



ORIGINAL ARTICLE

Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study

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ABSTRACT

Objective Changes in the occurrence of gastro-oesophageal reflux symptoms (GORS) in the population remain uncertain. This study aimed to determine the prevalence changes, the incidence and the spontaneous loss of GORS.

Design This population-based cohort study was conducted within the Nord-Trøndelag Health Study (the HUNT study), a longitudinal series of population-based health surveys in Nord-Trøndelag County, Norway. The study base encompassed all adult residents in the county, and the participants reported the degree of GORS during the previous 12 months. The number of participants included were 58 869 (64% response rate) in 1995–7 and 44 997 (49%) in 2006–9. Of these, 29 610 persons (61%) were prospectively followed up for an average of 11 years.

Results Between 1995–7 and 2006–9, the prevalence of any, severe and at least weekly GORS increased by 30% (from 31.4% to 40.9%), 24% (from 5.4% to 6.7%) and 47% (from 11.6% to 17.1%), respectively. The average annual incidence of any and severe GORS was 3.07% and 0.23%, respectively. In women, but not men, the incidence of GORS increased with increasing age. The average annual spontaneous loss (not due to antireflux medication) of any and severe GORS was 2.32% and 1.22%, respectively. The spontaneous loss of GORS decreased with increasing age.

Conclusion Between 1995–7 and 2006–9 the prevalence of GORS increased substantially. At least weekly GORS increased by 47%. The average annual incidence of severe GORS was 0.23%, and the corresponding spontaneous loss was 1.22%. The incidence and spontaneous loss of GORS were influenced by sex and age.

Gastro-oesophageal reflux disease (GORD) is defined by its cardinal symptoms, heartburn and acid regurgitation, occurring at least weekly.^{1–2} Gastro-oesophageal reflux symptoms (GORS) are associated with a decreased health-related quality of life^{3–4} and an increased risk of adenocarcinoma of the oesophagus,^{5–6} a disease with poor prognosis and rapidly rising incidence in western countries.^{7–9} The prevalence of at least weekly GORS among adults has been reported to be in the range of 10–20% in the western world,^{10–11} with a higher prevalence in more recent studies.¹² However, the population-based changes in prevalence remain

Significance of this study**What is already known about the subject?**

- The prevalence of at least weekly GORS among adults has been reported to be in the range of 10–20% in the western world.
- GORS are associated with a decreased health-related quality of life.
- GORS are established risk factors for adenocarcinoma of the oesophagus.

What are the new findings?

- The prevalence of at least weekly GORS increased by 47% (from 11.6% to 17.1%) between 1995–7 and 2006–9.
- The average annual incidence of severe GORS was 0.23%. In women, but not men, the incidence of GORS increased with increasing age.
- The average annual spontaneous loss of severe GORS (not due to antireflux medication) was 1.22%. The spontaneous loss of GORS decreased with increasing age.

How might it impact on clinical practice in the foreseeable future?

- The increasing prevalence of GORS found in this study may call for a strengthened effort to investigate and treat this patient population, both due to the impact on health-related quality of life and the increasing incidence of adenocarcinoma of the oesophagus related to GORS.

uncertain, and the few studies that have addressed the incidence of GORS have small sample sizes, short follow-up times, or the use of a selected population. In addition, GORS are not always persistent and the level of spontaneous loss of GORS, not due to antireflux medication, is unknown. The aim of this study was to provide valid data on the changes in prevalence, the incidence and the spontaneous loss of GORS in an unselected western population.

MATERIALS AND METHODS**Study population and design**

GORS were studied as part of the Nord-Trøndelag Health Study (the HUNT study), a longitudinal

series of population-based health surveys conducted in the Norwegian county of Nord-Trøndelag. The county has a stable population that is representative of the Norwegian population at large.¹³ All adult residents in Nord-Trøndelag county who turned 20 years of age during the survey year were invited to participate. The first survey (HUNT 1), which was conducted in the mid-1980s, was not included in the present study because GORS data were not collected. However, the second survey (HUNT 2) conducted from August 1995 to June 1997 and the third survey (HUNT 3) conducted from October 2006 to June 2008 included an assessment of GORS. Moreover, in 2009, a postal questionnaire study (Mini-Q) of the non-participants in HUNT 3 was conducted, also including an assessment of GORS and as such was eligible in our study. The HUNT database contains approximately 5500 health-related variables, including variables on exposures, complaints and diseases, collected through self-administered questionnaires, clinical measurements and blood samples taken at the screening stations.

