

Psychological Predictors of Peptic Ulcer Incidence in the Alameda County Study

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It has often been suggested that mood and personality predispose to peptic ulcer, but little prospective evidence exists. We used longitudinal data from the Alameda County Study to seek associations of psychological characteristics with later ulcer development, taking into account the possible confounding or mediating roles of nonpsychological factors. Among 4,595 Alameda County Study subjects ulcer-free in 1965, we studied five baseline psychological measures (depression, hostility, ego resiliency, social alienation or anomie, and personal uncertainty) with respect to reported ulcer in 1973-1974. All five measures had significant age-adjusted associations with incident ulcer [odds ratio (O.R.) 1.8-2.6]. After adjustment for smoking, drinking, skipping breakfast, lack of sleep, painful medical conditions, and liver disease, three measures remained significant: depression, anomie, and hostility. The age-adjusted O.R. of 2.8 [95% confidence interval (C.I.) 1.6, 4.8] for an upper versus a lower tertile index of independently predictive psychological factors fell to 2.1 with adjustment for health-related behaviors and medical conditions, and reached 1.7 (C.I. 1.0, 3.1) after addition of education to the model. We conclude that depression, maladjustment, and hostility are prospectively associated with peptic ulcer. These associations are partially accounted for by confounding or mediation by standard risk factors, and are to some extent related to socioeconomic status.

Key Words: Cohort study—Gender—Peptic ulcer—Psychology—Socioeconomic factors—Anomie—Anomie—Depression—Hostility.

Specific personality traits, particularly repressed hostility and dependency, may predispose to peptic ulcer (1,2). In various controlled studies, peptic ulcer patients have been found high in neuroticism (3,4), dependency (5,6), hostility (7), introversion (6,8), and personality disorders (9). In recent years, however, skepticism has been gaining ground (10), a recent review concluding, "There

is no convincing evidence for a causal link between particular personality types and DU [duodenal ulcer]" (11). This skepticism is in part related to better recognition of the limitations of cross-sectional data for evaluating psychological causes of disease: illness can itself be a source of distress, and sick persons also tend to exaggerate their recent life stress (so-called "effort after meaning") (12). Many measures of "mood" or "personality" are contaminated with items that, in organically ill patients, can be physically rather than psychologically based (13,14). Finally, the personality of ulcer patients seems to become more distinctive as the years pass since first diagnosis (15), raising the possibility that traits associated with ulcer may principally represent a response to illness.

Another reason for waning of interest has been a shift of emphasis in the field of psychosomatics from classic personality descriptors to external stressors (16,17), relegating the role of intrapsychic structures to their conditioning effects on coping style (18,19). Furthermore, the advent of endoscopy has greatly reduced confusion of ulcer with nonulcer dyspepsia, whose strong psychogenic component (20,21) may have biased past descriptions of peptic ulcer patients. Finally, in the eyes of many the discovery of *Helicobacter pylori* (22) has given the coup de grâce to the concept of a psychological component in ulcer pathogenesis.

Despite much current sentiment in favor of laying the whole question to rest, the older literature as well as several recent studies linking psychological stress to the onset and course of peptic ulcer (23-28) suggest that there may be some truth in the concept of a psychological predisposition to ulcer. Among the few attempts to demonstrate prospective links between personality traits and subsequent ulcer development, one old but methodologically sound study reported that susceptibility to ulcer was increased by dependency (2), and a more recent one suggested an association with the hypomania (Ma) scale of the Minnesota Multiphasic

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Personality Inventory (15). Neither of these studies addressed possible confounding by known ulcer risk factors. The Alameda County Study (ACS), a longitudinal study of behavioral, social, psychological, and economic influences on health (29), generated extensive descriptive data in 1965 regarding a large general population sample of adults and has reassessed their health status periodically. This offers an unusual opportunity for detecting an association of psychological characteristics with the development of peptic ulcer and for exploring the possible confounding or mediating roles of biomedical, behavioral, and sociodemographic factors (30). In our present analysis, we take on this task by examining reports of new peptic ulcer at the first ACS follow-up in relation to the baseline psychological characteristics of ACS subjects, while taking known ulcer risk factors into account.

