Long-Term Medical Conditions and Major Depression: Strength of Association for Specific Conditions in the General Population

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Background: The prevalence of major depression (MD) in persons with nonpsychiatric medical conditions is an indicator of clinical need in those groups, an indicator of the feasibility of screening and case-finding efforts, and a source of etiologic hypotheses. This analysis explores the prevalence of MD in the general population in relation to various long-term medical conditions.

Methods: We used a dataset from a large-scale Canadian national health survey, the Canadian Community Health Survey (CCHS). The sample consisted of 115 071 subjects aged 18 years and over, randomly sampled from the Canadian population. The survey interview recorded self-reported diagnoses of various long-term medical conditions and employed a brief predictive interview for MD, the Composite International Diagnostic Interview Short Form for Major Depression. Logistic regression was used to adjust estimates of association for age and sex.

Results: The conditions most strongly associated with MD were chronic fatigue syndrome (adjusted odds ratio [AOR] 7.2) and fibromyalgia (AOR 3.4). The conditions least strongly associated were hypertension (AOR 1.2), diabetes, heart disease, and thyroid disease (AOR 1.4 in each case). We found associations with various gastrointestinal, neurologic, and respiratory conditions.

Conclusions: A diverse set of long-term medical conditions are associated with MD, although previous studies might have lacked power to detect some of these associations. The strength of association in prevalence data, however, varies across specific conditions.

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Clinical Implications

- Patients with long-term medical conditions are generally more likely to have major depression (MD) than are those without such conditions.
- Associations between medical conditions and MD are not restricted to those conditions known to be linked to depression through physiological mechanisms.
- Young people with long-term medical conditions have a particularly high prevalence of MD.

Limitations

- Because these are cross-sectional data, it was not possible to evaluate causal effects.
- A brief predictive measure of MD was employed.
- The study relied on self-reported medical diagnoses.

Key Words: *depressive disorder, health surveys, chronic disease, prevalence*

Epidemiologic studies have documented an elevated prevalence of major depression (MD) in association with various long-term medical conditions. Some of these studies used data from large-scale investigations (1–5), but none have had sample sizes large enough to provide precise comparisons of the strength of association linking MD and specific conditions. Associations between prevalent medical conditions and prevalent MD reflect the end result of a set of complex underlying factors, including the incidence of medical conditions in people with MD, the incidence of MD in people with medical conditions, and the effect of MD and medical conditions on each others' mortality and prognosis. Isolating such factors typically requires specialized clinical studies, whereas exploration of prevalence requires large-scale population-based data collection. The objective of this study reflects the latter aim—to explore the prevalence of MD in relation to a set of medical conditions in a large sample from the general population.

Associations between MD and some conditions, such as migraine headaches, have been replicated consistently (2–4), whereas predominantly negative results have been reported from population-based studies for some other conditions, most notably, hypertension (1–3,5) and diabetes (1–5). However, where negative results for common illnesses have been reported in population studies, the possibility remains that a weak or modest effect might have been missed because of type II error.

Irrespective of causal mechanisms, the impact of depressive disorders on quality of life and clinical management highlight the importance of depressive comorbidity in many medical conditions (6–11). Some studies conducted in clinical settings have identified high frequencies of MD. For example, Kovacs and others reported a 27.5% prevalence of MD during a 20-year follow-up of youths diagnosed with insulin-dependent diabetes mellitus (12). The study sample, however, derived from a tertiary level hospital, and the reported prevalence from this and other clinically based studies may not be applicable to the general population or to populations seen in primary care.

Associations between long-term medical conditions and MD in the population are important for clinical practice and for health service planning. Clinically, these associations provide an index of suspicion when patients are assessed in specific clinical groups. Also, they provide useful information about the interpretation of screening or case-finding instruments in these groups. Because the positive predictive value of a case-finding or screening test depends on the base rate in the population screened, the predictive value of a test will generally be higher in clinical circumstances characterized by higher prevalence. For service-planning purposes, information about MD prevalence in various clinical groups may be an important indicator of treatment need. Finally, the pattern of prevalence may help to generate hypotheses about etiologic associations that were not previously held. Unfortunately, population-based estimates of depression prevalence in people with medical conditions are often unavailable. For example, in the case of asthma and chronic obstructive pulmonary disease, most studies have been conducted on a small scale and have not been population-based (13). Many studies have used symptom ratings rather than diagnostic instruments (14).

