International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	DEPRESSION AND ANXIETY IN ADVANCED CANCER: DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN PALLIATIVE CARE – A REVIEW
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5573
RECEIVED	14 March 2026
ACCEPTED	23 June 2026
PUBLISHED	30 June 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

DEPRESSION AND ANXIETY IN ADVANCED CANCER: DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN PALLIATIVE CARE – A REVIEW

Anna Wyżykowska *(Corresponding Author, Email: anna.wyzykowskaa@gmail.com)*
J. Gromkowski Regional Specialist Hospital, Wrocław, Poland
ORCID ID: 0009-0003-7351-4221

Monika Maruszak
J. Gromkowski Regional Specialist Hospital, Wrocław, Poland
ORCID ID: 0009-0007-6734-4974

Julia Grygorowicz
J. Gromkowski Regional Specialist Hospital, Wrocław, Poland
ORCID ID: 0009-0006-1646-1938

Michał Niedziela
4. Wojskowy Szpital Kliniczny z Poliklinika, Wrocław, Poland
ORCID ID: 0009-0000-5606-4036

Gabriela Faria
J. Gromkowski Regional Specialist Hospital, Wrocław, Poland
ORCID ID: 0009-0009-0418-8809

Monika Sas-Wyżykowska
Faculty of Medicine, College of Medical Sciences, University of Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0009-8900-7922

Alina Mykhalevych
Lower Silesian Centre for Oncology, Pulmonology and Haematology, Wrocław, Poland
ORCID ID: 0009-0003-6335-2900

Aliaksandr Kryshtofik
Provincial Specialist Hospital in Wrocław, Wrocław, Poland
ORCID ID: 0009-0006-5138-259X

Aleksandra Blachucik
4. Wojskowy Szpital Kliniczny z Poliklinika, Wrocław, Poland
ORCID ID: 0009-0002-6768-0680

ABSTRACT

Psychological distress, including depression and anxiety, represents a major clinical concern in patients with advanced cancer, particularly in palliative care settings, where it is associated with reduced quality of life, increased symptom severity, and impaired adherence to oncological treatment. The diagnosis of these conditions remains challenging due to the overlap between psychiatric and disease-related somatic symptoms, as well as the complex and multidimensional nature of distress in this population.

This review examines key diagnostic challenges and current approaches to pharmacological management of depression and anxiety in advanced cancer, with particular emphasis on palliative care populations. The analysis is based on selected clinical guidelines and relevant clinical studies addressing both diagnostic and therapeutic aspects of care.

Available evidence indicates that standard diagnostic criteria may have limited applicability in medically ill patients, requiring careful clinical interpretation and individualized assessment. Pharmacological treatment remains an important component of care, while symptom-oriented strategies and selected adjunctive agents may provide additional clinical benefit, and rapid-acting therapies represent a promising but still evolving area of research.

Effective management requires a flexible, patient-centered approach that integrates clinical context, symptom profile, and treatment goals. Further research is needed to improve diagnostic strategies and to develop more effective and rapidly acting therapeutic options in palliative care settings.

KEYWORDS

Depression, Anxiety, Advanced Cancer, Palliative Care, Pharmacological Treatment, Diagnostic Challenges

CITATION

Anna Wyżykowska, Monika Maruszak, Julia Grygorowicz, Michał Niedziela, Gabriela Faria, Monika Sas-Wyżykowska, Alina Mykhalevych, Aliaksandr Kryshtofik, Aleksandra Blachucik. (2026). Depression and Anxiety in Advanced Cancer: Diagnostic and Therapeutic Challenges in Palliative Care – A Review. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5573

1. Introduction

Depression and anxiety are among the most common psychiatric comorbidities in patients with cancer and represent a substantial component of overall disease impact, particularly in advanced stages [1–3]. Their presence is associated with reduced quality of life, increased symptom severity, and impaired adherence to oncological treatment, with potential consequences for clinical outcomes [4]. In this population, the identification of depressive and anxiety disorders remains particularly challenging. The clinical presentation of psychological distress is often complex and multidimensional, involving emotional, somatic, and existential components. The overlap between disease-related symptoms and psychiatric manifestations further complicates diagnosis, increasing the risk of both underrecognition and misclassification. In palliative care settings, where symptom intensity is high and disease trajectories are dynamic, these challenges become even more pronounced [3,5]. At the same time, the management of depression and anxiety is complicated by factors such as polypharmacy, comorbidities, and the need for rapid symptom control in patients with limited life expectancy. Pharmacological treatment remains a key component of care, but requires careful individualization and consideration of safety, tolerability, and potential drug-drug interactions. Given these complexities, a focused synthesis of current evidence addressing both diagnostic and therapeutic challenges is needed. This review aims to examine key issues in the diagnosis of depression and anxiety in advanced cancer and to evaluate the role of pharmacological management, including conventional antidepressants, symptom-oriented strategies, and emerging rapid-acting therapies. Non-pharmacological interventions are beyond the scope of this review.

2. Methodology

This study was conducted as a narrative literature review aimed at synthesizing current evidence on the diagnosis and pharmacological management of depression and anxiety in patients with advanced cancer. A structured search of the literature was performed using electronic databases, including PubMed, focusing on peer-reviewed publications addressing epidemiology, diagnostic challenges, and pharmacological treatment in oncology and palliative care settings. Relevant sources included clinical guidelines, systematic reviews, meta-analyses, randomized controlled trials, and observational studies. Priority was given to studies involving patients with advanced cancer and those conducted in palliative care populations. Seminal and conceptually important earlier publications were also included where relevant to diagnostic frameworks or therapeutic approaches. The selected literature was evaluated qualitatively and organized into thematic sections addressing epidemiology, diagnostic complexity, and pharmacological treatment strategies, including conventional antidepressants, symptom-oriented approaches, and emerging rapid-acting therapies.

3. Results

3.1. Epidemiology and clinical significance

Depressive and anxiety symptoms are among the most prevalent psychiatric complications observed across the cancer continuum [1–3]. Estimates from the literature indicate a broad prevalence range for depressive spectrum disorders, approximately 5% to 60%, reflecting significant methodological heterogeneity. Evidence from methodologically rigorous studies further indicates that the prevalence of depression differs markedly across clinical contexts [2,3]. More robust data based on structured psychiatric interviews suggest lower rates in general oncology populations (approximately 5-16% in outpatients and 4-14% in hospitalized patients), with markedly higher prevalence observed in palliative care settings, reaching up to 49% [3]. These findings highlight the critical influence of clinical context, with the highest burden of depressive disorders consistently observed in patients with advanced disease [2,3].

