



Observational Study

Current and forecasted 10-year prevalence and incidence of inflammatory bowel disease in Hong Kong, Japan, and the United States

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Abstract

BACKGROUND

The rising incidence of inflammatory bowel disease (IBD) globally has increased disease burden and economic impact. Gaps remain in understanding the IBD burden between Asian and Western populations.

AIM

To estimate the current and following 10-year prevalence and incidence of IBD in Hong Kong, Japan, and the United States.

METHODS

Patients diagnosed with IBD were identified from a territory-wide electronic medical records database in Hong Kong (2003-2022, including all ages) and two large employment-based healthcare claims databases in Japan and the United States (2010-2022, including < 65 age). We used Autoregressive Integrated Moving Average models to predict prevalence and incidence from 2023 to 2032, stratified by disease subtype [ulcerative colitis (UC); Crohn's disease (CD)], sex, and age, with 95% prediction intervals (PIs). The forecasted annual average percentage change (AAPC) with 95% confidence intervals was calculated.

RESULTS

The age-standardized prevalence of IBD for 2032 is forecasted at 105.88 per 100000 in Hong Kong (95%PI: 83.01-128.75, AAPC: 5.85%), 645.79 in Japan (95%PI: 562.51-741.39, AAPC: 5.78%), and 629.85 in the United States (95%PI: 569.09-690.63, AAPC: 2.85%). Prevalence is estimated to rise most significantly among those under 18 in Japan and the United States. Over the next decade, the incidence of IBD is estimated to increase annually by 3.3% in Hong Kong with forecasted increases across all age groups (although the AAPC for each group is not statistically significant); by 2.88% in Japan with a significant rise in those under 18 and stability in 18-65; and remaining stable in the United States. By 2032, the prevalence of CD is estimated to surpass UC in Hong Kong and the United States, whereas UC will continue to be more prevalent in Japan. A higher prevalence and incidence of IBD is forecast for males in Hong Kong and Japan, whereas rates will be similar for both males and females in the United States.

CONCLUSION

The prevalence of IBD is forecasted to increase in Hong Kong, Japan, and the United States, while estimates of incidence vary. The forecasts show distinct patterns across disease subtype, sex, and age groups. Health systems will need to plan for the predicted increasing prevalence among different demographics.

Key Words: Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Epidemiology; Forecast modeling

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Core Tip: The global rise in inflammatory bowel disease (IBD) has escalated the disease burden and economic impact, with notable differences between Asian and Western populations. Over the next decade, IBD prevalence is estimated to increase in Hong Kong, Japan, and the United States, with varying estimates of incidence, and forecasts by disease subtype, sex, and age group are expected to show distinct patterns across different regions. The study shows the rising burden and distinct patterns these regions are experiencing, thus healthcare systems are advised to develop targeted healthcare strategies to manage the escalating challenges.

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INTRODUCTION

Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic, relapsing disease[1]. Patients with IBD require long-term medications, potential complications often result in frequent hospitalization and surgery, significantly impairing quality of life and imposing substantial socioeconomic burdens[2,3]. With rapid socioeconomic development and lifestyle changes, IBD is no longer confined to Western countries and is increasing globally, including in newly industrialized regions of Asia, Africa, and Latin America. According to the four epidemiological stages, IBD in Western countries has entered the stage of 'compounding prevalence' where incidence has stabilized or declined, yet prevalence continues to rise[4]. Projections indicate that by 2035, IBD prevalence in Canada will

reach 1.1%[5,6], and 1.02% in Lothian, Scotland by 2028[7]. By contrast, regions such as Asia and Latin America are experiencing the ‘acceleration in incidence’ stage, with rapid surges in both incidence and prevalence of IBD[4,8].

Significant differences in disease subtype, sex, and age distribution of patients with IBD exist between Eastern and Western countries. CD is becoming dominant in many Western countries, while UC remains more common in less developed areas[9,10]. Sex differences are also notable; IBD appears to be more prevalent among women in the West, while in Asia, CD appears to be more frequently diagnosed in men[10]. Although IBD primarily affects young and middle-aged adults, there is a rising incidence in children globally[11], and some developed countries are experiencing an age shift towards older patients[5]. This distinct epidemiological profile of IBD poses new challenges to the global health system, requiring a deeper understanding of these features and trends to effectively manage the increasing complexity of care.

The rising number of patients with IBD in developed and newly industrialized countries, along with high treatment costs and negative economic impacts, is placing significant pressure on healthcare systems to deliver affordable, high-quality care[12,13]. Despite more extensive data on IBD in Western countries, it remains unclear whether the epidemiological patterns, disease subtypes, sex, and age differences in the Asia-Pacific region will mimic similar trends to those in the West[4]. Therefore, this study investigates Hong Kong, Japan, and the United States, where the prevalence and incidence of IBD vary significantly to explore trends in Asia and the West under different epidemiological progression. In Asia, Hong Kong exhibits moderate prevalence and incidence of IBD; Japan, with its relatively high prevalence and incidence, provides a leading perspective in Asia on the epidemiological curve[14]. The United States, with its consistently high prevalence and incidence of IBD, provides a Western perspective of a mature healthcare system[10]. We estimated the prevalence and incidence of IBD in Hong Kong (2003-2022), Japan (2010-2022), and the United States (2010-2022) and forecasted trends over the next 10 years by subtype, sex, and age group to prepare health systems for the burgeoning disease burden.

MATERIALS AND METHODS

Data sources

We utilized one territory-wide database from Hong Kong, the clinical data analysis and reporting system (CDARS), and two large claims databases: The Japan Medical Data Centre (JMDC) from Japan and Merative™ MarketScan® database (Merative) from the United States.

The CDARS is a territory-wide electronic medical record (EMR) database developed and managed by the Hong Kong Hospital Authority (HA)[15]. As the sole public healthcare provider of primary, secondary, and tertiary healthcare services in Hong Kong, HA manages all public hospitals and clinics, serving approximately 7.4 million residents. The available data in CDARS, dating back to 1993, include demographic data, date of registered death, date of hospitalization and consultation, diagnosis, and prescription, all of which are centrally stored for auditing and research purposes, and have been de-identified to protect patient privacy. Diagnoses are coded in the International Classification of Diseases, Ninth revision (ICD-9) format. The accuracy and quality of coding and records in CDARS have been validated through high-quality epidemiological studies[16].

The JMDC is an employment health insurance claims database that began in 2005[17]. It collects inpatient, outpatient, and drug treatment claims data from more than 250 payers nationwide[18]. The database covers non-government employees between 18 and 65 years old, and their dependents (including children under 18 and adults under 75). The cumulative dataset includes about 17 million people in 2024, approximately 13.6% of the total population of Japan. Diagnoses are coded in ICD-10 format, and medications are coded in the Anatomical Therapeutic Chemical format.

The Merative™ MarketScan® (previously IBM MarketScan Commercial Claims and Encounters) database includes health insurance claims data from over 155 million employees under 65 years old across the United States, with data available from 2000[19]. The database records detailed information on inpatient, outpatient, outpatient pharmacy, and behavioral healthcare events, along with enrolment information for employees of large corporations and health plans. All diagnoses are coded in ICD-9 and ICD-10 formats.

This study related to the analysis of CDARS was approved by the Institutional Review Board of The University of Hong Kong/HA Hong Kong West Cluster (No. UW22-280). Data from JMDC and Merative were de-identified and are fully compliant with relevant patient confidentiality requirements, including the Japanese Personal Information Protection Law and the United States Health Insurance Portability and Accountability Act of 1996. Ethical approval and individual informed consent are not required for JMDC and Merative.

Study population

In CDARS, patients with IBD between January 1, 2003 and December 31, 2022 were identified. In Merative and JMDC, patients aged < 65 who had been continuously enrolled in health insurance for at least 12 months were eligible for this study, and patients with IBD between January 1, 2010 and December 31, 2022 were identified. IBD cases were confirmed using previously reported methods, which included having at least two healthcare encounters with IBD-related ICD-9 codes 555.x (CD), 556.x (UC) or ICD-10 codes K50.x (CD) and K51.x (UC) on separate dates or receiving IBD-related drug therapy within ± 1 year of diagnosis[20,21]. The earliest diagnosis was noted as the index date. For patients with both CD and UC codes, the subtype was assigned based on the most frequent code in the most recent year or, if equal, the latest diagnosis. For Hong Kong, we performed sensitivity analysis using a single ICD diagnostic code as the case identification criterion, a commonly used criterion in CDARS as the EMR database, and the results were similar to those for the primary identification criterion (Supplementary Figure 1). The study tracked patients until they exited the health plan (JMDC and

Merative), died (CDARS), or December 31, 2022, whichever came first.

Statistical analyses

Annual prevalence was the number of patients per 100000 population meeting the IBD case definition. Annual incidence was the number of newly identified IBD patients per 100000 population in each database for the corresponding year. Incident cases were identified based on the first observed IBD diagnosis, starting from 1993 in CDARS, 2000 in Merative, and 2005 in JMDC, without any prior IBD codes recorded. For Hong Kong, the prevalence and incidence denominators were derived from midyear population estimates provided by the Census and Statistics Department of the Hong Kong SAR Government[22]. For Japan and the United States, the prevalence denominators were the total number of unique persons who had whole (12-month) or partial (coverage across mid-year) insurance coverage in the calendar year in their respective databases. The incidence denominators were calculated similarly but excluded individuals previously diagnosed with IBD. Prevalence and incidence were age-standardized using World Health Organization (WHO) standard populations with age intervals (< 18, 28-44, 44-64, Hong Kong additionally includes 65 + years) to ensure comparability across time periods. Age-specific prevalence and incidence were crude rates.

