ORIGINAL ARTICLE

Biologic treatment of inflammatory bowel disease in Poland, 2012–2020: nationwide data

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KEY WORDS

biologic treatment, inflammatory bowel disease, population data

EDITORIAL

by Myrelid and Eberhardson

ABSTRACT

INTRODUCTION The frequency of biologic drug treatment for Polish patients diagnosed with ulcerative colitis (UC) or Crohn disease (CD) has been insufficiently studied.

OBJECTIVES We aimed to analyze the use of biologic treatments among Polish patients suffering from inflammatory bowel diseases (IBDs).

PATIENTS AND METHODS We used administrative data collected by the National Health Fund (Narodowy Fundusz Zdrowia [NFZ]), Poland's sole public health care payer. IBD cases were defined as cases with at least 2 records assigned code K50 or K51 according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (ICD-10) and either at least 2 reimbursed prescriptions for IBD drugs or intestinal surgery preceding the record. We identified IBD patients receiving biologic treatments reimbursed by the NFZ in the years 2012–2020. We assessed the percentages of patients receiving biologic treatments in terms of disease type, sex, age group, and place of residence.

RESULTS While 6.8% of Polish CD patients received biologic treatment in 2012, that figure reached 7.9% by 2020. Biologic treatments were given to 0.4% of UC patients in 2014, and 1.6% in 2020. Among patients with both CD and UC, significantly fewer women received biologic therapy than men. The highest percentages of patients receiving biologic treatment for CD and UC were found in the 10–19 age group, while patients over 70 were the adults most rarely treated with biologic drugs.

CONCLUSIONS We showed a growing use of biologic agents in the treatment of IBD in Poland. Women receive biologic treatment for IBD significantly less frequently than men. The pediatric population features the highest proportion of patients receiving such treatment.

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INTRODUCTION Disclaimer: For the purpose of this work, the authors use the term "biologic drugs" to denote any of the innovative drugs used in the treatment of inflammatory bowel disease (IBD), including infliximab, adalimumab, vedolizumab, ustekinumab, and tofacitinib. Strictly speaking, tofacitinib is not a biologic drug but treating it as one fits best with the governmental therapeutic programs being pursued in Poland.

Crohn disease (CD) and ulcerative colitis (UC) are brought together under the general heading of IBD. While the first case of UC was described in 1859 by Sir Samuel Wilks, it was a Polish surgeon Antoni Leśniowski who in 1903 first reported a series of ileitis cases later classified as CD, long before the first detailed description (1932) of a patients' series by BB Crohn and his collaborators.[1-3] The etiology of both diseases remains unclear, though the suspected contributing factors include genetic predispositions, changes in immune system functioning, and environmental factors.[4-6] Both diseases are chronic in nature but with periods of relapse alternating with remissions; and both tend to develop complications, including some extraintestinal manifestations.

The prevalence of IBD is increasing steadily across the world. According to *The Global Burden of Diseases, Injuries and Risk Factors Study*,[7] there

WHAT'S NEW?

To the best of our knowledge, this article is the first to describe the population of Polish patients suffering from inflammatory bowel diseases (IBDs) and treated with innovative biologic drugs, which are the best treatment options known for patients with a moderate to severe disease course. Using administrative data, we estimated and discussed significant differences in the use of biologic drugs across different regions of Poland. We also showed a higher treatment rate for men than for women, as well as a high and rising rate for the youngest population. Access to modern therapies is crucial for improving the quality of life for the substantially growing population of IBD patients. We believe our work will be a helpful reference for evaluating the current situation of those patients and for predicting future demands.

were 6.8 million people living with IBD in 2017. In 2020, Poland reported 23 574 patients diagnosed with CD, as well as 73 235 with UC,[8] out of a national population of some 38 million inhabitants.

Given the lack of clarity as to the cause(s) of IBD, there is no causative treatment. Rather, the management of IBD includes the use of 5-aminosalicylates, budesonide, systemic steroids, immunosuppressive agents (azathioprine, 6-mercaptopurine), and the newest therapeutic innovations: biologic drugs and small-molecule immunosuppressive drugs. Two treatment approaches have been implemented into clinical practice: a "step-up" one, whereby the introduction of biologic drugs follows a failure of a conventional therapy, and a "top-down" approach in which biologic drugs represent a first-line therapy. So far there has been no strong evidence favoring one over another,[9-12] however, a majority of gastroenterological associations recommend the "step-up" strategy as a standard approach in moderate to severe disease course, limiting the use of the "top-down" one to patients with poor prognosis on the disease onset.

