Article

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Abstract

Objective
A population-based sample of 4,948 men and women aged 40 or older who did not have heart disease in 1994/1995 were followed to 2006/2007 to determine if depression was associated with increased risk of heart disease diagnosis or death.

Data sources
Data from seven cycles of the National Population Health Survey (NPHS), 1994/1995 through 2006/2007, were used for longitudinal analysis. Prevalence estimates of heart disease and depression in the population aged 40 years or older were based on the 2002 Canadian Community Health Survey 1.2: Mental Health and Well-being.

Analytical techniques
The association between depression and heart disease was analyzed with separate proportional hazards models for men and women, adjusting for socio-demographic characteristics and heart disease risk factors.

Main results
Among people aged 40 or older and free of heart disease in 1994/1995, 19% of men and 15% of women had developed or died from heart disease by 2006/2007. The risk of heart disease was significantly higher for women who had depression, but not for men. When heart disease events occurring within two years of baseline were removed, depression was not significantly associated with heart disease risk among women or men.

Keywords
death, major depressive disorder, longitudinal studies, National Population Health Survey (NPHS), proportional hazards models, risk factors

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Both heart disease and depression are associated with a considerable health burden.[1] Worldwide, coronary heart disease is the second leading cause of disability for men and the third leading cause for women; depression is the fourth leading cause of disability among men and the leading cause among women.[2]

In Canada, according to the 2002 Canadian Community Health Survey (CCHS) 1.2: Mental Health and Well-being, 9.9% of men (an estimated 682,000) and 8.2% of women (606,000) aged 40 or older reported a diagnosis of heart disease. Among this same age group, 2.7% of men (184,000) and 4.1% of women (302,000) met the criteria for having had a major depressive episode in the year preceding the survey.

In addition to common risk factors such as smoking, diabetes, hypertension, alcohol use, physical activity and obesity, psychosocial characteristics have been associated with heart disease.[3] Depression, in particular, has been found to worsen the prognosis of individuals who have suffered acute myocardial infarction (heart attack), and has been studied as a risk factor for the development of heart disease.[4-7] Despite some negative results,[8,9] etiologic studies of populations initially free of heart disease generally support the link between depression and heart disease.[10-23]

Behavioural and physiological factors have been proposed as mechanisms that may explain the relationship between depression and heart disease.[24] Since depression is associated with health behaviours that are, themselves, risk factors for heart disease,[25] it is possible that the link with depression operates via these behaviours. Nonetheless, many studies[10-15] have shown depression to be independently associated with cardiac outcomes when risk factors such as smoking, obesity, diabetes, alcohol use, physical activity, and hypertension are taken into account. The role of physiologic factors that are related to both depression and heart disease, such as shared genetic determinants, heart rate variability and inflammatory processes,[24] may help to explain the association.

This article reports the results of a 12-year prospective study of the relationship between depression and subsequent heart disease diagnosis or death in people initially free of heart

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disease, when common heart disease risk factors are controlled.

Data and methods

Data sources

National Population Health Survey
This analysis is based on longitudinal data from the first seven cycles (1994/1995 through 2006/2007) of the National Population Health Survey (NPHS). The household component covers the population living in private households in the 10 provinces in 1994/1995. It excludes people on Indian reserves, in the territories, on Canadian Forces bases, and in some remote areas.

In 1994/1995, 20,095 individuals were selected for the longitudinal panel, 17,276 of whom agreed to participate—a response rate of 86.0%. The response rates for subsequent cycles, based on these 17,276 respondents, were: 92.8% in 1996/1997; 88.2% in 1998/1999; 84.8% in 2000/2001; 80.6% in 2002/2003; 77.4% 2004/2005; and 77.0% in 2006/2007.

This analysis uses the cycle 7 (2006/2007) longitudinal "square" file, which contains records for all members of the original panel, regardless of whether information about them was obtained in every subsequent cycle. More detailed descriptions of the design, sample and interview procedures can be found in published reports.[26,27]

Canadian Community Health Survey: Mental Health and Well-being
Prevalence estimates of heart disease and depression are based on the 2002 Canadian Community Health Survey (CCHS) 1.2: Mental Health and Well-being, which collected information from a sample of 36,984 household residents aged 15 or older living in the 10 provinces. Residents of the three territories, Indian reserves, institutions, and certain remote areas, full-time members of the Canadian Forces, and residents (military and civilian) of military bases were excluded. The response rate was 77%. More detailed descriptions of the design, sample and

interview procedures can be found in other reports and on the Statistics Canada Web site.[28,29]

Study sample

The study sample was selected from the 17,276 participants in the NPHS longitudinal panel in 1994/1995 (Chart 1). Respondents whose vital status in 2006/2007 was not known (n=3,889) or who did not have a complete questionnaire response in 1994/1995 (n=294) were excluded, as were those younger than 40 at cycle 1 (1994/1995) (n=6,646). Those who, in 1994/1995, reported a diagnosis of heart disease, had a missing response to the question about heart disease, or reported taking "medicine for the heart" in the previous month (even though they did not report a diagnosis of heart disease) were excluded (n=852). Also excluded were 264 respondents with incomplete depression data in 1994/1995; 220 respondents who had all missing or inconsistent heart disease responses after cycle 1 that could not be confirmed by other survey questions (having heart failure, angina, or ever having had a heart attack in cycles 4 to 7; or taking heart medication in cycles 2 to 7); and 143 respondents for whom cause of death was unknown. Finally, 20 respondents whose first episode of depression in the observation period and first report of heart disease occurred in the same cycle (1994/1995) were removed. The final study sample was 4,948 (2,851 women and 2,097 men).

