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Title: A Systematic Review of Quantitative Observational Studies Investigating Psychological Distress in Testicular Cancer Survivors

Running Head: Review of Psychological Distress in Testicular Cancer Survivors

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Abstract

Objective

Testicular cancer (TC) affects young men and may cause psychological distress despite a good prognosis. This systematic review evaluated the prevalence, severity and correlates of anxiety, depression, fear of cancer recurrence (FCR) and distress in TC survivors.

Methods

A systematic search of literature published 1977-2017 was conducted to find quantitative studies including TC survivor-reported outcomes relevant to review objectives. The quality of included articles was assessed, and a narrative synthesis conducted.

Results

Of 6717 articles identified, 66 (39 good, 20 fair, 7 poor quality) reporting results from 36 studies were included. TC survivors' mean anxiety levels were higher than in the general population, while mean depression and distress were no different. Clinically significant anxiety (≈ 1 in 5) and to a lesser extent distress (≈ 1 in 7), but not depression, were more prevalent in TC survivors than the general population. Approximately 1 in 3 TC survivors experienced elevated FCR. Poorer psychological outcomes were more common among TC survivors who were: single, unemployed/low socioeconomic status (SES), suffering from comorbidities, experiencing worse symptoms/side effects, and using passive coping strategies.

Conclusions

Many TC survivors do not experience significant psychological morbidity, but anxiety and FCR are prevalent. Inadequate coping resources (e.g. low SES and social support) and strategies (e.g. avoidance) and greater symptoms/side effects were associated with poorer outcomes. Theoretically-driven prospective studies would aid understanding of how outcomes change over time and how to screen for risk. Age and gender appropriate interventions that prevent and manage issues specific to TC survivors are also needed.

Keywords

Testicular cancer, Survivorship, Anxiety, Depression, Fear of Cancer Recurrence, Patient-reported Outcomes, Oncology, Systematic Review

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Introduction

Testicular cancer (TC) is the second most common malignancy in men aged 15-35 years [1]. The existential challenge of receiving a life-threatening diagnosis at a relatively young age may cause considerable psychological distress [2]. This may be exacerbated by TC being diagnosed at a stage of life when many men are engaged in self-defining activities such as growing their family and career. The young age of diagnosis also means many men will live with the consequences of TC long after finishing treatment.

Treatment for TC may cause further psychological morbidity. The primary treatment for TC, removal of a testicle via orchidectomy, may result in body image disturbance [3]. Additional treatments for TC (chemotherapy and radiotherapy) have side effects such as infertility, altered neurological, respiratory and sexual function, and increased risk of cardiovascular disease and secondary malignancy [4], potentially increasing cancer-specific and general health anxiety and distress regarding functional impairments. More than 95% of men diagnosed with TC are treated successfully, but many survivors have persistent worries that TC will return [5].

Given the potential impact of TC, the extended duration of survivorship for the young men affected, and growing TC survivor numbers, it is critical that the extent and severity of psychological distress is evaluated to establish the scope of related healthcare needs and inform future interventions.

Psychological distress in TC survivors has been evaluated in numerous studies with variable results. Three reviews including distress have been reported in the past 13 years [6-8], with the most recent published in 2008 [8]. These reviews were focused more broadly on quality of life, rather than psychological distress, and only included eight [6], 13 [7], and seven [8] articles on psychological distress respectively. None of these reviews were systematic (i.e. they did not meet one or more key systematic review criteria such as: conducting an exhaustive search of relevant literature to address pre-defined specific objectives, using duplicate study selection and data extraction, and outlining reasons for including/excluding studies). Only three articles were included in more than one review, despite the similar review publication dates (2004-2008), highlighting their non-systematic nature.

Furthermore, the quality of included studies was generally poor. Flerer, et al. [7] alone rated the quality of included studies and only 7/23 were considered methodologically rigorous. Methodological shortcomings, particularly a predominance of small samples and study-specific questionnaires, were noted in all three reviews [6-8]. Good and poor quality studies produced quite different results (e.g. Greater depression in TC survivors versus controls in poor but not good studies) [7]. The most comprehensive review by Flerer, et al. [7] concludes that because of methodological shortcomings of the literature “it would not be justified to provide a general conclusion on the quality of life of TC survivors.” (p485) All three reviews noted a particular need for more methodologically rigorous investigation of factors associated with psychological morbidity [6-8].

The literature on TC survivors’ psychological distress is expanding rapidly. As many high quality studies have been published in the eight years since the last review, a systematic review was needed to provide a more authoritative appraisal of the prevalence, severity and correlates of psychological distress in TC survivors.