Assessment of GORS

In HUNT 2 and HUNT 3/Mini-Q the participants were asked the following question through self-administered questionnaires: 'To what degree have you had heartburn or acid regurgitation during the previous 12 months?' and replied with one of three response alternatives: 'no complaints', 'minor complaints', or 'severe complaints'. In the analyses, those who reported minor or severe complaints were included in the category 'any GORS', while those who reported severe complaints were included in the category 'severe GORS'. In HUNT 2, the GORS question was part of the initial questionnaire sent by mail along with the study invitation and returned at the screening station. In HUNT 3/Mini-Q, the GORS question was part of a second questionnaire given to the participants at the screening station (HUNT 3) or the questionnaire sent to the non-participants (Mini-Q). As the frequency of GORS was not directly assessed in HUNT 2 and HUNT 3, the participants were asked to report both their degree and frequency of GORS in a validation study after HUNT 2¹⁴ and in Mini-Q. The following question was asked to assess the frequency of GORS: 'If you have had heartburn or acid regurgitation during the previous 12 months, how often do you have complaints?' and replied with one of three response alternatives: 'daily', 'weekly', or 'less frequently'.

Assessment of antireflux medication

Data on antireflux medication were collected from the HUNT questionnaires as well as from the Norwegian Prescription Database (NorPD). The NorPD is a Norwegian national health register, established in 2004, which contains data on all prescribed medication dispensed from all Norwegian pharmacies. Through the use of the unique national identity number assigned to all Norwegian residents, it was possible to link the HUNT study to the NorPD and gather information on the prescribed medication among the participants during HUNT 3. The prescription rules in Norway during the study period required a prescription from a physician for all proton pump inhibitors or H₂-receptor antagonists (H₂RA), except for small packages of low-dose H₂RA. The information retrieved from the NorPD included dosage, package size and number of packages for each single prescription. In addition, the participants in HUNT 3 reported their use of over-the-counter antireflux medication, i.e. small packages of low-dose H₂RA and antacids during the past month, with the response alternatives 'never or rarely', '1–3 times per week', '4–6 times per week', or 'daily'.

All antireflux medication in the study population during HUNT 3 should thus be accounted for.

Statistical analyses

The prevalence of GORS was calculated as the proportion of persons in HUNT 2 and HUNT 3/Mini-Q who reported any (minor or severe) GORS or severe GORS, respectively. The prevalence of individuals with at least weekly GORS in HUNT 2 and HUNT 3/Mini-Q was estimated through assessment of both the degree and frequency of complaints reported by those participating in the HUNT 2 validation¹⁴ or in Mini-Q. The proportion of individuals with severe GORS and at least weekly GORS and the proportion of individuals with minor GORS and at least weekly GORS in the HUNT 2 validation and in Mini-Q were calculated. These proportions were multiplied by the number of individuals with severe and minor GORS in HUNT 2 and HUNT 3, respectively, to assess at least weekly GORS.¹¹ When calculating response rates, those who had died or were no longer resident in the county (non-eligible) were excluded from the denominator. The incidence of GORS was calculated from the proportion of those who reported no GORS in HUNT 2 and any or severe GORS in HUNT 3/Mini-Q (cumulative incidence), respectively. The loss of GORS was calculated from the proportion of those who reported any or severe GORS in HUNT 2, respectively, but no GORS in HUNT 3/Mini-Q (cumulative loss). In the latter analysis, those using antireflux medication at least weekly in HUNT 3/Mini-Q were excluded to assess the spontaneous loss of GORS only. The average annual cumulative incidence and spontaneous loss of GORS were calculated using the formula $(\exp(\text{cumulative proportion}) - 1) / 11$ years (average annual percentage change). In addition, 95% CIs for the proportions were calculated. The prevalence, incidence and spontaneous loss of GORS were stratified by sex and age (<40, 40–49, 50–59, 60–69 and ≥70 years). ORs between the time points were estimated to assess statistically the changes in the prevalence of GORS, and adjustments were made for sex and age by using the interaction term between sex and age groups as covariable. Generalised estimating equations with an exchangeable correlation structure were used to account for the repeated assessments of GORS among many of the participants. ORs were also estimated by logistic regression to assess differences in the incidence and spontaneous loss of GORS by sex and age, using the interaction term as explanatory variable. The statistical analyses were performed using the software Stata/IC V.11.1 for Windows by StataCorp LP.

The study was approved by the Regional Committee for Medical and Health Research Ethics, Central Norway. All participants signed a written consent form when they participated in the HUNT study, which stated that the data collected could be linked with health registries and patient records for research purposes in future studies.

RESULTS

Participants

The degree of GORS was reported by 58 869 individuals (64% response rate) in HUNT 2 (1995–7) and by 44 997 individuals (49% response rate) in HUNT 3/Mini-Q (2006–9). The number of participants in HUNT 3 and Mini-Q were 37 406 and 7591, respectively. These participants were included in the assessment of the prevalence of GORS (figure 1). In HUNT 2, the mean age was 48.5 years (SD 16.8 years; range 19–101 years) compared with 52.1 years (SD 16.0 years; range 19–102 years) in HUNT 3/Mini-Q. The female response rate was 52% in HUNT 2 and 55% in HUNT 3/Mini-Q, and 570 and 237 women reported to

be pregnant, respectively. All analyses included pregnant women, as analyses excluding them made no difference in the results (data not shown).