Ten-year forecasting of age-standardized prevalence and incidence was conducted using autoregressive integral moving average (ARIMA) models. The ARIMA models, which predict future values by combining trends and patterns in historical data, are suitable for dealing with the natural dependence and continuity of prevalence and incidence and are reported to be used in IBD[5,6]. We used the Kwiatkowski-Phillips-Schmidt-Shin test to verify the stationarity of the data and then applied differencing to achieve this stationarity. Log transformation was applied to the original data for stationarity. Using R package auto ARIMA, the optimal orders for the autoregressive and moving average components and the application of logarithmic transformation were determined by iteratively searching through a series of potential ARIMA models based on a combination of Akaike information criterion (AIC), Bayesian information criterion (BIC), and mean squared error of residuals (MSE). The models with the lowest AIC/BIC and MSE were selected. Prevalence and incidence were forecasted to 2032 with 95% prediction intervals (PIs).

We calculated the average annual percentage change (AAPC) with 95% confidence interval (CI). Poisson regression was used to calculate the AAPC for the forecasted incidence, and log-binomial regression was used for the forecasted prevalence, with year as the dependent variable. All analyses were stratified by disease subtype, sex, and age groups (< 18, 28-44, 44-64, with Hong Kong additionally including 65 + years). Data analyses were performed using R software version 4.2.2, Aginity Workbench for Amazon Redshift (version 4.9.3.2778) and SAS Enterprise Guide 7.15.

RESULTS

There were 5257 prevalent cases diagnosed in 2022 in CDARS (Hong Kong), 35830 in JMDC (Japan), and 84053 in Merative (United States). The background population and number of patients with IBD for each database are shown in Table 1, and crude prevalence and incidence in Figure 1.

Prevalence

From 2003 to 2022, the age-standardized prevalence of IBD per 100000 in Hong Kong increased from 13.63 to 58.12 (Table 2, Figure 2). From 2010 to 2022, the prevalence rose from 187.78 to 368.34 in Japan, and from 284.32 to 472.79 in the United States. By 2032, the forecasted prevalence of IBD per 100000 population will be 105.88 in Hong Kong (95%PI: 83.01-128.75) with an AAPC of 5.85% (95%CI: 3.38-8.40), 645.79 in Japan (95%PI: 562.51-741.39, AAPC = 5.78%, 95%CI: 4.76-6.80), and 629.85 in the United States (95%PI: 569.09-690.63, AAPC = 2.85%, 95%CI: 1.91-3.79). Stratified by disease subtypes, the prevalence of UC and CD in 2032 is estimated to be 56.72 (95%PI: 43.43-74.06) and 11.89 (95%PI: 8.29-15.48) per 100000 in Hong Kong, 545.88 (95%PI: 470.77-632.99) and 101.91 (95%PI: 84.89-122.33) in Japan, 311.90 (95%PI: 280.58-343.22) and 307.06 (95%PI: 275.04-339.08) in the United States.

Stratified by sex, the prevalence of IBD per 100000 population in 2032 is forecast to be higher for males than females in Hong Kong (male: 171.40, female: 78.87) and Japan (male: 730.24, female: 556.79), but similar between males and females in the United States (male: 628.03, female: 630.68) (Table 2, Figure 3). Forecasts of UC prevalence show consistent sex-specific differences with overall IBD. However, CD prevalence is forecast to be higher among females than males in Japan.

Stratified by age, the prevalence of IBD in Hong Kong is forecast to rise significantly in the three groups over 18 years by 2032, but not significantly in those under 18 years with an AAPC of 3.28% (95%CI: -6.77 to 14.55) (Table 2, Figure 4). In Japan and the United States, the prevalence of IBD is estimated to rise significantly in all three age groups < 65 years, with the greatest AAPC in the < 18 years group in both countries. The 18-45 age group is forecast to show the highest IBD prevalence than other respective age groups in Hong Kong (163.21 per 100000; 95%PI: 152.56-174.61), Japan (983.77; 95%PI: 828.63-1167.95), and the United States (883.45; 95%PI: 795.75-971.16). However, for UC, the prevalence in the 45-64 age group in Hong Kong is forecast to be the highest over other age groups.

Incidence

From 2022 to 2032, IBD incidence per 100000 is estimated to increase from 4.67 to 6.20 (95%PI: 5.22-7.18, AAPC = 3.10, 95%CI: -5.93 to 13.09) in Hong Kong, from 26.48 to 39.03 (95%PI: 24.93-53.13, AAPC = 2.88, 95%CI: -0.83 to 6.75) in Japan, and from 39.62 to 41.86 (95%PI: 35.65-48.08, AAPC = 0, 95%CI: -3.28 to 3.39) in the United States (Table 3, Figure 2). The forecasted incidence per 100000 for UC and CD in 2032 will be 2.90 (95%PI: 2.26-3.54) and 4.86 (95%PI: 2.73-8.63) respectively in Hong Kong, 33.28 (95%PI: 20.33-46.24) and 5.68 (95%PI: 3.74-7.62) respectively in Japan, and 23.57 (95%PI:

Table 1 Background populations and numbers of cases with inflammatory bowel disease for each database

Year	CDARS (Hong Kong)			JMDC (Japan)			Merative (United States)		
	Background population ¹	Prevalent cases	Incident cases	Background population ²	Prevalent cases	Incident cases	Background population ²	Prevalent cases	Incident cases
2003	6730800	1058	117						
2004	6783500	1180	145						
2005	6813200	1318	141						
2006	6857100	1443	152						
2007	6916300	1591	173						
2008	6957800	1744	192						
2009	6972800	1954	249						
2010	7024200	2179	235	957720	1973	178	40585148	121720	17192
2011	7071600	2392	218	1493943	3201	238	47340044	152199	22854
2012	7150100	2608	270	1708625	3827	422	47687942	159425	25225
2013	7178900	2831	254	2683156	6475	519	39731680	138599	18171
2014	7229500	3062	276	2869962	7361	734	41037026	151898	19690
2015	7291300	3302	230	4191243	11039	809	26139419	101611	13998
2016	7336600	3516	275	5373179	14573	1110	25676785	102867	13189
2017	7393200	3797	353	7212775	20593	1573	24022882	99699	11440
2018	7452600	4078	320	7955602	23831	2213	24380360	101296	11162
2019	7507900	4361	343	9230836	28815	2469	22777234	97095	11756
2020	7481000	4632	284	9523091	31174	2870	21414079	91267	9126
2021	7413100	4927	399	10257371	36301	3172	20797305	91415	9596
2022	7346100	5257	334	9530324	35830	2456	17353409	84053	7659

¹The background population for Hong Kong was the mid-year population data provided by the Census and Statistics Department of the Hong Kong Special Administrative Region Government (https://www.censtatd.gov.hk/tc/web_table.html?id=1A).

²The background populations for Japan Medical Data Center (Japan) and Merative (United States) were the number of individuals enrolled ≥ 1 year in Japan Medical Data Center and Merative database per year.

CDARS: Clinical data analysis and reporting system; JMDC: Japan Medical Data Center; Merative: The Merative™ MarketScan® (“Merative” previously IBM MarketScan Commercial Claims and Encounters) database.

20.21-26.93) and 18.31 (95%PI: 15.32-21.30) respectively in the United States.

In Hong Kong (males: 8.90, females: 4.19) and Japan (males: 44.61, females: 33.08), the forecasted incidence of IBD per 100000 population in 2032 is higher for males than females, although they are similar in the United States (males: 40.60, females: 42.96) (Table 3, Figure 3). The pattern for UC and CD will be similar to overall IBD in 2032, except that the incidence of UC in Hong Kong may be similar between males and females.

The forecasted incidence of IBD by 2032 is estimated to increase across all age groups in Hong Kong, with the highest incidence estimated for 18-44 years (Table 3, Figure 4). In Japan, IBD incidence among the < 18 age group is forecast to rise significantly (AAPC = 9.06%, 95%CI: 4.11-14.31), while remaining stable in the other two 18-65 age groups. In the United States, the incidence of IBD is forecast to increase in the < 18 age group and stabilize in the 18-65 age group.

