

**Inflammatory bowel disease incidence, prevalence and twelve-month initial disease course
in Tasmania, Australia**

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ABSTRACT

Background:

High inflammatory bowel disease (IBD) rates have been reported in Australasia, but no state-wide studies have yet been performed.

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Aims:

This study estimates the one-year incidence and point prevalence of IBD in the state of Tasmania, Australia. It also reports clinical outcomes after twelve months of diagnosis in an incident cohort.

Methods

A prospective, population-based study was performed collecting prevalent and incident state-wide cases from 1st June 2013 to 31st May 2014. Case data were identified from specialist doctors, pathology databases and hospital records. Age-standardised rates (ASRs) were calculated based on World Health Organization 2000 standard population characteristics. Incident cases were followed up twelve months after diagnosis.

Results

There were 1719 prevalent cases: ASRs for IBD, Crohn's disease (CD), ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBDU) prevalence were 303.9, 165.5, 131.4 and 6.9 per 100,000 respectively. Prevalent CD cases were younger, with greater immunomodulator/biologic use and bowel resections. There were 149 incident cases: ASRs for IBD, CD, UC and IBDU incidence were 29.5, 15.4, 12.4, and 1.7 per 100,000 respectively. Incident CD cases were more likely than UC or IBDU to require escalation of medical therapy, hospitalisation, and bowel resection especially among

those with penetrating or stricturing disease. They had longer duration of symptoms prior to diagnosis.

Conclusions

IBD prevalence and incidence rates are high in Tasmania, comparable to data from other Australasian studies and those from Northern Europe and America. Poorer twelve month clinical outcomes occurred in complicated CD, with greater use of healthcare resources.

KEY WORDS

Epidemiology; hospitalization; treatment outcome; Crohn's disease; ulcerative colitis

INTRODUCTION

Inflammatory bowel disease (IBD), a significant global health burden¹⁻³, includes distinct phenotypes of Crohn's disease (CD), ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBDU)^{4, 5}. Few studies have explored the epidemiology of IBD in Australasia. Gearry et al reported on IBD epidemiology in the Canterbury region of New Zealand in 2006⁶ and 2014⁷. Wilson et al⁸, Studd et al⁹ and Niewiadomski et al¹⁰ conducted similar research in the Barwon region of Victoria, Australia between 2010 and 2016. These studies reports epidemiological rates similar to Northern Europe and America, which are among the highest in the world.

This study aimed to calculate the population-based one-year incidence of IBD from 1st June 2013 to 31st May 2014, and point prevalence of IBD on 31st May 2014, in Tasmania, an island state off the south coast of Australia. We hypothesised that the IBD burden in Tasmania may be higher than in Barwon due to greater distance from the equator, which has been suggested as a risk factor in Northern hemisphere studies^{2, 11}; as well as genetic enrichment for IBD susceptibility genes¹² in a geographically enclosed population through a founder effect^{13, 14}. We also aimed to describe phenotypes and disease course in the first twelve months after diagnosis, and determine predictors of outcomes such as escalation of medical therapy or bowel resection.

MATERIALS AND METHODS

Population

A population-based, epidemiological prospective cohort study was performed in Tasmania during the study period from 1st June 2013 to 31st May 2014, with incident cases during this period also followed up twelve months after diagnosis. Tasmania has a population of 513,100 as per 2013 census results with over 80% of its population of Caucasian background¹⁵. It lies approximately 200 kilometres further south of the equator than Barwon: the latitude of Geelong, the population centre of Barwon, is 38.14° south; the latitudes of Launceston and Hobart, the two major population centres of Tasmania, are 41.43° and 42.88° south.

Case Capture

Data about IBD cases were obtained using a modification of multiple case-capture methodologies used in the Barwon study⁹. Incident and prevalent cases were obtained from two sources: 30 specialists treating IBD during the one-year study period, including gastroenterologists, paediatricians and surgeons; and state-wide pathology databases. Case data were submitted to the primary author (RB) by specialists after relevant consultations. Specialists were also reminded every 2 months to contribute cases. There were no demographic exclusion criteria.

