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Weight loss and reduction in gastroesophageal reflux : a prospective population-based cohort study : the HUNT study

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TITLE PAGE

Title

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Short title

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Weight loss and gastroesophageal reflux

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ABSTRACT

Objective High body mass index (BMI) is an established risk factor of gastroesophageal reflux symptoms (GERS). The aim of this study was to clarify if weight loss reduces GERS.

Design The study was part of the Nord-Trøndelag health study (the HUNT study), a prospective population-based cohort study conducted in Nord-Trøndelag County, Norway. All residents of the county from 20 years of age were invited. In 1995-7 (HUNT 2) and 2006-9 (HUNT 3), 58,869 and 44,997 persons, respectively, responded to a questionnaire on heartburn and acid regurgitation. Among these, 29,610 persons (61% response rate) participated at both times and were included in the present study. The association between weight loss and reduction of GERS was calculated using logistic regression. The analyses were stratified by antireflux medication and the results adjusted for sex, age, cigarette smoking, alcohol consumption, education, and physical exercise.

Results Weight loss was dose-dependently associated with a reduction of GERS and an increased treatment success with antireflux medication. Among persons with >3.5 units decrease in BMI, the adjusted OR of loss of any (minor or severe) GERS was 1.98 (95% CI 1.45 to 2.72) when using no or less than weekly antireflux medication, and 3.95 (95% CI 2.03 to 7.65) when using at least weekly antireflux medication. The corresponding ORs of loss of severe GERS was 0.90 (95% CI 0.32 to 2.55) and 3.11 (95% CI 1.13 to 8.58).

Conclusion Weight loss was dose-dependently associated with both a reduction of GERS and an increased treatment success with antireflux medication in the general population.

STUDY HIGHLIGHTS

WHAT IS CURRENT KNOWLEDGE

- The prevalence of gastroesophageal reflux symptoms (GERS) is high and increasing in Western populations
- High body mass index is a risk factor of GERS
- The effect of weight loss on GERS is not clear

WHAT IS NEW HERE

- Weight loss was associated with a reduction of GERS in the general population
- There was a dose-response relationship between weight loss and reduction of GERS
- Weight loss was associated with an increased treatment success with antireflux medication

MAIN TEXT

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a highly prevalent disease in Western populations,(1, 2) associated with a decreased health-related quality of life(3, 4) and an increased risk of esophageal adenocarcinoma.(5, 6) The Montreal definition and classification of GERD states that: “GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications” and the definition recognizes that heartburn and acid regurgitation are characteristic symptoms of GERD.(7, 8) Overweight, defined according to the World Health Organization’s classification as body mass index (BMI) ≥25 kg/m^2,(9) increases the risk of gastroesophageal reflux symptoms (GERS)(10-12) and is independently associated with esophageal adenocarcinoma.(11) The increasing weight seen in the general population will have unfortunate effects on the prevalence of GERD.(13-15) Weight loss may be of great importance in the prevention and treatment of the many individuals suffering from GERD. The aim of this study was to clarify if weight loss reduces GERS in a large population-based cohort followed prospectively over time.

METHODS

Study population and design

The study was performed as part of a large population-based study, the Nord-Trøndelag health study (the HUNT study). The HUNT study is an on-going prospective cohort study based on repeated health surveys of the entire adult population of Nord-Trøndelag County, Norway. All residents in the county from 20 years of age have been invited to participate in three surveys, entitled HUNT 1 (1984-6), HUNT 2 (1995-7), and HUNT 3 (2006-8). The HUNT study includes data on a wide range of health related items gathered from written questionnaires answered by the participants, clinical examinations performed by trained personnel, and blood samples taken from the participants.(16) GERS were assessed in HUNT 2 and HUNT 3, and these two surveys constituted the base of the present study. In addition, GERS were assessed in a 'non-responder study' (Mini-Q) after HUNT 3 in 2009, where those who did not participate in HUNT 3 were invited.(2, 16) The individuals who participated in HUNT 2 and were followed up in Mini-Q were also eligible for inclusion in the present study (figure 1).