DISCUSSION

This study forecasts the prevalence and incidence of IBD up to 2032 using historical data from a territory-wide EMR database from Hong Kong and two large claims databases covering employees and their dependents from Japan and the United States. We estimate that the prevalence of IBD in Hong Kong will increase by 1.82-fold, from 58.12 in 2022 to 105.88 per 100000 in 2032, with an annual growth rate of 5.85%. In Japan, the prevalence is estimated to rise by 1.75-fold, from 368.34 to 645.79 per 100000, increasing at 5.78% per year. In the United States, it will grow by 1.33-fold, from 472.79 to 629.85 per 100000, at a slower annual rate of 2.85%. Furthermore, the forecasted IBD incidence in Hong Kong is estimated to rise by 3.3%, with forecasted increases in all age groups, although the AAPC for each group was not statist-

Table 2 Age- and sex-stratified current and forecasted prevalence of inflammatory bowel disease, Crohn's disease, and ulcerative colitis in Hong Kong, Japan, and the United States

	CDARS (Hong Kong)				JMDC (Japan)				Merative (United States)			
	Prevalence		Forecasted prevalence		Prevalence		Forecasted prevalence		Prevalence		Forecasted prevalence	
	2003	2022	2032 (95%PI)	Forecasted AAPC (%, 95%CI)	2010	2022	2032 (95%PI)	Forecasted AAPC (%, 95%CI)	2010	2022	2032 (95%PI)	Forecasted AAPC (%, 95%CI)
IBD	13.63	58.12	105.88 (83.01 to 128.75)	5.85 (3.38 to 8.40) ¹	187.78	368.34	645.79 (562.51 to 741.39)	5.78 (4.76 to 6.80) ¹	284.32	472.79	629.86 (569.09 to 690.63)	2.85 (1.91 to 3.79) ¹
Age (IBD)												
< 18	2.01	11.06	15.82 (11.46 to 20.18)	3.45 (-2.43 to 9.73)	16.45	75.55	269.20 (166.46 to 435.35)	13.52 (11.55 to 15.55) ¹	61.83	176.92	272.82 (242.69 to 302.95)	4.27 (2.79 to 5.77) ¹
18-44	17.74	75.94	163.21 (152.56 to 174.61)	7.95 (5.81 to 10.15) ¹	281.97	557.46	983.77 (828.63 to 1167.95)	5.84 (5.02 to 6.67) ¹	366.71	648.57	883.45 (795.75 to 971.16)	3.06 (2.27 to 3.86) ¹
45-64	21.34	89.22	144.93 (123.80 to 166.07)	4.76 (2.71 to 6.86) ¹	264.32	440.66	589.50 (561.33 to 617.68)	2.80 (1.83 to 3.77) ¹	466.59	577.72	670.33 (583.13 to 757.52)	1.48 (0.61 to 2.36) ¹
65 +	18.86	74.04	109.06 (90.95 to 127.17)	3.81 (1.51 to 6.16) ¹								
Sex (IBD)												
Male	16.52	81.31	171.40 (128.68 to 228.31)	7.71 (5.63 to 9.84) ¹	217.52	421.11	730.24 (643.26 to 828.99)	5.65 (4.70 to 6.61) ¹	274.96	467.54	628.03 (565.96 to 690.11)	2.92 (1.99 to 3.87) ¹
Female	11.01	39.51	78.87 (55.40 to 112.29)	7.25 (4.25 to 10.36) ¹	146.54	303.51	556.79 (461.24 to 672.14)	6.25 (5.14 to 7.37) ¹	292.64	477.03	630.68 (569.90 to 691.46)	2.78 (1.85 to 3.72) ¹
UC	8.91	30.03	56.72 (43.43 to 74.06)	6.62 (3.16 to 10.23) ¹	149.82	303.30	545.88 (470.77 to 632.99)	6.05 (4.94 to 7.17) ¹	137.13	232.46	311.90 (280.58 to 343.22)	2.95 (1.62 to 4.29) ¹
Age (UC)												
< 18	0.54	2.77	3.94 (1.88 to 5.99)	4.38 (-7.16 to 17.60)	12.84	50.70	159.29 (103.38 to 245.46)	12.12 (9.66 to 14.65) ¹	21.51	58.41	89.17 (77.73 to 100.62)	4.15 (1.58 to 6.78) ¹
18-44	10.18	29.93	52.79 (45.60 to 61.13)	5.79 (2.29 to 9.43) ¹	217.13	454.66	841.71 (700.68 to 1011.13)	6.35 (5.44 to 7.26) ¹	173.27	322.52	446.90 (402.66 to 491.13)	3.24 (2.12 to 4.37) ¹
45-64	16.82	61.50	85.54 (77.83 to 93.24)	3.04 (0.51 to 5.64) ¹	227.63	390.15	526.33 (504.47 to 548.19)	2.88 (1.86 to 3.91) ¹	245.73	321.87	377.06 (188.43 to 754.54)	1.54 (0.38 to 2.72) ¹
65 +	15.46	58.80	81.61 (75.02 to 88.20)	3.28 (0.67 to 5.96) ¹								
Sex (UC)												
Male	10.46	37.73	74.12 (66.27 to 82.00)	7.07 (3.99 to 10.26) ¹	165.33	332.19	594.17 (519.19 to 669.19)	5.99 (4.93 to 7.06) ¹	136.58	229.57	307.06 (275.04 to 339.08)	2.89 (1.56 to 4.25) ¹

			82.89)				679.98)				339.08)		
Female	7.50	23.86	43.85 (38.89 to 49.45)	6.37 (2.47 to 10.45) ¹	128.45	267.82	494.06 (406.66 to 600.23)	6.31 (5.13 to 7.50) ¹	137.66	235.24	316.56 (285.08 to 348.03)	2.94 (1.62 to 4.28) ¹	
CD	4.72	28.09	66.03 (44.21 to 98.64)	8.95 (5.50 to 12.54) ¹	37.96	65.05	101.91 (84.89 to 122.33)	4.60 (2.16 to 7.11) ¹	147.18	240.33	317.96 (287.07 to 348.84)	2.78 (1.47 to 4.11) ¹	
Age (CD)													
< 18	1.47	8.30	11.89 (8.29 to 15.48)	3.66 (-3.08 to 10.94)	3.61	24.85	124.03 (53.78 to 286.00)	17.55 (14.31 to 20.92) ¹	40.33	118.50	183.65 (163.90 to 203.40)	4.32 (2.52 to 6.16) ¹	
18-44	7.57	46.01	116.68 (96.94 to 140.46)	9.92 (7.24 to 12.69) ¹	64.84	102.80	150.93 (124.77 to 182.59)	3.92 (1.95 to 5.93) ¹	193.44	326.05	436.55 (391.41 to 481.70)	2.92 (1.79 to 4.05) ¹	
45-64	4.52	27.72	43.93 (36.27 to 51.59)	4.55 (0.88 to 8.38) ¹	36.69	50.51	52.15 (18.18 to 86.13)	0.28 (-2.69 to 3.34)	220.86	255.85	285.01 (249.96 to 320.05)	1.06 (-0.26 to 2.39)	
65 +	3.39	15.24	22.93 (14.04 to 31.82)	3.91 (-1.06 to 9.15)									
Sex (CD)													
Male	6.06	43.58	104.55 (67.43 to 162.11)	9.1 (6.34 to 11.96) ¹	52.19	88.91	138.61 (113.68 to 169.03)	4.57 (2.47 to 6.71) ¹	138.37	237.97	320.97 (289.33 to 352.62)	2.98 (1.66 to 4.31) ¹	
Female	3.51	15.65	28.31 (19.45 to 37.17)	5.83 (1.11 to 10.81) ¹	45.84	94.14	171.49 (148.86 to 197.55)	6.16 (4.18 to 8.19) ¹	154.99	241.79	314.13 (282.74 to 345.51)	2.61 (1.30 to 3.94) ¹	

¹Significantly increasing/decreasing average annual percentage change.

AAPC: Average annual percentage change; CD: Crohn's disease; CDARS: Clinical data analysis and reporting system; CI: Confidence interval; IBD: Inflammatory bowel disease; JMDC: Japan Medical Data Center; Merative: The Merative™ MarketScan® ("Merative" previously IBM MarketScan Commercial Claims and Encounters) database; PI: Prediction interval; UC: Ulcerative colitis. Prevalence is expressed per 100000 population. Prevalence was age-standardized using the World Health Organization standard population, except for age-stratified prevalence, which consisted of crude rates.

ically significant. In Japan, the incidence is projected to increase by 2.88% per year, with a significant increase in the < 18 age group but remaining stable in the 18-65 age group. Incidence is estimated to remain stable in the United States. Our findings suggest that although the prevalence and incidence of IBD will continue to rise in Hong Kong and Japan, there are some differences in the epidemiological progression between regions. Hong Kong is experiencing an Acceleration in Incidence stage, whereas in Japan, the IBD incidence among adults is expected to remain stable. Meanwhile, the United States is encountering a compounding prevalence stage, suggesting a continued need for effective disease management strategies.

The prevalence and incidence in our study generally align with those reported previously. In Hong Kong, a study showed a prevalence of 21.14 per 100000 for UC and 14.17 for CD from 2011-2014, close to 19.11 and 15.35 in 2014 in our study[23]. Our results are similar with previous studies of UC and CD in Japan and the United States using the same database[20,21]. Furthermore, in Japan, two national hospital survey studies reported UC prevalence of 133.2-172.9 per 100000 and CD prevalence of 31.9-55.6 per 100000 in 2014[24,25], similar to our figures of 200 for UC and 47.8 for CD, with comparable sex distributions. The 2021 Global Burden of Disease report showed that the estimated annual percentage change in IBD incidence in Japan from 1991 to 2021 was among the highest levels in the world (0.9968-2.933)

Table 3 Age- and sex-stratified current and forecasted incidence of inflammatory bowel disease, Crohn's disease, and ulcerative colitis in Hong Kong, Japan, and the United States

