

# ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

Section Editor: Stephen B. Hanauer, MD

## Update on the Incidence and Prevalence of Inflammatory Bowel Disease in the United States



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### **G&H** What is the current incidence of Crohn's disease in the United States?

**EL** This question is surprisingly complicated to answer because the incidence likely varies across different demographic categories, and each region has a different mix of demographics. There is no overall incidence for the US population as a whole, but incidence has been reported for specific regions. For example, there has been a lot of research on the incidence of inflammatory bowel disease (IBD) in Olmsted County, Minnesota because the county has only 2 health care providers, and they share a linked diagnostic index called the Rochester Epidemiology Project, which is funded by the National Institutes of Health. My colleagues and I recently reported on updated incidence data on IBD because there have been conflicting data regarding whether rates have plateaued in the United States or whether they are still rising. We know that there has been a large increase in IBD since the end of World War II, but several studies have suggested that the incidence of IBD has plateaued over the past 10 to 15 years, while other studies have disagreed. From 2000 to 2010 (the most recent decade for which we have data), the annual adjusted incidence for Crohn's disease in Olmsted County was 10.7 cases per 100,000 person-years.

However, it is important to note that the racial and ethnic mix of Olmsted County is not reflective of the United States as a whole, despite a recent change in county demographics (96% non-Hispanic white in 1990, compared with 83% in 2010). Thus, even though the majority of IBD cases in the United

States are white, extrapolating Olmsted County incidence to the entire country may be an overestimate because Olmsted County has a lower prevalence of African Americans, Hispanic Americans, and probably also Asian Americans.

### **G&H** What is the incidence of Crohn's disease in other geographic regions in the United States?

**EL** Current incidence is only available for a few places in the United States. Outside of Olmsted County, the most recent estimate for Crohn's disease probably comes from Kaiser Permanente in northern California, which reported rates in the mid-1990s to the early 2000s that were a little lower—6 cases per 100,000 person-years. Most incidence data come from places with single-payer systems (eg, Canadian provinces) because they have data on every person in the area. Because the United States has many different insurance plans, it is harder to track this information.

### **G&H** How do these data compare with the current incidence of ulcerative colitis?

**EL** At least in North America, ulcerative colitis is slightly more prevalent than Crohn's disease. The incidence of ulcerative colitis in Olmsted County for the period of 2000 to 2010 was 12.2 cases per 100,000 person-years. The data from Kaiser Permanente from 1996 to 2002 were fairly comparable—12 cases per 100,000 person-years.

### G&H What is the current prevalence of these diseases in the United States?

**EL** There has been a fairly remarkable similarity across different North American sites. In general, when combining Crohn's disease and ulcerative colitis, the North American prevalence comes out to between 400 and 600 cases per 100,000 persons (0.4%-0.6% of the population). In Olmsted County, approximately 1 in 200 people have IBD, which can be extrapolated to between 1.5 and 1.6 million people out of the entire US population (approximately 320 million people). In other US studies (eg, members of Kaiser Permanente Northern California in 2002, members of 9 health maintenance organizations from 1999 to 2001, and persons with commercial insurance listed in the MarketScan database from 2003 to 2004), the combined prevalence of IBD has ranged from 252 to 439 cases per 100,000 persons. As for Canada, the prevalence of IBD from 1998 to 2000 was estimated to be 473 cases per 100,000 persons.

However, as previously mentioned, the major caveat is that these data have historically come from places where there is a high prevalence of whites, potentially leading to extrapolations being overestimated.

### G&H According to the most recent data available, is IBD increasing in the United States or has it reached a plateau?

**EL** Over the past 10 to 15 years, some studies have reported increasing rates, while others have suggested a plateau in rates. At the 2014 American College of Gastroenterology meeting, my colleagues and I presented, in abstract form, a statistical analysis called a Poisson regression, which is a multivariate analysis with incidence as its endpoint. We were able to show that for Olmsted County, the calendar year of diagnosis was significantly associated with incidence. When plotted, Crohn's disease demonstrated a statistically significant increase in incidence over time. The slope of the curve was shallower than for ulcerative colitis. In fact, when we performed the same Poisson regression for ulcerative colitis, we could not prove with statistical significance that there was a change in incidence over time. This suggests the possible start of a plateau in the incidence of ulcerative colitis, at least in Olmsted County.

