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Association between stress, depression or anxiety and cancer: Rapid review of reviews

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ABSTRACT

Background: Several studies have suggested links between psychological stress, depression or anxiety, and cancer incidence or outcomes. Existing systematic reviews have addressed this question, with differing results.
Aims: This rapid systematic umbrella review summarises existing reviews assessing the association between psychological stress, depression or anxiety and cancer incidence or cancer outcomes.
Methods: Systematic reviews assessing stress, depression or anxiety and cancer were identified via searches of MEDLINE, PsycInfo and Cochrane Database of Systematic Reviews from 2010 to November 2020.
Results: Twelve systematic reviews were included, summarising cohort and case-control studies, most of which adjusted for confounders. Regarding cancer incidence, one large meta-analysis reported a significant association between depression/anxiety and cancer incidence, while another showed a non-significant trend. Two further meta-analyses reported significant associations between stressful life events and cancer incidence. Conversely, two meta-analyses of work stress showed no significant association with cancer incidence. Regarding outcomes among cancer patients, three meta-analyses reported significant associations between depression/anxiety and cancer mortality, while another reported a non-significant trend for depression and cancer recurrence. One meta-analysis reported a significant association between partner bereavement and cancer mortality, while another showed no significant association between work stress and cancer mortality.
Conclusions: There is consistent evidence for an association between psychological stress, depression or anxiety and cancer incidence in general populations, and some evidence for an association with mortality in cancer populations. Future research may focus on confirmation of these findings, as well as the role of social support and stress-reducing interventions in buffering against these effects.

1. Introduction

Many studies over the years have suggested an association between chronic stress, depression, anxiety or stressful life events and cancer, both in terms of cancer incidence and cancer mortality [1–3]. However, until the last few decades, the potential physiological mechanisms for this were unclear. More recently, chronic psychological stress has been demonstrated to cause physiological effects on the body through signalling pathways including the neuroendocrine system, the sympathetic nervous system and stress hormones such as cortisol, adrenaline and noradrenaline [2,3]. Studies have also shown that the immune system has a key role in preventing cancer growth, and that chronic stress can suppress immune function [3–6]. It has also been shown that chronic stress can contribute to unhealthy behaviours such as poor diet, reduced physical activity, smoking and alcohol consumption, which may indirectly increase cancer incidence and progression [3].

Alongside this elucidation of biological mechanisms, epidemiological studies have also been conducted to gather data on whether there is an association between psychological stress, depression or anxiety and either cancer incidence (in general populations) or cancer mortality, progression and recurrence (in people with cancer). On an individual study level, such epidemiological studies have shown mixed results [7]. However, several systematic reviews and meta-analyses have been conducted with the aim of collating and pooling results of individual studies. These meta-analyses have differed in their focus (e.g. stress type, population type, cancer-related outcome). There is a need for an

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overarching summary of the findings of recent relevant systematic reviews in the area of stress and cancer.

This rapid systematic umbrella review of systematic reviews aims to summarise evidence on the association between psychological stress, depression or anxiety and the following: i) cancer incidence in general populations and ii) cancer progression, recurrence or survival in people with cancer.

2. Methods

2.1. Rapid review methodology

This rapid review was undertaken within a limited time and budget on behalf of the World Cancer Research Fund (WCRF) International to provide a high-level overview of existing knowledge in this area and to identify evidence gaps for a potential full systematic review of this topic.

2.2. Literature search methods

Existing systematic reviews assessing the link between psychological stress, depression or anxiety and cancer incidence, progression, recurrence or survival were identified via a literature search of MEDLINE and MEDLINE In-Process, PsycInfo and the Cochrane Database of Systematic Reviews in November 2020. To focus on recent literature, literature searching was limited to reviews published since 2010. The search strategy (Appendix 1) used free-text and thesaurus terms for psychological stress combined with terms for cancer and terms for risk, progression or survival. In addition, a wider search using broader terms was undertaken as part of a wider review on stress and cancer (broader terms not reported here), and the results of this wider search were also screened. Review filters from McMaster University for MEDLINE [8] and University of Texas for PsycINFO [9] were applied to restrict the findings to review articles. Key references within included reviews were also checked for inclusion.

