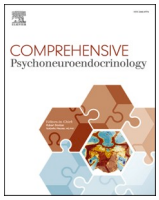
Comprehensive Psychoneuroendocrinology 16 (2023) 100210

Contents lists available at ScienceDirect

Comprehensive Psychoneuroendocrinology

journal homepage: www.sciencedirect.com/journal/comprehensive-psychoneuroendocrinology



The association between adverse events in later life and mortality in older individuals

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ARTICLE INFO

Keywords:
Stress
Older
Later-life
Bereavement
Caregiver
Mortality
Death
Cancer

ABSTRACT

Background: Stress can have adverse impacts on health, particularly when it is chronic or resulting from major adverse events. Our study investigated whether relatively common adverse events in older individuals were associated with an increased risk of death, as well as cause-specific death and potential gender differences.
Methods: Participants were 12896 community-dwelling Australians aged ≥70 years at enrolment into the ASPREE (ASPirin in Reducing Events in the Elderly) study and without known life-limiting disease. A questionnaire administered in the year after enrolment, collected information on ten adverse events experienced in the past year. Mortality status was verified by multiple sources including health records and the National Death Index across a maximum of 10 years. Underlying causes of death were determined using clinical information by two adjudicators. Cox-proportional hazards regression models were used to estimate mortality risk.
Results: Two of the ten adverse events were associated with an increased risk of mortality in fully adjusted models. A 69% increased risk of mortality was observed in participants who reported their spouse/partner had recently died (95% CI: 1.19–2.39, $P < 0.01$). Cancer-related but not cardiovascular deaths also increased. Participants with a seriously ill spouse/partner also had a 23% increased risk of mortality (HR: 1.23, 95% CI: 1.02–1.48, $P = 0.03$). There was a tendency for these associations to be stronger among men than women.
Limitations: Perceived stress and cortisol were not measured, thus limiting our understanding of the psychological and physiological impacts of adverse events.
Conclusions: Experiencing adverse events in later-life, especially the death of a spouse/partner, may be a risk factor for earlier mortality. These findings may increase public health awareness and better inform initiatives for particular groups, including bereaved men.

1. Introduction

Life expectancy has improved during the 21st century, with a global increase of more than six years in life expectancy between the year 2000 and 2019 [1]. As a result, there is a larger proportion of people who enter later-adulthood, and this can be associated with an assortment of psychosocial challenges which often occur sequentially within a short time frame, and can contribute to declines in physical health and vitality [2]. These may include loss of autonomy (e.g. driving cessation), and relationships with loved ones [3]. It can also be a period of added responsibilities (e.g. providing care for an ill spouse), and uncertainties (e.g. financial hardship and downsizing residence). It is possible that the mental distress and changes to life circumstances followed by these psychosocial pressures may impact somatic morbidity, and influence mortality risk [4,5].

The association between experiencing adverse events and mortality may be due to a series of internal mechanisms which enhance the progression and severity in pre-morbid, and life-limiting illnesses [6]. Experiencing a stressor can disrupt the body's natural homeostatic processes, and cause a redistribution of resources, or the 'adaptive stress

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https://doi.org/10.1016/j.cpnec.2023.100210
Received 12 September 2023; Accepted 12 September 2023
Available online 15 September 2023
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response' [7]. This response may include alterations to typical cardiovascular (e.g. increased heart rate and blood pressure), respiratory (e.g. hyperventilation), metabolic (redistribution of glucose to essential tissues) and behavioural (e.g. poor sleep hygiene) functions. Furthermore, chronic stress can diminish the integrity of these functions and body systems, leading to damage or 'wear and tear' of major organs and tissues, and can accelerate ageing and mortality [8,9]. Previous studies have linked psychological stress with coronary heart disease, and Alzheimer's Disease, the leading causes of geriatric death in Australian men and women respectively [10].

Current literature exploring the role of stress and mortality predominantly include younger populations (under 65 years of age) [11–15], which limits the ability to quantify the effects of later-life stress on mortality. It is highly likely that in comparison to their younger counterparts, older people are more vulnerable to stress, as the reserve capacity to adapt to changes in their external environment declines with ageing [16]. Older individuals are also likely to experience different types of stressful events to those who are younger, with personal decline in health and spousal loss being more commonplace with ageing [17]. The limited studies which have focussed on stress in later life have largely analysed the impact of bereavement, which is widely known to be associated with increased mortality risks [18,19]. Thus, there is a need to explore the effects of a more diverse range of stressors.

