## **LETTER**

## No association between urbanisation, neighbourhood deprivation and IBD: a population-based study of 4 million individuals

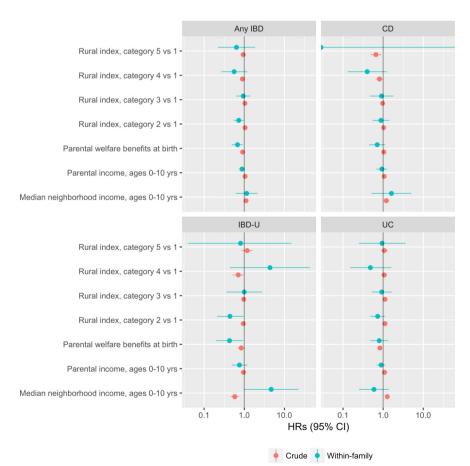
We read with interest the recently published work in *Gut* by Imhann *et al.*<sup>1</sup> Although this paper suggests that genetics plays an important role in IBD, <sup>1</sup> environmental factors clearly contribute to its aetiology.<sup>2</sup> When Ng *et al*<sup>2</sup> reviewed environmental risk factors for IBD in this journal they noted that urbanisation may be linked to both Crohn's disease (CD) and ulcerative colitis (UC).

We used Cox regression to estimate the effect of urbanisation and deprivation during childhood on future IBD.

From the Swedish Total Population Register,<sup>3</sup> the government agency Statistics Sweden selected all individuals born in Sweden between 1973 and 2013 (n=4 161 280). Among these there were 3 177 828 siblings nested within

2 331 062 families. Within this cohort we identified individuals with IBD, defined as having ≥2 relevant International Classification of Diseases codes in the Swedish National Patient Register, as earlier described.<sup>4</sup> Data from the Swedish Agency for Economic and Regional Growth were used to construct a rural index. Rural index category 1 represents major urban area. with increasing level of rurality in categories 4 and 5. Neighbourhood was defined according to the government agency Statistics Sweden's 'Small Area Marketing Statistics' (SAMS) classification system. We estimated the neighbourhood deprivation for each SAMS area based on school qualification, proportion of unmarried individuals, proportion born outside the Nordic countries and neighbourhood crime rate. The crude intraclass correlations for the neighbourhood factors were calculated to capture an aggregate of all factors. These estimates assume that individuals live in different areas randomly.

Individuals who had been diagnosed with IBD prior to the age of 10 years



**Figure 1** Crude and within-family HRs for future IBD. CD, Crohn's disease; UC, Ulcerative colitis; IBD-U. IBD unclassified.

**Table 1** Intraclass correlation (with 95% CI), adjusted for sex, birth year and birth order, and IBD as well as subtypes of the disease

	Neighbourhood (at birth)
Any IBD	2.1% (1.7% to 2.6%)
CD	3.3% (2.4% to 4.5%)
UC	3.0% (2.3% to 3.8%)
IBD-U	3.7% (2.4% to 5.9%)

CD. Crohn's disease: IBD-U. IBD unclassified.

were excluded in the models examining parental income measured across the first 10 years (to avoid reverse causation).

In total, 20183 individuals had an incident diagnosis of IBD after the age of 10 years (CD: n=6598; UC: n=10332; IBD unclassified (IBD-U): n=3253). We found no statistically significant association between childhood rural living and risk of developing IBD after the age of 10 years (figure 1). Except for a negative association between low median neighbourhood income (where a high income was linked to a lower risk of IBD-U) which was not supported controlling for familial effects (figure 1), there were no associations between deprivation and CD, UC or IBD-U (table 1). The intraclass correlation estimates for neighbourhood were small.

While neighbourhood deprivation has been linked to health and disease,<sup>5</sup> data on IBD are scarce.<sup>6</sup> In this nationwide study of more than 4 million Swedish residents, some 20 000 individuals developed IBD after the age of 10 years. We found no consistent associations between childhood living areas and future IBD.

Agnieszka Butwicka, <sup>1,2</sup> Amir Sariaslan, <sup>1</sup> Henrik Larsson, <sup>1</sup> Jonas Halfvarson, <sup>3</sup> Pär E Myrelid, <sup>4</sup> Ola Olén, <sup>5,6</sup> Louise Frisen, <sup>7,8</sup> Paul Lichtenstein, <sup>1</sup> Jonas F Ludvigsson <sup>1,9</sup>

<sup>1</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden <sup>2</sup>Department of Child Psychiatry, Medical University of

<sup>2</sup>Department of Child Psychiatry, Medical University o Warsaw, Warsaw, Poland

 <sup>3</sup>Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden
<sup>4</sup>Division of Surgery, Department of Clinical and Experimental Medicine, Faulty of Health Sciences, Linköping University and Department of Surgery, County Council of Östergötland, Linköping, Sweden
<sup>5</sup>Sachs' Children and Youth Hospital, Stockholm South General Hospital, Stockholm, Sweden

<sup>6</sup>Clinical Epidemiology Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden <sup>7</sup>Child and Adolescent Psychiatry Research Center, Stockholm, Sweden

<sup>8</sup>Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden

<sup>9</sup>Department of Pediatrics, Örebro University Hospital, Örebro University, Örebro, Sweden





## **PostScript**

Correspondence to Dr Jonas F Ludvigsson, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm 17177, Sweden; jonasludvigsson@yahoo.com

**Contributors** AB, JFL and AS wrote the first draft of the paper. AB and AS performed the statistics.

**Funding** This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

**Ethics approval** Stockholm Ethics Review Board, Sweden.

**Provenance and peer review** Not commissioned; internally peer reviewed.

**Data sharing statement** Data can be obtained from the National Board of Health and Welfare in Sweden.

© Article author(s) (or their employer(s) unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.



**To cite** Butwicka A, Sariaslan A, Larsson H, *et al. Gut* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/gutjnl-2018-316326

Received 26 February 2018 Revised 8 April 2018 Accepted 12 April 2018

Gut 2018; 0:1-2. doi:10.1136/gutinl-2018-316326

## REFERENCES

1 Imhann F, Vich Vila A, Bonder MJ, *et al.* Interplay of host genetics and gut microbiota underlying the onset and

- clinical presentation of inflammatory bowel disease. *Gut* 2018;67:108–19.
- 2 Ng SC, Bernstein CN, Vatn MH, et al. Geographical variability and environmental risk factors in inflammatory bowel disease. Gut 2013;62:630–49.
- 3 Ludvigsson JF, Almqvist C, Bonamy AK, et al. Registers of the Swedish total population and their use in medical research. Eur J Epidemiol 2016;31:125–36.
- 4 Olén O, Askling J, Sachs MC, et al. Childhood onset inflammatory bowel disease and risk of cancer: a Swedish nationwide cohort study 1964-2014. BMJ 2017;358:j3951.
- 5 Sariaslan A, Larsson H, D'Onofrio B, et al. Does population density and neighborhood deprivation predict schizophrenia? A nationwide Swedish familybased study of 2.4 million individuals. Schizophr Bull 2015;41:494–502.
- 6 Benchimol El, Kaplan GG, Otley AR, et al. Rural and urban residence during early life is associated with a lower risk of inflammatory bowel disease: a population-based inception and birth cohort study. Am J Gastroenterol 2017.

2 Gut Month 2018 Vol 0 No 0