

Smoking, alcohol, and analgesics in dyspepsia and among dyspepsia subgroups: lack of an association in a community

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Abstract

Dyspepsia is common in the general population, and despite a paucity of data, smoking, alcohol, and analgesics are believed to be important risk factors. The role of these environmental factors in subjects with uninvestigated dyspepsia was evaluated in a representative population sample. An age and gender stratified random sample of residents of Olmsted County, Minnesota, aged 20 to 64 years was mailed a valid self report questionnaire; 77% responded (n=1644). Age and gender adjusted (1990 US white population) prevalence rates for dyspepsia (defined as frequent pain located in the upper abdomen, or nausea in the absence of a history of peptic ulcer disease) were calculated. Logistic regression analysis was used to estimate the association between dyspepsia and potential risk factors. The age and gender adjusted prevalence (per 100) of dyspepsia in the community was 21.8 (95% confidence interval 19.6, 23.9). Dyspepsia was significantly more common in younger subjects and females. Adjusting for age and gender, paracetamol (odds ratio (OR)=2.2), aspirin (OR=1.8), and smoking (OR=1.5), but not alcohol (OR=0.9), were associated with dyspepsia (all $p < 0.05$). When non-gastrointestinal somatic complaints were included in the logistic models, however, these environmental factors were no longer significant (OR=1.3, 1.1, 1.2 and 0.9, respectively). Similar results were obtained when ulcer-like, dysmotility-like, and reflux-like dyspepsia were considered separately. The results were not significantly changed when subjects with a history of ulcer disease were included in the analyses. Smoking, alcohol, and analgesics may not therefore be important risk factors for dyspepsia in the community.

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Dyspepsia is recognised to be a very common condition.¹⁻³ Although it has often been recommended that people with dyspepsia avoid aspirin, cigarettes, and alcohol,⁴⁻⁶ few data address the risk of these environmental factors specifically.⁷⁻⁸ Functional (or non-ulcer) dyspepsia is the most frequent diagnosis made in patients with upper abdominal pain or nausea who are investigated, but the pathogenesis of this entity is not established. In a case-control study from Australia, paracetamol exposure was associated with functional dyspepsia.⁷ However, whether this reflected a true cause and effect relationship, whether paracetamol use was a 'marker' for an underlying psychopathological

process, or whether other painful somatic complaints accounted for the drug ingestion could not be assessed directly.

Symptoms have been used to classify subjects with uninvestigated dyspepsia into subgroups. Thus, those with classic ulcer symptoms (for example, pain relieved by food or antacids, night pain, periodic pain) have been labelled as having ulcer-like dyspepsia, while those with symptoms suggestive of a motility disorder (for example, bloating, retching, anorexia) have been classified as having dysmotility-like dyspepsia, and those with coexistent heartburn or acid regurgitation have been considered to have reflux-like dyspepsia.^{1,3,6,9,10} Although this classification has recently been questioned because these subgroups often overlap,¹ and while it is quite uncertain whether the pathophysiology of these subgroups is distinct, the classification has gained wide acceptance.^{3,6,9,11}

Population based data on the importance of smoking, alcohol, and analgesics in uninvestigated dyspepsia are lacking. Furthermore, there are no studies of the role of these environmental factors in the dyspepsia subgroups. We therefore aimed to estimate the prevalence of and risk factors for dyspepsia and the dyspepsia subgroups in subjects from the community, aged 20 to 64 years. In particular, we wished to determine whether specific environmental factors (namely, smoking, alcohol, aspirin, and paracetamol use) were associated with uninvestigated dyspepsia. We postulated that smoking, alcohol, and aspirin would be linked to subjects with typical ulcer-like dyspepsia but not to those with other forms of dyspepsia.

Methods

SURVEY

Approval was provided by the Institutional Review Board of the Mayo Clinic to approach the inhabitants of Olmsted County. The Olmsted County population comprises over 100 000 persons (70% urban, 30% rural), of which 96% were white in 1990. In terms of sociodemography, the community is similar to the white US population, and the Mayo Clinic is the major provider of medical care. It has been determined previously that about 15% of all Mayo Clinic registrations are from the local population, and that each year over half of the Olmsted County population is seen at one of the clinic facilities or by another local care provider, most notably the Olmsted Medical Group. During any given four year period, over 95% of local residents will have had at least one medical contact with a local care

provider. Consequently, the local residents in this sampling frame do not constitute primarily 'consultation-prone' individuals as these medical contacts include routine dental x rays, sports physical examinations, refractions, pre-employment examinations, insurance physical examinations and immunisations, as well as routine medical care.