Furthermore, most studies pertaining to stress and mortality use composite [11,13,20], perceived [12,14,15], or clinical measures (including Posttraumatic Stress Disorder) [21] of stress. Thus, it is difficult to quantify the extent to which different adverse events, especially those specific to later life, influence death. We identified limited studies with such criteria, including a study of 2152 participants from France, which reported increased mortality with adverse events such as recent illness and financial problems [22]. However, other common stress-inducing events in later-life were not examined, such as spousal death or illness. Furthermore, despite well-known differences in mortality rates between men and women (with women generally outliving men), there are still limited studies exploring gender differences in the associations between stress and mortality [23].

Thus, the primary aim of the present study is to determine whether there is an association between adverse life events experienced in the previous year and mortality risk, in a large cohort of initially healthy and community-dwelling Australian older adults. The secondary aims are to determine whether these associations differ by cause of death, and gender.

2. Methods

2.1. Participants

The study population comprised of Australian community-dwelling men and women over 70 years of age, who participated in the ASPirin in Reducing Events in the Elderly (ASPREE) study, and subsequent ASPREE Longitudinal Study of Older Persons (ALSOP) sub-study [24,25] (N = 16,439). ASPREE was a bi-national clinical trial conducted in the United States (US) and Australia, to determine the effect of daily low-dose aspirin on maintaining disability-free survival in healthy older adults. Eligible participants were cognitively healthy and were free of known cardiovascular disease, major physical disability, and terminal illness. The ASPREE clinical trial concluded in 2017 and results have previously been published [24]. Participants continue to be observed in a follow-up longitudinal study (ASPREE-XT study).

In Australia, ASPREE participant recruitment occurred between March 2010 and December 2014 through invitation by general practitioners (GPs), and ASPREE participants were also invited to participate in the ALSOP sub-study, generally within the first year after randomisation into the ASPREE trial (89% response rate). The present analysis uses data from the ALSOP social health questionnaire, which collected data regarding socioeconomic status, social engagement, physical activity, adverse life events, and optimism, and was generally administered approximately 9–12 months after randomisation. This study presents findings on the 12896 participants who returned the social health questionnaire, and were followed for a maximum of 10 years.

2.2. Measuring adverse life events

The ALSOP social health questionnaire collected data on whether or not participants have experienced ten adverse life events within the last 12 months (Supplementary Appendix A) [25]. These included death or illness within their social network, financial problems, relationship and employment difficulties in friends or family, major accidents, and loss of a pet.

2.3. Ascertaining mortality

Death status was determined within the follow-up period, through notification by the deceased participant's next of kin or close contact, or by searching health records. All cases of mortality were confirmed from two independent sources (e.g. public death notice and verification by GP) [26]. Furthermore, regular data linkage with The Ryerson Index, an online index of death notices compiled using a volunteer-based crowdsourcing model, was conducted. To account for selection bias, participants who were lost to follow-up were linked to the National Death Index (NDI), which contains the records of all registered deaths in Australia since 1980. Vital status was thus ascertained on all participants.

2.3.1. Underlying cause of mortality

Two adjudicators determined a primary underlying cause of death for each deceased participant using clinical information (including autopsy reports, hospital discharge summaries, and death certificates) [26]. In cases where insufficient documentation was provided to adjudicators, the underlying cause of death was obtained using the International Classification of Diseases, 10th Revision (ICD-10) codes presented on either the death certificate, or NDI. In the present study, deaths were categorised as deaths related to cancer, cardiovascular disease (including coronary heart disease and stroke), and other (including cases in which cause of death could not be determined).

2.4. Ethical approval

The ASPREE trial was conducted in accordance with the 2008 Declaration of Helsinki, and all participants provided their informed consent. Monash University Human Research Ethics Committee and the Alfred Hospital Human Research Ethics Committee approved the ASPREE-XT and ALSOP (project numbers Alfred HREC 593/17 and Monash 4HREC CF11/1935/2011001094) studies. Further information regarding the ASPREE trial can be located at Clinicaltrials.gov (NCT01038583).

