

# BMJ Open Cohort profile: the Nordic Antireflux Surgery Cohort (NordASCo)

John Maret-Ouda,<sup>1</sup> Karl Wahlin,<sup>1</sup> Miia Artama,<sup>2</sup> Nele Brusselaers,<sup>3,4</sup> Martti Färkkilä,<sup>5</sup> Elsebeth Lyngé,<sup>6</sup> Fredrik Mattsson,<sup>1</sup> Eero Pukkala,<sup>7,8</sup> Pål Romundstad,<sup>9</sup> Laufey Tryggvadóttir,<sup>10,11</sup> My von Euler-Chelpin,<sup>6</sup> Jesper Lagergren<sup>1,12</sup>

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## ABSTRACT

**Purpose** To describe a newly created all-Nordic cohort of patients with gastro-oesophageal reflux disease (GORD), entitled the Nordic Antireflux Surgery Cohort (NordASCo), which will be used to compare participants having undergone antireflux surgery with those who have not regarding risk of cancers, other diseases and mortality. **Participants** Included were individuals with a GORD diagnosis recorded in any of the nationwide patient registries in the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) in 1964–2014 (with various start and end years in different countries). Data regarding cancer, other diseases and mortality were retrieved from the nationwide registries for cancer, patients and causes of death, respectively. **Findings to date** The NordASCo includes 945 153 individuals with a diagnosis of GORD. Of these, 48 433 (5.1%) have undergone primary antireflux surgery. Median age at primary antireflux surgery ranged from 47 to 52 years in the different countries. The coding practices of GORD seem to have differed between the Nordic countries. **Future plans** The NordASCo will initially be used to analyse the risk of developing known or potential GORD-related cancers, that is, tumours of the oesophagus, stomach, larynx, pharynx and lung, and to evaluate the mortality in the short-term and long-term perspectives. Additionally, the cohort will be used to evaluate the risk of non-malignant respiratory conditions that might be caused by aspiration of gastric contents.

**INTRODUCTION**  
The Nordic Antireflux Surgery Cohort (NordASCo) was set up with the purpose of examining the consequences of surgery for gastro-oesophageal reflux disease (GORD). GORD is defined as a ‘condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications’.<sup>1</sup> GORD can occur as a result of pathological levels of regurgitation of acidic stomach contents, often also including alkaline bile salts and pancreatic enzymes, into the oesophagus. The primary symptoms of GORD are heartburn and regurgitation of stomach contents.<sup>2</sup> Other, less common symptoms include chest pain, nausea, hoarseness and symptoms associated with bronchial

## Strengths and limitations of this study

- The main strength of the Nordic Antireflux Surgery Cohort is the large number of individuals included, constituting the largest cohort to date of patients who have undergone antireflux surgery.
- The population-based design counteracts selection bias and facilitates the generalisability of the findings.
- The long and complete follow-up in the registries enables studies of conditions with an expected long latency interval between antireflux surgery and disease.
- There are variations in clinical practice and coding of diagnoses and procedures between the countries, including the codes associated with gastro-oesophageal reflux disease and antireflux surgery.

aspiration of reflux contents reaching the oropharynx, for example, pneumonia, cough and other respiratory disorders.<sup>2</sup> The prevalence of GORD is estimated at 10%–20% in the USA and Europe, and less than 5% in Asia.<sup>3</sup> The prevalence has increased during the last few decades,<sup>4</sup> an increase that correlates with the increasing prevalence of obesity, a known risk factor for developing GORD.<sup>5–7</sup> Other established risk factors for GORD are heredity and tobacco smoking.<sup>8–11</sup> GORD can lead to complications, including erosive oesophagitis, oesophageal strictures, premalignant Barrett’s oesophagus and oesophageal adenocarcinoma.<sup>2</sup> The primary treatment is medical, most often using a proton pump inhibitor. An alternative but less often used treatment is antireflux surgery, during which the fundus of the stomach is wrapped partly or completely around the lower oesophagus, mechanically hindering GORD.<sup>2</sup> Antireflux surgery should be considered in patients with severe GORD or poor response to medical treatment, especially in young, physically fit and healthy adults in whom pharmacological treatment otherwise would be necessary for a long period of time.<sup>12</sup>

