Changing incidence of peptic ulcer—facts or artefacts? A cohort study from Tromsø

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Abstract

Study objective—The aim was to estimate the age and sex specific incidences of duodenal and gastric ulcers censored for death and migration.

Design—A population based cohort was followed seven years through records of x ray examinations, endoscopies, and operations in the only hospital serving the area.

Setting—The study was conducted in the municipality of Tromsø, Northern Norway, where all men aged 20 to 54 years and women aged 20 to 49 years in 1980, a total of 21 440, were included.

Main results—We found an incidence of 1·47 (95% CI 1·21–1·76) and 0·88 (0·67–1·14) per 1000 person-years for gastric and 1·98 (1·69–2·31) and 0·85 (0·64–1·11) for duodenal ulcers in men and women, respectively. A small and insignificant sex difference for gastric ulcer was noted. The duodenal preponderance in men was only recognised among the ulcers identified by x ray, not among ulcers diagnosed by endoscopy.

Conclusions—This population based study has, in contrast to recent studies from other areas, revealed an unchanged high incidence of gastric and duodenal ulcer in both sexes. Compared to earlier studies from this area it indicates a preponderance of duodenal ulcers. The study also shows the impact of attendance rate, death, and migration, and of diagnostic methods on the incidence estimates. Ignoring these potential biases may lead to conclusions on peptic ulcer trends that reflect artefacts rather than real changes in peptic ulcer occurrence.

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The pattern of peptic ulcer incidence has changed throughout this century, starting with predominantly gastric ulcer among young women, followed by a period with a predominance of duodenal ulcer in middle aged men, and subsequently as either gastric or duodenal ulcers occurring mainly in older men and women since the 1950s.[1] Both Sussex and Stein[2] and Sonnenberg[3] ascribe the changing incidence to different risk patterns in successive age cohorts. But during the first three decades of this century both the duodenal to gastric ulcer ratio and the sex ratio differed considerably depending on whether the results were based on necropsy data or on clinical studies.[4] The recently asserted decline in inci-dence of peptic ulcer in some western countries is mainly based on mortality rates,[1–3][5–8] perforation rates,[5–7][9] and hospital admissions and physician visit rates.[5][6][9–11] Besides reflecting changes in peptic ulcer occurrence, these findings may mirror changes in clinical and coding practice as well.[6] The few published prospective studies are neither consistent regarding a declining inci-dence,[12–17] nor are they directly comparable due to disparities in design, diagnostic techniques, and definitions of peptic ulcer. Apparently in contrast to findings from all other western societies, a duodenal to gastric ulcer ratio of one or less has been observed in several studies[15][18][19] from northern Norway.

Both the identification of population at risk and the verification of diseased subjects appear to be major methodological problems in most incidence studies, and Sturdevant[20] has requested future studies to secure "a precise ascertainment of affected individuals, and precise definitions of population under study".

A comprehensive health survey of 21 440 inhabitants of the municipality of Tromsø gave us the opportunity to study the incidence of diag-nosed peptic ulcers, in a defined population, censored for death and migration.

Methods

In a health survey in the municipality of Tromsø in 1979–80, all men born between 1925 and 1959, and all women born between 1930 and 1959 were invited to participate, a total of 21 440. At the screening 16 621 attended, of whom 14 667 returned a supplementary questionnaire on several items concerning health and lifestyle.[21]

The University Hospital in Tromsø serves as the only hospital in the area, and all first occurring peptic ulcers diagnosed by x ray examination, upper gastrointestinal endoscopy, or operation in the study population were registered during the period 1979 and 1987. To ensure that all registered ulcers were "new" or incident, the medical records of all cases were examined.

The double contrast method of x ray examin-ations has been the standard in the department of radiology since 1976.[15] A gastric or a duodenal ulcer was diagnosed if a radiological niche was demonstrated 3 cm proximal or distal to the pylorus, respectively; or if an endoscopic ulcera-tion of at least 0·5 cm was seen proximal or distal to the pylorus, respectively. Only one ulcer epi-sode was recorded in each subject, except for combined ulcers, diagnosed at different points in time. Thus when the total number of peptic ulcers is given this corresponds to the number of subjects with new peptic ulcers.