	CDARS (Hong Kong)				JMDC (Japan)				Merative (United States)			
	Incidence		Forecasted incidence		Incidence		Forecasted incidence		Incidence		Forecasted incidence	
	2003	2022	2032 (95%PI)	Forecasted AAPC (% , 95%CI)	2010	2022	2032 (95%PI)	Forecasted AAPC (% , 95%CI)	2010	2022	2032 (95%PI)	Forecasted AAPC (% , 95%CI)
IBD	1.63	4.67	6.20 (5.22 to 7.18)	3.10 (-5.93 to 13.09)	17.36	26.48	39.03 (24.93 to 53.13)	2.88 (-0.83 to 6.75)	36.60	39.62	41.86 (35.65 to 48.08)	0 (-3.28 to 3.39)
Age (IBD)												
< 18	0.93	3.62	5.11 (2.61 to 7.60)	3.28 (-6.77 to 14.55)	4.81	12.93	31.78 (18.85 to 53.56)	9.06 (4.11 to 14.31) ¹	10.39	17.48	26.95 (14.26 to 50.94)	4.43 (-0.24 to 9.35)
18-44	2.08	5.92	10.92 (7.09 to 16.81)	5.78 (-1.75 to 14.01)	26.35	37.03	39.36 (18.79 to 82.47)	-0.15 (-3.52 to 3.34)	43.83	48.33	50.43 (43.01 to 57.85)	0 (-2.99 to 3.09)
45-64	1.92	4.46	7.39 (3.24 to 16.82)	4.14 (-4.53 to 13.73)	18.61	26.08	26.08 (-12.24 to 64.39)	0 (-4.14 to 4.32)	63.19	56.72	56.72 (11.04 to 102.41)	0 (-2.83 to 2.91)
65 +	1.38	3.01	4.34 (2.64 to 6.04)	2.08 (-8.43 to 13.90)								
Sex (IBD)												
Male	1.92	6.38	8.90 (7.41 to 10.38)	3.15 (-4.45 to 11.44)	22.64	30.49	44.61 (26.81 to 62.41)	2.71 (-0.75 to 6.30)	34.71	39.36	40.60 (34.39 to 46.81)	0 (-3.33 to 3.45)
Female	1.35	3.21	4.19 (2.81 to 5.58)	2.82 (-8.06 to 15.12)	10.27	21.68	33.08 (21.34 to 44.82)	3.37 (-0.71 to 7.65)	38.30	39.79	42.96 (36.55 to 49.37)	0 (-3.24 to 3.35)
UC	0.94	2.25	2.90 (2.26 to 3.54)	2.55 (-10.11 to 17.17)	14.41	22.21	33.28 (20.33 to 46.24)	2.98 (-1.05 to 7.18)	21.12	22.79	23.57 (20.21 to 26.93)	0 (-4.35 to 4.55)
Age (UC)												
< 18	0.08	0.85	0.85 (-0.62 to 2.32)	0 (-21.28 to 27.04)	3.21	8.42	21.36 (10.35 to 44.07)	9.24 (3.20 to 15.73) ¹	4.45	6.62	8.46 (6.06 to 10.85)	2.49 (-5.23 to 10.89)
18-44	1.26	2.76	2.76 (0.83 to 9.23)	0 (-12.26 to 13.97)	22.03	31.86	55.34 (26.54 to 115.40)	4.54 (1.24 to 7.97) ¹	25.07	28.11	28.44 (24.34 to 32.54)	0 (-3.97 to 4.13)
45-64	1.55	3.41	3.66 (1.18 to 6.07)	-0.12 (-10.86 to 11.92)	16.40	24.06	24.06 (-10.91 to 59.03)	0 (-4.31 to 4.50)	39.40	37.44	42.08 (34.93 to 49.24)	0 (-3.27 to 3.38)
65 +	1.26	2.22	2.56 (1.03 to 4.09)	0 (-12.70 to 14.55)								
Sex (UC)												
Male	1.03	2.37	2.37 (0.54 to 10.43)	0 (-13.17 to 15.17)	18.24	24.80	44.01 (21.46 to 90.30)	4.57 (0.89 to 8.42) ¹	20.06	22.32	22.80 (19.43 to 26.18)	0 (-4.42 to 4.63)

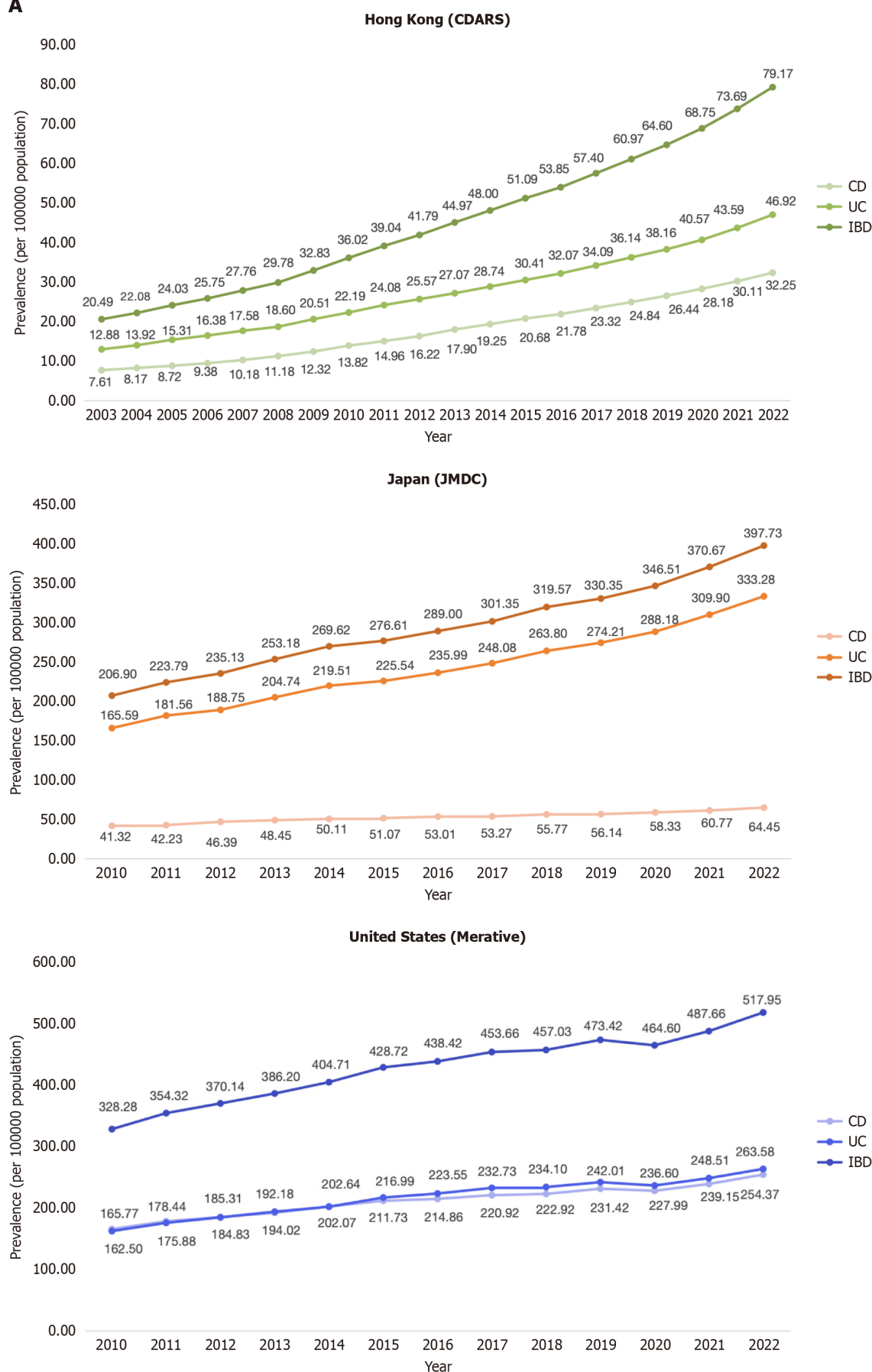
Female	0.88	2.17	2.93 (1.88 to 4.57)	4.46 (-8.80 to 19.98)	9.29	19.08	29.20 (18.49 to 39.91)	3.42 (-0.93 to 7.98)	21.82	23.23	24.23 (20.77 to 27.70)	0 (-4.29 to 4.48)
CD	0.69	2.43	4.86 (2.73 to 8.63)	6.96 (-4.5 to 20.14)	2.94	4.27	5.68 (3.74 to 7.62)	2.35 (-6.96 to 12.66)	15.61	16.83	18.31 (15.32 to 21.30)	0 (-4.92 to 5.18)
Age (CD)												
< 18	0.85	2.77	5.83 (2.05 to 16.57)	6.93 (-3.58 to 18.88)	1.60	4.51	10.35 (4.15 to 25.82)	8.69 (0.29 to 18.01) ¹	6.35	10.86	10.86 (4.22 to 17.50)	0 (-6.35 to 6.78)
18-44	0.83	3.16	4.51 (3.75 to 5.28)	3.26 (-7.52 to 15.45)	4.32	5.17	4.78 (3.30 to 6.26)	0 (-9.44 to 10.42)	18.76	20.22	21.99 (18.38 to 25.59)	0 (-4.50 to 4.71)
45-64	0.37	1.05	1.11 (0.02 to 2.20)	0 (-18.79 to 23.14)	2.22	2.02	2.66 (1.77 to 3.55)	0 (-12.48 to 14.26)	23.79	19.28	19.28 (1.89 to 36.68)	0 (-4.80 to 5.04)
65 +	0.13	0.78	0.73 (-0.33 to 1.78)	0 (-22.91 to 29.72)								
Sex (CD)												
Male	0.90	4.01	5.28 (4.20 to 6.37)	3.67 (-6.26 to 14.79)	4.40	5.68	5.78 (2.71 to 8.86)	-0.05 (-8.65 to 9.35)	14.65	17.04	17.80 (14.84 to 20.76)	0 (-4.99 to 5.25)
Female	0.47	1.05	1.07 (0.21 to 1.93)	0 (-19.14 to 23.67)	0.98	2.61	5.00 (2.57 to 9.70)	6.10 (-4.75 to 18.46)	16.48	16.56	18.73 (15.54 to 21.92)	0 (-4.87 to 5.12)

¹Significantly increasing/decreasing average annual percentage change.