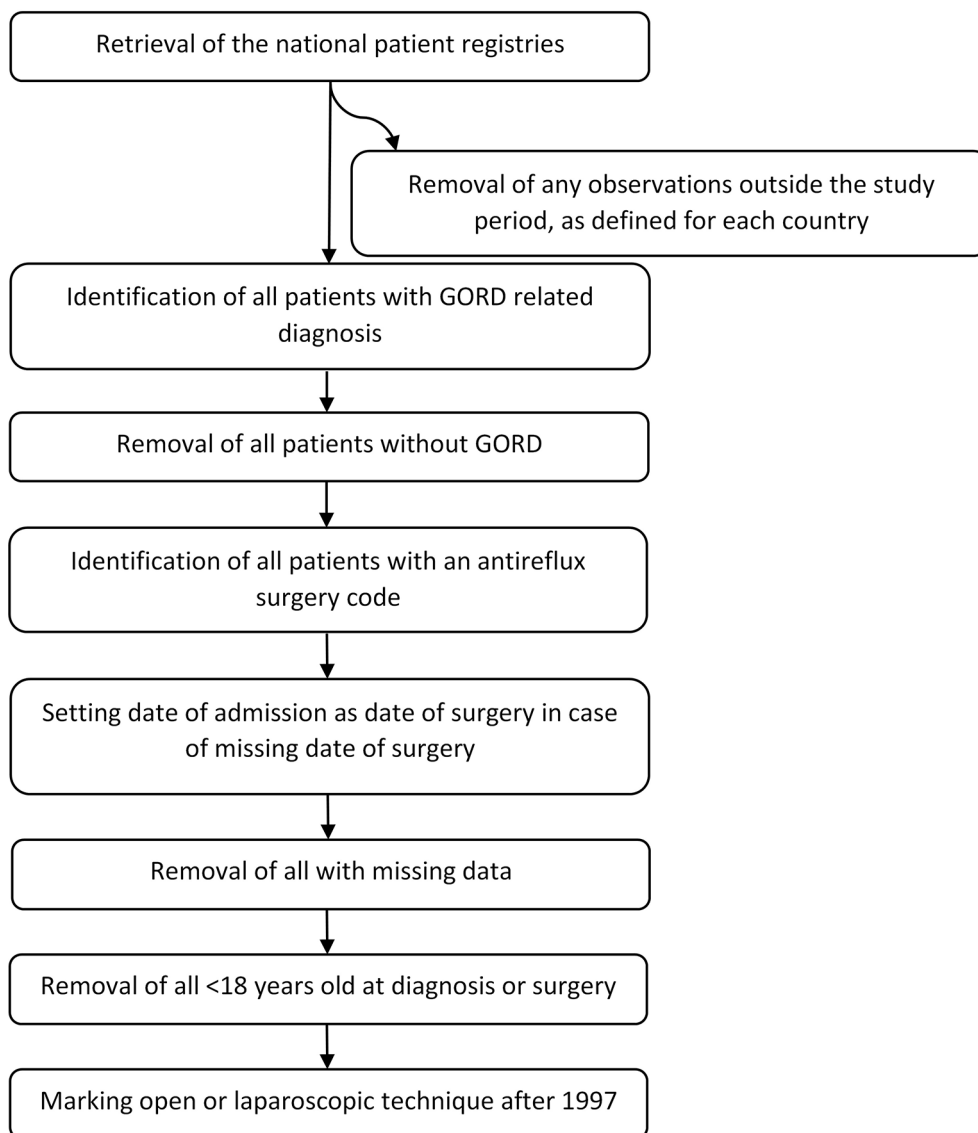


For numbered affiliations see end of article.

