaemia and anaemia subtypes in CD and UC patients at diagnosis and at 1-year follow-up is shown in Table 2. Overall, at diagnosis the prevalence of anaemia was 45% [n = 179] in CD, 34% [n = 196] in UC, and 27% [n = 28] in IBDU patients. At 1-year follow-up, the prevalence of anaemia was 18% [n = 75] in CD, 17% [n = 100] in UC, and 11% [n = 10] in IBDU patients. Regarding predictors of anaemia, logistic regression analysis found that CD patients had a higher risk of anaemia at diagnosis when compared with UC and IBDU patients (UC vs CD odds ratio [OR]: 0.6, 95% confidence interval [CI]: 0.5–0.8; IBDU vs CD OR: 0.5, 95% CI: 0.3–0.8). Predictors of anaemia in CD and UC patients are show in Table 3.

Among the patients with HgB values available at diagnosis, there were no differences in clinical or sociodemographic characteristics for CD and UC when compared with the total cohort. At 1-year

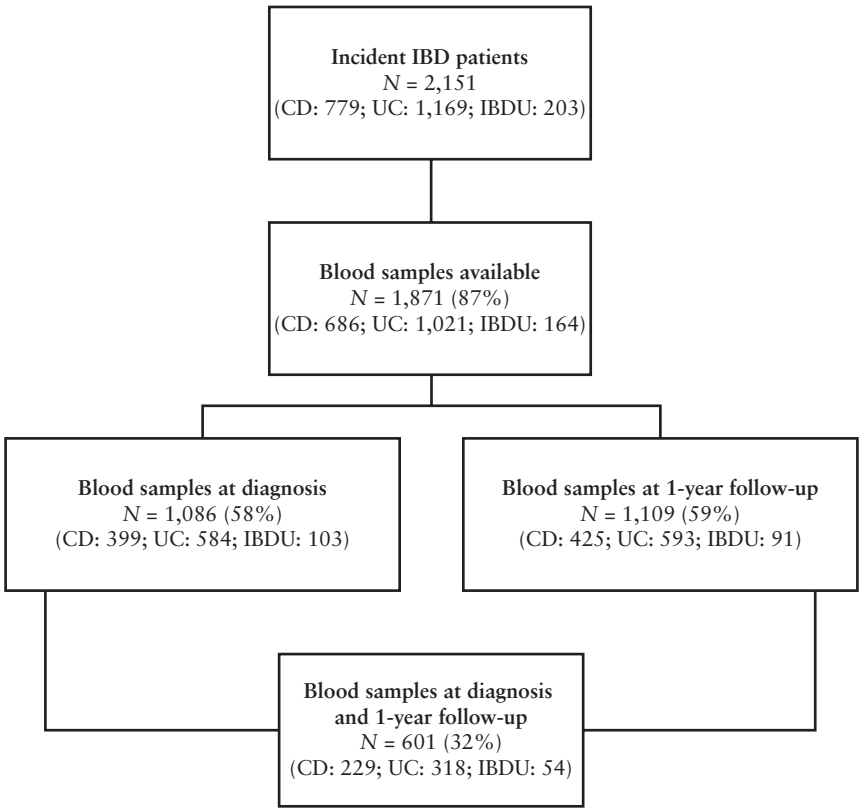

Figure 1. Flowchart of the study population.

Table 1. Characteristics of 1871 incident inflammatory bowel disease patients from the EpiCom-cohort