AAPC: Average annual percentage change; CD: Crohn's disease; CDARS: Clinical data analysis and reporting system; CI: Confidence interval; IBD: Inflammatory bowel disease; JMD: Japan Medical Data Center; Merative: The Merative™ MarketScan® ("Merative" previously IBM MarketScan Commercial Claims and Encounters) database; PI: Prediction interval; UC: Ulcerative colitis. Incidence is expressed per 100000 population. Incidence was age-standardized using the World Health Organization standard population, except for age-stratified prevalence, which consisted of crude rates.

[26], similar to the high AAPC (3.57%, 95%CI: 2.36-4.8) observed from 2010 to 2032 in our study. In the United States, a 2016 report recorded prevalence of 181.1 for UC and 197.7 for CD per 100000 adults[27], closely resembling our 2016 data of 193 for UC and 198 for CD. Additionally, a study in 2023 showed UC prevalence of 347 (344-350) and CD 378 (375-382) per 100000 people at a registration requirement period of 4 years in the United States[28], which is higher than our findings. However, their secondary estimates at a 1-year enrollment requirement period, 258 (256-260) for UC and 312 (310-314) for CD, are similar to our findings of 232.46 for UC and 240.33 for CD using the same requirement period. Other discrepancies may be related to differences in the databases, such as ethnicity, socio-economic, and geographic location, and age standardization using WHO standard populations, but we have consistent upward trends.

Consistent with our study, projection studies from other countries and regions have also shown a rising trend in IBD prevalence. A Canadian study predicted that by 2035, IBD prevalence will reach 1098 per 100000 (95%PI: 1068-1127), with an AAPC of 2.43% (95%CI: 2.32-2.54), with the highest prevalence in the elderly[6]. Similarly, a study in Lothian, United Kingdom, estimated that by 2028, prevalence will reach 1023 per 100000 (95%CI: 975-1071), peaking in the 60-79 age group[7]. In Asia, a Korean study projected that by 2028, IBD prevalence will rise to 149.59 per 100000 (95%CI: 134.47-164.71), increasing by 4.51 cases per 100000 annually[29]. Unlike Western projections, this study predicted that the fastest-growing prevalence will be in the 20-39 age group, while prevalence in the elderly (≥ 60 years) will decline. While these

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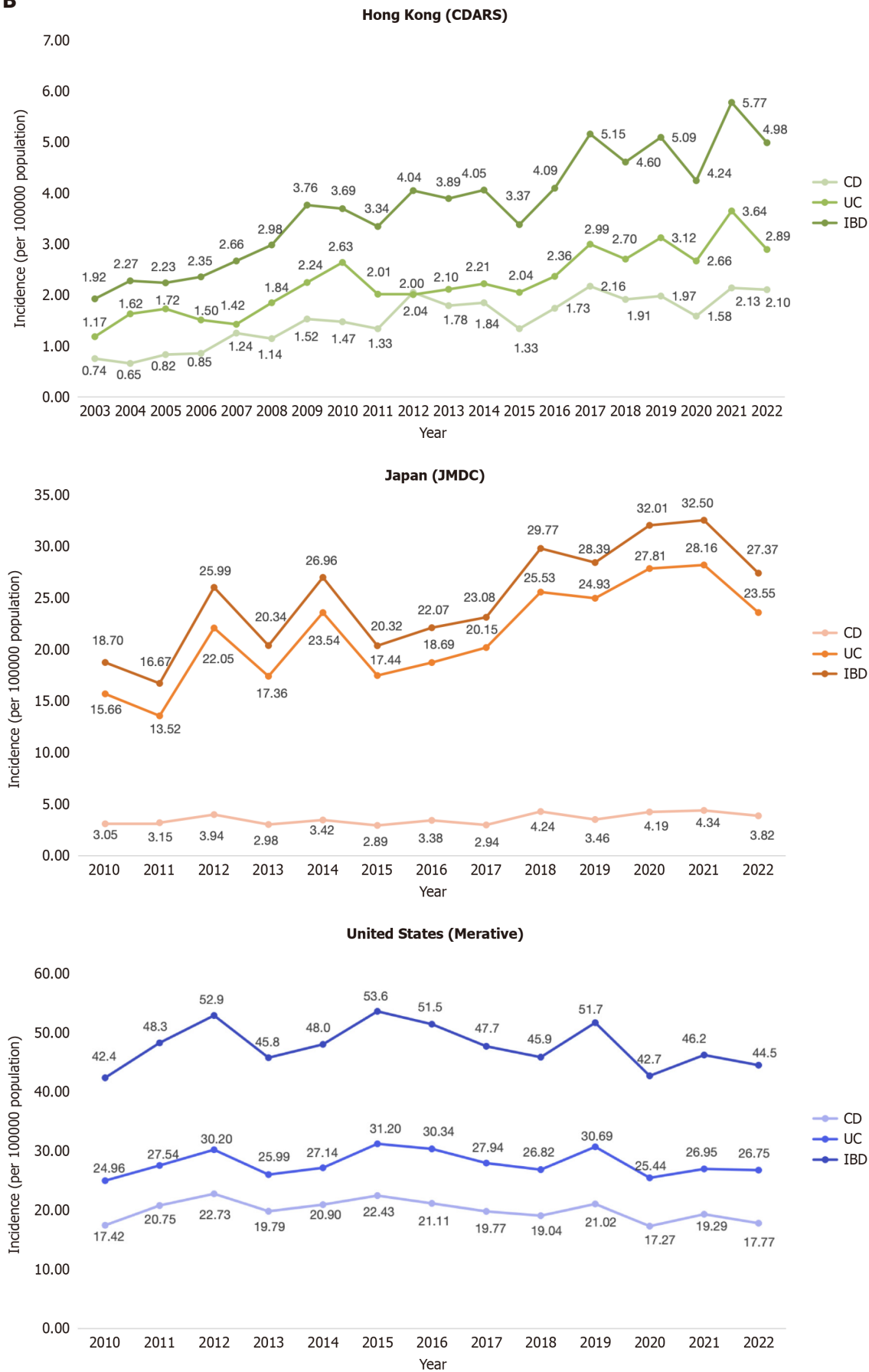


Figure 1 Crude prevalence and incidence of inflammatory bowel disease, Crohn's disease, and ulcerative colitis in Hong Kong, Japan,

and the United States. A: Crude prevalence in Hong Kong, Japan and the United States; B: Crude incidence in Hong Kong, Japan and the United States. Crude prevalence and incidence in Hong Kong were estimated using one diagnostic code definition. IBD: CD: Crohn's disease; CDARS: Clinical data analysis and reporting system; Inflammatory bowel disease; JMDC: Japan Medical Data Center; Merative: The Merative™ MarketScan® ("Merative" previously IBM MarketScan Commercial Claims and Encounters) database; UC: Ulcerative colitis.

projections, including ours, indicate a global rise in IBD prevalence, the most affected age groups differ. Our study predicts that by 2032, IBD prevalence will be highest in the 18-45 age group in Hong Kong, Japan, and the United States. These variations may reflect differences in disease epidemiology, healthcare systems, and demographic transitions across regions. Moreover, by incorporating data from both Asia and the West, our study provides a unique comparative perspective. In particular, Hong Kong, with its intermediate IBD prevalence in Asia, may serve as a valuable reference for understanding epidemiological trends in the region.

The forecasted prevalence and incidence for UC and CD in Hong Kong, Japan, and the United States show different trends. In Hong Kong and Japan, the prevalence and incidence of overall IBD are expected to continue their rapid increase, although with differences. This trend may be partly attributed to changes in lifestyle, socio-economic status, and environmental factors[30]. The populations in these areas have experienced westernization, characterized by a greater uptake of a Western diet rich in fats and sugars, which are risk factors for the rising incidence of IBD[31,32]. Specifically, a high-fat and high-sugar diet disrupts gut microbial homeostasis, increasing *Enterobacteriaceae* while reducing beneficial bacteria, leading to dysbiosis[33]. This imbalance also decreases short-chain fatty acid production, which weakens the intestinal barrier and promotes inflammation[33]. Beyond westernization, trends may be partly attributable to improved disease surveillance and diagnostic capabilities, and increased healthcare awareness and accessibility. In Hong Kong, more advanced healthcare infrastructure and broader use of colonoscopy may account for the rising trends. In Japan, several updates of evidence-based clinical practice guidelines for IBD in recent years and the release of pediatric guidelines, concurrent with a significant increase in incidence and prevalence among those under 18, reflect growing awareness and management efforts[34-36]. Meanwhile, the stable forecasted incidence among some age or subtype groups in these regions, including IBD in adults in Japan, also demonstrated some exposure transitions, such as stabilization or decline of antibiotic use[37,38]. Antibiotic exposure has been linked to an increased risk of IBD by altering gut microbiota, reducing beneficial bacteria such as *Bacteroidetes* and *Firmicutes*, and promoting the overgrowth of *Enterobacteriaceae*, which is associated with intestinal inflammation[33]. Whereas the incidence will remain stable in the United States, the prevalence will continue to rise. Given the chronic and incurable nature of IBD, its prevalence will steadily increase as long as morbidity exceeds mortality[4]. These projections underscore the complexity of IBD epidemiology and highlight the escalating burden of IBD across both Asian and Western contexts.

