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# Stressful life events exposure is associated with 17-year mortality, but it is health-related events that prove predictive.

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**Abstract**

**Objectives.** Despite the widely held view that psychological stress is a major cause of poor health, few studies have examined the relationship between stressful life events exposure and death. The present analyses examined the association between overall life events stress load, health-related and health-unrelated stress, and subsequent all-cause mortality.

**Design.** This study employed a prospective longitudinal design incorporating time-varying covariates.

**Methods.** Participants were 968 56-year old Scottish men and women. Stressful life events experience for the preceding two years was assessed at baseline, 8/9 years and 12/13 years later. Mortality was tracked for the subsequent 17 years during which time 266 participants had died. Cox's regression models with time varying covariates were applied. We adjusted for sex, occupational status, smoking, BMI, and systolic blood pressure.

**Results.** Overall life events numbers and their impact scores at the time of exposure and the time of assessment were associated 17-year mortality. Health-related event numbers and impact scores were strongly predictive of mortality. This was not the case for health-unrelated events.

**Conclusions.** The frequency of life events and the stress load they imposed were associated with all-cause mortality. However, it was the experience and impact of health-related, not health-unrelated, events that proved predictive. This reinforces the need to disaggregate these two classes of exposures in studies of stress and health outcomes.

**Keywords** Stressful life events, health-related events, health-unrelated events, mortality

It is now common knowledge, both in the lay (Davison, Davey Smith, & Frankel, 1991) and scientific (Greenwood, Muir, Packham, & Madeley, 1996; Hemingway & Marmot, 1999) communities, that psychosocial stress holds negative consequences for physical health. However, the evidence, particularly with regard to more objective measures of disease outcomes, is often less compelling than it first appears (Macleod et al., 2002; Macleod et al., 2001). In addition, the conceptualization and measurement of psychosocial stress remains a matter of debate. Two major approaches can be identified. The first approach conceives of stress as a personal attribute, and endeavours to measure individuals' perception of how stressful they regard their general life, or some specific aspect of it such as the work place, to be. Although popular, such measures are susceptible to reporting bias, as a function of individual variations in such things as plaintive set, and the specific discourse patterns that predominate in particular societies at particular times (Heslop et al., 2001; Macleod et al., 2001). The second approach conceives of stress as exposure to life events presumed to be negative and undesirable, and assesses stress as the number of such events experienced over a given period. Although this approach has a subjective component, it is less liable to reporting bias and variations in prevailing discourse. However, it fails to recognise that the same objective event can impact quite differently on different individuals. Accordingly, it is appreciated that the total psychosocial stress load is probably best captured as the product of life event exposures and some measure of their individual impact (Holmes & Rahe, 1967).

Stressful life events experience has been linked to both cardiovascular (Rosengren et al., 2004) and infectious (Cohen, Tyrell, & Smith, 1993) disease morbidity. Remarkably few substantial prospective studies, however, have examined the association between stressful life events experience and mortality, particularly all-cause mortality. In a 7-year follow-up of 752 Swedish men, those who had experienced three or more stressful life events during the year prior to entry were more likely to have died from all causes than those with no life events (Rosengren, Orth-Gomer, Wedel, & Wilhelmsen, 1993). The association between life events exposure and mortality survived adjustment for smoking, perceived health, and occupational class. In contrast, in a study of breast cancer in 673 women, stressful life events and their impact in the five years or one year prior to diagnosis did not predict either all-cause and or breast cancer-specific mortality during the seven years following diagnosis (Maunsell, Brisson, Mondor, Verreault, & Deschcnes, 2001). In the largest analyses to date, of over 12,000 men from the Multiple Risk Factor Intervention Trial (MRFIT) cohort, the number of life events during the previous year accumulated for five yearly assessment visits was negatively related to all-cause mortality; those who had accumulated more events were somewhat less likely to have died during the 6-year follow-up (Hollis, Connett, Stevens, & Greenlick, 1990).