The prevalence of depression and anxiety also differs according to tumour type. Higher rates are reported in patients with lung, gynaecological, breast, and haematological malignancies, whereas lower prevalence is observed in colorectal, prostate, and genitourinary cancer [6,7]. These differences likely reflect variations in prognosis, symptom burden, and treatment intensity across cancer types [2].

Sociodemographic factors further contribute to variability in psychological morbidity. Younger age has been associated with increased risk of depressive symptoms, potentially due to greater disruption of social and occupational roles [6]. Female sex is consistently linked to higher levels of depression and anxiety, mirroring patterns observed in the general population [7]. Additionally, socioeconomic deprivation has been identified as an independent predictor of major depression, suggesting that financial stress, reduced access to resources, and broader social inequalities contribute to increased vulnerability in oncology populations [6].

From a clinical perspective, depression and anxiety significantly impact multiple aspects of cancer care. Psychological distress is associated with poorer quality of life, greater symptom burden, and impaired functional status [1,4]. Furthermore, untreated depression and anxiety may adversely affect treatment adherence and engagement with medical care, with potential implications for clinical outcomes [4]. In advanced cancer, depression and hopelessness are also strongly associated with the desire for hastened death, underscoring the critical importance of timely recognition and management of psychological distress in palliative care settings [5].

3.2. Diagnostic challenges in depression and anxiety in advanced cancer

Limitations of standard diagnostic criteria in oncology populations

The application of standard psychiatric diagnostic criteria to patients with cancer presents significant challenges, as systems such as DSM-5 and ICD-11 were developed in general psychiatric populations and may not fully capture the complexity of psychological distress observed in oncology settings [8,9]. In this population, particularly in advanced disease, emotional, cognitive, and somatic symptoms frequently coexist and interact, complicating the identification of discrete psychiatric disorders [10]. The multidimensional nature of distress, encompassing psychological, physical, and existential components, further limits the applicability of categorical diagnostic frameworks and contributes to both underrecognition and misclassification of depressive and anxiety disorders in oncology and palliative care settings [11].

A major limitation of standard diagnostic criteria in oncology arises from the overlap between somatic symptoms of cancer and those used to define depressive disorders. Fatigue, appetite loss, weight loss, sleep disturbance, and reduced energy are highly prevalent as a direct consequence of cancer or its treatment,

complicating attribution to a primary psychiatric condition [9,10,12]. This overlap is particularly pronounced in advanced disease, where symptom burden is high and multifactorial, reducing the specificity of somatic criteria for depression and anxiety [11,13]. Furthermore, commonly used screening instruments may not adequately distinguish between somatic symptoms related to cancer and those reflecting psychiatric disorders, limiting their diagnostic accuracy in this population [14,15]. Consequently, reliance on symptom-based frameworks may result in both overdiagnosis, when cancer-related symptoms are interpreted as depressive features, and underrecognition, when psychological distress is attributed solely to the underlying medical condition [9,11]. These limitations support the need for adapted diagnostic approaches in oncology, with greater emphasis placed on affective and cognitive symptoms rather than somatic criteria [12].

Differential diagnosis of depression in advanced cancer

Differential diagnosis of depression in patients with advanced cancer represents a critical component of psychiatric assessment in palliative care, as a wide range of psychological responses may mimic depressive disorders. Individuals facing a life-limiting illness commonly experience sadness, fear, uncertainty, and emotional distress, which may constitute proportionate reactions to disease rather than a distinct psychiatric condition [9]. The high prevalence of multidimensional distress, encompassing affective, cognitive, and existential components, further complicates differentiation between adaptive responses and clinically significant depressive syndromes [13,16]. Consequently, accurate distinction is essential, as misclassification may lead to inappropriate management and suboptimal patient care [11].

A central diagnostic challenge lies in distinguishing major depressive disorder from adjustment disorder and normative emotional responses. Emotional reactions such as sadness, anxiety, irritability, or transient hopelessness are common following diagnosis or disease progression and may be clinically appropriate [17]. In contrast, depression is characterized by persistent and pervasive mood disturbance, including anhedonia, feelings of worthlessness or excessive guilt, and sustained hopelessness disproportionate to the clinical context [9]. Adjustment disorder occupies an intermediate position, with symptoms arising in response to identifiable stressors without fulfilling criteria for major depression. In oncology populations, these distinctions are frequently blurred due to ongoing disease-related stress, uncertain prognosis, and cumulative psychological burden [10,11]. This ambiguity is further compounded in palliative care, where emotional states fluctuate over time and are influenced by symptom burden and functional decline, necessitating longitudinal clinical assessment [18].

Differentiation between depression and existential distress, including demoralization, constitutes an additional key challenge in advanced cancer. Demoralization is characterized by helplessness, loss of meaning, and perceived inability to cope, while preserving emotional reactivity and lacking the pervasive anhedonia typical of major depressive disorder [19]. Existential concerns such as fear of death, loss of autonomy, and disruption of identity are highly prevalent in advanced illness and may resemble depressive symptomatology [16,20]. Although both conditions are associated with significant distress, their underlying mechanisms and therapeutic implications differ. Misinterpretation of existential distress as depression may lead to inappropriate pharmacological treatment, whereas such patients may benefit more from psychotherapeutic or meaning-centered interventions [19,21].

Screening tools for depression and anxiety in oncology

Recognition of depressive and anxiety symptoms in patients with cancer remains a significant clinical challenge, as a substantial proportion of cases are not identified in routine oncological practice [22,23]. Even when clinically relevant distress is present, it may remain undetected, particularly in settings focused primarily on somatic disease management [23]. This underrecognition is compounded by the nonspecific presentation of symptoms, where emotional distress overlaps with cancer-related physical manifestations such as fatigue, sleep disturbance, or appetite changes [24], as well as by time constraints and the lack of systematic assessment strategies in clinical practice [25]. Consequently, structured screening approaches have been recommended to improve detection and facilitate timely referral for further evaluation [25]. However, screening tools should be considered adjunctive rather than diagnostic instruments, and their results must be interpreted within the broader clinical and psychosocial context [26]. These range from ultra-brief case-finding approaches to structured questionnaires and measures developed specifically for individuals with advanced malignancy. Ultra-brief screening tools, including two-question approaches, are used as initial case-finding strategies in oncology and palliative care and demonstrate high sensitivity but lower specificity, supporting their role in identifying individuals requiring further assessment [14,27].

