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A link between physician-diagnosed ulcer and anxiety disorders among adults

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ABSTRACT

Purpose: Previous studies have suggested an association between mood and anxiety disorders and peptic ulcer, yet extant work suffers from methodologic limitations. Centrally, previous epidemiologic studies have relied exclusively on self-report of ulcer. This study aimed to investigate the relationship between DSM-IV depression and anxiety disorders and physician-diagnosed ulcer among adults in the general population.
Methods: Data were drawn from a population-based, representative sample of 4181 adults aged 18 to 79 in the German National Health Interview and Examination Survey.
Results: Any anxiety disorder (odds ratio [OR], 2.6), panic disorder (OR, 5.2), panic attacks (OR, 3.8), and social phobia (OR, 3.3) were associated with increased likelihood of physician-diagnosed ulcer, compared with those without ulcer. There was evidence of a dose–response relationship between number of mental disorders and likelihood of current ulcer.
Conclusions: These findings provide initial evidence of a link between anxiety disorders and physician-diagnosed ulcer among adults in the community. Future work, ideally taking into account *Helicobacter pylori* infection, stress, and mental health problems is needed to improve our understanding of the possible mechanisms that can provide insight into the etiology of peptic ulcers.

Introduction

Peptic ulcer (gastric ulcer and/or duodenal ulcer) occurs in more than 1 in 10 adults in the United States (an estimated 14% past year prevalence) [1]. Peptic ulcers are associated with pain, dyspepsia, functional impairment, increased risk of comorbid gastrointestinal conditions, and medical complications as well as increased health care costs [2]. Although treatable, if not diagnosed and treated, ulcers can perforate or bleed, resulting in premature mortality.

The identification of *Helicobacter pylori* as an infectious cause for ulcer resulted in a near exclusive focus on infectious causes of peptic ulcer [3,4], with virtual abandonment of interest in stress or emotional factors both clinically and in research. However, as it has become clear that *H. pylori* is an important risk factor for ulcer, epidemiologic work has shown that the majority of people with *H. pylori* infection do not develop ulcers, those effectively treated for *H. pylori* can develop new ulcers and that ulcers develop in people without *H. pylori* infection [5]. Therefore, it seems that other factors, potentially in combination with *H. pylori* infection, must be considered in the etiology of peptic ulcer [6]. This insight has contributed to an increase in interest in the possible role of mental health in ulcer etiology [7–12]. Several studies have shown a link between mood and anxiety disorders and peptic ulcer that have not been explained by confounding owing to sociodemographic data, alcohol/drug dependence, or help-seeking bias [8–11].

Studies that have explored the relationship between mental disorders and peptic ulcer have several limitations. First, epidemiologic studies to date have relied exclusively on self-report diagnosis of ulcer, which is subject to report bias. There has been concern in particular, that those with depression/anxiety may be over-reporting physical health problems, including ulcer, because it has been shown that depression/anxiety is associated with perception of poorer health [13]. Second, timeframes have been unclear when comparing mental disorders and ulcer. Specifically, it is not clear whether mental health problems and ulcer are

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associated only when they occur concurrently, or at any point in the lifecourse. Third, it also has not been clear whether amount/level of psychopathology is related to likelihood of ulcer. No previous study has examined the potential dose–response relationship between mental health problems and ulcer.

This study had three specific goals toward filling these gaps. First, we aimed to investigate the relationship between Composite International Diagnostic Interview (CIDI) assessed mental disorders and physician-diagnosed peptic ulcer in a representative sample of adults in Germany. Second, we attempted to examine the relationship between current (past 12 months) mental disorders and both current (past 12 months) and remitted (before the past 12 months) ulcer. Third, we aimed to examine the relationship between level of psychopathology and likelihood of ulcer. We took into account potential confounding by demographic factors and drug and alcohol disorders in these relationships.