Objectives

The current authors set out to review the literature to:

1. Determine the prevalence and severity of patient-reported anxiety, depression, fear of cancer recurrence (FCR) and distress in TC survivors (compared with the general population and other cancer survivors where possible);
2. Identify TC survivors at risk of poor outcomes by exploring correlates of patient-reported anxiety, depression, FCR, and distress, such as sociodemographic (e.g. age, employment, and relationship status), disease and treatment (e.g. stage of disease, type of medical treatment for TC (i.e. treatment type), and time since treatment), and psychosocial (e.g. personality, coping style, and social support) variables;

3. Evaluate relationships between anxiety, depression, FCR, distress, and other patient-reported outcomes (PROs) in TC survivors;
4. Assess study quality to guide conclusions regarding the objectives above.

Methods

Search Methods

AMED, EMBASE, Medline, PsycInfo, Scopus and Web of Knowledge were searched from 1977 (when cisplatin-based chemotherapy was widely introduced) to 10/04/2017. Searches were limited to human studies reported in English. The search strategy included key words: (testicular OR testis OR testes) AND (cancer* OR neoplasm* OR carcino* OR sarcoma* OR malignan* OR tumour* OR tumor* OR metasta*) AND (anx* OR depress* OR fear of recurrence OR distress* OR stress* OR emotion* OR mental health OR post-traumatic stress disorder). Subject Heading (MESH) terms were used to broaden the search where possible. Electronic searches were supplemented with: 1) hand searching reference lists of previous reviews and recent articles; 2) searches of key researchers in the field.

Eligibility criteria

Quantitative studies reporting PROs relevant to the review objectives from a sample of men who had completed treatment for TC (i.e. TC survivors) were included if:

1. At least 50% of the sample comprised unilateral TC survivors aged ≥ 18 years who had completed treatment after 1977 or TC survivor data could be separately extracted if heterogeneous cancer survivors were sampled;
2. They reported observational quantitative PRO data (i.e. unaffected by any intervention) for a specific time point (as opposed to change scores);

Conference abstracts, reviews, theoretical articles, and policy documents were excluded.

One reviewer (ABS) scanned titles and abstracts to exclude any references that were clearly irrelevant. Those considered possibly relevant were obtained in full. Two reviewers (ABS and TL) independently applied eligibility criteria to 20 randomly selected articles. Inter-rater reliability was high (Kappa=0.88, $p<0.001$) so ABS completed eligibility assessment of remaining potentially relevant articles. Any articles not clearly eligible were brought to the research team for discussion and consensus.

Data Collection

A data abstraction form assessing study design, methods, sample, measures and results was developed and piloted on 10 randomly selected articles. One reviewer (ABS or CR) extracted data from included articles, with 15% of data extraction cross-checked by a second reviewer.

Quality assessment

The methodological quality of included articles was evaluated using a checklist designed to assess quality of healthcare intervention studies, modified to remove items not applicable to observational studies [9]. The resulting 14-item checklist assessed: quality of reporting (5 items), external validity (2 items), internal validity (6 items), and power (1 item). Items were scored 1 if the quality criterion was met, or 0 if not met or unable to be determined. Not applicable criteria (e.g. attrition in a cross-sectional article) were not considered in the overall article quality rating.

Two reviewers (ABS and TL) initially independently evaluated study quality of 14 included articles. Observed agreement ranged from 0.60 to 0.95 across items, and was above 0.75 for 12/14. Kappa values ranged from .29 to .70, with 9/11 in the range indicating moderate to substantial agreement ($\kappa=0.41 - 0.80$)[10]. Kappa was not calculated for three items due to the presence of zero cells. Having established inter-rater reliability, 33 of the remaining studies were rated solely by ABS and 19 solely by TL.