Assessment of gastroesophageal reflux symptoms

GERS were assessed by a questionnaire in HUNT 2 (1995-7) and HUNT 3/Mini-Q (2006-9). The participants replied to the question: 'To what degree have you had heartburn or acid regurgitation during the previous 12 months?' with one of three response alternatives: 'no complaints', 'minor complaints', or 'severe complaints'. In a validation study after HUNT 2, 25% of those reporting minor complaints and 95% of those reporting severe complaints had at least weekly symptoms.(10) In Mini-Q,

where frequency of complaints also was assessed, the corresponding proportions were 31% and 98%.(2) We defined 'any GERS' to include all participants reporting minor or severe complaints and 'severe GERS' to include only those reporting severe complaints.

Assessment of body mass index

BMI equals weight in kilograms divided by the square height in meters (kg/m^2). Weight and height were objectively measured under standardized conditions and by trained personnel at screening stations in both HUNT 2 and HUNT 3. In Mini-Q, weight and height measurements were self-reported.

Assessment of co-variables

Co-variables in the analyses were chosen using accepted criteria for a confounding factor, i.e. being associated with the outcome (GERS), associated with the exposure (weight loss), and not an effect of the exposure or outcome under study.(17) The variables selected as potential confounders were sex, age, cigarette smoking, alcohol consumption, education, and physical exercise. These co-variables were assessed through questionnaires in HUNT 3/Mini-Q, except for education which was assessed in HUNT 2. The participants reported cigarette smoking status, frequency of alcohol drinking during the previous 12 months, length of education, and average frequency of physical exercise.

Assessment of antireflux medication

Data on antireflux medication, i.e. proton pump inhibitors (PPIs), histamine-2-receptor antagonists (H2RAs), or antacids, was gathered from HUNT 3 and from the Norwegian Prescription Database (NorPD). Until 2010, PPIs and H2RAs (except small packages of low dose H2RAs) have only been available in Norway through a prescription from a physician, and only small packages of low dose H2RAs and antacids have been available over the counter (OTC). In HUNT 3, frequency of OTC antireflux medication use was assessed through written questionnaires. Since 2004, data on all prescribed medication in Norway has been collected in the NorPD. By linkage of the HUNT study and the NorPD, data on all prescribed antireflux medication among the study participants was gathered. Using number of prescriptions and number of tablets in each prescription, average frequency of antireflux medication was estimated during the HUNT 3 study period. Thus, all antireflux medication should be accounted for in HUNT 3: OTC use through the HUNT 3 questionnaires and prescribed use through the NorPD. Only those who actually were prescribed an antireflux medication were included in the data from the NorPD and therefore it was not possible to distinguish between never users and participants with missing information on medication use. All participants with missing data on antireflux medication were therefore regarded as never users.

Statistical methods

Logistic regression was used to analyze the association between weight loss and reduction of GERS, providing odds ratios (ORs) with 95% confidence intervals (CIs). The participants who had any GERS at baseline (HUNT 2) and no GERS at follow-up

(HUNT 3/Mini-Q), defined as 'loss of any GERS', were compared with those who had any GERS at both time points, i.e. 'stable any GERS'. The participants who had severe GERS at baseline and no or minor GERS at follow-up, defined as 'reduction of severe GERS', were compared with those who had severe GERS at both time points, i.e. 'stable severe GERS'. Finally, those who had severe GERS at baseline and no GERS at follow-up, defined as 'loss of severe GERS', were compared with those who had severe GERS at both time points, i.e. 'stable severe GERS'. The absolute change in BMI units between the two time points was calculated and five categories reflecting this change were used in the analyses: <0.5 units change (reference category), 0.5-1.5 units decrease, >1.5-3.5 units decrease, >3.5 units decrease, and ≥0.5 units increase. In the statistical model adjustments were made by categorization of age (<40, 40-49, 50-59, 60-69, or ≥70 years), cigarette smoking status (never smoker, previous smoker, or current smoker), frequency of alcohol consumption (less than weekly or at least weekly), years of education (≤12 years or >12 years), and frequency of physical exercise (less than weekly or at least weekly). Antireflux medication was not considered a confounder according to the definition above. Instead, the analyses were stratified into two groups of antireflux medication use at follow-up: no or less than weekly or at least weekly. The analyses were performed with the statistics and data analysis software Stata, version 11.2, by StataCorp LP, Texas, US.

