Gastro-oesophageal reflux symptoms (GORS) are highly prevalent in Western nations, and may be increasing in incidence in Asia for unknown reasons. Similarly, the development of obesity has reached epidemic proportions in the Western world, which also remains largely unexplained. Obesity is important because it induces a major psychological burden and has a substantial impact on morbidity and quality of life.

We have previously reported that body mass index (BMI) appeared to be an independent risk factor for the presence of heartburn and acid regurgitation in a community based population study in the USA. Others have observed similar associations in Sweden but there have also been contradictory reports. We have also observed an association between obesity and symptoms of diarrhea in population based studies from the USA, Australia, and in a New Zealand birth cohort of young adults. However, these studies were all in uninvestigated subjects, and the relationship between BMI and unexplained upper and lower gastrointestinal symptoms remains to be clarified.

A number of drugs have been reported to lower oesophageal sphincter pressure and an association between the use of such drugs and an increased risk of oesophageal adenocarcinoma has also been observed. However, population based studies that include endoscopic data have not investigated how important medications are in causing oesophagitis, and whether their use mediates the possible association between BMI and GORS.

In this study, we aimed to evaluate the relationship between measured BMI and specific gastrointestinal symptoms in a community based population that was being evaluated by oesophagogastroduodenoscopy. We hypothesised that the association of obesity with symptoms of GORS would be largely explained by underlying oesophagitis or by medications that could potentially aggravate gastro-oesophageal reflux.

**Material and Methods**

**Setting**

The setting consisted of two neighbouring communities in Northern Sweden, Kalix and Haparanda, with 18,408 and 10,580 inhabitants (as of December 1998); 78% lived in city populated areas during the year 2000 compared with the Swedish national average of 84%. The distribution of age and sex was similar to the national average in Sweden in both communities, although unemployment status, income, and the proportion with a higher education were slightly lower.

**Sampling**

Using the computerised national population register, covering all citizens in the two communities by date of birth order, a representative sample was generated. Every seventh adult (n = 3000) from the target population (20–80 years of age, n = 21,610 in September 1998) was drawn, a procedure equivalent to random sampling. The sample was then, by a computerised process, given an identity number (ID 1–3000) in random order.

**Abbreviations:** ASQ, abdominal symptom questionnaire; BMI, body mass index; OEG, oesophagogastroduodenoscopy; GORD, gastro-oesophageal reflux disease; GORS, gastro-oesophageal reflux symptoms; ID, identity number; IBS, irritable bowel syndrome; LOS, lower oesophageal sphincter; OR, odds ratio
Study design and logistics

The study population (n = 3000) was contacted by mail and invited to take part; this invitation included a validated questionnaire, the abdominal symptom questionnaire (ASQ) (see below) to be returned by mail. Up to two reminders were applied when necessary; 140 subjects were unavailable at the time of invitation (21 dead; 38 migrated or questioned returned by relatives; 17 mentally retarded or having dementia; and 76 for other reasons). Thus 2860 of the original study population were eligible for inclusion.

Responders were invited to a visit in the clinic in 1D order, starting with the lowest available ID. Subjects reported the absence/presence of gastrointestinal symptoms using the ASQ questionnaire at the visit, as described below. The study population was divided into five parts in ascending order for logistic reasons, ID 1–600, 601–1200, and so forth, and the first subset of study subjects was approached with the mailed ASQ questionnaire in December 1998. The study was approved by the Umeå University ethics committee and conducted in accordance with the revised Declaration of Helsinki.

Assessments

Abdominal symptom questionnaire (ASQ)

This self-administered questionnaire assesses symptoms from the upper and lower part of the abdomen and has been validated in Sweden.26 A standardised procedure for the administration of the questionnaire at the visit was used. The ASQ includes questions describing the presence or absence (yes/no) of 27 troublesome gastrointestinal symptoms over the preceding three months. In order to better assess the Rome criteria in Sweden, 28 all participants were also asked if they had been troubled by any of 11 listed descriptors of abdominal pain, 26 in addition to symptom location (upper, centre, or lower abdominal, right and left flank, respectively).

