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

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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 drugs¹². 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 1997.¹³ 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 gastrointestinal reflux, many people still use over-the-counter antacids in less severe forms of dyspepsia, especially those suffering from heartburn.¹⁵ 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 surveillance.¹⁶¹¹. 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...
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.

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 individuals.16 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

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**Figure 1.** Flow chart for invited and attending individuals in the Finnmark Health Study 1987-88 and 1996-97.
the dependency or correlation between the repeated measures by robust estimation of the variances of the regression coefficients\(^\text{19}\). 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 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 heartburn\(^\text{19}\). 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 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 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 | Men Antacid users | Women Antacid users | 1987-88 | 1996-97 |
| | n | % | n | % | n | % |
| 20-39 | 924 | 9.7 | 1019 | 7.4 | 117 | 5.1 | 146 | 7.5 |
| 40-49 | 2216 | 11.2 | 2044 | 9.3 | 1716 | 12.7 | 1834 | 8.8 |
| 50-59 | 1821 | 11.9 | 1820 | 11.4 | 886 | 13.4 | 833 | 10.3 |
| 60-62 | 598 | 13.2 | 612 | 13.1 | 805 | 13.7 | 840 | 12.3 |
| 20-62 | 5559 | 11.4 | 5495 | 10.0 | 300 | 14.3 | 382 | 14.4 |
| p (age trend) | 0.02 | <0.001 | 0.08 | <0.001 |
| p (gender) | 0.02 | | | |

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).

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonusers of antacids in both surveys</td>
<td>1789 (82.2%)</td>
<td>1662 (80.0%)</td>
</tr>
<tr>
<td>Users of antacids only in 1996-97</td>
<td>152 (7.0%)</td>
<td>187 (9.0%)</td>
</tr>
<tr>
<td>Users of antacids only in 1987-88</td>
<td>134 (6.2%)</td>
<td>115 (5.5%)</td>
</tr>
<tr>
<td>Users of antacids in both surveys</td>
<td>101 (4.6%)</td>
<td>113 (5.4%)</td>
</tr>
</tbody>
</table>
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 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 attended 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 findings. 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.

<table>
<thead>
<tr>
<th>Code</th>
<th>Men</th>
<th>Women</th>
<th>p-value&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Men</th>
<th>Women</th>
<th>p-value&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>3471</td>
<td>2.5</td>
<td>3668</td>
<td>2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>2092</td>
<td>26.4</td>
<td>1830</td>
<td>25.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>4344</td>
<td>6.1</td>
<td>4255</td>
<td>4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>1219</td>
<td>30.4</td>
<td>1243</td>
<td>27.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>4986</td>
<td>9.1</td>
<td>5159</td>
<td>8.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>577</td>
<td>32.1</td>
<td>339</td>
<td>34.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Self-evaluated health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>1</td>
<td>191</td>
<td>17.3</td>
<td>190</td>
<td>22.1</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>2</td>
<td>1108</td>
<td>18.3</td>
<td>1247</td>
<td>17.0</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>3</td>
<td>3214</td>
<td>11.0</td>
<td>3154</td>
<td>8.2</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>4</td>
<td>1050</td>
<td>4.7</td>
<td>907</td>
<td>4.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

1987-88 (N=11,061)

| Heartburn | | | | | | |
| No | 0 | 2668 | 6.2 | 2746 | 3.6 | |
| Yes | 1 | 680 | 42.5 | 685 | 40.7 | <0.001 |
| Epigastric pain | | | | | | |
| No | 0 | 2933 | 8.1 | 2913 | 5.7 | |
| Yes | 1 | 552 | 32.6 | 668 | 26.2 | <0.001 |
| Peptic ulcer | | | | | | |
| No | 0 | 3001 | 10.2 | 3103 | 7.3 | |
| Yes | 1 | 515 | 28.7 | 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 | 541 | 3.7 | <0.001 |

1996-97 (N=7,854)

| Heartburn | | | | | | |
| No | 0 | 2668 | 6.2 | 2746 | 3.6 | |
| Yes | 1 | 680 | 42.5 | 685 | 40.7 | <0.001 |
| Epigastric pain | | | | | | |
| No | 0 | 2933 | 8.1 | 2913 | 5.7 | |
| Yes | 1 | 552 | 32.6 | 668 | 26.2 | <0.001 |
| Peptic ulcer | | | | | | |
| No | 0 | 3001 | 10.2 | 3103 | 7.3 | |
| Yes | 1 | 515 | 28.7 | 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 | 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).

<table>
<thead>
<tr>
<th>Main effects of time, heartburn, and gender</th>
<th>Adjusted model with four interaction terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude odds ratio [95% CI]</td>
<td>Adjusted odds ratio&lt;sup&gt;1&lt;/sup&gt; [95% CI]</td>
</tr>
<tr>
<td>Period (T1-T2)</td>
<td>1.43 [1.32-1.54]</td>
</tr>
<tr>
<td>Gender</td>
<td>0.83 [0.75-0.91]</td>
</tr>
<tr>
<td>Age</td>
<td>1.02 [1.01-1.02]</td>
</tr>
</tbody>
</table>

*Men without heartburn at both T1 and T2
*Men with heartburn at both T1 and T2
*Women without heartburn at both T1 and T2
*Women with heartburn at both T1 and T2

<sup>1</sup> 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 dyspepsia with more 
severe symptoms. The unit of measurement in whole-
sale 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 corre-
lation between the technical value DDD and the actual 
dose used. For drugs used intermittently in different 
dooses, 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 de-
velopment of antacid use in individuals over time\textsuperscript{22}.

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 in-
dicate 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- 
97\textsuperscript{21}. Other studies are showing that prevalence of dys-
pepsia varies from 15 to 40%, depending on the defini-
tion of dyspepsia and on the time frame of the preva-
ience\textsuperscript{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 pe-
riod 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 indi-
cations 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

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