Today, in the European Union, and so also in Poland, there are 5 innovative drugs registered for use in IBD treatment: infliximab, adalimumab, vedolizumab, ustekinumab, and tofacitinib.

In Poland, due to the high costs of treatment with innovative drugs, the abovementioned medications are fully reimbursed by the National Health Fund (Narodowy Fundusz Zdrowia [NFZ]) through so-called therapeutic programs approved by the Ministry of Health. The therapeutic program for CD (B.32)[13] was established in November 2007; its counterpart for UC (B.55)[14] was established in October 2013. Both have undergone many changes, most significantly, extensions of maximum treatment duration and introduction of new drugs.

The current B.32 therapeutic program "The treatment of patients with Crohn disease" makes infliximab or adalimumab available for use in patients aged 6 years and above, while vedolizumab or ustekinumab can be used in those of at least 18 years of age. Criteria to be met by the patients are: a severe flare of the disease defined by a score of more than 300 points on the Crohn Disease Activity Index (CDAI) scale, or over 50 points on the Pediatrics Crohn Disease Activity Index (PCDAI) scale and a previous failure of a conventional therapy, for example, glucocorticoids or immunosuppressive drugs. In the case of ustekinumab, an additional condition is the exclusion of anti-tumor necrosis factor (TNF) as a first-line biologic medicine, due to its proven prior failure. In the presence of a perianal fistula, infliximab or adalimumab may be used irrespective of the CDAI or PCDAI score.[13]

The current therapeutic B.55 program "The treatment of patients with ulcerative colitis" provides the treatment for patients aged 6 and over with infliximab, as well as with vedolizumab, tofacitinib, or ustekinumab for patients aged 18 and over. The criteria to be met by patients in this context are: a moderate to severe flare of the disease defined as 6 or more points on the Mayo scale for adults, and 65 or more points on the Pediatric Ulcerative Colitis Activity Index scale for patients aged 6–18, including a previous failure of the conventional therapy, or counterindications where its use is concerned, with simultaneous counterindications as regards the administration of cyclosporine.[14]

Until 2022, the treatments available in both therapeutic programs were time-limited, that is, could be administered for 12 to 24 months. In their latest versions (applicable from 2022 and beyond), the time limits have ceased to be imposed.

The analysis of such NFZ-reimbursed usage of biologic treatment among Polish patients with the 2 types of IBD represented both the aim and the subject matter of the research detailed in this paper.

PATIENTS AND METHODS **Data source** Our analysis centered on administrative health care–related claims in Poland, collected in the databases of the NFZ, the sole entire state health care payer. We searched the records for health services taking the form of individual claims reported to the NFZ by the service providers. The initial assessment concerned the prevalence of IBD in Poland in the years 2012–2020, with reference to the prevalent and incident cases in the NFZ database assigned a K50 or K51 code according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (ICD-10).[8] Due to a lack of electronic data, there was no possibility of assessing the prevalence of IBD for the years 2008–2011, a period in which the CD therapeutic program was already active. In the next step, we calculated the rates of the therapeutic program treatment in CD and UC patients with reference to age, sex, and place of residence. We further looked for an association between the use of biologic drugs in different regions of Poland (voivodeships), as set against the number of gastroenterologists practicing in each region. The latter data for individual years were obtained from the Polish Chamber of Physicians and Dentists.

TABLE 1 Percentage of Crohn disease patients treated under B.32 therapeutic program in Poland in the years 2012–2020

Year	Number of CD patients treated with biologic drugs	Total number of CD patients	Rate of use of biologic drugs per 100 cases
2012	751	11 107	6.8
2013	863	13 022	6.6
2014	1084	14 953	7.2
2015	1239	16 784	7.4
2016	1312	18 477	7.1
2017	1454	20 125	7.2
2018	1663	21 712	7.7
2019	1823	23 058	7.9
2020	1863	23 574	7.9

Abbreviations: CD, Crohn disease

Biologic drug therapies for Crohn disease and ulcerative colitis Services associated with the biologic treatment of CD or UC were identified in the NFZ service database with relation to specific products covered by the NFZ contracts (Supplementary material, *Table S1*). Each patient receiving at least 1 service over the 2012–2020 period was identified and assigned to a specific voivodeship in line with the location of the hospital involved and not their place of residence. The patients treated in more than 1 voivodeship in a given year were assigned to each voivodeship involved.

