

Changes in antacid use over a 9-year period in a general population adjusted for changes in dyspeptic complaints

Kari Furu¹ and Bjørn Straume²

1) Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway

2) Department of Epidemiology and Medical Statistics, Institute of Community Medicine, University of Tromsø, N-9037 Tromsø, Norway

Correspondence: Kari Furu, Division of Epidemiology, Norwegian Institute of Public Health, P.O. Box 4404 Nydalen, N-0403 Oslo, Norway
E-mail: kari.furu@fhi.no

ABSTRACT

Purpose: To explore changes in self-reported use of antacids over a 9-year period in a general population adjusted for changes in dyspeptic complaints.

Methods: Data is based on two health surveys carried out in the same population in Norway in 1987-88 and 1996-97. 15,523 individuals, who responded to the questions concerning drug use in either the first survey and/or in the second survey, were included in the analyses. Generalized estimating equation (GEE) was chosen for the multivariate analyses.

Results: From 1987-88 to 1996-97 the proportion of antacid users in this region increased among men from 11.2% to 12.7% (40-49 years) and from 11.9% to 13.4% (50-59 years), while the proportion of women using antacids decreased. The proportion of antacid users increased with age in both genders. In the same period, the frequency of self-reported dyspeptic complaints such as heartburn decreased. GEE analyses showed an overall increasing trend in antacid use over the 9 years (OR=2.0, 95% CI=1.8, 2.3) adjusted for self-reported heartburn and age. The effect of heartburn on antacid use is very strong (OR=14.6, 95% CI=12.9-16.7). The gender effect indicates that women are less likely to use antacids than men (OR=0.86, 95% CI= 0.77-0.95). Antacid use increased among those with dyspeptic complaints and also among those reporting no dyspeptic symptoms.

Conclusion: The prevalence of antacid users in 1996-97 was higher than in 1987-88 adjusted for age, gender and heartburn. The proportion of antacid users increased among those with dyspeptic complaints and also among those reporting no dyspeptic symptoms.

Key words: Antacid use, dyspeptic complaints, heartburn, longitudinal, generalized estimating equation, pharmacoepidemiology

INTRODUCTION

Antacids have been available for many years, and are still commonly used self-prescribed drugs^{1,2}. However, their importance has diminished since the development of histamine-2-receptor antagonists and more recently proton pump inhibitors. Based on the drug wholesale statistics in Norway, the sale of antacids decreased from 7.6 DDD/1000 inhabitants/day in 1988 to 4.3 DDD/1000 inhabitants/day in 1997^{3,4}. The histamine receptor antagonists (H₂RA) and proton pump inhibitors (PPI) have in the same period increased from 4.0 DDD/1000 inhabitants/day (only H₂RA) in 1988 to 5.2 and 7.8 DDD/1000 inhabitants/day in 1997, H₂RA and PPI, respectively. However, no information regarding drugs used at an individual level is available from the wholesale statistics. Although there are now drugs available that are more effective than antacids in healing ulcers and relieving the symptoms of gastro-oesophageal reflux, many people still use over-the-counter antacids in less severe forms of dyspepsia, especially those suffering from heartburn⁵⁻⁸. Dyspepsia is one of the commonest complaints in the community, usually including all symptoms referable to the upper

gastrointestinal tract. The reported prevalence of dyspepsia varies to some extent depending on the definitions used and also on the period of time patients are under surveillance⁹⁻¹¹. A reduction in the sale of antacids may reflect various changes in individual drug use, i.e. decreasing number of users or smaller doses used. From a Norwegian health survey performed in 1987-88 we have reported a prevalence of antacid use of about 10% in the general population¹². Heartburn was the most important predictor for using antacids in both men and women. The survey was repeated in 1996-97 in the same population thus offering the possibility of performing an analysis of the changes in use of antacids over time corrected for changes in dyspeptic complaints. In this paper we will explore the changes in the prevalence of self-reported use of antacids over a 9-year period in a general population.

MATERIALS AND METHODS

This study is based on data from two population-based health surveys carried out in the same population in the northernmost county of Norway in 1987-88 and 1996-97. The health care system in the region is rela-

tively uniform and almost exclusively public. Financial barriers with regard to the use of health services do not exist.