Demographics and history

Demographic data were collected at the clinic visit (sex, age, weight, tobacco use, and language). The subject’s level of education and number of inhabitants in their household was confirmed by questions in the ASQ at the visit to the clinic.

Definitions of symptom groups

Subjects were classified according to their symptom patterns as defined below:

(1) Gastro-oesophageal reflux symptoms (GORS)

GORS were defined as the presence of any troublesome heartburn and/or acid regurgitation over the past three months.20 30

(2) Dyspepsia

Dyspepsia was defined as any troublesome pain or discomfort expressed as one or more of the 11 listed pain modalities located in the upper (epigastric) part of the abdomen, and/or nausea, early satiety, or uncomfortable feeling of fullness after a meal. This is consistent with the Rome II definition (except for upper abdominal bloating which was not asked about in the ASQ).24

(3) Irritable bowel syndrome (IBS)

IBS was defined as any of the troublesome abdominal pain modalities located at any site plus concomitant bowel habit disturbances (constipation, diarrhoea, or alternating constipation and diarrhoea).24 This simple definition has been used previously and shown to produce results reasonably concordant with the Rome criteria in Sweden.24

(4) Epigastric pain or discomfort

Epigastric pain in the ASQ was defined as troublesome pain or discomfort expressed as one or more of the 11 listed pain or discomfort modalities indicated in the epigastric part of the abdomen only. This definition is based on the Rome I definition of dyspepsia.

(5) Abdominal pain

Abdominal pain was defined as troublesome pain or discomfort expressed as one or more of the 11 listed pain or discomfort modalities indicated anywhere in the abdomen.

Response rate

A total of 2122 individuals completed the postal questionnaire, which corresponds to a response rate of 74.2% after two postal reminders. These responders were representative of the local population.31 In order to complete the 1001 upper endoscopies, 1563 responders to the ASQ were approached; 364 declined, 74 had moved or could not be reached, and 124 had medical contraindications. Thus the response rate for those eligible for investigation was 73.3%. Sex and age distribution for the 1001 subjects (488 males (48.8%)) who responded to the questionnaire at both assessments (mean age 54 years) closely reflect the pattern in the Swedish population.31 The study subjects who refused endoscopy were very similar demographically to the 1001 subjects evaluated (data not shown). Hence a representative cohort of 1001 invited for upper endoscopy was evaluated. Of the subjects endoscoped, 10 did not have BMI data collected, leaving 991 for analysis.

Oesophagoscopy (OEG)

Upper endoscopies were performed by both primary and secondary care physicians in the two clinics who provided sole medical care in the area. The endoscopists were unaware of the symptoms of the subjects before and during endoscopy.24

Body mass index categories

Height and weight were measured at the endoscopy visit. Data on weight and height were used to calculate BMI (kg/m2). Participants were categorised based on BMI as underweight (BMI <18.5), normal (BMI 18.5 and <25), overweight (BMI 25 and <30), obese class I (BMI 30 and <35), class II (>35 and <40), and class III (>40).35 Because there were relatively few subjects in the extreme obesity categories, these were all combined.

Medications

Data on medication use were recorded after endoscopy. In addition to any acid suppressing drug, medications that were concurrently being taken that may reduce lower oesophageal sphincter (LOS) pressure (nitrates, theophylline, calcium channel blockers, opiates, beta agonists, phenothiazines, tricyclic antidepressive drugs, nicotine substitutes, anticholinergics, and benzodiazepines) were recorded.19-26

Statistical analysis

Prevalence is shown as percentage with 95% confidence interval (CI). We used a logistic regression analysis to assess the association between the presence of each specific gastrointestinal symptom (the binary dependent variable) and BMI (entered as a categorised independent variable), adjusting for age, sex, and education use. The odds ratios
status. Smoking was independently associated by gender, age groups, education levels, smoking and alcohol use. The prevalence of being overweight was 46% (n = 456 (95% CI 42.9, 49.1)) while the prevalence of obesity was 16% (n = 162 (95% CI 14.0, 18.7)). Table 1 shows the proportion of patients in each BMI category, as a whole and separated oesophagitis, adjusting for medication use as well as age, sex, and education level. Linear regression analysis was applied to analyse the independent associations between BMI and possible exposure variables.