Among structured instruments, the Hospital Anxiety and Depression Scale (HADS) is widely used in oncological settings and was designed to minimize the confounding influence of somatic symptoms by

focusing on psychological and cognitive domains [28]. It enables simultaneous assessment of anxiety and depression and demonstrates acceptable diagnostic accuracy, including sensitivity and specificity, in this population [15].

The Patient Health Questionnaire-9 (PHQ-9), based on DSM criteria, provides a standardized measure of depressive symptom severity and is widely used for both screening and monitoring symptom intensity over time [15]. Its alignment with diagnostic criteria may facilitate communication between oncology and mental health services and support structured follow-up. However, the inclusion of somatic items may complicate interpretation in patients with advanced disease [29].

In palliative care, multidimensional instruments such as the Edmonton Symptom Assessment System (ESAS) are frequently used to assess both physical and psychological symptoms [30]. This approach enables ongoing monitoring of symptom burden and allows evaluation of psychological distress within the broader context of physical illness [31], which is particularly relevant in patients requiring repeated assessments over time.

Additionally, methods specifically developed for oncology populations, such as the Brief Edinburgh Depression Scale (BEDS), have been designed to minimize the influence of somatic symptoms by focusing on cognitive and affective features of depression [32]. As a brief, patient-reported screening tool, BEDS may be particularly useful in clinical situations where high physical symptom burden complicates the interpretation of standard screening measures [33].

From a clinical perspective, screening instruments are most effective when integrated into structured diagnostic pathways rather than used in isolation. Despite their practicality, they demonstrate reduced diagnostic accuracy when applied as standalone measures [27]. A stepwise approach, involving initial screening followed by targeted clinical assessment in individuals with positive findings, improves identification of clinically significant psychological distress while maintaining feasibility in routine oncology and palliative care practice [25]. Interpretation of screening results is complicated by overlapping somatic and psychological symptoms, particularly in advanced disease [29,33], while variability in diagnostic performance across instruments, including differences in sensitivity, specificity, and optimal cutoff thresholds, further limits comparability and generalizability of findings [34]. Additionally, feasibility and acceptability may be influenced by patient condition and clinical context, especially in palliative care settings [35,36].

3.3. Pharmacological management of depression and anxiety in advanced cancer

General principles of pharmacological treatment in palliative care

Pharmacological management is a central component in the treatment of depression and anxiety in patients with advanced cancer. It is particularly relevant in cases of moderate to severe symptoms or when psychological distress significantly interferes with quality of life and clinical outcomes [37]. Untreated or inadequately managed symptoms are associated with increased symptom burden, reduced adherence to oncological treatment, and poorer overall functioning, underscoring the importance of timely intervention [38]. This approach is inherently complex due to the coexistence of advanced somatic illness, high prevalence of polypharmacy, and increased susceptibility to adverse effects and drug-drug interactions. In addition, the clinical presentation of depression and anxiety is influenced by disease-related factors such as pain, fatigue, and cachexia, which may affect both treatment selection and therapeutic response [39]. Importantly, the delayed onset of action of many antidepressants represents a critical consideration in palliative care, where life expectancy may be limited and rapid symptom control is often required [40]. This has led to increasing interest in both conventional antidepressants and alternative strategies with faster onset of action, particularly in patients with severe distress or acute clinical deterioration [41]. Treatment should therefore be individualized and patient-centered, taking into account symptom profile, prognosis, comorbidities, potential interactions, and patient preferences [39,42]. Pharmacotherapy is generally indicated in moderate to severe depression or clinically significant anxiety, particularly when non-pharmacological interventions are insufficient [38]. Selection of an appropriate agent requires careful consideration of clinical factors, including prognosis, comorbidities, concomitant medications, and potential drug-drug interactions [39]. In oncology populations, where polypharmacy is common, particular attention must be paid to interactions with anticancer therapies and supportive medications, which may influence both the efficacy and safety of psychotropic agents [39,43]. An additional consideration is the pharmacokinetic and pharmacodynamic profile of antidepressant and anxiolytic agents, including onset of action, tolerability, and route of administration, especially in patients with impaired functional status [41]. Agents with faster onset may be preferred in situations requiring urgent symptom relief [40]. A symptom-oriented approach is particularly relevant in palliative care, as certain pharmacological agents

may provide additional benefits such as analgesia, anxiolysis, sedation, or appetite stimulation [43]. Regular monitoring of treatment response and adverse effects remains essential, with therapeutic adjustments guided by clinical response, tolerability, and changes in the patient's condition over time [41]. Close collaboration between oncology, psychiatry, and palliative care teams is crucial to ensure safe and effective management of depression and anxiety in patients with advanced cancer [42]

Conventional antidepressants

Conventional antidepressants, including selective serotonin reuptake inhibitors (SSRIs) and serotonin-noradrenaline reuptake inhibitors (SNRIs), remain the most commonly used pharmacological options for the treatment of depression in patients with advanced cancer, although the overall evidence base remains limited and methodologically heterogeneous [40,44]. SSRIs are generally considered first-line pharmacological agents due to their favourable tolerability profile and relative safety in medically ill populations [43]. Among SSRIs, agents such as fluoxetine and paroxetine have been evaluated in randomized studies, with available data suggesting potential benefit in reducing depressive symptoms [40,44]. Importantly, head-to-head comparisons have not demonstrated clear superiority of SSRIs over other antidepressant classes, including tricyclic antidepressants (TCAs), reflecting limitations of the evidence base rather than equivalence of efficacy [44]. From a clinical perspective, SSRIs may be considered when a conventional antidepressant strategy is feasible and when a delayed onset of action is acceptable [40,43]. Evidence for SNRIs in oncology remains limited and is largely based primarily on studies of individual agents rather than the class as a whole [41]. Duloxetine has demonstrated efficacy in reducing cancer-related neuropathic pain in randomized and observational studies, including in patients with refractory symptoms, with effects consistent with its pharmacological action on descending serotonergic and noradrenergic inhibitory pathways [45–47]. Accordingly, in clinical practice, SNRIs may be considered in patients with advanced cancer in whom depressive symptoms coexist with neuropathic pain, although the evidence supporting this approach is driven primarily by analgesic rather than antidepressant outcomes in cancer-specific studies [43]. The use of conventional antidepressants requires careful consideration of potential drug-drug interactions, particularly in oncology populations receiving complex systemic treatment. Reviews of pharmacotherapy in cancer have specifically highlighted interactions between paroxetine and tamoxifen through CYP2D6 inhibition, as well as other drugs affecting serotonin pathways [37,43]. Moreover, the safety profile of SNRIs also requires careful consideration in palliative care populations. Studies in oncology indicate that noradrenergic effects may contribute to increases in blood pressure, while serotonergic adverse effects overlap with those observed for SSRIs and include gastrointestinal symptoms, sleep disturbances, and hyponatraemia [41]. In addition, duloxetine has been associated with potential hepatotoxicity, and venlafaxine with dose-dependent hypertension and discontinuation symptoms [43]. For this reason, the choice of an SSRI or SNRI in advanced cancer should be individualized, with careful attention to concomitant anticancer treatment, expected survival, and the overall burden of adverse effects and interactions [43].

