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Journal of Clinical Epidemiology 61 (2008) 958–963

Journal of Clinical Epidemiology

Loss to follow up did not bias associations between early life factors and adult depression

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Accepted 9 November 2007

Abstract

Objective: This study examines the consequences of nonresponse in a follow-up survey for the associations of early life factors with adult depression.

Study Design and Setting: A cohort of 11,532 Danish men born in 1953 had nearly complete follow up for outcomes retrieved from the Danish Psychiatric Register and the National Prescription Register, but only 66% of 9,507 eligible cohort members participated in a follow-up survey in 2004. We examined whether characteristics measured at birth and at ages 12 and 18 years, were associated with survey response. Associations between early life characteristics and four measures of depression were described by odd ratios (OR), estimated by logistic regression. For the register-based measures the effect of nonresponse was described by a relative OR($OR_{responders}/OR_{entire\ cohort}$ = ROR).

Results: Nonresponse at 50 years of age was related to having a single mother at birth, low educational attainment at age 18, and low cognitive function at ages 12 and 18. Hospitalizations for depression and having claimed a prescription for an antidepressive drug were also most frequent among men who did not respond in the follow up. However, the effect of this nonresponse on the estimated ORs was small, and all ROR were nonsignificant.

Conclusion: Although early life characteristics were related to response in a follow-up survey, the ORs for the exposure-risk associations were not biased by nonresponse.

Keywords: Response rate; Bias; Cohort study; Depression; Birth weight; Cognitive function

1. Introduction

Nonresponse is a serious methodological problem in population-based cohort studies of mental health. Nonresponse at baseline has been well investigated [1,2] and several population studies have shown that nonresponders have poorer mental health and lower socioeconomic status than responders [3–9]. Another area of concern is that of drop-out during follow up due to unavoidable (death, emigration, and disappearance) and avoidable (refusal) causes. Refusal is particularly problematic for follow ups on health outcomes that depend on subjects' willingness to participate in an interview or health examination. If the rate of drop out is high in a cohort study, it will raise serious doubts about the validity of study results [10,11]. A selection bias effect might occur if study losses are systematic and survey response modifies the associations under study. In such a situation, the effect estimates among those who respond differ from those found in the source population. Several studies have explored differences in baseline characteristics between those who participate and those who do not participate in cohort study follow ups [6,12–15]; but we have only found two studies, both from the UK, that have examined the relationship between factors measured early in life and survey response in epidemiological studies of adults [14,15]. Both of these studies have shown that factors early in life are related to response rates in later follow up, and both strongly recommend analyses that explore the extent of the potential biases of this selection. The increasing number of cohort studies on the importance of childhood environment in the etiology of depression later in life have yielded inconsistent results [16–22]. Many of these studies have been based on self-reported measures of depression;

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0895-4356/08/$ – see front matter
doi: 10.1016/j.jclinepi.2007.11.005

and, although some of the studies have had rather high rates of nonresponse in their follow up, we are not aware of any studies that explore whether selective loss to follow up influences the risk estimate obtained from epidemiological studies of the association between early life factors and later mental health.

Thus, in the present study, we first analyzed whether the prevalence of selected indicators of childhood development (birth weight, social circumstances, and cognitive function in early life) and two register-based measures of depression (a psychiatric ward diagnosis of depression or antidepressive drug prescriptions) differed between responders and nonresponders to a postal follow-up survey conducted in middle age. We then explored whether the relationships between early life factors and register-based depression outcomes among responders differed from those found in the entire cohort. We also investigated whether the relationship between early life factors and register-based outcomes differed from those obtained for two self-reported measures of depression.

2. Methods

2.1. Subjects

The Metropolit cohort is defined as the 11,532 men born in 1953 in the Copenhagen Metropolitan area who were living in Denmark in 1968. The cohort has been described in detail elsewhere [23]. Data from birth certificates, including information on birth dimensions and father's occupational status at time of delivery, were manually collected on all members of the original study population, in 1965. In the same year, 7,987 (69.2%) of these males participated in a school-based survey that included a questionnaire administered by their class teachers. The questionnaire involved tests of cognition and enquiries regarding social aspirations and leisure time activities. For decades, nearly all Danish men have had to register with the conscription board, complete a cognitive test, the Boerge Priens test, and undergo a health examination by a medical doctor at the age of 18 [24]. In 2004, the results of these exams were collected manually from all Danish conscript district registers for 11,108 of the 11,494 cohort members who were alive and living in Denmark in 1971. In recent years, cohort members have been followed through register linkages to the Cause of Death Registry, the Danish Psychiatric Central Registry, and the National Drug Prescription Registry. We had very little loss to follow up in the population covering registers, but we expected a considerable number of dropouts in the 2004 follow up, which was based on postal questionnaires. At follow up, there were 384 (3.3%) emigrations (to areas outside Denmark, Greenland, and the Faroe Islands), 47 subjects (0.2%) with unknown address, and 1,018 (8.9%) deaths. Furthermore, a total of 576 subjects had asked the Civil Registration System not to pass their contact information on for research purposes. Consequently, a total of 9,507 men with available address in Denmark were sent a questionnaire in September 2004.

2.2. Measurements

2.2.1. Early life factors

We chose early life factors expected to be associated with survey response [14,15] and depression [16–22]. From the *birth register data* we used the *marital status of the mother at time of delivery* coded in three categories: married, unmarried (i.e., single, divorced, widowed), and unknown. *Birth weight* was recorded in 100-g groups and, in the present study, categorized into two groups ($<$2,500 g and $>$2,500 g). From the *school and conscript examinations* we included information on *cognitive performance at age 12*, measured by the Härnquist school test, and *cognitive performance at age 18*, measured by a 45-min validated cognitive test, the Boerge Prien test. Both cognitive scores were categorized into quartiles. At conscript, *educational attainment*, primarily reflecting school education, was also registered on a scale ranging from leaving school after seventh grade (basic education) to the highest school level (Studentereksamen), which is approximately equivalent to the British Advanced Level General Certificate of Education (high school). These data were recoded into two categories (basic education and all other educations).

2.2.2. Depression outcome variables

Information on time of admission to psychiatric wards, from 1969 to December 2002, and diagnosis on discharge was obtained from the *Danish Psychiatric Central Registry* [25]. Diagnoses from the hospital register were classified according to the 8th Revision of the International Classification of Diseases (ICD-8) for the years from 1969 to 1993, and according to the ICD-10 from 1994, onward. Both bipolar disorders (code number 296.19, 296.39, 298.19, in ICD-8 and code number F30, F31, F34.0 and F38.0 in ICD-10) and unipolar depression (including the code numbers 296.09, 296.29, 296.89, 296.99, 298.09, 300.49, 301.19 in ICD-8, and F32, F33, F34.1 and F38.1 in ICD-10) were included as diagnoses for *depression* in the present study. *The National Drug Prescription Registry* (Registry of Medicinal Product Statistics) contains information on outpatient prescription drug use by all citizens of Denmark since 1995. Each prescription record contains detailed information on the drug dispensed (anatomical therapeutic classification [ATC] system name, strength, and package size), the date, and the civil registration number of the person purchasing the drug. From this database, we retrieved all prescriptions claimed by members of the Metropolit cohort for *antidepressive drugs* (including lithium ATC; N06, N05AN01) in the period 1995–2002. On this basis, we calculated whether a cohort member had purchased these drugs at any time. A subject was defined as receiving treatment if he had ever purchased these drugs at