MATERIALS AND METHODS

Population

The ACS began in 1965 with the distribution of 8,038 self-administered questionnaires to a stratified random sample of the adult inhabitants of Alameda County, California, obtaining responses for 6,928 individuals: 3,158 men and 3,770 women (29). The first follow-up of the cohort was performed in 1973–1974, when panel members not known to be dead were mailed a similar second questionnaire; 4,864 eventually answered, corresponding to 85% of located respondents. Further details on sampling and follow-up have been reported elsewhere (29).

Variables

The outcome variable for the present study was report of a new ulcer at the 1973–1974 follow-up survey. Respondents were questioned at both mailings regarding "stomach or duodenal ulcer" ("Here is a list of medical conditions that usually last for some time. Have you had any of these conditions during the past 12 months?"), and in 1973–1974 they were also asked, "What year did it start?" Subjects were excluded from the present analyses if they reported ulcer in 1965, or if they reported an ulcer in 1973–1974 with an onset before 1966. Among this at-risk population, all those reporting peptic ulcer in 1973–1974 were considered to have developed new ulcers.

Independent variables were five psychological measures from the 1965 questionnaire, selected either because of demonstrated associations with health outcomes in the ACS (personal uncertainty) or because they have been thought to be characteristic of ulcer patients (social maladjustment, low ego strength, depression, hostility).

The personal uncertainty scale, a seven-item measure that emerged from factor analysis of the psychological items on the 1965 ACS questionnaire (29), contains such items as "I have a hard time making up my mind about things I should do." Personal uncertainty has proved to be associated with health risk behaviors and also to have an independent impact on mortality rates in the ACS (29).

The ACS depression scale contains 18 items similar in content to other self-report depression measures (insomnia, low energy level, lack of enjoyment, etc.). Its psychometric char-

acteristics include a coefficient α of 0.77 and a correlation of $r = 0.66$ with the Beck Depression Scale (31,32).

McCloskey's nine-item scale assessing "anomy" (the psychological equivalent of the sociological concept of anomie) is a well-validated measure of social unease, alienation, or maladjustment (33) including such items as, "The trouble with the world today is that most people really don't believe in anything."

The ego resiliency scale (34) is composed of 19 items such as, "I think I am usually a leader in my group," and was designed to measure "resourcefulness, adaptability, and engagement in the world."

The hostility scale was created for this study from three items chosen for appropriate content. Two of them are near-identical to items from the Cook-Medley Hostility Scale ("I am sometimes cross and grouchy without any good reason" and "I lose my temper easily"); the third is, "I tend to be on my guard with people who are somewhat more friendly than I had expected."

Several 1965 risk factors were considered as possible adjustment variables: smoking (categorized as former, currently less than one pack per day, one pack per day, more than one pack per day), heavy alcohol use (81+ drinks/month for men, 61+ drinks/month for women), "often" or "always" skipping breakfast, chronic liver disease, and chronic bronchitis, all previously shown to be associated with ulcer in either men or women in this population (30), as well as sleeping habitually <7 h/night, and how much "hard physical work" they did on the job (asked only of men).

Use of nonsteroidal antiinflammatory drugs, an important cause of peptic ulcer, was not directly assessed in the 1965 ACS. Several items regarding painful conditions that might lead to use of such medications ("arthritis or rheumatism," "frequent headaches," and "stiffness, swelling, or aching in any joint or muscle") were therefore combined to provide a proxy for nonsteroidal antiinflammatory drug use (scored as no painful condition, one painful condition, or two to three painful conditions). The validity of this variable as a measure of nonsteroidal antiinflammatory drug use was tested using data from a separate population survey by the Human Population Laboratory, the Alameda County 1974 Cohort (35), which in addition to ascertaining the painful conditions also asked, "How often do you take aspirin, Bufferin, etc.?" ("almost daily, pretty often, not often, never"). These analyses showed that 185 of the 402 subjects reporting two or three of the three painful conditions (46.0%) took aspirin "pretty often" or "almost daily," as compared with 213 of 667 (31.9%) of those with one painful condition and 165 of 2,036 (8.1%) of those with none ($p < 0.001$); vice versa, 70.6% of all frequent aspirin users reported at least one of the three painful conditions. We concluded that the "painful conditions" variable is an adequate proxy for nonsteroidal antiinflammatory drug use.