2.5. Statistical analyses

The relationship between the independent variables (adverse life events experienced in the previous year) and dependent variable (mortality reported over a maximum 10 years follow-up) was determined using Cox proportional hazards regression, which reported Hazard Ratio (HR) estimates (with corresponding 95% confidence intervals (CIs) and p-values). Stepwise adjustments of covariates were conducted in our analyses, to account for variables which could theoretically also be considered as possible mediators, e.g. depression. Analyses initially adjusted for socioeconomic covariates (age, binary gender, and education level), and was followed by further adjustment for lifestyle behaviours and health factors. These include the presence of hypertension (defined by systemic blood pressure of ≥140 mmHg, diastolic blood pressure of ≥90 mmHg, or on treatment for high blood pressure) or

diabetes mellitus (defined by fasting glucose ≥126 mg/dL, on treatment for diabetes, or self-reported), smoking status (current/former/never), alcohol consumption (current/former/never), and symptoms of depression (as determined by a score of ≥8 on the ten-item Center for Epidemiologic Studies Depression Scale (CES-D 10)) [27].

To explore our secondary aims, we tested gender interactions (reporting p-values), and subsequently conducted gender-stratified analysis (adjusted for age, and education level). In order to determine whether cause of death influenced the associations, competing risk regression models were conducted (Fine and Grey method) estimating the Sub-hazard Ratios (SHRs) (with corresponding 95% CI and p-values), which accounted for mutual exclusivity regarding cause of death (e.g. an individual reported as dying from cancer-related causes, cannot also die from cardiovascular disease-related causes). Cumulative incidence functions were plotted to visually demonstrate the cumulative probability of cause-specific death, over the study period. We deemed p-value ≤0.05 to be of statistical significance. Statistical tests were performed using Stata 17 (StataCorp, 2021).

3. Results

3.1. Participant characteristics

During the study period (range: 0.4–10 years), a total of 1102 participants died, of whom 57.8% were men (Table 1). Among these individuals, 447 died from causes which were cardiovascular disease-related, 861 cancer-related, and 578 from other causes. Participants who died were more likely to be older (78.3 (5.4) versus 74.9 (4.1)), and were more likely to report various clinical and lifestyle risk factors at baseline (including hypertension, diabetes, and living alone). The frequency of 'current' smoking at baseline among deceased participants was more than double that of still living participants (5.9% vs 2.5%), and they had fewer years of formal education.

3.2. Association between adverse life events and all-cause mortality

The most commonly experienced adverse life event was the death or serious illness of a family member or close friend, followed by the serious illness of a spouse or partner (Table 1). The least experienced events were having had a recent divorce or break up, a major accident or disaster. Across ten adverse events, only two events were associated with increased mortality risk in the fully adjusted models (adjusted for covariates including age, gender, formal education, smoking and alcohol status, diabetes, hypertension, and depressive symptoms). This included an increased time-to-death amongst participants whose spouse or partner had died (HR: 1.69, 95% CI: 1.19–2.39, P < 0.01), or had a serious illness in the past year (HR: 1.23, 95% CI: 1.02–1.48, P = 0.03), in Model 3 (Table 2).

Three other life events were associated with mortality, but not after adjustment for health and lifestyle factors. A 35% increased risk of mortality was observed amongst individuals with major money problems in the past year (95% CI: 1.02–1.79, P = 0.03) when adjusted for age, gender, and formal education (Table 2). Loss of a job or retirement of a close family or friend was associated with a reduced risk of mortality (HR: 0.81, 95% CI: 0.67–0.98, P = 0.03) (Table 2). However, these associations were not significant after further adjustment in Model 3. No associations with mortality were found with the other five life events measured (death of a close family/friend, divorce or breakup, divorce or breakup of close family/friend, major conflict with children or grandchildren, and major accident or disaster).

3.3. Effect modification by gender

Significant gender differences in the association with the death of a spouse or partner (P = 0.03), and major accident or disaster (P = 0.02) were found (Supplementary Appendix B). Following gender-stratified analyses, the significant association with death of a spouse or partner was only found for men. Similarly, only men who had experienced a major accident or disaster in the past year showed an increased risk of mortality over the follow-up period (HR: 1.89, 95% CI: 1.23–2.84, P < 0.01) (Supplementary Appendix B), however this was not significant with the inclusion of hypertension in the model.

Table 1
Participants' characteristics at baseline (*N = 12896*).