Histopathology databases were searched to identify additional IBD cases at the end of the study period. Searches were conducted using the terms “IBD”, “ulcerative colitis”, “Crohn’s disease”, “colitis” and “ulcerative proctitis”, from 1st Jan 1986 up to the end of the study period. Neither self-referrals from the broader community nor referrals from primary care practitioners were sought. Hospital International Classification of Disease (ICD) discharge codes were not analysed as a source of eligible cases. It was felt that these methods of case recruitment had potentially poor specificity.

Case confirmation

Among patients submitted by specialists, incident cases were defined as those newly diagnosed during the study period; and included only if independently confirmed to be a true case by a co-author (CS) using the Copenhagen diagnostic criteria, a composite of clinical, endoscopic, histological and radiological findings^{16, 17}. Prevalent cases included were those defined as having IBD, diagnosed at any time, according to a specialist’s professional opinion.

Among cases identified through histopathology databases, those with acute or self-limited infectious colitis (with no signs of chronicity on histology and corresponding pathogens found on microbiological testing) and microscopic colitis were excluded, as were those previously submitted by specialists. Among the remaining cases, those newly diagnosed with IBD during the study period and fulfilling Copenhagen criteria were included as additional incident cases. Cases were included as additional prevalent

cases if they had recently engaged in health care, either through outpatient consultation with IBD specialists or attendance to hospital, during the 18 month period prior to 31st May 2014. This cut-off was implemented to maximise the likelihood of them living in Tasmania at this date.

Epidemiological data collection

Epidemiological endpoints were IBD, CD, UC and IBDU point prevalence rates at 31st May 2014 and incidence rates between 1st June 2013 and 31st May 2014. Crude prevalence and incidence rates of IBD, with sub-analyses for CD, UC and IBDU, were calculated using the state population as the denominator. Rates were expressed as cases per 100,000 population. Age-standardised rates (ASRs) were calculated using the direct method, based on World Health Organization (WHO) year 2000 standard population characteristics¹⁸. Rates were presented with 95% confidence intervals (CI) based on an assumed Poisson distribution.

Clinical data collection

Case data were collected from treating specialists and/or hospital medical records. This included patient demographics, smoking status (current, former or never), disease duration and phenotype, bowel resections and use of immunomodulators and biologics. For incident cases, additional data included endoscopy, histology and radiology investigations, Montreal criteria sub-classifications¹⁹, hospitalisation, surgery

and/or pharmacotherapy during the first month after diagnosis as well as at twelve months after diagnosis.

For UC, disease distribution was divided into proctitis (E1), left-sided colitis up to the splenic flexure (E2) and extensive colitis (E3). For CD, distribution was divided into ileal (L1), colonic (L2) and ileocolonic (L3). For CD, behaviour was divided into non-stricturing/ non-penetrating (inflammatory) (B1), stricturing (B2) and penetrating (B3). B2 necessitated obstructive symptoms or radiological demonstration of proximal bowel dilatation. B3 required intra-abdominal fistula or abscesses, but excluded isolated perianal fistulae.

Data analysis

Statistical analysis was conducted using R Software, Version 3.0.1; (R Foundation for Statistical Computing, Vienna, Austria). Categorical data were analysed with Pearson χ^2 tests. Non-parametric continuous data were summarised as medians and interquartile ranges (IQR) and group differences were analysed by Mann-Whitney U-testing and Kruskal-Wallis analysis of variance by ranks. P-values <0.05 were considered statistically significant.

Ethics

This study was approved by the Tasmanian Human Research Ethics Committee (approval number: H0013057). Each case was allocated a study code and patient information was de-identified. Direct contact with patients was not made.

RESULTS

Prevalent cohort

On 31st May 2014 there were 1719 prevalent IBD cases, 792 (41.6%) males and 927 (58.4%) females, including 874 (50.8%) CD, 803 (46.7%) UC and 42 (2.4%) IBDU. Crude point prevalence per 100,000 of overall IBD, CD, UC and IBDU was 335.0 (95% CI: 319.2, 350.9), 170.3 (159.0, 181.6), 156.5 (145.7, 167.3) and 8.2 (5.7, 10.7) respectively. The ASR for overall IBD prevalence was 303.9 per 100,000 (CI: 288.6, 319.2); the ASRs were 165.5 (154.0, 177.1) for CD; 131.4 (121.7, 141.1) for UC; and 6.9 (4.7, 9.2) for IBDU. Median duration of disease was 8 years (IQR= 10) and median age at diagnosis was 36 years (IQR=28). A peak in IBD prevalence occurred among those in the sixth decade of life (Figure 1).

