



# Is familial risk for depression confounded by individual and familial socioeconomic factors and neighborhood environmental factors? A 7-year follow-up study in Sweden

Tsuyoshi Hamano<sup>a,b,\*</sup>, Xinjun Li<sup>c</sup>, Sara Larsson Lönn<sup>c</sup>, Toru Nabika<sup>b,d</sup>, Jan Sundquist<sup>c,d,e</sup>,  
Kristina Sundquist<sup>c,d,e</sup>

<sup>a</sup> Department of Sports Sociology and Health Sciences, Kyoto Sangyo University, Kyoto, Japan

<sup>b</sup> Department of Functional Pathology, Shimane University School of Medicine, Izumo, Japan

<sup>c</sup> Center for Primary Health Care Research, Lund University, Malmö, Sweden

<sup>d</sup> Center for Community-Based Health Research and Education (CoHRE), Shimane University, Izumo, Japan

<sup>e</sup> Departments of Family Medicine and Community Health and of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York, USA

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## ABSTRACT

Family history of depression is an important risk factor for depression. The aim of this study was to examine whether the effect of family history of depression is confounded by individual and familial socioeconomic factors (i.e., country of origin, educational attainment, family income and mobility) and neighborhood environmental factors (i.e., neighborhood deprivation and neighborhood social capital). The study population comprised 188,907 individuals aged 20–44 years from a nationwide sample of primary care centers in Sweden. Among these individuals, 22,014 with a first event of depression (6,486 men and 15,528 women) were identified during the 7-year follow-up period. Family history of depression was defined as depression in at least one parent. Cross-classified multilevel logistic regression models were used to calculate odds ratios with 95% credible intervals. Increased familial odds were observed after adjustment for individual and familial socioeconomic factors and neighborhood environmental factors for both men and women. Our results suggest that family history of depression is an independent risk factor for depression. Offspring of parents with depression are important targets for disease prevention, regardless of individual and familial socioeconomic factors and neighborhood environmental factors.

## 1. Introduction

Depression is a common mental disorder and the proportion of the global population with depression in 2015 is estimated to be 4.4% (World Health Organization, 2017). Many studies have revealed risk factors related to depression, including socioeconomic factors (e.g., educational attainment and income), physical inactivity, and other health-related factors, e.g., current history of the disease (Tani et al., 2016; Mammen et al., 2013; Huang et al., 2010). It is also important to note that family history of depression is an important risk factor for depression (Levinson, 2006).

A review and meta-analysis of the genetic epidemiology in major depression has indicated that major depression is considered a familial disorder, which mostly or entirely results from genetic influences (Sullivan et al., 2000). There are now numerous established twin studies, indicating the heritability of major depression (Kendler et al.,

2006; Dunn et al., 2015). In addition, genome-wide studies were able to identify risk loci (CONVERGE consortium, 2015; Hyde et al., 2016). For a deeper understanding of the etiology of depression, it is necessary to construct a model that considers individual, familial, and environmental factors simultaneously to reveal the potential influence of these factors (Avenevoli and Merikangas, 2006; Mitjans et al., 2012; Dunn et al., 2015).

The social determinants of depression have been investigated in several studies. A previous meta-analysis found that lower socioeconomic factors (e.g., educational attainment and family income) were associated with a higher risk of depression (Lorant et al., 2003). Similar to socioeconomic factors at the individual and familial level, the neighborhood environment (e.g., neighborhood deprivation and neighborhood social capital) could also play an important role in the development of depression (Lofors and Sundquist, 2007; Richardson et al., 2015). To our knowledge, no large-scale follow-up study has yet

\* Corresponding author at: Department of Sports Sociology and Health Sciences, Kyoto Sangyo University, Kyoto, Japan.  
E-mail address: [thamano@cc.kyoto-su.ac.jp](mailto:thamano@cc.kyoto-su.ac.jp) (T. Hamano).

examined the effect of familial depression, individual and familial socioeconomic factors, and neighborhood environmental factors, simultaneously.

The first aim of this large-scale 7-year follow-up study was to examine the association between family history of depression and depression. The second aim was to examine whether the familial risk for depression remains significant after adjustment for individual and familial socioeconomic factors (i.e., country of origin, educational attainment, family income, and mobility) and neighborhood environmental factors (i.e., neighborhood deprivation and neighborhood social capital).

## 2. Methods

### 2.1. Participants

The study population comprised 80,072 men and 108,835 women from a nationwide sample of primary care centers in Sweden. The data used in this study were retrieved from national registers (Mezuk et al., 2013; Sundquist et al., 2011). Complete medical records were obtained from a nationally representative sample of 75 primary healthcare centers beginning on January 1, 2001. These records were then linked to national inpatient (available from 1964), outpatient (available from 2001), and prescription drug (available from 2005) registries provided by the National Board of Health and Welfare. Additional linkages were performed using several national Swedish data registers, including but not limited to the following: the Swedish national population and housing census (1960–1990), the total population register, the multi-generation register, and the cause of death register. These registers contain individual-level information on, for example, the following factors: age, sex, parents, siblings, children, occupation, education, region of residence, hospital diagnoses, and dates of hospital admissions for the period 1964–2010. The registers also include information on country of origin, date of emigration, and date and cause of death. In the Multi-Generation register, offspring born in Sweden since 1932 are linked to their parents. All linkages were performed using an individual national identification number that is assigned to each person in Sweden for their lifetime. This number was replaced by a serial number for analysis to ensure anonymity of individuals. The quality and validity of primary care electronic medical records in Sweden is high (Grimsmo et al., 2001; Nilsson et al., 2003). The participants were restricted to individuals aged 20–44 years by January 1, 2001, and followed until onset of depression, death, or censoring at the end of the study period, on December 31, 2007.

