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The role of self-reported stress in the development of breast cancer and prostate cancer: A prospective cohort study of employed males and females with 30 years of follow-up

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ABSTRACT

We investigate the association between psychological stress and breast cancer and, as oestrogen may provide a common mechanism, the association between stress and prostate cancer. A prospective study of 991 women and 5743 men employed in Scotland in the 1970s provided data. Risk exposure was measured by questionnaire and physical examination, routine data collection provided cancer outcomes over the subsequent 30 years. There was weak evidence of elevated incidences in those reporting moderate (breast cancer: hazard ratio [HR] 2.16, 95% CI 1.00–4.71; prostate cancer: HR 1.65, 95% CI 1.20–2.27) and high stress (breast cancer: HR 1.92, 95% CI 0.81–4.55; prostate cancer: HR 1.35, 95% CI 0.87–2.10) compared to those reporting low stress. These estimates are adjusted for socioeconomic circumstances and health-related behaviours. With no dose–response relationship and no established mechanism linking stress with breast and prostate cancer, confounding is the parsimonious explanation of these findings.

1. Introduction

A number of recent prospective studies have provided evidence that relatively high levels of psychological stress are associated with the subsequent diagnosis of breast cancer in women. A lower incidence of breast cancer has been linked with psychological stress[1] and, in the Nurses' Health Study, high job demands.[2] In contrast, a higher incidence of breast cancer has been linked with greater psychological stress[3] and, in the Finnish Twin Cohort,[4] stressful life events. Oestrogen secretion has been suggested as a mechanism by which stress can affect the risk of breast cancer, with chronic psychological stress suppressing[1] or amplifying[2] oestrogen secretion according to these hypotheses.

In this context of conflicting results and hypotheses, it is not surprising that not all recent studies find evidence of an association. Notably there was no association between caregiving stress and breast cancer in the Nurses' Health Study,[5] nor between stress of daily activities and breast cancer in the Finnish Twin Cohort,[6] both of these studies having been cited above in support of an association. In addition, two recent meta-analyses on the association between stressful life

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events and breast cancer have failed to find convincing evidence of an association once study quality and publication bias have been accounted for.[7,8] Earlier studies have been criticised for using retrospective or cross-sectional designs,[9,10] which leave reported psychological stress prone to recall bias, and for failing to control all relevant confounding factors.[9] With regards to the latter issue, it has been reported that women reporting high levels of psychological stress are more likely to be less physically active, to have finished full-time education earlier, to have a manual occupation, to be heavy drinkers, to be a current smoker, and to have undergone hormone therapy.[1,6]

We have previously suggested that confounding by factors associated with social position may have been underestimated when inferring causality from associations between measures of psychological distress and chronic physical disease. Social position often varies with both reported distress and health outcomes, so potentially confounding observed associations between these two factors. Hence in a population where social advantage is associated with perceived stress and social disadvantage with lung cancer, higher stress appears associated with lower risk of lung cancer despite an association between higher stress and heavier smoking.[11] Conversely, in a population where social disadvantage is associated with perceived stress and social advantage is associated with breast cancer, higher stress appears associated with a lower risk of breast cancer.[1,11,12]

This study is based upon a cohort of women for whom reported stress is not strongly associated with social position,[13] limiting the extent to which social position can confound the observed association between psychological stress and breast cancer. Furthermore, extensive data are available on social position and other potentially confounding factors, allowing better control than in many previous studies. We also look at the association between reported daily stress and prostate cancer in men. If psychological stress is affecting the rate of breast cancer through a hormonal mechanism, a similar mechanism may also influence hormone-dependent cancer in males.[14]

2. Materials and methods

2.1. Participants

The data for this analysis come from the West of Scotland Collaborative Study.[15,16] In brief, a cohort of 6022 men and 1006 women were recruited from a variety of workplaces in the west of Scotland between 1970 and 1973. At enrollment, all members of the cohort were invited to complete a questionnaire and undergo a physical examination. The present analysis is based upon 5743 men and 991 women, aged 35–64 years old at recruitment, who provided full data on the variables used. Only 11 individuals were lost to follow-up.

2.2. Outcome variables

Each cohort member was followed up through linkage to the National Health Service (NHS) Central Register until they left the United Kingdom, until they died, or otherwise until 31st March 2004. Breast cancer events (deaths, cancer registrations and hospital discharge diagnoses) were detected as International Classification of Diseases 9th revision (ICD-9) code 174 or ICD-10 code C50, whereas prostate cancer events were detected as ICD-9 code 185 or ICD-10 code C61. Death due to breast cancer, and first recorded instance of breast cancer were used as outcome measures for women. Death due to prostate cancer, and first recorded instance of prostate cancer were used as outcome measures for men. The small number of breast cancers occurring in men were not included in the analysis.

2.3. Risk factors and confounding variables

Psychological stress was measured at enrollment using the Reeder Stress Inventory,[17] a self-report measure of daily stress we have described in detail elsewhere.[18] Respondents are asked whether each of the four statements describes them ‘exactly’, ‘to some extent’, ‘not very accurately’, or ‘not at all’. The four statements are ‘In general I am usually tense or nervous’, ‘There is a great amount of nervous strain connected with my daily activities’, ‘At the end of the day I am completely exhausted mentally and physically’, and ‘My daily activities are extremely trying and stressful’. Scores range from 1 (low stress) to 8 (high stress), with three categories of stress being used in the presentation of the results: low stress (scores 1–3), medium stress (scores 4 and 5) and high stress (scores 6 and 7). Despite its age, the factor structure,[13] construct validity and test–retest reliability of the Reeder Stress Inventory support its continued use.[18]

Measures of social position in adulthood and childhood were available. Social position in adulthood was captured through the individual’s reported occupation at enrollment (manual versus non-manual according to the Registrar General’s classification[19]), their age at leaving full-time education (up to 14 years versus 15 years or older) and the Carstairs and Morris Index for their usual area of residence (categorised as affluent scores 1–3, intermediate scores 4 and 5, deprived scores 6 and 7[20]). An individual’s social circumstances in childhood were ascertained from their father’s main occupation (manual versus non-manual), how many siblings they had (0–2, 3–4, 5–6 and 7 or more siblings), and their height.

Height and weight were recorded using standard methods.[15,16] Exercise outside work was reported in hours per week and was categorised as less than 5 h, 5 h or more but less than 10 h, and 10 h or more, for men and women. Each participant’s average consumption of alcohol per week was derived from reported consumption of wine, beer and spirits.[21] For women three categories of alcohol consumption were derived, these being zero units, one to seven units, and eight or more units per week where one UK unit is 10 g of alcohol. For men six categories were derived, these being 0 units, 1–7 units, 8–14 units, 15–21 units, 22–34 units, and 35 or more units. The following aspects of each individual’s reported cigarette smoking history were used in the current analysis: number of cigarettes smoked per day if a current smoker (categorised as 1–14, 15–24, and 25 or more), whether an ex-smoker if not currently smoking, age at starting smoking, and whether or not the individual inhaled whilst smoking. Current cigarette smokers included those who reported having given up less than a year previously.[15,16] Only cigarette