Definitions

Depression

Using the methodology of Kessler et al.,[30] the NPHS measures *depression* with a subset of questions from the Composite International Diagnostic Interview (CIDI-SF). These questions cover a cluster of symptoms for a depressive disorder, which are listed in the *Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R)*.[31] Respondents were asked about feeling

sad, blue or depressed or losing interest in most things for a period of two weeks or more, along with other symptoms including decreased energy, appetite or sleep disturbance, difficulty concentrating, feelings of worthlessness, and/or thoughts about death. Scores were totaled and the results transformed into a probability estimate that the respondent would have met the criteria of a major depressive episode in the past year if he or she had completed the full version of the CIDI. For this article, if the estimate was 0.9 or more, the respondent was considered to have experienced depression in the previous 12 months. The specific questions in the depression module of the NPHS questionnaire can be found at www.statcan.ca/english/sdds/instrument/3225_Q1_V7_E.pdf.
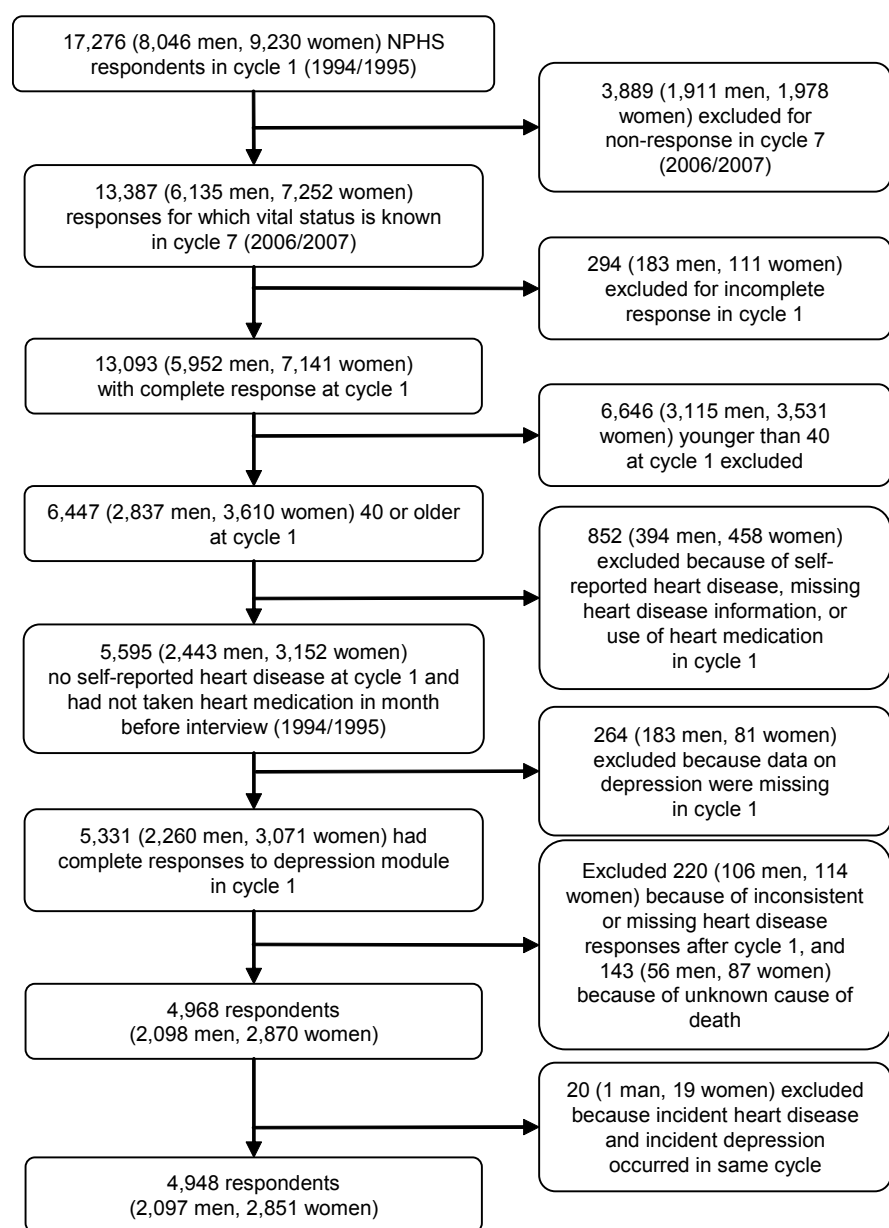
The prevalence estimate of depression from the CCHS 1.2 is based on the World Mental Health version of the Composite International Diagnostic Interview (WMH-CIDI). The WMH-CIDI was designed to be administered by lay interviewers and is generally based on diagnostic criteria outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV®-TR).[32] The CCHS questionnaire is available at http://www.statcan.ca/english/sdds/instrument/5015_Q1_V1_E.pdf. The algorithm used to measure the 12-month prevalence of depression is available in the Annex of the 2004 *Health Reports* supplement.[33]

Depression estimates from CCHS 1.2 exclude respondents who had also experienced an episode of mania in their lifetime, but NPHS estimates do not.

