

Death anxiety interventions in patients with advanced cancer: A systematic review

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Abstract

Background: Death anxiety is a common issue in adult patients with advanced cancer and can have a large impact on quality of life and end-of-life care. Interventions are available to assist but are scarcely used in everyday practice.

Aim: To assess quantitative studies on interventions for adult patients with advanced cancer suffering from death anxiety.

Data sources: MEDLINE, PsycINFO, Embase and CINAHL were searched to identify quantitative or mixed studies on death anxiety or relatable existential intervention studies in advanced cancer patients published from 1990 to December 2016. Two reviewers independently screened titles and abstracts and assessed relevant studies for eligibility. Data were then extracted from included studies for analysis.

Results: Nine unique quantitative studies were identified, including five randomised controlled trials, involving a total overall of 1179 advanced cancer patients. All studies were psychotherapeutic in nature and centred on existential themes such as meaning, dignity, relationships and spiritual well-being. The therapies investigated shared overlapping themes but varied in duration, therapist experience, training required and burden on patient. Heterogeneity of studies and measures prevented determination of an overall effect size.

Conclusion: Interventions were identified for this clinical scenario of death anxiety in patients with advanced cancer. Therapies of short duration incorporating spiritual well-being and those evoking a sense of meaning were claimed to be the most beneficial, despite lacking rigorous statistical analysis. More high-quality studies with tailored outcome measures are required to fully evaluate the most effective interventions for death anxiety in patients with advanced cancer.

Keywords

Palliative care, advanced cancer, death anxiety, systematic review, psychotherapy, qualitative research

What is already known about the topic?

- Death anxiety is a common concern in advanced cancer patients.
- Relief of death anxiety for all patients is a primary goal of palliative medicine.
- Psychotherapeutic interventions are available that may help death anxiety and existential concerns, but few studies have attempted interventions on advanced cancer patients.

What this paper adds?

- Psychological interventions for patients with advanced cancer are being developed and implemented around the world that may improve existential outcomes.
- Updated quantitative tools measuring death anxiety are now available.

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Implications for practice, theory or policy

- More research is needed on all interventions to assist patients with death anxiety and advanced cancer.
- Targeted psychological outcome measures for death anxiety may allow comparison of interventions in future reviews.
- · More research on psychopharmacological agents for death anxiety and existential concerns is now emerging.

Introduction

Death is a universal human concern which has inspired much artistic, philosophic and medical reflection throughout the ages. As individuals, we all live with knowledge of finite lifespans and adapt accordingly. This is particularly salient for those with life-limiting illnesses such as advanced cancer or heart failure, where patients may be forewarned of their impending death by worsening symptomatology as their disease progresses. Such a predicament can trigger existential concerns. Death anxiety is a term used to conceptualise the worry generated by this unique concern of death awareness.

Yalom⁵ saw death anxiety as a primitive, pervasive and deeply held dread of nonexistence, which is found to underpin many mental disorders. Such a basic fear may be at the core of psychiatric disorders such as hypochondriasis, panic, phobias, separation anxiety, post-traumatic stress and even obsessive-compulsive disorders. Its contribution to so many variations of mental illness has led death anxiety to be termed a 'transdiagnostic' construct,⁶ which is basic to any formulation of the differential diagnosis of anxiety, uncertainty and fear of recurrence in palliative care.

The proportion of patients with advanced cancer suffering distressing thoughts around death may approach 80%,7 with associated symptoms of demoralisation, dependency, depression and fears of suffering and mortality.8 Psychooncology researchers describe the difficult challenge of 'double awareness' for palliative care patients, who try to balance two conflicting thought streams: remaining engaged and enjoying what remains of their life, while being aware of their near-certain physical deterioration and death.9 Death anxiety may predispose patients towards a desire for hastened death. When not addressed, death anxiety may lead to requests for euthanasia or physician-assisted suicide. 11

Death anxiety can affect people to varying degrees, depending on factors such as age, health, spiritual beliefs and culture. In recognition of this, scales to measure death anxiety were designed, such as Templer's original work on the 'Death Anxiety Scale' (DAS) in 1970, and the more recently clinically validated 'Death and Dying Distress Scale' (DADDS) from Lo et al. These scales have allowed for further research and evaluation of potential interventions targeted towards those with symptomatic and severe death anxiety. More recent studies have utilised death anxiety scales to trial interventions in advanced cancer patient cohorts, is aiming to improve the following: quality of life, it, it treatment compliance, caregiver distress and appropriate healthcare utilisation.