**Correspondence to**  
Dr John Maret-Ouda;  
[john.maret.ouda@ki.se](mailto:john.maret.ouda@ki.se)







**Figure 2** Data management of the patient registries in the Nordic Antireflux Surgery Cohort. GORD, gastro-oesophageal reflux disease.

numbers that were used to replace the personal identity codes used for linkage are kept in each of the relevant agencies in each country. These arbitrary numbers can be used for future follow-up of all cohort members as well as adding data from additional registries for assessing other exposures and outcomes of interest. Furthermore, the arbitrary numbers could be used if data need to be checked regarding completeness and correctness.

## STUDIES

The NordASCo will be used to measure the risk of developing known or potential GORD-related cancers following antireflux surgery. The initial focus will be on how the risk of oesophageal adenocarcinoma develops over time after surgery, compared with the risk development of oesophageal squamous cell carcinoma and gastric adenocarcinoma. Other tumours of potential interest are cancer of the larynx, pharynx and lung, which might be

associated with GORD, although fewer studies support these associations and any association with lung cancer is controversial.<sup>22–24</sup> Additionally, the NordASCo will be used to evaluate whether antireflux surgery decreases the risk of non-malignant conditions that might be caused by aspiration of acidic gastric contents, for example, asthma, pneumonia and cardiovascular morbidity and mortality.<sup>25 26</sup> Due to a general decrease in the number of antireflux procedures performed, with one explanation being the risk of postoperative mortality and complications following antireflux surgery, further studies are needed to assess these risks and to identify individuals who would benefit most from such surgery.

## Findings to date

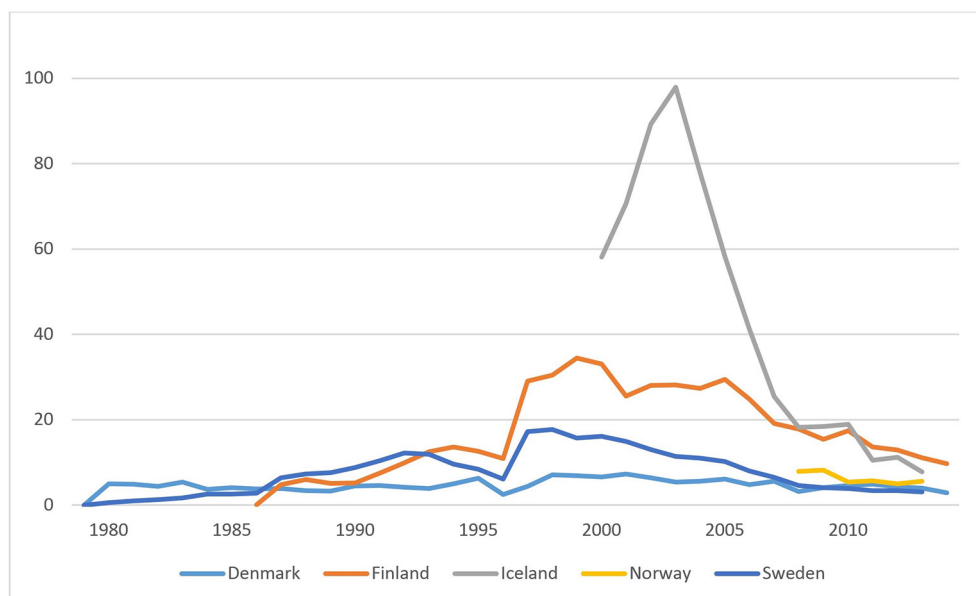
In total, 945 153 individuals with a GORD diagnosis have been included in the NordASCo. Characteristics of the cohort members are presented in [table 1](#). Of all

**Table 1** Characteristics of individuals included in the entire Nordic Antireflux Surgery Cohort (NordASCo), as well as the numbers and percentage within each characteristic category undergoing antireflux surgery