RESULTS
Prevalence of obesity
The prevalence of those underweight was 0.8% (n = 8); these subjects were excluded leaving 983 subjects in the subsequent analyses. The prevalence of being overweight was 46% (n = 456 (95% CI 42.9, 49.1)) while the prevalence of obesity was 16% (n = 162 (95% CI 14.0, 18.7)). Table 1 shows the proportion of patients in each BMI category, as a whole and by gender, age groups, education levels, smoking and alcohol status. Smoking was independently associated with increased BMI by linear regression analysis (beta coefficient 0.6); low education was associated with increased BMI (beta coefficient 0.6); alcohol use was not significant.

Prevalence of troublesome gastrointestinal complaints and upper endoscopy findings
At the time of endoscopy, 65.6% of 1001 subjects reported one or more troublesome gastrointestinal complaints on the questionnaire completed prior to endoscopy. The prevalence of major endoscopic findings by BMI category is summarised in table 2. Of those with oesophagitis (n = 155), most were grade A (n = 109); 39 had grade B, three grade C, two grade D, and two were unable to be classified. There were more endoscopic findings in obese subjects than in normal weight subjects, and the differences were significant for oesophagitis and gastric ulcer; the prevalence of oesophagitis in obesity was 26.5% (95% CI 19.7, 33.3) versus 9.3% (95% CI 6.3, 12.3) in normal weight subjects while the prevalence of gastric ulcer in obesity was 5.6% (95% CI 2.0, 9.1) versus 1.4% (95% CI 0.2, 2.6) in normal weight subjects.

Relationship between BMI, gastrointestinal symptoms, and other exposure factors
In the total cohort, the distribution of individual gastrointestinal symptoms by BMI categories is summarised in table 3. There were significant associations between obesity and GORS (OR 2.05 (95% CI 1.39, 3.01)), epigastric pain (OR 1.63 (95% CI 1.05, 2.55)), IBS (OR 1.58 (95% CI 1.05, 2.38)), any abdominal pain (OR 1.59 (95% CI 1.08, 2.35)), vomiting (OR 3.11 (95% CI 1.18, 8.20)), retching (OR 1.74 (95% CI 1.13, 2.67)), diarrhoea (OR 2.21 (95% CI 1.38, 3.46)), any stool urgency (OR 1.60 (95% CI 1.04, 2.47)), nocturnal urgency (OR 2.57 (95% CI 1.33, 4.98)), and feelings of incomplete rectal evacuation (OR 1.64 (95% CI 1.09, 2.47)), adjusting for age, sex, and education (table 4). When subjects with oesophagitis, peptic ulcer, and cancer at endoscopy were excluded, diarrhoea (OR 1.94 (95% CI 1.13, 3.32)), feelings of incomplete rectal evacuation (OR 1.68

### Table 1
**Distribution of demographic variables by body mass index (BMI) categories**

<table>
<thead>
<tr>
<th>BMI category</th>
<th>Age &lt; 54*</th>
<th>Age &gt; 54*</th>
<th>Sex Female*</th>
<th>Sex Male*</th>
<th>Education Low*</th>
<th>Education High*</th>
<th>Smoking†</th>
<th>Alcohol/week &lt; 100 g*</th>
<th>Alcohol/week &gt; 100 g*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>8 (0.3–1.4)</td>
<td>0.8 (0.0–0.16)</td>
<td>0.4 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>365 (0.3–1.4)</td>
<td>200 (0.0–0.16)</td>
<td>0.4 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
</tr>
<tr>
<td>Overweight</td>
<td>456 (0.3–1.4)</td>
<td>211 (0.0–0.16)</td>
<td>0.4 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
</tr>
<tr>
<td>Obese</td>
<td>162 (0.3–1.4)</td>
<td>72 (0.0–0.16)</td>
<td>0.4 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
<td>0.7 (0.0–0.1)</td>
</tr>
</tbody>
</table>