Some medical conditions are thought to be capable of causing depression through physiological mechanisms. Such conditions include epilepsy (15), hypothyroidism, multiple sclerosis (16), and pancreatic cancer (17,18). Many other conditions, such as chronic pain (19) and cardiovascular disease (20), may contribute to the etiology of depression through biological as well as psychosocial mechanisms, and for these conditions, it has often also been suspected that depression may contribute to the etiology of the medical conditions. Some conditions may have biological links to depression that have not previously been suspected. For example, regional cerebral hypoperfusion has recently been reported in patients with untreated celiac disease (21).

Methods

This analysis included 115 071 (of a total of 130 880) members of the Canadian Community Health Survey (CCHS) sample aged 18 years or over at the time of data collection. The CCHS sample was a geographically based probability sample that used a sampling frame developed by the Canadian national statistical agency, Statistics Canada. Data for the CCHS were collected in 2000 and 2001. Additional information about the survey can be found at http://stcwww.statcan.ca/english/sdds/3226.htm.

The CCHS interview incorporated a brief predictive instrument to identify major depressive episodes (MDEs) occurring during the year preceding the CCHS interview. This instrument, called the Composite International Diagnostic Interview-Short Form for Major Depression (CIDI-SFMD), was developed by Kessler and colleagues (22). Subjects endorsing 5 CIDI-SFMD symptoms, approximating those listed in the DSM-IV A criterion for MD (23), were regarded as having probable MD in this analysis. Validation studies have suggested that 75% to 90% of subjects endorsing 5 or more major depressive symptoms on the CIDI-SFMD have had an episode of MD during the preceding year (22,24).

The CCHS included questions about several health conditions. The selection of specific conditions to be included in the interview was made by Statistics Canada, based on input from an expert committee. The list of conditions is by no means exhaustive and was not formulated with reference to any specific hypotheses about MD. In each case, self-reported

diagnoses were obtained with the following item: "Now I'd like to ask about certain long-term conditions that have lasted or are expected to last 6 months or more and that have been diagnosed by a health professional . . . Do you have . . . (*interviewer inserts the name of each specific condition)*." The CCHS did not include clinical confirmation of the validity of the self-reported diagnoses. However, since the items inquiring about these diagnoses all referred to those made by health professionals, the self-reported diagnoses should have represented clinical diagnoses and not merely survey subjects' opinions. All the conditions that were evaluated in the CCHS were included in the current analysis, except Alzheimer's disease, since the CIDI-SFMD has not been validated in people with cognitive impairment.

We calculated the annual prevalence of MD and 95% confidence intervals (CIs) for subjects with and without various long-term conditions. Odds ratios (ORs) were also calculated, and we used logistic regression to evaluate possible interactions between chronic conditions, age, and sex. The sampling procedures employed in the CCHS involved both stratification and clustering. We used a bootstrap procedure developed by Statistics Canada for statistical analysis. This procedure accounts for design effects owing to the complex sampling procedures.

Results

The overall 12-month prevalence of MD in the CCHS was 7.4% (95%CI, 7.2% to 7.6%). This is higher than the annual prevalence reported from the National Population Health Survey (25,26), the Edmonton study (27), and the Mental Health Supplement of the Ontario Health Survey (28) but lower than some other Canadian estimates (29,30). As expected, having one or more reported long-term medical conditions was associated with MD. The annual prevalence of major depressive disorder in subjects reporting one or more conditions was 9.2% (95%CI, 8.% to 9.4%), compared with 4.0% (95%CI, 3.7% to 4.3%) in those not reporting a condition. Table 1 presents MD prevalence tabulated by specific chronic condition.

