

A 13-NATION POPULATION SURVEY OF UPPER GASTROINTESTINAL SYMPTOMS: PREVALENCE OF SYMPTOMS AND SOCIOECONOMIC FACTORS

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A 13-NATION POPULATION SURVEY OF UPPER GASTROINTESTINAL SYMPTOMS: PREVALENCE OF SYMPTOMS AND SOCIOECONOMIC FACTORS

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Revised manuscript APT-0871-2010-R2 for publication in: 13-Dec-10 Aliment Pharm & Ther A 13-NATION POPULATION SURVEY OF UPPER GASTROINTESTINAL SYMPTOMS: PREVALENCE OF SYMPTOMS AND SOCIOECONOMIC FACTORS Short-title: A 13-nation study on upper GI symptoms Keywords: gastroesophageal reflux, epidemiology, upper gastrointestinal symptoms Sebastian Haag (1), Jane M Andrews (2), Judith Gapasin (2, 3), Guido Gerken (1), Andreas Keller (4), Gerald Holtmann (5) (1) Dept. of Gastroenterology and Hepatology, University Hospital Essen, Essen, Germany (2) Dept of Gastroenterology and Hepatology, Royal Adelaide Hospital and School of Medicine, University of Adelaide, SA, Australia (3) Institute of Digestive Diseases, St. Luke's Medical Center, Quezon City, Philippines (4) Nycomed International, Switzerland (5) University Hospital Essen and University of Adelaide, Faculty of Health Sciences, Adelaide, Australia Address for correspondence: Prof Gerald Holtmann. MD, PhD, MBA, FRCP, FRACP

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SUMMARY

Background: <u>We aimed to</u> determine the prevalence of upper gastrointestinal (UGI) symptoms in 13 European countries and the association between socioeconomic factors and symptoms using a standardised method.

Methods: A representative age- and gender stratified sample of 23.110 subjects (aged 18-69 years) was surveyed.

Results: The prevalence of UGI symptoms was 38%. UGI symptoms were most prevalent in Hungary (45.3%, 95% confidence interval (CI) 42.2-48.4) and lowest in the Netherlands (23.6%, 95%CI 21.0-26.2). UGI symptoms were more prevalent in females (39%, 95%CI 38.4-39.6) vs. males (37%, 95%CI 36.4-37.6). Heartburn (24%, 95%CI 23.4-24.6) and acidic reflux (14%, 95%CI 13.6-14.4) were most common. With age, the prevalence of UGI symptoms decreased (e.g. 18-29 yrs: 42.8%, 95%CI 41.4-44.3 vs. 50-69yrs: 33.4%, 95%CI 32.3-34.4); in contrast, the frequency of symptom episodes/year increased with age (e.g. 18-29yrs: 11.3 episodes per years, 95%CI 10.5-12.1 vs. 50-69 yrs: 21.8, 95%CI 20.7-22.9). Socioeconomic status as measured by gross domestic product was inversely associated with symptoms and in total, socioeconomic factors, gender, body mass index, smoking habits and alcohol consumption explained 83.4% of the variance of UGI symptoms.

Conclusions: There are marked differences in the country specific prevalence of UGI complaints. Socioeconomic factors are closely associated with the prevalence of UGI symptoms.

INTRODUCTION

Upper gastrointestinal (UGI) symptoms such as heartburn, acidic reflux, indigestion, epigastric pain and/or discomfort are common and widely prevalent. They present with a broad spectrum of intensity and/or frequency

While chronic or relapsing UGI symptoms including symptoms of gastrooesophageal reflux (GOR) are most frequently due to so called functional gastrointestinal disorders or gastroesophageal reflux disease (GORD), they significantly impair health-related quality of life and cause a significant burden to society due to reduced work productivity and increased health-care resource utilization (1-5). Studies from specific countries and *post-hoc* analyses reported that the prevalence of dyspepsia, (upper) abdominal pain and the severity of reflux symptoms decreases with advancing age (6-9). However, despite their decreasing overall prevalence, more serious GORD-complications like complicated ulcers (i.e. life-threatening bleeding) and adenocarcinoma (10) appear to occur predominantly in elderly patients (11).