Prevalence of Crohn disease and ulcerative colitis As a basis for calculating the percentage of patients receiving the biologic drugs for CD or UC, we used the respective prevalence for these diseases, as estimated previously.[8] The patients were selected based on the following criteria: 1) at least 2 services in a hospital, or an outpatient specialist clinic, reported with the K50 or K51 ICD-10 code, and either 2) at least 2 prescriptions filled out for IBD drugs (as listed in Supplementary material, *Table S2*) with an interval of at least 2 months, or 3) an episode of intestinal surgery assigned 1 of the defined *International Classification of Diseases, Ninth Revision* codes (Supplementary material, *Table S3*), prior to at least 1 service reported with K50 or K51 ICD-10 codes.

The next step classified the patients as suffering from either CD or UC, on the basis of the ICD-10 code reported for the last service received, so that each patient was assigned to the group with CD, UC, or both of these diagnoses.

Migration analysis To assess the use of the biologic drugs in individual voivodeships and the scale of patient migration, we calculated the percentage of patients who could be regarded as external to each of the 16 voivodeships in Poland. We also calculated the percentage of residing patients treated in other voivodeships and the migration balance, defined as the difference between 1) the number of patients treated in a given voivodeship residing outside that voivodeship and, 2) the number of patients residing in a given voivodeship treated in another one. All these migration rates were calculated for 2020.

Statistical analysis The prescription rates for biologic therapies for CD in Poland in a given year between 2012 and 2020 were calculated as the number of patients registered in the therapeutic program for CD, as divided by 100 prevalent CD cases. An analogous process was run for UC. However, as biologic therapies for UC had not been reimbursed before 2014, we calculated the rates for the 2014–2020 period only. Differences in rates for women and men were compared using the χ^2 test, while voivodeship-based relationships between the number of gastroenterologists and the rates of patients participating in biologic therapy were assessed by calculating the Pearson correlation coefficients using R statistical software (version 3.6.2) (R Foundation for Statistical Computing, Vienna, Austria) with the "data.table" package (version 1.12.8). All the tests were 2-sided and significance level was set at a P value of 0.05.

Ethical Committee The study representing the basis for this paper gained approval from the Bioethical Committee of the Maria Sklodowska-Curie National Research Institute of Oncology (73/2021).

RESULTS

Crohn disease The official number of CD patients in Poland rose from 11 107 in 2012 to 23 574 in 2020. The rates of biologic drug use among these patients in the years 2012–2020 are presented in TABLE 1. As many as 751 patients with CD received biologic treatment in 2012, constituting 6.8% of their total number (751/11 107). The number of such patients in 2020 was 1863, representing 7.9% of the total number. Thus, even though the absolute numbers of CD patients receiving biologic drugs in the analyzed period doubled, the proportion of prevalent CD patients treated with biologic drugs increased only slightly (TABLE 1).

For most of the analyzed years, there was a significant difference in the frequency of using biologic drugs in men and women. In 2012, 6.4% of women diagnosed with CD were registered in the therapeutic program, as compared with 7.2% of men (TABLE 2). In 2020, the difference was more pronounced, with respective rates of 6.7% and 9.0% (P <0.001).

Over the analyzed period as a whole, the group of patients with CD showing the highest frequency of treatment with biologic drugs were those aged 10–19 years. Furthermore, it was in this group that the most marked increase in the share of patients receiving biologic treatment was recorded (from 11.8% in 2012 to 21.7% in 2020) (FIGURE 1; Supplementary material, *Table S4*).