2.3. Inclusion criteria, screening and selection of reviews

This rapid systematic review aimed to identify relevant systematic reviews evaluating the association between psychological stress and cancer incidence (in general populations) or cancer outcomes (in people with cancer), written in English or containing sufficient information in an English language abstract.

2.4. Data extraction and synthesis

In order to undertake the review with rapid timelines, key study characteristics together with a brief summary of results for relevant outcomes were extracted directly into tables. Data were initially extracted from review abstracts, supplemented by key data from the full texts. Findings are summarised via tabulation and narrative synthesis.

2.5. Consideration of study quality

This rapid review provides an overview of a number of existing systematic reviews. For some included reviews, only a small proportion of the reported data was relevant here. The main limitation was the sparseness and heterogeneity of the primary research, rather than the methodological quality of the included reviews. Therefore, it was felt that formal quality assessment of each review article would not be particularly informative. Instead, a general commentary is presented regarding the quality and limitations of available evidence (both for the included reviews and the primary study evidence within the reviews).

3. Results

3.1. Number of articles screened and included

A total of 2957 references were identified via the searches (Fig. 1). Of these 30 were checked at the full text stage, and 12 systematic reviews met the inclusion criteria for this rapid review. The majority of reviews were published since 2010 in line with the database search limits; however one review published in 2009 [10] was identified from a later review and was included due to its relevance to the review question and lack of overlap with later reviews in terms of included studies.

In total, 12 systematic reviews were included. Nine reviews addressed the relationship between psychological stress, depression or anxiety and cancer incidence, while eight assessed psychological stress, depression or anxiety and cancer progression, recurrence or survival (some reviews addressed both). Eight reviews included a meta-analysis while four did not.

All the primary studies included within these reviews were cohort studies or case-control studies. The majority of included reviews stated that the included primary studies adjusted for at least some patient characteristics to minimise confounding.

3.2. Psychological stress, depression or anxiety and cancer incidence

Nine systematic reviews (seven with a meta-analysis and two without) assessed the association between stress, depression or anxiety and cancer incidence (Table 1). The included reviews addressed three types of psychological stress: depression and anxiety, stressful life events, and work stress. The majority of reviews adjusted their analyses to account for potential confounders such as age, sex and other cancer risk factors (see Table 1 for details).

3.2.1. Depression and anxiety

The association between depression/anxiety and cancer incidence was assessed in two systematic reviews, both with meta-analyses. Firstly, a meta-analysis of 21 cohort studies [7] reported a significant association between depression/anxiety and cancer incidence (relative risk [RR] 1.13; 95% confidence interval [CI] 1.06 to 1.19). This review also reported significant associations for some individual cancers including lung cancer (RR 1.41), oral cancer (RR 1.47), prostate cancer (RR 1.37) and skin cancer (RR 1.09), while associations were not significant for the other 17 individual cancers analysed. A second meta-analysis [11] pooled data from three previously unpublished cohort studies (not included in the meta-analysis by Wang et al.). This review reported a positive but non-significant trend for a relationship between depression/anxiety symptoms and cancer incidence (hazard ratio [HR] 1.16; 95% CI 0.90 to 1.49). Positive but non-significant trends were also reported for individual cancers (lung, colorectal and breast cancers).

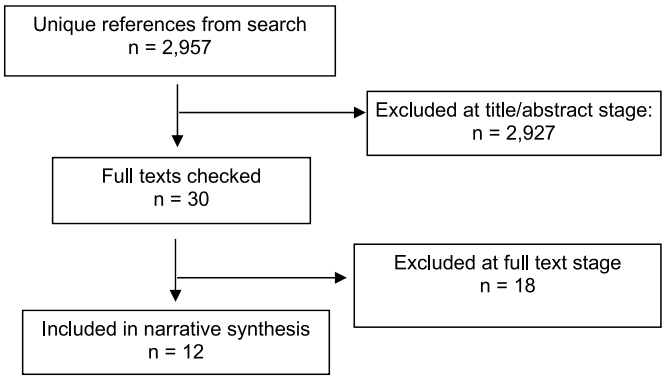

Fig. 1. PRISMA flow diagram for study identification and inclusion.

Table 1
Stress, depression or anxiety and cancer incidence.