The prevalence of GORD is currently estimated to be in the range from 10-20% (12), but a recent systematic review suggested significant geographic variations (13). Other studies suggest an increase of GORD prevalence in recent years (14;15). However, studies on the influence of age and gender on GORD and GOR symptoms have yielded inconsistent results (13;16-18) and a low

socioeconomic status has been reported to be associated with upper GI symptoms in some countries (3;19).

Therefore <u>we aimed to</u> assess the prevalence of upper GI symptoms and the influence of age and gender on upper gastrointestinal symptoms in 13 European countries using a standardized previously validated methodology. Furthermore we assessed the influence of socioeconomic variables (individual income, individual education level as well as gross domestic productivity, use of telephones [main lines, cell phones], internet use, and electricity consumption) on the prevalence of UGI symptoms in these countries.

METHODS

Subjects

Data were assessed by an online survey with a total of 23.110 interviews taken in a panel of overall 662.700 subjects which represent age- and gender stratified cohorts that are representative for the respective 13 countries. Subjects were members of a fixed panel, and a subset of panellists (n=33135, 5%) was invited to participate in this survey by mail, randomly selected from a telephone directory from the overall panel. To take part in this study, an internet access was required; however, subjects were free to enter this study at any computer with internet access. Predefined numbers of subjects for the various age-strata were included and upon achievement of the predefined numbers, strata were closed. Thus, even if all invited panellist would possibly be interested to take part in this

study, no further study entry was possible. All completed interviews were gratified with a voucher, valued €5. Countries included were Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Italy, Netherlands, Poland, Portugal, Spain and Switzerland. To ensure a sufficient statistical power, sample size were > 1.000 per country, while the five largest European countries (France, Germany, Italy, Poland, and Spain) had samples of more than 3.000 subjects each.

The individual highest achieved educational level and actual income were also documented. Data on gross domestic product (GDP) and GDP per capita (purchase power parity); mean body mass index (BMI, kg/m²), current tobacco use in adults >15yrs; per capita alcohol consumption (litres of pure alcohol) in adults >15yrs; use of telephones [main lines in use, mobile cellular] (million); internet users (million) and electricity consumption (billion kWh) in the various countries were acquired from available sources (20;21).

Upper gastrointestinal symptom questionnaire

The questions were designed by a group of experts in the field. Internal consistency was reviewed by a steering committee consisting of natives from all countries involved in this trial. After testing for test-retest reliability, the questions were utilized. Two days after study begin, a plausibility check was done to test for responsiveness and construct validity.

Assessment of the predominant upper gastrointestinal symptom

In the questionnaire, the following definitions were used to assess the key UGI symptoms. Heartburn was defined as a restrosternal burning sensation (behind the breastbone). Stomach acid complaints were defined as symptoms (pain, burning sensation) between the region of the umbilicus and lower end of the sternum, marked by the medioclavicular lines. Reflux/ acid taste in the mouth was defined as regurgitation of liquid gastric content into the oesophagus/ mouth. Dyspepsia was defined as pain or discomfort in the upper abdomen.

Statistical analysis

Demographical data are reported as the mean and standard deviation for numerical factors and as percentages and 95% confidence intervals (CI) for discrete characteristics. Initial bivariate categorical associations were tested for using the chi-squared test and continuous data by the Student's *t*-test or non-parametric tests when appropriate. All p-values calculated were two-tailed and the α -level was set at 5%. After testing for distribution, multivariate correlation analysis was performed. Two multiple linear regression models assessed the associations of age, gender and socioeconomic variables with the prevalence of any UGI symptom (model 1) and dyspeptic symptoms (model 2). The associations are reported using partial r^2 values, adjusted for all other variables in the model. All analyses were performed with the Statistical Package for the Social Sciences 17.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Prevalence of upper GI symptoms across countries

While upper gastrointestinal and dyspeptic symptoms were highly prevalent in all thirteen countries (overall 37.8%, 95%Cl 37.2-38.4 and 11.8%, 95%Cl 11.4-12.2), there were marked differences in the prevalence of symptoms, e.g. dyspeptic symptoms ranging from 23.6% in the Netherlands up to 45.3% in Hungary (table 1). The predominant symptoms in all countries were heartburn and symptoms of gastrointestinal reflux (table 1). In subjects with heartburn, symptoms occurred on average 16.5±41.2 times during the previous 12 months (figure 1).