Methods

Sample

The German National Health Interview and Examination Survey (GHS) sample was drawn from the population registries of subjects aged 18 to 79 living in Germany in 1997. It represents a stratified random sample from 113 communities throughout Germany with 130 sampling units. The first sampling step was the selection of communities; the second step was the selection of sampling units. The third step was the selection of inhabitants. Reasons for nonparticipation, analyses of nonrespondents, and further information on samples and weighting are provided elsewhere [14,15]. The sample is representative of adults in Germany. After the study was described to the participants, written informed consent was obtained.

The current analyses include only the subsample that also underwent comprehensive mental health assessment (participants of the Mental Health Supplement [MHS]). The GHS-MHS included only persons aged 18 to 65 years of age. The conditional response rate of the GHS-MHS was 87.6%, resulting in a total of 4181 respondents who completed both core survey (physical assessment) and mental health assessment.

Assessment of ulcer

The core survey assessment included a standardized computer-assisted medical interview conducted by study physicians. Ulcer was diagnosed within the medical interview and diagnoses were made by a medical doctor. Questions in the medical interview included: (1) Have you ever been diagnosed with peptic or duodenal ulcer (doctors could ask additional questions or explain the condition if a respondent was not sure)? If Yes, (2) When was the first onset (age), and when did you have that condition last time (within last 4 weeks/within last 12 months/>1 year ago)? Study physicians considered the answers to these questions and any other clinically relevant information (e.g., whether the participant had had diagnostic tests, specific symptoms) in making a diagnosis.

Assessment of mental disorders

Most interviews of the GHS-MHS took place within 2 to 4 weeks of the core survey medical examination to ensure that data gathered in both examinations were contemporaneous. Psychopathologic and diagnostic assessments were based on the computer-assisted version of the Munich CIDI (DIA-X/M-CIDI) [16–18]. The DIA-X/M-CIDI is a modified version of the World Health Organization CIDI, version 1.2, supplemented with questions to cover *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* (DSM-IV) and *International Statistical Classification of Diseases and Related Health Problems-10* criteria. The DIA-X/M-CIDI is a fully structured interview that allows for the assessment of symptoms, syndromes, and current and lifetime diagnoses of DSM-IV mental disorders [19]. The following diagnoses were included in these analyses: Any mood disorders (including unipolar major depression, dysthymia, and bipolar disorders), major depression, any anxiety disorders (including panic disorder with or without agoraphobia, social phobia, specific phobia, generalized anxiety disorder, and obsessive-compulsive disorder), and panic disorder with or without agoraphobia, panic attacks, and social phobia.

Analytic strategy

First, multiple logistic regression analyses were used to examine the association between mood and anxiety disorder and odds of physician-diagnosed ulcer by comparing the prevalence of ulcer among those with and without each. These analyses were adjusted for differences in gender, socioeconomic status, and age. Analyses were then additionally adjusted for drug and alcohol use disorders. Odds ratios (OR) with 95% confidence intervals (CI) were calculated with Stata software package, release 7.0 [20]. Second, bivariate analyses were used to investigate the relationships between past 12-month mood and anxiety disorders and current and remitted ulcer. Finally, logistic regression analyses were used to examine the relationship between anxiety/mood symptoms and likelihood of ulcer. All tests were 2 tailed; the alpha level of significance was set at $P < 0.05$.

Results

Cohort characteristics

Adults with ulcer during the past year at the time of the survey were significantly older ($P < .0001$) and more likely to be male (Table 1) than were adults without ulcer. There were no socioeconomic status differences between those with and without ulcer.

Current mental disorders and current ulcer

Any anxiety disorder, panic disorder, panic attacks, and social phobia were associated with a significantly increased likelihood of current ulcer (Table 2), compared with those without anxiety disorders. These associations remained significant and their strength remained essentially unchanged after adjusting for age,

Table 1
Demographics associated with current and remitted ulcer among adults in Germany

	No lifetime ulcer (n = 3885) n (%)	Remitted ulcer (lifetime; not past 12 months; n = 246) n (%)	Current (past 12 months; n = 40) n (%)	*P*
Age (yrs)				<.0001
18–35	1327 (34.2)	20 (8.1)	8 (20.0)	
36–55	1379 (35.5)	69 (28.1)	14 (35.0)	
≥55	1179 (30.4)	157 (63.8)	18 (45.0)	
Gender				.01
Male	1756 (45.2)	131 (53.3)	21 (52.5)	
Female	2129 (54.8)	115 (46.8)	19 (47.5)	
Socioeconomic status				.6
Lower	759 (19.9)	49 (20.5)	8 (20.5)	
Middle	2198 (57.7)	141 (59.0)	21 (53.9)	
Upper	851 (22.4)	49 (20.5)	10 (25.6)	