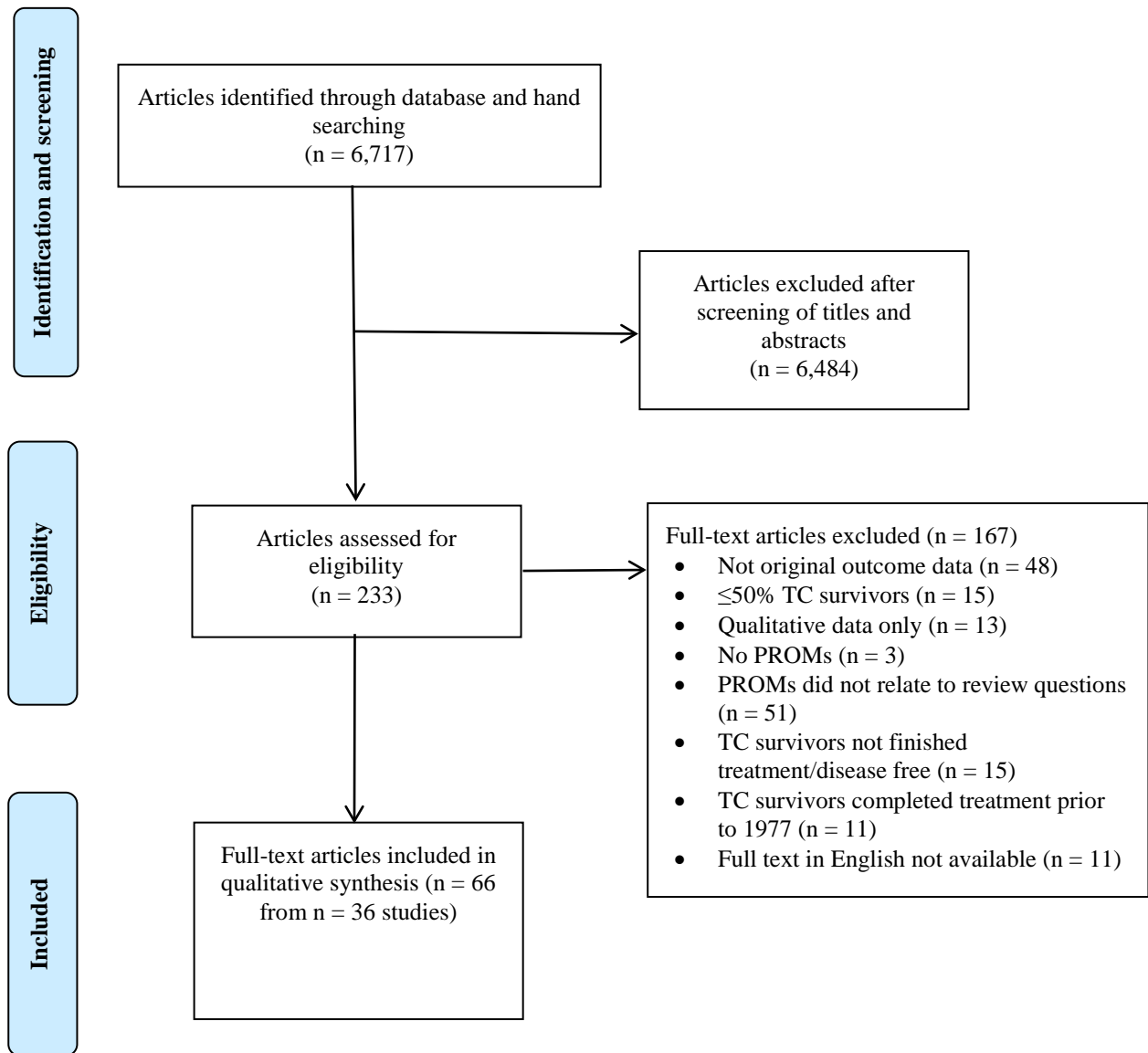
Data analysis

Meta-analysis was not feasible given the heterogeneity in outcome measures (many of them study-specific) and reporting of results, along with the limited number of studies pertaining to some outcomes (e.g. FCR). We used narrative synthesis to describe psychological distress in terms of: prevalence (preferably according to validated clinical cut-offs, but sometimes as indicated by a study-specific questionnaire (SSQ), which were often used in fair/poor quality studies), severity (mean scale scores or proportion of respondents falling within distinct response categories on a single item) and correlates. We included comparisons with members of the general population or other cancer survivors if reported. Results were considered within each quality category, with greater weight being placed on studies of high quality in overall synthesis.

Results

Of 6717 articles identified, 66 articles reporting 36 studies met eligibility criteria (Figure 1). Fifty of the 66 articles had not been included in previous reviews [6-8] and 32 of the new articles were considered good quality. Sixteen of the 25 articles on psychological distress contained in previous reviews were included. The remainder were primarily older studies where it was unclear whether participating TC survivors had completed treatment after 1977. Thirty-nine articles were considered good quality ($\geq 80\%$ of relevant criteria met), 20 fair quality (50-79% criteria met), and seven poor quality ($< 50\%$ criteria met). Hereafter, studies are simply referred to as good, fair and poor. Appendix S1 summarises characteristics of included studies.