Ref	Review type (search)	Incl. studies N participants Follow-up	Cancer type	Stress type	Outcome	Associations: Positive[a] (brackets show 95% CI)	Associations: Mixed or non-significant (brackets show 95% CI)	Associations: Negative (brackets show 95% CI)
Depression and anxiety								
Wang 2020 [7]	SR + MA (2018)	Cohort (N = 21) N = 1,685,782 14y (mean)	Various	Depression/anxiety (clinical diagnosis or via symptom scales)	Cancer incidence	Sig. association: adj[b] RR 1.13 (1.06–1.19) Individual cancers: Sig. association for lung (1.41), oral (1.47), prostate (1.37), skin (1.09)	Individual cancers: No sig. association for any of the 17 other cancers analysed	
Batty 2017 [11]	MA of IPD (NR)	Cohort (N = 3, previously unpublished) N = 20,485 5.7y to 13.8y	Various	Psychological distress (depression & anxiety symptoms) via general health questionnaire	Cancer incidence		No sig. association: adj[b] HR 1.16 (0.90–1.49) Individual cancers: Positive trends but not significant (lung, colorectal, breast)	
Stressful life events								
Bahri 2019 [12]	SR + MA (2018)	Cohort (N = 11) NR 1-40y (range)	Breast	Stressful life events	Breast cancer incidence	Significant association (RR 1.11 (1.03–1.19)		
Lin 2013 [13]	MA (2012)	Cohort (N = 3) + case-control (N = 4) N = 99,807 NR	Breast	Stressful life events Severe life events	Breast cancer incidence	Sig. association: adj[b] OR 1.51 (1.15–1.97) Sig. association: adj[b] OR 2.07 (1.06–4.03)		
Chiriac 2018[14]	SR (2016)	Cohort + case-control (N = 44) N = 700,000 NR	Breast	Stressful life events	Breast cancer incidence		Of 44 studies, positive association in 26, no association in 18	
Wong 2020 [15]	MA (NR)	Cohort (N = 2) N = 5,434,965 4-7y (range)	Melanoma	Partner bereavement	Melanoma incidence			Sig. reduction: adj[b] HR 0.88 (0.84–0.92). Possible delayed detection after bereavement
Work stress								
Heikkila 2013[16]	MA of IPD (NR)	Cohort (N = 12) N = 116,056 12y (median)	Various	Work stress (job strain)	Cancer incidence		No association: adj[b] HR 0.97 (0.90–1.04) Individual cancers: No significant associations (lung, colorectal, breast or prostate cancer)	
Trudel-Fitzgerald 2017[17]	MA (NR)	Cohort (N = 1) case-control (N = 1) N = 106,210 4.5y to 8.0y	Ovarian	Work stress (high job strain via questionnaire)	Ovarian cancer incidence		No sig. association: adj[b] RR 1.06 (0.72–1.55) Social support from co-worker or supervisor did not moderate association	
Stress (various types)								
Kruk 2019 [18]	SR (2019)	Reviews (N = 9); cohort + case-control (N = 10) NR; NR	Breast	Stress (life events, anxiety, depression, lack of social support, avoidant coping strategies)	Cancer incidence		Very mixed results; positive correlation in 5 of 9 previous reviews. Sig. positive association in 7 of 10 observational studies (4 cohort and 6 case-control; adj[b])	

Adj, adjusted; CI, confidence interval; HR, hazard ratio; incl, included; IPD, individual patient data; MA, meta-analysis; NR, not reported; OR, odds ratio; RR, relative risk; sig, significant; SR, systematic review; y, year.
[a]Positive association indicates that stress was associated with increased cancer incidence. [b]Included studies adjusted for the following [7]: maximally adjusted estimates included [11];: age and sex [18];: adjusted for confounders (NR which) [15];: comorbidities [13];: adjusted for confounders e.g. age, oral contraceptive use, hormone replacement, menopause, alcohol, smoking, socioeconomic status, family history [17];: age, socioeconomic status, marital status, oral contraceptive use, parity, tubal ligation, family history, menopause, hormone therapy, BMI, physical activity, caffeine, caloric intake, alcohol, smoking [16];: age, sex, socioeconomic status, BMI, alcohol, smoking.