In the first health survey, 21,066 individuals aged 20-62 years were invited to participate. This part of the survey was, to a large extent, a replication of two former health surveys performed in 1974-1975 and 1977-78, respectively^{13,14}. A detailed presentation of the material and method of the full survey, including analyses of participants who did not answer all three questionnaires, has been published elsewhere^{12,15}. Among those under 40 years a randomised sample was invited whilst all of those 40 years and older were invited to participate. 11,061 individuals who completed and returned a total of three questionnaires (52.5% of those invited) were included in the analyses (figure 1). The survey was repeated nine years later in 1996-97 in the same population where 12,366 individuals aged 20-71 years were invited to participate. 10,509 (85.0% of those invited) attended a physical examination and answered questionnaire 1. In addition 7,880 (63.7% of those invited) answered also a second questionnaire (figure 1). All of those aged 40-42 years were invited, whilst a randomised sample was invited in the other age groups. 4,253 attended and answered the questions regarding use of drugs in both surveys.

One self-administered questionnaire (Questionnaire 1) was part of the letter of invitation in both surveys, whereas supplementary questionnaires were handed out at the survey, and returned in pre-stamped envelopes. The questionnaires provided information on various aspects of health; health status, occurrence of different symptoms, self-reports of a number of diseases and a set of questions on use of drugs.

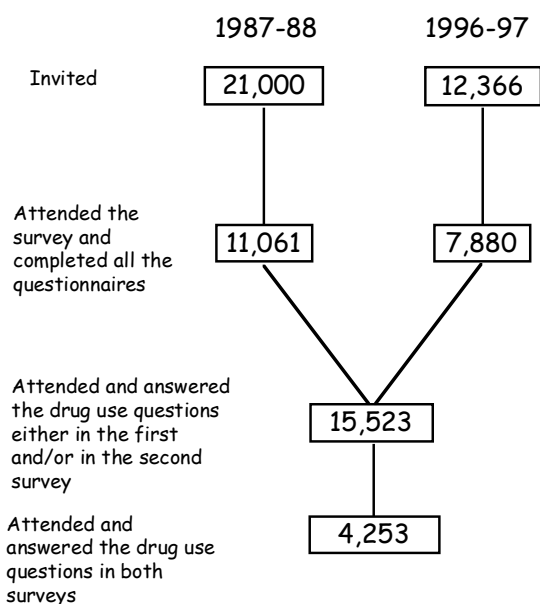


Figure 1. Flow chart for invited and attending individuals in the Finnmark Health Study 1987-88 and 1996-97.

In our study 15,523 individuals who responded to the questions concerning drug use in either the first survey and/or in the second survey, were included in the longitudinal analyses. The participants were asked if they had used any medication from different drug categories specified in the questionnaire assessing drug use. In this study the answer to the following question has been analysed (the same question was used in both surveys): "Have you taken antacids during the preceding 14 days?" Individuals who answered "yes" to the question were defined as users. The others were defined as non-users. In the 1996-97 survey a new question on drug use was added: "Did you use other drugs for peptic ulcer?"

Participants in 1987-88 responded to the following questions about dyspeptic complaints (yes/no):

- *has acid regurgitation or heartburn bothered you?*
- *have you been or are you bothered by pain in the upper abdomen?*
- *have you had an ulcer in your stomach or duodenum?*

Participants in 1996-97 responded to the following three questions about dyspeptic complaints (yes/no):

- Have you in periods had:*
- *pain located to the upper abdomen of at least 2 weeks' duration?*
 - *acid regurgitation or heartburn of at least 1 weeks' duration?*
- Have you during the preceding 5 years been examined for peptic ulcer?*

Those who answered yes to one or more of the above three questions, including the question regarding peptic ulcer, were defined as individuals with dyspeptic complaints. The others were defined as individuals with no complaints.

Both surveys included self-evaluated health, rated as excellent, good, fair or poor. Since heartburn was the strongest predictor for antacid use in the first survey, this variable was included in the multivariate analyses together with period, age and gender. Age is used as a continuous variable in the multivariate analyses.

Statistical methods

All statistical analyses were performed using the SAS statistical package, version 8.02. Differences between proportions were tested by chi square or chi square for trend as applicable. In epidemiology, longitudinal studies have been used in many situations, such as prospective studies of exposure-disease relations, and repeated health services utilisation surveys. Analyses of repeated measures of data need to accommodate the statistical dependence among the repeated observations within individuals¹⁶. The generalized estimating equations (GEE) method of Liang and Zeger is commonly used to estimate population-averaged effects and is suitable for the analyses of repeated measures of binary variables^{17,18}. This method takes into account

the dependency or correlation between the repeated measures by robust estimation of the variances of the regression coefficients¹⁹. While more complex than the traditional approaches, GEE use all available data and can produce more efficient estimates. By using GEE we can utilise the full potential of the longitudinal data. Consequently, the GEE method in the GENMOD procedure was chosen for the multivariate analyses. The working correlation was unstructured. A 0.05 level of significance was used for all the analyses.