An important feature of the Rochester environment is that each of the providers uses a dossier (or unit record) system whereby all medical information for each individual is accumulated in a single record. The pertinent clinical data are accessible because since 1910 the Mayo Clinic has maintained extensive indices based on clinical and histological diagnoses and surgical procedures.¹² The system was further developed by the Rochester Epidemiology Project, which created similar indices for the records of the other providers of medical care to residents of Rochester and Olmsted County. The Rochester Epidemiology Project records linkage system therefore provides what is essentially an enumeration of the population from which samples can be drawn. Using this system, we randomly selected Olmsted County residents aged 20 to 64 years, stratified by age (in five year intervals) and gender (equal numbers of men and women). The study population should therefore have been a representative sample of Olmsted County residents 20 to 64 years of age.

Initially, the medical records of candidate subjects were reviewed. Because their small number did not constitute a reliable sample, non-whites (n=32) were excluded. Also excluded were those diagnosed as having a major psychotic episode (n=39), those who had undergone major abdominal surgery (n=20), or those who currently had a major organic medical disease or were in very poor health (n=49). Subjects who were no longer residents of the county at the time of sampling were considered ineligible.

A letter was sent to all remaining eligible subjects (n=2135), outlining the study and requesting their participation. Included with the letter was the Bowel Disease Questionnaire (BDQ), which has been shown to be an understandable, easily completed, and highly reliable (medium kappa=0.78) measure of symptoms in the outpatient setting; it has also been demonstrated to have adequate content, predictive, and construct validity.^{13,14} The questionnaire consists of 46 gastrointestinal symptom-related items; 25 items that measure past illness, health care use, and sociodemographic variables; and 17 items from the Psychosomatic Symptom Checklist (PSC) that measure the frequency and severity of somatic complaints and other conditions (namely headaches, backaches, stiffness, insomnia, fatigue, depression, palpitations, dizziness, weakness, eye pain from reading, asthma, high blood pressure, stomach pain, nausea, peptic ulcer, diarrhoea/constipation and spastic colon).¹⁵ Data on the prevalence of dyspepsia (but not environmental factors) in an initial sample of these subjects aged 30 to 64 years (n=835) has been reported elsewhere.¹

Reminder letters were sent, as needed, to non-responders after two weeks, four weeks, and seven weeks. Subjects who indicated at any point

that they did not wish to participate were not contacted further.

CLASSIFICATION OF DYSPEPSIA

Subjects who reported pain centred in the upper abdomen more than six times in the previous year, or nausea once a month or more, or both, were classified as having dyspepsia. We did not include subjects with infrequent dyspepsia in order to exclude from consideration episodes of gastroenteritis and other acute illnesses.¹² Subjects were grouped further into the symptom categories set out below a priori based on their responses to the BDQ.

Ulcer-like dyspepsia

Upper abdominal pain or nausea and classic ulcer symptoms defined as two or more of the following (1): (a) pain often (>25% of the time) relieved by food; (b) pain often relieved by antacids; (c) periodic pain (periods of at least one month with no pain, with periods in between of weeks to months when there is pain); (d) pain before meals or when hungry, often; and/or (e) night pain (waking the subject from sleep).

Dysmotility-like dyspepsia

Upper abdominal pain or nausea and three or more of the following symptoms suggestive of gastric stasis or upper intestinal dysmotility (1): (a) vomiting once a month or more; (b) abdominal bloating and distension, often; (c) anorexia or weight loss (≥ 7 lb); (d) pain often aggravated by food or milk; (e) pain often after meals; and/or (f) pain often relieved by belching.

Reflux-like dyspepsia

Upper abdominal pain or nausea accompanied by one or both of the following symptoms (1): (a) heartburn once a week or more and/or (b) acid regurgitation once a week or more.

