

Small-area Variations and Sociodemographic Correlates for the Incidence of Crohn's Disease and Ulcerative Colitis

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The objectives of this study were to describe variations in the incidence of inflammatory bowel disease (IBD) within the Canadian province of Manitoba and to analyze sociodemographic factors associated with these variations. The authors used the Manitoba Health insurance databases to measure incidence rates of Crohn's disease and ulcerative colitis for each of 52 postal areas in Manitoba, in 1987–1996. The sociodemographic characteristics of the postal areas were based on data from the 1996 Canadian census. The overall incidence rates of Crohn's disease and ulcerative colitis were identical—15.6 per 100,000. Both diseases showed substantial geographic variation, with incidence rates differing significantly from the provincial average in 15 postal areas for Crohn's disease and in 13 postal areas for ulcerative colitis. There was a significant geographic correlation in the incidence of Crohn's disease and ulcerative colitis ($r = 0.49$, $p < 0.001$). The incidence of IBD was higher in urban areas (incidence rate ratio (IRR) = 1.21, 95% confidence interval (CI): 1.00, 1.45). Aboriginal Canadians had significantly lower rates of both Crohn's disease (IRR = 0.11, 95% CI: 0.05, 0.22) and ulcerative colitis (IRR = 0.57, 95% CI: 0.42, 0.79). A higher incidence of IBD was ecologically associated with a higher average family income, a lower proportion of immigrant and Aboriginal Canadian populations, and a smaller average family size. *Am J Epidemiol* 2001;154:328–35.

colitis, ulcerative; Crohn disease; incidence; inflammatory bowel diseases

Inflammatory bowel disease (IBD) is composed of two clinical entities, Crohn's disease and ulcerative colitis, which are chronic, spontaneously relapsing disorders of the gastrointestinal tract characterized by an inflammatory process. Whereas Crohn's disease can cause inflammation in all parts of the gastrointestinal tract, ulcerative colitis is restricted to the colon. The causes of these diseases are not known. There is evidence that both conditions are immunologically mediated and that genetic factors play an important etiologic role (1). However, the dynamic epidemiology of both conditions suggests that extrinsic environmental factors also play an important role in their pathogenesis. Numerous studies in various populations have documented substantial temporal trends in the incidence rates of both Crohn's disease and ulcerative colitis over the past century.

The general observations in northern European and North American populations are that the incidence of ulcerative colitis rose substantially through the early to mid-1900s and has since stabilized or declined, while the incidence of Crohn's disease has been increasing since the mid-1900s (2–12). These findings suggest that new patterns of environmental exposures that play an important causal role have emerged.

In addition to temporal trends, some investigators have pointed to geographic variations in the incidence of Crohn's disease and ulcerative colitis as evidence of environmental etiologic factors (13, 14). In general, the prevalence of both is highest in countries in northern latitudes (15). There is also limited evidence for epidemiologic variability within countries. For example, a study of IBD mortality and hospitalization rates in the United States demonstrated high variability between states, with IBD being more common in northern than in southern states (16). Another study found significant differences in the incidence of Crohn's disease and ulcerative colitis between four counties in Norway (17, 18). The reasons for these geographic variations are not clear, but they may result from variations in the geographic distribution of important environmental etiologic agents. Alternatively, they may be largely due to regional variations in the sociodemographic characteristics of populations.

We have recently reported that the central Canadian province of Manitoba has among the highest documented rates of both Crohn's disease and ulcerative colitis in the world (19). Other than its northern geographic location, the reasons for the very high rates of IBD, and especially

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Abbreviations: CI, confidence interval; IBD, inflammatory bowel disease; IRR, incidence rate ratio.

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Crohn's disease, in Manitoba are not clear. In this paper, we further explore the descriptive epidemiology of IBD in Manitoba. Our specific focus is to describe variations in the incidence of Crohn's disease and ulcerative colitis within Manitoba and to analyze sociodemographic factors that are associated with these variations.