Those with CD, compared to both UC and IBDU, were both younger and diagnosed at an earlier age; more likely to be using immunomodulators and biologics at time of referral for study inclusion; and more likely to have had bowel resections. Compared to UC, those with CD were more likely female and have a history of smoking. Further details are provided in Table 1.

Incident cohort

There were 149 incident cases during the study period from 1st June 2013 to 31st May 2014, 84 (56.4%) males and 65 (43.6%) females, including 74 (49.6%) CD, 63 (42.2%) UC and 12 (8.1%) IBDU. Crude incidence per 100,000 of overall IBD, CD, UC and IBDU was 29.0 (CI: 24.4, 33.7), 14.4 (11.1, 17.7), 12.3 (9.2, 15.3) and 2.4 (1.0, 3.7)

respectively. The ASR for overall IBD incidence per 100,000 was 29.5 (CI: 24.5, 34.5). The ASRs were 15.4 (11.7, 19.1) for CD; 12.4 (9.2, 15.6) for UC; and 1.7 (0.7, 2.8) for IBDU. Median age at diagnosis was 41 years (IQR= 34). A peak in IBD incidence occurred among those in the third decade of life. A second peak of IBD in the sixth decade of life was largely attributable to UC (Figure 2). Median length of symptoms prior to diagnosis was 13 weeks (IQR= 28, range= 1-748),

There was a predominance of males in UC and females in IBDU. CD cases were younger than UC at diagnosis with a trend toward significance. IBDU cases were significantly older than CD and UC cases. More CD cases had a positive IBD family history than UC. Current smoking rates were higher in CD than in UC: however there were no significant differences in former smoking rates. CD cases also reported longer length of symptoms prior to diagnosis. Further details are provided in Table 2.

Incident diagnosis and classifications

Among UC cases, colonic disease extent was quite evenly split between E1 (n= 20, 31.7%), E2 (n=20, 31.7%) and E3 (n=23 36.5%). Among CD cases, locations were quite evenly split between L1 (n=21, 28.3%), L2 (n=27, 36.5%) and L3 (n=25, 33.8%). CD behaviour was predominantly B1 (n=60, 81.1%). Eleven cases (14.9%) had B2 disease and 3 (4.1%) had B3 disease.

Disease progress

Data for follow-up was provided for 141 of 149 cases (94.6%) at the twelfth month after diagnosis. Median number of outpatient visits (clinic or endoscopy) per case was 6 (IQR 4, range 1-19). 45 cases (30.2%) had at least 1 IBD-related hospitalisation. Among those hospitalised, median total length of inpatient time was 8 days (IQR 10, range 1-55). Fifteen (10%) cases had bowel resections, five (4 CD, 1 UC) having total colectomies for severe disease. Two cases had resections for colonic lesions (1 CD for caecal adenocarcinoma, 1 UC for large caecal adenoma).

CD cases were more likely than UC or IBDU to be hospitalised within the first twelve months, however there was no significant difference between median total time of inpatient stay between IBD phenotypes. CD cases had longer length of symptoms prior to diagnosis, more bowel resections, and more combined outpatient and endoscopy sessions. Table 3 provides further details.

With B2 and B3 CD combined as a subgroup of 'complicated disease', this subgroup had significantly higher rates of bowel resection (66.7%) than B1 CD (8.1%, $p < 0.001$). Those with L1 CD had longer median length of symptoms (in weeks) pre-diagnosis (52, IQR 359) than those with L2 (13, IQR 20, $p=0.003$), L3 (2, IQR 24, $p=0.027$) or a combined subgroup of L2 and L3 CD (18, IQR 24, $p=0.213$). Those with E3 UC (30.4% vs 0%, $p=0.023$), or E2 UC (25% vs 0%, $p=0.056$), were more likely to be hospitalised than those with E1 UC.