Relief of death anxiety is now deemed to be a central tenant of palliative medicine.²⁰ Frustratingly, little is known about effective strategies to ameliorate death anxiety,²¹ particularly in the vulnerable group of unwell advanced cancer patients. Interventions, whether they be existential psychotherapy or pharmacotherapy, are difficult to evaluate and scarcely studied.²² This is thought to be due to the large variation and heterogeneity of outcome measures in this field,²³ the previous lack of validated death anxiety scales for terminally ill patients^{24,25} and the inability to blind participants and personnel to psychotherapeutic interventions.²³ Additional concerns have included the potential burden of intervention on patients and families²⁶ and the terminal nature of the cohort, leading to poor retention rates for prolonged interventional studies.²⁷

Previous systematic reviews of existential therapies for suffering²⁸ and general death anxiety¹² have been published, but to our knowledge, no review has been conducted focussing specifically on death anxiety and related existential issues in a palliative cohort with advanced cancer.

Aim

The aim of this systematic review was to identify and evaluate quantitative studies, published since 1990, on interventions for adult patients with advanced cancer suffering from death anxiety and hence inform further research into this difficult but important clinical area.

Methods

A systematic review was conducted and reported according to the checklist of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).²⁹ A patient, problem or population, intervention, comparison, control or comparator, outcome, study design (PICOS) model³⁰ was used to develop our search approach (Table 1). As per National Health and Medical Research Council (NHMRC) guidelines, ethics committee approval was deemed unnecessary,³¹ as the study was a literature review with no direct patient contact.

The study was limited to interventions with quantitative data in the hope of assessing and comparing the potential effect size and significance of any interventions, offering potential for statistical comparison between cohorts. Mixed studies with qualitative and quantitative results were included for review, with only quantitative outcomes examined.

Table 1. PICOS framework^a used to define the search approach.

PICOS element	Definition
Population	Adult patients with advanced (incurable) cancer
Intervention	Any intervention targeting death anxiety or related existential aspects of distress in a systematic fashion
Comparison	Usual care, no intervention or other control population
Outcomes	All outcome measures for death anxiety or related existential aspects of distress
Study design	Any intervention study design which included quantitative measures

PICOS: patient, problem or population, intervention, comparison, control or comparator, outcome, study design.

A preliminary literature search found few relevant studies prior to the year 1990, and relevant journals, such as *Psycho-Oncology*,³² had not been published prior to this time. As such, a comprehensive search of bibliographic databases was initially conducted on 30 September 2016 and updated on 15 December 2016 to identify eligible studies published since 1 January 1990.

Eligibility criteria

The review focused on interventions for death anxiety specific to the cohort of adult patients with advanced cancer. A study was also included for review if it examined a closely related existential theme of death anxiety, such as spirituality, meaning, hope or quality of life.^{25,33,34} For the purposes of this review, cancer was deemed to be 'advanced' if in Stage III or IV or incurable solid organ disease, or poorer prognosis haematological conditions such as high-grade non-Hodgkin's lymphoma (NHL). Interventions of any nature, including pharmacological, psychological, spiritual or existential, were reviewed. For studies with mixed samples that also included non-malignant or early-stage curable cancer patients, it was decided to include these studies if greater than 90% of the cohort had advanced cancer. Inclusion criteria are summarised below, and exclusion reasons are shown in Figure 1.

Study inclusion criteria

- 1. Evaluation of adult patients with advanced (incurable) cancer, at least 90% of cohort;
- Measured 'death anxiety' or closely related existential themes;
- 3. Use of an intervention (psychological or pharmacological), intended to alleviate death anxiety;
- 4. Controlled studies or a pre–post methodology with quantitative reporting;

- Published in a peer-reviewed journal from 1990 onwards;
- English language.

Search strategy

Electronic searching. The search strategy was refined using published search filters^{35–37} and reviewed prior to searching by a professional medical librarian. Databases searched were as follows: MEDLINE, PsycINFO and Embase via OvidSP and CINAHL via EBSCO. Keywords and Medical Subject Headings (MeSH) terms included death anxiety, attitudes to death, neoplasms and psychotherapy. Notable synonyms for 'death anxiety' such as 'mortality salience' or 'terror management theory'³⁸ were also used. Full text and English filters were applied (see Appendix 1 for full search strategies).

Hand-searching. This was performed on the following sources:

- Previous reviews of psychological, spiritual and existential interventions for cancer patients;
- 2. Reference lists of identified studies;
- 3. Studies that cited identified studies;
- 4. Intervention studies published in the journal *Psycho-Oncology*.³²

Data extraction

All titles and abstracts retrieved by the electronic search were downloaded to a reference management database and duplicates were removed.

Titles and abstracts were screened by two researchers (C.H.G. and J.B.) to assess eligibility for inclusion. A third researcher (N.M.) reviewed 10% of selected citations for quality assurance. Full-text articles were retrieved when the information from the abstract was viewed as insufficient for a decision about inclusion. If consensus could not be reached about study inclusion between the researchers, a senior research colleague (D.K.) arbitrated on review of full-text articles. Any disagreements were resolved with full team discussions. Figure 1 outlines search protocol results.