Education (less than high school, high school diploma only, more than high school) was used as a measure of socioeconomic status, which is associated with ulcer development in this population (30).

Statistical Methods

Depression and personal uncertainty were trichotomized using previously determined cutoff points (29,31), whereas anomy and personal uncertainty were classed as low, moderate, or high, and hostility (a score based on only three items) as absent or present, by dividing the population in as close as possible to equal splits based on the marginal distributions of the variables.

Logistic regression analysis was used to determine the age-adjusted association of each baseline psychological and physical variable with later ulcer development in the entire study population. Further logistic regression analyses added the other risk factors to each logistic model. Dummy variables were used to adjust for age (25–39, 40–49, 50–59, and ≥59 years), for smoking (former, <1 pack, 1 pack, >1 pack), and for pain (one painful condition, two to three painful conditions).

To determine the independence of the various psychological measures, a multivariate logistic model was examined, including all five of them plus age. In addition, an ulcer risk index of psychological characteristics was constructed by summing the tertile scores (0 for lowest tertile, 1 for middle tertile, and 2 for highest tertile) of trichotomized variables that retained a substantial independent association with incident ulcer [odds ratio (O.R.) ≥ 1.5 for either moderate or high level in the multivariate model]; hostility was scored as 0–1. This a posteriori index was then used to explore the relative importance of psychological factors in subject subgroups, to examine the mediating or confounding roles of known ulcer risk factors, and to correct for possible bias that could have been introduced by misreporting of diagnoses.

RESULTS

Outcomes

New ulcers were reported by 55 women and 49 men in 1973–1974, among 4,595 individuals at risk. Because the age-adjusted risk of new ulcer was similar in women and men [O.R. for male sex = 1.1, 95% confidence interval (C.I.) 0.8, 1.6], the principal analyses were performed with both sexes combined.

Adjustment Variables

The age-adjusted associations of incident ulcer with the nonpsychological risk factors examined are reported in Table 1. All except chronic bronchitis were significantly associated with ulcer development and were therefore used as adjustment variables; hard physical labor was used only in the separate analyses of men, because the question was not asked of women in the 1965 wave of the ACS.

Individual Psychological Risk Factors

All five psychological measures were significantly associated with incident ulcer, with age-adjusted O.R.s ranging between 1.9 and 2.6 (Table 2). Adjustment for smoking, heavy drinking, skipping breakfast, little sleep, painful medical conditions, and liver disease weakened these associations to some extent, but moderate and/or high scores on depression, anxiety, and hostility were still associated with ulcer development even after adjustment for all physical risk factors. Further adjustment for sex did not alter these results.

Psychological Index

In a multivariate logistic regression model along with age (Table 3), four of the five psychological characteris-

TABLE 1. Prospective age-adjusted association between individual non-psychological variables and peptic ulcer development, Alameda County Study, 1965–1974