Predictors of bowel resection in CD

Univariate logistic regression was performed analysing predictors of bowel resection in CD (excluding carcinoma). Predictive factors identified included older age (OR 1.03, CI: 1.01-1.07, $p < 0.01$), current or former smoking (OR 5.5, CI: 1.37-22.1, $p = 0.016$) and B2/B3 behaviour (OR 13.1, CI: 3.15-54.2, $p < 0.01$). Use of steroids in the first month was protective against resection (OR 0.25, CI: 0.074-0.885, $p = 0.032$). However gender, CD location, length of symptoms pre-diagnosis and use of immunomodulators or biologics were not predictive. Predictive factors were entered into a stepwise multivariate logistic regression model. Only B2/B3 behaviour remained independently predictive of resection (OR 7.16, CI: 1.51-33.92, $p = 0.013$).

Medications

Overall, at both one month and twelve months post-diagnosis, there was higher use of systemic steroids, immunomodulators and biologics in CD compared to UC, and less use of aminosalicylates. Further details are provided in Table 4.

Medications were classified into five levels of increasing potency: no treatment, aminosalicylates +/- topical steroids, systemic steroids, immunomodulators, and biologics. Using this classification, 47 cases had an escalation in their most potent level of therapy between first month and twelfth month after diagnosis including 37 with CD (50%), 8 with UC (12.7%) and 2 with IBDU (16.7%).

Univariate logistic regression was performed analysing predictors of escalation.

Predictive factors identified included younger age (OR 0.97, CI: 0.96, 0.99, $p = 0.015$), having CD (OR 6.17, CI: 2.56-14.83, $p < 0.001$) and longer length of symptoms (in weeks) prior to diagnosis (OR 1.006, CI: 1.001-1.01, $p = 0.011$). Gender and smoking were not predictive. Predictive factors were entered into a stepwise multivariate logistic regression model. Only CD (OR 5.01, CI: 2.02-12.4, $p = 0.001$) and longer length of symptoms (OR 1.005, CI: 1.001-1.009, $p = 0.21$) remained independently predictive of escalation.

DISCUSSION

Prevalent cohort

Prevalence rates of IBD in our study were comparable with previous Australasian data. Data from Barwon in 2010-2011 report similar crude twelve-month period prevalence rates for IBD, CD, UC and IBDU of 344.6, 197.3, 136 and 8.5 per 100,000 respectively⁹. In Canterbury, crude point prevalence rates on 1st June 2005 were 308.2, 155.2, 145.0 and 8.0 per 100,000 respectively⁶. The 95% CIs for crude IBD prevalence rates per 100,000 in Barwon (309.6, 383.4), Canterbury (292.2, 324.3) and our study (319.2, 350.9) overlapped, suggesting similar prevalence across the Australasian region. These rates are comparable to those reported from Scandinavia and Canada²⁰⁻²³, with similar peaks in the sixth decade of life²¹.

Incident cohort

Crude IBD, CD, UC and IBDU one-year incidence rates in our study were also comparable with previous Australasian data. Data from Barwon in 2010-2011 report an incidence of 24.2, 14.7, 7.5 and 2.0 per 100,000 respectively⁹. The 95% CIs for crude IBD incidence rates per 100,000 in the most recent Barwon data (18.9, 30.5) and our study (24.4, 33.7) overlapped, suggesting no significant difference in incidence across Australian regions. In Canterbury, New Zealand in 2004⁶, crude IBD, CD and UC one-year incidence rates were of 25.2, 16.5 and 7.6 per 100,000 respectively. However, by 2014, these rates had significantly increased to 39.5, 26.4 and 12.6 per 100,000 respectively⁷, with the IBD incidence rate (CI: 34.4, 45.3) significantly higher than both Australian studies. Potential explanations included increased colonoscopy uptake and increased health-seeking among the population. Australasian IBD incidence rates are comparable to those in Scandinavia and Canada which are among the highest in the world^{24, 25}, with similar peaks in the third decade of life²². They are also higher than rates of between 1-2 per 100,000 in other areas of the Asia-Pacific region^{1,26}; genetic, dietary and climate-related factors may explain these differences.

Studies from Europe²⁷⁻²⁹ and North America^{11, 30} suggest IBD incidence increases with latitudes further from the equator. However among Australasian data from Barwon, Tasmania, and the more southerly Canterbury region of New Zealand (latitude of the population centre of Christchurch 43.52° south), latitude differences between the three regions may not be large enough to exert consistent effects on IBD epidemiology. Further studies from tropical northern Australia are awaited.