Each included research paper was read, and inclusion was confirmed against eligibility criteria. Intervention details, outcome measures, sample sizes, characteristics of subjects and main findings were identified and recorded.

Quality assessment and risk of bias

Randomised controlled trials (RCTs) were assessed using the seven-item risk of bias developed by the Cochrane Bias Method Group.³⁹ Non-RCT studies were assessed by the Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS).⁴⁰ Criteria included random sequence generation, allocation concealment, blinding of participants and personnel, incomplete outcome data, selective

^aThis framework was developed according to the strategy described by the Centre for Reviews and Dissemination, University of York.³⁰

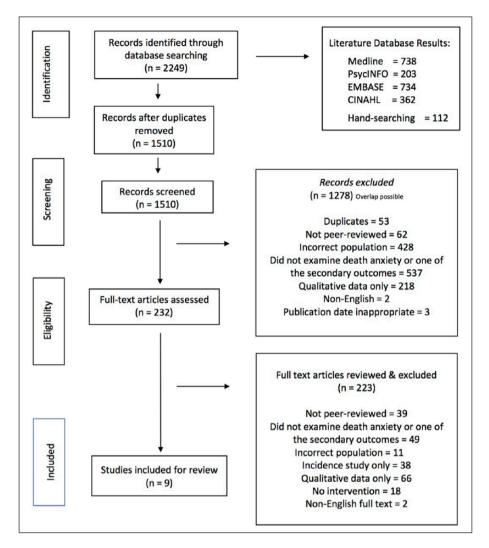


Figure 1. Flow of information through the different phases of this review. Based on recommendation of Moher et al. 29

reporting or other, and each criterion was graded high/unknown or low. On the basis of these ratings, each study was provided with an overall risk of bias.

Analysis

Given the heterogeneity in the types of measures used, we were not able to calculate an overall effect size for outcomes.

Results

Summary of studies

Nine studies satisfied all inclusion criteria, with outcome measures pertaining to death anxiety or related existential aspects in patients with advanced cancer. 15,24,26,27,41-45 Designs, types of interventions, samples and outcomes are summarised in Table 2. A brief description of the

interventions, interventionist and time burden of the interventions is shown in Table 3.

Despite searching for studies from 1990 onwards, the oldest study identified in the review was published in 2003.²⁴ Nearly half of the included studies were published within 5 years of the time of searching. Five studies were RCTs,^{26,42–45} and four involved pretest–posttest methodology.^{15,24,27,41} Seven studies were conducted in Australia, United States or Canada, with two of these studies^{41,42} being multinational. The remaining two studies were conducted in Asia.^{27,43}

The interventions involved 'Life Review', 'Dignity Therapy', 'Meaning-Centred' or 'Meaning-Making' therapy, 'Couples Therapy with Existential Focus' and 'Managing Cancer and Living Meaningfully (CALM)' psychotherapy. 'Supportive Group Therapy' was used as a control for one study and did not have any statistically significant effect on death anxiety or existential distress outcomes.²⁶ The interventions varied in duration from two sessions over 2–3 days, to up to eight sessions over

6 months. The interventions aimed to improve meaning, sense of control over life, spiritual well-being, quality of life, relationships, identity and dignity, addressing mostly existential concerns. Assessed outcomes included death anxiety, spiritual well-being, quality of life, non-specific anxiety, depression, control of symptoms, sense of meaning and existential well-being.

Despite our search terms attempting to identify relevant pharmaceutical interventions, all studies captured described psychological interventions. Three study interventions involved training of nurses in palliative care to respond to patients' existential needs, ^{27,41,42} and these studies were also the least time intensive in terms of their delivery. The majority of studies involved psychologist-led interventions.

Two studies showed improvements in the outcome of death anxiety, using a validated¹⁵ and non-validated measure, respectively.²⁴

Types of intervention

Five studies described meaning-based therapy, ^{15,26,27,44,45} two of which were group interventions. These meaning-based interventions were highly structured and psychoeducational interventions, with detailed manuals, incorporating between two and eight face-to-face sessions. These involved discussing, summarising and assisting clients to act directly and positively in finding meaning in their current life. Most were led by trained psychotherapists, with one study led by trained nurses or other healthcare workers.²⁷

Three studies focused on 'Dignity Therapy' and 'Life Review', 41–43 which similarly aimed to relieve existential distress by inspiring meaning. In contrast to the meaning-based therapies, these interventions aimed to be brief and individualised, 41 which is of particular relevance to terminally ill populations. An edited transcript or album of the session was also returned to the patient as a 'legacy document' that affirms the life lived and can be bequeathed as seen fit, principally to assist family and friends with impending bereavement and inspire discussion. 41