Figure 1. PRISMA Study Selection Flowchart



Depression

Appendix S2 summarises findings for the prevalence, severity, and correlates of depression in TC survivors from 22 good, 14 fair and 4 poor quality articles from 25 studies.

Prevalence of Depression

Depression prevalence estimates from eight good studies ranged from 5% [e.g. 11] to 20% [e.g. 12], and from 12 fair/poor studies from 5% [e.g. 13] to 36% [e.g. 14], potentially reflecting the wide range of questionnaires (many study-specific) used to assess depression in the latter studies. Eight studies (2 good, 3 fair, 1 poor) reported rates of clinical depression based on a validated cut-off score of ≥ 8 on the Hospital Anxiety and Depression Scale (HADS). Estimates ranged from 8% [e.g. 3] to 10% [e.g. 15] in good studies and 5% [e.g. 13] to 11% [e.g. 16] in fair studies, ***suggesting approximately one in ten TC survivors experience clinically significant depression.***

Depression rates did not differ from age-matched population norms in one large good Norwegian study (9.7% vs. 10.1%) [15], but were higher than population norms in a good Australian study (20% vs. 13%) [12], suggesting possible cross-cultural differences. Two fair studies found a significantly higher prevalence of depression compared with general population controls (12% versus 0% [17], 36% versus 14% [14]).

Severity of Depression

Findings from 12 good, seven fair, and three poor studies consistently indicate low levels of depression (*in the bottom quartile*) in TC survivors, irrespective of the measure used. Depression levels were no different [e.g. 18, 19] or lower [e.g. 15] than age- and gender-matched comparators in all except one good [12] and two fair studies [17, 20].

Correlates of Depression

Ten good, nine fair and two poor studies explored sociodemographic, clinical and psychological correlates of depression in TC survivors.

Consistently absent (i.e. non-significant) associations were found between depression and *treatment type* (six good [12, 21-25], and six [13, 14, 16, 26-28] of seven fair/poor studies); and *time since diagnosis/treatment* (four [12, 21, 23, 29] of five good studies), although a single good study found depression decreased slightly in the first year post-orchidectomy then plateaued [25].

Consistent significant associations were found between depression and *being unmarried* (three good studies [22, 23, 25]); and *lower social support* more generally, although Tuinman et al [25] found that higher rates of clinically significant depressive symptoms in single versus partnered TC survivors immediately post-orchidectomy resolved one year later. Also consistently associated were *fatigue* (three good studies [23, 30, 31]; *negative health behaviours* (two good studies [32, 33]); *avoidant* [34] and *helpless/hopeless coping* [12] (two good studies); *poorer sexual functioning* (two good studies [25, 35]); *previous psychological distress* (one good [22] and one fair study [26]); and *altered body image and sense of masculinity* in one good [3] and one fair [17] study.

Conflicting evidence regarding associations with depression were found for: a) *older age* (significantly associated in two good [22, 31] and one poor study [36], not associated in one good study [33] and two fair studies [17, 26]); b) *lower education* (significantly associated in one good [22] and one fair [17] study, not associated in one fair study [26]); c) *hormone levels* (significantly associated in one poor study [36], not associated in two fair/poor studies [13, 37]).

Single good studies reported associations between depression and: *comorbidity* [22]; *low physical activity* [33]; *anxiety* [33], *neuroticism* [38], and *self-reported cognitive problems* [24] but not *number of impairments* and *overall impairment on neuropsychological tests* [28].

Anxiety

Appendix S3 summarises findings for the prevalence, severity, and correlates of anxiety in TC survivors from 19 good, 12 fair and 4 poor quality articles from 21 studies.

Prevalence of Anxiety

Four good, seven fair and two poor studies evaluated the prevalence of anxiety. Prevalence estimates from three good studies (two using the HADS) ranged from 17% [e.g. 3] to 20% [e.g. 35], significantly higher (by $\geq 5\%$) than age- and gender-adjusted normative data. The other good study [29] found only 6% of TC survivors experienced anxiety. Three fair studies using the HADS-A also found approximately one in five (17-19%) TC survivors had anxiety [13, 37, 39], while prevalence estimates from other fair/poor studies were higher and more variable (27% [e.g. 40] - 62% [e.g. 41]), likely due to the use of non-validated study-specific questionnaires and/or small samples. ***These results suggest that approximately one in five TC survivors experience clinically significant anxiety.***

Severity of Anxiety

Nine good, five fair and two poor studies evaluated anxiety severity. Mean HADS-A scores of 4.2 to 4.8 were reported in three good studies [3, 18, 35]. All five (three good, two fair) studies comparing TC survivors with healthy controls *found significantly higher anxiety in TC survivors* [12, 15, 17-19]. Anxiety levels were comparable to Hodgkin's disease survivors' in a good study [21] and no different to spouses' in a fair study [42].