Interestingly, studies in eastern Canada have suggested that the incidence of Crohn's disease and ulcerative colitis may be decreasing.

### G&H Is it known why IBD (at least Crohn's disease) may still be increasing in the United States?

**EL** It is hard to know for sure. Various factors have been suggested, such as increased diagnostic awareness. My colleagues and I tried to examine this issue in 2007 by looking at the median interval between symptom onset and diagnosis. If there was increased diagnostic awareness over time, it would seem reasonable that the median interval between symptom onset and diagnosis would shorten over time. We found an increase in incidence in 2007, but we did not see a difference in the interval between symptoms and diagnosis. This was circumstantial evidence that perhaps there was not increased diagnostic awareness. However, we only looked at the cohort until approximately the year 2000, so perhaps some of the increase in IBD since then has been due to increased diagnostic awareness; it is difficult to determine.

There has also been speculation that an increase in incidence may involve the hygiene hypothesis. According to this hypothesis, as children grow up in more sanitary environments and, thus, are not exposed to various antigens and infectious agents, they do not develop certain conditions such as *Helicobacter pylori* gastritis or intestinal parasite infections, which can be protective for certain immune-mediated conditions, including IBD. Thus, one of the consequences of growing up in a clean environment may be an increase in immune-mediated conditions. In other words, according to this hypothesis, someone raised on a farm who is exposed to dirt and farm animals all the time is less likely to develop IBD than someone who grew up in an apartment building in a city.

The other factor that may be playing a role in any increase in IBD incidence is the Western diet. There is an emerging sense that a diet high in dairy, sugar, and processed foods (and perhaps emulsifiers, which are used in some processed foods) may be contributing to a higher incidence of IBD. However, more research is needed for confirmation.

### G&H What are the most recent data on the incidence of IBD in different races and ethnic groups in the United States?

**EL** A study from southern California in the early 1990s from Kaiser Permanente showed that African Americans have an incidence approximately two-thirds of that of whites. However, the data may have changed since then; unfortunately, there has not been much recent research in this area.

In addition, there have been increasing reports of Hispanic Americans developing IBD, although exact numbers are not currently available. However, the incidence is probably still lower than that of whites. In general, as socioeconomic status improves, the incidence of IBD increases. In addition, as previously mentioned, studies

have shown that having *H pylori* is protective against the development of IBD. At one point, the people with the highest rate of *H pylori* infection in the United States were Hispanic Americans. However, that has been changing over time; as socioeconomic status improves and *H pylori* rates go down, the incidence of IBD will likely increase.

### G&H How does IBD compare in incidence and characteristics between men and women?

**EL** In Crohn's disease, most studies have found nearly even rates in men and women. However, there is definitely a suggestion that men are slightly more likely than women to develop ulcerative colitis; in most studies, there is a 60/40 breakdown of men vs women, respectively. It has also been observed that men generally have worse outcomes than women for both conditions, although this seems more apparent in ulcerative colitis. My colleagues and I conducted a study in Olmsted County looking at colectomy rates and found that men were twice as likely to require colectomy than women. In addition, several studies looking at colon cancer risk in ulcerative colitis have suggested that men are twice as likely to develop colon cancer than women.

It is interesting to speculate why there are differences. My own simplistic theory is that men may not go to the doctor until they have uncontrolled symptoms and inflammation, whereas women may go to the doctor more often and are thus treated before the disease progresses.

### G&H What is the current US incidence of IBD in terms of age?

**EL** In general, both conditions are diagnosed in younger patients, but there are many exceptions. In Crohn's disease, the incidence rapidly increases in the late teens and in the 20s and then begins dropping off in the 30s and 40s; basically, two-thirds of patients will be diagnosed before the age of 40 years. The median age at diagnosis in Olmsted County is approximately 28 or 29 years, and then it tails off, even though some people are being diagnosed in their 50s, 60s, and 70s.