Table 2
Mood and anxiety disorders and active and remitted ulcer among adults in Germany

	No lifetime ulcer (n = 385), n (%)	Remitted ulcer (lifetime; not past 12 mos; n = 246), n (%)	OR (95% CI)	Current ulcer (past 12 months; n = 40)	OR (95% CI)	AOR* (95% CI)	AOR†(95% CI)
Any anxiety	668 (17.2)	42 (17.1)	1.0 (0.7–1.4)	13 (32.5)	2.3 (1.2–4.5)‡	2.6 (1.3–5.2)‡	2.6 (1.3–5.2)‡
Panic disorder	108 (2.8)	8 (3.3)	1.2 (0.6–2.4)	5 (12.5)	5.0 (1.9–13.0)‡	5.3 (2.0–14.0)‡	5.2 (1.9–13.8)‡
Panic attack	212 (5.5)	22 (8.9)	1.7§ (1.1–2.7)‡	7 (17.5)	3.7 (1.6–8.4)‡	3.9 (1.7–9.1)‡	3.8 (1.6–9.0)‡
Social phobia	350 (9.0)	27 (11.0)	1.2 (0.8–1.9)	9 (22.5)	2.9 (1.4–6.2)‡	3.4 (1.6–7.4)‡	3.3 (1.5–7.3)‡
Any mood disorder	508 (13.1)	38 (15.5)	1.2 (0.8–1.7)	8 (20.0)	1.7 (0.8–3.6)	1.8 (0.8–3.9)	1.7 (0.8–3.9)
MDD	462 (11.9)	36 (14.6)	1.3 (0.9–1.8)	7 (17.5)	1.6 (0.7–3.6)	1.7 (0.7–3.8)	1.6 (0.7–3.8)

AOR = adjusted odds ratio; MDD = major depressive disorder.
* Adjusted for age, gender, and socioeconomic status.
† Adjusted for age, gender, socioeconomic status, and alcohol and drug use disorders.
‡ Odds ratio significant if $P < .05$.
§ Association was no longer significant after adjusting for age, gender, and socioeconomic status.

gender, socioeconomic status, and drug and alcohol use disorders. Current mood disorders were not associated with ulcer.

Current mental disorders and remitted ulcer

Current panic attacks were associated with increased odds of remitted ulcer (Table 2), compared with those without panic attacks, although this association was no longer significant after adjusting for age, gender, socioeconomic status, and drug and alcohol disorders. No other mood/anxiety disorders were associated with remitted ulcer.

Dose–response relationship between current mental disorders and current ulcer

There was evidence of a dose–response relationship between current mental disorders and current ulcer (Table 3) with increased prevalence of ulcer among adults with three or more current mental disorders (OR, 3.2; 95% CI, 1.4–7.3) and one or two mental disorders (OR, 2.0; 95% CI, 1.0–4.3), compared with those with none.

Discussion

The study has three key findings. First, anxiety disorders (past 12 months) are associated with significantly increased prevalence of physician-diagnosed ulcer (past 12 months) among adults in the general population. Second, anxiety disorders (past 12 months) are not associated with remitted ulcer (i.e., lifetime but not past 12 months). Third, there is evidence in support of a dose–response relationship between current mood/anxiety disorders and ulcer.

Our results suggest a relationship between anxiety disorders and physician-diagnosed ulcer belie concerns that the previously observed link between mental disorders and ulcer was owing to self-report bias. Consistent with previous studies using self-report of ulcer, the relationship between anxiety and ulcer is stronger than mood disorders. Our findings are also consistent with previous studies (e.g., Goodwin et al. [7]) in other population-based samples of adults in the United States, in which panic disorder was among the most strongly associated with ulcer as was also the case in the current study.