Symptom-oriented and adjunctive pharmacotherapy

Mirtazapine represents a pharmacological option in oncology and palliative care distinguished by its noradrenergic and specific serotonergic mechanism of action, as well as its clinically relevant sedative and appetite-stimulating properties [48]. It has been described as particularly useful in individuals with coexisting insomnia, anorexia, or cachexia, as its pharmacodynamic profile may address multiple symptom domains simultaneously [49]. Clinical studies in oncology populations indicate that mirtazapine is associated with significant reductions in depressive and anxiety symptoms, as reflected by improvements in total HADS scores and corresponding subscales [50]. Its use in advanced disease is further illustrated in palliative care settings, where it may serve as a baseline antidepressant, often requiring augmentation to achieve more rapid symptom control due to delayed onset of action [51]. This reflects the clinical reality in which conventional antidepressants, including mirtazapine, may require augmentation due to delayed onset of action in patients with limited life expectancy [51]. Although these features support its clinical utility in symptom-oriented management, the overall evidence for mirtazapine in cancer-related populations remains limited and heterogeneous, highlighting the need for further randomized controlled trials [48].

Other antidepressants, including trazodone and bupropion, have a more limited and context-dependent role in oncology and palliative care compared with SSRIs, SNRIs, and TCAs, with their use largely guided by predominant clinical features rather than strong disease-specific antidepressant evidence [38,52]. In this setting, trazodone is used mainly as a symptom-oriented agent for insomnia and anxiety, with clinical data indicating improvement in sleep in patients with advanced malignancy, particularly in cases refractory to standard hypnotics [53,54]. Bupropion has been investigated mainly in relation to fatigue and mood disturbances, with

preliminary studies suggesting potential benefits in energy levels, depressive features, and quality of life, although available evidence is limited and largely based on non-randomized data [55]. Their role in palliative care is nevertheless constrained by tolerability concerns, especially anticholinergic adverse effects, sedation, orthostatic hypotension, and cardiac toxicity, which are particularly relevant in medically fragile patients with advanced cancer [43]. Overall, these agents may be considered in selected clinical scenarios, such as sleep disturbances or adjustment-related distress for trazodone and fatigue-dominant presentations for bupropion - but their application in advanced disease is constrained by limited oncology-specific evidence and considerations related to tolerability [38,43,52].

Benzodiazepines are widely used in palliative oncology for the management of acute anxiety, particularly when associated with insomnia, agitation, or dyspnoea, although their use is largely based on clinical practice rather than high-quality randomized evidence [56,57]. Observational data indicate that anxiety is highly prevalent in palliative care settings, and these agents are frequently prescribed, especially in individuals with a high symptom burden [58]. Despite their widespread use, evidence supporting benzodiazepines for anxiety in palliative care remains limited, with no randomized controlled trials meeting inclusion criteria identified in systematic reviews [56]. Clinical response appears variable, and some individuals may require alternative or adjunctive approaches [59]. From a practical perspective, benzodiazepines may be appropriate in selected situations requiring rapid anxiolysis or short-term symptom control. They are commonly used as adjuncts in the management of dyspnoea [60] and may also be beneficial in agitation associated with delirium, as demonstrated in a randomized trial in which lorazepam combined with haloperidol resulted in greater reduction in agitation compared with haloperidol alone [61]. However, their use is limited by adverse effects, including sedation, cognitive impairment, and increased risk of falls, particularly in frail patients [56,58]. Consequently, benzodiazepines should be regarded as short-term, symptom-oriented interventions in carefully selected cases rather than first-line treatment for anxiety disorders in palliative care [56,57].

Rapid-acting and emerging therapies

Methylphenidate has been investigated in oncology and palliative care as a pharmacological option for depressive symptoms, fatigue, and apathy, particularly in advanced disease. Its dopaminergic and noradrenergic mechanism has been associated with improvements in energy, motivation, and mood in medically ill populations [62]. Clinical evidence suggests that it can provide relatively rapid improvement in depressive symptoms when used as an adjunct to antidepressant therapy [51]. Nevertheless, data regarding its effectiveness in cancer-related fatigue remain inconsistent, with more recent randomized evidence failing to demonstrate superiority over placebo [63–65]. In clinical practice, methylphenidate may be considered in selected patients with advanced cancer, particularly when depressive symptoms are accompanied by apathy or low energy and when a more rapid therapeutic effect is desirable. At the same time, treatment requires careful monitoring, as adverse effects such as insomnia, agitation, and cardiovascular stimulation can limit tolerability in frail patients [62].

Ketamine has emerged as a rapid-acting pharmacological intervention investigated in oncology and palliative care for the management of depressive symptoms, anxiety, and acute psychological distress, particularly when the delayed onset of conventional antidepressants limits their clinical utility [66,67]. Randomized clinical data support its short-term efficacy in selected clinical settings. In patients with cancer, a single subanesthetic ketamine infusion has been associated with a significant reduction in suicidal ideation compared with midazolam, with effects evident as early as the first day following administration [68]. Additional evidence from palliative care suggests potential benefits in symptom control. In a retrospective pilot study, S-ketamine administration was associated with a reduction in anxiety symptoms [69]. Qualitative and mixed-methods data further indicate improvements in subjective well-being and emotional state, although these findings remain exploratory [70]. Despite these encouraging observations, the evidence base remains constrained by methodological heterogeneity, small sample sizes, short-term outcomes, and variability in dosing, administration, and patient selection, limiting both interpretation and generalizability [66,67]. Clinically, safety considerations are essential, as ketamine may be associated with transient dissociative or psychotomimetic symptoms and hemodynamic changes, necessitating careful monitoring and appropriate patient selection [68,69].