The dependent variable is the repeated measure of using antacids at two time points, 1987-88 (T1) and 1996-97 (T2). The independent variables include a period effect, the clinical variable heartburn, age and gender. The period effect implies the changes from T1 to T2. We examined two models. The first model examined the association between use of antacids and period effect, heartburn, gender, and age. There was no significant interaction between period and age. However, significant interactions between period and heartburn, and between period and gender were identified. Therefore, the second model included four separate period effects described by the interaction terms in addition to the main effects of age, gender and heartburn. To allow for different period effects depending on gender and heartburn, four interaction terms were constructed, representing the period effect on antacid use within each combination of gender and heartburn²⁰. The effects of gender and heartburn are average effects over the two periods, thus having the same interpretation as in the first model. The four period effects represented by the interaction variables are computed for individuals who do not change their heartburn status from T1 to T2.

The GEE-analyses were done for both the 15,523 participants and the 4,253 individuals that participated in both surveys and therefore had longitudinal data for all individuals (figure 1).

RESULTS

Table 1 gives the proportion of antacid users stratified by gender and age. There was an increase in the proportion of antacid users over the nine-year period for men from 11.2% to 12.7% (40-49 years) and from 11.9% to 13.4% (50-59 years). There was, however, a weak decrease among women, from 9.3% to 8.8% (40-49 years) and from 11.4% to 10.3% (50-59 years). The proportion of antacid users increased with age in both genders.

Table 2 is confined to individuals that participated and answered the drug use questions in both surveys. Eighty-two % of men and 80% of women reported no use of antacids at any time (p=0.07).

Table 3 gives the proportion of drug users according to dyspeptic complaints. The proportion of antacid users among those with no dyspeptic complaints increased from 1.5% to 4.0%. Among those with one or two dyspeptic complaints there was an increase in the proportion of antacid users, while among those with all three complaints there was practically no change in the proportion of antacid users. In the 1996-97 survey, 146 (1.9%) individuals reported use of other drugs for peptic ulcer and the proportion of users increased with number of complaints (Table 3). Seventy individuals reported simultaneous use of antacids and other drugs for peptic ulcer. Fifty-nine of these had two or more dyspeptic complaints.

Table 2. Use of antacids during the preceding 14 days among participants in both the Finnmark Health Survey **1987-88** and **1996-97** (N=4,253).

	Men	Women
Nonusers of antacids in both surveys	1789 (82.2%)	1662 (80.0%)
Users of antacids only in 1996-97	152 (7.0%)	187 (9.0%)
Users of antacids only in 1987-88	134 (6.2%)	115 (5.5%)
Users of antacids in both surveys	101 (4.6%)	113 (5.4%)

Table 1. Proportion of antacid users during the preceding 14 days according to age and gender. The Finnmark Health Survey **1987-88** (N=11,054) and **1996-97** (N=7859).

Age group	1987-88				1996-97				
	Men n	Antacid users %	Women n	Antacid users %	Age group	Men n	Antacid users %	Women n	Antacid users %
20-39	924	9.7	1019	7.4	20-39	117	5.1	146	7.5
40-49	2216	11.2	2044	9.3	40-49	1716	12.7	1834	8.8
50-59	1821	11.9	1820	11.4	50-59	886	13.4	833	10.3
60-62	598	13.2	612	13.1	60-69	805	13.7	840	12.3
					70-71	300	14.3	382	14.4
20-62	5559	11.4	5495	10.0	20-71	3824	12.9	4035	10.3
p (age trend)		0.02		<0.001			0.08		<0.001
p (gender)			0.02					<0.001	

Table 3. Proportion of antacid users and users of other peptic ulcer agents (%) during the preceding 14 days according to number of dyspeptic complaints. The Finnmark Health Survey 1987-88 and 1996-97.

	1987-88 (N=11,061)		1996-97 (N=7,880)		
	Antacid users		Antacid users	Users of other peptic ulcer agents	
	n	%	n	%	%
No complaint	6388	1.5	5593	4.0	0.1
One complaint	2549	14.0	1299	23.0	2.3
Two complaints	1621	30.0	664	36.0	9.2
Three complaints	503	46.0	324	44.0	15.4
p (trend)		<0.001		<0.001	<0.001