Table 1 indicates that the prevalence of MD within various disease groups differs considerably. Table 2 presents a series of logistic regression analyses. In each case, the median age for subjects reporting a long-term condition was included in the model as a categorical variable, along with interaction terms. For most conditions, age and sex interactions were not evident, and simplified models are depicted in Table 2.

In the case of a category containing bowel disorders, Crohn's disease, and colitis, the association with MD was found to be stronger in subjects falling below the median age (52 years) for these conditions (Wald $\chi^2 = 5.88$, $P = 0.015$). The ORs were elevated in each age category (1.9 and 2.8 in the older and younger age category, respectively). For food allergies and chemical sensitivities, there was an interaction between these conditions and sex, with the condition being more strongly associated with MD in men than in women. Wald tests for the interaction terms were significant both for food allergies (Wald $\chi^2 = 4.89$, $P = 0.027$) and for "chemical sensitivities" (Wald $\chi^2 = 7.56$, $P = 0.006$). These regression models are presented in Table 3. For food allergies, the fitted ORs from this model were 2.1 for men and 1.6 for women. For "chemical sensitivities," the fitted ORs were 3.7 for men and 2.1 for women.

For several other conditions, the logistic regression analysis was inconclusive as a result of data-release conditions. Some data release conditions are put in place by Statistics Canada to deter the release of highly imprecise estimates. In the case of cataracts, glaucoma, and Parkinson's disease, coefficients of variation associated with terms in the regression analyses exceeded levels suitable for release. For urinary incontinence, significant positive interactions were observed for below median age and female sex, but it was not possible to evaluate third-order interactions because of data-release prohibitions.

Discussion

For some of the long-term conditions evaluated in this analysis, there is already an extensive literature documenting an association with MD. This is true, for example, for multiple sclerosis and stroke. The evidence from population-based studies has been mixed or predominantly negative for 2 important and commonly occurring conditions: hypertension and diabetes. The data presented here clarify that the previous negative associations between hypertension and diabetes probably represented type II errors. With the benefit of an extremely large sample size, it has been possible to show in this analysis that these conditions are associated with MD in the general population but that the strength of association is not as strong as for some other conditions. Since the CCHS was a general health survey and did not specifically evaluate all medical conditions potentially associated with MD, it is not possible to conclude that all chronic conditions are associated with MD. However, associations were found for most of the conditions evaluated in this analysis. Aside from chronic fatigue and "chemical sensitivities," the strongest associations were observed for gastroenterological, neurological, and respiratory conditions, and also for conditions associated with pain.

One limitation of the data used in this analysis was the reliance on self-report. Some of the diagnostic data may be inaccurate, and the categories investigated were, by necessity, somewhat crude. For example, the term "arthritis" did not differentiate between rheumatoid arthritis and osteoarthritis. Also, responses to other items, for example, the question on back problems, might have overlapped with other diagnostic

Table 1 Prevalence of major depression in persons with self-reported long-term medical conditions

Chronic medical condition	Prevalence of condition (%)	Annual MD prevalence (%)	95%CI for MD prevalence (%)
Chronic fatigue syndrome	0.8	36.4	32.0 to 40.7
Fibromyalgia	1.2	22.2	19.4 to 24.9
Stomach or intestinal ulcers	3.2	16.7	15.0 to 18.3
Chemical sensitivities	2.0	16.5	14.3 to 18.7
Bowel disorders, Crohn's disease, and colitis	2.3	16.4	14.6 to 18.2
Multiple sclerosis	0.2	15.7	10.9 to 20.6
Urinary incontinence	2.3	14.5	12.7 to 16.3
Epilepsy	0.6	13.6	10.0 to 17.2
Asthma	7.9	13.4	12.4 to 14.4
Food allergies	7.4	12.7	11.7 to 13.7
Back problems	18.8	12.6	12.0 to 13.3
Cancer	1.9	11.8	9.7 to 13.8
Emphysema or COPD	1.2	11.7	8.8 to 14.6
Migraine	9.4	10.2	8.2 to 12.3
Thyroid conditions	5.2	10.1	9.0 to 11.1
Arthritis or rheumatism	16.7	10.0	9.4 to 10.6
Stroke	1.1	8.6	6.7 to 10.6
Parkinson's disease	0.1	7.9	2.2 to 13.7
Diabetes	4.5	7.7	6.7 to 8.6
Heart disease	5.4	7.3	6.4 to 8.2
High blood pressure	13.9	6.9	6.4 to 7.4
Glaucoma	1.4	6.6	4.9 to 8.2
Cataracts	4.1	5.2	4.3 to 6.0
Any chronic condition	65.7	9.2	8.9 to 9.5
No chronic condition	34.3	4.0	3.7 to 4.3