The influence of age and gender on upper GI symptoms

Overall, females reported a greater prevalence of UGI symptoms than men (table 1). Interestingly, this was not true in all countries with men in Belgium and Poland, having a higher prevalence of UGI symptoms than females. Women also generally experienced a greater frequency of UGI symptoms compared to men (figure 2). Twenty-seven percent of women (95%CI 26.2-27.8) and 22% men (95%CI 21.2-22.8) reported 13 or more episodes of UGI symptoms. With increasing age, the number of UGI symptom episodes per year increased significantly. Considering the most prevalent UGI symptom "heartburn", the mean frequency of symptomatic episodes was significantly greater in women than in men (18.1±43.5 vs. 14.7±38.5 episodes/ 12 months) and increasing with age.

Overall, the prevalence of UGI symptoms decreased from 42.8% in the group of subjects between 18-29 yrs to 32.9% in the 50 to 69yrs old group (p<0.001). The age related decrease of symptoms was in particular clear for heartburn and dyspepsia while reflux and stomach acid complaints were not affected by age (figure 3).

The influence of socioeconomic variables on upper GI symptom prevalence In the bivariate analyses UGI symptoms and dyspepsia were significantly and negatively correlated with GDP per capita (r=-0.579, p=0.004, figure 4), highest achieved level of education (r=-0.397, p=0.02), number of phones (main lines in use, r=-0.122, p=0.02) and internet use (r=-0.152, p=0.02) as indirect markers of a high socioeconomic status and positively with body mass index (r=0.180, p=0.04), smoking habits (r=0.176, p=0.33), alcohol consumption (r=0.334, p=0.01), proportion of subjects with a monthly income of less than \in 1500 (r=0.507, p=0.01, figure 5). After adjusting for age, gender and body mass index, smoking and alcohol consumption were no longer significantly associated with either UGI symptoms or dyspepsia (table 2). However, there was a trend for alcohol consumption being associated with dyspepsia, but it failed to reach statistical significance. Similar associations were found for dyspepsia (data not shown).

The per capita GDP was negatively correlated with UGI symptoms and dyspepsia. After stratification for individual income, subjects with a monthly income of less than 1500€/month reported higher rates of UGI symptoms or

dyspepsia compared to those with a monthly income > 1500€/month. The overall numbers of phones (main lines in use) as well as internet use were negatively correlated with UGI symptoms in general, and along with electricity consumption were negatively correlated with dyspepsia in particular.

DISCUSSION

In our study, utilising a large age and gender stratified sample from thirteen countries, the overall prevalence of upper gastrointestinal symptoms was 38% with a marked inter-country variation. However, our data clearly support the notion that there are marked geographic differences in the prevalence of UGI symptoms. Even more importantly besides well recognised risk factors such as BMI and alcohol or nicotine consumption, dyspepsia and the prevalence of UGI symptoms are inversely associated with the GDP per capita and other indicators of wealth such as education, electricity consumption per capita and other markers. This association was still evident after adjusting for potential confounding factors.

In all countries, acidic reflux and heartburn were the most prevalent symptoms. All symptoms were more prevalent in females. While the proportion of subjects with symptoms decreased with age, symptom episodes were more frequent in the elderly. Relationships between age and gastrointestinal symptoms have been previously reported (3;22). However, different studies have found different relationships between aging and the prevalence of UGI symptoms, with some studies finding an increasing prevalence with age until the age of 69 or 55 years, from which point the trend was reversed (3;13), whereas in the Kalixanda study the prevalence decreased even for subjects above 34 years (23), and others who did not report an association of GOR symptoms with age (24). The reasons for the variation between studies and countries, in this relationship amongst ageing and UGI symptoms, are still unknown and need to be elucidated further.