The population at risk was censored for all deaths, recorded by the Central Bureau of Statistics of Norway during the period (237 men and 67 women). We got information from the Bureau on individual migration in the study population (2234 men and 2099 women), but no the exact date of their migration. As an approximation for censoring purposes all migrations were recorded as having occurred in the middle of the follow up period, ie, we used 3·5 years as the mean observation time for these persons.

STATISTICS
Incidence rates were estimated as numbers of first time peptic ulcers per 1000 person-years, censored for the time of diagnoses of petic ulcers, for deaths during the period, and for migration.[22] The relationship between age, sex, and incidence of peptic ulcers was tested by Cochran-Mantel-Haenszel statistics.[22] Confidence intervals were calculated from the binomial distribution.

Results
Of the 21 440 subjects invited to the screening, 328 experienced their first peptic ulcer episode during follow up, and the majority were diagnosed by x ray. Table I illustrates that the pattern of peptic ulcer location depended on whether diagnoses where made by endoscopy or x ray. Exploring whether the difference could be explained by patient selection failed to reveal significant differences according to age, sex, or the relevant symptoms recorded in 1979/80. Excluding combined ulcers and deformities of the bulb, there were still more duodenal ulcers diagnosed by x ray. During the observation period, 83 persons had surgery because of their ulcer disease: 49 persons were operated electively while 34 had emergency surgery because of bleeding or perfor-

ation. Of these 34 persons only 11 had "new" or incident ulcers.

A separate analysis showed a somewhat higher incidence of total peptic ulcer among responders compared to non-responders, though statistically non-significant. However, the incidence among the youngest male responders, aged 20 to 34 years, of 2·17 per 1000 person-years (95% CI: 1·74–2·79) was twice that of the non-responders, 1·08 (0·57–1·84).

The age and sex specific incidences of gastric, duodenal and total ulcers, respectively, are shown in table II. Excluding from the analysis 532 subjects who reported having had a peptic ulcer before 1979/80 gave an overall peptic ulcer incidence per 1000 person-year of 3·29 among men and 1·63 in women, compared to 3·18 and 1·61 as shown in table II. Duodenal ulcers included 28 first diagnoses of deformity of the duodenal bulb in 21 men and seven women. Twenty two men and eight women had combined ulcers.

A significant linear trend with increasing age was found, both for gastric ($p < 0.001$) and duodenal ulcer ($p < 0.001$). A duodenal predominance was found among young females, and, most pronounced, in middle aged males. Overall, the ratios between duodenal and gastric ulcers were 1·4 (1·0–1·8) and 1·0 (0·6–1·4) for men and women, respectively. Among the youngest females, aged 20 to 29 years, the ratio was 2·2 (0·7–7·2).

The effect of censoring for death and migration is illustrated by contrasting table III with table II. The censored incidences of peptic ulcer were 13% higher than the uncensored in both sexes. The consequence (an underestimate) of not censoring was greatest among the youngest urbans, with approximately a 20% difference between uncensored and censored incidences.

Discussion
The changing pattern in incidence of peptic ulcer disease in different age and sex cohorts has been ascribed to the adoption of industrialised civilisation.[2] However, to some degree new diagnostic technology, change in treatment from surgical to medical therapy,[23] and a shift in coding practice[6] may also have influenced the perceived trends in peptic ulcer epidemiology. In addition expensive

Table I   Number of subjects with peptic ulcers by ulcer location and methods[a] of diagnosis. Tromsø 1980–87

	Gastric ulcer	Duodenal ulcer	Combined ulcer	Deformity of the bulb	Total
Endoscopy	65	52	21	1	139
X ray	59	83	9	27	178
Operation	7	4	–	–	11

[a]Ulcers diagnosed both by x ray and endoscopy are grouped under endoscopy

Table II   The incidences (per 1000 person-years) of new peptic ulcers by age, censored for death and migration, among 11 483 men and 9957 women. Tromsø 1980–87. 95% Confidence intervals in brackets