In the assessment of the incidence and spontaneous loss of GORS between HUNT 2 and HUNT 3/Mini-Q, the 29 610 individuals who reported their degree of GORS at both occasions were included. This corresponds to a response rate of 61%, excluding the 10 535 non-eligible participants who reported GORS in HUNT 2 but had died or were no longer resident in the county at HUNT 3 (figure 1). The mean age of this cohort was 57.3 years at follow-up (SD 13.1 years; range 29–100 years) and 54% were women.

Changes in prevalence of GORS

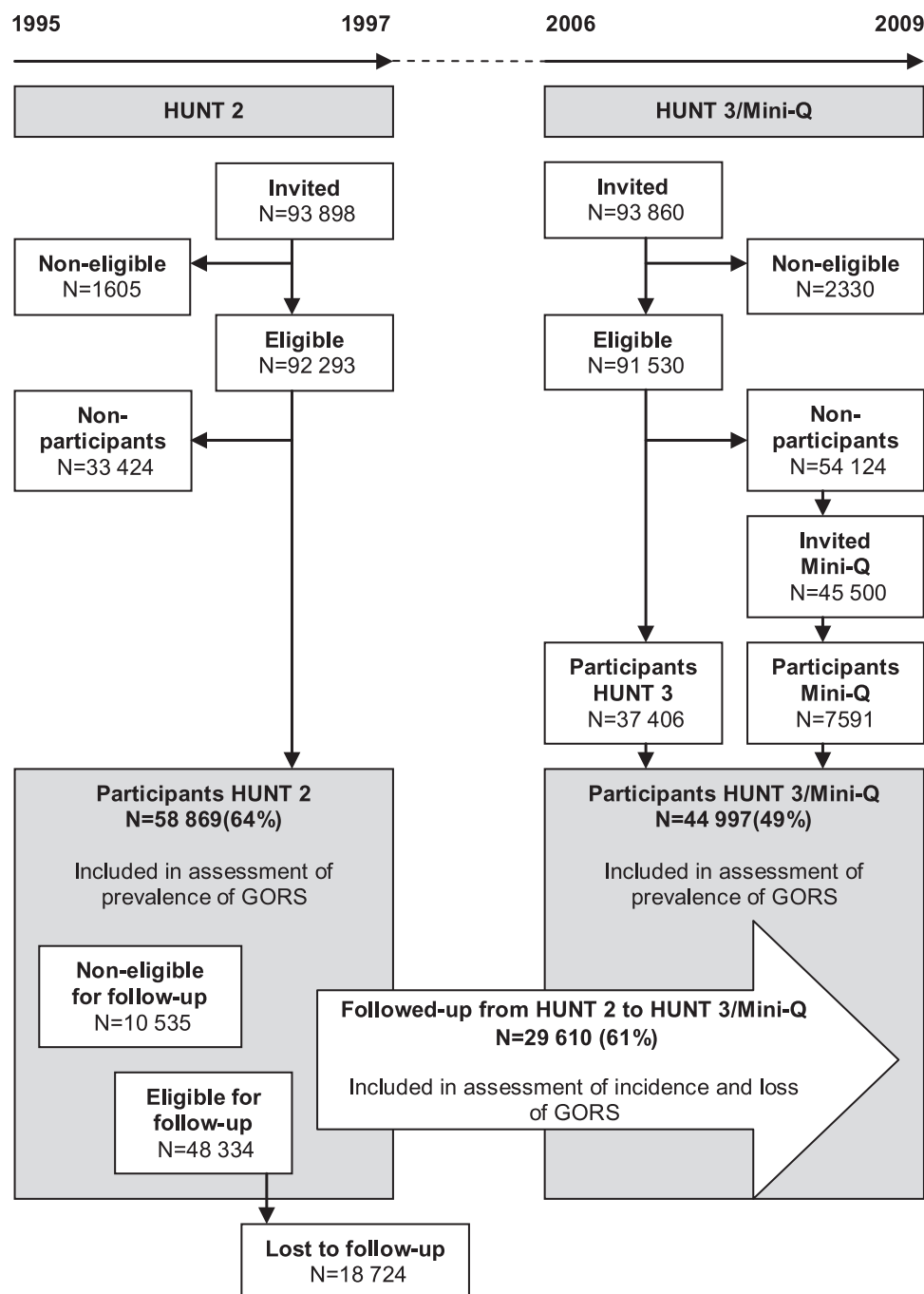
Between 1995–7 and 2006–9, the prevalence of any GORS increased by 30%, from 31.4% (95% CI 31.0% to 31.7%) to

40.9% (95% CI 40.4% to 41.3%), and the prevalence of severe GORS increased by 24%, from 5.4% (95% CI 5.2% to 5.6%) to 6.7% (95% CI 6.4% to 6.9%). Adjusted for sex and age, the OR of any and severe GORS in 2006–9 compared with 1995–7 was 1.46 (95% CI 1.43 to 1.49) and 1.20 (95% CI 1.15 to 1.26), respectively. For any GORS the prevalence increased for both sexes and all age groups, but for severe GORS the prevalence increased mainly among the middle aged (table 1).