Study approval

The study was approved by the Regional Committee for Medical and Health Research Ethics, Central-Norway (ID 4.2009.328). All participants in the HUNT study

signed a written consent form before participating, which stated the purpose of the study and the possibility of future research and linkage to other registries.

RESULTS

Participants

In HUNT 2 (1995-7) and HUNT 3/Mini-Q (2006-9), 58,869 individuals (64% response rate) and 44,997 individuals (49% response rate) reported their complaints with GERS, respectively. Among these, 29,610 individuals participated in both surveys and were included in the present study. This corresponds to a response rate of 61% at follow-up, after excluding the 10,535 participants in HUNT 2 who were no longer resident in the county at the time of HUNT 3/Mini-Q or had deceased before HUNT 3/Mini-Q (non-eligible for follow-up) (figure 1).

Characteristics

At baseline (HUNT 2), 9299 individuals (31.4%) reported any GERS (any GERS cohort) and 1553 individuals (5.2%) reported severe GERS (severe GERS cohort). Of the any GERS cohort, 2398 individuals (25.8%) reported no GERS at follow-up in HUNT 3/Mini-Q, i.e. 'loss of any GERS' (table 1). Of the severe GERS cohort, 284 individuals (18.3%) reported no GERS at follow-up in HUNT 3/Mini-Q, i.e. 'loss of severe GERS' (table 1), 729 individuals (46.9%) reported minor GERS, and 1013 (65.2%) reported no or minor GERS, i.e. 'reduction of severe GERS' (table 1).

The mean BMI among all the participants increased between the two time points. The participants with loss or reduction of GERS had a lower increase in BMI than those with stable GERS (table 1). Those with loss or reduction of GERS were younger, had higher education, and used less antireflux medication than those with stable GERS for both cohorts (table 1). There was no difference in the proportion of current

cigarette smokers among the subgroups (table 1). In the any GERS cohort, the proportion of women was higher among those with loss of GERS compared to those with stable GERS (table 1). In the severe GERS cohort, alcohol consumption was more frequent among those with loss or reduction of GERS compared to those with stable GERS, and physical exercise was more frequent among those with loss or reduction of GERS (table 1).

Table 1 Characteristics of cohort reporting gastroesophageal reflux symptoms (GERS)* in HUNT 2 & HUNT 3/Mini-Q (N=29,610)