Correlates of Anxiety

Nine good, eight fair and two poor studies evaluated correlates of anxiety. Associations between anxiety and *treatment type* were *consistently non-significant* in five good [12, 15, 21, 22, 24], two fair [14, 16] and one poor study [27]. One fair study [13] found anxiety was more prevalent in TC survivors treated with five or more chemotherapy cycles, but this may be due to the sample having recurrent or refractory disease, which in itself may be anxiety provoking.

Consistent significant associations were found between anxiety and *self-reported physical symptoms and side effects (particularly peripheral neuropathy)* in three good studies [12, 15, 29]; as well as *avoidant* [34] and *helpless/hopeless coping* [12] (both good studies).

Conflicting evidence regarding relationships with anxiety were found for *time since treatment* (no association in three good studies [21, 43, 44] versus significant decreases in anxiety with increasing time since diagnosis in another [29]); and *younger age* (two good studies found anxiety was higher in younger men [15, 29], while two good studies found no relationship [12, 21]).

A single study of 1408 Norwegian TC survivors [15] reported associations between anxiety and *alcohol problems, economic problems, treatment for mental problems, and relapse anxiety*. Other single studies reported associations with *sexual problems* [35], *chronic fatigue* [30], *reduced working capacity* [22], *high neuroticism* [38], *depression* [33], *occurrence of cognitive problems* [24] but not specifically the level of bother caused by them [45], *body image disturbance* [3], and *greater unmet needs* [12].

Fear of Cancer Recurrence

Appendix S4 summarises findings for the prevalence, severity, and correlates of FCR in TC survivors from three good, four fair and zero poor quality articles from six studies.

Prevalence of FCR

Two good studies using single-items found 28% [11] and 31% [5] of TC survivors reported 'quite a bit' or 'very much' FCR 10 years post-diagnosis, although one fair study found FCR reduced from 45% at six months post-treatment to 12% four years post-treatment [37], perhaps due to regular follow-up during this time period. FCR prevalence estimates from two fair studies were also generally high (42% - 45%) [42, 46].

These results suggest approximately one in three TC survivors experience FCR.

Severity of FCR

One good and three fair studies assessed FCR severity. The good study found FCR was one of the most concerning issues to TC survivors [47]. In contrast, the only fair study to use a FCR-specific validated measure (FoP-Q-12), found TC survivors' FCR levels compared to survivors of 15 other cancers were the second lowest, although no statistical comparisons were made [48]. One fair study reported a mean score of 40.1 (SD=29.2) on the EORTC QLQ-TC26 future perspective subscale [49]. Another fair study found that FCR severity was equivalent in TC survivors and their spouses [42].

Correlates of FCR

Two good studies and one fair study assessed FCR correlates. *Consistently absent associations* were found between FCR and *disease or treatment characteristics* [5, 11].

Conflicting evidence regarding relationships with FCR were found for *sociodemographics*. One good study found no relationship [11]. Another good study found higher FCR associated with *moderate education level* (11-12 years) in multivariate analyses and various other sociodemographic factors in univariate analyses [5].

Single good studies reported associations between FCR and *neuroticism and intrusive/avoidant thoughts* [5], and *depression* and *attributing the development of TC to psychological stress* [11] in multivariate analyses. One fair study found FCR was associated with higher perceived stress & lower physical wellbeing [49].

Distress

Appendix S5 summarises findings for the prevalence, severity, and correlates of distress (i.e. psychological morbidity in TC survivors not specifically concerning anxiety, depression, or FCR) in TC survivors from 20 good, 8 fair and 5 poor quality articles from 21 studies.

Prevalence of Distress

The prevalence of distress was evaluated in eight good, three fair and three poor studies. Distress was most commonly measured using the Impact of Event Scale (IES) (score ≥ 26 indicative of clinically significant cancer-related distress). Four good studies found 9% [e.g. 50] to 16% [e.g. 51] of TC survivors were above this cut-off. Similar prevalence estimates emerged from good studies using other measures (13% [24] and 17% [12]). Distress prevalence estimates from fair and poor studies were more variable, ranging from 23% [e.g. 27] to 55% [e.g. 52]. ***These data suggest that approximately one in seven TC survivors experience clinically significant distress.***

Two good studies found a higher prevalence of distress in TC survivors (17%, 22%) compared to age-adjusted normative controls (13%, 18%) [12, 53].