Unspecified (non-specific) dyspepsia

Upper abdominal pain or nausea that did not fit into the three categories above.¹

MEASUREMENT OF RISK FACTORS

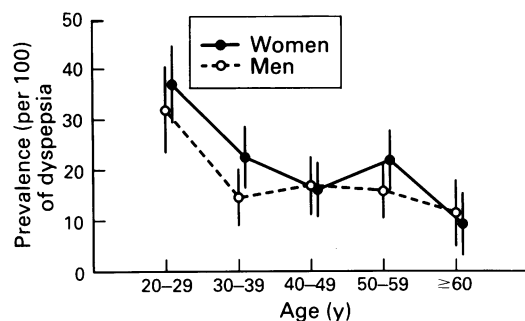
Health habits

Smoking, alcohol, aspirin, and paracetamol use in the previous year was obtained from responses to the questionnaire.

Psychosocial factors

Socioeconomic status (based on education level), marital status, and employment status were obtained from the responses to the questionnaire. Scores from the PSC were used to identify the frequency and severity of 12 non-gastrointestinal somatic complaints or conditions and five gastrointestinal complaints or conditions; this checklist has been validated in outpatients.¹⁵

Figure 1: The age-specific prevalence (per 100) and 95% CI of dyspepsia in men and women with no history of peptic ulceration based on a random sample (n=1528) of Olmsted County, MN, residents.



Past health

Previous gastrointestinal consultations and a history of peptic ulcer disease were obtained from responses to the questionnaire. These data were checked against a review of the medical records in a subsample of the eligible candidates (n=732) of which 538 had responded to the survey. Those subjects who indicated a past history of peptic ulcer disease were excluded from the primary analyses in an attempt to minimise confounding by this disease.

STATISTICAL ANALYSIS

Age adjusted, gender specific, and overall age and gender adjusted prevalence rates of upper gastrointestinal symptoms in the community were obtained by adjusting directly the age and gender specific observed proportions to the population structure of 1990 US whites.¹⁶ Ninety five per cent confidence intervals (95% CI) for the prevalence rates were based on the binomial distribution for the proportion of responders reporting the presence of specific symptoms.¹

Stepwise logistic discriminant analysis, adjusting for age and gender, was used to identify which of the 12 non-gastrointestinal somatic complaints or conditions from the PSC was significant in discriminating between subjects with and without dyspepsia. All p values calculated were two tailed; the alpha level of significance for the residual χ^2 test to stop adding variables to the model was set at 0.05.

The odds of dyspepsia were estimated for potential risk factors based on two separate logistic regression models – firstly, adjusting only for age and gender, and secondly, adjusting for age, gender, the significant non-gastrointestinal somatic complaints, marital status, and socio-economic status. Adjustment was made for these factors in the analysis since they were considered to be potential confounders. Because of the known overlap of the dyspepsia subgroups,¹

TABLE 1 Prevalence (per 100) of dyspeptic symptoms in 20–64 year old Olmsted County, Minnesota, residents (n=1528) (95% confidence intervals)

Symptoms in previous year	Women*	Men*	Overall †
Upper abdominal pain >6 times	15.7 (13.1, 18.3)	16.6 (13.6, 19.5)	16.1 (14.2, 18.1)
Nausea ≥once per month	12.3 (9.9, 14.7)	6.4 (4.5, 8.4)	9.4 (7.8, 10.9)
Ulcer-like dyspepsia	8.3 (6.3, 10.2)	12.6 (10.0, 15.2)	10.4 (8.8, 12.1)
Dysmotility-like dyspepsia	5.6 (4.0, 7.3)	3.6 (2.2, 5.1)	4.6 (3.5, 5.7)
Reflux-like dyspepsia	7.1 (5.2, 8.9)	8.1 (5.9, 10.2)	7.6 (6.1, 9.0)
Non-specific dyspepsia	10.5 (8.2, 12.7)	4.6 (2.9, 6.3)	7.5 (6.1, 8.9)

Note: Subjects with a history of peptic ulcer disease are not included in the calculated prevalence rates.

*Directly age adjusted to the population structure of US whites in 1990.

†Directly age and gender adjusted to the population structure of US whites in 1990.