In Mini-Q, in which the participants reported both their degree and frequency of GORS, 98% of the participants with severe GORS had at least weekly symptoms or used antireflux medication at least weekly. The corresponding rate was 31% among participants with minor GORS.

The prevalence of at least weekly GORS, estimated through the assessment of data from the HUNT 2 validation and Mini-Q, increased by 47% from 11.6% (95% CI 11.4% to 11.9%) to

Figure 1 Flowchart of participants reporting gastro-oesophageal reflux symptoms (GORS) in HUNT 2 (1995–7) and HUNT 3/Mini-Q (2006–9) with the number (N) of individuals at each stage and response rates (%). Response rates were calculated from those eligible, excluding those who had died or were no longer resident in the county (non-eligible).



Oesophagus

Table 1 Prevalence of GORS in the HUNT study, stratified by degree of GORS, time point, sex and age groups

Prevalence of any GORS*																			
1995–7 (HUNT 2)							2006–9 (HUNT 3/Mini-Q)							Relative change†					
Total N = 58 869														Total					
Number			%			95% CI			Number			%			95% CI			%	
18 460			31.4			31.0 to 31.7			18 389			40.9			40.4 to 41.3			30.3	
Women N = 30 608				Men N = 28 261				Women N = 24 550				Men N = 20 440				Women		Men	
Age (years)§	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	%	%		
All ages	9104	29.7	29.2 to 30.3	9356	33.1	32.6 to 33.7	9526	38.8	38.2 to 39.4	8860	43.3	42.7 to 44.0	30.5					30.9	
<40	2528	23.9	23.1 to 24.7	2695	29.4	28.5 to 30.3	1886	28.3	27.2 to 29.4	1516	34.5	33.1 to 35.9	18.3					17.5	
40–49	1852	28.0	26.9 to 29.0	2197	35.0	33.9 to 36.2	1762	35.7	34.4 to 37.0	1761	43.4	41.9 to 44.9	27.7					23.8	
50–59	1635	31.9	30.6 to 33.1	1823	36.0	34.7 to 37.3	2157	42.1	40.7 to 43.4	2258	46.7	45.3 to 48.1	32.0					29.8	
60–69	1432	36.9	35.3 to 38.4	1347	34.7	33.2 to 36.2	2092	48.3	46.9 to 49.8	1971	47.1	45.6 to 48.6	31.2					35.9	
≥70	1657	37.6	36.2 to 39.1	1294	33.5	32.0 to 35.0	1629	46.6	44.9 to 48.2	1354	45.6	43.8 to 47.4	23.7					36.2	

Prevalence of severe GORS*																			
1995–7 (HUNT 2)							2006–9 (HUNT 3/Mini-Q)							Relative change†					
Total N = 58 869														Total					
Number			%			95% CI			Number			%			95% CI			%	
3167			5.4			5.2 to 5.6			2994			6.7			6.4 to 6.9			23.7	
Women N = 30 608				Men N = 28 261				Women N = 24 550				Men N = 20 440				Women		Men	
Age (years)§	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	%	%		
All ages	1603	5.2	5.0 to 5.5	1564	5.5	5.3 to 5.8	1629	6.6	6.3 to 6.9	1364	6.7	6.3 to 7.0	26.7					20.6	
<40	396	3.7	3.4 to 4.1	436	4.8	4.3 to 5.2	290	4.4	3.9 to 4.8	223	5.1	4.4 to 5.7	16.2					6.8	
40–49	286	4.3	3.8 to 4.8	372	5.9	5.3 to 6.5	289	5.9	5.2 to 6.5	275	6.8	6.0 to 7.5	35.6					14.2	
50–59	281	5.5	4.9 to 6.1	312	6.2	5.5 to 6.8	372	7.3	6.5 to 8.0	390	8.1	7.3 to 8.8	32.5					31.0	
60–69	299	7.7	6.9 to 8.5	238	6.1	5.4 to 6.9	385	8.9	8.0 to 9.7	288	6.9	6.1 to 7.6	15.6					12.4	
≥70	341	7.7	7.0 to 8.5	206	5.3	4.6 to 6.0	293	8.4	7.5 to 9.3	188	6.3	5.5 to 7.2	8.1					18.8	

*Any gastro-oesophageal reflux symptoms (GORS): minor or severe complaints with heartburn or acid regurgitation; severe GORS: severe complaints with heartburn or acid regurgitation.

†Relative change in prevalence = (prevalence HUNT 3/Mini-Q—prevalence HUNT 2)/prevalence HUNT 2.

‡Seven participants in HUNT 3/Mini-Q had missing information on sex.