	Western European centres			Eastern European centres		
	CD	UC	IBDU	CD	UC	IBDU
No. of patients	520 [36%]	777 [53%]	157 [11%]	166 [40%]	244 [59%]	7 [2%]
Male	280 [54%]	441 [57%]	78 [50%]	88 [53%]	130 [53%]	5 [71%]
Female	240 [46%]	336 [43%]	79 [50%]	78 [47%]	114 [47%]	2 [29%]
Age at diagnosis, years	37 [16–89]	39 [15–89]	38 [17–78]	38 [15–78]	35 [15–87]	28 [20–34]
Median time to diagnosis, months	4.0 [0–31 yr]	2.5 [0–30 yr]	2.6 [0–30 yr]	3.2 [0–10 yr]	2.2 [0–26 yr]	2.0 [0–3 yr]
Extra-intestinal manifestations at diagnosis	70 [13%]	59 [8%]	22 [14%]	26 [16%]	25 [10%]	1 [14%]
Smoking status at diagnosis						
Never smoker	223 [44%]	395 [53%]	77 [52%]	68 [42%]	140 [59%]	4 [57%]
Current smoker	177 [35%]	78 [11%]	17 [11%]	56 [35%]	24 [10%]	3 [43%]
Former smoker	109 [21%]	262 [36%]	55 [37%]	38 [23%]	75 [31%]	0 [0%]
Disease extent						
E1: Proctitis		156 [20%]			21 [21%]	
E2: Left-sided		314 [41%]			112 [46%]	
E3: Extensive colitis		306 [39%]			81 [33%]	
Disease location*						
L1: Terminal ileum	148 [29%]			63 [38%]		
L2: Colon	141 [27%]			31 [19%]		
L3: Terminal ileum + colon	110 [21%]			43 [26%]		
L4: Upper GI	35 [7%]			3 [2%]		
L1+L4	34 [7%]			10 [6%]		
L2+L4	15 [3%]			7 [4%]		
L3+L4	32 [6%]			8 [5%]		
Disease behaviour						
B1: non-stricturing, non-penetrating	331 [64%]			105 [64%]		
B2: stricturing	95 [18%]			35 [21%]		
B3: penetrating	44 [8%]			14 [8%]		
B1p: B1 + perianal	39 [8%]			6 [4%]		
B2p: B2 + perianal	6 [1%]			2 [1%]		
B3p: B3 + perianal	5 [1%]			3 [2%]		
Highest level of treatment during follow-up						
No treatment	27 [5%]	27 [3%]	0 [0%]	3 [2%]	2 [1%]	0 [0%]
5-ASA	78 [15%]	395 [51%]	88 [56%]	41 [25%]	164 [67%]	4 [57%]
GCS	90 [17%]	185 [24%]	33 [21%]	30 [18%]	40 [16%]	2 [29%]
Immunomodulators	154 [30%]	118 [15%]	21 [13%]	57 [34%]	29 [12%]	1 [14%]
Biological therapy	97 [19%]	31 [4%]	10 [6%]	12 [7%]	6 [2%]	0 [0%]
Surgery	74 [14%]	21 [3%]	5 [3%]	23 [14%]	3 [1%]	0 [0%]

*Differences between geographical regions $p < 0.05$.

CD, Crohn's disease; UC, ulcerative colitis; IBDU, inflammatory bowel disease unclassified; yr, years; GI, gastrointestinal; GCS, glucocorticosteroids; 5-ASA, 5-aminosalicylic acid.

Table 2. Prevalence of anaemia in Crohn's disease and ulcerative colitis patients at diagnosis [$n = 983$] and at 1-year follow-up [$n = 1018$].

	Crohn's disease				Ulcerative colitis			
	Diagnosis		Follow-up		Diagnosis		Follow-up	
	Eastern Europe	Western Europe	Eastern Europe	Western Europe	Eastern Europe	Western Europe	Eastern Europe	Western Europe
Anaemia overall	52 [46%]	127 [44%]	19 [25%]	56 [16%]	72 [38%]	124 [31%]	32 [27%]*	68 [14%]
Iron deficiency	6 [12%]	3 [2%]	2 [11%]*	7 [13%]	12 [17%]	9 [7%]	3 [9%]*	24 [35%]
Chronic disease	14 [27%]	30 [24%]	1 [5%]*	4 [7%]	12 [17%]	13 [10%]	4 [13%]*	5 [7%]
Mixed anaemia	12 [23%]	39 [31%]	5 [25%]*	6 [11%]	20 [28%]	30 [24%]	0 [0%]*	7 [10%]
Other anaemia	2 [4%]	17 [13%]	0 [0%]*	8 [14%]	5 [7%]	16 [13%]	4 [13%]*	7 [10%]
Unclassified	18 [35%]	38 [30%]	11 [58%]*	31 [55%]	23 [32%]	56 [45%]	21 [66%]*	25 [37%]

*Differences between geographical regions $p < 0.05$.

follow-up, in CD the proportion of patients receiving immunomodulators or biological therapy was larger than that seen in the cohort as a whole. In UC, the proportion of patients with extensive colitis, as well as the proportion of patients receiving corticosteroids, immunomodulators, or biological therapy, were larger than those seen in the cohort as a whole [data not shown].