Though more incident cases of UC were male in our study, a systemic review of the international literature suggests no sex-specific trends in IBD incidence³¹. Our finding that CD is diagnosed at an earlier age than UC (31.5 years vs 42 years) does reflect international findings³². Our observed 'second peak' of UC in the 6th decade of life has also been described in other studies³³. The proportions of incident disease location (L1-L3, E1-E3) in our study were similar to other Australasian studies^{7,9}, and CD behaviour was predominantly B1, reflecting both Australian and international literature³⁴.

Consistent with other studies, we found a significantly longer length of preceding symptoms in CD compared to UC and IBDU, driven by a longer length of symptoms in L1 compared to L2 or L3 disease. A lack of frank PR bleeding or diarrhoea in such cases may increase diagnostic delay³⁵. Those with longer symptoms pre-diagnosis were also more likely to require therapeutic escalation, independent of IBD phenotype, perhaps due to a greater inflammatory burden of disease at diagnosis.

Medications in first twelve months after diagnosis

We found significant differences in the medication regimens prescribed between different phenotypes of IBD, with CD more likely than UC or IBDU to be treated with steroids, immunomodulators, biologics and have therapy escalated between the first and twelfth month after diagnosis. In a large 2011 European cohort³⁶, 56% of CD cases

had used immunomodulators by the first year of therapy. We report an even higher proportion of 74% of CD cases, and similarly use of biologics in 21.6% of CD cases, higher than recent cohorts from Barwon (18.1%)¹⁰ and Western Europe (19%)³⁶. Of note, there were no significant differences in immunomodulator or biologic use between different phenotypes of CD or extent of UC. This differs from other studies in CD, wherein those with B1 behaviour had lower rates^{36, 37}.

Complications in first twelve months after diagnosis

CD hospitalisation rates were higher than UC (41.9% vs 19%), consistent with findings from the Barwon cohort (28% vs 17%)¹⁰ and European studies³⁸. However, unlike other studies, we found no association between ileocolonic location or penetrating behaviour and hospitalisation rates¹⁰. Among those with CD, B2 or B3 behaviour independently increased the risk of surgical bowel resection compared to B1 behaviour, also demonstrated in the Barwon cohort¹⁰ and European studies^{39, 40}. Conversely, we did not find that other commonly described risk factors such as ileal location, younger age at diagnosis or steroids at diagnosis independently associated with increased resection rates, perhaps due to low absolute numbers.

Strengths and Limitations

This is the first Australasian state-wide study of IBD. Strengths include using the whole state as the reference population, intensive capture-recapture methodology, and

rigorous case definition. However data were not collected about patients' socioeconomic analysis, ethnicity, or geographical proximity to health services; nor about laboratory results, medication doses or extra-intestinal manifestations, which may be predictors of surgical resection⁴¹. Only two discrete data points were chosen at one month and twelve months post-diagnosis in the incident cohort. Other studies³ collected data in shorter intervals and thus described outcome timing in finer detail.

Patients may have been missed due to investigators recruiting almost exclusively from specialists rather than any other medical professionals or hospital discharge codes. However the general consensus of specialists involved in recruitment was that that IBD patients in Tasmania (even those with stable disease) are likely to have in-state specialist review at a minimum frequency of 12 months, rather than be managed exclusively in primary care or elsewhere. Furthermore, IBD patients missed by specialists (either due to clinic non-attendance during the 12-month study period or management elsewhere) were likely to be picked up by the histopathology database search and subsequent medical record review. This methodology recruited additional patients with histological findings of IBD collected in Tasmania since 1st January 1986, strengthening the specificity of the recruitment process. Nonetheless, some IBD patients may have had histological diagnosis elsewhere before moving to Tasmania and also missed specialist review during the study period. Potential omission of such patients is a limitation of this study that may underestimate IBD prevalence.

CONCLUSION:

High IBD incidence and prevalence rates in Tasmania are similar to other studies in Australasia as well as Northern Europe and America. CD cases experienced greater complications, health resource utilisation, medical therapy escalation and bowel resection than other phenotypes. Those with isolated ileal IBD experienced diagnostic delay; stricturing and penetrating CD behaviours were independent risk factors for bowel resection; and the extent of UC was an independent risk factor for hospitalisation.