The number of hospitals offering biologic treatment for CD increased from 53 in 2012 to 62

TABLE 2 Treatment rates for men and women with Crohn disease under B.32 therapeutic program in Poland in the years 2012–2020

Year	Women with CD under B.32 program	Men with CD under B.32 program	Total number of women with CD	Total number of men with CD	Percentage of women under B.32 program	Percentage of men under B.32 program	*P* value
2012	363	388	5683	5424	6.4	7.2	0.11
2013	406	457	6638	6384	6.1	7.2	0.02
2014	489	595	7562	7391	6.5	8.1	<0.001
2015	557	682	8505	8279	6.5	8.2	<0.001
2016	563	749	9309	9168	6	8.2	<0.001
2017	624	830	10 100	10 025	6.2	8.3	<0.001
2018	716	947	10 876	10 836	6.6	8.7	<0.001
2019	777	1046	11 529	11 529	6.7	9.1	<0.001
2020	790	1073	11 713	11 861	6.7	9	<0.001

Abbreviations: see **TABLE 1**

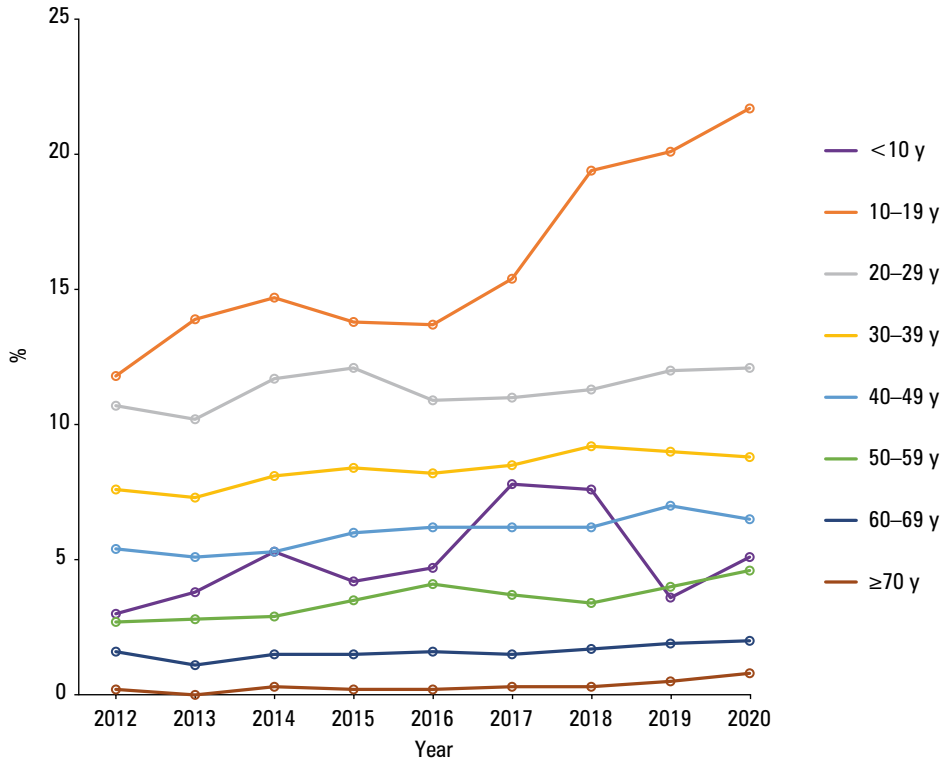

FIGURE 1 Percentage of patients with Crohn disease treated under B.32 therapeutic program in the years 2012–2020, by age group

in 2020. In 2020, the highest number of such centers was 10 noted for Mazowieckie voivodeship, whereas both Opolskie and Świętokrzyskie voivodeships had only 1 such center. **FIGURE 2** and Supplementary material, *Table S5* present shares of patients with CD receiving biologic drugs in 2020 per voivodeship. Substantial differences are to be noted. In Mazowieckie voivodeship (that includes Warsaw, the capital of Poland), 13.8% of all patients with CD received treatment with biologic drugs—a sharp contrast with Lubuskie voivodeship, for which the rate was as low as 1.2%. It further emerged that Mazowieckie was the region of Poland treating the highest percentage of patients from other voivodeships. The patients treated in Mazowieckie but residing in other voivodeships accounted for 34.9% of all patients treated with biologic drugs in this voivodeship. Conversely, Lubuskie voivodeship had the highest percentage of patients receiving biologic treatment outside of their voivodeship of residence, at frequency up to 88.6%. This means that, roughly speaking, only 1 in 10 CD patients from Lubuskie voivodeship received biologic treatment close to their place of residence.