*Prevalence and 95% confidence interval (CI)/column.
†Current smokers at the time of endoscopy.

### Table 2
**Prevalence (%) of peptic ulcer disease, oesophagitis, and gastric cancer in different body mass index (BMI) categories**

<table>
<thead>
<tr>
<th>Endoscopic finding</th>
<th>BMI category (n %)</th>
<th>BMI category (n %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Underweight (n = 456)</td>
<td>Normal (n = 365)</td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td>0 (0)</td>
<td>5 (1.4)</td>
</tr>
<tr>
<td>Duodenal ulcer</td>
<td>0 (0)</td>
<td>7 (1.9)</td>
</tr>
<tr>
<td>Oesophagitis</td>
<td>1 (12.5)</td>
<td>34 (9.3)</td>
</tr>
<tr>
<td>Cancer</td>
<td>0 (0)</td>
<td>1 (0.2)</td>
</tr>
</tbody>
</table>

*Prevalence and 95% confidence interval (CI)/column.
Medication use, BMI, and reflux

Use of acid reducing drugs was a significant predictor for overall GORS (OR 9.8 (95% CI 6.5, 14.7)) and for the following individual symptoms: heartburn (OR 6.4 (95% CI 4.5, 9.2)), acid regurgitation (OR 6.2 (95% CI 4.3, 8.8)), and retching (OR 3.0 (95% CI 2.1, 4.2)). Drugs that potentially reduce LOS pressure (nitrates (n = 24), theophylline (n = 10), calcium channel blockers (n = 44), opiates (n = 20), beta agonists (n = 22), phenothiazines (n = 2), tricyclic antidepressants (n = 2), nicotine substitutes (n = 0), anticholinergics (n = 0), and benzodiazepines (n = 2)) as a group were univariately associated with the symptom of a burning feeling rising in the chest (Carlsson-Dent question) (OR 1.8 (95% CI 1.1, 3.1)) and with central chest pain (OR 1.6 (95% CI 1.0, 2.6)), but were not significantly associated with overall GORS. Only calcium channel blockers (OR 3.0 (95% CI 1.5, 5.9)) were univariately associated with the symptom of a burning feeling rising in the chest; none of the other individual drug classes was significant. LOS relaxing drugs were not individually or as a group significantly associated with oesophagitis. Adjusting for medication use, the association between GORS and being overweight remained significant (OR 1.4 (95% CI 1.04, 2.0)) and similarly, the association between GORS and obesity remained significant (OR 1.9 (95% CI 1.3, 3.0)). The association between oesophagitis and BMI did not alter substantially adjusting for medication use (OR for overweight 1.7 (95% CI 1.1, 2.6) and OR for obesity 3.4 (95% CI 2.0, 5.8)).
DISCUSSION