MATERIALS AND METHODS

Study setting

This study was conducted in the central Canadian province of Manitoba. Manitoba has a population of 1.14 million (as of 1997) that is ethnically diverse. More than 60 percent of the residents live in the only major urban center, Winnipeg (population, 647,000). The remainder of the population is distributed among small regional centers and farming communities in the rural southern half of the province and remote, mining, forestry, and Aboriginal Canadian communities in the subarctic northern half of the province. The majority of Manitobans are of European descent, with most recent immigrants coming from the Philippines, China, India, or the United Kingdom.

Data sources

The main source of data for this study was the University of Manitoba IBD Database. The creation of this database has been described previously (19). Briefly, the database is derived from the Manitoba Health insurance databases, which are based on the universal provincial health insurance system. The utility, accuracy, and completeness of these databases have been documented (20, 21). To identify persons with IBD in the province, physician billing claims and hospital discharge abstracts were searched for a diagnosis of Crohn's disease (*International Classification of Diseases*, Ninth Revision, Clinical Modification code 555.xx) or ulcerative colitis (*International Classification of Diseases*, Ninth Revision, Clinical Modification code 556.xx) between 1984 and 1998 inclusive. To improve the specificity of case definition using the administrative data for persons who had been resident and registered with the insurance system for at least 2 years, we included as cases only those with at least five separate physician contacts and/or hospitalizations for an IBD diagnosis. For residents who had been insured for less than 2 years, we required three physician contacts and/or hospitalizations. We have previously reported that this case definition strategy identifies persons with IBD with a high sensitivity and specificity compared with self-report and chart review (19). To define incident cases, we identified those persons whose first medical claim or hospitalization occurred between 1987 and 1996. This excluded those with initial medical contacts between 1984 and 1986, the first 3 years of observation in our database. In this study, First Nation status refers to those Aboriginal Canadians who are registered as North American Indian under the Indian Act of Canada. This designation is based on self-report during the insurance registration process with the Manitoba health insurance system. It is estimated that more than 70 percent of all registered Indians were so identified

in the Manitoba Health insurance registry during the study period. Urban residence was assigned to those who lived in the city of Winnipeg, which is the only urban center with a population greater than 50,000.

Data from the 1996 Census of Canada were used to estimate the average family income, ethnic composition, immigrant population, and average family size (Statistics Canada, Microdata Release File).

To examine variations, we organized the data into postal forward sortation areas. During the study period, there were 63 of these postal areas within the province. We excluded 11 small postal areas with annual populations of less than 350 people, since reliable estimates of incidence and sociodemographic characteristics could not be calculated. Of the remaining 52 postal areas, 32 were in the city of Winnipeg, and the remaining 20 were nonurban.

Analysis of incidence rates

Incidence rates were calculated based on the total number of incident cases that occurred from 1987 to 1996 inclusive, with the person-years denominator being the sum of the annual population estimates for each of those years. Age-standardized rates were calculated by the direct method using the total person-years distribution of 1987–1996 as the standard. The geographic correlation between age-adjusted incidence rates of Crohn's disease and ulcerative colitis was assessed by using the Pearson correlation coefficient (r), weighted by the postal-area population size.

To examine associations between the incidence rates of IBD and family income, the ethnic and Aboriginal population distribution, and average family size, we organized the 52 postal areas into tertiles for ecologic analyses. To examine the relation between urban residence and First Nation status and IBD incidence rates, we assigned these characteristics to persons for analysis. Poisson regression was used for multivariate analyses to calculate adjusted incidence rate ratios.

To assess whether differences in diagnostic practices and health care utilization might account for variations in incidence rates, we analyzed geographic differences in the average age of first IBD-related health care contact and the average annual number of IBD-related outpatient physician visits and hospitalizations. To do this, we divided the postal areas into quartiles based on the incidence rates of Crohn's disease and ulcerative colitis and compared those postal areas in the upper quartile (i.e., the 13 postal areas with the highest incidence rates) with those in the lowest quartile.

RESULTS

Geographic variations in incidence rates

During the study period (1987–1996), there were 11.3 million person-years of observation, with 3,528 incident cases of IBD (1,765 Crohn's disease and 1,763 ulcerative colitis). Figures 1 and 2 show the incidence rates of Crohn's disease and ulcerative colitis, respectively, in each of the 52 study postal areas in Manitoba. The overall incidence rate of Crohn's disease was 15.6 per 100,000 person-years (figure 1).