Very recently one study by Gururatsakul et al. (25), demonstrated diminished sensory responses in elderly patients with peptic ulcer disease and elder healthy controls as compared to younger patients and controls. Thus the decrease in the prevalence of dyspeptic symptoms in the elderly might be explained by diminished sensory responses (or a decreased prevalence of functional GI disorders). The decrease of symptoms in the elder subjects thus occurs despite of the well known fact, that the prevalence of *H. pylori* is higher in the elderly as compared to younger subjects. In additions elderly are more likely to be on medications that may cause dyspepsia (e.g., non-steroidal anti-inflammatory drugs, bisphosphonates) that increase their risk for dyspeptic symptoms and acid-related disorders (26-28). On the other hand, difference in the *H. pylori* prevalence and differences in the alcohol consumption - while not specifically assessed in our study – might be potential.

In our study, the associations between symptoms and smoking or alcohol consumption did not yield significance. On the other hand, an association with GORD symptoms and smoking has been reported previously (22;29), while the results of an association of GORD symptoms with alcohol consumption are still controversial. The Georgia Medicaid study identified a significant association between a GORD diagnosis and alcohol consumption with an OR 1.8 (95% CI 1.4–2.4). Another study, also, found an association between GORD and alcohol consumption, but only if it was judged excessive (30). In contrast, alcohol consumption did not significantly affect the risk of a first time diagnosis of GORD in data from the UK GP database study (22). An excess body mass/ higher body mass index has been reported to be associated with the prevalence of GORD (18;30;31), although the OR was small (OR 1.3 (95%CI 1.2–1.4) for BMI >25 and OR 1.3 (95%CI 1.2–1.5) for BMI >30) (22).

In our study, upper GI symptom prevalence was inversely associated with educational level. This is in line with some data from EI Serag et al. (31) and Isolauri et al. (18). However, neither the lowest, nor the highest achieved level of education but rather, graduation from senior high school, was negatively associated with upper GI symptom and dyspepsia prevalence in our study. However, this association was observed in the univariate analysis, but did not significantly affect the upper GI symptom prevalence in the multivariate analysis. The reason for this finding might be the correlation of educational level and monthly income, which also ultimately affect nutritional factors, which were not

assessed in this study. We furthermore analyzed the association of individual monthly income with the prevalence of symptoms and demonstrated that a monthly income of less than €1499 was associated with higher rates of upper GI symptoms, while an income exceeding €1500/month was negatively associated with these symptoms. There was also a significant negative association between gross domestic productivity and the reported prevalence of upper GI symptoms and dyspepsia.

To determine whether a higher social status/ income may also result in an increased intake of antacids, we assessed the individual medication taken for upper GI symptoms in various countries. However, we did not find a significant association of PPI use with a decreased rate of upper GI symptoms or dyspepsia, while the use of H2RAs and antacids were associated with higher rates of upper GI symptoms and dyspepsia. Due to the nature of the study, individual co-medication as well as current or past medical history were not assessed. However, it is unlikely that these potential confounders significantly influenced our results.

While our results are based on very large stratified cohorts, there are some limitations of this study that need consideration. The nature of online surveys requires internet access. However, since the subjects were randomly selected from a telephone directory and received their invitation per mail, a personal internet access which may cause bias, was not necessarily required but the questionnaire could have been assessed and answered from any computer with internet access. In our study, predefined numbers of subjects for the various agestrata were included and upon achievement of these predefined numbers, the strata were closed. Therefore data on response rates are not available. Incentives are often used to maximize study participation in epidemiological studies which in turn raises the question of selection bias. Because bias is

closely linked to the value of the incentive, we have rewarded study participation with a €5 voucher to compensate potential costs associated with study participation only, as previous studies have demonstrated that low-price vouchers are not causing a significant selection bias (32). The questionnaire only included four predominant upper gastrointestinal symptoms (heartburn, stomach acid complaints, reflux/ acid taste in the mouth and dyspepsia). Whilst focusing on these core symptoms appears justified by the results of a recent factor analytic study that revealed that these as main factors for the assessment of upper GI symptoms (33), it is possible that the lack of assessment of other symptoms has limited our understanding of all UGI symptomatology. In our study, for example, we did not assess extra-oesophageal symptoms. On the other hand it can be argued that members of a panel for questionnaire studies are likely to talk about their health and we may thus have overestimated the prevalence of UGI symptoms. We found various associations between sociodemographic and ecologic data and GI symptoms. While it is very unlikely that e.g. the number of mobile phones per 1000 directly affects GI symptoms or underlying disease, there are many factors that might be correlated with mobile utilization that ultimately affect the symptom manifestation. However, the key finding of our study is the fact that beyond reasonable doubt, environmental factors are associated with symptoms. Thus, the ecologic "indicators" tested are indeed linked with the prevalence of symptoms. However, despite these limitations, our findings are in accordance with population- based studies from various Western nations (3;7;18;24;34-36).