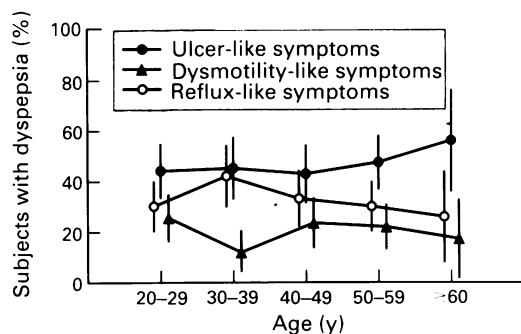


Figure 2: Proportions (95% CI) of ulcer-like, dysmotility-like, and reflux-like dyspepsia in subjects with dyspepsia and no history of peptic ulceration (n=310) by age group.

the risk factors were assessed for each of them in separate models versus those subjects without dyspepsia. The odds ratios (and 95% CI) were calculated based on the estimated coefficients from the logistic regression models.

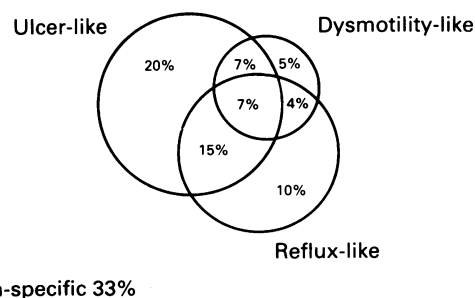
Results

DYSPEPSIA IN THE COMMUNITY

A completed questionnaire was returned by 1644 subjects, giving a response rate of 77%. No significant age, gender, or age by gender differences were detected between responders and non-responders except that younger men had a significantly lower response rate (p<0.05). The review of medical records in a subsample of 538 respondents indicated a 98% overall agreement between a previous diagnosis of peptic ulcer and responses on the questionnaire. Altogether, 116 of 1644 respondents (7%) indicated a past history of peptic ulcer disease. The remaining 1528 subjects with no history of peptic ulcer were considered in the primary analyses below.

A total of 439 persons (29%) reported pain located in the upper abdomen or nausea in the previous year and no history of peptic ulcer; 310 of these subjects (20% of the total) were classified as having dyspepsia. Their median age was 37 years (range 20–64), and 58% were women. Of those with dyspepsia, 9% (n=29) had undergone cholecystectomy in the past, compared with 5% (n=59) in those with no history of dyspepsia (p<0.001, adjusting for age and gender).

The age adjusted prevalence (per 100) of dyspepsia, excluding a history of peptic ulceration, was 23.9 in women (95% CI 20.9, 27.0) and 19.6 in men (95% CI 16.5, 22.7), with an overall age and gender adjusted prevalence of 21.8 (95%



Non-specific 33%

Figure 3: Overlap of the dyspepsia subgroups in subjects with dyspepsia and no history of peptic ulceration (n=310).

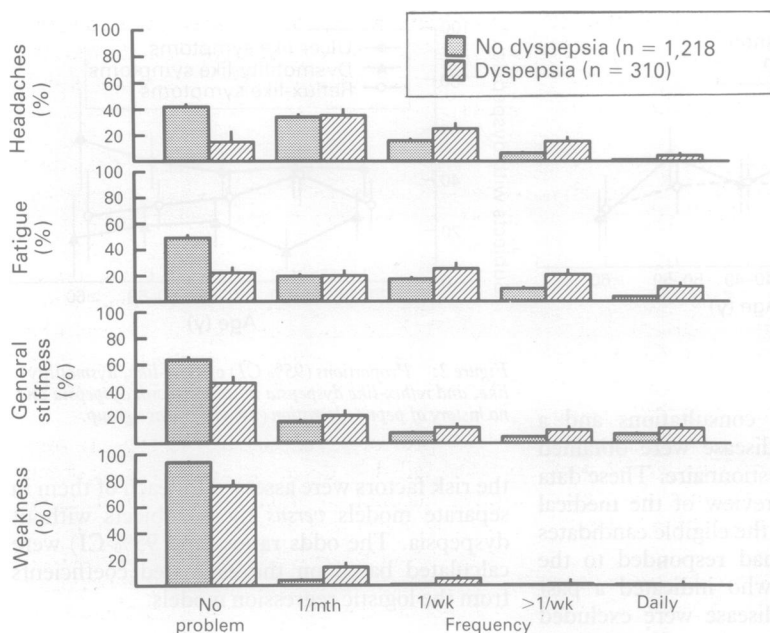


Figure 4: Distribution (%) and upper bound of the 95% CI of the frequency of headaches, fatigue, general stiffness and weakness in subjects with and without dyspepsia who had no history of peptic ulceration.