Psychedelic-assisted therapies, particularly those involving psilocybin, have been investigated in oncology and palliative care as novel approaches for the treatment of depression, anxiety, and existential distress in patients with life-threatening illness, although their use remains experimental and confined to controlled clinical settings [71,72]. These interventions appear to target not only affective symptoms but also

broader dimensions of psychological suffering, including demoralization, fear of death, and loss of meaning [72]. Clinical trials provide some of the most robust data in this field. In a randomized, double-blind study involving patients with life-threatening cancer, psilocybin administration was associated with substantial and sustained reductions in symptoms of depression and anxiety, with clinically significant improvements persisting for several months following a single treatment session [73]. Broader analyses of serotonergic hallucinogens support these findings, indicating rapid and durable improvements in mood and anxiety when administered within structured therapeutic frameworks [74]. Systematic reviews further emphasize that psychedelic-assisted therapy differs fundamentally from conventional pharmacotherapy, as its effects are closely linked to the therapeutic setting, psychological support, and the subjective experience induced by the substance [71]. This integrated model, combining pharmacological and psychotherapeutic elements, may contribute to improvements in psychological well-being that extend beyond symptom reduction alone [72]. However, the available evidence is derived from small, highly selected populations and controlled settings, and, together with regulatory and practical constraints, limit generalizability to routine clinical practice [71,72,74]. Accordingly, these therapies remain investigational and require further large-scale studies.

4. Conclusion

The findings of this review highlight the complexity of diagnosing and managing depression and anxiety in patients with advanced cancer, where psychological distress is closely intertwined with somatic and disease-related factors. Across the analyzed literature, no single diagnostic or therapeutic approach has been shown to be consistently effective in this population, underscoring the need for clinically nuanced assessment and individualized treatment strategies.

Pharmacological interventions remain a central component of care. However, their effectiveness is often constrained by delayed onset of action, tolerability issues, and the clinical realities of advanced disease. Symptom-oriented and adjunctive approaches may provide additional benefit in selected cases, while emerging rapid-acting therapies represent a promising but still evolving area of research.

These observations emphasize the importance of integrating psychiatric expertise into palliative and oncological care, with a focus on flexible, patient-centered decision-making. Further research is needed to refine diagnostic frameworks applicable to medically ill populations and to develop therapeutic strategies that address both the complexity and urgency of psychological symptoms in advanced cancer.

Conflicts of Interest: The authors declare no conflict of interest.

REFERENCES

1. Grassi, L., Caruso, R., Riba, M. B., Lloyd-Williams, M., Kissane, D., Rodin, G., McFarland, D., Campos-Ródenas, R., Zachariae, R., Santini, D., & Ripamonti, C. I. (2023). Anxiety and depression in adult cancer patients: ESMO clinical practice guideline. *ESMO Open, 8*(2), 101155. https://doi.org/10.1016/j.esmoop.2023.101155
2. Caruso, R., Nanni, M. G., Riba, M., Sabato, S., Mitchell, A. J., Croce, E., & Grassi, L. (2017). Depressive spectrum disorders in cancer: Prevalence, risk factors and screening for depression: A critical review. *Acta Oncologica, 56*(2), 146–155. https://doi.org/10.1080/0284186X.2016.1266090
3. Walker, J., Holm Hansen, C., Martin, P., Sawhney, A., Thekkumpurath, P., Beale, C., Symeonides, S., Wall, L., Murray, G., & Sharpe, M. (2013). Prevalence of depression in adults with cancer: A systematic review. *Annals of Oncology, 24*(4), 895–900. https://doi.org/10.1093/annonc/mds575
4. Andersen, B. L., DeRubeis, R. J., Berman, B. S., Gruman, J., Champion, V. L., Massie, M. J., Holland, J. C., Partridge, A. H., Bak, K., Somerfield, M. R., & Rowland, J. H. (2014). Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: An American Society of Clinical Oncology guideline adaptation. *Journal of Clinical Oncology, 32*(15), 1605–1619. https://doi.org/10.1200/JCO.2013.52.4611
5. Rodin, G., Lo, C., Mikulincer, M., Donner, A., Gagliese, L., & Zimmermann, C. (2009). Pathways to distress: The multiple determinants of depression, hopelessness, and the desire for hastened death in metastatic cancer patients. *Social Science & Medicine, 68*(3), 562–569. https://doi.org/10.1016/j.socscimed.2008.10.037
6. Walker, J., Hansen, C. H., Martin, P., Symeonides, S., Ramessur, R., Murray, G., & Sharpe, M. (2014). Prevalence, associations, and adequacy of treatment of major depression in patients with cancer: A cross-sectional analysis of routinely collected clinical data. *The Lancet Psychiatry, 1*(5), 343–350. https://doi.org/10.1016/S2215-0366(14)70313-X
7. Linden, W., Vodermaier, A., MacKenzie, R., & Greig, D. (2012). Anxiety and depression after cancer diagnosis: Prevalence rates by cancer type, gender, and age. *Journal of Affective Disorders, 141*(2–3), 343–351. https://doi.org/10.1016/j.jad.2012.03.025