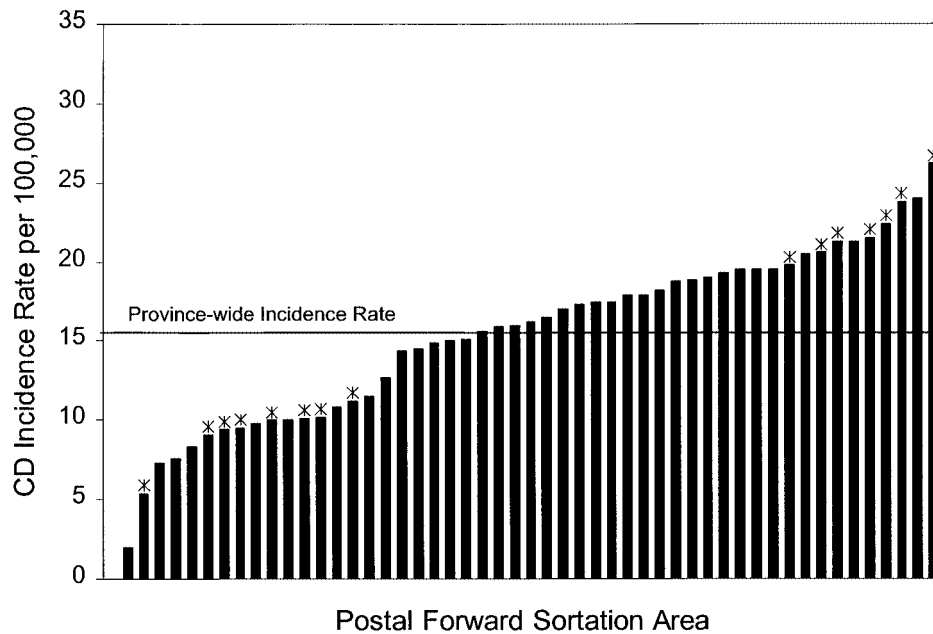


FIGURE 1. The age-standardized incidence rates per 100,000 person-years of Crohn's disease (CD) by postal forward sortation area in Manitoba, Canada, 1987–1996. The asterisk above the bars indicates rates that are significantly lower or higher (i.e., $p < 0.05$) than the provincial average.

The age-adjusted incidence rate ranged from 0.0 to 26.2 per 100,000, and the incidence rate was significantly ($p < 0.05$) below the provincial average in eight of the postal areas and

significantly above average in seven. The overall incidence rate of ulcerative colitis was also 15.6 per 100,000, with the age-adjusted incidence rates ranging from 6.1 to 31.8 per

