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Research report

Depression and mortality: Artifact of measurement and analysis?

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ABSTRACT

Background: Previous research demonstrates various associations between depression, cardiovascular disease (CVD) incidence and mortality, possibly as a result of the different methodologies used to measure depression and analyse relationships. This analysis investigated the association between depression, CVD incidence (CVDI) and mortality from CVD (MCVD), smoking related conditions (MSRC), and all causes (MALL), in a sample data set, where depression was measured using items from a validated questionnaire and using items derived from the factor analysis of a larger questionnaire, and analyses were conducted based on continuous data and grouped data.
Methods: Data from the PRIME Study ($N=9798$ men) on depression and 10-year CVD incidence and mortality were analysed using Cox proportional hazards models.
Results: Using continuous data, both measures of depression resulted in the emergence of positive associations between depression and mortality (MCVD, MSRC, MALL). Using grouped data, however, associations between a validated measure of depression and MCVD, and between a measure of depression derived from factor analysis and all measures of mortality were lost.
Limitations: Low levels of depression, low numbers of individuals with high depression and low numbers of outcome events may limit these analyses, but levels are usual for the population studied.
Conclusions: These data demonstrate a possible association between depression and mortality but detecting this association is dependent on the measurement used and method of analysis. Different findings based on methodology present clear problems for the elucidation and determination of relationships. The differences here argue for the use of validated scales where possible and suggest against over-reduction via factor analysis and grouping.

1. Introduction

Various researchers report a link between depression, cardiovascular disease, and mortality, while others also report no association, or an association that results purely from confounders (see Atlantis et al., 2012; Baune et al., 2012; Leung et al., 2012; Schulz et al., 2002; Wulsin et al., 1999). These different conclusions between studies are often attributed partly to differing methodologies. Studies investigating methodological effects have largely focussed on details such as depression subtype, time course effects, and confounding variables (Atlantis et al., 2012; Baune et al., 2012; Leung et al., 2012; Schulz et al., 2002; Wulsin et al., 1999), but two purely methodological aspects of limited study include the method by which depression is assessed and the analyses subsequently conducted. Measures of depression can range from clinical interviews to self-rating scales and single questions (Nezu et al., 2000). Analyses can be conducted using continuous data, allowing the emergence of continuous patterns and effects, or data which is grouped dichotomously as depressed/not depressed, or grouped by quartiles or quintiles, which may more easily elucidate extreme differences and detect non-linear associations (Kline, 2000; Biswas et al., 2008). Use of different methods of measurement and analysis could potentially result in different outcomes. This analysis aimed to investigate the link between depression, cardiovascular disease incidence and mortality in a sample data set, when comparing the use of items from a

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validated questionnaire and items from the factor analysis of a larger questionnaire for the assessment of depression, and using analyses based on continuous data and grouped data.

2. Methods

Analyses were conducted on the data set gained from the Prospective Epidemiological Study of Myocardial Infarction (PRIME) study, where data on depression, cardiovascular disease incidence and mortality are available over a 10-year follow-up period for 9798 men from France and Northern Ireland. Full details of the PRIME study are provided elsewhere (The PRIME Study Group, 1998).

Depression was assessed in the PRIME study using 10 questions from a validated questionnaire – the Welsh Pure Depression Inventory (Rodda et al., 1971), plus three additional questions, all contained within a larger 70-item psychosocial questionnaire. The psychosocial questionnaire was derived by including questions from a number of validated questionnaires – the Framingham Type A scale (Haynes et al., 1978), the Cook–Medley Hostility scale (Cook and Medley, 1954) and the MONICA scales for the assessment of social support (WHO, 1989), plus additional questions derived by researchers (Sykes et al., 2002). The questionnaire was completed by all participants at the start of the study.

Data on depression via a validated questionnaire were obtained by combination of the 10 items from the Welsh Pure Depression Inventory. Questions were responded to on a 2 point scale (true/false: scored 1/0), then combined and divided by the number of questions to result in a single depression score (depV) per person between 0 and 1, where higher scores denote greater depression. Individual questions are provided in Table 1. All questions were responded to using the full extent of possible answers.