We have examined the associations between gastrointestinal symptoms and BMI in a population sample who were then investigated for an upper gastrointestinal tract structural explanation by oesophagogastroduodenoscopy. We found that reflux symptoms were linked to obesity and specifically, the presence of GORS was linked to reflux oesophagitis in the present study. However, others have reported concordant observations.\(^\text{16–18}\) The finding of a link between obesity and diarrhoea, however, has now been confirmed in three population based studies, although these were all in uninvestigated subjects.\(^\text{16–18}\) Crowell et al also observed more frequent lower gastrointestinal symptoms in overweight females attending a weight management centre compared with normal weight women recruited from the community,\(^\text{40}\) although obese patients seeking treatment may not be representative of obese individuals in the community. Why does diarrhoea occur in obesity rather than, as might be expected in this generally more sedentary population, constipation? We hypothesise that excess intake of poorly absorbed products causing osmotic diarrhoea could explain the increased lower gastrointestinal symptoms in obesity. For example, there has been a very substantial increase in the use of corn syrup containing fructose in the USA, and excess ingestion of this could induce fructose malabsorption.\(^\text{41,42}\) Other mechanisms that might explain the increased bowel frequency associated with increased BMI include abnormal bile salt turnover because of rapid small intestinal transit or rapid gastric emptying, which has been reported in some groups of obese patients.\(^\text{41,42}\) Obesity was also associated with symptoms consistent with IBS in the present study. However, whether obesity is truly linked to IBS remains unclear; we did not apply the Rome II criteria for IBS as the questionnaire

<table>
<thead>
<tr>
<th>Table 4: Association of individual gastrointestinal symptoms with being overweight and obese based on BMI versus those of normal weight, among the study subjects (n=973)</th>
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</thead>
<tbody>
<tr>
<td>Symptom</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Weight loss</td>
</tr>
<tr>
<td>Anorexia</td>
</tr>
<tr>
<td>Un accounted feeling of fullness</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
</tr>
<tr>
<td>Retching</td>
</tr>
<tr>
<td>Acid regurgitation</td>
</tr>
<tr>
<td>Early satiation</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Heartburn</td>
</tr>
<tr>
<td>Central chest pain</td>
</tr>
<tr>
<td>Burning feeling rising in chest</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Alternating constipation/diarrhoea</td>
</tr>
<tr>
<td>Feeling incomplete rectal evacuation</td>
</tr>
<tr>
<td>Pain at defecation</td>
</tr>
<tr>
<td>Pain relieved by defecation</td>
</tr>
<tr>
<td>Straining</td>
</tr>
<tr>
<td>Urgency</td>
</tr>
<tr>
<td>Flatus</td>
</tr>
<tr>
<td>Borborygmi</td>
</tr>
<tr>
<td>Abdominal distension</td>
</tr>
<tr>
<td>Nightly urge to defecate</td>
</tr>
<tr>
<td>Black stools</td>
</tr>
<tr>
<td>Blood in stool</td>
</tr>
<tr>
<td>Mucous</td>
</tr>
<tr>
<td>Epigastric pain</td>
</tr>
<tr>
<td>Dyspepsia</td>
</tr>
<tr>
<td>IBS</td>
</tr>
<tr>
<td>Abdominal pain</td>
</tr>
</tbody>
</table>

Logistic regression adjusted for education, age and sex.
OR (95% CI) odds ratio (95% confidence interval).
IBS, irritable bowel syndrome; GORS, gastro-oesophageal reflux symptoms.
was not designed to assess these specifically. Others have observed a trend for more IBS symptoms in obesity but this has yet to be confirmed, and severe obesity has not been studied.45

Mechanisms that control food intake and energy expenditure may be dysregulated in obesity. A number of hormonal satiation factors, including cholecystokinin, enterostatin, and peptide YY from the gut, may contribute to meal termination, and thus may influence meal size.46 47 Whether a decreased satiation response to food intake plays a role in the development of obesity is uncertain.48 49 Early satiation, defined as an inability to finish a normal size meal, has been linked to impaired fundic accommodation in some studies although not all studies agree and the association is controversial.50 51 For this reason, we investigated the association between obesity and the symptom early satiation; we speculated there would be more people with this symptom in those who were normal weight and less in the obese group. However, we did not observe increased reporting of early satiety in normal weight persons. This is contrary to previous observations in uninvestigated subjects with obesity52 53; whether this reflects population or measurement differences is unknown.