The one remaining study combined meaning therapy and couples' therapy principles, with guided exploration of existential themes and distress.²⁴

Types of outcome

There was large variation in outcome measures used; the most common outcome measure was the Functional Assessment of Chronic Illness Therapy – Spiritual Well-Being (FACIT-Sp) in six studies. Few studies directly used a validated death anxiety measure with only one using the DADDS¹⁵ and another using a Likert scale of death anxiety.²⁴ No study used Templer's DAS or the Death Attitude Profile.⁴⁶ Multiple authors commented on the frustrating nature of attempting to measure death anxiety and existential distress in their cohorts, ^{15,24} with larger

RCTs resorting to the Schedule of Attitudes towards Hastened Death (SAHD),⁴⁴ or non-validated tools such as two-question Likert scales of death anxiety.²⁴

Despite the well-established link between existential concerns and severity of physical symptoms, ⁴⁷ few studies attempted to evaluate physical symptoms. ^{26,41,42,45}

Effects on psychopathology

Five studies (total of 876 participants) examined the impact of interventions on psychopathology and existential suffering, compared with control populations. ^{26,42–45} These RCTs yielded statistically significant improvements in areas such as spiritual well-being and existential distress. Life Review, ⁴³ comprising a mixture of dignity and meaning-centred approaches, showed significant improvement in existential suffering. However, Chochinov's large multinational RCT of dignity therapy ⁴² yielded no significant improvement in existential domains.

Discussion

Only nine studies were found that sought to assuage death anxiety in patients with advanced cancer. The majority of the studies were published in the last 5 years, which suggests that death anxiety is potentially being more widely recognised in recent times. However, this are still a low number of studies given the universality of death anxiety in cancer patients,³⁴ and the relief of existential distress being a specific focus of the 'whole-person approach' in palliative medicine.^{20,48}

Research on death anxiety has been rare. ^{49,50} It has been argued that previous research has been hindered by a lack of a clear, comprehensive definition of death anxiety. ⁵¹ Other reasons hypothesised include difficulties in researching the terminally ill, ⁵² the lack of tailored measurement tools²⁴ and reluctance of researchers to draw attention to death anxiety for fear of harm. ¹

Recent increase in research in this area may be attributed to the resurgence of interest in new validated measures, such as the DADDS in 2015.²⁵ In its design, the DADDS hoped to address the concerns of some potentially irrelevant questions found in older measures, such as Templer's DAS¹³ and Conte's Death Anxiety Questionnaire⁵³, where advanced cancer patients were asked whether they were 'afraid of getting cancer'.²⁵

Intervention themes and design

The development of psychotherapeutic interventions for death anxiety is built on the nature of the existential distress underpinning the problem. Ando et al.⁴³ noted the significant association between desire for hastened death and death anxiety when hopelessness and clinical depression are present and used this as a framework to develop an intervention

Table 2. Des	criptive summa	ary of studies	identified with death	h anxiety–relatable	Descriptive summary of studies identified with death anxiety—relatable outcome measures.			
Author/s	Country	Design	Intervention	Subjects	Outcome tools	Findings	Attrition rate (%)	Risk of bias
Ando et al. ⁴³	Japan	RCT	Short-Term Life Review	68 Terminally ill cancer patients	FACIT-Sp HADS-A HADS-D GDI ECOG-PSR	Significant improvements in spiritual well-being ($p < 0.001$), anxiety and depression ($p < 0.001$), life completion ($p < 0.001$), hope ($p < 0.001$) and existential suffering ($p < 0.001$).	17	High
Breitbart et al. ⁴⁴	USA	RCT	Meaning- Centred Group Psychotherapy	90 Advanced solid organ tumours (Stage III or IV) or NHL	FACIT-Sp BHS SAHD LOT HADS	Significant improvements in spiritual well-being (p =0.0001), meaning (p =0.0001), faith (p =0.006), decreased anxiety (p =0.02) and desire for death (p =0.04).	39	Low
Breitbart et al.²6	USA	RCT	Meaning- Centred Group Psychotherapy	253 Advanced solid organ tumours (Stage III or IV) or NHL	FACIT-Sp BDI HADS-A SAHD MSAS HAI	Significant improvements in quality of life ($\rho < 0.01$), spiritual well-being ($\rho < 0.001$), depression ($\rho < 0.001$), hopelessness ($\rho < 0.001$), desire for hastened death ($\rho < 0.05$) and physical symptom distress ($\rho < 0.001$).	78	Low
Chochinov et al. ⁴¹	Australia, Canada	Pretest—posttest	Dignity Therapy	I 60 Terminally ill patients (97% cancer)	ESAS Single-item screening for depression, dignity, anxiety, suffering, hopefulness, desire for death, suicide and sense of well-being Two-item quality-of-life tool	Significant improvements in suffering $(p=0.023)$ and depressed mood $(p=0.05)$. Non-significant changes favouring improvement in hopelessness, desire for death, anxiety and will to live.	22	High
Chochinov et al. ⁴²	Australia Canada USA	RCT	Dignity Therapy	441 Terminally ill patients (96% cancer)	FACIT-Sp PDI HADS PPI ESAS Will to live visual scale	No significant changes in distress. Significant improvement in quality of life $(p=0.001)$ and dignity $(p=0.002)$.	26	High
Henry et al. ⁴⁵	Canada	RCT	Meaning-Making Intervention	24 Stage III or IV ovarian cancer patients	FACIT-Sp MQOL HADS GSES	Significant improvements in spiritual well-being ($p=0.04$) and support ($p=0.03$). Non-significant trends towards improved quality of life ($p=0.07$) and existential well-being ($p=0.06$).	20	High