In 1987-88, 42.2% reported one or more dyspeptic complaints while in 1996-97 only 29.0% reported at least one dyspeptic complaint. The prevalence of heartburn decreased from 37.6% to 20.3% and from 33.3% to 20.0% in men and women, respectively. The prevalence of epigastric pain was reduced from 21.9% to 15.8% and from 22.6% to 18.7% in men and women, respectively. The prevalence of self-reported peptic ulcer increased in the same period from 10.4% to 14.6% and from 6.2% to 13.8% in men and women, respectively. Table 4 gives the proportion of antacid users during the preceding 14 days according to specific dyspeptic complaints and self-evaluated health, the 1987-88 and the 1996-97 survey, respectively. The proportion of antacid users among those with complaints of heartburn increased strongly from 26.4% to 42.5% and from 25.9% to 40.7% in men and women, respectively. Among men not reporting heartburn, the proportion of antacid users also increased from 2.5% to 6.2%. However, among those with epigastric pain there was virtually no change in the proportion of antacid users. There were virtually no changes in self-evaluated health from 1987-88 to 1996-97. Neither did the proportion of antacid users change according to self-evaluated health.

Table 5 shows the odds ratios for being an antacid user in two models. The period effect on antacid use gives an OR=2.0 at the second time point (reference is T1), indicating an overall increasing trend in antacid use. The effect of heartburn on antacid use is very strong, OR=14.2, showing that persons reporting heartburn are much more likely to use antacids than those not reporting heartburn. In addition, the odds ratio of gender effect equals 0.86, indicating that women are less likely to use antacids than men. Age is significant ($p<0.001$) in both models, indicating an increase in antacid use with increasing age independent of the period effect. In the model including interaction terms, the increase in antacid use among men without heartburn at any time gives OR=2.9 and among men with heartburn OR=2.0. The increase in antacid use among women without heartburn gives OR=2.0 and among women having heartburn at both time points OR=1.7. The GEE-analyses with the 4,253 individuals that at-

tended both surveys lead to nearly identical odds ratios (data not shown).

DISCUSSION

From 1987-88 to 1996-97 the proportion of antacid users in this region increased among men from 11.2% to 12.7% (40-49 years) and from 11.9% to 13.4% (50-59 years), while the proportion of women using antacids decreased. The proportion of antacid users increased with age in both genders. In the same period, the frequency of self-reported dyspeptic complaints such as heartburn, which was the main predictor for antacid use, decreased. The GEE analyses showed an overall increasing trend in antacid use across the nine-year period, even when adjusted for self-reported heartburn and age. Antacid use increased among those with dyspeptic complaints and also among those reporting no dyspeptic symptoms. This finding was consistent in both the bivariate and the multivariate analyses.

One main problem in this study as in longitudinal studies in general is missing data, i.e. when not all individuals have data at both or all time points. We therefore made GEE-analyses for both the total population with missing data (N=15,523) and the population where all individuals participated in both surveys (N=4,253). The analyses gave the same results and this indicates there was no selection by missing in our study, i.e. the missing data were ignorable.

Antacid use

One of the strengths in our study is that the questions about antacid use were not changed from 1987 to 1996. There are, however, some limitations to this study. We had no information regarding doses, frequency or duration of the antacid use i.e. the amount of antacid the individual user is exposed to, is not known. We do not, however, consider these limitations essential for interpreting the change of antacid use during the time period of our study. A nationwide health survey performed in Norway in 1995 reported that 8% used non-prescription drugs and 1.9% used prescription drugs for dyspeptic symptoms, which is in accordance with our findings²¹. Our results may indicate that

Table 4. Proportion of antacid users during the preceding 14 days according to dyspeptic complaints and self-evaluated health. The Finnmark Health Survey **1987-88** and **1996-97**.

	Code	Men			Women		
		n	Antacid Users %	p-value ¹	n	Antacid users %	p-value ¹
1987-88 (N=11,061)							
Heartburn							
No	0	3471	2.5		3668	2.1	
Yes	1	2092	26.4	<0.001	1830	25.9	<0.001
Epigastric pain							
No	0	4344	6.1		4255	4.8	
Yes	1	1219	30.4	<0.001	1243	27.8	<0.001
Peptic ulcer							
No	0	4986	9.1		5159	8.4	
Yes	1	577	32.1	<0.001	339	34.5	<0.001
Self-evaluated health							
Poor	1	191	17.3		190	22.1	
Fair	2	1108	18.3		1247	17.0	
Good	3	3214	11.0		3154	8.2	
Excellent	4	1050	4.7	<0.001	907	4.1	<0.001
1996-97 (N=7,854)							
Heartburn							
No	0	2668	6.2		2746	3.6	
Yes	1	680	42.5	<0.001	685	40.7	<0.001
Epigastric pain							
No	0	2933	8.1		2913	5.7	
Yes	1	552	32.6	<0.001	668	26.2	<0.001
Peptic ulcer							
No	0	3001	10.2		3103	7.3	
Yes	1	515	28.7	<0.001	496	27.0	<0.001
Self-evaluated health							
Poor	1	135	21.5		111	16.2	
Fair	2	1153	18.0		1354	15.7	
Good	3	2084	11.5		2029	8.2	
Excellent	4	447	4.5	<0.001	541	3.7	<0.001

¹ chi square or chi square for trend when applicable

Table 5. Crude and adjusted odds ratio for being an antacid user estimated by generalized estimating equations. The period effect implies the changes from T1 to T2. The Finnmark Health Survey **1987-88 (T1)** and **1996-97 (T2)** (N=15,523).