Table 3. Predictors of anaemia in Crohn's disease and ulcerative colitis patients at diagnosis [*n* = 983], 1-year follow-up [*n* = 1018] and overall during follow-up [*n* = 1707].

	Diagnosis		At 1-year follow-up		Any time during follow-up	
	Crohn's disease [OR, 95% CI]	Ulcerative colitis [OR, 95% CI]	Crohn's disease [OR, 95% CI]	Ulcerative colitis [OR, 95% CI]	Crohn's disease [OR, 95% CI]	Ulcerative colitis [OR, 95% CI]
Number of patients	399	584	425	593	686	1,021
Age [per year]	0.99 [0.98–1.00]	1.00 [0.99–1.01]	1.02 [1.00–1.03]	1.01 [0.99–1.02]	1.00 [0.99–1.01]	1.00 [0.99–1.01]
Female gender	1.15 [0.75–1.77]	1.18 [0.82–1.71]	0.89 [0.52–1.54]	1.13 [0.71–1.79]	1.36 [0.97–1.92]	1.21 [0.91–1.62]
Coming from Eastern Europe	1.15 [0.71–1.85]	1.46 [1.00–2.14]	1.26 [0.65–2.47]	2.66 [1.60–4.45]	1.00 [0.67–1.50]	2.36 [1.70–3.27]
Smoking status						
Current	1.15 [0.71–1.88]	0.88 [0.48–1.63]	0.89 [0.47–1.67]	0.44 [0.15–1.29]	0.80 [0.54–1.19]	0.86 [0.53–1.39]
Former	1.53 [0.85–2.73]	1.04 [0.69–1.58]	1.00 [0.50–2.02]	1.25 [0.77–2.05]	1.06 [0.67–1.67]	1.12 [0.81–1.54]
Never	Reference	Reference	Reference	Reference	Reference	Reference
No extra-intestinal manifestation at diagnosis	1.08 [0.59–1.99]	1.41 [0.72–2.77]	0.65 [0.31–1.37]	0.83 [0.39–1.74]	0.73 [0.45–1.20]	1.07 [0.65–1.76]
Disease behaviour ± perianal						
B3: penetrating	3.47 [1.73–6.99]		3.02 [1.11–8.26]		2.73 [1.35–5.52]	
B2: structuring	2.13 [1.20–3.78]	-	2.42 [1.23–4.76]	-	1.42 [0.91–2.22]	-
B1: non-stricturing, non-penetrating	Reference		Reference		Reference	
Disease location						
L4: Upper GI [± L1-L3]	1.98 [1.06–3.68]		1.10 [0.50–2.43]		0.97 [0.60–1.56]	
L3: Terminal ileum + colon	3.14 [1.69–5.84]	-	1.77 [0.81–3.87]	-	1.66 [1.03–2.69]	-
L2: Colon	5.14 [2.73–9.68]		1.59 [0.72–3.53]		2.50 [1.54–4.07]	
L1: Terminal ileum	Reference		Reference		Reference	
Disease extent						
E3: Extensive colitis	-	5.20 [2.82–9.59]	-	1.28 [0.62–2.65]	-	2.94 [1.89–4.57]
E2: Left-sided		3.60 [1.96–6.64]		1.33 [0.66–2.71]		2.40 [1.56–3.68]
E1: Proctitis		Reference		Reference		Reference
Highest treatment level						
No treatment	-	-	0.00 [NA*]	0.54 [0.07–4.47]	0.12 [0.03–0.47]	0.05 [0.01–0.27]
5-aminosalicylates			0.56 [0.15–2.05]	0.35 [0.08–1.52]	0.25 [0.13–0.50]	0.16 [0.06–0.41]
Corticosteroids			1.73 [0.57–5.29]	0.50 [0.11–2.22]	0.48 [0.25–0.91]	0.32 [0.13–0.81]
Immunomodulators			2.66 [0.98–7.23]	1.32 [0.30–5.83]	0.97 [0.54–1.72]	0.71 [0.27–1.86]
Biological therapy			0.84 [0.26–2.70]	0.86 [0.15–4.89]	0.90 [0.46–1.73]	1.01 [0.32–3.47]
Surgery [reference]			Reference	Reference	Reference	Reference

OR, odds ratio; 95% CI, 95% confidence interval; GI, gastrointestinal.
*No cases of anaemia in this treatment group.