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Author/s	Country	Design	Country Design Intervention	Subjects	Outcome tools	Findings	Attrition rate (%)	Risk of bias
Lo et al. ¹⁵	Canada	Pretest- posttest	САГМ	50 Incurable cancer patients	FACIT-Sp DADDS ECR-M16 PTGI PHQ-9	Significant improvements in death anxiety ($p < 0.009$), depressive symptoms ($p < 0.019$) and spiritual wellbeing ($p < 0.017$).	42	High
Mohr et al. ²⁴	USA	Pretest- posttest	Couples Therapy and facilitating discussion around disease and dying	9 patients with incurable cancer and their partners	Death Anxiety and Quality of Life – Likert scale BDI-II Relationship quality	Significant reduction in 'distress about dying' for patient ($p = 0.04$) and reduction in 'worry about dying' for partner ($p = 0.049$). Significant positive relationship outcome for patient ($p = 0.049$).	33	High
Mok et al. ²⁷	Hong Kong	Pretest— posttest	Meaning of Life Intervention	84 Patients with incurable cancer	QOLC-E	Significant reduction in existential distress ($p < 0.05$) and improvement in quality of life ($p < 0.05$).	3	High

Depression subscale of Hospital Anxiety and Depression Scale; GDI: Good Death Inventory; ECOG-PSR: Eastern Cooperative Oncology Group-Performance Status Rating; BHS: Beck Hopelessness Scale; Index; PPI: Palliative Performance Index; GSES: General Self-Efficacy Scale; CALM: Managing Cancer and Living Meaningfully Psychotherapy; DADDS: Death and Dying Distress Scale; ECR-M16; Modified Experiences in Close Relationships; PTGI: Post-Traumatic Growth Inventory; PHQ-9; Patient Health Questionnaire-9; BDI-II: Beck Depression Index-II; QOLC-E: Quality-of-Life Concerns in End-of-Life. SAHD: Schedule of Attitudes towards Hastened Death; LOT: Life Orientation Test; HADS: Hospital Anxiety and Depression Scale; NHL: non-Hodgkin's lymphoma; BDI: Beck Depression Index; MSAS: RCT: randomised controlled trial; FACIT-5p: Functional Assessment of Chronic Illness Therapy – Spiritual Well-Being; HADS-A: Anxiety subscale of Hospital Anxiety and Depression Scale; HADS-D: Memorial Symptom Assessment Scale; HAI: Hopelessness Assessment in Illness Questionnaire; MQOL: McGill Quality of Life Scale; ESAS; Edmonton Symptom Assessment Scale; PDI: Patient Dignity

Table 3. A summary of the interventional therapies used to target existential concerns in patients with advanced cancer.