3.2.2. *Stressful life events*

The effect of stressful life events on cancer incidence was reported in four systematic reviews. Two meta-analyses in breast cancer both suggested a significant association between stressful life events and breast cancer risk. Firstly, a meta-analysis of 11 cohort studies [12] reported a significant association between stressful life events and breast cancer incidence (RR 1.11; 95% CI 1.03 to 1.19). Secondly, an earlier meta-analysis of three cohort studies and four case-control studies [13] also reported a significant association between stressful life events and breast cancer incidence (odds ratio [OR] 1.51; 95% CI 1.15 to 1.97) as

well as between severe life events and breast cancer incidence (OR 2.07; 95% CI 1.06 to 4.03)[13]. A further systematic review in breast cancer (without a meta-analysis) summarised 44 cohort and case-control studies, with 26 studies reporting positive associations between stressful life events and breast cancer incidence and the other 18 studies showing no association [14].

In addition, a meta-analysis of two large cohort studies assessed the effect of partner bereavement on melanoma incidence [15]. This review reported an inverse relationship whereby bereavement was associated with a significant reduction in melanoma incidence; however, the authors noted that this could be due to delayed detection of skin changes rather than a true reduction in incidence. The same review showed that partner bereavement in people with melanoma was associated with increased melanoma mortality (described later).

3.2.3. Work-related stress

Two meta-analyses assessed the effect of work stress on cancer incidence, neither reporting a significant association. A meta-analysis of 12 cohort studies [16] reported no association across all cancers (hazard ratio [HR] 0.97; 95% CI 0.90 to 1.04) or for any of the individual cancers assessed. A meta-analysis of one cohort and one case-control study in ovarian cancer [17] also showed no association between work stress and ovarian cancer incidence (RR 1.06; 95% CI 0.72 to 1.55).

3.2.4. Stress (various types)

One systematic review assessed various types of psychological stress including life events, anxiety, depression, lack of social support and avoidant coping strategies [18]. This review reported very mixed results, with a positive correlation between stress and cancer incidence being observed in 5 of 9 previous reviews and 7 of 10 observational studies. However, no meta-analysis was conducted.

3.3. Psychological stress, depression or anxiety and cancer progression, recurrence or survival

Eight systematic reviews (five with a meta-analysis and three without) assessed the association between stress, depression or anxiety and cancer progression, recurrence or survival (Table 2). The included reviews addressed three types of psychological stress: depression and anxiety, stressful life events, work stress. The majority of reviews adjusted their analyses to account for potential confounders such as age, sex and other cancer risk factors (see Table 2 for details).

3.3.1. Depression and anxiety

Three meta-analyses showed a significant association between depression/anxiety and cancer mortality. A meta-analysis of 16 cohort studies [7] reported a significant association between depression/anxiety and cancer mortality (RR 1.21; 95% CI 1.16 to 1.26). Similarly, an older meta-analysis of 14 studies [10], with little overlap with the studies included in Wang et al., also reported a significant association between depressive symptoms and cancer mortality (RR 1.25; 95% CI 1.12 to 1.40). An analysis pooling 16 previously unpublished cohort studies [11] also showed a significant association between depression/anxiety symptoms and cancer mortality (HR 1.26; 95% CI 1.11, 1.42).

There was some limited evidence for an association between depression/anxiety and cancer recurrence. A meta-analysis of three studies [10] showed a non-significant positive trend for association between depressive symptoms and cancer recurrence (RR 1.23, 95% CI 0.85 to 1.77). In addition, a systematic review of bladder cancer [19] suggested that people with more severe depression/anxiety scores had worse prognosis in terms of post-surgical complications, progression and survival (based on one study each).

3.3.2. Stressful life events

There was limited evidence addressing the relationship between stressful life events and cancer outcomes. A meta-analysis of two large cohort studies [15] reported a significant association between partner bereavement and melanoma mortality (HR 1.17; 95% CI 1.06 to 1.30).

3.3.3. Work-related stress

There was limited evidence on the relationship between work stress and cancer outcomes. A meta-analysis of two observational studies in ovarian cancer [17] showed no significant association between work stress and ovarian cancer mortality (RR 1.08; 95% CI 0.64 to 1.82), and social support from a co-worker or supervisor did not moderate the association.