Obesity is now considered to be a major health problem worldwide. Data from the National Centre for Health Statistics show that 31% of the US population aged 20 years or above is clinically obese (BMI ≥ 30 kg/m²).54 The prevalence of obesity in Northern Sweden was less (16%) but still substantial; moreover, the rates of obesity in this cohort were only modestly higher than those reported across Sweden as a whole (10%).55 The present study had a number of other strengths. The ASQ is a reliable and adequately validated measure.56 57 The study was performed in the northern part of Sweden, but the population studied appears to be representative of the Swedish population in terms of most sociodemographic factors, and the response rates were excellent. The proportion with higher education was slightly lower in these communities and a low education rates were excellent. The proportion with higher education appears to be representative of the Swedish population in Sweden and thus may influence meal size.56 57 Whether a decreased satiation response to food intake plays a role in the development of obesity is uncertain.50 51 For this reason, we investigated the association between obesity and the symptom early satiation; we speculated there would be more people with this symptom in those who were normal weight and less in the obese group. However, we did not observe increased reporting of early satiety in normal weight persons. This is contrary to previous observations in uninvestigated subjects with obesity52 53; whether this reflects population or measurement differences is unknown.

In conclusion, in this population based study, reflux symptoms were independently associated with BMI. Importantly, the association was explained by increased upper endoscopy findings in obesity.

ACKNOWLEDGEMENTS
This study was supported in part by the Swedish Research Council, the National Board of Health and Welfare, 1998. The study was supported by the Swedish Research Council, the National Board of Health and Welfare, 1998. The present study had a number of other strengths. The ASQ is a reliable and adequately validated measure.56 57 The study was performed in the northern part of Sweden, but the population studied appears to be representative of the Swedish population in terms of most sociodemographic factors, and the response rates were excellent. The proportion with higher education was slightly lower in these communities and a low education rates were excellent. The proportion with higher education appears to be representative of the Swedish population in Sweden and thus may influence meal size.56 57 Whether a decreased satiation response to food intake plays a role in the development of obesity is uncertain.50 51 For this reason, we investigated the association between obesity and the symptom early satiation; we speculated there would be more people with this symptom in those who were normal weight and less in the obese group. However, we did not observe increased reporting of early satiety in normal weight persons. This is contrary to previous observations in uninvestigated subjects with obesity52 53; whether this reflects population or measurement differences is unknown.

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REFERENCES
EDITOR’S QUIZ: GI SNAPSHOT

A case of jaundice with a mediastinal mass

Clinical presentation
An elderly male presented with acute upper abdominal pain and tenderness with dyspnoea. On examination he had tachypnoea, tachycardia, hepatomegaly, and tenderness in the right upper quadrant and epigastrium. He also appeared jaundiced and had peripheral oedema of the lower limbs.

Laboratory findings were: aspartate transaminase 118 IU/l (normal range 0–32); alkaline phosphatase 430 IU/l (normal range 0–320); bilirubin 40 µmol/l (normal range < 20).

Chest radiograph performed at presentation suggested a large lobulated mass involving the pericardium causing luminal compromise of the atria. (B) Coronal reformatted image along the plane of the right atrium and inferior vena cava shows large mass (arrow) with near total obliteration of the right atrial chamber.

Question
What is the diagnosis?
See page 1390 for answer

This case is submitted by:

R Sinha
Department of Radiology, Glenfield Hospital, Leicester, UK

D Clarke
Department of Radiology, Derby City General Hospital, Derby, UK

Correspondence to: Dr R Sinha, Department of Radiology, Glenfield Hospital, Leicester LE3 9QP, UK; rakesh.sinha@uhl-tr.nhs.uk
doi: 10.1136/gut.2005.066134

Figure 1 (A) Large lobulated mass involving the pericardium causing luminal compromise of the atria. (B) Coronal reformatted image along the plane of the right atrium and inferior vena cava shows large mass (arrow) with near total obliteration of the right atrial chamber.