Clearly, further investigation is warranted. Since life events span a number of domains, from finance to bereavement, it is also important to examine the consequences for mortality of events in different classes of domains. Although neither of the two substantial previous studies of relatively healthy participants (Hollis et al., 1990) included health-related life events, most life events inventories include items about health-related experiences (Dohrenwend, Dohrenwend, Dodson, & Shrout, 1984). Accordingly, a comparison of the impact of health-related and health-unrelated events would seem important. It has been argued that life events which reflect symptoms of physical illness confound the measurement of stress with the measurement of health outcomes (Dohrenwend et al., 1984). Essentially, health-related life events, as well as being stressful, can be indicators of morbidity, which clearly has consequences for mortality. The present study revisited the issue of life events and mortality in a cohort of 56-year old Scottish men and women. Stressful life events experience for the two years prior to baseline was measured and mortality tracked for the subsequent 17 years. Life event assessment was repeated 8/9 years and 12/13 years later. As well as determining the association between overall stress load and mortality, the analyses also examined the consequences for mortality of life events experience in health-related and –unrelated domains. It was hypothesised that stressful life events would be positively associated with all-cause mortality, but that the association would be stronger for health-related than health-unrelated events because they reflect morbidity.

## Methods

### Participants

Data are derived from eldest of the three age cohorts of the West of Scotland Twenty-07 Study (Ford, Ecob, Hunt, Macintyre, & West, 1994) who were around 56 years old at the baseline in 1988. They were all from the Glasgow area and have been followed up on three subsequent occasions in 1992/93 (wave 2), 1995/96 (wave 3) and 2000/01(wave 4). Demographic, and health-related data, such as smoking, body mass index, and blood pressure, were collected at each wave, but life event information was not collected at wave 2, and so the life events referred to in this paper are derived from baseline, and waves 3 and 4.

**Data collection**

On each of the occasions, participants completed questionnaires and were interviewed in their own homes by trained nurses. Household occupational status was classified as manual and non-manual from the occupational status of the head of household, using the Registrar General's (*Classification of Occupations*, 1980) classification of occupations. Smoking behaviour was determined by responses to the question, 'Do you ever smoke tobacco now? I am thinking of a pipe, cigars and your own roll ups as well as cigarettes you might buy.' If the answer was 'No', participants were asked, 'Did you ever used to smoke any kind of tobacco?' On this basis, participants were characterised as 'never smokers', 'ex smokers', or 'current smokers'. Height and weight were measured and body mass index computed. Systolic blood pressure was determined by a Hawksley random zero sphygmomanometer at baseline and an Omron (model 705CP) semi-automatic sphygmomanometer thereafter. The Omron is recommended by the European Society of Hypertension (O'Brien, Waeber, Parati, Staessen, & Myers, 2001). Following interview and questionnaire completion (approximately an hour), there was then a formal 5-minute period of relaxed sitting, at the end of which a resting blood pressure reading was taken.

Major life events over the two years prior to interview and their initial and current impact were assessed by presenting participants with eight cards each of which listed a number of major life events in one particular domain. The domains were as follows: health, marriage, relationships, bereavement, work, housing, finance, and general. The full list of events is presented in the Appendix. Participants were asked to indicate up to six events which had happened either to them or to someone they cared about. In addition, participants could endorse a final item in each domain if they had experienced an event not listed on the cards without specifying the nature of the event (see Appendix). This was rarely used. The present analyses focused on those events that had happened directly to the participant. Following identification of the events, participants were asked to specify, for each event, how much the event disrupted or changed their life and how stressful it was at the time of occurrence, as well as how disruptive and stressful it was 'now' (i.e. at the time of the interview). All of these responses were scored on a 5-point scale, where 1 = a very great deal and 5 = not at all; for the analyses, the values were reversed so that the greater the impact the higher the score. The present assessment method is based on the well-established Life Events and Difficulties Schedule (Brown & Harris, 1989) and included the same domains of personal experience. It has been argued that the interview method adopted here produces better reliability than self-administration of life events checklists (Raphael, Cloitre, & Dohrenwend, 1991). As concern lay with the *overall* stress load on participants, four measures were derived for each life event experienced by summing its disruptiveness and stressfulness, both at the time of its occurrence and now.

Mortality was tracked for the next 17 years until December, 2005. Deaths among the study participants were flagged at the UK's National Health Service Central Registry, which records all births, marriages, and deaths. Whenever a study participant died, the registry sent a copy of the death certificate, containing date and cause of death to the study office in Glasgow.

**Statistical Methods and Analyses**

Cox's regression models were used to analyse all cause mortality. For each of the four life event summary measures a separate model was fitted, adjusting for sex, occupational status, smoking, BMI, and systolic blood pressure. These models were repeated for events from all domains together then separately for health related events and other events. For life event impact scores, hazard ratios are expressed per standard deviation.