§Age at time of GORS assessment (HUNT 2 and HUNT 3/Mini-Q, respectively).

17.1% (95% CI 16.7% to 17.4%). The prevalence of at least weekly GORS increased for both sexes and all age groups and most among the middle aged (table 2; see supplementary figure 2, available online only).

Incidence of GORS

During the average 11 years of follow-up from 1995–7 to 2006–9, the cumulative incidence of any GORS was 29.1%

(95% CI 28.4% to 29.7%), which corresponded to an average annual incidence of 3.07% (95% CI 2.99% to 3.14%). Women younger than 40 years of age had the lowest incidence of any GORS. The incidence increased with increasing age for women, while it was stable with age for men. In older age groups there was no difference in the incidence of any GORS between the sexes (table 3; see supplementary figure 3, available online only).

Table 2 Prevalence of at least weekly GORS in the HUNT study, stratified by time point, sex and age groups

Prevalence of at least weekly GORS*																			
1995–7 (HUNT 2)							2006–9 (HUNT 3/Mini-Q)							Relative change†					
Total N = 58 869														Total					
Number			%			95% CI			Number			%			95% CI			%	
6835			11.6			11.4 to 11.9			7692			17.1			16.7 to 17.4			47.2	
Women N = 30 608				Men N = 28 261				Women N = 24 550				Men N = 20 440				Women		Men	
Age (years)§	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	Number	%	95% CI	%	%		
All ages	3400	11.1	10.8 to 11.5	3435	12.2	11.8 to 12.5	4036	16.4	16.0 to 16.9	3654	17.9	17.4 to 18.4	48.0					47.1	
<40	910	8.6	8.1 to 9.2	979	10.7	10.0 to 11.3	778	11.7	10.9 to 12.5	618	14.1	13.1 to 15.1	35.6					31.9	
40–49	663	10.0	9.3 to 10.8	810	12.9	12.1 to 13.8	738	14.9	14.0 to 16.0	729	18.0	16.8 to 19.2	49.4					39.0	
50–59	606	11.8	10.9 to 12.7	674	13.3	12.4 to 14.3	916	17.9	16.8 to 18.9	959	19.8	18.7 to 21.0	51.3					49.1	
60–69	568	14.6	13.5 to 15.8	504	13.0	11.9 to 14.1	905	20.9	19.7 to 22.2	803	19.2	18.0 to 20.4	43.1					47.9	
≥70	653	14.8	13.8 to 15.9	468	12.1	11.1 to 13.2	700	20.0	18.7 to 21.4	545	18.4	17.0 to 19.8	34.9					51.6	

*At least weekly gastro-oesophageal reflux symptoms (GORS): at least weekly complaints with heartburn or acid regurgitation.

†Relative change in prevalence = (prevalence HUNT 3/Mini-Q—prevalence HUNT 2)/prevalence HUNT 2.

‡Seven participants in HUNT 3/Mini-Q had missing information on sex.

§Age at time of GORS assessment (HUNT 2 and HUNT 3/Mini-Q, respectively).

Table 3 Cumulative incidence of GORS from 1995–7 (HUNT 2) to 2006–9 (HUNT3/Mini-Q), stratified by degree of GORS, sex and age groups*

Any GORS†												
Cumulative incidence												
Total N=20 311												
Number												
%												
95% CI												
5904												
29.1												
28.4 to 29.7												
OR and 95% CI‡												
Women N=11 394												
Men N=8917												
Women												
Men												
Age (years)§	Number	%	95% CI	Number	%	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
All ages	3209	28.2	27.3 to 29.0	2695	30.2	29.3 to 31.2						
<40	283	20.5	18.3 to 22.6	243	29.3	26.2 to 32.4	1.00	Reference	1.61	1.32 to 1.96		
40–49	704	25.9	24.2 to 27.5	548	29.6	27.5 to 31.7	1.36	1.16 to 1.59	1.63	1.38 to 1.92		
50–59	900	29.1	27.5 to 30.7	775	31.3	29.4 to 33.1	1.59	1.37 to 1.85	1.77	1.51 to 2.07		
60–69	823	33.3	31.5 to 35.2	666	30.6	28.6 to 32.5	1.94	1.66 to 2.27	1.71	1.46 to 2.01		
≥70	499	28.9	26.8 to 31.1	463	29.4	27.1 to 31.6	1.58	1.34 to 1.87	1.62	1.36 to 1.92		
Severe GORS†												
Cumulative incidence												
Total N=20 311												
Number												
%												
95% CI												
510												
2.5												
2.3 to 2.7												
OR and 95% CI‡												
Women N=11 394												
Men N=8917												
Women												
Men												
Age (years)§	Number	%	95% CI	Number	%	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
All ages	319	2.8	2.5 to 3.1	191	2.1	1.8 to 2.4						
<40	31	2.2	1.5 to 3.0	15	1.8	0.9 to 2.7	1.00	Reference	0.80	0.43 to 1.50		
40–49	66	2.4	1.8 to 3.0	40	2.2	1.5 to 2.8	1.08	0.70 to 1.67	0.96	0.60 to 1.55		
50–59	95	3.1	2.5 to 3.7	53	2.1	1.6 to 2.7	1.38	0.92 to 2.08	0.95	0.61 to 1.49		
60–69	85	3.4	2.7 to 4.2	48	2.2	1.6 to 2.8	1.55	1.03 to 2.36	0.98	0.62 to 1.55		
≥70	42	2.4	1.7 to 3.2	35	2.2	1.5 to 2.9	1.09	0.68 to 1.74	0.99	0.61 to 1.62		