In ulcerative colitis, the age demographics are slightly different. Age is shifted a little later, so the median age, instead of being in the late 20s, is in the mid-30s (about 5 years later than for Crohn's disease). There is also more of a divergence in men and women later in life. The incidence drops more in women later in life than it does in men; more men are diagnosed in their 50s and 60s than women.

### G&H How do the prevalence and incidence of IBD in the United States compare with the rest of the world?

**EL** The United States has one of the highest rates of IBD (with the highest rate probably being Canada). In general, northern Europe, along with Canada and the United States, has the highest prevalence, and this has been the case for decades.

However, IBD has become a global phenomenon. For example, the first case of Crohn's disease was reported in Korea in the late 1980s, yet Korea now has an incidence of approximately 3 cases per 100,000 person-years. This rate is still much lower than that of the United States, but it is rising. The same goes for Japan, China, and India. These are countries that were historically thought not to have any or very low incidence and prevalence of IBD, but they are now seeing IBD more and more, to the point that these countries now have gastroenterologists who specialize in IBD, just like in the United States.

In addition, some interesting epidemiologic studies from Europe (particularly France) and the United States (from the Nurses' Health Study) have suggested that there may be a north-south gradient of incidence for IBD. It has been observed that the incidence of autoimmune diseases increases further away from the equator. Thus, the highest incidence of IBD has been reported in Canada, Iceland, and Greenland. This pattern holds true even within the United States; the incidence of IBD can vary by as much as 30% to 40%, depending upon whether a person is in a far northern or southern latitude.

### G&H Why is it important to study the prevalence and incidence of IBD?

**EL** Some of the factors that might be associated with the incidence of IBD might also be associated with disease severity over time. For example, there is a sense that IBD in Western countries still might be more severe than in Asia. The incidence of IBD might also provide clues to its pathogenesis. In addition, it is important for policy planners and payers to understand the global burden of disease. Proving that IBD is contributing a significant burden of disease to the population as a whole might also affect research funding from national authorities.

### G&H What are the next steps in research?

**EL** It would be ideal to have prospective registries in which patients could be enrolled at the time of their diagnosis. This could lead to a bio-bank of IBD patients for collecting longitudinal data on serum blood, stool, or tissue and then following these patients over time. Such a registry could help identify biomarkers for inflammation, cancer risk, or treatment response. The ultimate goal would be to identify either a single biomarker or panels of biomarkers that could tell doctors at the time

of diagnosis which type of medication might be most effective in a particular patient.

### G&H Are there any notable studies currently ongoing in this area?

**EL** The GEM (Genetics, Environmental, Microbial) Project, which is being funded by Crohn's and Colitis Canada, is following a group of first-degree relatives of IBD patients and is prospectively collecting their blood, stool, and so on. Owing to their familial relationships, these patients have a higher-than-expected incidence of IBD. Therefore, if and when these high-risk patients develop IBD, researchers of this study can examine biospecimens that were collected from these patients prediagnosis, thereby potentially enabling the identification of genetic, environmental, or microbial triggers of disease. The hope is that someday these data may be able to answer questions regarding the final triggers of IBD. We have information on some of the risk factors, including genetic ones, but we still do not understand why some people with the same genetic mutations as IBD patients do not develop IBD.

### G&H What have recent studies reported regarding risk factors for IBD?

**EL** Recent research has largely confirmed what we already know—for example, cigarette smoking is a risk factor for Crohn's disease but is protective for ulcerative colitis, and nonsteroidal anti-inflammatory drugs may be a risk factor for flares of IBD. Some interesting findings have been that ingestion of certain fibers (in particular, fruit fibers as opposed to cereals or legumes) is protective against the development of Crohn's disease. In addition, depression and anxiety symptoms might increase the risk

of developing Crohn's disease. Another important area of research is the role of stress on not only the incidence of IBD but also the management or triggering of IBD flares.

*Dr Loftus has no relevant conflicts of interest to disclose.*

### Suggested Reading

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