Severity of Distress

Distress levels were assessed in nine good, four fair and one poor study. Despite a significant proportion of TC survivors experiencing clinically significant distress, *mean distress levels* appear relatively low and comparable to various comparison groups. In two good studies, IES total scores ranged from 10.2 [54] to 14.0 [51] out of 75, while one fair study using different scoring found an IES total score of 6.6 out of 35 [26]. Similarly low mean scores on other distress measures were reported by three good studies, with HADS total scores of 7.1 [55] and 7.5 [34] out of 42 and a HSCL-25 total score of 8.5 out of 100 [24]. Three good studies found no significant difference in TC survivors' mean distress levels compared with matched controls [55], breast cancer [55] or Hodgkin's disease [21] survivors, while one fair study found elevated distress levels relative to prostate cancer survivors [49]. ***Evidence suggests that TC survivors experience mean distress levels comparable to similar men in the general population and other cancer survivor populations.***

Correlates of Distress

Correlates of distress were assessed in six good, four fair and zero poor studies. In good studies, *consistently absent* associations were found between distress and *age* [12, 21, 56-58], *education level* [12, 56, 58, 59], *treatment type* [12, 21, 24, 28, 56-58], *tumour type* [21, 58], *disease stage* [12, 58, 59], or *diagnosis with a second cancer* [60].

Consistent significant associations were found in good studies between distress and *unemployment* [60] or *lower SES* [58], *patient-reported side effects* [12, 57], *self-reported cognitive complaints* [24, 61], but not

cognitive impairment according to neuropsychological testing [51], and a *maladaptive coping style* [12, 34]. Distress showed a *significant positive association with FCR* in one good [5] and one fair study [49].

Conflicting evidence from good studies regarding relationships with distress were found for *not having a partner or children* (significantly associated in one study [60], not associated in three studies [12, 54, 58]) and *shorter time since treatment* (significantly associated in one study [56] and not associated in two studies [12, 58]). One fair study [62] found various aspects of distress were elevated six months post-treatment before subsequently decreasing, but a good study [54] found lower distress levels three months post-treatment versus immediately post-treatment, which however, rose again by 12 months post-treatment. These results indicate that distress may fluctuate in the period shortly after treatment, and may still be present 12-months post-treatment.

Single good studies reported positive relationships between distress and *sexual dysfunction* [35], *low life fulfilment* [60], *low social support* [12], *neuroticism* [38], and *poorer quality of life* [57].

Discussion

Despite their excellent prognosis (>95% 5-year survival), the findings of this review suggest that TC survivors experience significantly more prevalent and severe anxiety than the general population, and fear of cancer recurrence (FCR) is also common. Overall about one in five TC survivors suffer from clinically significant anxiety, versus approximately one in eight of general population controls. TC survivors' mean anxiety levels also appear higher than the general population and are comparable to that of other cancer survivors of similar age and gender. Approximately one third of TC survivors experience elevated FCR, close to the average of 49% (range 22-87%) found in a 2013 systematic review of FCR in heterogeneous cancer survivors [63]. As in other cancers, FCR was rated as one of the most concerning issues to TC survivors [47]. Likewise, observed associations between FCR and various negative outcomes, such as intrusive thoughts, depression, stress and poorer physical wellbeing in TC survivors are consistent with findings in other cancer survivors [63].

It appears that being diagnosed with TC shatters many men's sense of invulnerability and raises unforeseen existential concerns. Qualitative research [64] suggests that, like other cancer survivors, they experience a sense of 'liminality', which is characterised by feeling isolated from those who have not shared an intense experience, questioning the meaning of one's existence and an increased awareness of the fragility of life

and ultimate inevitability of death [65]. A recent study found that some TC survivors believe their initial cancer was caused by a susceptibility to stress and may feel that the same susceptibility makes recurrence inevitable [11]. This may also explain why some men continue to experience high levels of FCR more than 10 years post-treatment [5] despite a recurrence risk of $\approx 1\%$ [66]. Some men may continue to require therapeutic intervention for many years post-treatment, to help them deal with these psychological consequences of their disease.

Depression appears to be less of an issue for TC survivors generally. Most good and fair studies found depression was no more prevalent than in the general population, although one good Australian study by the current authors did find higher rates of, and more severe, depression in TC survivors than population norms [12]. While statistically significant, TC survivors' elevated mean levels of depression in Smith et al [12] were small in effect according to Cohen's rule of thumb [67] and therefore unlikely to be clinically important. The increased prevalence found in that study may also have been an artefact of the measure used (DASS-21), which enabled comparison with Australian general population norms, but is not specifically designed to screen for clinically significant depression.