Heart disease

The prevalence of chronic conditions was based on self-reports of diagnosed illness. Respondents were asked about any "long-term health conditions that have lasted or are expected to last six months or more and that have been diagnosed by a health professional." The NPHS used a checklist of

Chart 1
Study sample

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┌─────────────────────────────────────────────┐
│ 17,276 (8,046 men, 9,230 women) NPHS         │
│ respondents in cycle 1 (1994/1995)           │
└─────────────────────────────────────────────┘
                 │        ┌──────────────────────────────────┐
                 │───────▶│ 3,889 (1,911 men, 1,978          │
                 │        │ women) excluded for              │
                 │        │ non-response in cycle 7          │
                 ▼        │ (2006/2007)                      │
┌─────────────────────────────────────────────┐ └──────────────────────────────────┘
│ 13,387 (6,135 men, 7,252 women)              │
│ responses for which vital status is known    │
│ in cycle 7 (2006/2007)                       │
└─────────────────────────────────────────────┘
                 │        ┌──────────────────────────────────┐
                 │───────▶│ 294 (183 men, 111 women)         │
                 │        │ excluded for incomplete          │
                 ▼        │ response in cycle 1              │
┌─────────────────────────────────────────────┐ └──────────────────────────────────┘
│ 13,093 (5,952 men, 7,141 women)              │
│ with complete response at cycle 1            │
└─────────────────────────────────────────────┘
                 │        ┌──────────────────────────────────┐
                 │───────▶│ 6,646 (3,115 men, 3,531          │
                 │        │ women) younger than 40           │
                 ▼        │ at cycle 1 excluded              │
┌─────────────────────────────────────────────┐ └──────────────────────────────────┘
│ 6,447 (2,837 men, 3,610 women) 40 or older   │
│ at cycle 1                                   │
└─────────────────────────────────────────────┘
                 │        ┌──────────────────────────────────┐
                 │───────▶│ 852 (394 men, 458 women)         │
                 │        │ excluded because of self-        │
                 │        │ reported heart disease, missing  │
                 │        │ heart disease information, or    │
                 │        │ use of heart medication          │
                 ▼        │ in cycle 1                       │
┌─────────────────────────────────────────────┐ └──────────────────────────────────┘
│ 5,595 (2,443 men, 3,152 women)               │
│ no self-reported heart disease at cycle 1 and│
│ had not taken heart medication in month      │
│ before interview (1994/1995)                 │
└─────────────────────────────────────────────┘
                 │        ┌──────────────────────────────────┐
                 │───────▶│ 264 (183 men, 81 women)          │
                 │        │ excluded because data on         │
                 │        │ depression were missing          │
                 ▼        │ in cycle 1                       │
┌─────────────────────────────────────────────┐ └──────────────────────────────────┘
│ 5,331 (2,260 men, 3,071 women) had           │
│ complete responses to depression module      │
│ in cycle 1                                   │
└─────────────────────────────────────────────┘
                 │        ┌──────────────────────────────────┐
                 │───────▶│ Excluded 220 (106 men, 114       │
                 │        │ women) because of inconsistent   │
                 │        │ or missing heart disease         │
                 │        │ responses after cycle 1, and     │
                 │        │ 143 (56 men, 87 women)           │
                 │        │ because of unknown cause of      │
                 ▼        │ death                            │
┌─────────────────────────────────────────────┐ └──────────────────────────────────┘
│ 4,968 respondents                            │
│ (2,098 men, 2,870 women)                     │
└─────────────────────────────────────────────┘
                 │        ┌──────────────────────────────────┐
                 │───────▶│ 20 (1 man, 19 women) excluded    │
                 │        │ because incident heart disease   │
                 │        │ and incident depression          │
                 ▼        │ occurred in same cycle           │
┌─────────────────────────────────────────────┐ └──────────────────────────────────┘
│ 4,948 respondents                            │
│ (2,097 men, 2,851 women)                     │
└─────────────────────────────────────────────┘
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Sources: 1994/1995 to 2006/2007 National Population Health Survey, longitudinal square file.

conditions, one of which was *heart disease.*

Use of *heart medication* was determined by asking respondents if, in the past month, they had taken "medicine for the heart."

Heart disease death was based on ICD-10 codes for ischaemic heart disease (I20-I25) or heart failure (I50.0-I50.9).

Covariates

Age in 1994/1995 was used as a continuous variable and contained values of 40 years or more.

Three *marital status* categories were specified: partner (married, common-law or living with partner); separated, divorced or widowed; and never married.

Household income was based on total self-reported household income from all sources in the previous 12 months. The ratio between total household income and the low-income cut-off corresponding to the number of people in the household and community size was calculated. The ratios were then adjusted by dividing them by the highest ratio for all NPHS respondents. The adjusted ratios were grouped into deciles, which were collapsed into five household income categories: low (deciles 1 and 2), low to middle (deciles 3 and 4), middle (deciles 5 and 6), high to middle (deciles 7 and 8) and high (deciles 9 and 10). More information on the income variable can be found in the NPHS derived variable documentation at www.statcan.ca/english/sdds/document/3225_DIO_T9_V3_E.pdf.

High blood pressure was measured by self-reported diagnosis of the condition or indication that the respondent had taken "medicine for blood pressure" in the past month.

Diabetes was measured by self-reported diagnosis of the condition.

Body mass index (BMI) is calculated by dividing self-reported weight in kilograms by the square of self-reported height in metres. The BMI groups used in this article were: underweight/acceptable (BMI less than $25 kg/m^2$), overweight ($25.0 kg/m^2$ to $29.9 kg/m^2$) and obese ($30 kg/m^2$ or more).

Smoking status was grouped into six categories based on current and former smoking habits: current daily/occasional smoker; former occasional smoker (smoked in the past, but not daily); quit daily smoking 0 to 4 years ago; quit daily smoking 5 to 9 years ago; quit daily smoking 10 or more years ago; and never smoker.

Leisure-time physical activity was based on total accumulated energy expenditure (EE) during leisure time. EE was calculated from the reported frequency and duration of all of a respondent's leisure-time physical activities in the three months before the interview and the energy cost of

the activity (kilocalories expended per kilogram of body weight per hour of activity). To calculate an average daily EE for an activity, the estimate was divided by 365. This calculation was repeated for each leisure-time activity reported, and the resulting estimates were summed to provide an aggregate average daily EE. Respondents whose leisure-time EE was 3.0 or more kcal/kg/day were considered active; 1.5 to 2.9 kcal/kg/day, moderately active; and less than 1.5 kcal/kg/day, inactive.

Identification of respondents who participate in *non-leisure physical activity* was based on usual daily activities and work habits over the previous three months. Those who reported that they "stand or walk quite a lot," "lift or carry light loads," or "do heavy work or carry very heavy loads" were considered to participate in non-leisure physical activity, compared with those who reported that they "usually sit and don't walk around very much."

Alcohol use was determined by asking:
- "During the past 12 months, have you had a drink of beer, wine, liquor or any other alcoholic beverage?"
- "Have you ever had a drink?"
- Thinking back over the past week, did you have a drink of beer, wine, liquor or any other alcoholic beverage?"

For each day in the past week the respondent was asked, "How many drinks did you have?" Five categories of alcohol use were established: never in lifetime; former drinker; light drinker (1 drink or less in past week); moderate drinker for men (2 to 14 drinks in the past week); and heavy drinker for men (15 or more drinks in the past week). Because few women were in the heavy drinker category, moderate drinking (2 to 9 drinks in past week) and heavy drinking (10 or more drinks in past week) were combined.

Use of *hormone replacement therapy* was determined during the 1994/1995 NPHS interview by asking women aged 30 or older if they had taken "hormones for menopause or aging symptoms" in the past month.

Statistical analyses

To identify variables that were associated with an increased or decreased risk of being diagnosed with or of dying from heart disease, Cox proportional hazards modeling was used. This technique allows for the study of relationships between individual characteristics and an outcome when that outcome can take place over a period of time. The method accounts for the possibility that respondents do not develop or die from heart disease during the study period, and it minimizes the bias associated with attrition.

Because heart disease is relatively rare at younger ages, the analysis was restricted to respondents aged 40 or older at cycle 1 (1994/1995). Since the prevalance of and characteristics associated with heart disease and depression differ between men and women,[3,4] the analysis was stratified by sex.

If a respondent reported a diagnosis of heart disease or died of ischaemic heart disease or heart failure after 1994/1995, this was considered an event. Given that the development of heart disease is a continuous process that was measured only at discrete intervals (the NPHS interviews every two years), many transitions to a heart disease event were recorded at the same time, after 2, 4, 6, 8, 10 or 12 years. Thus, the complementary log-log model was used.[35]

If self-reported heart disease information was missing for one or more survey cycles but values for subsequent cycles were available, the cases were retained. This creates intervals of varying lengths between observations. To control for the fact that the longer the interval, the more likely a respondent was to develop heart disease, values for interval length and interval length square were entered as independent variables in the model.

An imputed value of "No" to the heart disease question was used if a missing response was bounded by "No's" in the previous and subsequent cycles. Of the 4,948 respondents, 493 (10.0%) contain imputed "No" response(s) to the heart disease question in one or more cycles.

The 4,948 respondents were followed until 2006/2007. During the follow-up period, there were 429 heart disease diagnoses or deaths among men, and 486 among women. Two models were applied. The first adjusted for depression, age and the varying lengths of time between observations. The second adjusted for these variables and also for socio-demographic variables, chronic conditions and health behaviours. Independent variables were measured as of 1994/1995, except for depression, which was measured at baseline and in subsequent cycles. A respondent was considered to have experienced depression from their first occurrence of depression during the study period, such that it became a "characteristic" of the respondent from that point onward. If data were missing for depression in a given cycle and the respondent had not experienced depression in a previous cycle, the respondent was considered not to have depression for that cycle.

In an effort to study the population without heart disease, respondents who reported a diagnosis of heart disease or use of heart medication at baseline were excluded. But since clinical examinations were not part of the survey, it is possible that some respondents who remained in the sample had undetected or sub-clinical heart disease. To minimize the possibility that sub-clinical or undetected disease at baseline biased the relationship between depression and heart disease, the analysis was repeated after excluding heart disease events that occurred in the first cycle of follow-up.

All the analyses were weighted using the longitudinal weights constructed to represent the total population in 1994. The bootstrap method was used to

account for the complex survey design in the calculation of confidence intervals and in the assessment of statistical significance.[36-38] The significance level was set at p < 0.05.

Results

Estimates from the study population indicate that 16.8% of women and 10.9% of men (p<0.001) experienced depression in at least one of the seven survey cycles. Both men and women who experienced depression were, on average, approximately 5 years younger at baseline, were more likely to be current smokers, and were more likely to be taking antidepressants, compared with those who did not experience depression (Appendix Table A). Women who experienced depression were less likely to be never drinkers and to have high blood pressure, and were more likely to be using hormone replacement therapy and to be in the high income group.

Among people who did not report heart disease or the use of heart medication in 1994/1995, 19% of men and 15% of women either reported a new diagnosis of heart disease or died from ischaemic heart disease or heart failure during the next 12 years (Table 1). Incident heart disease diagnoses (rather than death) represented 81.6% of the heart disease events for men and 86.8% of the events for women.

Women with depression were more likely to have a heart disease event,

compared with those without depression (HR=1.8, 95% CI=1.3, 2.7); men with depression did not have a significantly higher risk of having a heart disease event (HR=1.4, 95% CI=0.8, 2.4) (Tables 2 and 3). When the model was adjusted for other heart disease risk factors, the risk was attenuated slightly for women with depression (HR=1.7, 95% CI=1.1, 2.5), but remained significant. For men with depression, the risk of heart disease was not significantly higher in the covariate-adjusted model (HR=1.2, 95% CI=0.7, 2.2).

When respondents with incident heart disease in the first two years after baseline (one survey cycle) were removed from the model (94 men, 90 women), depression was not significantly associated with heart disease for either men (HR= 1.6, 95% C.I.=0.8, 3.0) or women (HR=1.5, 95% C.I.=0.9, 2.4). The excluded respondents represented 21.9% of incident heart disease events for men and 18.5% for women.

Discussion

This is the first nationally representative study of the association between depression and incident heart disease in the Canadian population. Depression was found to be associated with incident heart disease among women, even when adjusting for other risk factors. The association between depression and

heart disease did not reach statistical significance for men. Although most previous studies did not stratify the analysis by sex, evidence from adequately adjusted studies indicates that the association between depression and heart disease exists in both men and women.[12,14,39] Since heart disease develops over a long period, the 12-year interval may not have been long enough for the full effect of associations between depression and heart disease to emerge among men.

When heart disease events that occurred in the first two years of follow-up (one survey cycle) were eliminated from the analysis, the relationship between depression and heart disease, although positive and consistent with the other models, did not reach statistical significance for either sex. Other studies that have used this technique[20,21,39] found that the association between depression and heart disease remained after eliminating the first two years of follow-up in their samples of men. The smaller sample in the present study may have reduced the statistical power of the models. However, it is possible that sub-clinical or undetected disease at baseline affected the results of analysis in the full sample.

Of the studies that did not find significant associations between depression and heart disease, the Framingham study[8] used a different depression instrument, a shorter follow-up (6 years), and included younger respondents (30 or older), all of which might contribute to differences from the present analysis. The Leiden-85 study[9] was confined to people aged 85 or older, and as noted in a recent review,[10] the results may be influenced by the inclusion of exceptionally healthy individuals who lived to an advanced age without heart disease, as well as to low statistical power due to a smaller sample.

Some factors that were treated as confounders in the present analysis may actually be in the causal pathway between depression and heart disease (for example, smoking, alcohol use,

Table 1

New diagnosis of or death from heart disease between 1994/1995 and 2006/2007, by sex, household population aged 40 or older with no diagnosis of heart disease or use of heart medication in 1994/1995, Canada excluding territories

	Women			Men		
		Estimated population			Estimated population	
	Sample size	'000	%	Sample size	'000	%
Total	2,851	3,792	100	2,097	3,195	100
No diagnosis of or death from heart disease	2,365	3,227	85.1	1,668	2,603	81.4
Diagnosis of or death from heart disease	486	566	14.9	429	594	18.6

Note: Deaths attributed to heart disease are based on records for which cause of death was available.
Sources: 1994/1995 to 2006/2007 National Population Health Survey, longitudinal square file.