3.3.4. Stress (various types)

Two reviews assessed various types of stress, with mixed findings. A systematic review of the effects of various stress measures on cancer recurrence [20] showed very mixed findings (of 15 studies, 5 showed a positive relationship on at least 1 stress measure, 12 showed no relationship on at least 1 measure, and 3 showed an inverse relationship on at least 1 measure). A further systematic review covering various types of stress [18] reported some effect on cancer growth and metastasis (based on earlier reviews) and an association with cancer mortality (based on 1 previous review). However, neither review conducted a meta-analysis.

4. Discussion

4.1. Summary of findings: stress, depression or anxiety and cancer incidence

This rapid systematic review aimed to summarise systematic reviews addressing the association between psychological stress, depression or anxiety and cancer. Overall there was a reasonable volume of evidence for an association between psychological stress, depression or anxiety and cancer incidence (in general populations). In summary, one large meta-analysis reported a significant association between depression/anxiety and cancer incidence [7], while another showed a non-significant trend [11]. Two meta-analyses reported a significant association between stressful life events and cancer incidence [12,13], while a further review without a meta-analysis reported mixed findings [14]. However, two meta-analyses of work stress showed no significant association with cancer incidence [16,17]. The majority of reviews adjusted their analyses to account for potential confounders such as age, sex and other cancer risk factors.

4.2. Summary of findings: stress, depression or anxiety and cancer outcomes (in cancer patients)

This review also assessed the link between psychological stress, depression or anxiety in patients with cancer and cancer outcomes, including progression, recurrence or survival. Overall there was some evidence for an association, particularly from reviews which included a meta-analysis. Three meta-analyses of various cancer types reported a significant association between depression/anxiety and cancer mortality [7,10,11] while a smaller meta-analysis showed a non-significant trend for an association between depressive symptoms and cancer recurrence [10]. In terms of stressful life events, one meta-analysis of two studies reported a significant association between partner bereavement and cancer mortality [15]. A further meta-analysis of two studies showed no significant association between work stress and cancer mortality [17]. Additional reviews did not include meta-analyses and reported mixed findings across their included studies.

4.3. Strengths, quality and limitations of the evidence base

All the included reviews and meta-analyses were based on cohort and case-control studies. Many of the included studies were very large cohorts with several years' follow-up, which is essential when assessing

Table 2
Stress, depression or anxiety and cancer progression, recurrence or survival.

Ref	Review type (search)	Incl. studies N participants Follow-up	Cancer type	Stress type	Outcome	Associations: Positive[a] (brackets indicate 95% CI)	Associations: Mixed or non-significant (brackets indicate 95% CI)	Associations: Negative
Depression and anxiety								
Wang 2020 [7]	SR + MA (2018)	Cohort (N = 16) N = 762,762 6.4y (mean)	Various	Depression/anxiety (clinical diagnosis or via symptom scales)	Cancer mortality	Sig. association: adj[b] RR 1.21 (1.16–1.26) Individual cancers: Sig. association for (RRs in brackets): breast (1.40), lung (1.40), colorectal (1.38), hematopoietic (1.66), prostate (1.87), kidney (1.85), bladder (2.22)	Individual cancers: Non-sig. trends for other cancers analysed	
Satin 2009 [10]	SR + MA (NR)	Obs[c] (N = 14) (NR, NR) Obs[c] (N = 3) Obs[c] (N = 3)	Various	Depressive symptoms Clinical depression (major or minor) Depressive symptoms	Cancer mortality Cancer mortality Cancer progression	Sig association: unadj RR 1.25 (1.12–1.40) Sig association: unadj RR 1.39 (1.03–1.89)	No sig association: unadj RR 1.23 (0.85–1.77)	
Batty 2017 [11]	MA of IPD (NR)	Cohort (N = 16, previously unpublished) N = 163,363 9.5y (mean)	Various	Psychological distress (depression & anxiety symptoms) via general health questionnaire	Cancer mortality	Sig. association: adj[b] HR 1.26 (1.11–1.42) Individual cancers: Sig. association for colorectal (1.84), breast (1.91), ovarian (2.37), prostate (2.42), oesophagus (2.59), stomach (2.67), bladder (2.69), pancreas (2.76), non-Hodgkin's lymphoma (3.14), leukemia (3.86)	Individual cancers: Non-sig. trend for other cancers analysed	
Pham 2019 [19]	SR (2018)	Cohort (N = 3)	Bladder	Depression/anxiety (distress scores or mental health scores)	Bladder cancer progression, mortality	Association with worse prognosis, including post-surgical complication rates (1 study), progression (1 study) and survival (1 study)		
Stressful life events								
Wong 2020 [15]	MA (NR)	Cohort (N = 2) N = 28,508 3.5-5y (range)	Melanoma	Partner bereavement	Melanoma mortality	Sig. association: adj[b] HR 1.17 (1.06–1.30)		
Work stress								
Trudel-Fitzgerald 2017[17]	MA (NR)	Cohort + case-control (N = 2) N = 396 2-3y (range)	Ovarian	Work stress (high job strain via questionnaire)	Ovarian cancer mortality		No sig. association: adj[b] RR 1.08 (0.64–1.82) Social support from co-worker or supervisor did not moderate association	
Stress (various types)								
Kruk 2019 [18]	SR (2019)	Reviews (NR) NR NR	Various (mainly breast)	Stress (life events, anxiety, depression, lack of social support, avoidant coping strategies)	Cancer growth, metastasis, mortality	Some effect on cancer growth, metastasis and cellular aging (various reviews) and with cancer mortality (1 previous review)		
Todd 2014 [20]	SR (2012)	Cohort (N = 12), RCTs (N = 3) N = 27,629 1-13y (range)	Breast + melanoma	Stress (life events, depression/anxiety or cortisol/immune markers)	Cancer recurrence		In summary, of 15 studies: −5 (33%) positive relationship on ≥1 stress measure −12 (80%) no relationship on ≥1 stress measure −3 (20%) inverse relationship on ≥1 stress measure	