Variable	Odds Ratio	95% C.I.
Male sex (N = 2008)	1.1	0.8, 1.6
Never smoked (N = 1881)	1.0	
Ex-smoker (N = 750)	1.2	0.6, 2.3
Smokes < 1 pack/day (N = 624)	1.9*	1.0, 3.6
Smokes 1 pack/day (N = 776)	2.8***	1.6, 4.8
Smokes > 1 pack/day (N = 538)	2.8***	1.6, 5.1
Skips breakfast (N = 2398)	1.9**	1.3, 2.9
Heavy drinker (N = 429)	1.9*	1.0, 3.6
Sleeps < 7 hours/night (N = 610)	1.7*	1.0, 2.8
No painful medical conditions (n = 3001)	1.0	
1 painful condition (N = 1074)	1.6*	1.0, 2.6
2 - 3 painful conditions (N = 537)	2.2**	1.3, 3.8
Liver disease (N = 38)	4.8*	1.1, 21.1
Chronic bronchitis (N = 238)	1.9	0.8, 4.3
No hard physical labor on the job (N = 869)†	1.0	
Hard on-the-job labor (N = 820)†	2/1†**	1.3, 3.4
Not working (N = 270)†	1.2†	0.8, 2.0
Attended college (N = 1741)	1.0	
High school dropout (N = 1371)	2.4***	1.4, 4.0
High school diploma only (N = 1485)	1.7*	1.0, 2.9

*p < 0.05

**p < 0.01

***p < 0.001

†Among men only.

tics retained some independent association with ulcer development. These four—anxiety, depression, hostility, and personal uncertainty—were therefore combined, as described in the Statistical Methods section, into a psychological ulcer risk index ranging from 0 (lowest category on all four scales) to 7 (upper half on hostility, highest tertile on the other three scales); scores of 0–1 were classified as low (N = 1,126), of 2–3 as medium (N = 1,678), and of 4–7 as high (N = 1,802).

Successive logistic regression models (Fig. 1) demonstrated that the age-adjusted risk of peptic ulcer fell from O.R. 2.8 for subjects with a high index (95% C.I. 1.6, 4.8) to O.R. 2.1 (95% C.I. 1.2, 3.7) after adjustment for smoking, heavy drinking, skipping breakfast, liver disease, lack of sleep, and painful medical conditions, a drop of 0.7/1.8 or 38.9% in excess risk. Similarly, the risk associated with a medium index fell from O.R. 1.7 (95% C.I. 0.9, 3.0) to O.R. 1.4 (95% C.I. 0.8, 2.6). The minimal impact on the O.R. of adjustment for each organic or behavioral risk factor individually suggests that none is by itself a major confounder or mediator of the effect of psychological characteristics on ulcer formation.

In this population, the sociodemographic predictors of peptic ulcer development are different for men and for women. Because women were more sensitive to stressors such as unemployment (30), we determined the sex-specific, age-adjusted risk associated with high index scores. As expected, it was much higher in women (O.R. 12.8,

TABLE 2. Prospective association between individual psychological factors and peptic ulcer development, Alameda County Study, 1965-1974

	Adjusted for:			
	Age Alone		All risk factors†	
	O.R.	95% C.I.	O.R.	95% C.I.
Low depression (N = 2425)	1.0		1.0	
Moderate depression (N = 1605)	1.7**	1.1, 2.7	1.6*	1.0, 2.5
High depression (N = 567)	2.1***	1.2, 3.7	1.5	0.8, 2.8
Low personal uncertainty (N = 1561)	1.0		1.0	
Moderate pers. uncertainty (N = 1741)	1.8*	1.1, 3.0	1.5	0.9, 2.5
High pers. uncertainty (N = 1285)	2.0**	1.2, 3.4	1.4	0.8, 2.4
Low anomy (N = 1468)	1.0		1.0	
Moderate anomy (N = 2183)	1.5	0.9, 2.5	1.3	0.8, 2.2
High anomy (N = 919)	2.6***	1.5, 4.6	2.2**	1.3, 3.9
High ego resiliency (N = 1009)	1.0		1.0	
Moderate ego resiliency (N = 2829)	1.1	0.7, 1.9	1.1	0.6, 1.8
Low ego resiliency (N = 749)	1.9*	1.1, 3.5	1.6	0.8, 2.9
Low hostility (N = 2924)	1.0		1.0	
High hostility (N = 1618)	1.8**	1.2, 2.7	1.6*	1.0, 2.3

†Age, smoking, skipping breakfast, alcohol abuse, lack of sleep, liver disease, painful medical conditions.