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Table 1: Demographic details and disease characteristics of prevalent IBD cases.

	CD (n=874)	UC (n=803)	IBDU (n=42)	P value (CD vs UC)	P value (CD vs IBDU)	P value (UC vs IBDU)
Male (%)	42.3	49.8	52.4	0.02	0.60	0.92
Age, (median, IQR) (years)	45 (26)	54 (24)	51 (20.75)	<0.001	0.008	0.94
Age at diagnosis (median, IQR) (years)	31 (23.7)	40 (25)	46.5 (29)	<0.001	<0.001	0.20
Smoking (current or former) (%)	32	21.4	23.9	<0.001	0.34	0.09
Immunomodulator use (%)	62.6	24.4	26.1	<0.001	<0.001	0.92
Biologic use (%)	27.2	4.3	11.9	<0.001	0.04	0.06
Previous bowel resections (%)	40.7	7.8	7.1	<0.001	<0.001	0.88
Previous total colectomy (%)	7.3	6.6	4.8	0.7	0.86	0.84

IBD= inflammatory bowel disease. CD= Crohn's disease. UC= ulcerative colitis. IBDU= inflammatory bowel disease-unclassified. IQR= interquartile range.

Table 2: Demographic details and disease characteristics of incident IBD cases

	CD (n=74)	UC (n=63)	IBDU (n=12)	P value (CD vs UC)	P value (CD vs IBDU)	P value (UC vs IBDU)
Male (%)	54.1	65.1	25	0.41	0.12	0.02
Age, (median, IQR) (years)	31.5 (25.5)	42 (27)	65 (20)	0.06	0.012	0.01
Smoking (current) (%)	21.6	6.3	8.3	0.01	0.35	0.71
Smoking (former) (%)	20.1	19	9.3	0.85	0.34	0.62
Family history of IBD (%)	29.7	9.5	8.3	0.003	0.23	0.68
Length of symptoms pre-diagnosis (median, IQR) (weeks)	26 (40)	12 (20)	12 (16)	0.003	0.039	0.95

IBD= inflammatory bowel disease. CD= Crohn's disease. UC= ulcerative colitis. IBDU= inflammatory bowel disease-unclassified. IQR= interquartile range.

Table 3: Disease characteristics and clinical progress in incident IBD cohort

	CD (n=74)	UC (n=63)	IBDU (n=12)	P value (CD vs UC)	P value (CD vs IBDU)	P value (UC vs IBDU)
Length of symptoms pre-diagnosis (median, IQR) (weeks)	26 (40)	12 (20)	12 (16)	0.003	0.039	0.95
Hospitalized (%)	43.2	17.4	16.7	0.002	0.025	0.67
Total days of inpatient stay (median, IQR)	9 (10)	7 (3.5)	32 (NA)	0.209	0.09	0.05
Surgery (total) (%)	25.7	3.2	8.3	0.002	0.004	0.72
Surgery (bowel resection) (%)	18.9	3.2	0	0.004	0.008	0.84
Outpatient/ endoscopy sessions (median, IQR)	7 (5)	4.5 (4)	5 (3.3)	0.001	0.037	0.865

IBD= inflammatory bowel disease. CD= Crohn's disease. UC= ulcerative colitis. IBDU= inflammatory bowel disease-unclassified. IQR= interquartile range.

Table 4: patterns of medication use in incident IBD cohort.

	CD (n=74)	UC (n=63)	IBDU (n=12)	P- value (CD vs UC)	P- value (CD vs IBDU)	P value= (UC vs IBDU)
1st month therapy						
Aminosalicylates +/- topical steroids(%)	25.7	84.1	91.7	0.001	0.001	0.81
Systemic steroids(%)	56.7	31.7	8.3	0.005	0.005	0.19
Immunomodulators(%)	27	3.2	0	0.0004	0.09	0.73
Biologics(%)	2.7	0	0	0.5	0.64	N/A
12th month therapy*						
Aminosalicylates +/- topical steroids (%)	33.7	84.1	100	0.0001	0.0001	0.30
Systemic steroids(%)	70.2	39.7	16.7	0.0006	0.0012	0.23
Immunomodulators(%)	75.7	12.7	0	0.001	0.001	0.42
Biologics(%)	21.6	0	0	0.001	0.16	N/A

*This denotes if patients had ever been treated with the listed medications in the first 12 months.