Ulcerative colitis The number of UC patients in Poland increased from 49 758 in 2014 to 73 235 in 2020. The rates of biologic drugs usage among these patients in the years 2014–2020 are presented in **TABLE 3**. There were 207 UC patients treated with biologic drugs in 2014, which was just 0.4% of the total number (207/49 758). In 2020, these numbers rose to 1174 and 1.6% (1174/73 235), respectively; both absolute and relative numbers of UC patients on biologic drugs were markedly higher than in 2014 (**TABLE 3**).

As with CD, we witnessed a significant difference in the use of these drugs between men and

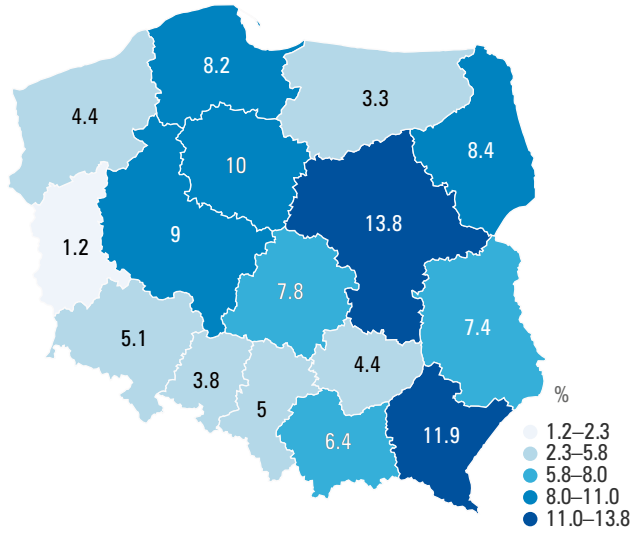

FIGURE 2 Percentage of patients with Crohn disease treated under B.32 therapeutic program in 2020, by Polish voivodeships

TABLE 3 Percentages of patients with ulcerative colitis treated under B.55 therapeutic program in Poland in the years 2014–2020[a]

Year	Number of UC patients treated with biologic drugs	Total number of UC patients	Rate of use of biologic drugs per 100 cases
2014	207	49 758	0.4
2015	298	55 005	0.5
2016	251	59 924	0.4
2017	407	64 468	0.6
2018	692	68 546	1
2019	1021	72 080	1.4
2020	1174	73 235	1.6

a The therapeutic program B.55 commenced in 2014

Abbreviations: UC, ulcerative colitis

TABLE 4 Treatment rates for men and women with ulcerative colitis under B.55 therapeutic program in Poland in the years 2014–2020[a]

Year	Women	Men	Number of women with UC	Number of men with UC	Percentage of affected women treated under B.55 program	Percentage of affected men treated under B.55 program	*P* value
2014	82	125	24 607	25 151	0.3	0.5	0.005
2015	124	174	27 182	27 823	0.5	0.6	0.007
2016	99	152	29 500	30 424	0.3	0.5	0.002
2017	166	241	31 730	32 738	0.5	0.7	0.001
2018	287	405	33 658	34 888	0.9	1.2	<0.001
2019	443	578	35 338	36 742	1.3	1.6	<0.001
2020	509	665	35 964	37 271	1.4	1.8	<0.001

a Therapeutic program B.55 was initiated in 2014

Abbreviations: see TABLE 2

women. In 2014, the rate for patients diagnosed with UC was 0.3% for women and 0.5% for men. By 2020, the difference was even greater, with rates for women and men reaching 1.4% and 1.8%, respectively (P <0.001) (TABLE 4).

In the years 2014–2016, the highest share of UC patients receiving innovative drugs were those in their twenties (0.9%). By 2017, however, that lead position had been taken by the patients aged 10–19 (FIGURE 3; Supplementary material, *Table S6*).