COPD = chronic obstructive pulmonary disease; MD = major depression

categories, such as arthritis or fibromyalgia. One recent literature review found a stronger association of depressive symptoms with rheumatoid arthritis than with osteoarthritis and a stronger association with back pain than with rheumatoid arthritis (31). These categories were not distinguished in the CCHS questionnaire. Similarly, MD may be more strongly associated with urge and mixed incontinence than with stress incontinence (9,10)—2 categories that were also not differentiated.

The reliance on self-report data resulted in an inability to differentiate between subjective perceptions of symptoms and objective signs. This is an important concern for some conditions. For example, in asthma, depression scores have been found to correlate with subjective symptoms but not with objective measures (that is, peak flow variability or response to methacholine) (32).

The instrument evaluating depression in the CCHS was a brief predictive instrument, which might have limited specificity (24). If inaccuracies in the CIDI-SFMD occurred equally in subjects with and without long-term medical conditions, then bias toward the null (nondifferential misclassification bias) would be expected. Conversely, if the CIDI-SFMD is less specific in people with medical conditions (for example, because of its lack of exclusion criteria for physiological effects of general medical conditions, resulting in differential misclassification), overestimation of these associations could occur as a result (33).

It is important to emphasize that the cross-sectional description presented here does not capture all the underlying epidemiologic determinants of prevalence in the groups studied. The prevalence of MDEs in persons with long-term medical conditions is influenced by the incidence of depressive episodes, but also by their duration and associated mortality. Also, the direction of causal effect cannot be clarified by the cross-sectional data presented here. Situations where depression might have caused or perpetuated a medical condition are not distinguishable in cross-sectional data from situations where the medical condition contributed to the etiology of depression. In diabetes, for example, an elevated incidence of MD has been reported in association with type I diabetes (12),

Table 2 Logistic regression analysis of associations between long-term medical conditions and major depression

Chronic medical condition[a]	Median age, years	Logistic regression adjusted OR[b] (95%CI)		
		Condition	< Median age	Female sex
Chronic fatigue syndrome	49	7.2 (5.9 to 8.8)	1.9 (1.8 to 2.1)	1.8 (1.7 to 2.0)
Fibromyalgia	52	3.4 (2.9 to 4.0)	2.1 (1.9 to 2.3)	1.8 (1.7 to 2.0)
Stomach or intestinal ulcers	50	2.8 (2.5 to 3.1)	2.8 (2.5 to 3.1)	1.9 (1.8 to 2.2)
Multiple sclerosis	45	2.3 (1.6 to 3.3)	1.8 (1.6 to 1.9)	1.9 (1.8 to 2.0)
Epilepsy	44	2.0 (1.4 to 2.7)	1.7 (1.6 to 1.8))	1.9 (1.8 to 2.0)
Asthma	43	1.9 (1.7 to 2.1)	1.6 (1.5 to 1.7)	1.8 (1.7 to 2.0)
Back problems	48	2.3 (2.1 to 2.5)	2.0 (1.8 to 2.1)	1.9 (1.8 to 2.0)
Cancer	66	2.3 (1.8 to 2.8)	2.8 (2.5 to 3.1)	1.9 (1.8 to 2.0)
Emphysema or COPD	68	2.7 (2.0 to 3.6)	2.6 (2.3 to 2.9)	1.9 (1.8 to 2.1)
Migraine	41	2.6 (2.4 to 2.9)	2.5 (2.2 to 2.8)	1.7 (1.6 to 1.8)
Thyroid conditions	59	1.4 (1.2 to 1.6)	2.6 (2.3 to 2.8)	1.9 (1.7 to 2.0)
Arthritis or rheumatism	62	1.9 (1.7 to 2.0)	3.3 (3.0 to 3.7)	1.8 (1.7 to 1.9)
Stroke	72	1.7 (1.3 to 2.2)	3.1 2.6 to 3.6)	1.9 (1.8 to 2.0)
Diabetes	64	1.4 (1.2 to 1.6)	2.8 (2.5 to 3.2)	1.9 (1.8 to 2.0)
Heart disease	70	1.4 (1.2 to 1.6)	3.0 (2.5 to 3.5)	1.9 (1.8 to 2.0)
High blood pressure	64	1.2 (1.1 to 1.3)	2.8 (2.5 to 3.1)	1.9 (1.8 to 2.0)