CI 19.6, 23.9). The prevalence of subjects with dyspepsia decreased with age ($p < 0.01$) and was higher in females ($p < 0.05$); the prevalence of dyspepsia in men and women by age is shown in Figure 1.

Of those with dyspepsia, 49% ($n = 152$) had ulcer-like, 23% ($n = 70$) dysmotility-like, and 35% ($n = 109$) reflux-like dyspepsia (Table I).

However, 33% ($n = 101$) were in more than one category and 33% ($n = 103$) had unspecified dyspepsia. The proportion of subjects in each of the dyspepsia subgroups by age is shown in Figure 2, while the overlap of the dyspepsia subgroups is displayed in Figure 3.

RISK FACTORS FOR DYSPEPSIA AND THE DYSPEPSIA SUBGROUPS

Of the 12 non-gastrointestinal somatic complaints or conditions measured by the PSC, only the frequency of headaches, fatigue, general stiffness, and weakness in the last year were independently associated with dyspepsia in those with no history of peptic ulcer, adjusting for age and gender (Fig 4). The distribution of the overall symptom scores are given in Table II by dyspepsia group.

The distribution of smoking, alcohol ingestion, and analgesic use in subjects with and without dyspepsia (excluding those with an ulcer history) is summarised in Table II. Adjusting for age and gender, paracetamol use was associated with dyspepsia; aspirin and smoking were also significant risk factors (Table III). No association between paracetamol, aspirin, or smoking and dyspepsia could be detected, however, when the significant non-gastrointestinal somatic complaints noted above were incorporated into the logistic model (Table III). Socioeconomic and employment status were not significantly associ-

TABLE II Distribution of potential risk factors for dyspepsia in Olmsted County, MN

Variable	No dyspepsia (n=1218)	Any dyspepsia (n=310)	Ulcer-like (n=152)	Dysmotility-like (n=70)	Reflux-like (n=109)
Age (mean, range) (y)	44 (20-64)	37 (20-64)	41 (20-64)	43 (20-63)	40 (20-63)
Gender (M:F)	598:620	130:180	85:67	26:44	56:53
Environmental exposures (%):					
Cigarette smoker					
Never smoked	625 (51.6)	153 (49.7)	72 (47.7)	30 (42.9)	49 (45.0)
Ex-smoker	373 (30.8)	81 (26.3)	49 (32.5)	19 (27.1)	30 (27.5)
<5 per day	22 (1.8)	7 (2.3)	2 (1.3)	3 (4.3)	3 (2.8)
5-15 per day	78 (6.4)	32 (10.4)	11 (7.3)	11 (15.7)	12 (11.0)
>15 per day	113 (9.3)	35 (11.4)	17 (11.3)	7 (10.0)	15 (13.8)
Alcoholic drinks					
None or rarely	428 (35.4)	124 (40.1)	60 (39.5)	33 (47.1)	45 (41.3)
1-2 per week	402 (33.3)	94 (30.4)	38 (25.0)	22 (31.4)	29 (26.6)
3-6 per week	219 (18.1)	38 (12.3)	20 (13.2)	4 (5.7)	12 (11.0)
7-10 per week	103 (8.5)	26 (8.4)	18 (11.8)	7 (10.0)	8 (7.3)
>10 per week	57 (4.7)	27 (8.7)	16 (10.5)	4 (5.7)	15 (13.8)
Aspirin					
None or rarely	623 (51.6)	140 (45.6)	65 (43.1)	24 (34.3)	42 (38.9)
1-2 per week	331 (27.4)	85 (27.7)	42 (27.8)	24 (34.3)	32 (29.6)
3-6 per week	132 (10.9)	47 (15.3)	27 (17.9)	13 (18.6)	18 (16.7)
7-10 per week	70 (5.8)	22 (7.2)	10 (6.6)	7 (10.0)	9 (8.3)
>10 per week	52 (4.3)	13 (4.2)	7 (4.6)	2 (2.9)	7 (6.5)
Paracetamol					
None or rarely	792 (66.0)	161 (52.6)	87 (58.0)	31 (45.6)	53 (50.0)
1-2 per week	295 (24.6)	81 (26.5)	42 (28.0)	18 (26.5)	25 (23.6)
3-6 per week	76 (6.3)	38 (12.4)	12 (8.0)	12 (17.7)	13 (12.3)
7-10 per week	17 (1.4)	14 (4.6)	5 (3.3)	5 (7.4)	8 (7.6)
>10 per week	20 (1.7)	12 (3.9)	4 (2.7)	2 (2.9)	7 (6.6)
Education					
Less than high school	59 (4.9)	12 (3.9)	6 (4.0)	4 (5.7)	3 (2.8)
High school	323 (26.7)	76 (24.5)	41 (27.0)	19 (27.1)	34 (31.2)
College	829 (68.5)	222 (71.6)	105 (69.1)	47 (67.1)	72 (66.1)
Marital status (% married)	981 (80.8)	218 (70.3)	109 (71.7)	50 (71.4)	81 (74.3)
Employment (% employed)	965 (79.6)	255 (82.3)	126 (82.9)	61 (87.1)	92 (84.4)
Non-GI PSC score (median, interquartile range):					
Frequency†	42.5 (38.2-49.0)	50.6 (44.5-58.5)	50.0 (42.7-58.7)	56.8 (49.1-63.7)	53.5 (46.9-61.6)
Severity‡	41.9 (37.4-48.6)	50.0 (43.5-57.6)	48.6 (42.8-57.0)	56.8 (48.8-62.8)	52.4 (45.6-61.0)
GI PSC score (median, interquartile range):					
Frequency*	36.1 (36.1-44.9)	55.8 (46.8-65.9)	56.1 (46.8-66.1)	62.9 (54.6-70.5)	62.9 (52.6-69.4)
Severity†	36.4 (36.4-45.2)	54.4 (46.5-65.4)	54.3 (45.6-66.1)	64.5 (52.5-69.1)	56.8 (46.5-68.0)