	% (N)	DECEASED N = 1102	ALIVE N = 11794
Sociodemographic	*Age, y*		
	Septuagenarians	63.5 (700)	86.8 (10240)
	Octogenarians	34.3 (378)	12.9 (1526)
	Nonagenarians	2.2 (24)	0.2 (28)
	Gender		
	Men	57.8 (637)	44.5 (5247)
	Women	42.2 (465)	55.5 (6547)
	Years of education		
	<12	62.8 (692)	58.75 (6929)
	>12	37.2 (410)	41.3 (4865)
Clinical	*Hypertension**	49.6 (547)	47.2 (5571)
	Diabetes†	12.1 (133)	7.5 (886)
	Depressive symptoms§	7.6 (84)	5.4 (639)
Lifestyle	*Smoking status*		
	Current	5.9 (65)	2.5 (295)
	Former	46.4 (511)	40.7 (4803)
	Never	47.7 (526)	56.8 (6696)
	Alcohol status		
	Current	76.41 (842)	80.08 (9445)
	Former	7.53 (83)	84.44 (514)
	Never	16.06 (177)	15.56 (1835)
	Living arrangements		
	Lives alone	37.0 (408)	29.1 (3435)
	Lives with others	63.0 (694)	70.9 (8359)
Adverse life events	*Death or serious illness of a family member of close friend*	41.5 (457)	42.3 (4986)
	Serious illness of spouse or partner	22.1 (243)	17.7 (2085)
	Divorce or break up of close family or friends	12.3 (136)	14.2 (1675)
	Lost job or retirement of close family or friend	10.5 (116)	13.2 (1559)
	Death of a pet	7.4 (82)	9.5 (1124)
	Major conflict with children or grandchildren	3.8 (42)	5.5 (652)
	Major money problems	4.7 (52)	4.0 (466)
	Death of spouse or partner	4.9 (54)	2.7 (317)
	Major accident, disasters	2.9 (32)	2.6 (308)
	Divorce or break up	2.3 (25)	2.0 (241)

* Hypertension as defined by the receipt of treatment for high blood pressure or a blood pressure of more than 140/90 mm Hg at trial entry.
† Diabetes as defined by participants' report of diabetes mellitus, a fasting glucose level of at least 126 mg per decilitre (≥7 mmol per litre) or receipt of treatment for diabetes.
§ Depressive symptoms as defined by a score of ≥8 on the 10-item Centre for Epidemiologic Studies Depression scale.

Table 2
Associations between adverse life events and mortality.

	HR, 95% CI, P-VALUE		
	Model 1[a]	*Model 2*[b]	*Model 3*[c]
Death of spouse or partner	1.84 (1.40–2.43), <0.0001	1.58 (1.20–2.09), <0.01	1.69 (1.19–2.39), <0.01
Serious illness of spouse or partner	1.35 (1.17–1.56), <0.0001	1.23 (1.06–1.42), <0.01	1.23 (1.02–1.48), 0.03
Death or serious illness of a family member of close friend	0.98 (0.87–1.11), 0.80	0.99 (0.87–1.12), 0.84	0.99 (0.84–1.16), 0.90
Major money problems	1.17 (0.89–1.55), 0.27	1.35 (1.02–1.79), 0.03	1.08 (0.73–1.61), 0.70
Divorce or break up	1.18 (0.79–1.76), 0.41	1.17 (0.78–1.73), 0.45	1.03 (0.60–1.75), 0.92
Divorce or break up of close family or friends	0.87 (0.73–1.04), 0.12	0.95 (0.79–1.13), 0.56	0.90 (0.71–1.14), 0.37
Major conflict with children or grandchildren	0.73 (0.54–0.99), 0.05	0.90 (0.66–1.22), 0.49	0.86 (0.57–1.30), 0.47
Major accident, disasters	1.19 (0.84–1.70), 0.32	1.33 (0.94–1.89), 0.11	1.20 (0.74–1.95), 0.45
Lost job or retirement of close family or friend	0.80 (0.66–0.97), 0.03	0.81 (0.67–0.98), 0.03	0.79 (0.61–1.02), 0.07
Death of a pet	0.79 (0.63–0.99), 0.04	0.86 (0.69–1.08), 0.19	0.86 (0.64–1.14), 0.30

[a] Univariate model.
[b] Adjusted for age, gender, education.
[c] Adjusted for age, gender, education, smoking status, alcohol status, diabetes, high blood pressure, depressive symptoms.