8. First, M. B., Gaebel, W., Maj, M., Stein, D. J., Kogan, C. S., Saunders, J. B., Poznyak, V. B., Gureje, O., Lewis-Fernández, R., Maercker, A., Brewin, C. R., Cloitre, M., Claudino, A., Pike, K. M., Baird, G., Skuse, D., Krueger, R. B., Burke, J. D., Lochman, J. E., & Reed, G. M. (2021). An organization- and category-level comparison of diagnostic requirements for mental disorders in ICD-11 and DSM-5. *World Psychiatry*, 34–51. https://doi.org/10.1002/wps.20825
9. Caruso, R., Nanni, M. G., Riba, M. B., Sabato, S., & Grassi, L. (2017). Depressive spectrum disorders in cancer: Diagnostic issues and intervention. A critical review. *Current Psychiatry Reports, 19*(6). https://doi.org/10.1007/s11920-017-0785-7
10. Mattsson, S., Olsson, E. M. G., Carlsson, M., & Johansson, B. B. K. (2019). Identification of anxiety and depression symptoms in patients with cancer: Comparison between short and long web-based questionnaires. *Journal of Medical Internet Research, 21*(4). https://doi.org/10.2196/11387
11. Keller, M., Sommerfeldt, S., Fischer, C., Knight, L., Riesbeck, M., Löwe, B., Herfarth, C., & Lehnert, T. (2004). Recognition of distress and psychiatric morbidity in cancer patients: A multi-method approach. *Annals of Oncology, 15*(8), 1243–1249. https://doi.org/10.1093/annonc/mdh318
12. Butow, P., Price, M. A., Shaw, J. M., Turner, J., Clayton, J. M., Grimison, P., Rankin, N., & Kirsten, L. (2015). Clinical pathway for the screening, assessment and management of anxiety and depression in adult cancer patients: Australian guidelines. *Psycho-Oncology, 24*(9), 987–1001. https://doi.org/10.1002/pon.3920
13. Niedzwiedz, C. L., Knifton, L., Robb, K. A., Katikireddi, S. V., & Smith, D. J. (2019). Depression and anxiety among people living with and beyond cancer: A growing clinical and research priority. *BMC Cancer, 19*(1). https://doi.org/10.1186/s12885-019-6181-4
14. Whooley, M. A., Avins, A. L., Miranda, J., & Browner, W. S. (1997). Case-finding instruments for depression: Two questions are as good as many. *Journal of General Internal Medicine*. https://doi.org/10.1046/j.1525-1497.1997.00076.x
15. Hartung, T. J., Friedrich, M., Johansen, C., Wittchen, H. U., Faller, H., Koch, U., Brähler, E., Härter, M., Keller, M., Schulz, H., Wegscheider, K., Weis, J., & Mehnert, A. (2017). The Hospital Anxiety and Depression Scale (HADS) and the 9-item Patient Health Questionnaire (PHQ-9) as screening instruments for depression in patients with cancer. *Cancer, 123*(21), 4236–4243. https://doi.org/10.1002/cncr.30846
16. Emanuel, L. L., Solomon, S., Chochinov, H. M., Delgado Guay, M. O., Handzo, G., Hauser, J., Kittelson, S., O'Mahony, S., Quest, T. E., Rabow, M. W., Schoppee, T. M., Wilkie, D. J., Yao, Y., & Fitchett, G. (2023). Death anxiety and correlates in cancer patients receiving palliative care. *Journal of Palliative Medicine, 26*(2), 235–243. https://doi.org/10.1089/jpm.2022.0052
17. Bonanno, G. A., & Malgaroli, M. (2020). Trajectories of grief: Comparing symptoms from the DSM-5 and ICD-11 diagnoses. *Depression and Anxiety, 37*(1), 17–25. https://doi.org/10.1002/da.22902
18. Zebrack, B., Kayser, K., Sundstrom, L., Savas, S. A., Henrickson, C., Acquati, C., & Tamas, R. L. (2015). Psychosocial distress screening implementation in cancer care: An analysis of adherence, responsiveness, and acceptability. *Journal of Clinical Oncology, 33*(10), 1165–1170. https://doi.org/10.1200/JCO.2014.57.4020
19. Robinson, S., Kissane, D. W., Brooker, J., & Burney, S. (2015). A systematic review of the demoralization syndrome in individuals with progressive disease and cancer: A decade of research. *Journal of Pain and Symptom Management, 49*(3), 595–610. https://doi.org/10.1016/j.jpainsymman.2014.07.008
20. Grossman, C. H., Brooker, J., Michael, N., & Kissane, D. (2018). Death anxiety interventions in patients with advanced cancer: A systematic review. *Palliative Medicine, 32*(1), 172–184. https://doi.org/10.1177/0269216317722123
21. Nowels, M. A., Kalra, S., Duberstein, P. R., Coakley, E., Saraiya, B., George, L., & Kozlov, E. (2023). Palliative care interventions effects on psychological distress: A systematic review & meta-analysis. *Journal of Pain and Symptom Management, 65*(6), e691–e713. https://doi.org/10.1016/j.jpainsymman.2023.02.001
22. Kissane, D. W. (2014). Unrecognised and untreated depression in cancer care. *The Lancet Psychiatry, 1*(5), 320–321. https://doi.org/10.1016/S2215-0366(14)70345-1
23. Passik, S., Dugan, W., McDonald, M. V., Rosenfeld, B., Theobald, D. E., & Edgerton, S. (1998). Oncologists' recognition of depression in their patients with cancer. *Journal of Clinical Oncology, 16*, 1594–1600. https://doi.org/10.1200/JCO.1998.16.4.1594
24. Caruso, R., Nanni, M. G., Riba, M. B., Sabato, S., & Grassi, L. (2017). The burden of psychosocial morbidity related to cancer: Patient and family issues. *International Review of Psychiatry, 29*(5), 389–402. https://doi.org/10.1080/09540261.2017.1288090
25. McCarter, K., Britton, B., Baker, A. L., Halpin, S. A., Beck, A. K., Carter, G., Wratten, C., Bauer, J., Forbes, E., Booth, D., & Wolfenden, L. (2018). Interventions to improve screening and appropriate referral of patients with cancer for psychosocial distress: Systematic review. *BMJ Open, 8*(1). https://doi.org/10.1136/bmjopen-2017-017959
26. Mitchell, A. J., Meader, N., Davies, E., Clover, K., Carter, G. L., Loscalzo, M. J., Linden, W., Grassi, L., Johansen, C., Carlson, L. E., & Zabora, J. (2012). Meta-analysis of screening and case finding tools for depression in cancer: Evidence based recommendations for clinical practice on behalf of the Depression in Cancer Care consensus group. *Journal of Affective Disorders, 140*(2), 149–160. https://doi.org/10.1016/j.jad.2011.12.043
27. Mitchell, A. J. (2008). Are one or two simple questions sufficient to detect depression in cancer and palliative care? A Bayesian meta-analysis. *British Journal of Cancer, 98*(12), 1934–1943. https://doi.org/10.1038/sj.bjc.6604396