Note: Data on subjects who did not answer a specific item are not shown. Subjects with a history of peptic ulcer disease were excluded. Ulcer-like, dysmotility-like, and reflux-like categories are not mutually exclusive. GI=gastrointestinal; PSC=Psychosomatic Symptom Checklist. *Frequency score is a composite score based on 12 non-GI items or 5 GI items (coded 0 to 4) from the PSC eliciting how often the symptom or illness occurred in the last year. These were converted to ranks and summed/scaled to give a score between 0 and 100. †Severity score is a composite score based on 12 non-GI items or 5 GI items (coded 0 to 4) from the PSC eliciting how bothersome the symptom or illness was in the last year. These were converted to ranks and summed/scaled to give a score between 0 and 100.

ated with dyspepsia in the final model. Marital status was significantly associated with dyspepsia ($p < 0.05$), but the odds ratio in unmarried subjects was only 1.4 (compared with married individuals).

When ulcer-like, dysmotility-like, and reflux-like dyspepsia were considered separately, similar results were obtained (Table IV).

RISK FACTORS FOR DYSPEPSIA IN SUBJECTS WITH AND WITHOUT A PAST HISTORY OF PEPTIC ULCER
Of those with a past history of ulcer, 56 subjects reported dyspepsia in the previous year while 60 subjects had been symptom free. Ulcer-like dyspepsia was described by 48 of the subjects with dyspepsia and an ulcer history (86%), but 30 subjects also reported reflux-like dyspepsia and 23 dysmotility-like dyspepsia (two had non-specific dyspepsia).

To determine if excluding subjects with a peptic ulcer history introduced bias, the logistic regression analyses were repeated on all subjects including those with a past history of peptic ulcer ($n = 1644$). Adjusting for age, gender, marital status, employment status, and education level, we found that smoking, aspirin, and paracetamol (but not alcohol) were associated with dyspepsia. After adjusting for non-gastrointestinal complaints, however, none of these factors was significant, confirming the initial findings.

Discussion

While dyspepsia is known to be very common in the general population, no community based

studies have systematically investigated the relationship between these complaints and exposure to analgesics, smoking, and alcohol. As only a minority of people with dyspepsia present for medical care,¹⁷ and as the decision to consult is likely to be associated with factors that may confound aetiological studies,¹⁸ a population based investigation is the preferable way of assessing the role of environmental factors. It must be noted, however, that with a population based approach it is not possible to distinguish accurately between uninvestigated subjects who have functional dyspepsia or other causes of dyspepsia such as reflux oesophagitis or peptic ulcer.

