



Research paper

Smoking status as a predictor of antidepressant medication use

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ABSTRACT

Background: Cigarette smoking and depression are major public health concerns, but longitudinal research on the association between smoking and antidepressant use is scarce. The purpose of this study was to investigate, whether smoking predicts antidepressant medication during a 10-year follow-up.

Methods: A questionnaire was administered to Finnish adult twins in 1990. Antidepressant prescription data during 1995–2004 were obtained from the register of the Finnish Social Insurance Institution and linked to the survey data. Cox Proportional Hazard Models among 10,652 individuals (1075 cases, 9577 controls) assessed the risk for depression in the cohort, whereas within-pair comparisons of smoking twins with their non-smoking co-twins controlled for shared familial influences.

Results: Daily smokers had a significantly elevated likelihood for having antidepressant prescriptions in the follow-up. Based on the analysis among those without baseline depression, heavy daily smokers had a significantly elevated likelihood (HR 1.56, 95% CI 1.17–2.08) for antidepressant prescription when adjusted for all confounders. Similar analysis using pairs discordant for antidepressant medication confirmed that daily smoking twins had a higher likelihood for prescriptions (HR 1.98, 95% CI 1.11–3.54) compared with their non-smoking co-twins. The estimates were for MZ pairs (HR 1.78, 95% CI 0.48–6.55) and DZ pairs (HR 1.92, 95% CI 0.99–3.72), respectively.

Limitations: Changes in smoking status after baseline cannot be accounted for. Reversed association between depression and smoking cannot be ruled out.

Conclusion: Daily smoking predicts antidepressant medication, even when controlling for essential confounders and familial factors. This study highlights the need of systematically assessing depressive symptoms among smokers.

1. Introduction

Smoking and depression are major public health concerns (Royal College of Psychiatrists, 2013; World Health Organization, 2013). Depression is common and poses a substantial burden both societally, economically and individually (Kessler and Bromet, 2013; World Health Organization, 2012). Daily smoking is reported among 19% of men and 13% of women in Finland (Helldan et al., 2013) and the prevalence of nicotine dependence among Finnish ever smokers is very high (48–52%) (Broms et al., 2012).

The nature of this association between smoking behavior, nicotine dependence and depression can be discussed under various scenarios (Fluharty et al., 2016). First, the association may be causal between smoking and depression and that cigarette smoking behavior increases

the risk of depressive symptoms (Goodman and Capitman, 2000; Korhonen et al., 2007, 2011) or, nicotine dependence does indeed increase the risk of depressive symptoms (Boden et al., 2010). Second, depression may increase the level of nicotine dependence and thus, urge for smoking through a self-medication mechanism (Balfour and Ridley, 2000; Royal College of Psychiatrists, 2013). A reciprocal relation between cigarette smoking and depression has also been reported (Breslau et al., 1998; John et al., 2004). Third, there may be underlying factors common to both that are responsible for the association between nicotine dependence and major depressive disorder. One such factor may be genetic, given that there is a genetic component shared by both conditions (Broms et al., 2012; Korhonen et al., 2014; Sullivan et al., 2000). It is still unclear whether smoking ameliorates the symptoms of depression or whether depression pro-

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notes nicotine addiction (Balfour and Ridley, 2000; Royal College of Psychiatrists, 2013). The longitudinal association between smoking and depression has been addressed in several studies (Boden et al., 2010; Breslau et al., 1998; John et al., 2004). However, hardly any longitudinal research has been conducted on the association between smoking behavior and future use of prescribed antidepressant medications.

Antidepressant prescription may be used as an indicator of depression in register based studies. Such an outcome measure is justified because it is independent of the study investigators and of the participation in follow-up assessments, therefore this methodological approach is robust. The aim of the present study was to investigate whether smoking predicts prescriptions of antidepressant medication during 10 years' follow-up in a large sample of twins who were analyzed as individuals and as pairs discordant for antidepressant medication.

2. Materials and methods

2.1. Sample

The Finnish Twin Cohort is a population based sample that is compiled from the Central Population registry comprising all same sex twin pairs born in Finland before 1958, who were alive in 1967. The first questionnaire survey of the twins was conducted in 1975 and the second in 1981. The present study is based upon the third survey conducted in 1990. A questionnaire was sent in 1990 to all twin pairs born in 1930–1957, who had replied to at least one of the previous surveys, and with both co-twins resident in Finland in 1987 ($n=16,177$). Among the 16,177 who had been sent the 1990 questionnaire, 12,502 responded (77.3% response rate).