The forecasted disease burden of IBD varies by disease subtype, sex, and age across regions. Forecasted trends suggest CD prevalence may catch up with UC in Hong Kong and the United States. However, in Japan, UC will continue to be the more common form. Some factors, such as smoking among adults and exposure to traffic-related air pollution, particularly nitrogen dioxide (NO₂), are recognized risk factors that increase the risk of CD[39,40]. Specifically, long-term exposure to particulate matter and NO₂ can induce oxidative stress, increase intestinal permeability, and alter gut microbiota composition, promoting the growth of pro-inflammatory bacteria such as *Gammaproteobacteria* while reducing anti-inflammatory species[33]. A United Kingdom study found that individuals residing in areas with higher NO₂ concentrations had an increased risk of CD in early life[38]. Sex differences were also evident in the projections[39]. In Hong Kong and Japan, the prevalence and incidence of IBD are expected to remain higher in males than females, whereas in the United States, it is similar for both males and females. This difference may be partly attributed to greater exposure of Asian males to environmental risk factors associated with industrialization (*e.g.*, ultra-processed foods, food additives, microplastics, air pollution, and heavy metals)[41-46], as they are more likely to move to industrialized regions for education or employment. Such environmental risk factors may contribute to IBD risk through mechanisms such as gut microbiota dysbiosis, increased intestinal permeability, and chronic inflammation. In contrast, in the United States, sex differences in exposure to industrialized environments may be less pronounced than in East Asia. For example, the consumption of ultra-processed foods is similar between males and females in the United States[47,48]. However, further research is needed to clarify how specific environmental exposures influence sex differences in IBD risk across regions. Additionally, substantially higher smoking rates in males compared to females in Hong Kong and Japan may further explain this gender disparity[49,50], whereas smoking rates in the United States are more evenly distributed between genders[49]. Moreover, differences in medical behaviors, such as higher colonoscopy uptake among males, might also partially contribute to this disparity, although evidence remains inconsistent[51,52]. Lastly, genetic backgrounds specific to Japanese and Hong Kong populations may also contribute to these sex differences, although empirical evidence remains limited. Among all age groups in Hong Kong and groups < 65 in Japan and the United States, adults aged 18-44 years are projected to continue facing the highest IBD prevalence in all three regions. Furthermore, in Japan and the United States, the most significant increase of both IBD prevalence and incidence among those under 18, compared to other 18-65 years groups, cannot be overlooked. Improved disease awareness and diagnosis might contribute to this increasing trend[11]. The update of pediatric IBD clinical guidelines in Japan has likely facilitated earlier diagnoses in children and adolescents[36], while the approval of more IBD-related pediatric medications during the study period in both Japan and the United States may have increased physician awareness of pediatric IBD[53,54]. Additionally, environmental factors, such as early exposure to Westernized diets high in fat and sugar, may also contribute to this trend. These differences underscore the importance of region-specific healthcare measures in anticipation of the increasing burden of IBD.

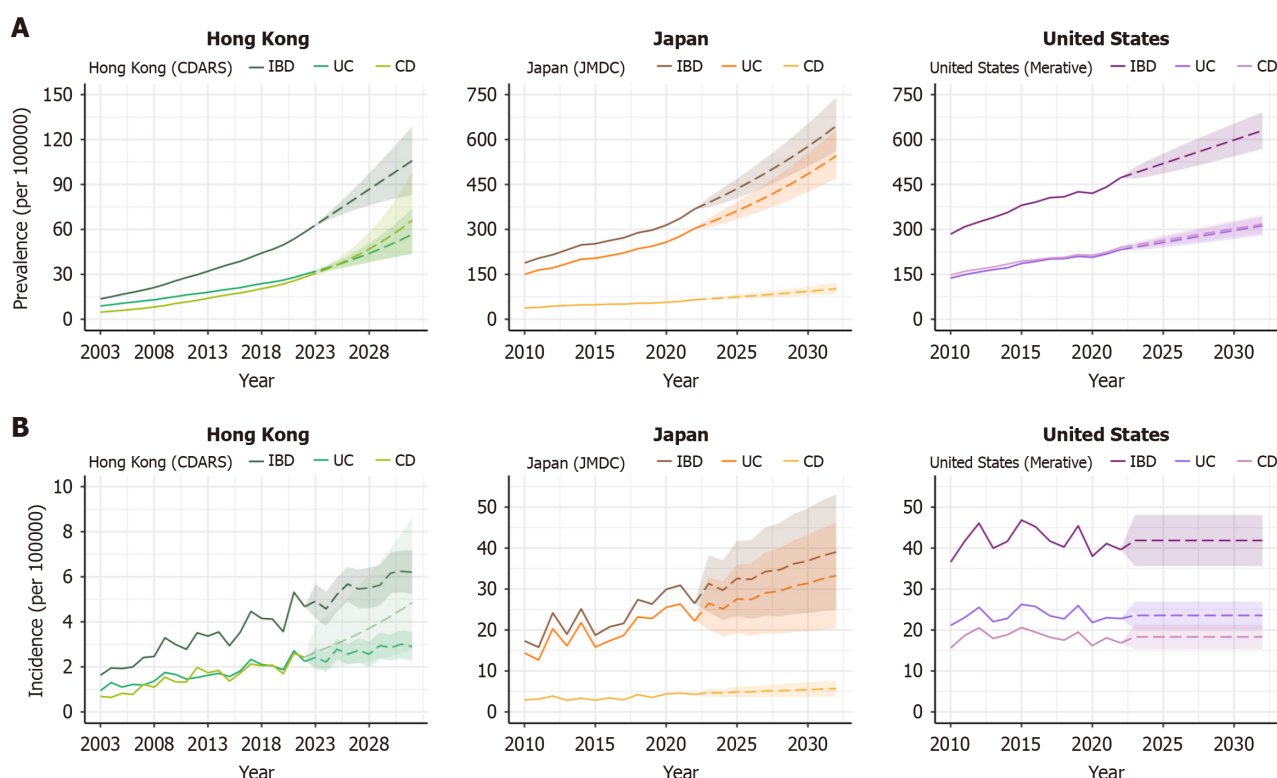


Figure 2 Current and forecasted prevalence and incidence of inflammatory bowel disease, Crohn's disease, and ulcerative colitis in Hong Kong, Japan and the United States. A: Prevalence in Hong Kong, Japan and the United States; B: Incidence in Hong Kong, Japan and the United States. The solid line represents the actual age-standardized prevalence and incidence of inflammatory bowel disease, ulcerative colitis, and Crohn's disease. The dashed lines indicate forecasted prevalence and incidence with the 95% projection intervals highlighted. Prevalence and incidence were age-standardized using the World Health Organization standard population. IBD: Inflammatory bowel disease; UC: Ulcerative colitis; CD: Crohn's disease; CDARS: Clinical data analysis and reporting system; JMDC: Japan Medical Data Center. Merative: The Merative™ MarketScan® ("Merative" previously IBM MarketScan Commercial Claims and Encounters) database.

Over the next decade, healthcare systems will face an escalating burden of IBD from both the increasing number of patients and the growing complexity of disease management, influenced by shifting disease demographics. The forecasted rise in childhood diagnoses in Japan and the United States will introduce specific challenges, including the psychological impact on patients and families, growth delays, and the need for lifelong care[55]. Compared to adults, pediatric patients with IBD typically have a broader disease extent, a higher incidence of acute severe colitis, and greater risks of growth retardation and delayed puberty[56]. Furthermore, pediatric IBD treatment pathways vary by region and differ from adult approaches, such as the use of biologics[57,58]. However, pediatric access to treatment remains limited as the approval of biologics and other novel therapies lag behind those for adults. Therefore, in response to the rising pediatric IBD diagnosis rate across regions, efforts should focus on strengthening pediatric IBD management by optimizing early biologic use, enhancing psychological support, and improving nutritional interventions to achieve better long-term outcomes for pediatric patients. While the majority of forecasted cases are among the young, the ageing IBD population and extended life expectancy will further increase the prevalence among older adults[4], especially given that the forecasted incidence is highest among those aged 45-64 years in the United States. Subsequent age-related comorbidities, such as cardiovascular disease and cancer, may present new management difficulties[55]. Therefore, in the United States, chronic disease management for middle-aged and elderly patients with IBD should be strengthened, and personalized treatment strategies should be optimized to improve disease control. Additionally, multidisciplinary collaboration should be promoted to ensure coordinated care among gastroenterology, geriatrics, and cardiology[59]. In Asia, the continued rapid increase of IBD necessitates greater awareness among the public and healthcare professionals, earlier diagnosis, and enhanced multidisciplinary management systems to improve overall IBD care and long-term patient outcomes, particularly for males who bear a higher disease burden.