	Entire NordASCo Number (% distribution)	Antireflux surgery Number (% within category)
Total	945 153 (100.0)	48 433 (5.1)
Country		
Denmark	243 137 (25.7)	6912 (2.8)
Finland	42 044 (4.4)	20 328 (48.3)
Iceland	4545 (0.5)	1296 (28.5)
Norway	192 290 (20.3)	1429 (0.7)
Sweden	463 137 (49.0)	18 468 (4.0)
Sex		
Male	462 755 (49.0)	27 169 (5.9)
Female	481 280 (51.0)	21 264 (4.4)
Age at entry (in years)		
18–29	64 033 (6.8)	3395 (5.3)
30–39	94 945 (10.0)	7379 (7.8)
40–49	141 323 (15.0)	11 717 (8.3)
50–59	181 894 (19.2)	13 614 (7.5)
≥60	462 958 (49.0)	12 328 (2.7)
Calendar period (year)		
1979–1984	38 161 (4.0)	1370 (3.6)
1985–1999	189 017 (20.0)	19 855 (10.5)
2000–2014	717 975 (76.0)	27 208 (3.8)

participants, 48 433 (5.1%) underwent a primary anti-reflux surgery during the study period and 896 720 (94.9%) did not. The proportion of patients with a registered GORD diagnosis who underwent antireflux surgery varied between countries, and was lower in Denmark, Norway and Sweden (2.8%, 0.7% and 4.0%, respectively) compared with Finland and Iceland (48.3% and 28.5%), which might also reflect substantial differences in clinical practice and registration routines. The sex distribution was more even among both the operated and non-operated cohort members. The surgery group was generally younger (25.5% ≥60 years at entry) than the non-surgery group (50.4% ≥60 years old at entry). The median age at primary antireflux surgery ranged from 47 to 52 years in the different countries. Most cohort members were included during the time periods 1985–1999 (41.0%) and 2000–2014 (56.2%) in the antireflux surgery group, and during the time period 2000–2014 in the non-operated group (76.0%).

Figure 3 shows the annual incidence of primary anti-reflux surgery among adults in the Nordic countries per 100 000 inhabitants, including both open and laparoscopic techniques. The rate in Denmark and Norway remained fairly stable during the study period. For both Finland and Sweden, a plateau was seen during the end of the 1990s, followed by a decrease. In Iceland, a similar pattern was seen, but with a later peak in 2003. Due to the relatively small population in Iceland, large variations in rates were seen but with only small differences in the absolute number of procedures. The total number of primary antireflux surgery conducted per year is shown in figure 4. This figure also shows a peak in the number of primary antireflux procedures in the Nordic countries



**Figure 3** Rate of primary antireflux procedures per 100 000 inhabitants in the five Nordic countries of the Nordic Antireflux Surgery Cohort, in 1980–2014.

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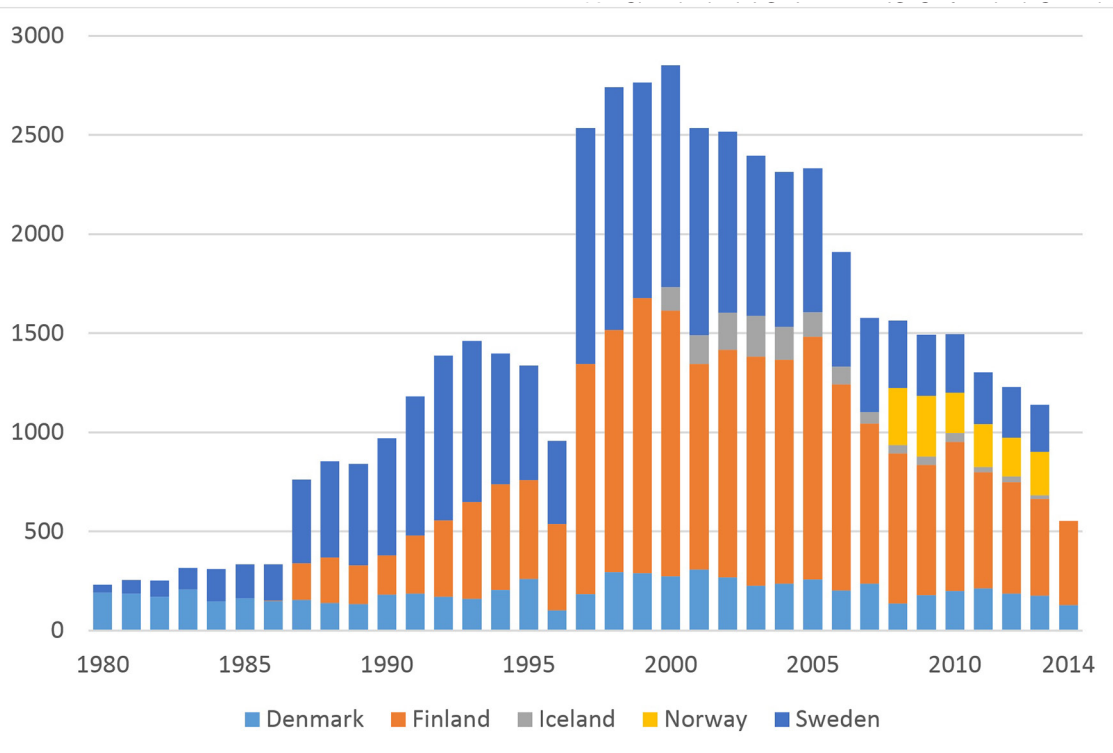