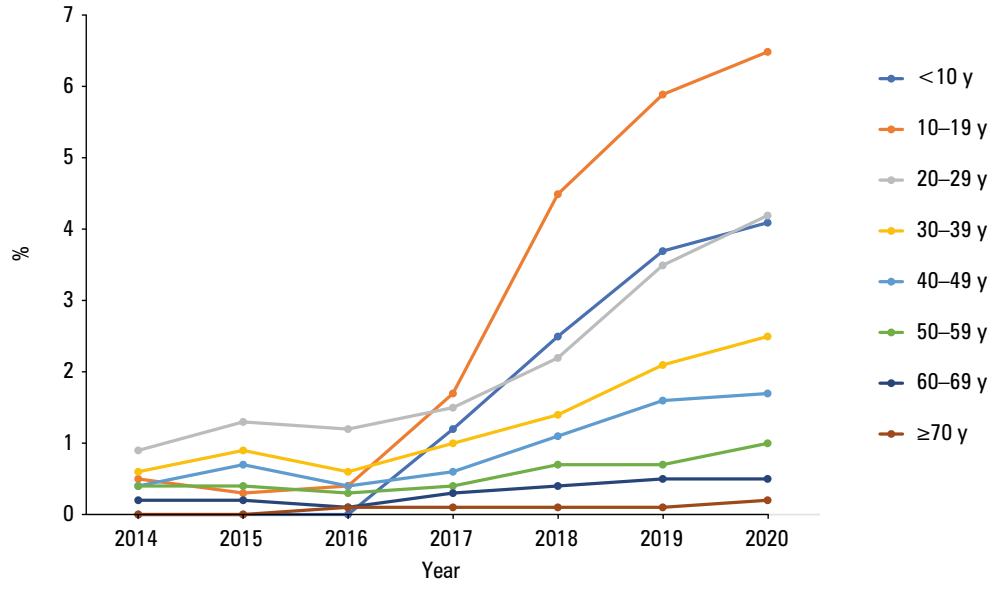

FIGURE 3 Percentage of patients with ulcerative colitis treated under B.55 therapeutic program in the years 2014–2020, by age group

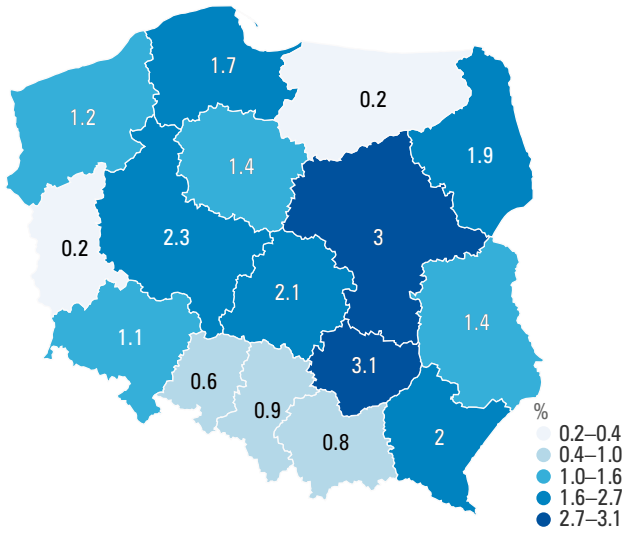

FIGURE 4 Percentage of patients with ulcerative colitis treated under B.55 therapeutic program in 2020, by Polish voivodeships

The number of hospitals offering the biologic treatment for UC rose from 31 in 2014 to 52 in 2020. In 2020, the highest number of such centers was 8 noted for Mazowieckie voivodeship, whereas Opolskie, Świętokrzyskie, and Warmińsko-Mazurskie voivodeships had only 1 center each. As for CD, we found clear voivodeship-to-voivodeship differences in the rates of using biologic treatment (FIGURE 4; Supplementary material, *Table S7*). The highest percentage of UC patients treated with innovative drugs in 2020 was 3.1% and 3.0%, noted for Świętokrzyskie and Mazowieckie voivodeships, respectively. The corresponding value for both Lubuskie and Warmińsko-Mazurskie voivodeships was just 0.2%.

The highest rate for patients with UC receiving treatment with biologic drugs in a voivodeship outside of their place of residence was 40% noted for Warmińsko-Mazurskie voivodeship. However, this result is perhaps misleading, given this region's absolute figure of just 5 patients with UC undergoing biologic treatments. However, as with CD, Lubuskie voivodeship emerged as the Polish region from which the highest proportion (93.1%) of UC patients sought treatment in a voivodeship other than their own.