Adj, adjusted; BMI, body mass index; CI, confidence interval; GHQ-12, General Health Questionnaire-12; HR, hazard ratio; incl, included; IPD, individual patient data; NR, not reported; obs, observational; RCT, randomised controlled trial; RR, relative risk; sig, significant; unadj, unadjusted.
[a]Positive association indicates that stress was associated with increased cancer mortality, recurrence or progression. [b]Included studies adjusted for the following [7]: maximally adjusted estimates included [11];: age, sex, education, socioeconomic status, BMI, smoking, alcohol [15];: age, sex, comorbidities [17];: age, socioeconomic status, marital status, oral contraceptive use, parity, tubal ligation, family history, menopause, hormone therapy, BMI, physical activity, caffeine, caloric intake, alcohol, smoking. [c]Not stated whether cohort or case-control studies [10].

rare, long-term outcomes such as cancer incidence. Any observational study can be subject to confounding, whereby both the exposure (i.e. stress) and the outcome (i.e. cancer incidence) are associated with a third, hidden, factor rather than to each other (e.g. social deprivation or other health issues). Most of the reviews included here noted that the majority of their included studies had adjusted their analyses for patient characteristics, which should address confounding to a large extent, though some residual bias may remain.

Associations involving rare outcomes (such as cancer incidence) may not be statistically significant in smaller studies due to insufficient size (study power); therefore, the included large meta-analyses which pool data across a number of primary studies are important. There is also a possibility of publication bias within the included studies (i.e. studies reporting a positive association may have a higher chance of publication). In addition, there was variability between studies in terms of types of stress, measures used to assess stress, and cancer outcomes; this is discussed in more detail in the following section.

4.4. Limitations of the rapid review methodology

Limitations of this review due to the rapid review methodology included the following. Due to limited time and budget, only one reviewer screened the reviews for inclusion and extracted the data (data were double-checked but by the same reviewer), which could have led to reviews being missed or data inaccuracies. Formal quality assessment of the included reviews was not undertaken.

4.5. Possible factors impacting the relationship between stress and cancer incidence

Some reviews discussed possible factors impacting the relationship between stressful life events and cancer incidence [1,14]. It was suggested that different types of event, as well as the number, duration and timing of events, may differ in the amount of stress they cause, and therefore in their effects on cancer incidence. Some types of event are thought to have greater impact on health than others, including events which threaten social status, self-esteem, identity, or physical wellbeing, or where demands exceed control [1]. Such events may include the death of a loved one; divorce; conflict with or exclusion by a spouse/friend/co-worker; job loss; retirement; and diagnosis of serious illness [1]. In terms of timing of event, childhood adverse experiences may have a substantial impact on health outcomes, while events such as losing a partner may have differing effects at different ages.