Two previous case-control studies in outpatients failed to detect an association between aspirin, alcohol, or tobacco and documented functional dyspepsia, but only limited numbers of highly selected patients were evaluated.^{7,8} One of the case-control studies, however, found that paracetamol was a significant risk factor for functional dyspepsia.⁷ In our study of subjects with uninvestigated dyspepsia, we postulated that any association with paracetamol would probably be spurious, either because these patients were taking paracetamol for other aches and pains or possibly because paracetamol use and dyspepsia both represent the expression of an underlying psychological disturbance. Thus, when we adjusted for non-gastrointestinal somatic symptoms, paracetamol was no longer a significant risk factor in our community subjects, implying that it is not causally linked to dyspepsia. Our findings are also consistent with data from outpatients with peptic ulcer disease; while it was initially reported that recurrent gastric ulcer was associated with paracetamol use, this association was later shown to be spurious because patients with dyspepsia avoided aspirin and took paracetamol.¹⁹ As paracetamol is recognised to lack toxicity for the gastric and duodenal mucosa,^{20,21} it seems biologically implausible that this drug would induce either ulcers or dyspepsia.

Aspirin use is linked to dyspepsia but the risk seems to be dose-dependent. Thus, dyspeptic symptoms were reported by 24% of patients given 1000 mg of aspirin and 15% given placebo in the Aspirin Myocardial Infarction Study, a significant difference.²² However, in the Physicians' Health Study, where 325 mg was administered on alternate days, symptoms were less common on aspirin and occurred as frequently in the placebo group.²³ A dose-response relationship between aspirin and gastrointestinal complaints was also reported in the United Kingdom Transient Ischaemic Attack Trial.²⁴ High dose aspirin use was uncommon in the 20 to 64 year olds in this community, which probably explains why no association with this drug was detected. Even though our data suggest that avoidance of low dose aspirin is unlikely to benefit most persons with uninvestigated dyspepsia in the community, this does not mean that use of aspirin is entirely safe as serious complications may occur, albeit uncommonly, particularly in those who have pre-existing (but not necessarily known) peptic ulcer disease.^{25,26} The role of other non-steroidal anti-inflammatory drugs

TABLE III Odds ratios (and 95% confidence intervals) of potential risk factors for dyspepsia

Risk factor	Initial model*	Final model†
Smoking (current <i>v</i> never)	1.5 (1.1, 2.0)‡	1.2 (0.9, 1.8)
Alcohol (≥ 3 drinks/week <i>v</i> none)	0.9 (0.6, 1.2)	0.9 (0.7, 1.3)
Aspirin (≥ 3 tablets/week <i>v</i> none)	1.8 (1.3, 2.5)‡	1.1 (0.8, 1.6)
Paracetamol (≥ 3 tablets/week <i>v</i> none)	2.2 (1.5, 3.1)‡	1.3 (0.9, 1.9)

Note: Subjects with a history of peptic ulcer disease were excluded.

*Adjusted for age and gender by logistic regression.

†Adjusted for age, gender, significant non-gastrointestinal somatic complaints from the Psychosomatic Symptom Checklist, marital status and socioeconomic status.

‡Note that a 95% CI which does not contain the value 1 corresponds to a significantly ($p < 0.05$) increased odds.

TABLE IV Odds ratios (and 95% confidence intervals) of potential risk factors for the dyspepsia subgroups