**p < 0.01.

*p < 0.05.

***p < 0.001.

95% C.I. 2.8, 49.3) than in men (O.R. 1.7, 95% C.I. 0.9, 3.3), although the C.I. for women was wide. Among men, this trend toward an influence of psychological factors was further weakened by adjustment first for the previous set of nonpsychosocial risk factors (O.R. 1.3, 95% C.I. 0.7, 2.7), and then for hard physical labor as well (O.R. 1.3, 95% C.I. 0.6, 2.6); adjusting only for hard physical labor yielded an O.R. of 1.5 (95% C.I. 0.8, 3.0). In contrast, the fully adjusted O.R. for women was 8.3 (95% C.I. 1.9, 35.5) for a high index and 7.3 (95% C.I. 1.7, 31.7) for a medium index.

The increased risk of ulcer development associated with psychological characteristics proved nearly identi-

cal for subjects under 40 years of age at baseline (O.R. 3.0 for a high index score, C.I. 1.4, 5.4) and for those 40 years or older (O.R. 2.6, C.I. 1.2, 5.6).

Addition of education to the logistic regression model lowered the age-adjusted O.R. to 2.3 (95% C.I. 1.3, 4.0) for a high psychological index and to 1.5 (95% C.I. 0.8, 2.7) for a medium index. In a final model including education in addition to health-related behaviors and medical conditions, the O.R. was 1.7 (95% C.I. 1.0, 3.1) for subjects with a high index and 1.3 (95% C.I. 0.7, 2.4) for subjects with a medium index.

Differential Misreporting: A Worst-Case Model

Because our outcome variable was determined by self-report, some misreporting could have been influenced by psychological factors. We attempted to correct for any resulting bias by constructing a worst-case model of the 2 × 3 contingency table displaying index tertile by ulcer incidence. The key assumption in creating a new, hypothetical contingency table was that all false-positive reports of ulcer would be among subjects scoring in the upper tertile on the psychological ulcer risk index. On the basis of a population-based endoscopy study, it can be estimated that the false-positive rate among self-reported peptic ulcer will be ≤17%, and that false-negative reports are negligible (36). Our worst-case model therefore reclassified 17% × 104 = 18 self-reported ulcer cases from the high-index ulcer cell to the high-index nonulcer cell. The crude O.R. for ulcer development associated with a high versus a low index, which had been 2.7 in the true contingency table, fell in this worst-case model to 1.8 ($\chi^2 = 3.76$, p = 0.05).

TABLE 3. Multivariate prospective associations between psychological factors and peptic ulcer development, Alameda County Study, 1965-1974

	O.R.	95% C.I.	p
Age			
25 - 39	2.5	1.1, 5.7	0.02
40 - 49	2.3	1.0, 5.4	0.05
50 - 59	1.8	0.7, 4.6	0.19
> 59	1.0	0.4, 3.0	0.89
Moderate depression	1.5	0.9, 2.4	0.08
High depression	1.5	0.8, 3.0	0.24
Moderate personal uncertainty	1.5	0.9, 2.6	0.14
High personal uncertainty	1.2	0.6, 2.2	0.62
Moderate anomy	1.4	0.8, 2.4	0.22
High anomy	2.1	1.1, 4.0	0.02
Moderate ego resiliency	0.7	0.4, 1.3	0.32
Low ego resiliency	0.8	0.4, 1.7	0.57
Hostility	1.5	0.9, 2.3	0.10