Table 3
Dose–response relationship between mood and anxiety disorders and current ulcer (past 12 months)

No. of mood/anxiety disorders	Current ulcer (past 12 months), n (%)	OR (95% CI)
None (n = 2925)	22 (0.8)	1.0
1–2 (n = 664)	10 (1.5)	2.0 (1.0–4.3)*
≥3 (n = 364)	8 (2.4)	3.2 (1.4–7.3)*

* Odds ratio significant if $P < .05$.

The mechanism of the relationship between anxiety disorders and ulcer remains unclear and cannot be determined from these data. There are several possibilities. First, there could be a causal relationship between the two. Having an ulcer could lead to an anxiety disorder (e.g., generalized anxiety disorder) owing to limitations on functioning or concern about one's physical health. Alternatively, extreme levels of anxiety could contribute to development of an ulcer through increased acid secretion. Another possibility is that there are a number of potential mediating factors. For instance, nonsteroidal anti-inflammatory drugs, such as aspirin and ibuprofen, are etiologically linked with ulcers and gastrointestinal complications [21,22]. Depression/anxiety have been linked to physical pain, which may increase the use of nonsteroidal anti-inflammatory drugs but whether this applies to anxiety is uncertain [23–25]. It remains possible that use of nonsteroidal anti-inflammatory drugs leads to both ulcer disease and anxiety explaining in part the links observed. Another potential explanation for the association between ulcer and anxiety disorders is the use of selective serotonin re-uptake inhibitors (SSRI) to treat anxiety. It has been shown that selective serotonin re-uptake inhibitors are associated with gastrointestinal bleeding via diminishing the efficacy of normal clotting mechanisms [26]. Current SSRI use in a Danish population-based case-control study were associated with uncomplicated peptic ulcers (OR 1.5, 95% CI,1.18–1.90) [27]. There are also common risk factors that could increase the risk of both. These include alcohol use disorders and drug use, although neither the current nor previous studies support this explanation. Another possibility is that increased levels of mast cells, which are associated with both heightened vulnerability to ulcer [28] and anxiety [29], could lead to increased susceptibility to their co-occurrence. Future studies are needed to examine these potential pathways.

There are a number of key study limitations that should be considered. First, although this study is the first population-based representative sample to include physician diagnoses of ulcer, there were no routine objective tests (e.g., endoscopy); therefore, misclassification is possible. Further, it is not known whether ulcers were duodenal or gastric. Because ulcers have different etiologies, lack of information on ulcer type limits interpretations. In addition, information on ulcer was provided to the physician by participants during the medical interview, and it is therefore based, in part, on self-report. However, the fact that physicians considered self-report of ulcer, as well as potential diagnostic tests, specific symptoms, and whatever other clinically relevant information seemed pertinent, make these diagnosis distinctly different from direct self-report, as

has been used in previous studies. Although the ideal might be to perform diagnostic tests on a representative sample, this is hindered by economic, and other potential obstacles to performing invasive diagnostic tests on a large, mostly health population. Second, we do not have information on medication use in this study and therefore cannot examine the possibility that medication use explains the relationship. Third, stressful life events were not measured in this study, so we could not examine the possibility that exposure to stress is a common risk factor that explains the relationship. Fourth, we do not have information on *H. pylori* infection. Although is it clear that *H. pylori* is a risk factor for peptic ulcer, but is not responsible for all cases, it would be ideal to examine the potentially overlapping and/or interactive role of both *H. pylori* and mental health in the same study. This should be a top priority for studies going forward.

In conclusion, the current study adds to the previous literature about the association between anxiety disorders and ulcer through the use of a more rigorous assessment of ulcer. Ideally, future studies would benefit from objective gastrointestinal testing. In addition, knowledge of whether patients have *H. pylori* would be useful in exploring whether there is a difference between the association of *H. pylori* or non-*H. pylori* ulcer with mental health disorders. More specific information about the type and etiology of ulcer being measured would allow future studies to begin assessing the mechanism of the relationship between ulcers and mood/anxiety disorders.

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