Relations between the number of gastroenterologists in a voivodeship and the use of biologic drugs During the 2012–2020 period, the number of certified gastroenterologists in Poland increased from 713 to 1136. Two of the regions boasting the highest number of gastroenterologists per inhabitant were Mazowieckie and Podlaskie voivodeships (each with 4.2/100 000 in 2020). This ratio was the lowest in Świętokrzyskie voivodeship (1.6/100 000 in 2020). The 2020 ratio of the number of gastroenterologists per 100 IBD patients proved to be the highest in Mazowieckie voivodeship (1.7/100), and the lowest in Lubuskie, Wielkopolskie, and Świętokrzyskie voivodships (0.7/100) (Supplementary material, *Table S8*). However, no significant correlation was noted between the number of gastroenterologists and the number of patients receiving biologic treatment in any voivodeship ($P = 0.166$).

DISCUSSION The analysis detailed here drew on Poland-wide data on the usage of biologic drugs to treat IBD patients, with costs as reimbursed by the NFZ. It showed a growing use of biologic drugs over the years 2012–2020, in terms of both absolute numbers of treated patients and shares of all patients in Poland diagnosed with either CD or UC. Treatment rates increased from 6.8% in 2012 to 7.9% in 2020 among CD patients, and from 0.4% in 2014 to 1.6% in 2020 within the population of those suffering from, and treated for, UC. The factors potentially accounting for this increase include, primarily, growing clinicians' confidence in biologics, arising from a better understanding of their modes of action, and secondly, a mounting evidence regarding both

their effectiveness and safety. Another probable factor is the introduction of biosimilar drugs that lowered the costs of the therapy. This was later accompanied by extensions of maximal periods of treatment under available treatment programs that further encouraged the gastroenterologists to enroll more patients in the hope of achieving prolonged remission. One more possible reason for the increased rate of using the biologics among Polish IBD patients may lie in improved access, with a growing number of centers offering this kind of treatment. Finally, the gradual increase in the number of drugs encompassed by therapeutic programs over the last 5 years may have allowed the patients failing to respond to the first-line therapy to re-enroll for new treatments.

The observed increase in the use of biologics in Poland resembles the situation in other countries. A Danish nationwide study[15] on enrolled patients diagnosed with IBD over the years 2003–2016 found the share of participants treated with biologic agents rising from 0% to 16% for CD, and from 0% to 5% for UC cases. A 2010–2016 Norwegian study[16] reported an increase in the rate of use of biologic drugs from 17% to 33% for CD patients, and from 7% to 13% for UC patients. Furthermore, a study from Sweden,[17] the most methodologically similar to ours (and which analyzed the population of IBD patients diagnosed in the years 1969–2017, and those treated with biologics in the years 2005–2017), pointed to the cumulative rate of use of the drugs being as high as 14.5% and 6.7% among patients with CD and UC, respectively. A Swiss study[18] noted an increase in the use of biologic drugs among IBD patients from 5.3% in 2010 to 12.8% in 2014, albeit with no distinction drawn between CD and UC. A further limitation of the latter study was its confinement to patients insured by a single Swiss payer, which covered only around 15% of the population of Switzerland.

While the share of Polish IBD patients receiving treatment has been on the rise, it remains below the levels noted in other countries for which data have been published. This would mainly seem to reflect the restrictive rules applied to Polish therapeutic programs. In particular, the minimum level the disease activity required for the treatment to commence is simply too high to allow many patients with moderate activity to be included, along with those for whom conventional treatment has failed and who experience postoperative relapse. For every patient taken on, there is an absolute requirement to establish a failure of the conventional therapy. This clearly stands in the way of any early-stage introduction of the biologic treatment, despite the fact that the biologic therapy is proven to be the most effective. Moreover, the 2 Polish programs were previously run under time limits, requiring withdrawal after 12 or 24 months, even if the treatment remained efficient.

A further key observation from our study concerned significant differences in the deployment of biologic drugs in IBD patients of different ages. The highest rate of biologics use was found for the patients aged 10–19 years, perhaps because these are the youngest patients that are more often affected by an aggressive course of the disease. A Hungarian population study[19] taking 30 years of practice into consideration established that small intestine involvement, perianal fistulas, a need for systemic steroids, and a need for surgery induced by the disease all arise more often in pediatric CD patients than in adults, while all of the factors referred to are associated with poor outcome prognoses. Moreover, just as in our study, Romberg-Camps et al[20] demonstrated that it was within their youngest (under 18 years old) population of IBD sufferers that the highest cumulative rate of use of biologics (19%) was to be found.

