Reviewer's report

Title: Annual pattern of peptic ulcer hospitalizations: a retrospective analysis of hospital discharge data of the Emilia-Romagna region of Italy.

Version: 2 Date: 13 December 2009

Reviewer: Reimar W Thomsen

Reviewer's report:

This is an interesting and generally well-written population-based study of the annual seasonal incidence of hospitalizations with peptic ulcer disease in an Italian region comprising ~4 million inhabitants. The data material is impressive and well-suited for conducting a study of this type, and the literature review is good.

I have the following comments, all for Major Revision:

Title:

1) I suggest to replace ‘annual pattern’ with ‘seasonal variation’ as this expression is used throughout the abstract.

2) I suggest to delete the term ‘retrospective’. All analyses are by nature made ‘retrospectively’, i.e., after data collection. However, the study is based on data collected prospectively in the hospital databases since 1998. Thus, I consider this a prospective study, if any.

Abstract:

3) I think the early introduced expression ‘admission due to acute PUD’ is a bit unclear at this point for the reader. Does this mean admission with complicated PUD, i.e. bleeding or perforation, or does it just mean acute admission with any form of PUD? Please rephrase.

4) Final outcome ‘fatal’ – please state the denominator/follow-up time for this outcome (unclear from abstract if this e.g. 30-day or in-hospital mortality is meant).

5) The expression ‘PUD hospital admission were lowest in summer (23.2%)’ etc. is unclear. Please be precise in the abstract: what means 'lowest', and 23.2% of what number? (doesn’t fit with the 62% and 61% cited for autumn and spring)?

6) Conclusions: The very last sentence in the conclusions is confusing, as it suddenly presents additional results on PUD events divided by total admissions. These results should be moved to the abstract’s results section. Moreover, these last results (‘main peak in August-September’) are the opposite of the previous results (‘nadir was consistently in summer (July/August’)”). This is confusing for two reasons:
1) The additional PUD admission / total admission analysis is not prespecified in the methods, and it should be. One place in the manuscript’s discussion section, the authors clearly state that they analyzed their data ‘in two ways’: counts per month, and versus total admissions. I recommend this to be clearly stated already in the abstract.

2) The additional analysis is called ‘analysis performed on hospital admission rates’. A better expression would be: ‘analysis of total admission proportions’, since period prevalence proportions, not rate ratios, are presented. Please see my later comment on this.

7) Finally, the phrase: ‘summer low which cannot depend from the expected reduction of admissions in that period’ is a bit cumbersome. I translate this to: ‘summer low that was independent of the observed general reduction in admissions during summer’. However, in my understanding the PUD summer low was not independent of the general admission reduction in the summer, since if PUD summer events were divided by total summer admissions, the proportion was actually highest during the summer. Please explain/rephrase.

Main text:

Introduction:

8) I miss some sentences about the potential biological mechanisms behind a seasonal variation of PUD. I feel there is no obvious relationship between the seasonality of CVD cited at this point, and PUD variation.

9) Table 1 provides a nice overview of previous studies. I suggest citing these studies’ main results (e.g. the winter peak) in the Introduction section.

10) The authors call the small size of previous studies ‘a major drawback’ – please explain why this would be major drawback.

Subjects and methods:

11) Data collection: Please explain why repeated admissions in the follow-up period can’t be excluded more precisely by using additional data (name etc.) than birth date only.

12) What about PUD admissions of the same person in the years before start of the follow-up period 1998, how were such admissions handled?

13) The authors state that they included ‘only admissions directly related to PUD’. In other words, ‘community’acquired PUD’. However, they include both first and second discharge diagnoses, with the risk of including admissions for other conditions than PUD. E.g. elderly patients admitted for acute COPD exacerbation or CVD events, for which an episode of PUD emerged during hospitalization, thus mimicking the seasonal variation of COPD or CVD. Analyses should be repeated for PUD as first diagnosis to test any differences in results.

14) Why is sea level vs. hilly level included as a covariate – please explain.
15) Statistical analysis: the authors use ‘rate’ in a wrong way here and throughout the paper: ‘we assessed hospital admission rates of PUD, i.e., total number of ulcer cases/month divided by the total number of all hospital admissions (…)’ This measure is not a rate, but a proportion. More specifically, it is a period prevalence proportion = the monthly prevalence of PUD admissions divided by the monthly prevalence of total admissions. Please reword.

Discussion:
16) I don’t understand the sentence in the beginning of the second page of the Discussion: “Recent epidemiological surveys show the incidence of PU bleeding has remained stable, being responsible for about 50% of all cases, followed by oesophagitis and erosive diseases”. 50% of what kind of cases?

17) Explanation of results: The authors seem to suggest that their finding of a PUD summer peak when examining PUD/total admissions is biased by fewer elective admissions in the summer. An alternative explanation might be that other common diseases, such as CVD, COPD, and community-acquired infections, have even more marked summer lows than PUD. Please discuss in the manuscript.

The review of the present literature is very good, and the presented hypotheses regarding seasonal variation of NSAID / steroid use and alcohol on the population level are interesting.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests