What characteristics are associated with earlier onset of first depressive episodes: A 16-year follow-up of a national population-based cohort

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ABSTRACT

This study examined characteristics associated with earlier onset of first depressive episodes. A nationally representative Canadian sample was randomly selected and followed from 1994 to 2011. At baseline complete data on depression history (Yes/No) and related diseases was available for *12,227* study subjects. Proportional hazard models were used. Meta-analyses were also applied to sync results across studies. Being younger, a woman, a Caucasian, a regular smoker, and having a chronic disease were significantly associated with the expedited trajectory for the onset of the first depressive episode. People were at the greater risk of having earlier onset of first depressive episodes at the 2-year follow-up ($p < 0.001$), with the risk declining after four years ($p < 0.001$). Women and men had different sets of characteristics associated with earlier onset of first depressive episodes. In meta-analyses, those having a chronic disease ($HR_{pooled} = 1.31$) and being a woman ($HR_{pooled} = 1.43$) were more likely to have earlier onset of first depressive episodes. This study provides solid evidence on the timing effect of these characteristics on first depressive episodes. Approaches focused on these identified risk characteristics should be prioritized to reduce the risk and postpone the onset of major depressive episode.

1. Introduction

The Global Burden of Disease 2012 systematic review of 291 diseases and injuries in 21 world regions from 1990 to 2010 concluded that major depressive disorder accounted for 2.5% of global DALYs, and its ranking increased from 15th to 11th (Murray et al., 2012). It has a profound impact on individuals and their families' quality of life, and also places a significant economic and social burden on society (Halfin, 2007).

From a preventive point of view there is a clear imperative for early detection or screening of major depressive disorder, identifying asymptomatic individuals at risk, and the application of effective treatments. The potential benefits such actions in altering the trajectory of disease is readily apparent. Early recognition and treatment of major depressive disorder can improve social function, increase productivity, and reduce absenteeism in the work places (Coulehan et al., 1997; Rost et al., 2004). Identifying those individuals at higher risk of earlier occurrence of first depressive episode is important, as prompt and appropriate interventions can then be applied to improve outcomes and quality of life.

Many epidemiological studies, mostly cross-sectional studies, have identified risk factors for major depression, including child abuse and adverse childhood experiences (Colman et al., 2009; Kessler et al., 2007; Li et al., 2016), low income (Salkever et al., 2014), unemployment (Pompili et al., 2014), smoking (He et al., 2014), physical inactivity (Meng and D'Arcy, 2013), unhealthy eating styles (Rawana et al., 2010), low social support (Theorell et al., 2015), stressful events, and neighbourhood deprivation (Mair et al., 2008).

Although few cohort studies have explored the risk profile of incident major depression among those having a comorbidity of another somatic or psychiatric disease (Aarts et al., 2009; Perng et al., 2014; Pan et al., 2015), little is known about the relationship between risk factors and earlier onset of first depressive episode in prospective, population-based community samples. This study was designed to investigate characteristics associated with the earlier onset of first depressive episode in a large, population-based, prospective cohort study. In addition, meta-analyses were used to synthesize this present study's results on risk factors for earlier onset of first depressive episode with other published studies.

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2. Methods

2.1. Data source and study design

Data analyzed was from the National Population Health Survey (NPHS), which is a population-based cohort study of a representative community sample of the Canadian population. The NPHS was designed to collect longitudinal information on population health from 1994/1995 to 2010/2011. Multistage stratification sampling was used to adjust geographic and socioeconomic characteristics and clustering. The NPHS longitudinal cohort initially included *17,726* participants in total. There was a 69.7% response rate for those who completed all nine cycles (Statistics Canada, 2012). The NPHS was approved by Statistics Canada ethics review process, and all respondents provided informed consent. More detailed information of this survey is described elsewhere (Tambay and Catlin, 1995; Swain et al., 1999).

2.2. Study sample

A total of *12,227* participants were selected for this study from the larger survey dataset. The eligibility criteria of the study sample selection was: 1) being aged 12 and more at the baseline who had been followed-up to 2010/2011; 2) being depressed-free at the baseline, and had depression values (Yes/No) during the follow-ups; and, 3) not reporting any history of Alzheimer's disease or other dementias.

2.3. Outcome and predicators

The NPHS survey used an internationally recognized diagnostic questionnaire to assess the presence of a major depressive episode, the Composite International Diagnostic Interview Short Form (Kessler et al., 1998), to assess the presence of diagnostic symptoms in the past 12-months prior to the interview. A 90% predicative probability cut-off point had been validated against the revision of Diagnostic and Statistical Manual of Mental Disorders 3rd edition diagnostic criteria for major depressive episode. It was used to indicate the incidence of first depressive episode.

Characteristics examined in this study included *socio-demographic* factors (age, sex, race, marital status, income, education, and immigration status), *history of chronic disease*, and *lifestyle factors* (type of drinkers, level of physical activity, and type of smokers). The variable of "history of chronic disease" was dichotomous. Participants reporting any of the following long-term conditions that had been diagnosed by a health professional, were seen as having a history of chronic disease: arthritis or rheumatism, high blood pressure, asthma, chronic bronchitis, or other lung or breathing condition, diabetes, epilepsy, heart disease, angina, effects of a heart attack, effects of stroke, paralysis, incontinence, Alzheimer's disease or other dementias, osteoporosis or brittle bones, glaucoma, digestive conditions, kidney failure or disease, cerebral palsy, spina bifida, cystic fibrosis, multiple sclerosis, deformity, orthopaedic impairment or absence of arms, legs, hands or feet, cancer, or any other long-term condition. The variable of "type of drinker" was based on participant's drinking frequency, including regular drinker, occasional drinker, former drinker, and abstainer. Physical activity was measured using criteria from Canadian Fitness and Lifestyle Research Institute that had been also used in other surveys, such as Ontario Health Survey (www.chass.utoronto.ca/ datalib/codebooks/utm/ohs/ohs90.htm), and the Campbell's Survey on Well-Being in Canada (www.cflri.ca/cflri/pa/surveys/88survey.html). Exposure to leisure time physical activity in the past three months prior to the interview was assessed through a series of questions, e.g. "Have you done any of following (physical activities) in the past three months?; "In the past three months, how many times did you participate in that activity?"; "How much time did you spend on each occasion?" Previously developed energy expenditure values were used to categorize an individuals' physical activity level, as active, moderate, and inactive (www.cflri.ca/cflri/pa/surveys/88survey.html). The variable of "type of smoker" was based on smoking frequency, which includes regular smoker (daily smoker), occasional smoker, former smoker, and non-smoker.

2.4. Statistical analyses

In order to examine the representativeness of the selected study sample, we compared the study sample to those not included in this study. Proportional hazard models were used to evaluate the relationship between characteristics and earlier onset of the first-episode of major depressive disorder. Schoenfeld residuals and –ln(-ln) survival plots were used to verify the proportional hazards assumption. In multivariate survival analyses, hazard ratios (HRs) were used to illustrate the relationship between characteristics and earlier onset of the first depressive episode. Interactions between factors were tested using Wald tests. The goodness of fit of the final model was tested. To correct for the sample design effect, Statistics Canada recommended a bootstrap procedure that uses a set of 500 replicate sampling weights.

2.5. Meta-analyses

Meta-analysis was used to synthesize our findings with the results from other published cohorts indexed in the database of PubMed. Using PubMed with search terms 'depression' or 'depressive', and 'first' or 'new' or 'incident', and 'predicator', 'factor' or 'characteristic*', cohort studies of the association between risk factor and the first depressive episode were identified as of April 2016. To be included in the meta-analyses, articles were evaluated for internal validity and following inclusion and exclusion criteria: 1) be published in English (before April 2016); 2) be a cohort study; 3) use clear diagnosis criteria for major depressive episode; and, 4) provide statistical indicators or original data to estimate the relationship between characteristics and major depressive episode. Meta-analyses were restricted to characteristics that were selected in this present study and consistently categorized across studies. Studies were excluded if characteristics studied were not found in this present study.

HRs for the contrast between the risk level and reference level of each selected factor were pooled using random-effects models. The inverse of the variance of the log HR was used to weight each HR from each study to calculate the pooled HR and its 95% confidence interval (CI). Heterogeneity between studies was tested by DerSimonian and Laird I^2 *statistic*, which is the proportion of variation in HRs attributable to heterogeneity (Schoenfeld and Loftus, 2005). Funnel plots and Egger's tests were used to check publication bias (Egger et al., 1997). Sensitivity analysis assessed the influence of each study on overall estimates by recalculating HR with each study being removed one at a time, and by only including those studies with large sample size (N > = *1000*). Stata v.12, statistical software (StataCorp., USA) was used for all analyses.

3. Results

3.1. Characteristics of the study sample

A total of *12,227* participants of NPHS were selected for this study. The study sample was 12 years and more and depression-free at the baseline, and followed up for a 16-year period from 1994/95 to 2010/11. Additionally, there was complete data on major depressive episode during the period. Compared to non-selected survey subjects, the study sample had a higher proportion of older population, women, Caucasians, people living married or in a common-law relationships, people with higher income and better education, immigrants, regular drinkers and smokers, less active people, and people suffering with chronic diseases (data not shown). There were fewer men than women (48.2% vs. 51.8%). Men were more likely to be younger, in a relationship (married or common-law), with higher income and more