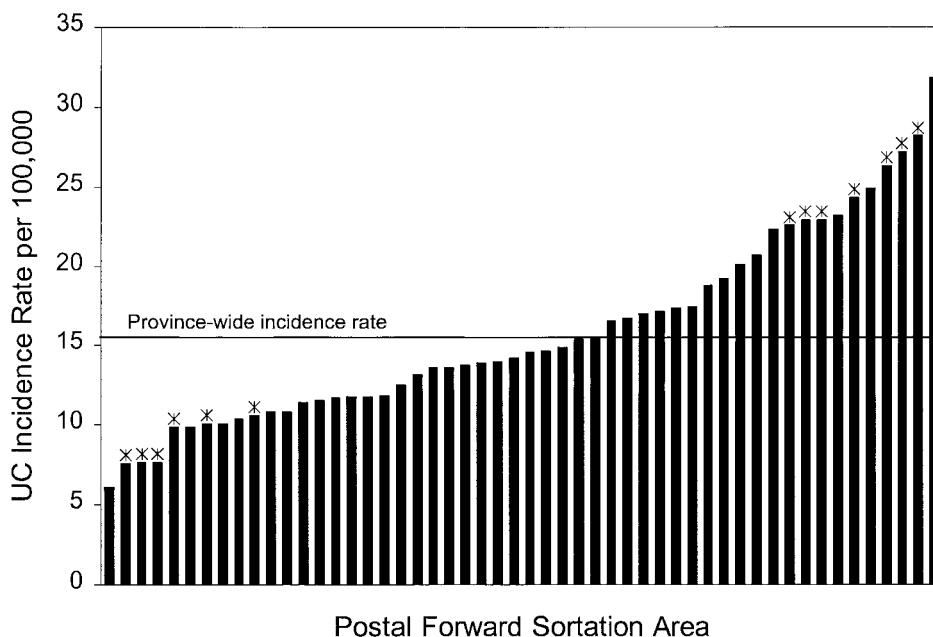


FIGURE 2. The age-standardized incidence rates per 100,000 person-years of ulcerative colitis (UC) by postal forward sortation area in Manitoba, Canada, 1987–1996. The asterisk above the bars indicates rates that are significantly (i.e., $p < 0.05$) lower or higher than the provincial average.

100,000 in the postal areas (figure 2). For ulcerative colitis, the incidence rate was significantly below the provincial average in six of the postal areas and significantly above average in seven. Figure 3 is a scatterplot showing the relation between the Crohn's disease and ulcerative colitis incidence rates at the level of the postal area. There was a significant correlation between Crohn's disease and ulcerative colitis incidence rates ($r = 0.49$, $p < 0.001$).

Associations with sociodemographic factors

Table 1 shows the relation between various sociodemographic variables and the incidence rates of Crohn's disease, ulcerative colitis, and all IBD. The age-adjusted incidence of Crohn's disease, but not of ulcerative colitis, was higher among those living in urban areas. However, after adjustment for other sociodemographic factors, the rates of both Crohn's disease (incidence rate ratio (IRR) = 1.19, 95 percent confidence interval (CI): 0.93, 1.52) and ulcerative colitis (IRR = 1.25, 95 percent CI: 0.94, 1.65) were slightly, but not significantly, higher in urban dwellers. The combined adjusted incidence of IBD was significantly higher in urban areas (IRR = 1.21, 95 percent CI: 1.00, 1.45). The age-adjusted incidence of IBD was significantly lower among First Nation persons than in the general population (10.6 vs. 32.3 per 100,000). This three-fold difference was maintained after adjustment for other sociodemographic factors (IRR = 0.33, 95 percent CI: 0.25, 0.44). The difference in incidence rates between First Nation persons and the general population was much more striking for Crohn's disease (IRR = 0.11, 95 percent CI:

0.05, 0.22) than for ulcerative colitis (IRR = 0.57, 95 percent CI: 0.42, 0.79).

There was a significant, positive association between the incidence of IBD and the average family income of the area of residence. Compared with the lowest tertile of average family income, the adjusted IRRs were 1.11 (95 percent CI: 1.01, 1.23) and 1.20 (95 percent CI: 1.06, 1.36) for the middle and highest tertiles, respectively. A significant positive association with average family income was also present for Crohn's disease, but not for ulcerative colitis. There was a significant, inverse association between the incidence of IBD and the percentage of immigrants and Aboriginals and the average family size in the area of residence. The adjusted IRRs comparing the highest with the lowest tertile were 0.77 (95 percent CI: 0.64, 0.94) for percent immigrant, 0.85 (95 percent CI: 0.76, 0.95) for percent Aboriginal, and 0.78 (95 percent CI: 0.71, 0.86) for average family size. Significant inverse relations were also observed between these variables and the incidence of ulcerative colitis, whereas only average family size was significantly associated with the incidence of Crohn's disease.

Geographic patterns of health care utilization

The average age of first IBD-related health care contact with physicians was slightly lower in the 13 postal areas in the lowest quartile of incidence rates than in postal areas in the highest quartile for both Crohn's disease (35.4 vs. 36.2 years) and ulcerative colitis (39.5 vs. 43.3 years).