	Stable any GERS	Loss of any GERS†	Stable severe GERS	Reduction of severe GERS†	Loss of severe GERS†
Number (%)	6901 (74.2)	2398 (25.8)	540 (34.8)	1013 (65.2)	284 (18.3)
BMI‡ (kg/m^2), HUNT 2					
Mean (sd)	27.3 (4.0)	27.2 (4.3)	27.7 (4.2)	28.1 (4.3)	27.9 (4.3)
Missing, no. (%)	23 (0.3)	21 (0.9)	2 (0.4)	5 (0.5)	2 (0.7)
BMI (kg/m^2) change§					
Mean (sd)	1.3 (2.4)	0.5 (2.7)	1.3 (2.4)	0.9 (2.7)	0.6 (2.8)
Missing, no. (%)	78 (1.1)	46 (1.9)	7 (1.3)	19 (1.9)	7 (2.5)
Sex					
Women, no. (%)	3415 (49)	1271 (53)	277 (51)	521 (51)	143 (50)
Age (years), HUNT 3/Mini-Q					
Mean (sd)	59.8 (12.6)	57.4 (14.1)	60.8 (12.7)	60.2 (13.6)	58.7 (14.5)
Cigarette smoking, HUNT 3/Mini-Q					
Never, no. (%)	2428 (35.2)	921 (38.4)	188 (34.8)	304 (30.0)	79 (27.8)
Previous, no. (%)	2332 (33.8)	737 (30.7)	182 (33.7)	383 (37.8)	120 (42.3)
Current, no. (%)	1822 (26.4)	631 (26.3)	141 (26.1)	279 (27.5)	73 (25.7)
Missing, no. (%)	319 (4.6)	109 (4.5)	29 (5.4)	47 (4.6)	12 (4.2)
Alcohol consumption, HUNT 3/Mini-Q					
<weekly, no. (%)	4292 (62.2)	1498 (62.5)	363 (67.2)	649 (64.1)	173 (60.9)
≥weekly, no. (%)	2377 (34.4)	816 (34.0)	153 (28.3)	327 (32.3)	103 (36.3)
Missing, no. (%)	232 (3.4)	84 (3.5)	24 (4.4)	37 (3.7)	8 (2.8)
Education, HUNT 2					
≤12 years, no. (%)	5602 (81.2)	1837 (76.6)	469 (86.9)	842 (83.1)	233 (82.0)
>12 years, no. (%)	1162 (16.8)	511 (21.3)	56 (10.4)	146 (14.4)	41 (14.4)
Missing, no. (%)	137 (2.0)	50 (2.1)	15 (2.8)	25 (2.5)	10 (3.5)
Physical exercise, HUNT 3/Mini-Q					
<weekly, no. (%)	1672 (24.2)	576 (24.0)	156 (28.9)	272 (26.9)	71 (25.0)
≥weekly, no. (%)	5047 (73.1)	1754 (73.1)	363 (67.2)	721 (71.2)	210 (73.9)
Missing, no. (%)	182 (2.6)	68 (2.8)	21 (3.9)	20 (2.0)	3 (1.1)
Antireflux medication‖, HUNT 3					
Never or <weekly, no. (%)¶	3742 (54.2)	2112 (88.1)	87 (16.1)	505 (49.9)	195 (68.7)
≥weekly, no. (%)	3159 (45.8)	286 (11.9)	453 (83.9)	508 (50.1)	89 (31.3)

* GERS: self-reported degree of complaints with heartburn or acid regurgitation during the previous 12 months.
† Loss of any GERS: any GERS at baseline, no GERS at follow-up; Reduction of severe GERS: severe GERS at baseline, no or minor GERS at follow-up; Loss of severe GERS: severe GERS at baseline, no GERS at follow-up. The severe GERS group is a subset of the any GERS group.
‡ BMI: body mass index.
§ BMI change: BMI HUNT 3/Mini-Q - BMI HUNT 2.
|| Antireflux medication: proton pump inhibitors, histamine-2-receptor antagonists, and antacids.
¶ Participants with no information on antireflux medication were included in never or <weekly category.

Association between weight loss and gastroesophageal reflux symptoms

In the crude analyses, without considering antireflux medication or any potential confounder, weight loss was dose-dependently associated with loss or reduction of GERS (p-value for trend ≤0.012) (table 2). When stratified by antireflux medication, weight loss was associated with an increased treatment success with antireflux medication when used at least weekly (table 2). Among participants with no or less than weekly antireflux medication, there was a 2-fold increase in the adjusted odds of loss of any GERS among participants with >3.5 units decrease in BMI compared to participants with <0.5 units change in BMI (OR 1.98, 95% CI 1.45 to 2.72) (table 2). Among participants with at least weekly antireflux medication, the corresponding odds increased 4-fold (OR 3.95, 95% CI 2.03 to 7.65) (table 2). The association between weight loss and any GERS was dose-dependent regardless of antireflux medication (p-value for trend <0.001) (table 2). In the severe GERS cohort, there was no association between weight loss and GERS among participants with no or less than weekly antireflux medication. The adjusted ORs of reduction and loss of severe GERS among those with >3.5 units decrease in BMI compared to those with <0.5 units change in BMI was 0.58 (95% CI 0.16 to 2.10) (table 2) and 0.90 (95% CI 0.32 to 2.55) (table 2), respectively, and there was no dose-response association (p-value for trend 0.804 and 0.189, respectively) (table 2). However, among those with at least weekly antireflux medication, the corresponding ORs was 2.12 (95% CI 0.89 to 5.02) (table 2, figure 2) and 3.11 (95% CI 1.13 to 8.58) (table 2, figure 3), respectively, and there was a dose-response association (p-value for trend 0.008 and 0.047, respectively) (table 2). Since the crude and adjusted ORs were similar when stratified by antireflux medication, only the adjusted data are presented in table 2.