As the event measures and risk factors (smoking, BMI and systolic blood pressure) were measured at baseline and again at waves 3 and 4, these were treated as time varying covariates. This approach uses the most recent values of these variables in estimating the hazards. For example, for survival times between waves 1 and 3, the baseline values at wave 1 are used; for survival times between waves 3 and 4, the wave 3 values are used and for survival beyond wave 4, the values from that wave are used. The assumption is that, when explanatory variables change during the follow up period, using the most recent values leads to more accurate estimates. Further details and examples of the method are provided by Andersen (1992).

## Results

At baseline 1,042 people took part in the survey and 968 of these had complete data for life events, covariates and survival. The majority of the missing data (N = 62) arose where the respondents declined the physical measures. Of the 968 with complete data, 46 % (442) were male, and 42% (440) in non-manual households. At baseline their mean age was 56 (SD 0.6), with mean BMI of 26 (SD 4.4) and systolic blood pressure of 137 (SD 21.1). At wave 3, there were 692 participants with complete data: 45% (312) male, 44% (305) in non-manual households, mean age 64 (SD 0.6), with mean BMI of 27 (SD 4.6) and systolic blood pressure of 147 (SD 22.8). 527 participants had complete data by wave 4: these were: 44% male (233); 47% (250) in non-manual households; mean age 69 (SD 1.0); with mean BMI of 27 (SD 4.4); and systolic blood pressure of 151 (SD 21.8).

## Life Events Exposure

Seventy-two percent of participants had experienced at least one major stressful event in the two years prior to baseline; and 54% and 47% had experienced at least one event in the two years prior to survey at waves 3 and 4, respectively. At wave 1, health-related events (36%) were the most common exposures, followed by work (13%), bereavement (11%), housing related (11%) and general (11%) events. With regard to the stress load at each wave, the descriptive statistics for disruption and stressfulness scores at the time of the event and now are presented in Table 1.

[Insert Table 1 about here]

**All-cause Mortality**

During the 17 years follow up 27% (266) of the participants died. The mean age at death was 66 (SD 5.0) years. The major causes of death were: cancers (34%), cardiovascular (24%), respiratory, (12%) other causes (30%). Thirty-three percent (144) of the men in the study sample had died during follow up and 23% (122) of the women, a difference that was statistically significant ($\chi^2$ (1) = 10.62, $p = 0.001$). However, a significantly higher proportion of those from manual, 32% (180), than non-manual, 21% (86), occupational households had died ($\chi^2$ (1) = 13.34, $p < 0.001$).

**Life Events and All-cause Mortality**

Overall life events experience significantly predicted 17-year mortality: for disruption at the time (HR = 1.15, 95%CI 1.03 – 1.28, $p = 0.01$); for disruption now (HR = 1.15, 95%CI 1.04 – 1.28, $p = 0.007$); for stressfulness now (HR = 1.13, 95%CI 1.02 – 1.26, $p = 0.02$). The higher the stress load scores, the greater the likelihood of dying. For stressfulness at the time, there was a trend for higher stressfulness to predict 10-year mortality (HR = 1.11, 95%CI 0.99 – 1.24, $p = 0.08$). These analyses adjusted for potential confounders including age, sex, household occupational status, smoking, body mass index, and systolic blood pressure.

**Domain Specific Life Events and All-cause Mortality**

In these analyses, attention focussed on the most commonly reported types of events. Health-related event scores were strongly predictive of mortality: for disruption at the time (HR = 1.27, 95%CI 1.15 – 1.39, $p$ <0.001); for disruption now (HR = 1.25, 95%CI 1.15 – 1.36, $p$ <0.001); for stressfulness at the time (HR = 1.24, 95%CI 1.13 – 1.37, $p$ <0.001); for stressfulness now (HR = 1.25, 95%CI 1.14 – 1.37, $p$ <0.001). These positive associations remained following adjustment for same potential confounders. Analyses of the aggregated life events scores for all seven of the health-unrelated domains were also undertaken. Aggregated health-unrelated stressful event experience was not significantly predictive of mortality: for disruption at the time (HR = 1.00, 95%CI 0.89 – 1.13) and now (HR = 0.99, 95%CI 0.88 – 1.11), and stressfulness at the time (HR = 0.97, 95%CI 0.85 – 1.09) and now (HR = 1.00, 95%CI 0.96 – 1.04). Finally, health-related and health-unrelated life events scores correlated positively ($r$ (966) = 0.15 – 0.20, $p$ <0.001, for the four life events scores).