The Finnish Twin Cohort was linked to the reimbursed prescriptions of anti-depressants purchased from community pharmacies, using the Prescription Register of the Finnish Social Insurance Institute (SII). The antidepressant prescriptions of these individuals were followed up for the 1995–2004 period (1995 was the first year when such data were available). Approval for the register linkages was obtained from the Ethics committee of the Department of Public Health, University of Helsinki and the appropriate authorities at SII. The zygosity of the twins, monozygotic (MZ) or dizygotic (DZ), had been determined by validated questionnaire in a previous study (Sarna et al., 1978).

2.2. Measures

2.2.1. Outcome

The outcome variable was having register-based antidepressant prescriptions (ATC code N06A) during years 1995–2004. The SII prescription register was set up in 1995, and our linkage was restricted to the end of 2004. The twins who had prescriptions were linked to the completed questionnaire via their personal national insurance number (assigned to each resident in Finland) as the identifier. Those who had at least four consecutive prescriptions within one year or four non-consecutive prescriptions during the 10 years of follow-up were considered as cases. Persons with 1–3 medication prescriptions were excluded from the analyses. Controls were those who had no antidepressant prescriptions; no missing data on antidepressant prescription existed.

The prescription register includes data on the diagnoses for which the fully reimbursed medicines had been received. We matched the individuals' antidepressant prescription data with those in the 1990 survey data and defined the case versus control status of the identified individuals. Data on depressive symptoms were available from 12,063 individuals, however, there was missing information on smoking status and/or on amount of smoking for 615 of them.

From the 12,502 persons available from the SII register, we

excluded persons with psychotic disorders or mental retardation. Further, from the merged data set we removed individuals with other serious chronic mental illnesses and persons who were in disability pensions. A total of 1116 cases identified in the register data were successfully matched with the 1990 survey data, whereas the number of persons with no antidepressant prescription (controls) was 9968. Our sample was restricted to those who provided data for both depression and smoking in 1990, thus there were valid data available for the analysis from total of 10 768 persons (1075 cases, 9693 controls). Finally, the time-to-event analysis removed those persons who were lost to follow-up (death or emigration) between 1990 and 1994, when the outcome events for survival analysis were started ($n=116$). Thus, our time-to-event analyses were restricted to 10,652 persons (1075 cases, 9577 controls).

2.2.2. Predictor

Participants were categorized according to their baseline smoking status as follows: 1) Never smokers ($n=5174$); 2) Non-daily smokers ($n=373$); 3) Former smokers ($n=2479$); 4) Light/moderate daily smokers, ($n=1785$), and 5) Heavy daily smokers ($n=957$). The subjects were asked if they have ever smoked more than 5–10 packs of cigarettes (100 cigarettes) during their lifetime. Those responding negatively were categorized as “never smokers” and were considered as the reference group. Those responding positively were asked “Do you smoke or have you smoked cigarettes regularly, say daily, or almost daily during your lifetime?” Positive responders were further asked if they still smoked regularly. If so, they were classified as current daily smokers. Persons who had smoked more than 100 cigarettes but were not regular smokers were considered as non-daily smokers. Former smokers were those regular smokers who had responded that they no longer smoked at the time of the survey. In our data the self-reported length of smoking abstinence among former smokers ranged mainly between 1 and 39 years. However, there was a minor group of participants (5.53%) who had quit smoking less than 12 months ago.

Among current daily smokers the mean daily cigarette consumption was defined. The response categories to the question “How many cigarettes do you smoke daily on average?” were as follows: < 5, 5–9, 10–14, 15–19, 20–24, 25–39, and > 40. Light/moderate daily smokers included those smoking < 20 cigarettes/day (CPD) and heavy daily smokers included those smoking ≥ 20 CPD (i.e. a pack a day).

2.2.3. Confounders

Potential confounders at the baseline included socio-demographic background (age, gender, social class), other substance use than smoking (binge drinking), and health status (somatic health) and these were used to adjust the analyses. Individuals were divided into three groups by years of education and physical activity performed during work to determine the individual's broad socio-economic class (Appelberg et al., 1991). Those with a minimum of 12 years of education and sedentary work were considered “white collar”; those with fewer than 9 years of education and ambulatory work consisting of walking and lifting or hard physical work were “blue collar” and the remainder formed an intermediate group of individual (Romanov et al., 2003).

Binge drinking was defined as drinking more than five bottles of beer, or more than a bottle of wine, or more than half a bottle of spirits on the same occasion at least once a month; only a “yes” or “no” response was recorded (Kaprio et al., 1987).

In the 1990 questionnaire the subjects were asked if they had ever been told by their physician that they have or have had any somatic disease listed. The response to each item was scored 0 if ‘No’ and 1 if ‘Yes’. A Somatic Disease Index (SDI) was formed in which the subject was considered to have ‘any somatic disease’ if in the 1990 questionnaire he/she had (i) any self-reported disease diagnosed by a physician, or (ii) a self-reported life event of serious injury/illness, or (iii) self-reported work disability. Other subjects were classified as

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