Table 2
Adjusted proportional hazards ratios relating selected characteristics to diagnosis or death from heart disease between 1996/1997 and 2006/2007, female household population aged 40 or older and free of heart disease in 1994/1995, Canada excluding territories

Characteristics in 1994/1995	Model 1 (adjusted for depression and age)		Model 2 (fully adjusted)		Model 3 (fully adjusted, excluding heart disease diagnoses and deaths during cycle after baseline)	
	Proportional hazards ratio	95% confidence interval	Proportional hazards ratio	95% confidence interval	Proportional hazards ratio	95% confidence interval
Depression in past 12 months[†]	1.8*	1.3 to 2.7	1.7*	1.1 to 2.5	1.5	0.9 to 2.4
Age (continuous)	1.07*	1.06 to 1.09	1.07*	1.05 to 1.08	1.06*	1.04 to 1.09
Household income						
High[‡]	...	...	1.0	...	1.0	...
Middle to high	...	...	1.3	0.8 to 2.2	0.8	0.4 to 1.4
Middle	...	...	1.2	0.7 to 1.9	1.0	0.6 to 1.8
Low to middle	...	...	1.1	0.6 to 1.9	1.0	0.5 to 1.9
Low	...	...	1.3	0.8 to 2.2	1.1	0.6 to 2.0
Marital status						
Partner[‡]	...	...	1.0	...	1.0	...
Widowed/Separated/Divorced	...	...	1.0	0.8 to 1.3	1.1	0.8 to 1.6
Never married	...	...	0.6	0.4 to 1.2	0.7	0.3 to 1.4
High blood pressure	...	...	1.9*	1.4 to 2.5	2.0*	1.4 to 2.9
Diabetes	...	...	1.9*	1.2 to 2.9	1.9*	1.2 to 3.1
Body mass index						
Underweight/Acceptable[‡]	...	...	1.0	...	1.0	...
Overweight	...	...	1.1	0.8 to 1.4	1.2	0.9 to 1.8
Obese	...	...	1.0	0.7 to 1.5	1.3	0.8 to 2.0
Smoking status						
Current daily or occasional smoker	...	...	1.8*	1.2 to 2.6	2.2*	1.3 to 3.5
Former occasional smoker	...	...	0.9	0.6 to 1.6	1.0	0.5 to 2.0
Quit daily smoking less than 4 years	...	...	2.4*	1.4 to 4.4	2.7*	1.3 to 5.4
Quit daily smoking 5 to 9 years	...	...	1.6	0.8 to 2.9	2.3*	1.1 to 4.8
Quit daily smoking 10 or more years	...	...	1.2	0.9 to 1.7	1.3	0.9 to 2.0
Never smoker[‡]	...	...	1.0	...	1.0	...
Leisure-time physical activity						
Inactive[‡]	...	...	1.0	...	1.0	...
Moderately active	...	...	0.9	0.6 to 1.2	0.9	0.6 to 1.5
Active	...	...	0.9	0.6 to 1.4	0.8	0.5 to 1.3
Non-leisure physical activity	...	...	0.8	0.6 to 1.1	0.7*	0.5 to 1.0
Alcohol use						
Never drank[‡]	...	...	1.0	...	1.0	...
Former drinker	...	...	0.8	0.5 to 1.2	0.8	0.5 to 1.2
Light drinker	...	...	0.7	0.5 to 1.0	0.7	0.4 to 1.1
Moderate/Heavy drinker	...	...	0.5*	0.3 to 0.8	0.4*	0.2 to 0.8
Hormone replacement therapy in past month	...	...	1.1	0.7 to 1.6	0.9	0.6 to 1.5

[†] time-varying co-variate
[‡] reference category
* significantly different from estimate for reference category (p < 0.05)
... not applicable

Note: Because of rounding, some hazards ratios with 1.0 as lower/upper confidence limit are statistically significant. To maximize sample size, "missing" categories were included for several variables, but hazards ratios are not shown. A variable was included to control for varying length of time between observations, but hazards ratios are not shown.
Source: 1994/1995 to 2006/2007 National Population Health Survey, longitudinal square file.

Table 3
Adjusted proportional hazards ratios relating selected characteristics to diagnosis or death from heart disease between 1996/1997 and 2006/2007, male household population of men aged 40 or older and free of heart disease in 1994/1995, Canada excluding territories