Table 2 Odds ratio (OR) with 95% confidence interval (95% CI) for loss or reduction of gastroesophageal reflux symptoms (GERS)* compared with stable GERS by change in body mass index (BMI)† and antireflux medication‡

	Loss of any GERS§			Reduction of severe GERS§			Loss of severe GERS§		
Crude									
Change in BMI (kg/m^2)	**No.**	**OR**	**95% CI**	**No.**	**OR**	**95% CI**	**No.**	**OR**	**95% CI**
≥0.5 increase	5542	0.72	0.63 to 0.82	897	0.83	0.63 to 1.10	897	0.77	0.55 to 1.09
<0.5 change	1589	1.00	Reference	278	1.00	Reference	278	1.00	Reference
0.5-1.5 decrease	970	1.22	1.03 to 1.46	157	0.88	0.59 to 1.33	157	0.90	0.55 to 1.48
>1.5-3.5 decrease	770	1.38	1.15 to 1.66	137	1.87	1.16 to 3.02	137	1.11	0.67 to 1.83
>3.5 decrease	304	2.42	1.88 to 3.11	58	1.32	0.70 to 2.47	58	1.51	0.79 to 2.88
p-value for trend‖		<0.001			0.001			0.012	
Missing (%)	124	(1.3)		26	(1.7)		26	(1.7)	
No or less than weekly antireflux medication									
Change in BMI (kg/m^2)	**No.**	**OR¶**	**95% CI**	**No.**	**OR¶**	**95% CI**	**No.**	**OR¶**	**95% CI**
≥0.5 increase	3100	0.67	0.57 to 0.78	304	0.74	0.36 to 1.51	304	0.72	0.43 to 1.19
<0.5 change	939	1.00	Reference	95	1.00	Reference	95	1.00	Reference
0.5-1.5 decrease	616	1.14	0.92 to 1.40	65	0.50	0.20 to 1.22	65	0.83	0.41 to 1.67
>1.5-3.5 decrease	485	1.25	0.99 to 1.56	54	1.64	0.49 to 5.48	54	1.13	0.56 to 2.31
>3.5 decrease	198	1.98	1.45 to 2.72	22	0.58	0.16 to 2.10	22	0.90	0.32 to 2.55
p-value for trend‖		<0.001			0.804			0.189	
Missing (%)	516	(8.8)		52	(8.8)		52	(8.8)	
At least weekly antireflux medication									
Change in BMI (kg/m^2)	**No.**	**OR¶**	**95% CI**	**No.**	**OR¶**	**95% CI**	**No.**	**OR¶**	**95% CI**
≥0.5 increase	2022	0.99	0.67 to 1.45	518	1.04	0.71 to 1.51	518	0.81	0.42 to 1.56
<0.5 change	507	1.00	Reference	145	1.00	Reference	145	1.00	Reference
0.5-1.5 decrease	267	1.29	0.75 to 2.19	78	1.16	0.66 to 2.03	78	0.94	0.36 to 2.48
>1.5-3.5 decrease	213	1.79	1.05 to 3.05	67	2.24	1.19 to 4.21	67	0.91	0.32 to 2.55
>3.5 decrease	66	3.95	2.03 to 7.65	30	2.12	0.89 to 5.02	30	3.11	1.13 to 8.58
p-value for trend‖		<0.001			0.008			0.047	
Missing (%)	370	(10.7)		123	(12.8)		123	(12.8)	