Author/s	Unit of intervention	Number of sessions and duration	Interventionist/s	Brief description of intervention
Ando et al. ⁴³	Individual	Two sessions, I week apart Duration: 30–60 min	Trained therapist	Semi-structured interview that facilitated discussion about meaning, relationships, memories and guidance for friends or family. Themes were transcribed in an album by the therapist along with visual imagery using photographs or drawings and presented to the patient in the second session.
Breitbart et al. ⁴⁴	Groups (8–10 patients)	Eight weekly sessions Duration: 90 min	Psychiatrist or clinical psychologist	Group-based therapy to enhance meaning, peace and purpose in life. Sessions explore meaning, relationships, impact of cancer on sense of self and placing one's life in a historical and personal context.
Breitbart et al. ²⁶	Groups (8–10 patients)	Eight weekly sessions Duration: 90 min	Psychiatrist or clinical psychologist or social worker	(As above)
Chochinov et al. ⁴¹	Individual	Three to four sessions, each 2–4 days apart Duration: 30–60 min	Psychiatrist, palliative care nurse or psychologist	Guided interview session exploring theme of generativity, self, pride, hope, post-death concerns and relationships. Sessions are transcribed and edited to produce a generativity document to bequeath to family or friends.
Chochinov et al. ⁴²	Individual	Three to four sessions, each 2–4 days apart Duration: 30–60 min	Psychiatrist, palliative care nurse or psychologist	(As above)
Henry et al. ⁴⁵	Individual	One to four sessions Duration: 30–90 min	Psychologist	Session length and number tailored to patient's needs. Review impact and meaning of cancer diagnosis, past significan life events and coping, life priorities going forward.
Lo et al. ¹⁵	Individual	Three to eight sessions over 6 months Duration: 60 min	Social worker or psychiatrist or oncologist	Individual psychotherapy sessions to address domains of symptom control and communication, change in self and relationships, spiritual well-being with meaning and purpose, preparing for the future, sustaining hope and facing mortality
Mohr et al. ²⁴	Couple	Eight weekly sessions Duration: 50–60 min	Psychologist or social worker	Psychotherapy aimed to reduce distress, improve communication and increase intimacy in couples with a terminal patient Assists shifts in meaning and provide support for the family unit, including discussions about assisting children.
Mok et al. ²⁷	Individual	Two sessions over 2–3 days. Duration: 30–60 min (initial) 15–30 min (follow-up)	Nursing staff	Initially a semi-structured interview that facilitated search for meaning. A follow-up session involved providing a written summary of themes from first session. Significant past life events, relationships and maintaining positive attitudes were covered.

for their 'Short-Term Life Review'. Similarly, an Institute of Medicine report identifying spiritual well-being and meaning as some of the most important influences on quality of life and end-of-life care⁵⁴ was quoted by Breitbart et al.⁴⁴ as inspirational for the development of Meaning-Centred Group Therapy. Virtually all therapies explored strategies to

relieve psycho-existential suffering based on themes of dignity, meaning and demoralisation.⁵⁵

In further support of the above, when terminally ill patients were asked to discuss matters important to them, existential themes such as meaning, purpose, relationships and death were recurring.²² Given this, Murata and

Morita³³ proposed a framework to better understand psycho-existential suffering using a theoretical model and 'good death' survey. They saw psycho-existential suffering as pain caused by the extinction of being and meaning of self through loss of relationships with others, loss of autonomy or loss of a proposed future.³³

Most of the studies reviewed employed the domains described by Murata and Morita to ameliorate existential suffering:⁴³

- 1. Maintaining and strengthening relationships;
- 2. Regaining a sense of control;
- 3. Sustaining a sense of continuity of self;
- 4. Decreasing sense of burden to others;
- Generativity documents or discussions with community, friends or family;
- Relief of concern around the dying process;
- 7. Maintaining hope.

Thoughts about death and themes of existential suffering have proven similar in both Eastern⁵⁶ and Western researches,⁵⁷ suggesting universal givens about human nature that cross cultural divides. This is echoed in the interventions by Ando et al.⁴³ and Mok et al.²⁷ in Japan and Hong Kong respectively, which incorporated aspects of Western existential interventions in their design.

Multiple authors commented on the difficulty in designing therapies for such an ill cohort, with the potential for patient deterioration (physical or cognitive), burden of intervention and competing with priorities of patient and family when time is short.^{26,27}

Intervention descriptions

The interventions described in these studies can be broadly grouped into two categories: meaning-based therapy and dignity-based therapy.

Dignity therapy was designed by Chochinov⁵⁸ as a brief, individualised psychotherapeutic intervention specifically to cater to the terminally ill and to engender purpose and sense of self. Promising results were elucidated in the initial pilot in 2005;⁴¹ however, the larger multinational RCT⁴² yielded non-significant primary outcomes, including existential distress markers. Despite this, other therapies based on dignity therapy principles such as Ando's 'Life Review' showed a significant improvement in existential suffering, burden and generalised anxiety in terminally ill cancer patients.⁴³

The larger RCTs of Meaning-Centred Group Psychotherapy^{26,44} (MCGP) by Breitbart et al. contained some of the most promising results of the review. MCGP was designed primarily to address spiritual well-being, sense of meaning and purpose.⁴⁴ Both well-powered RCTs showed significant improvements in desire for hastened death and spiritual well-being as well as physical symptom

distress.^{26,44} Death anxiety itself was not a direct outcome measure for these studies, but given the correlation between death anxiety and each of the above domains,^{10,34} these results are very promising. These studies are also unique in that they are group-orientated.

Mok et al.'s²⁷ 'Meaning of Life Intervention' is noteworthy as the intervention was predominantly led by trained nurses, utilising the most available staffing resource.