3.4. Change in haemoglobin value during follow-up

In total, 601 IBD patients had HgB measured both at diagnosis and at 1-year follow-up. Changes in anaemia status in CD and UC patients between diagnosis and 1-year follow-up are shown in Figure 2. Regarding CD, low HgB at diagnosis, female gender, penetrating or stricturing disease behaviour compared with non-stricturing, non-penetrating disease, and colonic or ileo-colonic location compared with ileal location, were associated with a relative increase in HgB value between diagnosis and 1-year follow-up [$p < 0.05$]. In UC, only female gender was associated with a relative increase in HgB value between diagnosis and 1-year follow-up [$p < 0.05$].

In order to analyse clinical factors associated with the final HgB value, a total of 6251 blood samples from 1707 CD and UC patients were included in the repeated measures analysis, and 1370 patients had at least one HgB measurement after 6 months of follow-up. Clinical factors associated with the final HgB value are shown in Table 4.

4. Discussion

We have described the prevalence of anaemia and the frequency of HgB assessment during the first year of disease in a European, prospective, population-based inception cohort. Anaemia was found to be frequent, with almost half of CD patients, and 40% of UC patients, being anaemic at some point during the observation period. UC patients with more extensive disease, or those originating in Eastern European countries, along with CD patients with penetrating disease or colonic disease location, all had higher risks of anaemia. CD and UC patients in need of only mild treatment or none at all had a lower risk of anaemia. In a significant proportion of patients, HgB was not measured until several months after diagnosis, and in almost half of all cases of anaemia, a thorough work-up was not performed and so the type of anaemia was indeterminable.

CD and UC are frequently complicated by manifestations, such as anaemia, that may not be apparent to the physician or patient, but might have a major impact on patients' well-being and disease course. A European meta-analysis found that the overall prevalence of anaemia was 27% for CD and 21% for UC,[3] but the range of prevalence estimates depends on study type and subpopulation and can vary from 6% to 74%.[9,24] IBD patients with anaemia report a lower perception of HRQoL, carry higher health care costs,[6,25] and are at higher risk of CD-related complications or surgery.[26] Anaemia should therefore be considered a serious complication in IBD which necessitates adequate monitoring and treatment of the underlying