The average number of medical contacts for an IBD diagnosis (including outpatient physician visits and hospitaliza-

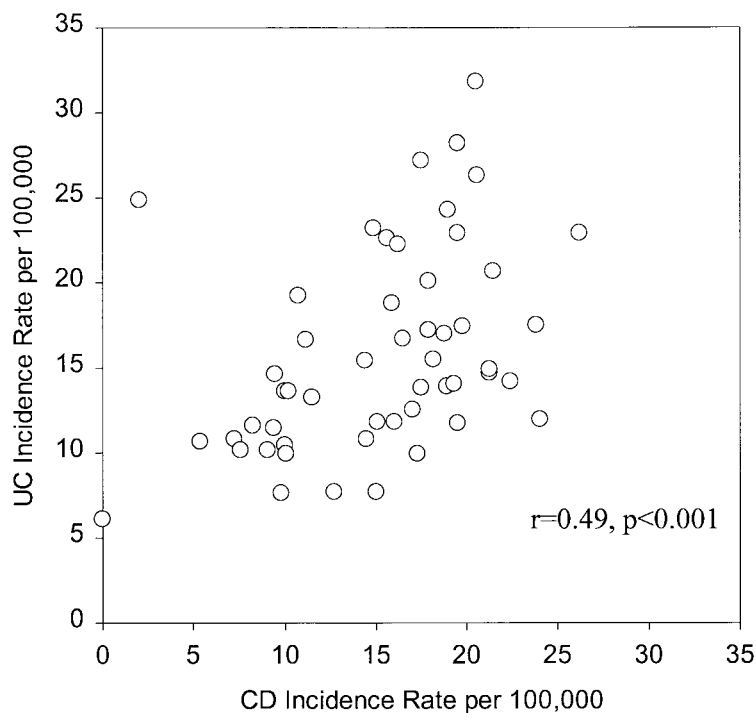


FIGURE 3. Scatterplot of the age-standardized incidence rates of Crohn's disease (CD) and ulcerative colitis (UC) by Manitoba postal forward sortation area, Manitoba, Canada, 1987-1996.

TABLE 1. Age-adjusted incidence rates, and incidence rate ratios and 95% confidence intervals derived from Poisson regression analysis, for Crohn's disease and ulcerative colitis according to sociodemographic characteristics, Manitoba, Canada, 1987–1996

Population characteristics	Crohn's disease			Ulcerative colitis			All IBD*		
	Incidence per 100,000	IRR [†] , ‡	95% CI*	Incidence per 100,000	IRR [†]	95% CI	Incidence per 100,000	IRR [†]	95% CI
Rural	13.1	1.00	Reference	15.8	1.00	Reference	29.0	1.00	Reference
Urban [‡]	17.5	1.19	0.93, 1.52	15.4	1.25	0.94, 1.65	32.9	1.21	1.00, 1.45
Other	16.4	1.00	Reference	15.9	1.00	Reference	32.3	1.00	Reference
First Nation ^{‡,§}	1.9	0.11	0.05, 0.22	8.7	0.57	0.42, 0.79	10.6	0.33	0.25, 0.44
Average family income (dollars) [¶]									
22,776–44,826	12.1	1.00	Reference	14.6	1.00	Reference	26.7	1.00	Reference
45,150–53,365	16.3	1.18	1.02, 1.36	14.9	1.05	0.92, 1.21	31.2	1.11	1.01, 1.23
53,504–110,632	19.2	1.29	1.08, 1.54	17.9	1.13	0.95, 1.34	37.2	1.20	1.06, 1.36
% Immigrant [¶]									
0.9–6.8	13.1	1.00	Reference	17.0	1.00	Reference	30.1	1.00	Reference
7.6–15.5	18.3	0.97	0.76, 1.25	16.0	0.70	0.53, 0.92	34.3	0.83	0.69, 0.99
15.6–34.3	15.9	0.94	0.72, 1.22	13.9	0.63	0.47, 0.85	29.8	0.77	0.64, 0.94
% Aboriginal [¶]									
0.3–3.7	18.4	1.00	Reference	18.0	1.00	Reference	36.4	1.00	Reference
3.9–11.0	16.4	1.03	0.90, 1.19	15.2	0.88	0.76, 1.00	31.6	0.95	0.87, 1.05
12.5–82.8	11.6	0.90	0.77, 1.06	13.3	0.80	0.68, 0.94	24.9	0.85	0.76, 0.95
Average family size [¶]									
2.6–3.0	16.2	1.00	Reference	17.1	1.00	Reference	33.3	1.00	Reference
3.1–3.2	17.6	1.03	0.91, 1.16	16.9	0.94	0.83, 1.06	34.5	0.98	0.90, 1.07
3.3–4.0	12.4	0.83	0.73, 0.95	11.5	0.73	0.63, 0.83	23.9	0.78	0.71, 0.86

* IBD, inflammatory bowel disease; IRR, incidence rate ratio; CI, confidence interval.