Similarly to depression, this review found that mean distress levels were generally comparable with those in the general population, with the exception of two good studies that found more prevalent clinically significant distress and higher rates of help-seeking in TC survivors [12, 53]. Levels of morbidity in TC survivors may appear similar to those in the general population because the measures used in many studies have not addressed specific concerns for TC survivors. General measures of anxiety, depression and distress may not target TC-specific issues, such as infertility worries [68], impacts on study/work [55], and body image/intimacy issues [69], which have been reported in this population and found to be associated with distress in some studies in this review [e.g. 12, 22].

Another potential reason for inconsistent findings is that, while some TC survivors may suffer poor outcomes, others may experience benefits from their experience, effectively cancelling out deficits when outcomes are averaged across TC survivors overall. A large proportion of both adolescent and young adult and older adult cancer survivors have reported both benefit finding and post-traumatic growth from six months to several years post-diagnosis [70, 71]. In addition, qualitative research has found that although the experience of TC was initially associated with physical and emotional trauma, it also engendered a renewed appreciation for life in many TC survivors [72].

In addition to bringing about a more positive mental outlook, experiencing TC may also lead men to make positive health behaviour changes. Support for this idea is provided by research showing that TC survivors display increased physical activity levels relative to men from the general population [73] and that a significant proportion of survivors reduce or quit smoking after TC [74]. These lifestyle changes may lead to improvements in psychological wellbeing that may nullify any initial deficits experienced.

Correlates of Poor Psychological Outcomes

Being single or having low social support, unemployed/low SES, and suffering from comorbid physical illness were the sociodemographic variables most consistently related to poor psychological outcomes. While risk factors more specific to TC survivors, such as negative treatment experiences, require further investigation, these general factors are still useful in identifying TC survivors at risk of poorer outcomes. It is likely that TC survivors who are single and lack a partner or a job have less emotional, cognitive, and material resources at their disposal to help them cope with stressful situations than those with partners and jobs. Further, trying to cope with having a comorbid chronic illness may exhaust the limited resources available to such individuals, resulting in poorer psychological wellbeing. Conversely, TC survivors experiencing psychological and physical morbidity may struggle to secure a partner and/or a job. The cross-sectional nature of much of the research on psychological distress in TC survivors makes the direction of associations difficult to infer. Disease and treatment variables were largely unrelated to psychological outcomes, except that concomitant symptoms and side-effects were associated with anxiety, FCR and distress. This is commonly reported; patients ascribe meaning to their symptoms, which they see as foreshadowing recurrence, reminding them of losses, and keeping memories of the disease and treatment alive [75].

Other correlates included coping strategies, with passive (i.e. avoidant or helpless-hopeless) coping styles associated with worse psychological outcomes compared to more active, problem-solving coping styles. This is consistent with the wider coping literature suggesting that actively addressing issues leads to better outcomes than trying to avoid them [76].

Clinical Implications

Overall, these findings suggest that interventions that address key concerns, such as FCR and anxiety, by facilitating adaptive coping, finding meaning in the TC experience and positive lifestyle changes (e.g. [77]) may benefit this population. Greater social support was associated with better psychological outcomes for TC survivors in this review and cancer survivors more generally in other reviews [63], so efforts to increase social support, either by strengthening existing social support networks or gaining additional support

networks may also be helpful.

As there appear to be almost no disease and treatment variables and only a few sociodemographic characteristics useful in identifying TC survivors at risk of psychological distress, screening for some of the issues highlighted above may prove worthwhile. A brief screening tool, such as the distress thermometer and accompanying problems list recommended by the National Comprehensive Cancer Network [78], which assesses distress and various physical and emotional problems (including FCR, fatigue, and appearance) has been found to be feasible and acceptable in other cancer contexts, with effectiveness dependent on appropriate referral and follow-up [79].

Study Limitations

While a relatively large literature was found describing psychological outcomes in TC survivors, it is possible some relevant literature was missed, as our search did not extend to grey literature. The overwhelming majority of studies were cross-sectional, limiting causal inferences, and undertook univariate analyses only, meaning that confounding, mediating and moderating variables could not be explored. Furthermore, many correlates of poorer psychological outcomes have been identified in only single studies, requiring corroboration. The small number of studies relating to some outcomes (e.g. FCR) and the variability in the assessment and reporting of outcomes precluded meta-analysis. Theoretically driven prospective longitudinal studies using validated measures and powerful statistics to explore changes over time, are still required.