Figure 4 Total numbers of primary antireflux procedures per year in the Nordic Antireflux Surgery Cohort, in 1980–2014.

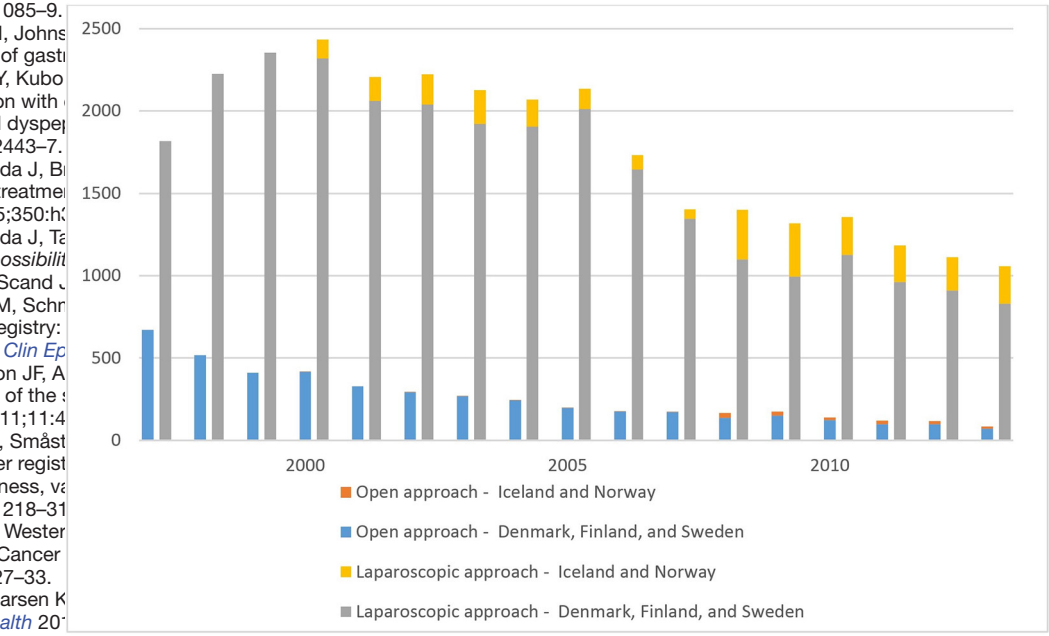


Figure 5 Number of primary antireflux procedures conducted using open or laparoscopic technique in the Nordic Antireflux Surgery Cohort, 1997–2013. Countries where data from the entire period were available are grouped (Denmark, Finland and Sweden), as are countries where only part of the study period was available (Iceland and Norway).

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