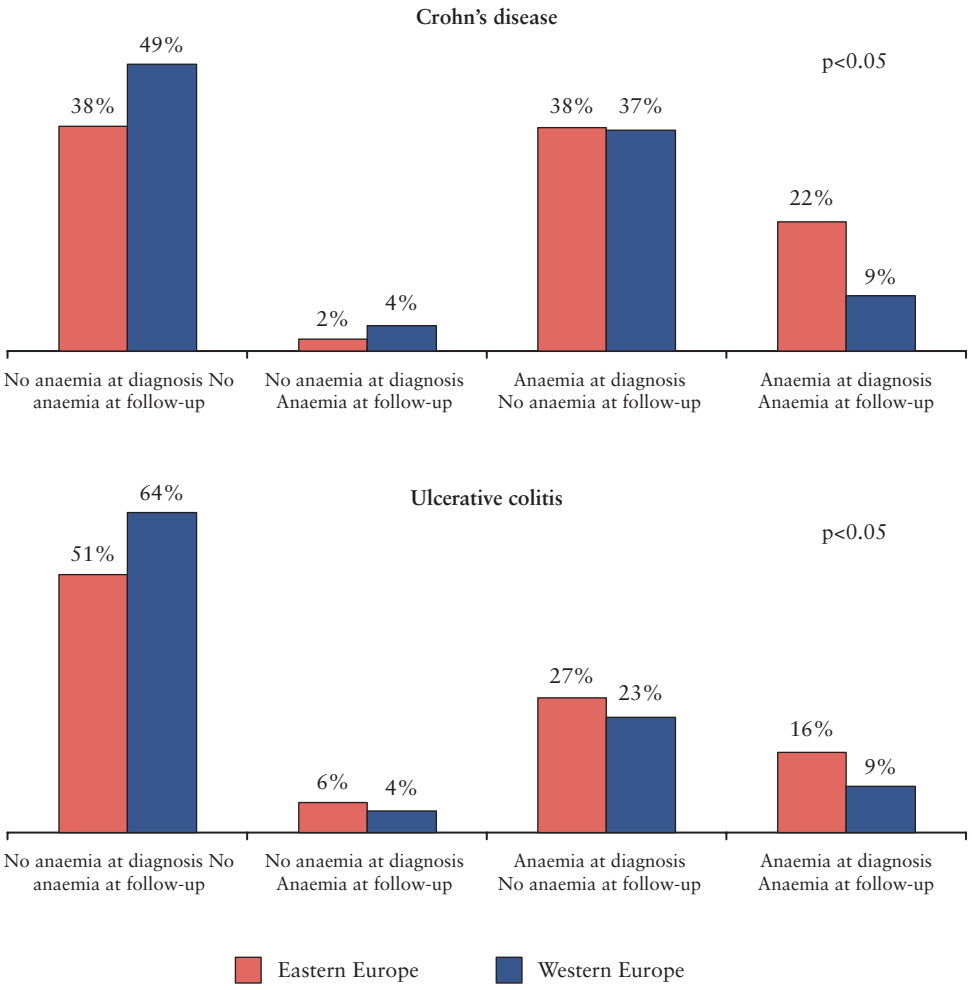

Figure 2. Change in anaemia status between diagnosis and 1-year follow-up in EpiCom cohort patients.

causes. Screening for anaemia at diagnosis and regular assessment for the presence of anaemia are therefore mandatory, according to guidelines.[7,8,23]

Surprisingly, in this unselected inception cohort representing real-life practices of IBD care of incident patients, we found that whereas the majority of patients had HgB measured three times during the 12-month observation period, a substantial number were not assessed until several months after diagnosis. Furthermore, serum ferritin was only determined occasionally and thus anaemia subtyping was not possible. No geographical difference regarding these observations was found. Iron deficiency in the absence of anaemia negatively affects HRQoL in IBD patients in remission,[27] further underlining the importance of regular anaemia work-ups. Our findings are somewhat in line with a German population-based cohort showing that 33% of patients with proven anaemia did not have further diagnostic work-ups performed,[11]

Our study found that approximately 40% of IBD patients had anaemia at any given time during the observation period, a proportion similar to that observed in previous studies.[11,25] However, although in our study the prevalence of anaemia in CD at the time of diagnosis was in accordance with previous studies, the prevalence in UC was higher.[9,10] At 1-year follow-up, the prevalence of anaemia in Western European patients was low and similar to other population-based cohorts, whereas Eastern European patients had higher prevalence rates. As only a selection of patients had HgB measured at diagnosis or follow-up, the findings may be biased, as these patients were more likely to have received immunomodulators or biologics, or to have extensive colitis. Furthermore, the prevalence of IDA in our cohort was low, but data on anaemia subtypes from population-based cohorts are limited. A Scandinavian cross-sectional study found that 20% of patients had IDA,[2] and a German population-based cohort with rates of full anaemia work-up found that 38% of anaemia patients had IDA.[11] As many patients did not have full anaemia work-up performed the reported prevalence of IDA might be underestimated. Consistently with previous studies, we found that disease classification [having more extensive colitis and colonic CD location], as well as the need for more immunomodulators, biological therapy, and surgery, as surrogate markers for disease severity, to be a predictor of anaemia.[9,10,28]

Most data on anaemia from population-based cohorts originate in Western, rather than Eastern, Europe.[29] In this study, we found that Eastern European UC patients had a higher risk of anaemia than those from Western Europe. Patient characteristics, as well as short-term outcomes, did not differ between geographical regions in this cohort[13,15] despite differences in treatment strategies. Therefore, the present findings might indicate differences in awareness of anaemia across Europe, as well as in overall quality of IBD care, as we have no reason to believe the disease course is influenced by region.