*Cumulative incidence was calculated from no GORS in HUNT 2 to any or severe GORS in HUNT 3/Mini-Q, respectively.

†Any gastro-oesophageal reflux symptoms (GORS): minor or severe complaints with heartburn or acid regurgitation; severe GORS: severe complaints with heartburn or acid regurgitation.

‡OR and 95% CI of incident GORS for each sex and age group.

§Age at follow-up in HUNT 3/Mini-Q.

The cumulative incidence of severe GORS was 2.5% (95% CI 2.3% to 2.7%), which corresponded to an average annual incidence of 0.23% (95% CI 0.21% to 0.25%). There was a slightly increased incidence of severe GORS with increasing age for women, but it was stable with age for men. Women aged 60–69 years had the highest incidence of severe GORS (table 3; see supplementary figure 3, available online only).

Spontaneous loss of GORS

The cumulative loss of any GORS during the study period was 22.7% (95% CI 21.9% to 23.6%), when excluding the 286 participants (12%) using antireflux medication at least weekly. This corresponded to an average annual spontaneous loss of 2.32% (95% CI 2.23% to 2.42%). Women younger than 40 years of age had the highest spontaneous loss of any GORS. The spontaneous loss decreased with increasing age for both sexes, but this was more pronounced among women. There was no difference in spontaneous loss of any GORS between the sexes in older age groups (table 4; see supplementary figure 4, available online only).

The cumulative loss of severe GORS was 12.6% (95% CI 10.9% to 14.2%), when excluding the 89 participants (31%) using antireflux medication at least weekly. This corresponded to an average annual spontaneous loss of 1.22% (95% CI 1.05% to 1.40%). The spontaneous loss decreased with increasing age for both sexes, but this was particularly evident among women (table 4; see supplementary figure 4, available online only).

Non-participant study

In Mini-Q and HUNT 3, respectively, 29.9% and 43.1% reported any GORS; 4.3% and 7.1% reported severe GORS; and 5.7% and 8.2% used antireflux medication at least weekly. These differences were also retained after stratification by sex and age (data not shown). Distributions of key variables associated with GORS were also assessed. In Mini-Q and HUNT 3, respectively, 49% and 56% were women; the mean age was 45.9 and 53.4 years; the mean body mass index (BMI) was 26.1 and 27.2 kg/m²; there were no differences in the proportions of none or daily cigarette smokers; 34% and 38% drank at least weekly alcohol; and 69% and 79% reported at least weekly physical exercise.

DISCUSSION

The present study found a substantial increase in the prevalence of GORS during the past decade. The absolute number of individuals with new GORS exceeded the number who lost GORS during the study period. Age was an important risk factor for the incidence of GORS among women, but for men the incidence was stable irrespective of age. GORS was frequently lost, especially among young women, but seemed to be more stable with increasing age. Analyses excluding pregnant women made no difference in the results. The use of regular antireflux medication could only explain the loss of GORS in a minority of participants.

There are a few methodological issues to be discussed. Major strengths were: (1) the population-based design, which reduced

Oesophagus

Table 4 Cumulative spontaneous loss of GORS from 1995–7 (HUNT 2) to 2006–9 (HUNT3/Mini-Q), stratified by degree of GORS, sex and age groups*

Any GORS†											
Cumulative spontaneous loss											
Total N = 9299											
	Number			%			95% CI			OR and 95% CI‡	
	2112			22.7			21.9 to 23.6				
	Women N = 4686			Men N = 4613			Women		Men		
Age (years)§	Number	%	95% CI	Number	%	95% CI	OR	95% CI	OR	95% CI	
All ages	1118	23.9	22.6 to 25.1	994	21.5	20.4 to 22.7	1.00	Reference	0.37	0.27 to 0.52	
<40	207	51.1	46.2 to 56.0	74	27.9	22.5 to 33.3	0.43	0.34 to 0.55	0.32	0.25 to 0.41	
40–49	279	31.1	28.0 to 34.1	209	25.0	22.1 to 27.9	0.28	0.22 to 0.35	0.26	0.20 to 0.33	
50–59	262	22.6	20.2 to 25.0	287	21.3	19.1 to 23.5	0.18	0.14 to 0.24	0.22	0.18 to 0.29	
60–69	181	16.1	14.0 to 18.3	229	19.0	16.7 to 21.2	0.20	0.15 to 0.25	0.24	0.19 to 0.31	
≥70	189	17.2	14.9 to 19.4	195	20.4	17.8 to 22.9					