Characteristics in 1994/1995	Model 1 (adjusted for depression and age)		Model 2 (fully adjusted)		Model 3 (fully adjusted, excluding heart disease diagnoses and deaths during cycle after baseline)	
	Proportional hazards ratio	95% confidence interval	Proportional hazards ratio	95% confidence interval	Proportional hazards ratio	95% confidence interval
Depression in past 12 months[†]	1.4	0.8 to 2.4	1.2	0.7 to 2.2	1.6	0.8 to 3.0
Age (continuous)	1.07*	1.06 to 1.08	1.07*	1.0 to 1.1	1.07*	1.05 to 1.08
Household income						
High[‡]	...	...	1.0	...	1.0	...
Middle to high	...	...	0.9	0.6 to 1.3	1.0	0.6 to 1.7
Middle	...	...	1.0	0.7 to 1.5	1.1	0.7 to 1.7
Low to middle	...	...	1.0	0.6 to 1.5	1.0	0.6 to 1.7
Low	...	...	1.0	0.7 to 1.6	0.9	0.5 to 1.7
Marital status						
Partner[‡]	...	...	1.0	...	1.0	...
Widowed/Separated/Divorced	...	...	0.7	0.5 to 1.0	0.8	0.6 to 1.3
Never married	...	...	0.9	0.6 to 1.4	0.9	0.5 to 1.6
High blood pressure	...	...	1.5*	1.1 to 2.0	1.5*	1.1 to 2.3
Diabetes	...	...	1.9*	1.2 to 3.1	1.8*	1.0 to 3.3
Body mass index						
Underweight/Acceptable[‡]	...	...	1.0	...	1.0	...
Overweight	...	...	1.3	1.0 to 1.9	1.1	0.8 to 1.6
Obese	...	...	1.9*	1.2 to 3.0	1.8*	1.1 to 2.8
Smoking status						
Current daily or occasional smoker	...	...	1.3	0.8 to 1.9	1.0	0.6 to 1.6
Former occasional smoker	...	...	1.1	0.6 to 1.9	0.8	0.4 to 1.8
Quit daily smoking less than 4 years	...	...	1.6	0.9 to 3.1	1.1	0.5 to 2.5
Quit daily smoking 5 to 9 years	...	...	0.8	0.4 to 1.6	0.6	0.2 to 1.6
Quit daily smoking 10 or more years	...	...	1.0	0.7 to 1.4	0.8	0.5 to 1.3
Never smoker[‡]	...	...	1.0	...	1.0	...
Leisure-time physical activity						
Inactive[‡]	...	...	1.0	...	1.0	...
Moderately active	...	...	0.6*	0.4 to 0.9	0.7	0.5 to 1.1
Active	...	...	1.2	0.9 to 1.7	1.2	0.8 to 1.8
Non-leisure physical activity	...	...	0.7*	0.5 to 0.9	0.8	0.5 to 1.2
Alcohol use						
Never drank[‡]	...	...	1.0	...	1.0	...
Former drinker	...	...	1.4	0.7 to 2.8	1.6	0.7 to 3.6
Light drinker	...	...	1.3	0.6 to 2.5	1.2	0.6 to 2.7
Moderate/Heavy drinker	...	...	1.1	0.5 to 2.1	1.1	0.5 to 2.3
Heavy drinker	...	...	0.7	0.3 to 1.6	0.8	0.3 to 2.3

[†] time-varying co-variate
[‡] reference category
* significantly different from estimate for reference category (p < 0.05)
... not applicable
Note: Because of rounding, some hazards ratios with 1.0 as lower/upper confidence limit are statistically significant. To maximize sample size, "missing" categories were included for several variables, but hazards ratios are not shown. A variable was included to control for varying length of time between observations, but hazards ratios are not shown.
Source: 1994/1995 to 2006/2007 National Population Health Survey, longitudinal square file.

Why is this study important?

■ From a public health and disease prevention perspective, it is important to understand the role of depression as a potential risk factor for heart disease.

What else is known on this topic?

■ The majority of population-based studies have found that depression is associated with increased risk of incident heart disease in an initially healthy population. However, some results have been inconsistent.

What does this study add?

■ For the first time, national population-based data are used to investigate the association between depression and incident heart disease in Canada. When other risk factors were controlled, depression was significantly associated with increased risk of heart disease among women, but not among men.

Limitations

NPHS respondents were asked if they had "heart disease," but no information was collected on the specific type. However, self-reports of heart disease diagnoses likely reflect common conditions such as coronary heart disease and myocardial disease. Although it would have been more precise to limit the outcome to confirmed ischemic heart disease fatalities and heart failure fatalities, the low number in the sample (102 men, 86 women) precluded this option. A small portion of sample respondents whose incident heart disease event was based on a self-reported diagnosis died of ischemic heart disease or heart failure during the follow-up period (6.6% of men and 5.2% of women).

The degree to which the self-reported diagnoses of chronic conditions, including heart disease, are inaccurate because of reporting error is unknown.

The CIDI-SF used to assess major depression on the NPHS is not a validated instrument, although the criteria it uses are consistent with the DSM-III-R. Moreover, the CIDI-SF does not discount symptoms due to physical illness, alcohol or drug use, or bereavement. Consequently, the symptoms of some respondents classified as having depression may actually have been due to physical illness, milder forms of depressive disorder, or bereavement.[40]

The NPHS collects data every two years, but the depression questions refer to the 12 months before the interview. Thus, there is a one-year period between survey cycles for which depression information is not available, so the prevalence of depression among the study population may be underestimated.

A dose-response relationship between depressive symptoms and incident heart disease has been found in other studies.[10,23] However, the CIDI-SF depression measure is designed for use as a dichotomous rather than a continuous variable. Thus, it was not possible to investigate whether the risk

of heart disease increased with the severity of depression.

Respondents with missing values for depression and who had not met the criteria for depression in previous NPHS cycles were considered not to have depression for that cycle. If cycle non-response to the depression questions was higher among individuals experiencing depression, the prevalence of depression in the sample would be underestimated.

It would be interesting to know the proportion of people who had repeated episodes of depression during the study period. However, respondents' length of exposure to risk of depression varied because nearly one-fifth of them (19.4%) died over the 12-year period, and values for depression were missing in some cycles. Nonetheless, this study addresses whether *any* episode of depression during the period was associated with incident heart disease, so the number of occurrences of depression is not directly relevant to the results of this analysis.