[a]Conditions included in Table 1 are included here, except for Parkinson's disease, cataracts, and urinary incontinence, where valid models could not be fit. Also, bowel disorders, Crohn's disease, colitis, food allergies, and "chemical sensitivities" (where interaction terms were required) are not included. (See Table 3 and the text for a more detailed explanation.)
[b]For above and below median age for each condition and sex
OR = odds ratio.

Table 3 Logistic regression analyses for food allergies and "chemical sensitivities"

	Food allergies			"Chemical sensitivities"		
	Regression coefficient	Wald	*P*	Regression coefficient	Wald	*P*
Intercept	–3.83	NA	NA	-3.37	NA	NA
Condition	0.74	62.6	0.001	1.30	50.3	0.001
Below median age	0.99	286.5	0.001	0.65	317.1	0.001
Female sex	0.64	318	0.001	0.63	325.7	0.001
Female by condition interaction	–0.24	4.9	0.027	–0.57	7.6	0.006

NA = Not applicable

and various mechanisms (34,35) could account for an increased incidence of type II diabetes in people with elevated depressive symptom ratings (36) and depressive disorders (37).

Migraine headaches are an example of a condition where prospective studies have previously been carried out in an attempt to explore causal relations. A recent study by Breslau and others reported an increased incidence of first-onset migraines in a cohort with MD (9.3%, compared with 2.9% in a control group) and an increased incidence of first-onset MD (10.5%, compared with 2.0% in a control group) in people with migraines in a community sample (38). In the Breslau study, the lifetime prevalence of MD, evaluated with the CIDI (39), was found to be 42.1%.

Coronary artery disease represents another clinical situation in which multiple and multidirectional effects may account for an epidemiologic association with depression in prevalence data. In a recent review, Joynt and colleagues proposed 7 mechanisms explaining interactions between cardiovascular disease and depression: treatment noncompliance, risk factor clustering, hypothalamic–pituitary–adrenocortical activation, circadian rhythm disturbances, inflammation, hypercoagulability, and common underlying causes (20).

The CCHS included only one item evaluating "arthritis or rheumatism." Most of the literature concerned with the association between osteoarthritis and MD has emphasized an important role for psychosocial factors, most notably, social support (40,41). However, painful conditions in general appear to be associated with depression, and a plurality of biological as well as psychological mechanisms may account for this association (see Bair and others, 19).

Previous studies have reported an elevated frequency of mood disorders in subjects reporting multiple chemical sensitivities (42,43). The results reported here, unlike these previous results, derive from a large population sample. They add refinement to the previous estimates by indicating that the association may be stronger in men reporting this condition. Interaction by sex of the association between depression and skin test–diagnosed atopy has been reported in the literature, but in the opposite direction, with a stronger association observed in women than in men (44).

In this investigation, the objective was to describe the strength of association across several long-term conditions. However, the CCHS also allowed for the estimation of MD prevalence in different population groups. For purposes of case finding and service planning, these results show that the highest prevalence will be found in young people and in women.