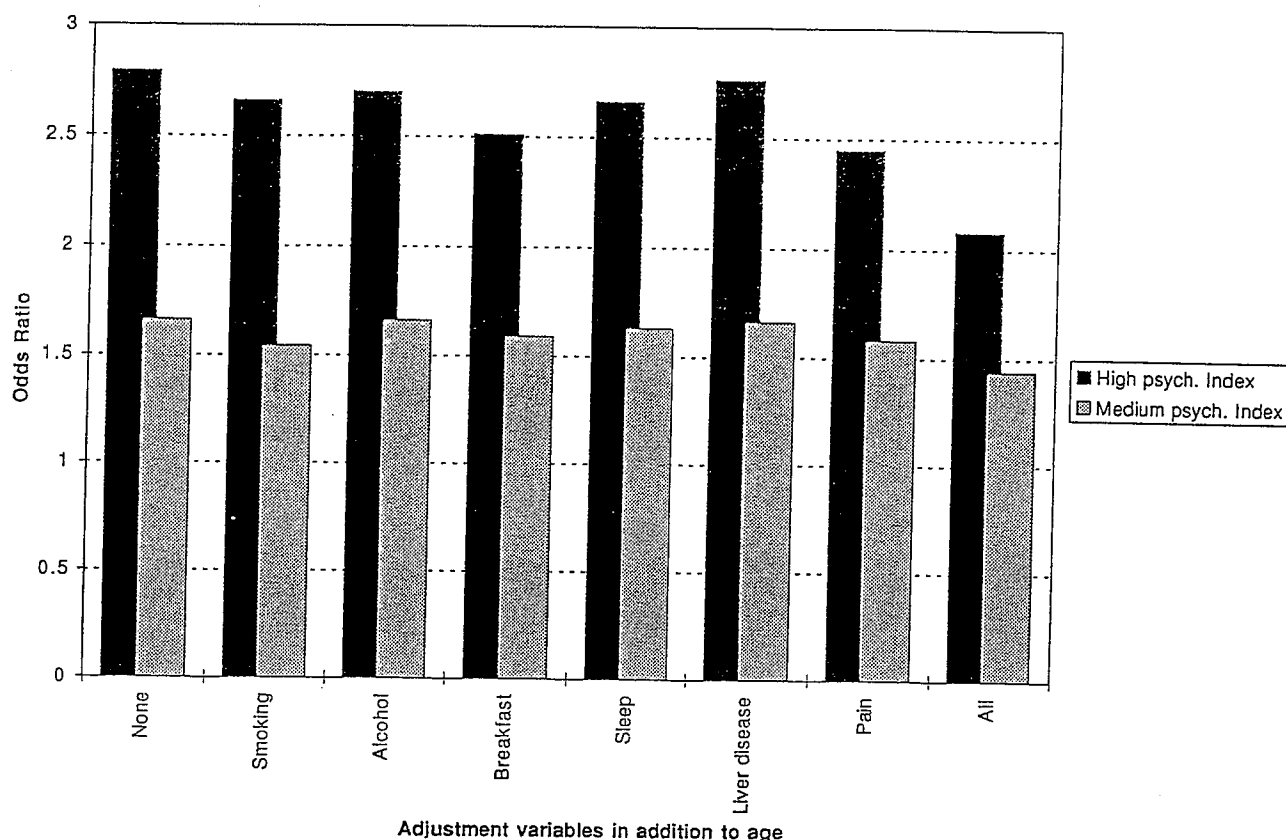


FIG. 1. Peptic ulcer development according to ulcer psychological risk index score: age-adjusted odds ratios for upper two tertiles with respect to lowest tertile, with adjustments for health behaviors and associated disease. Alameda County Study, 1965–1974.

DISCUSSION

Among a general population sample initially free of peptic ulcer, psychological characteristics including depression, personal uncertainty, "anomy" or social alienation, low ego resiliency, and hostility were significantly associated with the development of ulcers during the following 9 years. To some extent these associations were accounted for by risk factors that could be considered confounders or mediators: smoking, heavy alcohol use, skipping breakfast, lack of sleep, and painful medical conditions. Even after complete adjustment for these factors, however, several traits (hostility, anomy, and depression) remained predictive of subsequent ulcer development.

Psychological predictors, like concrete life stressors (30), proved to be more strongly associated with ulcer in women than in men in this population. These results are consistent with studies finding gender differences in psychological influences on cardiovascular disease (37,38).