IBD= inflammatory bowel disease. CD= Crohn's disease. UC= ulcerative colitis. IBDU= inflammatory bowel disease-unclassified.

FIGURE LEGENDS

Figure 1: histogram of age distribution of prevalent IBD cases with stacked proportions (expressed as percentage of total cases) according to IBD phenotype.

IBD= inflammatory bowel disease. CD= Crohn's disease. UC= ulcerative colitis. IBDU= inflammatory bowel disease-unclassified.

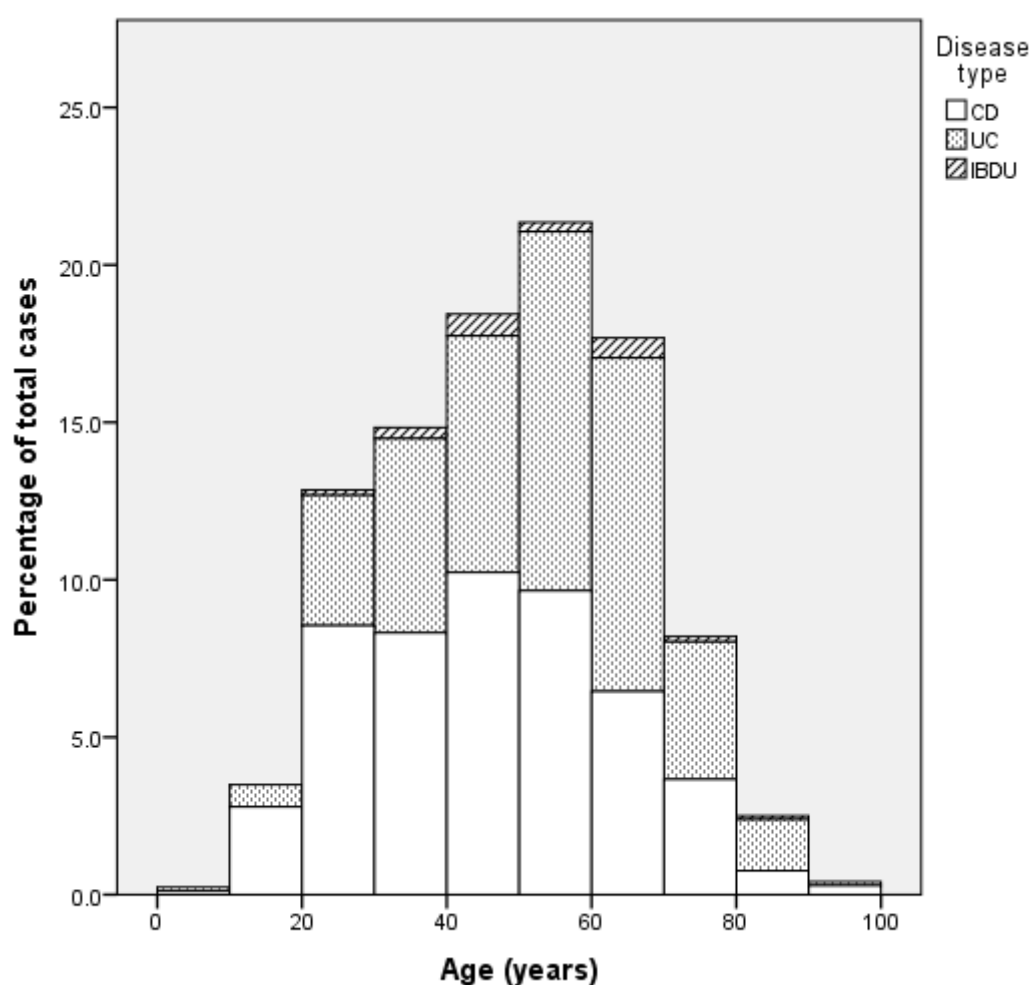


Figure 2: histogram of age distribution of incident IBD cases with stacked proportions (expressed as percentage of total cases) according to IBD phenotype.

IBD= inflammatory bowel disease. CD= Crohn's disease. UC= ulcerative colitis. IBDU= inflammatory bowel disease-unclassified.