In summary, there are marked differences in the country specific prevalence of upper GI complaints. These differences are associated with socioeconomic indicators such as the GDP per capita. Whether these socioeconomic factors and the prevalence of UGI symptoms are linked via specific environmental factors (e.g. nutritional) needs to be elucidated further.

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Tables, Figures

Table 1: Prevalence rates of upper gastrointestinal symptoms (%, 95%CI)

	Overall (n=23.163)	Austria (n=1.000)	Belgium (n=1.010)	Denmark (n=1025)	Finland (n=1014)	France (n=3.020)	Germany (n=3.000)
Any upper GI symptom	37.8 [37.2-38.4]	36.8 [33.8-39.8]	35.1 [32.1-38.1]**	25.4 [22.7-28.1]***	36.4 [33.4-39.4]	36.4 [34.7-38.1]	34.2 [32.5-35.9]*
heartburn	24.2 [23.6-24.8]	21.4 [18.9-23.9]**	20.0 [17.5-22.5]***	16.2 [13.9-18.5]***	30.9 [28.0-33.8]***	17.0 [15.7-18.3]***	23.7 [22.2-25.2]
stomach acid complaints	13.0 [12.6-13.4]	16.3 [14.0-18.6]***	15.4 [13.2-17.6]***	7.5 [5.9-9.3]***	11.7 [9.7-13.7]*	23.4 [21.9-24.9]***	12.3 [11.1-13.5]
reflux/ acid taste in the mouth	14.2 [13.7-14.7]	13.4 [11.3-15.5]	15.7 [13.4-18.0]*	14.7 [12.5-16.9]	9.4 [7.7-11.4]***	16.9 [15.6-18.2]***	12.1 [10.9-13.3]'
dyspepsia	11.8 [11.4-12.2]	7.5 [5.9-9.3]***	9.7 [7.9-11.7]**	1.9 [1.2-3.0]***	3.0 [2.0-4.3]***	7.5 [6.6-8.5]***	8.0 [7.1-9.0]***
females	38.9 [38.3-39.5]	37.3 [33.2-41.6]*	31.4 [27.3-35.5]***	26.1 [22.3-30.1]***	37.6 [33.4-41.8]	37.8 [35.3-40.3]	34.6 [32.2-37.0]*
males	36.7 [36.1-37.3]	36.3 [32.2-40.6]	38.7 [34.5-43.1]	24.8 [21.0-28.6]***	35.2 [31.0-39.4]*	35.0 [32.6-37.4]*	33.9 [31.5-36.3]
Prevalence of upper (GI symptoms by age						
18-29 yrs	42.8 [42.2-43.4]	49.6 [43.4-55.8]**	43.2 [37.1-49.3]	31.5 [25.8-37.4]***	38.8 [32.8-44.8]*	44.1 [40.6-47.7]	36.7 [33.2-40.1]*
30-39 yrs	41.6 41.0-42.2	36.9 30.8-42.8	34.8 [28.9-40.7]***	28.5 [22.8-34.0]***	43.4 [37.5-49.7]	37.1 33.6-40.5	38.3 34.8-41.7
40-49 yrs	37.4 36.8-38.0	29.4 23.6-34.8	32.4 26.6-38.2 **	20.7 [15.8-25.8]***	37.6 31.6-43.6	38.2 34.8-41.7	34.6 31.3-38.1
50-68 yrs	32.9 32.3-33.5	35.0 29.3-41.1	32.7 27.0-38.6	23.6 18.3-28.9	31.1 25.5-36.9	30.4 27.1-33.7	30.5 27.2-33.8