To date, CALM psychotherapy was the only intervention shown to significantly decrease death anxiety (p < 0.009) on a validated measure (DADDS) in patients with advanced cancer. ¹⁵ CALM is described as a brief, individualised, semi-structured psychotherapy designed to relieve distress and promote psychological well-being. ¹⁵ Participants also reported significantly reduced depressive symptoms (p < 0.019) and improved spiritual well-being (p < 0.017). ¹⁵ A feasibility study has been completed, ⁵⁹ and a phase III RCT trial is ongoing.

Mohr et al.²⁴ developed two brief questions: 'In the past week, how often have you thought about dying?' and 'When you have these thoughts or worries about dying, how distressed does it make you feel?' graded on a 7-point Likert scale.²⁴ Despite the apparent simplicity of this measure, they were able to show a significant decrease in death anxiety (p < 0.04) in response to their tailored couples therapy.

Quality assessment

Virtually all the included studies had methodological issues. Given these were studies of psychological interventions, blinding of random allocation for the participants and personnel was not possible. As most used a variety of psychological outcome tools, no studies published full breakdowns of their entire results and all reported selective data.

Many studies did not report directly on dropouts, but some had attrition rates of 39%⁴⁴ and 26%.²⁶ Even an RCT with only 24 participants had attrition of 20%.⁴⁵ Death was a key reason for dropout in the included studies. CALM therapy also had considerable attrition, with only 48% of patients available at 3 months and 32% at 6 months, most withdrawing due to deteriorating health or death.¹⁵

Four studies included assessment of patient's physical symptomatology as part of their study designs. ^{26,41,42,45} Only occasionally was comment made about symptoms, with all studies selectively reporting either no outcomes or only significant outcomes. No studies described whether, or how, patients with high symptom scores were treated, for example, offered analgesia for severe pain. Existential distress and physical symptoms are acknowledged as being strongly associated, ^{3,60} with death anxiety being described as a consequence of unresolved psychological and physical distress. ³⁴ Hence, physical symptoms add another confounder and a potential source of bias to studies in this area.

Pharmacotherapy

Despite this review attempting to capture pharmacotherapy as a primary intervention for cancer patients with death anxiety, there was a lack of high-quality studies about this. One study showed promising results with intravenous pharmacotherapy with tricyclic antidepressants to treat distress in the imminently dying, but unfortunately was not significantly powered for more intensive quantitative analysis.⁶¹ Other studies examined terminal sedation for relief of severe death anxiety and existential distress,^{62,63} but given the nature of the intervention involved, there were no outcome tools available for analysis. It is hoped that with greater clinical awareness and better screening tools, patients experiencing death anxiety may be identified earlier and treated proactively.

No studies mention pharmacotherapy as a potential confounding variable in their study designs. Previous research has indicated that treatment of severe depression and death anxiety with pharmacotherapy may be promising.⁶⁴

Indeed, a recent RCT by Ross et al.⁶⁵ of psilocybin (derived from mushrooms) psychopharmacotherapy for patients with advanced disease found promising results with significant improvements in demoralisation, hopelessness and quality of life. However, psilocybin therapy was not associated with decreased death anxiety. This trial was excluded from our review as the cohort contained only 62% advanced cancer patients.⁶⁵

Limitations and recommendations

This review was limited to examining quantitative data from intervention studies focused on existential domains. Study measures may only capture part of the benefits of intervention, given the psychospiritual nature of the work and the subjective benefit that may follow.^{23,66} In future, we recommend that a synthesis of qualitative research and studies of clinical experience be undertaken.⁶⁶

Our review was limited to patients with advanced cancer, whereas death anxiety is also found in patients with early-stage cancers, where 'Cognitive Existential Group Therapy'⁵⁵ and 'Supportive-Affective Group Therapy'⁶⁷ have shown benefits. Similarly, 'Acceptance and Commitment Therapy'⁶⁸ shows much promise, but lay beyond this review as a non-cancer trial.

Further studies may choose to examine death anxiety in paediatric patients, non-malignant patients or caregivers. Caregivers supporting terminal patients with death anxiety are known to potentially be at risk of symptomatic existential concerns themselves.⁶⁹ The cohort of cancer survivors, who may also suffer from death anxiety and fears of relapse, was beyond the scope of this review.⁷⁰

Conclusion

Given the universality and importance of death anxiety and the dearth of studies to date, existential psychotherapies are a promising group of interventions.

It is recommended that the scientific quality of future research be improved with more specific outcome measures, chosen for the aims of an intervention, rather than broad outcome tools recording levels of general psychopathology. With the recent publication of a validated death anxiety measurement for cancer patients, the DADDS,²⁵ hopefully more studies will use similar outcome measures to simplify analysis and enable comparison.