The strength of this study lies in using territory-wide or large claims databases from three territories under different healthcare systems, enabling robust comparisons of future disease burdens across Western and Asian locales. The large population-based samples and long historical data of 13 to 20 years facilitate reliable analysis of disease trends and forecasts by subtype, sex, and age. However, there are some limitations. Firstly, since JMDC and Merative are employment-based databases, we include only employees and their dependents under 65 years. Nevertheless, IBD is usually diagnosed during adulthood, and the data from these databases can be considered representative of the adult population with IBD in their respective countries. Future studies in Japan and the United States among elderly > 65 years may provide supplemental insights. Moreover, since employment-based databases may not capture individuals unable to work due to severe illness, particularly older adults and those with frequent hospitalizations or severe complications, there is potential for an underestimation of IBD incidence and prevalence in these groups. Secondly, insufficient clinical

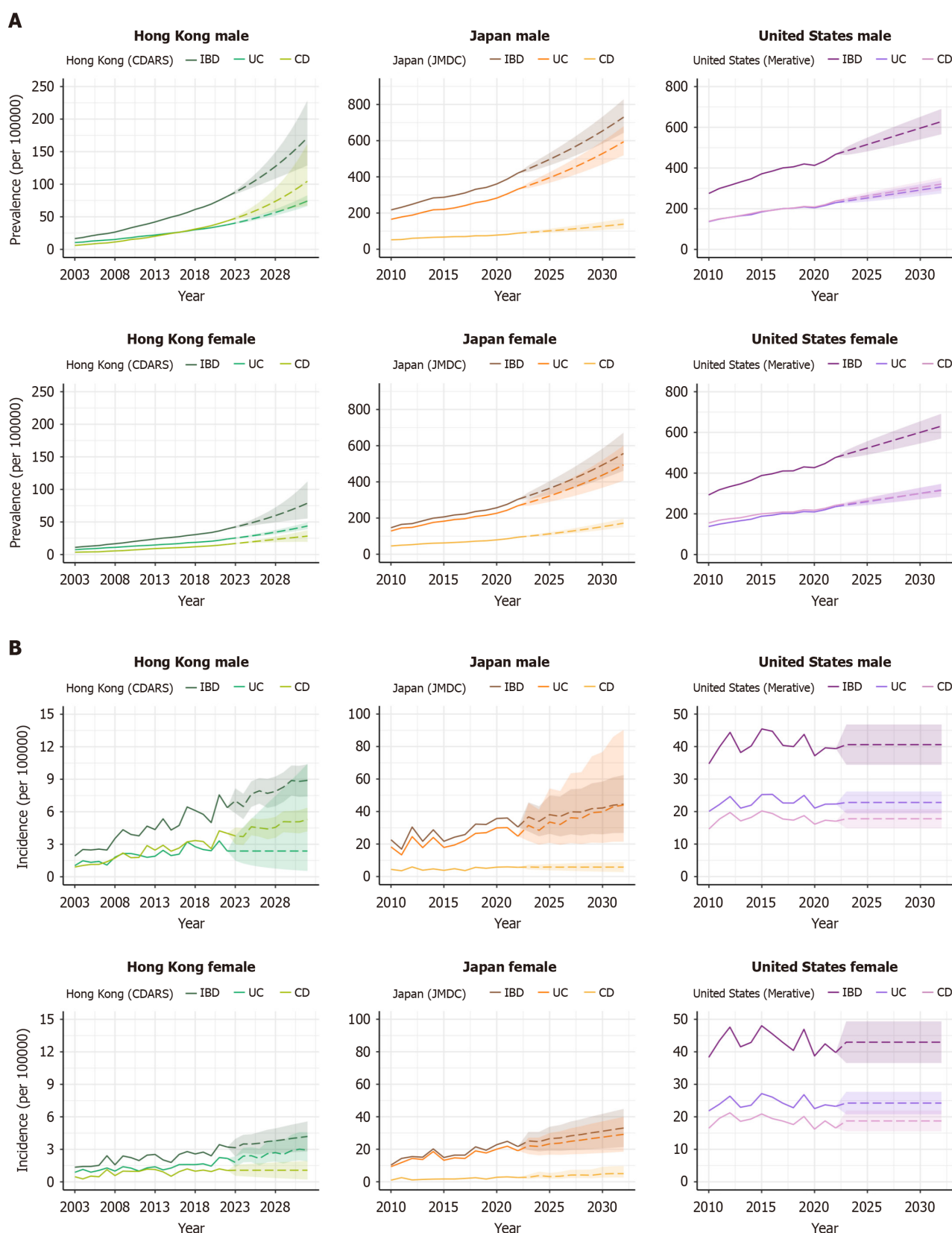
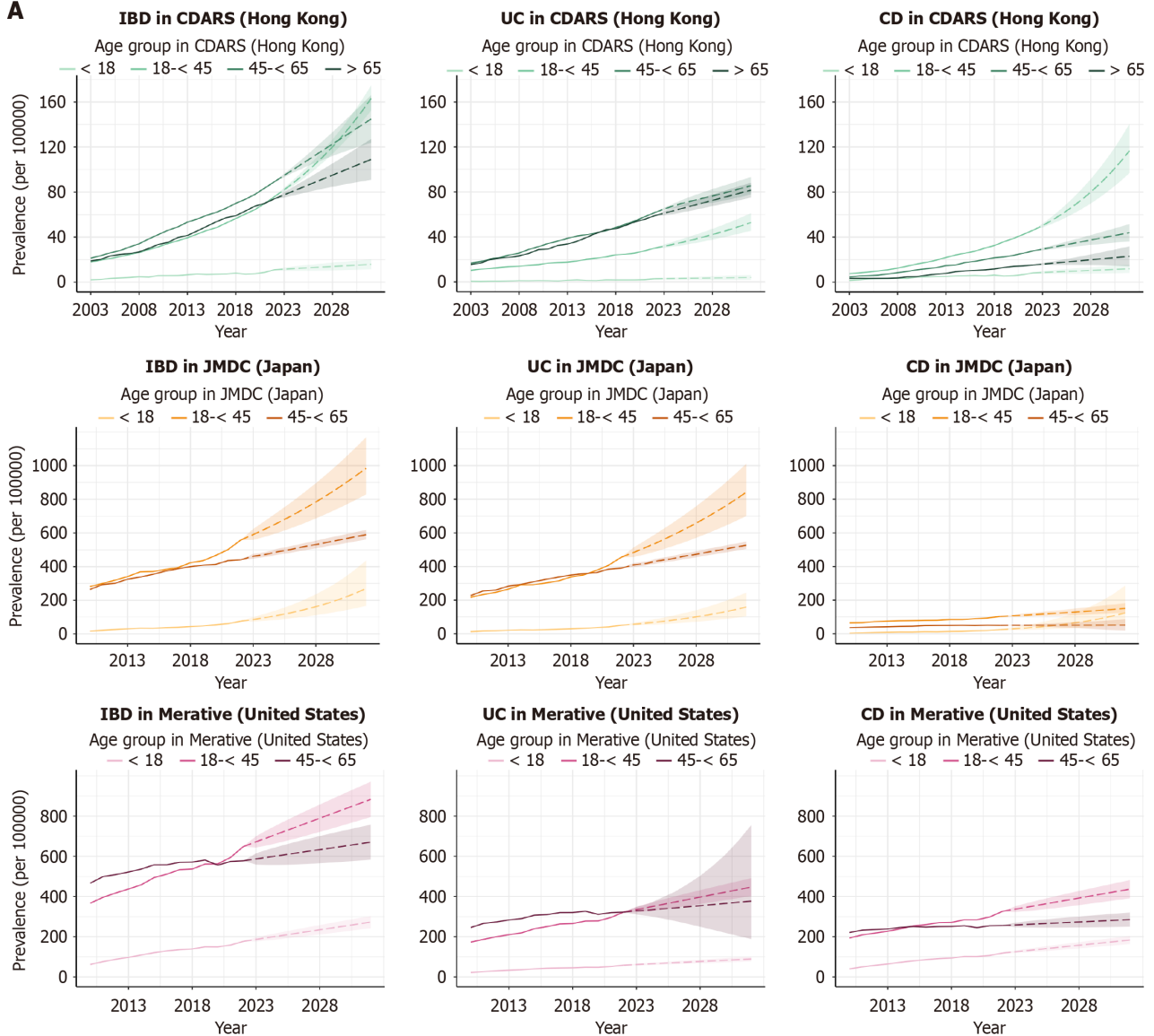
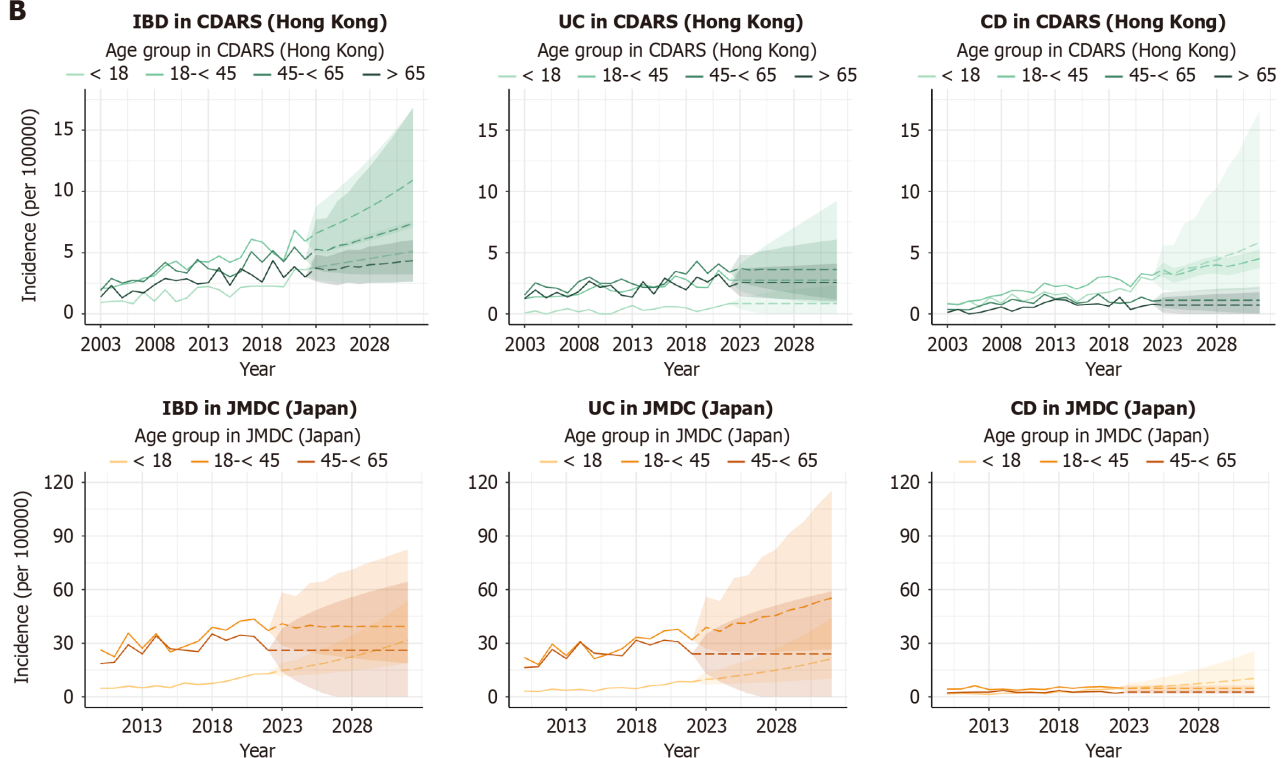