## Number of Life Events and All-cause Mortality

Additional analyses were conducted to assess the impact of the number of life events separately from their self-reported impact. In these analyses, the hazard ratios are expressed per life event. The overall number of life events predicted mortality (HR = 1.11, 95%CI 1.01 – 1.22, $p$ = .03). The number of health-related events strongly predicted mortality, (HR = 1.42, 95%CI 1.22 – 1.65, $p$ <0.001), but health-unrelated events were not predictive (HR = 0.99, 95%CI 0.87 – 1.12).

## Discussion

The number and overall disruption and stress attributed to nominated life events, both at the time of occurrence and now, were positively related to subsequent 17-year all-cause mortality. On closer examination of the different domains of events, however, it was clear that these associations were driven by health-related events; whereas the number and impact of health-related events predicted mortality, no significant associations were found for other sorts of events. This result emphasizes the importance of distinguishing between health-related and health-unrelated events. Indeed, the inclusion of events that could be symptoms or consequences of physical or mental illness has been regarded a major limitation of the traditional style of stressful life events assessment (Holmes & Rahe, 1967) when applied to predict health outcomes and mortality (Dohrenwend et al., 1984).

The present findings are seemingly at odds with expectations based on the hypothesis that the frequency and impact of negative psychosocial exposures contribute to disease outcomes. They also contrast with the results of a study of Swedish men, where higher numbers of stressful events over the previous year were positively associated with all-cause mortality across the subsequent seven years (Rosengren et al., 1993). Moreover, the life events measure used in this study did not include health-related events and the association with mortality was not attenuated following adjustment for self-rated health at entry. However, the association between life events and mortality was restricted to those men with low levels of emotional support. This is similar to the observation that, in male survivors of acute myocardial infarction, life event stress predicted 3-year mortality in the socially isolated patients (Ruberman, Weinblatt, Goldberg, & Chaudhary, 1984).

In the present study, participants seemed to be particularly well-integrated, reporting a mean number of five close friends, and a mean of four close friends that they had seen in the past four weeks; only 2% of participants indicated that they were lonely most of the time, whereas 70% reported never feeling lonely. Further, it is also worth noting that the majority of the 10 events included in the scale used by Rosengren et al. appear to relate specifically to situations redolent of social isolation (serious illness or death of family member; divorce/separation; forced to move house or change job; made redundant; feeling insecure at work) rather than the broad range of stressful life events used to assess stress exposure in the present study. Accordingly, it is possible that the effect for life events in Swedish men was actually an effect of social isolation.

In further contrast, a study of life events stress, which included health-related events, and mortality in women found that the frequency and impact of stressful events did not predict all-cause mortality over the next seven years (Dohrenwend et al., 1984). However, health-related events were infrequently reported by these women; 22% registered such a health-related event at least once over the 5-year assessment period, whereas 44% of participants in the present study reported a health-related life event at least once over the six years covered by the assessment. In addition, although not included in the scale, the major health-related event of breast cancer, which characterized all the study's participants, and accounted for 80% of the deaths observed, may have rendered immaterial any other stressful events. It is also possible the impact of life events may vary between samples with proven pathology and those who are generally healthy (Rahe, Romo, Bennett, & Siltanen, 1974; Ruberman et al., 1984).

The participants in the MRFIT study, although healthy, were selected for being in the top 10-15% of risk for coronary heart disease (Hollis et al., 1990). The focus was again on non-health related events. Contrary to expectations, a small negative association emerged between the number of life events experienced and 6-year all cause mortality. Only for those with high type A behaviour scores was there any indication of a positive association between life events exposure and death. It is clearly difficult to forge any kind of consensus out of the available data. However, it would appear that, only in very particular circumstances, can we muster much evidence that health-unrelated life events are associated with reduced longevity.