Age (years)	Person-years		Gastric ulcer[a]				Duodenal ulcer[b]				Total ulcers			
	Men	Women	Men		Women		Men		Women		Men		Women	
			n	Incidence	n	Incidence	n	Incidence	n	Incidence	n	Incidence	n	Incidence
20–24	10 847	11 597	7	0·65 (0·26–1·33)	2	0·17 (0·02–0·62)	9	0·83 (0·38–1·58)	4	0·34 (0·09–0·88)	14	1·29 (0·71–2·16)	6	0·52 (0·19–1·13)
25–29	13 468	13 603	12	0·89 (0·46–1·55)	3	0·22 (0·04–0·64)	16	1·19 (0·68–1·90)	7	0·51 (0·21–1·06)	26	1·93 (1·26–2·41)	9	0·66 (0·30–1·26)
30–34	14 017	13 322	12	0·86 (0·44–1·49)	11	0·83 (0·41–1·48)	22	1·57 (1·04–2·64)	8	0·60 (0·26–1·19)	31	2·21 (1·51–3·12)	18	1·35 (0·80–2·13)
35–39	11 369	10 127	12	1·06 (0·79–2·68)	11	1·09 (0·54–1·95)	31	2·73 (2·09–4·33)	11	1·09 (0·54–1·95)	40	3·52 (2·52–4·76)	21	2·07 (1·28–3·16)
40–44	7809	7201	13	1·66 (0·88–2·84)	12	1·67 (0·86–2·90)	23	2·95 (1·87–4·41)	16	2·22 (1·28–3·60)	33	4·23 (2·92–5·90)	26	3·61 (2·36–5·26)
45–49	7086	6352	28	3·95 (2·64–5·69)	16	2·52 (1·85–4·08)	20	2·82 (1·72–4·35)	7	1·10 (0·44–2·27)	43	6·07 (4·42–8·11)	20	3·15 (1·92–4·85)
50–54	6987	–	21	3·01 (1·86–4·58)	–		24	3·43 (2·20–5·08)	–		41	5·87 (4·24–7·91)	–	
Total	71 589	62 202	105	1·47 (1·21–1·76)	–		142	1·98 (1·69–2·31)	–		228	3·18 (2·83–3·57)	–	
Total (20–49)			84	1·30 (1·05–1·59)	55	0·88 (0·67–1·14)	118	1·83 (1·53–2·16)	53	0·85 (0·64–1·11)	187	2·89 (2·53–3·29)	100	1·61 (1·32–1·93)

[a]Combined ulcers are included in both locations

new drugs are refunded in many countries, Norway included, only if a peptic ulcer is documented by *x* ray or endoscopy. This presumably increases the referral rates among dyspeptics, and thereby the possibility of detecting an ulcer. Still, the occurrence of silent and undiagnosed peptic ulcer is surprisingly high, indicating that peptic ulcer disease is considerably more frequent than is clinically recognised.[24] Furthermore, a variety of selection mechanisms hampers comparisons of ulcer incidences based on admission rates, necropsy studies, and prospective studies on differing patient groups, with considerable bias. Even perforation rates and mortality rates are unreliable as estimates of peptic ulcer incidences, reflecting differences in rates of complications rather than true differences in peptic ulcer occurrence.

This study was population based, with explicitly defined end points including ulcers diagnosed by *x* ray, endoscopy, and at operation. It was also an unbiased assessment of the population at risk, which implies controlling for sex and age distribution, and censoring for death and migration.

The reported decline in hospital admissions,[5 9 10] perforation, and mortality rates[5 7 8] is somewhat inconsistent regarding its relation to age and sex. Besides, in the United Kingdom the decrease in peptic ulcer is mainly accounted for by gastric ulcer, while the decline in the USA affects the duodenal location. Kurata claims that the decline in the USA can partly be ascribed to changes in coding practices, hospital admission criteria, and diagnostic procedures.[6] However, perforation rates and cause specific mortality of peptic ulcer, as opposed to diagnosis, are hard end points, and the evidence of a shift in the presentation and complication rates of peptic ulcer seems difficult to disregard.