Data on depression via the factor analysis were obtained through principal component analysis (with varimax rotation) on 69 items from the psychosocial questionnaire. (One item was optional and due to low response rates was excluded from the analysis). This analysis revealed eight factors, explaining 37% of the variance, but inspection of individual factor loadings and composite factors, and reference to an earlier analysis of the same data set (Sykes et al., 2002) resulted in a decision to limit the analysis outcomes to five factors, explaining 29% of the variance. These five factors utilized 58 items from the questionnaire. All items with a factor loading less than 0.30 on any factor were ignored. Based on their component questions, these factors were labelled Depression (16 items), Competitiveness (14 items), Hostility (10 items), Social Support (8 items) and Anger/Impatience (10 items). Individual questions for the Depression factor are provided in Table 2. Cronbach's alpha for reliability = 0.71. All questions were responded to using a variety of response formats, but all response formats were subsequently re-scaled to result in a score per question of between 0 and 1. All questions were responded to using the full extent of possible answers. Scores on the depression factor were created per person by adding scores for all relevant items and dividing by the number of items, to result in a score (depFA) between 0 and 1, where higher scores again denote greater depression.

For the analyses, either calculated continuous depression scores (depV/depFA) were used, or depression scores were grouped into approximate fifths (depVG/depFAG). Grouping into exact quintiles was not possible due to the limited gradations and responses in the depression scales.

Cardiovascular disease incidence (CVDI), mortality (MCVD), mortality from smoking related conditions (MSRC) and mortality from all causes (MALL) were assessed for a 10-year period from the start of the study via hospital records. All reported cases were verified by study personnel (The PRIME Study Group, 1998).

Cox proportional hazards models were used to predict incidence or not of CVDI, MCVD, MSRC and MALL using depression scores (Model 1), depression scores plus two demographic confounders (Model 2), and depression scores, demographic confounders and ten lifestyle confounders known to be associated with mortality (Model 3) (The PRIME Study Group, 1998; Wulsin et al., 1999; Schulz et al., 2002). The two demographic confounders were age and country of residence (NI/France). The ten lifestyle confounders were: systolic blood pressure, cholesterol, HDL cholesterol, height, BMI, fruit and vegetable intakes (portions of fruit, fruit juice and vegetables/day), physical activity (metabolic equivalent scores/week), lifetime smoking (five categories: never smoked; smoked other than cigarettes; smoked less than 15 cigarette pack-years; smoked 15 or more but less than 30 cigarette pack-years; smoked 30 or more cigarette pack-years), alcohol intakes (five categories: none; 1–128 ml/week; 129–265 ml/week; 266–461 ml/week; and 462 ml or more/week) and diabetes (present/absent). Similar analyses were conducted using continuous data and using grouped data. The grouped analyses investigated evidence of a linear trend to allow comparison with continuous data. Analyses were also attempted using two groups (depressed/not depressed), but cut offs for depression/no depression are not available for the Welsh Pure Depression Inventory (Rodda et al., 1971), and are clearly not available for the scale derived from factor analysis. Analyses were conducted for two groups using scores of 0 vs. 0.1 or more on each scale, but this resulted in classification of 60% of the sample as depressed using depV, and

Table 1
Question items from the Welsh Pure Depression Inventory (Rodda et al., 1971).

Item	
1.	I get tired for no reason
2.	Life seems dull to me
3.	I do not seem to have the energy to do things
4.	I have a good appetite
5.	I am usually bored
6.	I feel that others would be better off if I were dead
7.	I awake in the morning feeling tired
8.	I have trouble sleeping at night
9.	In thinking of my life I often wonder why I exist
10.	I feel useless

Table 2
Question items for the Depression scale derived by Factor Analysis from the 70-item Psychosocial Questionnaire.

Item	
1.	I get tired for no reason
2.	Life seems dull to me
3.	I do not seem to have the energy to do things
4.	I am usually bored
5.	I awake in the morning feeling tired
6.	I have trouble sleeping at night
7.	In thinking of my life I often wonder why I exist
8.	I feel useless
9.	I feel powerless to effect changes in my life
10.	I feel helpless
11.	I often feel uncertain, uncomfortable or dissatisfied with how well I am doing
12.	How often in the last month, did you have trouble falling asleep?
13.	How often in the last month, did you have trouble staying asleep (e.g. waking up too early)?
14.	How often in the past month, did you wake up two or more times per night?
15.	How often in the past month, did you wake up after your usual amount of sleep feeling tired and worn out?
16.	How many hours of sleep do you usually get each night?