Not all factors known to be associated with incident heart disease could be examined. For example, the NPHS does not collect data on diet, aspirin use, or biological measures such as blood lipids. Family history of heart disease was collected in cycle 3 (1998/1999), but because this information was not available for respondents who had died by that time, it was not used. Similarly, lifetime history of depression was not collected until cycle 6 (2004/2005), and as a result, the possible influence of depression before the baseline year was not assessed.

The lack of association between heart disease and some common risk factors, such as smoking and household income in men and leisure-time physical activity and BMI in women, is unexpected. This may reflect limitations in how these covariates were measured. For example, smoking status does not indicate smoking intensity, which may have contributed to the weak association between smoking and heart disease in men in the full model. Also, obesity

obesity, physical activity). The fact that the hazards ratios for depression were somewhat attenuated when controlling for these other risk factors suggests that the impact of depression on heart disease may operate, at least in part, via these health behaviours.

Most previous studies measured depression only at baseline, which may have underestimated associations between depression and heart disease. A strength of the present study is that the measure of depression was repeated at each survey cycle.

was based on self-reported weight and height, which tend to yield lower estimates than those based on measured data.[41] The result for this analysis could be an underestimation of the association between obesity and heart disease, which, in turn, might influence the observed association between depression and heart disease. However, household income and smoking were significantly associated with heart disease in restricted models that controlled for them individually along with depression and a variable to control for the varying length of time between observations; leisure-time physical activity and BMI were not (data not shown).

The exclusion of 3,899 records for non-response in cycle 7 (some of which may be due to the death of the respondent) and 143 deaths for which cause of death was not available limited the statistical power of the analysis. For these reasons, the analysis may underestimate associations that could emerge when more complete data for these records become available.

Conclusion

Although this and other studies indicate an association between depression and heart disease, a causal link between the two disorders has not been confirmed. Future research can help illuminate the mechanisms underlying this association, whether they be health behaviours, physiologic factors, or other unmeasured or yet unidentified variables. The results of this study highlight the importance of monitoring people with depression for the development of heart disease. ■

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Appendix

Table A
Baseline (1994/1995) characteristics of study sample, by depression, household respondents aged 40 or older free of heart disease in 1994/1995, Canada excluding territories

Characteristics in 1994/1995	Had depression in any survey cycle			
	Women		Men	
	No	Yes	No	Yes
Mean age (years)	57.5	51.2**	55.2	50.1**
	%		%	
Income				
High[†]	19.7	25.6*	27.9	20.7[E]
Middle to high	18.2	17.7	18.8	24.9[E]
Middle	18.2	15.4	19.2	14.5[E]
Low to middle	20.3	17.4	15.7	16.5[E]
Low	16.8	17.4	12.3	13.8[E]
Marital status				
Partner[†]	67.8	69.4	82.4	80.1
Widowed/Separated/Divorced	26.6	24.9	11.4	13.3[E]
Never married	5.6	5.7[E]	6.2	6.6[E]
High blood pressure	19.4	14.8*	13.1	17.1[E]
Diabetes	3.8	5.2[E]	4.8	6.4[E]
Body mass index				
Underweight/Acceptable[†]	48.1	48.7	35.1	37.9
Overweight	35.1	35.2	49.3	50.7
Obese	15.1	15.1	15.4	11.4[E]
Smoking status				
Current daily or occasional smoker	19.7	31.8**	29.1	42.1*
Former occasional smoker	6.3	6.2[E]	7.1	F
Quit daily smoking less than 4 years ago	4.1	2.9[E]	4.2	4.7[E]
Quit daily smoking 5 to 9 years ago	4.1	4.9[E]	5.9	8.4[E]
Quit daily smoking 10 or more years ago	15.4	14.6	28.7	15.6[E**]
Never smoker[†]	50.5	39.1**	25.0	26.4
Leisure-time physical activity				
Inactive[†]	63.6	66.4	58.7	58.4
Moderately active	22.5	21.4	22.5	20.3
Active	13.9	12.3	18.8	21.3[E]
Non-leisure physical activity	79.3	74.8	78.4	71.8
Alcohol use				
Never drank[†]	13.0	7.1[E**]	5.3	F
Light drinker	41.6	50.5*	32.2	34.2
Moderate drinker[‡]	29.3	25.5	40.6	39.8
Heavy drinker	…	…	9.0	7.1[E]
Former drinker	16.0	16.7	12.7	14.5[E]
Hormone replacement therapy in past month	13.0	20.9*	…	…
Antidepressant use in past month	2.9	17.5**	1.0[E]	7.5[E*]

[†] reference category
[‡] For women, moderate and heavy drinkers were grouped because of small number who were heavy drinkers.
* significantly different from estimate for group of the same sex without depression (p<0.05)
** significantly different from estimate for group of the same sex without depression (p<0.001)
[E] use with caution (coefficient of variation 16.6% to 33.3%)
F too unreliable to be published (coefficient of variation greater than 33.3%)
… not applicable
Source: 1994/1995 to 2006/2007 National Population Health Survey (NPHS), longitudinal square file.