Incidence studies published in the United Kingdom,[13 14] the USA,[12] and Scandinavia,[15–17] are not conclusive in showing a decline in the occurrence of peptic ulcer. The Scandinavian studies of Østensen *et al*[15] and Bonnevie,[16 17] in particular, give no indication of a declining incidence. However, the studies are not comparable, due to differences in the selection of the populations at risk, diagnostic criteria, and diagnostic methods applied. Our study shows that the pattern of ulcer location depends on the method of the diagnostic examination. Both *x* ray examination and endoscopy are, according to Dooley *et al*,[25] specific, but the low sensitivity inherent in *x* ray examinations may result in numerous false negative findings. The uncertainties caused by these methodological problems make it difficult to be confident that there is a declining incidence of peptic ulcer. Schache *et al* even claim that there has been no change in the incidence of duodenal ulcer, but only in the pattern of presentation.[26]

The high incidences in our study may reflect an increasing diagnostic intensity, due to refunding of the cost of drugs prescribed for ulcers, as well as to more efficient diagnostic investigations. The number of examinations has, however, been constant during the follow up period with a declining use of *x* ray examinations with a corresponding increase in endoscopies. The frequency of positive findings varied throughout the period, with no significant trend.

Contrary to the duodenal ulcer predominance found in Denmark,[16 17] the USA,[12] and the United Kingdom[13 14] a gastric ulcer predominance has been observed in northern Norway.[15 18 19] Our findings of a predominance of duodenal ulcers in men and maybe even among the youngest women, support the trend indicated by Østensen *et al*.[15] But the duodenal to gastric ulcer ratio depends to some extent on the diagnostic method applied. There is no duodenal preponderance among endoscopically diagnosed ulcers. However, as the previous studies[15 18 19] are based on ulcers diagnosed by *x* ray, a shift in the location is most likely, and is also in accordance with the results from the gastrointestinal study in Sørreisa,[24] a rural municipality in the county of Troms.

Our almost equal gender specific risk of gastric ulcer was another somewhat surprising finding in this geographical area. Both Schanke[19] and Østensen *et al*[15] found a male preponderance of peptic ulcer. In this study the highest difference between the sexes was observed among the youngest, aged 20 to 29 years. This may reflect a true cohort effect, or merely a change in gender related diagnostic intensity, as indicated in the Sørreisa study[24] and the follow up study of Krag.[27]

None of the previously reported studies on peptic ulcer incidence has been censored for death and migration. As shown in the present study, censoring the population for death and migration is mandatory for a precise incidence estimate. Although not an earth shattering revelation, the difference between the uncensored and censored incidences of up to 20% should not be neglected.

The selection of patients for investigation still probably represents the major source of error. Both patient self selection and referral pattern will greatly influence the number of diagnosed cases. The ideal alternative—regular examinations of a population of the present size—is an insurmountable task. Thus we have to depend on incidences based on diagnostic routines, prescribed by our clinical practice in force at the time in question. This insight invites caution when comparing studies differing in time and geographical area.

In conclusion, our population based study has, in contrast to other recent studies, revealed an unchanged high incidence of gastric and duodenal ulcer in both sexes. Compared to previous studies from the area it indicates a change towards a preponderance of duodenal ulcers. The study has

Table III The uncensored incidences (per 1000 person-years) of new peptic ulcers by age in 11 483 men and 9957 women. Tromsø 1987

Age (years)	Men			Women		
	Person-years	Peptic ulcer		Person-years	Peptic ulcer	
		n	*Incidence*		*n*	*Incidence*
20–24	12 522	14	1·12	14 099	6	0·43
25–29	15 864	26	1·64	16 167	9	0·56
30–34	16 042	31	1·93	14 809	18	1·22
35–39	12 486	40	3·20	10 866	21	1·93
40–44	8461	33	3·90	7635	26	3·41
45–49	7517	43	5·72	6689	20	2·99
50–54	7518	41	5·45	–	–	–
Total	80 416	228	2·87[a] (2·52–3·17)[b]	70 263	100	1·47[a] (1·17–1·71)[b]

[a]Age adjusted by direct standardisation
[b]95% confidence interval

also demonstrated the impact of attendance rate, death and migration, and diagnostic methods on the incidences. Ignoring these potential biases may lead to conclusions on peptic ulcer trends that reflect artefacts rather than real changes in the epidemiology of peptic ulcer.

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