Conclusion

The literature to date suggests that many TC survivors, particularly those with substantial treatment side effects and passive coping styles grapple with anxiety and FCR, and would potentially benefit from intervention. Studies evaluating TC-specific prevention and management interventions targeting issues pertinent to this group are needed.

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Conflicts of Interest

The authors have no conflicts of interest to disclose.

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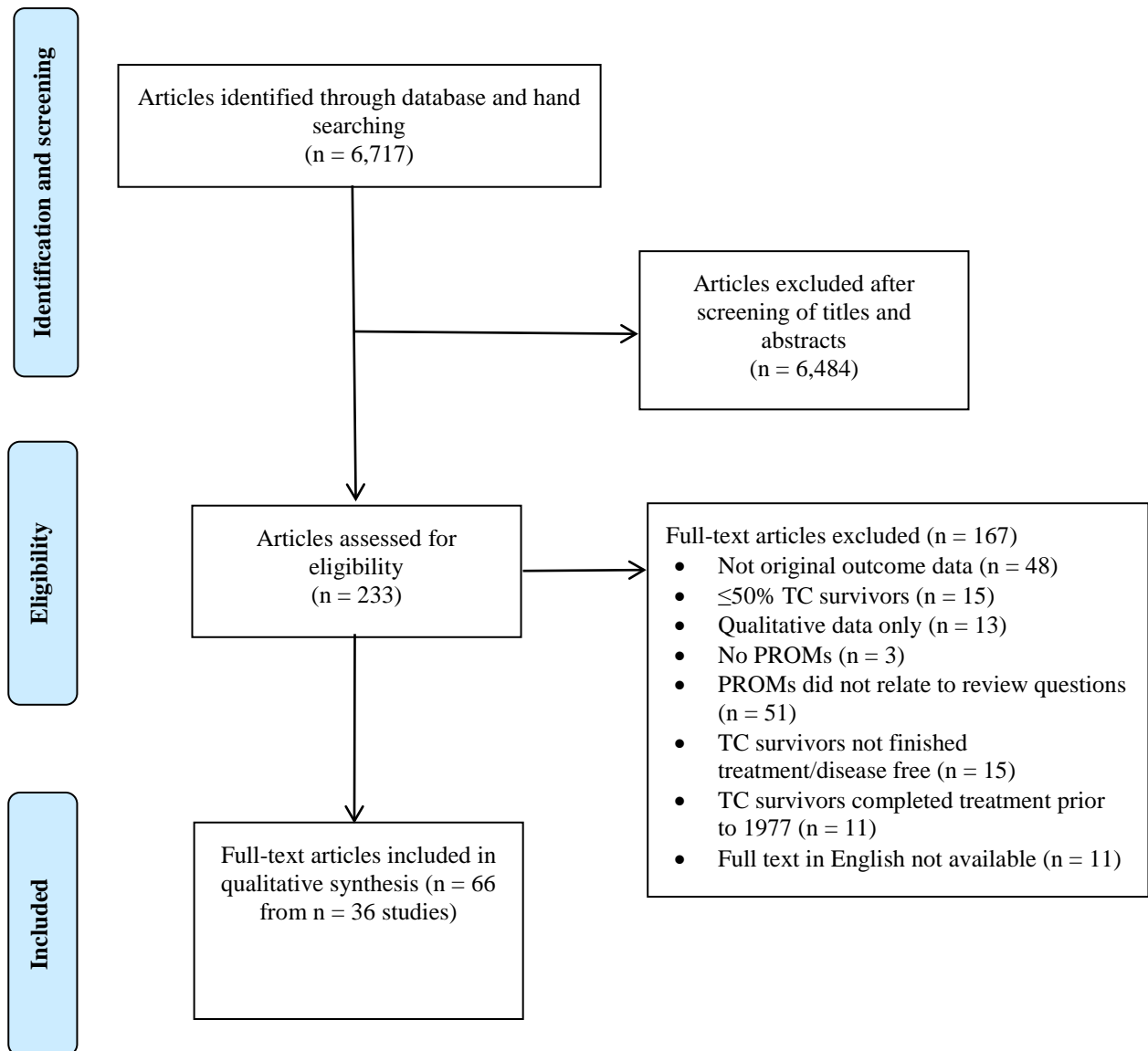
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Figure 1. PRISMA Study Selection Flowchart





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