The strength of the present study is the prospective population-based inclusion and follow-up of incident IBD patients diagnosed

Table 4. Factors influencing final value of haemoglobin during follow-up in inflammatory bowel disease patients.

	Crohn's disease		Ulcerative colitis	
	Adjusted mean HgB[a]	Adjusted mean HgB[b]	Adjusted mean HgB[a]	Adjusted mean HgB[b]
No. of patients	569	686	801	1,021
No. of samples	-	2688	-	3,563
Gender				
Female	8.1*	8.0*	8.2*	8.1*
Male [reference]	8.8	8.7	8.9	8.9
Region				
Eastern Europe	8.4	8.3	8.4*	8.3*
Western Europe [reference]	8.5	8.4	8.6	8.6
Smoking status				
Current	8.5	8.4	8.9*	8.7*
Former	8.3	8.3	8.6	8.5
Never [reference]	8.5	8.5	8.5	8.5
Extra-intestinal manifestation				
No	8.5	8.4	8.6	8.5
Yes [reference]	8.4	8.3	8.5	8.4
Disease behaviour ± perianal				
B3: penetrating	8.4	8.3	-	-
B2: stricturing	8.3*	8.2*		
B1: non-stricturing, non-penetrating [reference]	8.5	8.5		
Disease location				
L4: Upper GI [± L1-L3]	8.5	8.5		
L3: Terminal ileum + colon	8.4	8.4*	-	-
L2: Colon	8.3*	8.2*		
L1: Terminal ileum [reference]	8.6	8.6		
Disease extent				
E3: Extensive colitis			8.6	8.4*
E2: Left-sided	-	-	8.6	8.5*
E1: Proctitis [reference]			8.6	8.7
Highest treatment level				
No treatment	8.7	8.6*	9.1*	9.2*
5-aminosalicylates	8.7	8.7*	8.7*	8.7*
Corticosteroids	8.4	8.4	8.6*	8.5*
Immunomodulators	8.3	8.3	8.2	8.1*
Biological therapy	8.6	8.4*	8.3	8.1*
Surgery [reference]	8.4	8.1	7.8	7.6

GI, gastrointestinal.

[a]ANCOVA [analysis of covariance] for final haemoglobin value in measurements taken more than 6 months after diagnosis.

[b]Repeated measures ANOVA [analysis of variance] including all available haemoglobin values.

*$p < 0.05$.

within well-defined geographical areas. Diagnostic criteria, case ascertainment methods, and recorded data were standardised, and patients were thereby made fully comparable. Several measures previously described ensured that all centres collected valid and high quality data.[13] The EpiCom cohort thereby constitutes a unique group of patients diagnosed after the introduction of biological agents and in the era of earlier and more aggressive treatment with immunomodulators or biological agents. The patients represent the natural spectrum of disease severity. The choices of treatment, as well as of monitoring of anaemia status, reflect community practices; however, they were implemented with a knowledge of the consensus of the European Crohn's and Colitis Organisation.

This study's limitations include the heterogeneity of the participating centres in terms of the health care systems of which they form a part. Decisions regarding treatment and follow-up are strongly linked to extra-medical considerations, and therefore the differences observed between Eastern and Western Europe might be explained by variations between health care systems across the continent. Furthermore, as the cohort represents real-life practices and no guidance for anaemia screening was provided specifically for this study, not all patients had HgB values or full anaemia work-ups available. Prevalence rates at diagnosis and at 1-year follow-up are influenced by the fact that patients with mild or no symptoms, or mild disease course, were to a lesser extent included in the analysis compared with those with more severe disease. Unfortunately we did not have data regarding iron treatment available, and the prevalence rates of anaemia in the relevant background populations were not collected for comparison. Finally, clinical data were collected only after diagnosis, and so data from patients monitored before diagnosis were not recorded for this study but might have influenced the decision on how to screen follow-up up patients.

To conclude, in this European prospective population-based inception cohort the prevalence of anaemia at diagnosis and during the first year of disease was found to be high, with 42% of patients having at least one instance of anaemia. Patients are assessed for anaemia frequently during the first year after a diagnosis of IBD; however, a full anaemia work-up is frequently neglected.