† Adjusted for age group and all other population characteristics listed in the table by using Poisson regression.

‡ Values for urban/rural residence and First Nation status are based on individual characteristics.

§ First Nation in this study refers to North American Indians who are registered under the Indian Act of Canada.

¶ Values for average family income, percent immigrant, percent Aboriginal, and average family size are derived ecologically, based on estimates from the 1991 Canadian census for the postal forward sortation area of residence, with the ranges representing tertiles of those variables within the province.

tions) was higher in the 13 postal areas in the lowest quartile of incidence rates for Crohn's disease (6.0 contacts per year in lowest quartile vs. 4.8 contacts per year in highest quartile). There was little difference between the lowest and the highest quartiles for ulcerative colitis (2.6 vs. 2.8 contacts per year).

DISCUSSION

In this study, we have demonstrated substantial variations in the incidence of both Crohn's disease and ulcerative colitis in the province of Manitoba, Canada, and have also shown that these variations are associated with differences in the sociodemographic characteristics of the population. Our study has several methodological limitations. We have relied exclusively on data derived from administrative health records to estimate IBD incidence rates. However, we previously studied the accuracy of this approach and found that the specificity was high—90 percent for Crohn's disease and 94 percent for ulcerative colitis—when compared

with a detailed chart review (19). It is possible that some of the variations that we observed are due to variability in health care access and diagnostic practices. However, Manitoba provides universal health care to its residents, so restricted access to physician and hospital services is not likely. Previous research in the Manitoba population suggests that the likelihood of medical care for chronic conditions is not lower among those of lower socioeconomic status (22, 23). We found that the mean number of medical contacts (including outpatient physician visits and hospitalizations) for an IBD diagnosis was higher in low-incidence areas for Crohn's disease and differed little for ulcerative colitis, suggesting that variations in health care utilization do not account for observed differences in incidence rates. Diagnostic practices likely vary across the province and probably explain some of our observed variations. However, we found substantial geographic variations in IBD incidence even within the city of Winnipeg (data not shown), where access to specialists and diagnostic practices are likely to be more evenly distributed. If the large geographic differences

in incidence that we observed are due to substantial variations in diagnostic practices, we might expect that the diagnosis of IBD would be delayed in areas of low incidence, which would be reflected by a later average age at first contact for IBD. However, we found that, compared with those areas in the highest incidence quartile, in those areas in the lowest quartile of incidence, the average age of first IBD-related contact was similar for Crohn's disease and younger for ulcerative colitis.

Other than for urban residence and First Nation status, we have relied on ecologic data to assess the relation between sociodemographic factors and the incidence of IBD. Therefore, as with any ecologic analysis, interpretation must be cautious. Specifically, our findings do not necessarily infer that these factors alter a person's risk of IBD.

The wide variation in the incidence of Crohn's disease and ulcerative colitis that we observed between different postal areas in Manitoba is consistent with some previous research showing geographic variability at an international or regional level of analysis (15–18). In fact, the severalfold variation in incidence rates that we observed is of a magnitude similar to that previously reported for international comparisons (15) and for the variability between states in the United States (16). Less geographic variability in incidence rates has been reported in studies conducted in Italy (24), Sweden (2, 25), and Norway (17, 18). One possible explanation for the greater variability seen in our study is that we examined smaller geographic areas. Studies of larger geographic units would tend to wash out regional variations by combining heterogeneous populations.