### 2.2. Measures

#### 2.2.1. Depression

Depression was defined as a clinical diagnosis from primary care, inpatient, or outpatient registries (ICD-10 code F32) in the time from January 1, 2001, to the end of the follow-up period. Depression was assessed as a binary indicator (never diagnosed with depression vs. diagnosed with depression at least once in any healthcare setting) for analysis. To ensure that all depression cases were new, we excluded those individuals in the study population (offspring) with pre-existing depression. However, parents with prevalent depression were not excluded. We identified 22,014 depression cases (6486 men and 15,528 women) during the follow-up period.

#### 2.2.2. Family history of depression

Family history of depression was assessed as a diagnosis of depression (ICD-10 code F32) in either biological parent from January 1, 2001, to December 31, 2007, from the primary care, outpatient, and inpatient registries, and the prescription drug registry (ATC code N06A).

#### 2.2.3. Individual and familial socioeconomic factors

Educational attainment was categorized as completion of compulsory school or less ( $\leq 9$  years or missing), practical high school, or some theoretical high school (10–11 years), and completion of theoretical high school or college ( $\geq 12$  years). Country of origin was classified as Swedish-born or foreign-born; the latter was based on the most common immigrant groups in Sweden, which resulted in the following groups: (1) Swedish-born, (2) born in Finland, (3) born in Western Europe or North America (e.g., Denmark, United Kingdom, France, Italy, Germany, and United States), (4) born in Eastern Europe (e.g., Bosnia–Herzegovina, former Yugoslavia, Czechoslovakia, Poland, Romania, and Russia), (5) born in the Middle East (e.g., Turkey, Lebanon, Iran, Iraq, and Morocco), and (6) all other nationalities. Family income was based on the annual family income divided by the number of people in the family (i.e., individual family income per capita) as calculated by Statistics Sweden. The income calculation was weighted, taking the ages of the family members into account. For example, children were given lower consumption weights than adults. The calculation was performed as follows: the sum of all family members' incomes was multiplied by the individual's consumption weight divided by the family members' total consumption weight. The final variable was calculated as empirical quartiles from the distribution and classified as low, middle-low, middle-high, and high. Mobility was included to partly account for length of time lived in the neighborhood, categorized as moved/not moved between Jan 1st 2001 and Dec 31st 2006.

#### 2.2.4. Neighborhood environmental factors

Neighborhoods were defined on the basis of *small areas for market statistics* (SAMS), which are small geographical units with boundaries defined by homogenous types of buildings as defined by Statistics Sweden. All Swedish individuals have been geocoded to these areas. There are approximately 9,200 SAMS throughout Sweden, with an average population of 1000 individuals. SAMS were used as proxies for neighborhoods, as in previous research (Calling et al., 2016; Li et al., 2016; Sundquist et al., 2014). In total, this study included 188,907 individuals, nested in 4,703 neighborhoods.

We identified deprivation indicators used by previous studies to characterize neighborhood environment, and performed principal component analysis to select deprivation indicators in the Swedish national database. Four variables were selected for those aged 25–64 years: low education level ( $< 10$  years of formal education), low income (income from all sources, including that from interest and dividends  $< 50\%$  of the median individual income), unemployment (excluding full-time students, those completing military service, and early retirees), and receipt of social welfare. Each variable loaded on the first principal component with similar loadings (+0.47 to +0.53) and explained 52% of variation between these variables. A z-score was calculated for each SAMS. The z scores, weighted by the coefficients for the eigenvectors, were then summed to create the index (Gilthorpe, 1995). The index was categorized into three groups:  $< 1$  standard deviation (SD) from the mean (low deprivation),  $> 1$  SD from the mean (high deprivation), and within 1 SD of the mean (moderate deprivation). Higher scores reflected more deprived neighborhoods, as depicted in previous studies (Winkleby et al., 2007).

Neighborhood social capital was also included in the analysis. This variable was measured as the number of people in the neighborhood who voted in local government elections divided by the number of people in the neighborhood who were entitled to vote, as previous studies have done (Sundquist et al., 2014a, b). Neighborhoods were divided into the following three groups based on the proportion of residents who voted: (1) low, (2) intermediate, and (3) high. Group 1 comprised 20% of neighborhoods with lowest proportions of voters ( $\leq 74.0\%$ ); group 2 comprised 60% of neighborhoods with intermediate proportions of voters (74.1–82.0%); and group 3 comprised 20% of neighborhoods with the highest proportions of voters ( $> 82.0\%$ ).

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