Severe GORS†											
Cumulative spontaneous loss											
Total N = 1553											
	Number			%			95% CI			OR and 95% CI‡	
	195			12.6			10.9 to 14.2				
	Women N = 798			Men N = 755			Women		Men		
Age (years)§	Number	%	95% CI	Number	%	95% CI	OR	95% CI	OR	95% CI	
All ages	93	11.7	9.4 to 13.9	102	13.5	11.1 to 16.0	1.00	Reference	0.60	0.24 to 1.50	
<40	25	37.3	25.6 to 49.0	9	26.5	11.4 to 41.5	0.36	0.18 to 0.70	0.31	0.16 to 0.62	
40–49	23	17.6	11.0 to 24.1	20	15.6	9.3 to 21.9	0.20	0.10 to 0.39	0.29	0.16 to 0.54	
50–59	19	10.4	6.0 to 14.9	32	14.7	10.0 to 19.5	0.13	0.06 to 0.27	0.20	0.10 to 0.39	
60–69	13	7.0	3.3 to 10.6	22	10.6	6.4 to 14.8	0.10	0.05 to 0.21	0.21	0.11 to 0.43	
≥70	13	5.6	2.6 to 8.6	19	11.3	6.5 to 16.1					

*Cumulative spontaneous loss was calculated from any or severe GORS in HUNT 2, respectively, to no GORS in HUNT 3/Mini-Q, excluding those using antireflux medication at least weekly.

†Any gastro-oesophageal reflux symptoms (GORS): minor or severe complaints with heartburn or acid regurgitation; severe GORS: severe complaints with heartburn or acid regurgitation.

‡OR and 95% CI of losing GORS for each sex and age group.

§Age at follow-up in HUNT 3/Mini-Q.

the risk of selection bias compared with studies of individuals consulting physicians or in other healthcare settings; (2) the large study population, which reduced the risk of chance findings and made subgroup analyses possible; and (3) the ability to account for the use of antireflux medication among participants with loss of GORS. Limitations of the study were: (1) the drop in participation rate from HUNT 2 to HUNT 3, making differences in selection bias between the surveys possible; and (2) the long time interval (11 years) between the surveys, which prevented the evaluation of additional fluctuations in GORS during the study period. The analysis of incident GORS may thus also have included recurrent symptoms and not only genuinely new cases, and the loss of GORS may not necessarily mean a true recovery, but rather a temporary relief of symptoms. The probability of fluctuating symptoms was, however, most likely reduced by the 12 months time period the individuals were asked to consider when reporting GORS. Selection bias is a major concern in all population-based studies including the present study. However, compared with other population-based cohort studies of this magnitude the overall response rate is high. In addition, the purpose of the HUNT study was to perform an extensive investigation of common diseases and exposures using a wide range of health-related variables. Therefore, non-participation due to GORS is highly unlikely as there were only two questions related to GORS in the HUNT study. In Mini-Q the prevalence of both any and severe GORS and the use of antireflux medication was lower than in HUNT 3, also after stratification by sex and age. The lower prevalence of GORS in Mini-Q may indicate a selection of individuals with

more complaints in the study population than in the target population and possibly an overestimation of the occurrence of GORS. However, this bias is reduced with the inclusion of the participants in Mini-Q in the study population. The lower prevalence of GORS in Mini-Q may be partly explained by the lower BMI of this population. Finally, the definition of GORD is arbitrary, but according to present guidelines it is based mainly on the frequency of GORS,² which is in line with the present study. Our previous validation study (HUNT 2 validation) showed that 95% of the participants with severe GORS had at least weekly symptoms or used antireflux medication at least weekly.¹⁴ The corresponding proportion of 98% in Mini-Q confirmed this result and implies reliability of the GORS assessment in the HUNT study.

Previous research on the population-based prevalence of GORS is heterogeneous and comparisons between prevalence studies are inherently difficult because GORS are subjective and the definition of GORD varies between studies. In addition, the sample size of previous studies is generally small. A few studies have assessed the change in prevalence of GORS by investigating the same source population at a minimum of two time points. Two US studies, conducted in the same source population in the 1980s and the 1990s, found an increase in the prevalence of at least weekly heartburn from 13.2% (n=835; aged 30–64 years) to 17.8% (n=1511; aged 25–74 years), but no change in at least weekly acid regurgitation (6.5% and 6.3%, respectively).^{15 16} In a Swedish study, the prevalence of any GORS increased from 20–21% in 1986 (n=337; aged 20–79 years) to 22–25% at follow-up 10 years later (n=197).^{17 18} In another Swedish

population, the prevalence of any GORS increased from 18.9% in 1988 (n=1156; aged 20–79 years) to 19.4% at follow-up in 1995 (n=877).¹⁹ In a recent Danish study, the prevalence of at least mild GORS at baseline in 1998–9 was 22% (n=6781; aged 40–65 years) and was reported to be stable at follow-up 5 years later (n=5578).²⁰ Except for this last study, there was an increasing prevalence of GORS over time in all populations, but this increase was not as pronounced as in the present study. The increasing prevalence of GORS is alarming because it will most likely contribute to the increasing incidence of adenocarcinoma of the oesophagus in the western population.^{5 6}