Since cardiovascular diseases and diabetes are associated with mortality, a differential impact of MD on the mortality associated with these conditions could weaken the association, as observed in cross-sectional data. An association between depression and mortality in people with coronary artery disease has been consistently reported (see reference 45). The literature also supports the existence of an association between MD and subsequent coronary events (46). In the case of thyroid disease, the association might have been weakened by an impact of treatment. Expectation holds that most people who have been diagnosed with thyroid disease by a health professional should also be receiving treatment, and by correcting the physiological disturbance, treatment of hypothyroidism might have weakened the association.

It is possible that the associations between MD and the 2 conditions most strongly associated with MD in this analysis, fibromyalgia and chronic fatigue syndrome, were exaggerated because of an overlap of these syndromes with MD symptoms. The CIDI-SFMD does not include exclusionary criteria addressing nonpsychiatric etiology, as are included in the full version of the CIDI. For example, fatigue is only counted toward fulfillment of diagnostic criteria by the full CIDI if the subject reports that the symptom was not due to the effects of a drug or illness. In the CIDI-SFMD, severity, persistence, and timing are addressed, but etiologic exclusions are not applied.

For certain conditions, including cataracts, glaucoma, and Parkinson's disease, even the large CCHS sample could not adequately support precise estimation at the population level. One previous study, which used a clinical sample, failed to identify improvement in depressive symptom ratings following cataract surgery (47). This study reported generally low levels of depression in both the treatment and control groups. In community populations, the prevalence of MD declines with age, and the low base rate in the elderly age groups affected by these conditions might have contributed to the nonsignificant results. The literature linking glaucoma to MD emphasizes the role of antiglaucoma drugs (including topical beta blockers) as potential triggers of depressive episodes (48–52), but the literature contains no population-based studies. The prevalence of Parkinson's disease in the CCHS survey was 0.12% (95% CI, 0.09 to 0.15), which is consistent with other recent estimates (53), but the small number of subjects with Parkinson's disease precluded additional analysis.

Finally, one role of exploratory epidemiologic analysis is to generate new hypotheses for research. Some of the surprising findings in this analysis suggest a need for additional research. For example, despite the prominence of the association between stroke and MD in the literature, the strength of association observed here was modest in relation to that of other conditions. Research into the occurrence of depression within the context of medical conditions may need to be extended beyond the core set of conditions that have traditionally been most strongly linked to depression.

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Résumé : Les affections médicales de longue durée et la dépression majeure : le degré d'association pour les affections spécifiques dans la population générale

Contexte : La prévalence de la dépression majeure (DM) chez les personnes souffrant d'affections médicales non psychiatriques est un indicateur du besoin clinique chez ces groupes, un indicateur de la faisabilité des initiatives de dépistage et de recherche des cas, et une source d'hypothèse étiologiques. Cette analyse explore la prévalence de la DM dans la population générale, en relation avec les diverses affections médicales de longue durée.

Méthodes : Nous avons utilisé un ensemble de données tirées d'une enquête de santé canadienne à grande échelle : l'Enquête sur la santé dans les collectivités canadiennes (ESCC). L'échantillon se composait de 115 071 sujets de 18 ans et plus, choisis au hasard dans la population canadienne. L'entrevue de l'enquête a rapporté des diagnostics auto-déclarés de diverses affections médicales de longue durée, et utilisait une brève entrevue prédictive de DM, la forme abrégée de l'entrevue diagnostique composite internationale de la dépression majeure. La régression logistique a servi à rajuster les estimations d'association selon l'âge et le sexe.

Résultats : Les affections les plus fortement associées avec la DM étaient le syndrome de fatigue chronique (risque relatif rajusté [RRR] 7,2) et la fibromyalgie (RRR 3,4). Les affections les moins fortement associées étaient l'hypertension (RRR 1,2), le diabète, la maladie cardiaque et la maladie thyroïdienne (RRR 1,4 dans chaque cas). Nous avons trouvé des associations avec diverses affections gastro-intestinales, neurologiques et respiratoires.

Conclusions : Diverses affections médicales de longue durée sont associées avec la DM, bien que des études antérieures n'aient pas eu la puissance de détecter certaines de ces associations. Cependant, le degré d'association dans les données de prévalence varie selon les affections spécifiques.