Risk factor	Initial model*	Final model†
Ulcer-like:		
Smoking (current <i>v</i> never)	1.2 (0.8, 1.9)	1.0 (0.6, 1.6)
Alcohol (≥ 3 drinks/week <i>v</i> none)	0.9 (0.6, 1.4)	1.0 (0.6, 1.5)
Aspirin (≥ 3 tablets/week <i>v</i> none)	1.9 (1.2, 2.9)‡	1.2 (0.7, 1.9)
Paracetamol (≥ 3 tablets/week <i>v</i> none)	1.8 (1.1, 2.9)	1.1 (0.6, 1.9)
Dysmotility-like:		
Smoking (current <i>v</i> never)	2.2 (1.2, 3.9)‡	1.6 (0.8, 3.0)
Alcohol (≥ 3 drinks/week <i>v</i> none)	0.6 (0.3, 1.0)	0.6 (0.3, 1.2)
Aspirin (≥ 3 tablets/week <i>v</i> none)	2.8 (1.5, 5.1)‡	1.3 (0.6, 2.5)
Paracetamol (≥ 3 tablets/week <i>v</i> none)	3.6 (1.9, 6.9)‡	1.8 (0.9, 3.6)
Reflux-like:		
Smoking (current <i>v</i> never)	1.8 (1.1, 2.9)	1.4 (0.8, 2.3)
Alcohol (≥ 3 drinks/week <i>v</i> none)	0.8 (0.5, 1.3)	0.9 (0.6, 1.6)
Aspirin (≥ 3 tablets/week <i>v</i> none)	2.4 (1.5, 3.9)‡	1.2 (0.7, 2.2)
Paracetamol (≥ 3 tablets/week <i>v</i> none)	3.5 (2.1, 6.0)‡	1.9 (1.1, 3.5)

Note: Subjects with a history of peptic ulcer disease were excluded.

*Adjusted for age and gender by logistic regression.

†Adjusted for age, gender, significant non-gastrointestinal somatic complaints from the Psychosomatic Symptom Checklist, marital status and socioeconomic status.

‡Note that a 95% CI which does not contain the value 1 corresponds to a significant ($p < 0.05$) increased odds, but at an adjusted α -level for these subgroups (0.017) only those odds ratios with an \ddagger were significant.

(NSAIDs) was not investigated in this survey, and we have no information on whether subjects had modified their aspirin use in the past as a consequence of chronic abdominal symptoms.

Although the pathophysiological basis for subdividing subjects with uninvestigated dyspepsia into symptom subgroups has been questioned, this approach has gained wide acceptance.^{1 3 6 9 10} We postulated that dividing subjects with dyspepsia a priori into symptom subgroups would reduce heterogeneity if this were a valid classification. We found that the distribution of risk factors was generally similar regardless of subject classification. Furthermore, we found that the age and gender distributions of the dyspepsia subgroups were remarkably similar, which further suggests that such a classification may not be helpful in identifying distinct pathophysiological clusters in subjects with dyspepsia. We cannot, however, discount the possibility that a classification based on subjects identifying their predominant complaint, rather than using clusters of individual symptoms, would be more useful; such an approach now needs to be tested.

The strengths of the present study include the use of a previously validated questionnaire to measure symptoms and environmental factors, the unbiased sampling of a representative community population, and the adequate response rate obtained. The exposure variables sought were such that their use is likely to be remembered, so we believe that subject recall of environmental exposures was reasonably accurate.⁷ Indeed, when we tested subject recall for ulcer disease we found that the survey responses were highly concordant with the chart data. We cannot exclude the possibility that subjects with dyspepsia were more likely to remember exposure to environmental factors than those without dyspepsia, but such recall bias should have led to spuriously positive associations. As the current study failed to detect a significant risk (after adjusting for potential confounders) such bias is unlikely. We used a stricter definition of dyspepsia in the current study than has been used by us previously to identify the dyspepsia subgroups,¹ which we believe was a strength. The current study also evaluated a larger cohort and surveyed younger subjects aged 20 to 29 years who had not previously been included.¹ One of the weaknesses of community epidemiological studies is that underlying structural causes of dyspepsia cannot be determined. Others have shown that most people with dyspepsia in the community do not have a peptic ulcer at endoscopy.²⁷ We also found that excluding subjects with a known history of peptic ulcer did not introduce bias into the study, but this would not have removed all subjects with an ulcer nor would it have insured the exclusion of subjects with other organic diseases such as reflux oesophagitis. Thus, our findings cannot be directly extrapolated to patients with functional dyspepsia.

In conclusion, this study suggests that smoking, alcohol, and analgesics are not important risk factors for subjects aged 20 to 64 years with uninvestigated dyspepsia in the community once

potential confounders are taken into account. Moreover, none of these factors seem to be linked to symptom subgroups in uninvestigated dyspepsia, raising additional doubts about the value of this classification.

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