	Hungary (n=1.020)	ltaly (n=3.018)	Netherlands (n=1.010)	Poland (n=3.015)	Portugal (n=1.017)	Spain (n=3.003)	Switzerland (n=1.011)
Any upper GI symptom*	45.3 [42.2-48.4]***	43.3 [41.5-45.1]***	23.6 [21.0-26.2]***	44.5 [42.7-46.3]***	29.0 [26.2-31.8]***	43.0 [41.2-44.8]***	27.4 [24.6-30.2]***
heartburn	21.1 [18.6-23.6]**	29.6 [28.0-31.2]***	9.1 [7.4-11.1]***	29.0 [27.4-30.6]***	18.9 [16.5-21.3]***	33.5 [31.8-35.2]***	16.2 [13.9-18.5]**
stomach acid complaints	17.4 [15.1-19.7]***	9.1 [8.1-10.2]***	14.1 [11.9-16.3]	10.8 [9.7-11.9]***	4.1 [3.0-5.5]***	8.2 [7.2-9.2]***	10.4 [8.5-12.3]***
reflux/ acid taste in the mouth	12.1 [10.1-14.1]*	17.9 [16.5-19.3]***	4.5 [3.3-6.0]***	14.9 [13.6-16.2]	12.6 [10.5-14.7]	14.5 [13.2-15.8]	10.6 [8.7-12.5]***
dyspepsia	24.9 [22.2-27.6]***	20.9 [19.4-22.4]***	6.5 [5.1-8.2]***	16.8 [15.5-18.1]***	7.0 [5.5-8.8]***	12.6 [11.4-13.8]	5.0 [3.7-6.5]***
females males	49.6 [45.2-54.0]*** 40.8 [36.5-45.1]***	44.6 [42.1-47.1]*** 41.9 [39.4-44.4]***	24.5 [20.8-28.4]*** 22.6 [18.9-26.3]***	44.3 [41.8-46.8]*** 44.6 [42.1-47.1]***	29.3 [25.4-33.4]*** 28.6 [24.6-32.6]***	44.4 [41.9-46.9]*** 41.7 [39.2-44.2]***	29.6 [25.6-33.6]** 25.2 [21.4-29.0]**
Prevalence of upper (GI symptoms by age						
18-29 yrs	50.2 [44.2-56.6]***	46.7 [43.1-50.2]**	27.7 [22.1-33.1]***	54.5 [51.0-58.1]***	27.7 [22.1-33.1]***	43.9 [40.3-47.4]*	26.3 [20.9-31.9]**
30-39 yrs	49.6 [43.4-55.8]***	47.6 [44.0-51.2]***	29.8 [24.3-35.7]***	51.8 [48.3-55.4]***	28.7 [23.2-34.4]***	47.9 [44.3-51.4]***	26.9 [21.3-32.3]**
40-49 yrs	43.4 [37.5-49.7]**	44.4 [40.8-48.0]***	20.9 [15.8-25.8]***	40.6 [37.2-44.2]**	34.0 [28.1-40.0]	42.5 [39.0-46.1]***	27.0 [21.7-32.7]**
50-68 yrs	41.0 [35.1-47.3]***	38.0 [34.5-41.5]***	19.4 [14.7-24.5]***	35.1 [31.7-38.5]	26.7 [21.3-32.3]**	38.8 [35.3-42.3]***	28.4 [22.8-34.0]**

CI = Confidence Interval; GI = gastrointestinal

*p<0.05, **p<0.01, ***p<0.001 compared to overall results

TABLE 2: Final model to predict the prevalence of any upper GI symptom and dyspeptic symptoms. R² values from the multiple linear regression models reflect all variables included in the model. (GDP = Gross Domestic Product, purchase power parity adjusted).

	Any upper GI symptom				Dyspeptic symptoms		
Variable	R ²	r (two-t	p-value ailed)	R ²	r (two-t	p-value ailed)	
Age	1.4	-0.120	0.59	0.3	-0.059	0.79	
Body Mass Index	0.6	-0.80	0.72	2.9	-0.171	0.43	
Prevalence of current tobacco use in adults >15yrs both sexes	0.6	0.076	0.73	<0.1	0.0	1	
Per capita recorded alcohol consumption (litres of pure alcohol) in adults >15yrs	11.2	-0.334	0.12	16.3	-0.404	0.06	
GDP in \$ per capita 2008	-33.5	-0.579	0.004	-39.8	-0.631	0.001	
Education							
Up to High School degree	15.8	0.397	0.06	17.2	-0.158	0.47	
Income/ Month							
<1500 €	25.7	0.507	0.01	33.8	0.884	<0.001	
Others							
Electricity consumption	-11.2	-0.335	0.12	-35.7	-0.598	0.003	
Telephones - main lines in use	-24.5	-0.495	0.02	-33.5	-0.579	0.004	
Telephones - mobile cellular	-2.6	-0.161	0.46	-15.6	0.394	0.06	
Internet users	-44.8	-0.669	<0.001	-59.8	-0.773	<0.001	