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Conflict of Interest

JB: lecture fees from AbbVie, Takeda, and MSD; consulting fees from AbbVie, Celgene, and Janssen. DD: lecture fees from AbbVie and Takeda; consulting fee from Janssen. RS: lecture fees from AbbVie, Takeda, and MSD. VA: consulting fees from MSD and Jansen. JFD: lecture fees from AbbVie, Takeda, MSD, and Pharmacosmos. All other authors reported no conflicts of interest.

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Author Contributions

All authors have participated in the study design, patient inclusion, and data acquisition, have critically reviewed the draft manuscript for content, and approved the final version for publication. JB had full access to all the data in the study and takes full responsibility for the veracity of the data and statistical analyses. JB, LUG, MH, JFD, and PM analysed and interpreted the data. JB drafted the manuscript.

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Supplementary Data

Supplementary data are available at *ECCO-JCC* online.

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Appendix. Members of the EpiCom study group

Ola Niewiadomski (Australia)
Sally Bell (Australia)
Niksa Turk (Croatia)
Silvija Cukovic-Cavka (Croatia)
Ioannis Kaimakliotis (Cyprus)
Anastasia Nicolaou (Cyprus)
Dana Duricova (Czech Republic)
Milan Lukas (Czech Republic)
Martin Bortlík (Czech Republic)
Olga Shonová (Czech Republic)
Johan Burisch (Denmark)
Pia Munkholm (Denmark)
Ebbe Langholz (Denmark)
Birgitte Blichfeldt (Denmark)
Dorte Marker (Denmark)
Katrine Carlsen (Denmark)
Petra Weimers (Denmark)
Natalia Pedersen (Denmark)
Jens Kjeldsen (Denmark)
Clays Aalykke (Denmark)
Jens Frederik Dahlerup (Denmark)
Karen Kudsk (Denmark)
Vibeke Andersen (Denmark)
Ida Vind (Denmark)
Niels Thorsgaard (Denmark)
Riina Salupere (Estonia)
Jóngerð Olsen (Faroe Islands)
Kári Rubek Nielsen (Faroe Islands)
Pia Oksanen (Finland)
Pekka Collin (Finland)
Konstantinnos H. Katsanos (Greece)
Dimitrios K. Christodoulou (Greece)
Alexandros Skamnelos (Greece)
Dimitrios Politis (Greece)
Karin Ladefoged (Greenland)
Peter Laszlo Lakatos (Hungary)
Zsuzsanna Vegh (Hungary)
Laszlo Lakatos (Hungary)
Peterne Demenyi (Hungary)
Szabina Nemethne Kramli (Hungary)
Colm O'Morain (Ireland)
Giualia Dal Piaz (Italy)
Alessia Santini (Italy)
Giulia Girardin (Italy)
Renata D'Inca (Italy)
Doron Schwartz (Israel)
Selwyn Odes (Israel)
Limas Kupcinskas (Lithuania)
Laimas Jonaitis (Lithuania)
Gediminas Kiudelis (Lithuania)
Irena Valantiene (Lithuania)
Romanas Zykus (Lithuania)
Ruta Kucinskiene (Lithuania)
Svetlana Turcan (Moldova)
Louisa Barros (Portugal)
Fernando Magro (Portugal)
Daniela Lazar (Romania)
Adrian Goldis (Romania)
Inna Nikulina (Russian Federation)
Elena Belousova (Russian Federation)
Vicent Hernandez (Spain)
Luisa de Castro (Spain)
Juan-Ramon Pineda (Spain)
Santos Pereira (Spain)
Jesus Martinez-Cadilla (Spain)
Luciano Sanroman (Spain)
Montserrat Figueira (Spain)
David Martinez Ares (Spain)
Jose-Ignacio Rodriguez-Prada (Spain)
Alberto Fernandez (Spain)
Amalia Carmona (Spain)
Carlos Gonzalez-Portela (Spain)
Sven Almer (Sweden)
Lotta Granberg, (Sweden)
Benoît Almer (Sweden),
Jonas Halfvarson (Sweden)
Ulla-Britt Widen (Sweden)
Shaji Sebastian (UK)
Sally Myers (UK)
Katherine Ashton (UK)
Emma whitehead (UK)
Naila Arebi (UK)