* GERS: self-reported degree of complaints with heartburn or acid regurgitation during the previous 12 months.
† Change in BMI: BMI HUNT 3/Mini-Q - BMI HUNT 2.
‡ Antireflux medication: proton pump inhibitors, histamin-2-receptor antagonists, and antacids.
§ Loss of any GERS: any GERS at baseline, no GERS at follow-up; Reduction of severe GERS: severe GERS at baseline, no or minor GERS at follow-up; Loss of severe GERS: severe GERS at baseline, no GERS at follow-up. The severe GERS group is a subset of the any GERS group.
|| p-value for trend: Wald test for linear trend.
¶ Adjusted for sex, age, cigarette smoking, alcohol consumption, education, and physical exercise

DISCUSSION

In this study, weight loss was dose-dependently associated with a reduction of GERS, especially among those with the highest decrease in BMI. Weight loss was also associated with an increased treatment success with antireflux medication.

The major strengths of this study are 1) the population-based design, reducing selection bias; 2) the large sample size, reducing the risk of chance findings and making subgroup analyses possible; 3) the prospective design, minimizing recall bias; 4) the large selection of variables assessed in the HUNT study, making adjustments for potential confounders possible; and 5) the linkage with the NorPD, complementing the data on antireflux medication. The limitations are 1) the loss to follow-up between the two time points, making selection bias possible; 2) the 12 months recall period used in the questionnaire, making recall bias possible; 3) the long time period between the assessments of GERS, making short term fluctuations in GERS impossible to evaluate; 4) residual confounding, which cannot be excluded in observational research, although the choice of co-variables was restrictive to avoid spurious effects; and 5) self-reported height and weight in Mini-Q, reducing the measurement accuracy of BMI.

Nord-Trøndelag County is representative of the Norwegian population at large, making the findings generalizable.(18) Selection bias due to loss of follow-up is probably small since there were only minor differences in the distribution of the study variables among all the HUNT 2 participants (N=58,869) compared with the cohort

which was followed-up (N=29,610): there was no difference in the mean BMI (26 kg/m^2) or mean alcohol consumption (2.5 times/month); the proportion of women was 52% and 54%; the mean age was 48.5 years and 45.8 years; the proportion of never smokers was 47% and 48% and of daily smokers 30% and 27%; the proportion with >12 years of education was 21% and 24%; and the proportion who did no exercise weekly was 9% and 6%, respectively. The 12 months recall period used in the questionnaire is a sub-optimal long period to recall GERS. However, this should not be a major threat to the validity of the study, since most people with GERS, at least of a more severe type, are likely to be able to report their symptoms. The passage of 11 to 12 years between the surveys does not capture the short-term fluctuations in symptoms in individual subject. Moreover, some people with GERS might have developed Barrett´s esophagus between the surveys, which might reduce symptoms although the reflux disease remains. However, this should be limited to only a few people in the study. In Mini-Q, height and weight were self-reported, reducing measurement accuracy of BMI in this subpopulation. However, the number of individuals from Mini-Q was limited to n=938 (10.1%) and n=190 (12.2%) in the any GERS cohort and the severe GERS cohort, respectively. Assuming that self-reported weight is an underestimate of the actual weight, this would overestimate any weight loss from baseline in the study, and dilute the effect of weight loss on loss or reduction of GERS, make the presented ORs closer to the null. In English, “heartburn” and “regurgitation” are known to be words that the general public not understands adequately. However, in Norwegian this is much less a problem. The Norwegian words “brystbrann”/”halsbrann” and “sure oppstøt” used in this study are frequently used in the common language and are understood by the general public in the same way as health care professionals and researchers do.