	Main effects of time, heartburn, and gender		Adjusted model with four interaction terms
	Crude odds ratio [95% CI]	Adjusted odds ratio ¹ [95% CI]	Adjusted odds ratio [95% CI]
Period (T1-T2)	1.43 [1.32-1.54]	2.03 [1.81-2.26]	
Heartburn	11.55 [10.23-13.03]	14.24 [12.58-16.13]	14.63 [12.85-16.66]
Gender	0.83 [0.75-0.91]	0.86 [0.77-0.95]	0.86 [0.77-0.97]
Age	1.02 [1.01-1.02]	1.01 [1.01-1.02]	1.01 [1.01-1.02]
*Men without heartburn at both T1 and T2			2.94 [2.19-3.96]
*Men with heartburn at both T1 and T2			2.02 [1.70-2.43]
*Women without heartburn at both T1 and T2			2.03 [1.55-2.66]
*Women with heartburn at both T1 and T2			1.73 [1.44-2.08]

¹ Odds ratio for period effects compares T2 to T1. Odds ratios for gender compare women to men and for heartburn yes to no.

* Four interaction terms representing the period effect on antacid use within each combination of gender and heartburn.

the overall decrease of antacid drug use estimated from the wholesale statistics do not reflect a decline in the proportion of individual users. Another reasonable consideration to the decrease in the wholesale statistics is that lower doses of antacids have been used after the introduction of the histamine-2-receptor antagonists and proton pump inhibitors for dyspeptics with more severe symptoms. The unit of measurement in wholesale statistics is usually the Defined Daily Dose (DDD), which is defined as the assumed average maintenance dose per day for a drug use on its main indication in adults. The estimated drug consumption based on wholesale statistics is only valid if the drug is used regularly on a daily basis and there is good correlation between the technical value DDD and the actual dose used. For drugs used intermittently in different doses, such as non-prescription antacids, wholesale statistics and DDD will not give an adequate estimate of the proportion of users in the population and the development of antacid use in individuals over time²².

Dyspeptic complaints

Dyspeptic complaints were measured differently in the two surveys. In the 1996-97 survey the duration of the complaints, "at least 1 week's duration" for heartburn and "at least 2 weeks' duration" for epigastric pain, were added. This may have influenced the change in prevalence estimates as specifying an exact duration of the complaints may contribute to the decrease in the prevalence. The prevalence of the main predictor of antacid use, heartburn, went down from 38% to 20%. We do not know if this is a real change, or if it is due to the questions being different. Nevertheless we doubt that the differences in the questions could explain the whole decrease in prevalence. Our study revealed no change in the self-evaluated health and this may indicate that the morbidity in this population did not increase in the period. In a health survey performed on

the Norwegian population in 1995-97 the prevalence of heartburn or regurgitation during the past 12 months was 31%, which is higher than our figures from 1996-97²³. Other studies are showing that prevalence of dyspepsia varies from 15 to 40%, depending on the definition of dyspepsia and on the time frame of the prevalence^{11,24}. The frequency and severity of dyspeptic symptoms were not incorporated in our study and therefore our figures may include individuals with trivial symptoms.

In summary, the traditional indication for antacid use is dyspepsia, and the strongest predictor of antacid use in our study at both cross-sections was heartburn. However, the longitudinal analyses showed that the increased prevalence of antacid users during this period was not a consequence of increased frequency of the predictor of the antacid use. In fact, the increased proportion of antacid users took place in dyspeptics as well as in non-dyspeptics. Thus we conclude that the increase in the prevalence of antacid users over the nine year period is not caused by the traditional indications for these medications.

"TAKE HOME" MESSAGES

- GEE analyses showed an overall increasing trend in antacid use over the 9-year period adjusted for self-reported heartburn and age.
- The gender effect indicates that women are less likely to use antacids than men.
- There is an increase in antacid use with increasing age independent of the period effect.

ACKNOWLEDGEMENTS

The data collection was conducted in collaboration with the National Health Screening Services of Norway, now a part of the Norwegian Institute of Public Health.

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