Reasons for the high degree of geographic variability in incidence rates within Manitoba are not clear. Our results suggest that some of the variability is related to differences in the sociodemographic characteristics of the populations. We found an increased incidence of IBD in areas of higher income, which is consistent with most, but not all, previous analytic studies (26–32). Some studies have suggested that higher rates among those of higher socioeconomic status may be due to a delayed and/or low-level exposure to common infectious agents during childhood, resulting in persistent infection or an altered immune response (33, 34). Others have hypothesized that it may be due to a higher risk in among those with indoor occupations (26).

We also found that areas with a higher percentage of immigrants had lower rates of ulcerative colitis, even after adjustment for family income, Aboriginal population, and family size. One explanation may be that these areas have a higher concentration of persons from Asia, Africa, and South America, where IBD rates are low. However, a recent study from the United Kingdom has shown that persons with a South Asian ethnicity have a higher incidence of ulcerative colitis than do Europeans (35). Further research, including analytic epidemiologic studies and epidemiologic studies of international migrants, is warranted to understand these findings better.

We found that areas with a larger average family size have significantly lower incidence rates of both Crohn's disease and ulcerative colitis. This association was independent of the average family income in the area. Because this find-

ing is based on ecologic data, we cannot conclude that persons from larger families have a lower risk of IBD. However, it is consistent with the hypothesis that less household crowding and delayed exposure to infections increase the risk of developing IBD (33, 34).

Our findings with respect to Manitoba's First Nation population are intriguing. Others have reported that Aboriginal populations, such as Native Americans in the United States (14) and Maoris in New Zealand (36), have a lower incidence of IBD than the rest of the population. Our data showing that the incidence in the First Nation population is only one third of that in the general population are consistent with those findings. However, we have shown that this difference is much more profound for Crohn's disease than for ulcerative colitis. This pattern is consistent with observations of the emergence of IBD in many populations in which the rising incidence of ulcerative colitis precedes that of Crohn's disease (11, 37). Etiopathologic explanations for these findings are not readily apparent. Since there is strong evidence that genetic factors play an important role in the etiology of IBD (1), it may be that First Nation persons have a low genetic predisposition to IBD. Cigarette smoking has been shown to increase the risk of Crohn's disease and reduce the risk of ulcerative colitis (38, 39). However, since the prevalence of smoking in Manitoba's First Nation population is high relative to the general population (40), this does not explain our findings. Dietary habits have been linked to the risk of IBD, with Crohn's disease patients tending to report higher intake of refined sugar and starch (41). However, traditional dietary habits are waning in the First Nation population. It has been reported that Crohn's disease, but not ulcerative colitis, is associated with greater domestic hygiene in the home during childhood (33), and it has been hypothesized that a high exposure to enteric organisms during infancy programs the immune system of the gut in such a way as to protect against IBD (15). Household crowding and the lack of running water are still common for Manitoba's First Nation persons, and their incidence of childhood infections, including enteric infections, is much higher than that in the general population (42, 43). More detailed epidemiologic studies and analytic research are required to better interpret the descriptive epidemiology of IBD in this population.

There has been much speculation about whether Crohn's disease and ulcerative colitis share a common etiology (1, 11, 44). Our study can provide only modest support for this hypothesis. We did find a significant ecologic correlation between Crohn's disease and the incidence of ulcerative colitis by postal area. However, the correlation was not as high as one might expect for diseases with common environmental risk factors. Further evidence from our study for differences in the pattern of environmental risk factors for Crohn's disease and ulcerative colitis is provided by the very discordant rates for these two entities found within the First Nation population. One explanation that has been offered to explain differences in the temporal patterns of incidence is the existence of some environmental exposure that predisposes to the development of IBD and an additional factor that is required to shift the inflammatory dis-

ease expression to Crohn's disease from ulcerative colitis (11). It will now be important to see whether Crohn's disease emerges in the First Nation population and, if it does, to study the epidemiologic patterns of emergence to illuminate the environmental risk factors.

This study has provided further evidence of the dynamic epidemiology of IBD. Wide variations and substantial differences in the incidence of both Crohn's disease and ulcerative colitis between First Nation persons and the rest of the population suggest that diligent research is warranted to identify environmental exposures that are etiologically important in these diseases.

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