Our study further showed that men were more likely than women to be treated with biologic drugs. Such a finding was in fact made previously in a multicenter Polish study on anti-TNF use in therapeutic programs in IBD.[21] The aforementioned Swedish analysis[17] also noted a sex-based difference in the rate of using the biologics (significant at $P = 0.02$).[17] However, this phenomenon has no obvious explanation, given conflicting data on sex-related differences in IBD courses and complications. There are nevertheless studies showing that male sex is a risk factor when it comes to IBD taking a more severe course, with this extending, in the case of CD, to a higher frequency of involvement of the upper gastrointestinal tract and small intestine. These circumstances may prompt clinicians to make more frequent use of biologics.[20,22,23] According to other studies, male sex is an independent risk factor for extensive abdominal surgery, including intestinal resections.[24] It is also worth mentioning that, within the IBD population, it is men who most often go on to suffer—often fatally—from cancer of the large bowel.[25,26]

Another possible explanation for the more limited usage of biologic drugs among women might involve discontinuation of treatment due to its adverse effects. Some studies suggest that the female sex is an independent risk factor when it comes to adverse effects of anti-TNF drugs.[27] Moreover, in the Polish case, pregnancy was a criterion that straightforwardly excluded the patients from the therapeutic programs. This was likely a further reason why women were treated with biologic drugs for IBD less often than men.

The remaining significant difference demonstrated for the rates of using biologics is the regionally-based one, given that as many as 27% of all instances of biologic therapy for Polish CD patients involved receipt of the drugs in Mazowieckie voivodeship. The corresponding figure for patients with UC was 24%. At the other extreme, the western voivodship of Lubuskie emerged as contributing the least to overall biologic treatment of Polish CD and UC patients. In 2020, just 0.27% of Polish patients with CD

treated with biologic drugs were cared for in that voivodeship. The corresponding figure for UC was just 0.34%. The key reason for this would seem to involve limited access to specialist gastroenterology care in many patients' respective regions of residence. Data from the Polish Chamber of Physicians and Dentists reveal that, while Mazowieckie voivodeship had 226 gastroenterologists in 2020 (or 1.7 per 100 IBD patients), Lubuskie voivodship had a mere 17 (or 0.7 per 100 IBD patients). Nevertheless, it was not possible to establish any significant correlation between the number of gastroenterologists in a given voivodeship and the number of patients treated with biologic drugs (with $P = 0.17$).

These last differences might be partly explained by migration of IBD patients in search of treatment, to the highly-specialized centers mainly located in the capital and at academic units. While there were several dozen centers offering biologic treatment across the country as of 2020 (62 for CD and 52 for UC), the 5 most-utilized ones served no fewer than 38.3% of the country's CD patients and 35.1% of the country's UC patients. Migration balance was thus definitely positive in the case of Mazowieckie voivodeship, with almost 35% of CD patients and nearly 26% of UC patients receiving biologic treatment there coming from beyond the region's borders. At the other extreme, in Lubuskie voivodeship, more than 88% of the resident CD patients on biologic drugs received this treatment in another voivodeship. In the case of UC, the figure was 93.1%.

Several limitations to our study include our confinement to IBD patients whose treatment gained NFZ reimbursement. Our analysis excluded patients treated as part of clinical trials. We have no insight on the proportion of IBD patients given biologic drugs in non-NFZ contexts. A further problem related to a lack of precise comparability reflects changing regulations of the therapeutic programs, above all regarding limited durations and the variety of drugs available. Equally, some IBD patients were enrolled in both of the therapeutic programs analyzed (B.32 and B.55), due to changes in diagnosis (most often from UC to CD). That confers a slight bias upon the percentage of patients treated for the particular diseases. Moreover, the aforementioned unequal geographic access to the therapeutic programs might also have generated a selection bias.

To conclude, our analysis of the use of biologic drugs among Polish IBD patients over the last decade confirmed a slow increase, sex-based differences, age-related differences, and an unequal geographic distribution of gastroenterological services providing the biologic therapy in individual Polish voivodeships. These results may in part reflect a limited access to innovative therapies due to tight reimbursement criteria. We believe these data are of importance at the national level, especially for those involved in the planning of the health policy, but also for medical professionals all over the world who deal with IBD patients.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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