It was also suggested that different individuals may experience different intensities of stress from similar events, based on differences in personality, coping strategies and resilience to stressors, which may lead to differences in physiological stress responses [3]. Some people are thought to be more resilient to stressful events; for example, people with greater self-efficacy, greater perceived control, and less negative affect and rumination [1,14].

In addition, other aspects of a person's life may moderate the impact of stressful events, in either direction. Positive social support has been suggested to buffer against the physiologic effects of stressful events [1]. Conversely, a narrative review reported that inadequate social support was associated with a substantial increase in breast cancer mortality (based on 15 studies), while greater social burden, such as caregiving responsibilities, was also found to be associated with increased risk of breast cancer mortality [21].

4.6. Potential mechanisms for the relationship between stress and cancer

Several authors have investigated the potential biological mechanisms linking psychological stress with cancer incidence or cancer outcomes. Possible mechanisms include the sympathetic nervous system and neuroendocrine signalling via stress hormones such as cortisol, adrenaline and noradrenaline, which suppress immune function, increase chronic inflammation, and increase tumour cell survival, proliferation and metastasis [2–6,22,23]. In addition, stress may lead to poor diet and decreased physical activity which indirectly affect cancer risk via stress pathways and other mechanisms [24,25].

4.7. Future research

Future research may benefit from more in-depth analyses of study cohorts to understand why psychological stress may influence cancer development in some individuals but not in others. This may include personal factors such as an individual's resilience to stress [3] or genetic predisposition to cancer, social factors such as stress-buffering effects of social support, as well as the impacts of different types and timing of stressors [1,14].

In addition, future research may focus on interventions to reduce psychological stress, both in general populations and cancer populations, and the extent to which these might reduce cancer incidence, cancer outcomes, or intermediate outcomes such as biological markers of the physiological stress response.

5. Conclusions

This review of systematic reviews identified some evidence for an association between psychological stress, depression or anxiety and both cancer incidence and cancer mortality, particularly within reviews which pooled data in a meta-analysis. In terms of type of stress, significant associations were seen for depression/anxiety and stressful life events, but not for work stress. Confirmation of these findings through further high-quality studies would be valuable; for example, by incorporating measures of different types of stress within major cohort studies. Future research may also focus on the role of social support and stress-reducing interventions in buffering against these effects.

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Author statement

Katy Cooper: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Writing - original draft. Fiona Campbell: Conceptualization, Data curation, Funding acquisition, Methodology, Writing - review & editing. Sue Harnan: Conceptualization, Data curation, Funding acquisition, Methodology, Writing - review & editing. Anthea Sutton: Conceptualization, Data curation, Funding acquisition, Methodology, Writing - review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Katy Cooper reports financial support was provided by World Cancer Research Fund (WCRF) International.

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Appendix A. Medline search strategy: stress-cancer association

Search run 10th November 2020.

MEDLINE: Search terms
1 Stress, Psychological/
2 ((psychological or psychosocial or long-term or chronic) adj3 (stress or distress)).ti,ab.
3 1 or 2
4 Neoplasms/
5 cancer.ti,ab.
6 Multiple Myeloma/
7 Leukemia, Myelogenous, Chronic, BCR-ABL Positive/or Precursor Cell Lymphoblastic Leukemia-Lymphoma/or Leukemia, Myeloid, Acute/or Leukemia, Lymphocytic, Chronic, B-Cell/or Leukemia/
8 Melanoma/
9 (myeloma or leuke?mia or lymphoma or melanoma).ti,ab.
10 or/4-9
11 (non-cancer or non-malignant).ti,ab.
12 10 not 11
13 3 and 12
14 Risk Factors/
15 Progression-Free Survival/or Disease Progression/
16 Survival Rate/or Survival/or Disease-Free Survival/
17 Neoplasm Metastasis/
18 Recurrence/or Neoplasm Recurrence, Local/
19 Mortality/
20 (risk* or progression or surviv* or metastas* or recurrence or secondary or mortality).ti,ab.
21 or/14-20
22 13 and 21
23 meta analysis.mp,pt. or review.pt. or search:.tw.
24 22 and 23

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