Previous research on the effect of weight loss on GERS is limited, conflicting, and suffers from varying definitions of GERD. Two randomized, double-blind, sham controlled trials of gastric balloon distension on 42 and 28 extremely obese patients with pH-verified reflux, but without grade C or D oesophagitis (Los Angeles classification(19)) or large (>3 cm) hiatus hernia on endoscopy, found that weight loss was followed by reduced reflux.(20, 21) An uncontrolled prospective study of 34 patients (mean BMI 23.5) with troublesome GERS, and either normal endoscopy or grade I oesophagitis (Savary-Miller classification(22)), found improvement in reflux symptom score after 6 weeks with a decrease of mean BMI of 1.7.(23) Another uncontrolled prospective study of 18 volunteers (mean BMI 43.5) with GERS, found improvement in symptom score after a mean of 4 days with an average weight loss of 1.7 kg.(24) In the Nurses' Health Study from the United States there was a 36% reduction in the risk of at least weekly GERS among women with at least 3.5 decrease in BMI compared with those with no change in BMI (OR 0.64, 95% CI 0.42 to 0.97).(25) However, a randomized trial of 20 obese patients (mean BMI 31.4 at inclusion) with pH-verified reflux, erosive oesophagitis, and daily GERS, did not find any effect on GERS with a mean decrease in BMI of 2.6 to 4.8 units.(26) This study included participants with hiatus hernia, which contributes to the occurrence of GERD and is irreversible with weight loss. The only previous population-based study of the effect of weight change on GERS was from the United States and followed 637 individuals over a median of 10.5 years (mean age 62 years and 53% females at follow-up) and found no relation between weight change and change in reported GERD symptoms.(27) A major limitation of that study was, however, the use of self-reported height and weight.

Our results favor the hypothesis that weight loss improves GERS. Due to the observational design of the study, strict causality cannot be implied. However, the consistent and dose related association between weight loss and reduction of GERS, which is preserved after adjustment for possible important confounders, argues for a valid conclusion. The data also indicates that even greater benefits might be seen in overweight individuals who achieve a larger weight loss. According to the Montreal definition and classification, “GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications” and it further states that “In population-based studies, mild symptoms occurring 2 or more days a week, or moderate/severe symptoms occurring more than 1 day a week, are often considered troublesome by patients”.(8) As the validation studies of our questionnaire showed that 95-98% of the participants who reported severe GERS had at least weekly complaints, those reporting severe GERS in our study can be regarded as having GERD according to the Montreal definition. It seems that the weight loss needs to be substantial to improve severe GERS. This is probably due to the strong association between BMI and GERS. Even BMI in the upper normal range has been shown to be associated with GERS compared with BMI in the lower normal range.(25) In addition, weight loss without regular use of antireflux medication does not seem to be sufficient. This probably reflects an advanced stage of disease in these subjects, i.e. esophagitis or symptoms related to the presence of hiatal hernia, which does not resolve only with weight loss. However, weight loss was associated with an increased chance of treatment success with antireflux medication.

CONCLUSION

In this large prospective population-based cohort study weight loss was dose-dependently associated with reduction of GERS and increased chance of treatment success with antireflux medication. The study also suggests that patients with GERD using regular antireflux medication might benefit from weight reduction.

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Guarantor of the article

EN-J accepts full responsibility for the conduct of the study and had access to the data and control of the decision to publish.

Specific author contributions

EN-J has provided substantial contributions in planning and conducting the study, interpreting data, drafting the manuscript, and he has approved the final draft submitted. AL has provided substantial contributions in planning and conducting the study, interpreting data, drafting the manuscript, and she has approved the final draft submitted. JL has provided substantial contributions in planning and conducting the study, interpreting data, drafting the manuscript, and he has approved the final draft submitted. KH has provided substantial contributions in planning and conducting the study, collecting and interpreting data, drafting the manuscript, and he has approved the final draft submitted.