28. Vodermaier, A., & Millman, R. D. (2011). Accuracy of the Hospital Anxiety and Depression Scale as a screening tool in cancer patients: A systematic review and meta-analysis. *Supportive Care in Cancer, 19*(12), 1899–1908. https://doi.org/10.1007/s00520-011-1251-4
29. Mitchell, A. J., Lord, K., & Symonds, P. (2012). Which symptoms are indicative of DSMIV depression in cancer settings? An analysis of the diagnostic significance of somatic and non-somatic symptoms. *Journal of Affective Disorders, 138*(1–2), 137–148. https://doi.org/10.1016/j.jad.2011.11.009
30. Bruera, E., Kuehn, N., Miller, M. J., & Macmillan, K. (1991). The Edmonton Symptom Assessment System (ESAS): A simple method for the assessment of palliative care patients. *Journal of Palliative Care, 7*(2), 6–9.
31. Solar, S., Wieditz, J., Lordick, F., Mehnert-Theuerkauf, A., Oechsle, K., van Oorschot, B., Thomas, M., Asendorf, T., Nauck, F., & Alt-Epping, B. (2023). Screening versus multidimensional assessment of symptoms and psychosocial distress in cancer patients from the time of incurability. *Frontiers in Oncology, 13*. https://doi.org/10.3389/fonc.2023.1002499
32. Lloyd-Williams, M., Shiels, C., & Dowrick, C. (2007). The development of the Brief Edinburgh Depression Scale (BEDS) to screen for depression in patients with advanced cancer. *Journal of Affective Disorders, 99*(1–3), 259–264. https://doi.org/10.1016/j.jad.2006.09.015
33. Rayner, L., Lee, W., Price, A., Monroe, B., Sykes, N., Hansford, P., Higginson, I. J., & Hotopf, M. (2011). The clinical epidemiology of depression in palliative care and the predictive value of somatic symptoms: Cross-sectional survey with four-week follow-up. *Palliative Medicine, 25*(3), 229–241. https://doi.org/10.1177/0269216310387458
34. Lloyd-Williams, M., Dennis, M., & Taylor, F. (2004). A prospective study to compare three depression screening tools in patients who are terminally ill. *General Hospital Psychiatry, 26*(5), 384–389. https://doi.org/10.1016/j.genhosppsych.2004.04.002
35. Mitchell, A. J., Kaar, S., Coggan, C., & Herdman, J. (2008). Acceptability of common screening methods used to detect distress and related mood disorders: Preferences of cancer specialists and non-specialists. *Psycho-Oncology, 17*(3), 226–236. https://doi.org/10.1002/pon.1228
36. Le Fevre, P., Hospital, R. E., Terrace, M., & Devereux, J. (1999). Screening for psychiatric illness in the palliative care inpatient setting: A comparison between the Hospital Anxiety and Depression Scale and the General Health Questionnaire-12. *Palliative Medicine, 13*, 399–407. https://doi.org/10.1191/026921699671260095
37. Grassi, L., Nanni, M. G., Uchitomi, Y., & Riba, M. (2010). Pharmacotherapy of depression in people with cancer. In D. W. Kissane, M. Maj, & N. Sartorius (Eds.), *Depression and cancer* (pp. 151–167). https://doi.org/10.1002/9780470972533.ch7
38. Rane, P. B., Sambamoorthi, U., & Madhavan, S. (2013). Depression treatment in individuals with cancer: A comparative analysis with cardio-metabolic conditions. *Health Psychology Research, 1*(1), 2. https://doi.org/10.4081/hpr.2013.e2
39. Caruso, R., Grassi, L., Nanni, M. G., & Riba, M. (2013). Psychopharmacology in psycho-oncology. *Current Psychiatry Reports, 15*(9). https://doi.org/10.1007/s11920-013-0393-0
40. Riblet, N., Larson, R., Watts, B. V., & Holtzheimer, P. (2014). Reevaluating the role of antidepressants in cancer-related depression: A systematic review and meta-analysis. *General Hospital Psychiatry, 36*(5), 466–473. https://doi.org/10.1016/j.genhosppsych.2014.05.010
41. Grassi, L., Caruso, R., Hammelef, K., Nanni, M. G., & Riba, M. (2014). Efficacy and safety of pharmacotherapy in cancer-related psychiatric disorders across the trajectory of cancer care: A review. *International Review of Psychiatry, 26*(1), 44–62. https://doi.org/10.3109/09540261.2013.842542
42. Rayner, L., Price, A., Hotopf, M., & Higginson, I. J. (2011). The development of evidence-based European guidelines on the management of depression in palliative cancer care. *European Journal of Cancer, 47*(5), 702–712. https://doi.org/10.1016/j.ejca.2010.11.027
43. Grassi, L., Nanni, M. G., Rodin, G., Li, M., & Caruso, R. (2018). The use of antidepressants in oncology: A review and practical tips for oncologists. *Annals of Oncology, 29*(1), 101–111. https://doi.org/10.1093/annonc/mdx526
44. Vita, G., Compri, B., Matcham, F., Barbui, C., & Ostuzzi, G. (2023). Antidepressants for the treatment of depression in people with cancer. *Cochrane Database of Systematic Reviews, 2023*(3). https://doi.org/10.1002/14651858.CD011006.pub4
45. Obata, H. (2017). Analgesic mechanisms of antidepressants for neuropathic pain. *International Journal of Molecular Sciences, 18*(11). https://doi.org/10.3390/ijms18112483
46. Matsuoka, H., Makimura, C., Koyama, A., Otsuka, M., Okamoto, W., Fujisaka, Y., Kaneda, H., Tsurutani, J., & Nakagawa, K. (2012). Pilot study of duloxetine for cancer patients with neuropathic pain non-responsive to pregabalin. *Anticancer Research, 32*, 1805–1810. https://pubmed.ncbi.nlm.nih.gov/22593465/
47. Matsuoka, H., Iwase, S., Miyaji, T., Kawaguchi, T., Ariyoshi, K., Oyamada, S., Satomi, E., Ishiki, H., Hasuo, H., Sakuma, H., Tokoro, A., Shinomiya, T., Otani, H., Ohtake, Y., Tsukuura, H., Matsumoto, Y., Hasegawa, Y., Kataoka, Y., Otsuka, M., & Yamaguchi, T. (2019). Additive duloxetine for cancer-related neuropathic pain nonresponsive or intolerant to opioid-pregabalin therapy: A randomized controlled trial (JORTC-PAL08). *Journal of Pain and Symptom Management, 58*(4), 645–653. https://doi.org/10.1016/j.jpainsymman.2019.06.020