Only a few population-based studies have assessed the prevalence of GORS in the same cohort during at least two time points and addressed the incidence or loss of GORS. Generally, these studies have a small sample size, a short follow-up time, or a selected population. A Danish study with baseline in 1982–4 and follow-up assessment in 1987–8 (n=2987; aged 30–60 years at baseline) reported an annual incidence of any GORS of 13–19% and an annual incidence of frequent GORS of 1–3%.²¹ A Swedish study with baseline in 1988 and 1 year follow-up (n=1059; aged 20–79 years at baseline) reported an annual incidence of predominant GORS of 0.05% and an annual incidence of GORS with other concurrent gastrointestinal symptoms of 0.75%.²² A US study from 1988 to 1991 with 12–20 months follow-up (n=690; aged 30–64 years at baseline) reported a cumulative onset rate of heartburn several times a week or daily of 2.7%, corresponding to average annual onset rates of 1.6–2.7%.²³ In another Swedish population with baseline assessment in 1986 and follow-up 10 years later (n=197; aged 20–79 years at baseline), the annual incidence of any GORS was 1.2–1.8%.¹⁸ In the most recent study from Denmark with baseline in 1998–9 and follow-up assessment 5 years later (n=5578; aged 40–65 years at baseline), an annual incidence of at least mild GORS of 2.2% was reported.²⁰ Except for the first Danish study, these incidence figures comply with the results of our study, and over the past two decades the incidence seems to have been quite stable among these populations. However, in our study we were able to show an effect of age on the incidence of GORS among women.

The first Danish study reported cumulative loss of any GORS of 27–37%, corresponding to an average annual loss of 6.2–9.0%, and cumulative loss of frequent GORS of 59–77%, corresponding to an average annual loss of 16.1–23.2%.²¹ The US study reported a cumulative loss of heartburn several times a week or daily of 47.8%, corresponding to an average annual loss of 36.9–61.3%.²³ The second Swedish study reported an annual loss of any GORS of 1.1–1.3%,¹⁸ and the most recent Danish study reported an annual loss of at least mild GORS of 8.6%.²⁰ Except for the second Swedish study, these figures on the loss of GORS deviate from our results, but our large sample size, long follow-up time, and ability to adjust for antireflux medication argue for validity. In addition, we showed a considerable effect of age on the spontaneous loss of GORS.

There might be several reasons why the prevalence of GORS has increased during the past decade. The body weight has increased in the population, and high BMI is an established risk factor for GORS. The increasing age of the cohort may contribute, but the prevalence also increased after adjustment for age. However, it is interesting that the incidence and spontaneous loss of GORS were influenced by age, particularly for women. Postmenopausal hormone replacement therapy seems to be a risk factor for GORS and may to some extent contribute to this pattern for women.^{14 24} The substantial loss of GORS, not due to antireflux medication, found in the present study, is

partly conflicting with the presumed chronic character of GORS and the large use of regular antireflux medication in this population. Besides antireflux medication, there are few data on the prevention and treatment of GORS in a population-based setting. These issues will be addressed in depth in future studies using the HUNT study.

CONCLUSION

In this large prospective population-based cohort study there was a considerable increase in the prevalence of GORS between 1995–7 and 2006–9, and the prevalence of at least weekly GORS increased by 47%. The average annual cumulative incidence of severe GORS was 0.23%, and the average annual spontaneous loss of severe GORS (not due to antireflux medication) was 1.22%. The incidence and spontaneous loss of GORS differed between the sexes and with age.

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Competing interests None.

Ethics approval As a result of the large number of participants in the HUNT study (58 869 and 44 997 participants in HUNT 2 and HUNT 3/Mini-Q, respectively) and the long time span of the study (from 1995), it would be an extremely demanding task to contact each participant, guardian or next of kin to gather a signed BMJ patient consent form. However, the study was approved by the Regional Committee for Medical and Health Research Ethics, Central Norway, and all participants signed a written consent form when they participated in the HUNT study, which stated that the data collected could be linked with health registries and patient records for research purposes in future studies. This is also stated in the manuscript. There is no information in the manuscript that could identify any participant.

Contributors EN-J: study concept and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, approval of the final version of the manuscript. AL: study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, statistical analysis, approval of the final version of the manuscript. JL: study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, approval of the final version of the manuscript. KH: study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, approval of the final version of the manuscript.

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Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study

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