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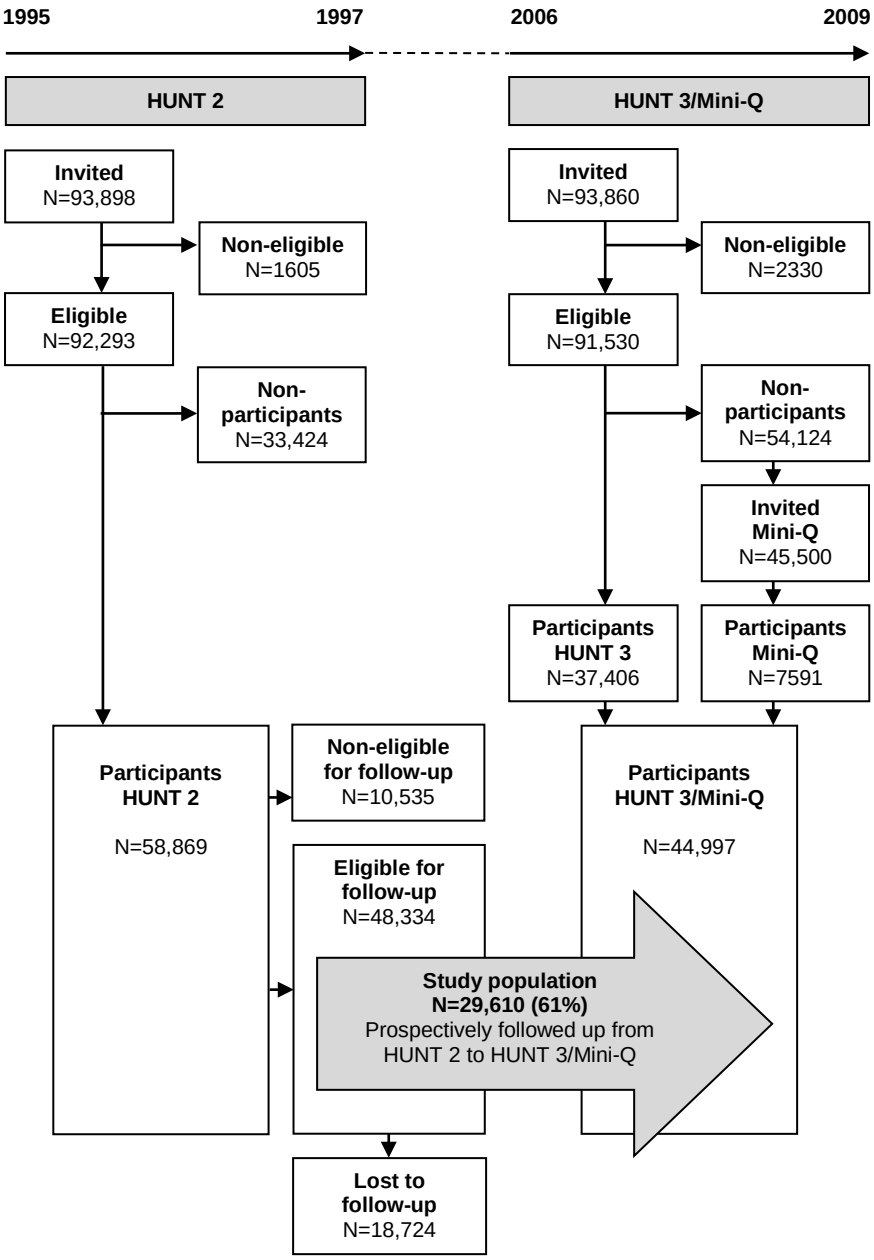
Potential competing interests

None

FIGURE LEGENDS

Figure 1 Flowchart of participants. Number of individuals (N) at each stage and the response rate (%). The response rate was calculated from those eligible for follow-up, excluding those who were no longer resident in the county or had deceased (non-eligible for follow-up).

Figure 1


1995
1997
2006
2009
HUNT 2
HUNT 3/Mini-Q
Invited
N=93,898
Non-eligible
N=1605
Eligible
N=92,293
Non-participants
N=33,424
Invited
N=93,860
Non-eligible
N=2330
Eligible
N=91,530
Non-participants
N=54,124
Invited Mini-Q
N=45,500
Participants HUNT 3
N=37,406
Participants Mini-Q
N=7591
Participants HUNT 2
N=58,869
Non-eligible for follow-up
N=10,535
Eligible for follow-up
N=48,334
Participants HUNT 3/Mini-Q
N=44,997
Study population
N=29,610 (61%)
Prospectively followed up from HUNT 2 to HUNT 3/Mini-Q
Lost to follow-up
N=18,724