3.4. Associations with cause-specific death

Multivariable competing-risks analyses were performed to determine the strength of the relationship between adverse life events and cause-specific mortality. Fig. 1 demonstrates that the increased risk of death in participants who lost a spouse or partner in the past year appeared to be driven primarily by cancer-related, rather than cardiovascular-related deaths. Adjustment for age, gender, formal education, smoking and alcohol status, diabetes, hypertension, and depressive symptoms, revealed a 92% increased risk of cancer-related mortality in individuals reporting spousal loss (95%CI: 1.18–3.15, P < 0.01). Full details are available in Supplementary Appendix C.

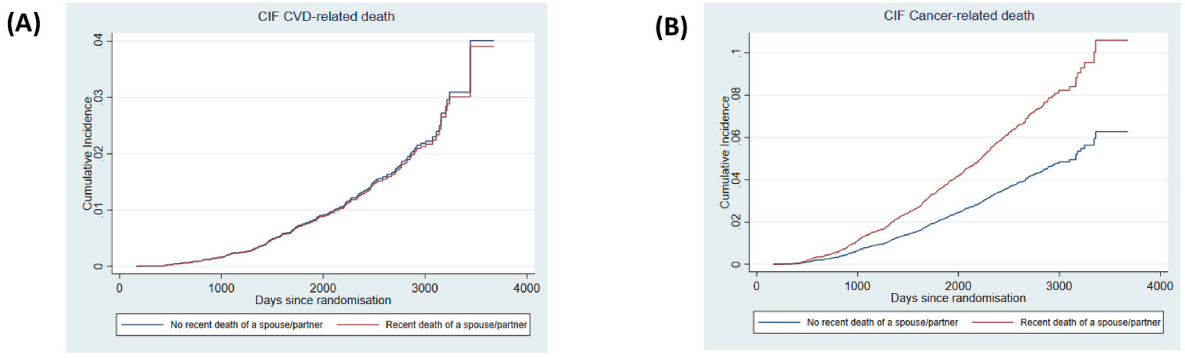
4. Discussion

4.1. Overall findings

We investigated the association between a broad range of adverse life events experienced in the past year by older adults, and all-cause mortality, over a maximum 10-year follow-up period. Only two out of the ten measured events were associated with an increased risk of mortality when adjusted for sociodemographic, health and lifestyle factors. Individuals who recently lost their spouse or partner (within the past 12 months) were found to be at 69% greater risk of dying within the follow-up period. We also found a 23% increased risk of mortality among participants who had a seriously ill spouse or partner. There was also some evidence that these findings differed according to gender, and cause of death. In particular, experiencing the death of a spouse or partner was a significant risk factor for earlier mortality in men (but not women), and was associated with an increased risk of cancer-related mortality.

A major finding of this study is the increased risk of death amongst participants whose spouse or partner have died in the past year. The somatic health impacts of bereavement on the surviving spouse have been extensively researched, with increased risks of cardiovascular disease [28] and inflammation [29] having been reported. Several studies have also reported a greater likelihood of earlier mortality in the bereaved. A meta-analysis of 26 independent studies (maximum follow-up time of 20 years) of marital status in adults (>50% aged 65 years), reported an 11% increased risk (95% CI: 1.08–1.14) of mortality among participants whose spouse had died, in comparison to individuals who were still married [30]. The review also found a slightly higher risk of death in participants who were divorced or separated (RR: 1.16, 95% CI: 1.09–1.23) – a finding that was not replicated in our analysis. A more recent meta-analysis (n > 500 million participants) on widowhood and mortality risk revealed a 23% increased risk of mortality amongst bereaved individuals of all ages in comparison to married people (95% CI: 1.19–1.28) [31]. This risk also remained significantly increased when analysing older individuals (aged 60–69 years HR: 1.24, 95% CI: 1.16–1.34; aged 70–79 years HR: 1.19, 95% CI: 1.07–1.32; aged ≥80 years HR: 1.18, 95% CI: 1.11–1.24). This study also suggests that mortality risk decreases with follow-up time, with a 51% increased risk of excess mortality within the first two years (95% CI: 1.27–1.79), tapering down to 11% in studies with a follow-up period of ≥25 years (95% CI: 1.02–1.20). We were unable to observe if similar associations occurred in our study, due to low numbers of participants dying within the first two years of follow-up (<5 who experienced the death of a spouse or partner).