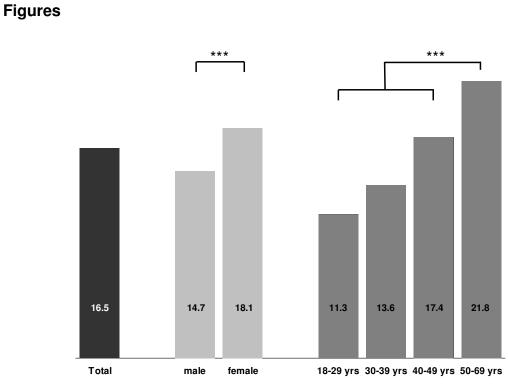


Figure 1: Episodes of heartburn in the previous 12 months (***p<0.001), stratified by age and gender.

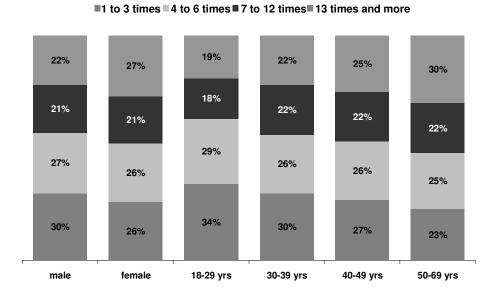
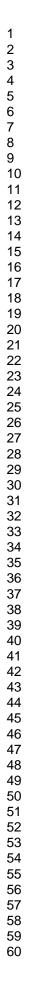


Figure 2: Frequency of upper gastrointestinal symptoms reported in the previous 12 months stratified by age and gender.



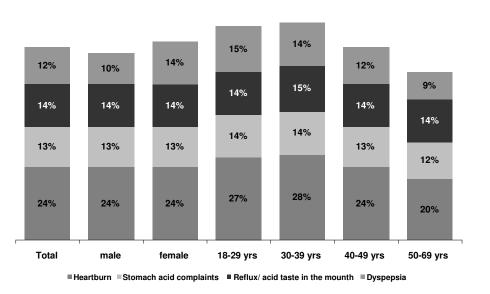


Figure 3: Age- and gender-specific prevalence of upper gastrointestinal symptoms

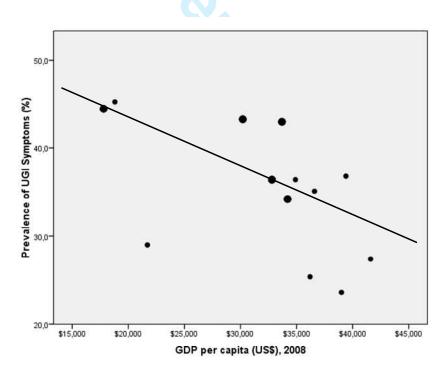


Figure 4: Correlation of Gross Domestic Productivity per capita in \$ with

prevalence of upper GI symptoms. (• = small countries, sample size n=1000; • = large countries, sample size n=3000). r=-0.58, p=0.004.

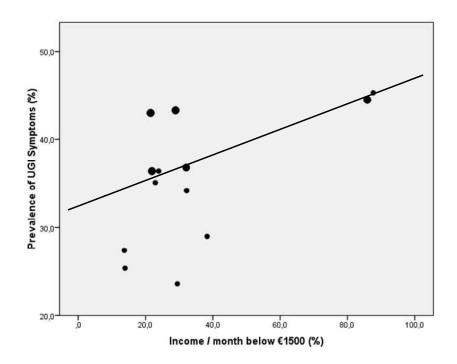


Figure 5: Correlation of income/ month below €1500 with prevalence of upper GI

symptoms. (• = small countries, sample size n=1000; • = large countries, sample size n=3000). r=0.51, p=0.01