The present study could be regarded as having a number of limitations. First, it is difficult to discern whether health-related events are associated with mortality because of the psychological impact of such events as ‘an operation’ or ‘serious illness diagnosed’, or simply as a result of scores in this domain reflecting serious morbidity. The latter is by far the more parsimonious explanation. Mortality was related not only to the reported psychological impact of such events but also their number. Further, many of the health-unrelated events (e.g., bereavement or divorce) were undoubtedly of similar psychological moment and, indeed, were regarded as such by participants. Second, it might be argued that health-unrelated events may only have an impact after health-related events have taken their toll and that there were insufficient deaths among the present sample to catch this effect. Again, however, this seems unlikely. In analyses not reported here, health-unrelated events still did not predict mortality even when the occurrence of health-related events was taken into account. Also, in the closest comparison study to report an association between health-unrelated life events and mortality, only just over 5% of their sample has died during follow-up (Rosengren et al., 1993), whereas in the current study 27% had died. Third, it might be argued that there were health-unrelated events not captured by the present inventory. However, the inventory provided comprehensive coverage, with 46 health-unrelated items and a facility for the participant to add events not listed. Finally, it is possible that interviews conducted by a trained nurse might bias participants towards emphasizing their health events in comparison with other domains. However, this is unlikely as life events were listed on cards shown to the participant, limiting the opportunity to over-report health events. In addition, any reporting bias in the form of a lower threshold for reporting health events would lead participants to include less serious health events; this, if anything, would make the present results less likely.

In conclusion, the present analyses reveal positive associations between the number of life events and the stress load they impose and subsequent all-cause mortality.

However, it is the experience and impact of health-related, rather than health-unrelated, events that are predictive. This reinforces the need to disaggregate these two classes of exposures in studies with health outcomes.

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Table 1: Mean (SD) Disruptiveness and Stressfulness Scores at the Time of the Event and Now for each Wave.

| **Wave** | **Disruptiveness Then** | **Disruptiveness Now** | **Stressfulness Then** | **Stressfulness Now** |
|---|---|---|---|---|
| 1 | 5.01 (5.04) | 3.74 (4.21) | 5.42 (5.36) | 3.69 (4.17) |
| 3 | 3.22 (4.31) | 2.33 (3.45) | 3.65 (4.69) | 2.34 (3.54) |
| 4 | 2.73 (4.07) | 1.95 (3.28) | 2.84 (4.15) | 1.85 (2.99) |

Table 2: Mean (SD) Disruptiveness and Stressfulness Scores of Health Events and Other Events at the Time of the Event and Now for each Wave.

| Wave | Events | Disruptiveness Then | Disruptiveness Now | Stressfulness Then | Stressfulness Now |
|---|---|---|---|---|---|
| 1 | Health | 1.85 (2.54) | 1.36 (2.09) | 1.96 (2.58) | 1.32 (2.02) |
| | Other | 3.16 (3.97) | 2.38 (3.25) | 3.47 (4.32) | 2.37 (3.30) |
| 3 | Health | 1.14 (2.27) | 0.85 (1.83) | 1.27 (2.42) | 0.83 (1.82) |
| | Other | 2.08 (3.26) | 1.49 (2.63) | 2.38 (3.67) | 1.51 (2.71) |
| 4 | Health | 1.19 (2.79) | 0.86 (2.26) | 1.21 (2.86) | 0.77 (1.92) |
| | Other | 1.54 (2.59) | 1.09 (2.05) | 1.63 (2.71) | 1.09 (1.99) |

**Appendix**

***Life Events Cards***

Card 1 health
An unexpected illness
Period in hospital
An operation
Serious illness diagnosed
An existing condition got worse
Depression or nerves
Painful or upsetting treatment
Serious accident causing injury
Developing a handicap
A period of poor health
Other worries about health
Problems with a pregnancy
Any other health problems

Card 2 marriage
Living apart or divorce
Serious rows or disagreements
Difficult spells in the marriage
Other problems in marriage

Card 3 relationships
Serious disagreement within family
Serious disagreement with friends
End of a relationship
Seeing much less of family
Seeing much less of friends
Problems with children
Other problems with relationships

Card 4 deaths
Spouse died
Other household member died
Other close family (parents, child, sib)
Other more distant family died
Friends died

Card 5 work
Paid off or changed work
On strike
Unemployment
Enforced retirement
Change for worse at work
Serious rows at work
Difficulty in business venture
Other work problems

Card 6 housing
Problems moving house
Worries over poor housing
Problem with landlord/council
Difficulties over mortgage/rent
Damage or repairs to house
Problems with neighbours
Problems in the neighbourhood
Other housing problems

Card 7 finances
Problems paying bills
A drop in income
Difficulties paying a loan
Other financial problems

Card 8 general
Having to give up an activity
Burglary or theft
Losing something important
Violence, being attacked
Problems with officials
Legal or police problems
Problems gambling or drinking
Problems driving or on the road
Giving someone bad news
Seeing something distressing

Finally is there anything else that you haven't told me about?