The psychological impact of losing a spouse or partner can include a



*Adjusted for age, gender and education

Fig. 1. Cumulative incidence functions between the death of a spouse or partner and (A) cardiovascular-related death or (B) cancer-related death*
*Adjusted for age, gender and education.

range of emotional responses including lowered mood as well as stress. For example, from a total of 43 life events, death of a spouse or partner was associated with the highest rating of stress on the Social Readjustment Rating Scale (based on the amount and duration of adaptation after experiencing the event) [32]. In terms of physiological responses to losing a spouse, increased levels of cortisol have been reported as a short-term effect of spousal loss [33]. It is possible that repeated activation of the Hypothalamic-Pituitary-Adrenal (HPA) Axis as a response to severe psychological distress may lead to hypercortisolemia, which in turn may exacerbate pathological mechanisms in the body, including disruptions to regular immune and cardiovascular functioning [5]. Another pathway could be through cognitive decline, as a prior study in our sample population identified that bereaved older adults had an increased risk of dementia [34]. In addition to the biological stress response of bereavement, psychosocial changes may contribute to the association between loss of a spouse and increased mortality risk. The death of a partner can be associated with various behavioural risk factors for poor health outcomes [35], including disruptions to sleep, increased alcohol and tobacco consumption, and decreased physical activity. While the present analysis did find a significant association between death of a spouse/partner and earlier mortality after adjusting for alcohol and smoking status, we were unable to take into consideration all possible factors. It is also important to consider other behavioural factors, which may be unrelated to the grief process. In some instances, a lack of self-care can result if the individual's deceased spouse was responsible for their health-related behaviours e.g. medication compliance, or attendance at medical appointments. The observed association may also be attributed to shared environmental risk factors between the deceased and bereaved spouse, such as similar diets and levels of social engagement. If the deceased spouse's death was related to poor nutrition or physical inactivity for example, it is possible that the bereaved spouse was similarly affected.

Further analyses revealed that spousal loss was associated with an increased risk of cancer-related mortality in particular. It is possible that the death of a spouse or partner may increase the progression of existing tumour pathologies, as suggested by previous literature demonstrating increased inflammatory processes in bereaved individuals [36]. However, it is also possible these associations could be explained by a change in health-related behaviours in grieving individuals, such as declining aggressive treatment. We did not observe an association between the death of a spouse/partner and cardiovascular disease-related death, despite a wealth of evidence linking bereavement to incident cardiovascular disease events [37]. Such events include Takotsubo Cardiomyopathy, a diagnosis which presents similarly to acute myocardial infarction, and commonly manifests as a result of psychological stress [38]. It is possible that we did not observe associations with cardiovascular-disease related deaths, as the ALSOP cohort analysed in this study were free of cardiovascular disease at baseline, and thus may be more resilient than the general population. This particular cohort also has a higher socioeconomic status than similarly aged Australians, thus it is possible that increased health literacy and access to healthcare may explain these null findings. Other results in our analyses pertain to the increased risk of mortality among participants whose spouse/partner were seriously ill, or had major money problems in the past year. However, the latter association was no longer significant when taking hypertension into consideration.

The present findings reflect previous research using ALSOP data, which found either a decline or constant low trajectory of physical health-related quality of life (HRQoL) in individuals who experienced these events [39]. Furthermore, having a seriously ill spouse/partner mediated the relationship between economic factors, and physical HRQoL trajectories, suggesting that caregiving is linked to financial strain [40]. Other research also supports our finding related to having a seriously ill spouse/partner, with a seminal study in the field finding a 63% increased risk of mortality in a study of older spousal caregivers (caregivers n = 392, non-caregivers n = 427) who reported mental and emotional strain, in comparison to non-caregiver controls [41]. However, more recent research on spousal caregiving has reported conflicting results in the opposite direction [42,43]. We also reported an observation in the reverse direction; which showed that having close family or friend who lost their job or retired had a protective effect against mortality. This is aligned with a prior study in our sample population reporting that older women with retired family or friends have a reduced risk of dementia [34]. The health-benefits from having family or friends who are retired has been linked to increased social engagement [44]. Specific types of social engagement, such as helping behaviour, has also been showed to buffer the association between stress and mortality [45].