Greater awareness is required of the need to investigate, identify and treat all terminally ill patients who suffer existential issues. Studies discussed above all claimed to be successful in introducing interventions to an unwell population, highlighting that more can certainly be done. With further research, education and training, the ability to offer even the most existentially distressed patients a positive death will hopefully be seen as a challenge rather than an impossibility.

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Appendix I

Search strategies

MEDLINE (OvidSP)

Subject headings: attitude to death, neoplasms, psychotherapy, self-help groups

- exp Attitude to Death/OR (Death Anxiety or Terror Management Theor* or Mortality Salience or Death Depression or Thanatophobia).mp.
- 2. ((attitude* or anx* or terror* or fear* or concern* or worr*) adj4 (death or dying or mortal*)).mp.
- 3. 1 OR 2
- 4. exp Neoplasms/OR (adenocarcinoma* or metasta* or tumo?r or cancer* or oncolog* or malig* or neoplas* or carcinom*).mp.
- 5. 3 AND 4
- 6. exp Psychotherapy/OR Self-Help Groups/OR (psychotherapy or psychol* intervention* or psychosocial intervention* or Health Education or Patient Education or Adaptation or Coping or intervention* or Quantitative or Treatment Outcome or

- Psychometrics or Empirical or assessment or psychopharmacology or screening or validation)).mp.
- 7. 5 AND 6
- 8. limit 7 to (english language and yr='1990–Current')

EMBASE (OvidSP)

Subject headings: attitude to death, neoplasm, psychotherapy, support group

- 1. 'Attitude to Death'/exp OR (Death Anxiety or Terror Management Theor* or Mortality Salience or Death Depression or Thanatophobia).mp.
- 2. ((attitude* or anx* or terror* or fear* or concern* or worr*) adj4 (death or dying or mortal*)).mp.
- 3. 1 OR 2
- 4. 'Neoplasm'/exp OR (adenocarcinoma* or metasta* or tumo?r or cancer* or oncolog* or malig* or neoplas* or carcinom*).mp.
- 5. 3 AND 4
- 6. 'Psychotherapy'/exp OR 'Support Group'/exp OR (psychotherapy or psychol* intervention* or psychosocial intervention* or Health Education or Patient Education or Adaptation or Coping or intervention* or Quantitative or Treatment Outcome or Psychometrics or Empirical or assessment or psychopharmacology or screening or validation).mp.
- 7. 5 AND 6
- 8. limit 7 to (english language and yr = '1990–Current')

CINAHL (EBSCO)

Subject terms: attitude to death, neoplasms, psychotherapy, coping

- 1. (MH 'Attitude to Death+') OR (Death Anxiety or Terror Management Theor* or Mortality Salience or Death Depression or Thanatophobia).mp.
- 2. ((attitude* or anx* or terror* or fear* or concern* or worr*) N4 (death or dying or mortal*)).mp.
- 3. 1 OR 2

- (MH 'Neoplasms+') OR (adenocarcinoma* or metasta* or tumo?r or cancer* or oncolog* or malig* or neoplas* or carcinom*).mp.
- 5. 3 AND 4
- 6. (MH 'Psychotherapy+') OR (MH 'Coping+') OR (psychotherapy or psychol* intervention* or psychosocial intervention* or Health Education or Patient Education or Adaptation or Coping or intervention* or Quantitative or Treatment Outcome or Psychometrics or Empirical or assessment or psychopharmacology or screening or validation).mp.
- 7. 5 AND 6
- 8. Limiters Publication Year: 1990–2016 (current)

PsycINFO (OvidSP)

Subject headings: death anxiety, neoplasms, psychotherapy, coping behaviour, support groups, group intervention

- 1. DE 'Death Anxiety'/Exp OR (Death Anxiety or Terror Management Theor* or Mortality Salience or Death Depression or Thanatophobia).mp.
- ((attitude* or anx* or terror* or fear* or concern* or worr*) adj4 (death or dying or mortal*)).mp.
- 3. 1 OR 2
- DE 'Neoplasms'/Exp OR (adenocarcinoma* or metasta* or tumo?r or cancer* or oncolog* or malig* or neoplas* or carcinom*).mp.
- 5. 3 AND 4
- 6. DE 'Psychotherapy'/Exp OR DE 'Support Groups' OR DE 'Group Intervention' OR DE 'Coping Behaviour' OR (psychotherapy or psychol* intervention* or psychosocial intervention* or Health Education or Patient Education or Adaptation or Coping or intervention* or Quantitative or Treatment Outcome or Psychometrics or Empirical or assessment or psychopharmacology or screening or validation).mp.
- 7. 5 AND 6
- 8. yr='1990-Current'