Although painful medical conditions were examined mainly as a proxy for nonsteroidal antiinflammatory drug use, it must be noted that their modest confounding of the distress–ulcer association reflects, in addition, an

association between pain and psychological states. The direction of causation could be in both directions: to the extent that distress increases pain (somaticizing), nonsteroidal antiinflammatory drug use will be a mediator between psychological factors and ulcer formation; if chronic pain causes psychological distress, on the other hand, it will be a confounder. Adjustment for educational achievement attenuated the association between psychological factors and ulcer, suggesting that part of the explanation for this association lies in the complex interactions between psychological states and socioeconomic status.

Our study has several limitations. The first is the use of self-reported ulcer diagnoses. We attempted to overcome this problem by using the best available rates of false-positive and false-negative ulcer reporting in population surveys to estimate to what extent our findings could be due to misreporting, and found the most conservative estimate of the increased ulcer risk related to psychological characteristics to remain substantial.

Another major limitation is that no information is available from the ACS regarding *H. pylori*, arguably the most important risk factor for peptic ulcer development (22,39,40). Differential distribution of this infection according to psychological characteristics is unlikely to

have generated the present results, because psychological distress seems, if anything, to be inversely rather than directly associated with *H. pylori* antibody titers among groups of patients with gastrointestinal disorders (41-43). It is possible, however, that in a general population there may be an association between *H. pylori* and adverse psychological characteristics due to confounding by a third factor, such as low socioeconomic status.

A final limitation is the choice of psychological characteristics for examination, which was dictated partially by their availability in the data base. Fortunately, the 1965 ACS questionnaire was rich in measures among which to choose. The constructs of low ego resiliency and personal uncertainty have clear affinities to dependency, said in the older literature to be a cardinal feature of ulcer patients (1,2). Depression, although perhaps less likely to be a lasting character trait and although reported inconsistently in ulcer patients (9,13,44,45), was examined because it has been hypothesized to be the major link between life stress and physical illness in general (46). It should be observed that of all the psychological characteristics studied, the strongest association with ulcer was found for anomie (the intrapsychic reflection of anomie), a global key for interpreting the human environment that has been little studied previously with regard to health outcomes (aside from suicide), but that has affinities with pessimism (47).

The possibility that certain psychological traits, especially dependency, anger, and low self-esteem, may predispose to ulcer has been repeatedly suggested in the past, but we take our study to be the first to demonstrate that psychological characteristics have a prospective association with peptic ulcer development while taking important confounders into account. If these results are valid, and if the concept of an "ulcer personality" thus deserves some degree of rehabilitation, the question must be asked: How might psychological characteristics predispose to ulcer?

Several contributing behavioral and psychophysiological mechanisms can be hypothesized. One pathway involves behavioral effects, because ulcer-related health risk behaviors seem likely to be distributed unevenly with respect to psychological characteristics. In fact, smoking, use of nonsteroidal antiinflammatory drugs, and other aspects of lifestyle accounted for a certain proportion of the association between personality and ulcer development in the present study. Another important mechanism is through effects on gastric mucosal function: Psychological distress has a well-established link with gastric acid hypersecretion (48-51), possibly through vagal pathways, and it has been shown that ulcer patients (52) and subjects with certain personality characteristics (53,54) are particularly likely to react to stress by increasing gastric acid secretion. Psychological factors could also increase the delivery of acid to the duode-

num by altering gastric motility (55), could decrease mucosal defenses by affecting gastric blood flow or mucus characteristics, and could promote or abet *H. pylori* infection by psychoneuroimmunologic or other mechanisms (56) in addition to the facilitation of *H. pylori* invasion of the duodenal mucosa that may result from gastric hypersecretion (57).

We conclude that psychological characteristics including depression, personal uncertainty, anomie, and hostility are prospectively associated with peptic ulcer in the general population, especially in women. These associations can be explained in part by distributions of health risk behaviors and other medical conditions, but they persist even after a broad set of such potential confounders or mediators have been taken into account.

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