4.2. Gender-specific associations

Significant gender differences were observed in participants who lost a spouse/partner, and who experienced a major accident/disaster, which were significant in men only. A recent review which included participants of all ages, reported 16 studies which found differences in mortality risk between widowed men and women, with the widowhood effect being more pronounced in men [37]. Further research is required to elucidate why spousal loss affects mortality in men more than women, but it may be attributed to biological sex differences in HPA-reactivity, as well as psychosocial factors. Indeed, widowed Australian men report greater levels of loneliness than women [46], which may disproportionately affect mortality in men [47]. It is possible that bereaved men are not receiving adequate support, due to widowhood being more likely in women, than in men [48]. Qualitative research has previously suggested that older bereaved men do not feel included in mixed-gendered support groups, as they can be dominated by women [49]. Furthermore, bereaved men may be faced with unique stressors if there was an unequal division of domestic tasks prior to spousal death [50]. It could be especially challenging for men to undertake traditionally women-associated household duties in later-life, including meal preparation [51], which in turn could lead to changing dietary habits and nutritional deficiencies, which may increase mortality risk [52].

4.3. Strengths and limitations

Our study adds to the limited body of literature which explores the associations between adverse events in later-life and all-cause mortality. We captured multiple adverse events, ranging from transitionary events which may be considered normative during the ageing process, to acute and traumatic experiences. Furthermore, we also investigated cause-specific death and whether the associations differed by gender. This study is strengthened by its longitudinal design and involvement of a large cohort of community-dwelling older individuals. Our participants were without known life-limiting disease at baseline unlike previous research in older cohorts analysing similar associations [22], which further eliminates potential confounders in the observed associations. Mortality was also verified from multiple sources, including the National Death Index.

However, several limitations should be considered in the interpretation of our findings. Adverse life events were measured only at one period in time, thus it is possible that our effect sizes may be underestimated, as the comparison groups could also include participants who experienced an event during the follow-up period. We also have to consider the possibility of Type I Errors in our results, due to the multiple comparisons having been analysed. Some of the events measured, including experiencing a divorce or breakup, were only reported by a small number of participants. As a result, our ability to detect small effects for uncommon events may be limited. Furthermore, it is possible that the observed associations were mediated by other adverse events e.g. the increased risk of mortality among participants who lost a spouse/partner may have been mediated by major money problems. While we measured a range of adverse events, some important ones were missing

(e.g. elder abuse) [53]. In addition, other specific information was not ascertained in relation to the event, including whether the individual felt stressed by the event. When considering spousal death in particular, information regarding whether the spouse unexpectedly died or was chronically ill before their death, could modify the impact in the bereaved individual [50]. Thus, future research should investigate the psychological impacts of adverse events, to gain better understanding as to why different events have varied consequences. Furthermore, due to the relatively infrequent occurrence of some events, combined with the number of deaths, we were unable to ascertain whether the finding related to losing a spouse and whether cancer-related deaths differed by gender or cancer subtype. Ascertaining this information in future research may support more targeted screening initiatives or interventions for bereaved spousal health and wellbeing. Our findings may also not be generalisable to all older Australians, as individuals participating in studies such as ASPREE are known to have higher health literacy and health-related quality of life (HRQoL) than the general population [54]; and our study also had an under-representation of individuals from different ethnic groups (including First Nations Australians). Thus, future research should consider replicating our findings in more diverse populations.

4.4. Conclusion

Our study indicates that in a relatively healthy older community dwelling cohort, adverse events overall were not consistently associated with earlier mortality risk, however death or serious illness of a spouse/partner was associated with an increased mortality risk. This study also highlighted groups who may be at greater risk, including bereaved men, who may benefit from tailored public health interventions.

Contributors

RLW and JM are responsible for the study conception and design of the ASPREE study. AO provided a major role in the acquisition of ALSOP data. JR, CG, and RFP conceived the current study. DN drafted the manuscript and takes responsibility for the accuracy of analysis of data. DN, JR, CG, and RFP interpreted the data, with input from AO, RLW, JM, MN, and NS. All authors read and gave final approval to the submitted manuscript.

Funding

ASPREE was supported by grants from the National Institute on Aging and the National Cancer Institute at the US National Institutes of Health (Grant Nos. U01AG029824 and U19AG062682); the National Health and Medical Research Council of Australia (Grant Nos. 334047 and 1127060); Monash University (Australia) and the Victorian Cancer Agency (Australia). The ALSOP sub-study was supported by Monash University. JR is supported by a National Health and Medical Research Council Dementia Research Leader Fellowship (1135727). Funders had no role in the design and conduct of the study, in the writing, and submission of the manuscript.

Data availability statement

Any requests for data can be sent to the corresponding author.

Declaration of competing interest

All authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cpnec.2023.100210.

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