



# High and increasing prevalence of inflammatory bowel disease in Finland with a clear North–South difference

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## Abstract

**Background and aim:** Inflammatory bowel disease (IBD) prevalence has increased and a North–South gradient has been reported. We estimated the nationwide prevalence of IBD, ulcerative colitis (UC) and Crohn's disease (CD) in 1993, and prevalence of IBD in 2008, and assessed the geographical distribution of IBD in Finland. In addition, we investigated the vitamin D levels in a study population from a large, nationally representative health examination survey, the Health 2000 Survey.

**Methods:** The register study for prevalences included all patients who had special reimbursement of medications for IBD in the years 1993 (n=10,958) and 2008 (31,703). The study for D-vitamin measurement consisted of 6134 persons who had participated in the Health 2000 Survey.

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**Results:** The nationwide point prevalence of IBD in 1993 was 216 per 100,000 inhabitants, and 595 in 2008. In 1993, the prevalence of UC (177) was fourfold higher than the prevalence of CD (38). The prevalence of IBD and UC in Finland increased from South to North. For CD, no geographical variation could be demonstrated. In the Health 2000 survey, vitamin D levels were lower in Northern than in Southern Finland.

**Conclusions:** Finland belongs to high prevalence area of IBD and this prevalence has increased nearly threefold during the past 15 years. A clear North–South gradient has been shown for IBD and UC, but not for CD. Slightly lower vitamin D levels in Northern Finland may be associated with the observed higher prevalence of IBD there.

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## 1. Introduction

Inflammatory bowel diseases (IBD), consisting of ulcerative colitis (UC) and Crohn's disease (CD), have become more common in different regions of the world over the past decades.<sup>1</sup> Both CD and UC are associated with substantial morbidity and excessive use of healthcare resources. In addition to the incidence of IBD, a knowledge of prevalence is important in estimating the overall disease burden due to IBD including special services, and the need for costly medical therapy and surgery to meet the various needs of IBD patients. Moreover, epidemiological studies may also provide clues to disease etiology. High prevalence of IBD has been reported in Northern Europe, the United Kingdom and North America.<sup>1–11</sup> The highest prevalence values for IBD are in Europe (UC, 505 per 100,000 persons; CD, 322 per 100,000 persons) and North America (UC, 249 per 100,000 persons; CD, 319 per 100,000 persons).<sup>1,6</sup>

A North–South gradient has long been known for IBD. In Europe, higher incidence rates have been found in Northern countries.<sup>12</sup> In several countries including the USA, UK, and France, North–South gradients have also been reported.<sup>13–17</sup> High incidence of CD has also been observed in Northern France based on EPIMAD registry.<sup>18</sup>

Etiology of IBD is unknown. Genetic predisposition has been established, especially in CD.<sup>19</sup> There is also evidence that environmental factors may play a role in the pathogenesis of IBD.<sup>20</sup> Dietary constituents, including linoleic acid have been suggested as contributing factors for IBD, especially UC.<sup>21,22</sup> Many autoimmune diseases have been linked to vitamin D deficiency including multiple sclerosis, rheumatoid arthritis, asthma, and type 1 diabetes among others.<sup>23,24</sup> Vitamin D deficiency is also common among adult, pediatric and young patients with inflammatory bowel disease.<sup>25–28</sup> A high prevalence of hypovitaminosis D has been found among pediatric patients with IBD, regardless of their diagnosis.<sup>26</sup> Lower 25(OH)D concentrations were found among young patients with more active disease, severe disease and those with upper gastrointestinal involvement in patients with CD.<sup>26</sup> In adult CD patients, vitamin D levels were lower in those with severe disease activity and less sun exposure.<sup>28</sup> Recently published data from the United States showed that higher predicted plasma levels of 25(OH)D significantly reduce the risk of incident CD, and nonsignificantly the risk for UC in women.<sup>29</sup> Vitamin D3 can be obtained from the diet, but it is mainly synthesized from

7-dehydrocholesterol in skin as a response to ultraviolet light exposure.<sup>24</sup> Vitamin D status may be one of the environmental factors influencing the prevalence of autoimmune diseases including IBD.<sup>23,24</sup> A recent geographic study from France also suggested that low sunlight exposure was associated with an increased incidence of CD.<sup>30</sup>

The aim of this study was to estimate for the first time the nationwide prevalence of IBD, changes from 1993 to 2008 in Finland, and further to test the North–South gradient hypothesis by analyzing the comprehensive drug reimbursement database. In addition, we had an opportunity to study the vitamin D levels in a large (n=8028), nationally representative (random sample) health examination survey, the Health 2000 Survey conducted in Finland in 2000–2001, to find out whether there is a geographical variation in vitamin D levels within the population of Finland.

## 2. Patients and methods

Finland has a National Health Insurance Policy that covers all residents, and a unique personal social security number which can be used to identify each insured person. This code identifies the owner and reveals his/her date of birth and gender. The costs for drugs prescribed by a physician are reimbursed by the Social Insurance Institution (SII) of Finland. The basic refund rate is 42%. Certain severe and chronic diseases such as IBD are entitled to special refunds (72% or 100% category) of the drug costs.

For IBD, the intestinal anti-inflammatory agents (e.g. mesalazine, sulfasalazine, and budesonide), the glucocorticoids for systemic use (e.g. prednisolone), the immunosuppressants (e.g. azathioprine), the nitroimidazole antibiotics (metronidazole), and also drugs for local therapy (glucocorticoids and mesalazine) are included in this special refund category. TNF- $\alpha$  inhibitor adalimumab has been in the refund category for IBD since December 2007. In Finland, the infliximab therapy is given only in hospital, and the hospital has to cover all costs without refund from the SII.

To be eligible for drug reimbursement under the special refund categories, the patient's condition and diagnosis must meet explicit, predefined criteria, and a written certificate is required from the treating physician. As a rule, the diagnosis of IBD has to be assessed by a specialist in gastroenterology, internal medicine, pediatrics, digestive surgery, or surgery. The drug certificates are checked by a medical examiner,

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