Figure 3 Sex-stratified prevalence and incidence of inflammatory bowel disease, Crohn's disease, and ulcerative colitis in Hong Kong, Japan and the United States. A: Prevalence in Hong Kong, Japan and the United States; B: Incidence in Hong Kong, Japan and the United States. The solid line represents the actual age-standardized prevalence and incidence of inflammatory bowel disease, ulcerative colitis, and Crohn's disease by sex. The dashed lines indicate forecasted prevalence and incidence with the 95% projection intervals highlighted. Prevalence and incidence were age-standardized using the World Health Organization standard population. IBD: Inflammatory bowel disease; UC: Ulcerative colitis; CD: Crohn's disease; CDARS: Clinical data analysis and reporting system; JMDC: Japan Medical Data Center. Merative: The Merative™ MarketScan® ("Merative" previously IBM MarketScan Commercial Claims and Encounters) database.

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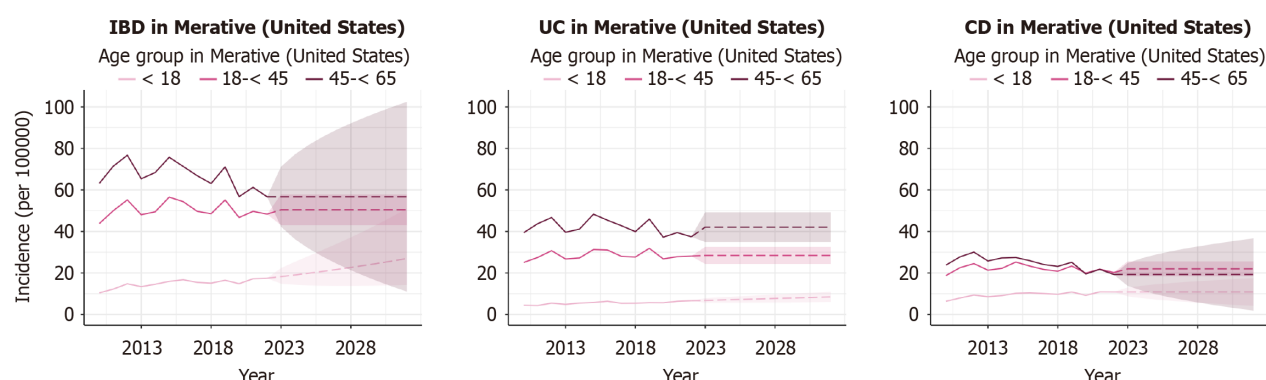


Figure 4 Age-stratified prevalence and incidence of inflammatory bowel disease, Crohn's disease, and ulcerative colitis in Hong Kong, Japan, and the United States. A: Prevalence in Hong Kong, Japan and the United States; B: Incidence in Hong Kong, Japan and the United States. The solid line represents the actual prevalence and incidence of inflammatory bowel disease (IBD), ulcerative colitis (US), and Crohn's disease (CD) by age. The dashed lines indicate forecasted prevalence and incidence with the 95% projection intervals highlighted. Prevalence and incidence were age-standardized using the World Health Organization standard population. CDARS: Clinical data analysis and reporting system; JMDC: Japan Medical Data Center; Merative: The Merative™ MarketScan® ("Merative" previously IBM MarketScan Commercial Claims and Encounters) database.

details in two health insurance databases increase the risk of misclassification. However, we adopted a combination of diagnosis and drug codes to identify cases, mitigating this risk. Lastly, due to the nature of the ARIMA model, the current forecasted disease burden is primarily based on historical data without considering other external factors that might influence the prevalence and incidence. For example, the introduction of new therapies may alter the IBD treatment pattern and further affect patients' survival and prognosis; adjustments in public health policies (*e.g.*, increased universal screening) and advances in medical technology could improve the early diagnosis; and changes in health policies may affect patients' access to healthcare services. Further research is required to assess the potential impact of these uncertainties on IBD prevalence, incidence, and overall disease burden. To mitigate these uncertainties, we chose the most appropriate models and utilized PIs to provide a range of plausible values for true prevalence and incidence.

CONCLUSION

The prevalence and incidence of overall IBD are estimated to increase in Hong Kong and Japan, with variations in patterns. In the United States, the forecasted IBD incidence remains stable, but the prevalence is forecasted to rise. These forecasts reveal significant differences across regions by subtype, sex, and age, highlighting the need for targeted healthcare strategies to manage the escalating challenge. Efforts should focus on strengthening pediatric IBD management in response to the rising trends across regions, including optimizing early biologic use. In the United States, where the burden of IBD is high among middle-aged and elderly patients, multidisciplinary collaboration and chronic disease management should be enhanced. In Asia, where IBD continues to rise rapidly, greater awareness among the public and healthcare professionals is needed, particularly for the heavily affected male population.

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FOOTNOTES

Author contributions: Li X and Qiu H designed and supervised the study; Wong ICK provided administrative and technical support for data access and clinical advice on results interpretation; Zhang Y and Chung H acquired the data; Zhang Y, Chung H, and Fang QW analyzed the data and performed cross-checking; Zhang Y and Li X drafted the manuscript; Leung WK provided clinical input and advice; Li X acquired the funding; Zhang Y, Chung H, Fang QW, Xu YR, Zhang YJ, Nakajo K, Wong ICH, Leung WK, Qiu H, Li X contributed equally to the interpretation of the results, and critically revised the manuscript for significant intellectual contribution.

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Institutional review board statement: Analysis of clinical data analysis and reporting system from Hong Kong was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster (No. UW22-280). Data from the Japan Medical Data Centre and Merative™ MarketScan® database (Merative) were de-identified and are fully compliant with relevant patient confidentiality requirements, including the Japanese Personal Information Protection Law and the United States Health

Insurance Portability and Accountability Act of 1996. Ethical approval are not required for Japan Medical Data Centre and Merative.

Informed consent statement: Informed consent from patients was waived because the study was retrospective and all patient data were fully de-identified.

Conflict-of-interest statement: Li X received research grants from the Research Fund Secretariat of the Health Bureau, Health and Medical Research Fund (HMRF, HKSAR), Health and Medical Research Fund Fellowship Scheme (HMRF Fellowship, HKSAR), Research Grants Council Early Career Scheme (RGC/ECS, HKSAR), commission grants from Hospital Authority of Hong Kong; educational and investigator initiate research fund from Janssen and Pfizer; internal funding from the University of Hong Kong; and consultancy fee from Pfizer, Merck Sharp and Dohme, Open Health. She was also the former non-executive director of ADAMS Limited Hong Kong, all outside the submitted work. ICKW reports grants from Amgen, Bristol-Myers Squibb, Pfizer, Janssen, Bayer, GSK and Novartis, the Hong Kong RGC, and the Hong Kong Health and Medical Research Fund in Hong Kong, National Institute for Health Research in England, European Commission, National Health and Medical Research Council in Australia, consulting fees from IQVIA and World Health Organization, payment for expert testimony for Appeal Court of Hong Kong and is a non-executive director of Jacobson Medical in Hong Kong and Therakind in England, outside of the submitted work. There are no other relationships or activities that could appear to have influenced the submitted work. Leung WK has received speaker's honoraria from AbbVie, Ferring Pharmaceuticals, and Janssen. Chung H, Xu YR, Zhang YJ, Nakajo K and Qiu H are employees of Janssen Research and Development, LLC at the time of the study. Qiu H holds stock in Johnson and Johnson Pty Ltd. All other authors have no conflicts of interest to declare.

Data sharing statement: Local academic institutions, government departments, or non-governmental organizations may apply for access to clinical data analysis and reporting system data through the Hospital Authority's data sharing portal (<https://www3.ha.org.hk/data>). The data from Japan Medical Data Centre (JMDC) and Merative underlying this article were provided by the JMDC and Merative under license. Data from JMDC and Merative will be shared on request to the corresponding authors with permission of JMDC and/or Merative.

STROBE statement: The authors have read the STROBE Statement—a checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-a checklist of items.

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