48. Economos, G., Lovell, N., Johnston, A., & Higginson, I. J. (2020). What is the evidence for mirtazapine in treating cancer-related symptomatology? A systematic review. *Supportive Care in Cancer, 28*(4), 1597–1606. https://doi.org/10.1007/s00520-019-05229-7
49. Imai, H., Kaira, K., & Kagamu, H. (2025). Clinical significance of mirtazapine for anorexia in patients with non-small cell lung cancer. *Journal of Thoracic Disease, 17*(5), 3478–3483. https://doi.org/10.21037/jtd-2024-2225
50. Cankurtaran, E. S., Ozalp, E., Soygur, H., Akbiyik, D. I., Turhan, L., & Alkis, N. (2008). Mirtazapine improves sleep and lowers anxiety and depression in cancer patients: Superiority over imipramine. *Supportive Care in Cancer, 16*(11), 1291–1298. https://doi.org/10.1007/s00520-008-0425-1
51. Ng, C. G., Boks, M. P. M., Roes, K. C. B., Zainal, N. Z., Sulaiman, A. H., Tan, S. B., & De Wit, N. J. (2014). Rapid response to methylphenidate as an add-on therapy to mirtazapine in the treatment of major depressive disorder in terminally ill cancer patients: A four-week, randomized, double-blinded, placebo-controlled study. *European Neuropsychopharmacology, 24*(4), 491–498. https://doi.org/10.1016/j.euroneuro.2014.01.016
52. Price, A., & Hotopf, M. (2009). The treatment of depression in patients with advanced cancer undergoing palliative care. *Current Opinion in Supportive and Palliative Care, 3*(1), 61–66. https://doi.org/10.1097/SPC.0b013e328325d17a
53. Davis, M. P. (2007). Does trazodone have a role in palliating symptoms? *Supportive Care in Cancer, 15*(2), 221–224. https://doi.org/10.1007/s00520-006-0111-0
54. Tanimukai, H., Murai, T., Okazaki, N., Matsuda, Y., Okamoto, Y., Kabeshita, Y., Ohno, Y., & Tsuneto, S. (2013). An observational study of insomnia and nightmare treated with trazodone in patients with advanced cancer. *American Journal of Hospice and Palliative Medicine, 30*(4), 359–362. https://doi.org/10.1177/1049909112452334
55. Moss, E. L., Simpson, J. S. A., Pelletier, G., & Forsyth, P. (2006). An open-label study of the effects of bupropion SR on fatigue, depression and quality of life of mixed-site cancer patients and their partners. *Psycho-Oncology, 15*(3), 259–267. https://doi.org/10.1002/pon.952
56. Salt, S., Mulvaney, C. A., & Preston, N. J. (2017). Drug therapy for symptoms associated with anxiety in adult palliative care patients. *Cochrane Database of Systematic Reviews, 2017*(5). https://doi.org/10.1002/14651858.CD004596.pub3
57. Bausewein, C., Simon, S. T., Pralong, A., Radbruch, L., Nauck, F., & Voltz, R. (2015). Palliativmedizinische Behandlung von erwachsenen Krebspatienten. *Deutsches Ärzteblatt International, 112*(50), 863–870. https://doi.org/10.3238/arztebl.2015.0863
58. Mercadante, S., Adile, C., Ferrera, P., Masedu, F., Valenti, M., & Aielli, F. (2017). Sleep disturbances in advanced cancer patients admitted to a supportive/palliative care unit. *Supportive Care in Cancer, 25*(4), 1301–1306. https://doi.org/10.1007/s00520-016-3524-4
59. Sakamoto, R., & Koyama, A. (2020). Effective therapy against severe anxiety caused by cancer: A case report and review of the literature. *Cureus*. https://doi.org/10.7759/cureus.8414
60. Matsuda, Y., Matsunuma, R., Suzuki, K., Mori, M., Watanabe, H., & Yamaguchi, T. (2020). Benzodiazepines for cancer dyspnoea: A nationwide survey of palliative care physicians. *BMJ Supportive & Palliative Care, 10*(2), 205–208. https://doi.org/10.1136/bmjspcare-2019-001997
61. Hui, D., Frisbee-Hume, S., Wilson, A., Dibaj, S. S., Nguyen, T., De La Cruz, M., Walker, P., Zhukovsky, D. S., Delgado-Guay, M., Vidal, M., Epner, D., Reddy, A., Tanco, K., Williams, J., Hall, S., Liu, D., Hess, K., Amin, S., Breitbart, W., & Bruera, E. (2017). Effect of lorazepam with haloperidol vs haloperidol alone on agitated delirium in patients with advanced cancer receiving palliative care: A randomized clinical trial. *JAMA, 318*(11), 1047–1056. https://doi.org/10.1001/jama.2017.11468
62. Hardy, S. E. (2009). Methylphenidate for the treatment of depressive symptoms, including fatigue and apathy, in medically ill older adults and terminally ill adults. *American Journal of Geriatric Pharmacotherapy, 7*(1), 34–59. https://doi.org/10.1016/j.amjopharm.2009.02.006
63. Chin-Yee, N., Yennurajalingam, S., & Zimmermann, C. (2024). Putting methylphenidate for cancer-related fatigue to rest? *Journal of Clinical Oncology, 42*(20), 2363–2366. https://doi.org/10.1200/JCO.24.00707
64. Sullivan, D. R., Mongoue-Tchokote, S., Mori, M., Goy, E., & Ganzini, L. (2017). Randomized, double-blind, placebo-controlled study of methylphenidate for the treatment of depression in SSRI-treated cancer patients receiving palliative care. *Psycho-Oncology, 26*(11), 1763–1769. https://doi.org/10.1002/pon.4220
65. Stone, P., Minton, O., Richardson, A., Buckle, P., Enayat, Z. E., Marston, L., & Freemantle, N. (2025). Methylphenidate versus placebo for fatigue in patients with advanced cancer: The MePFAC randomised controlled trial. *Health Technology Assessment, 29*(36). https://doi.org/10.3310/GJPS6321
66. Garcia, G. T., & Sarin, L. M. (2023). Efficacy and safety of ketamine for the treatment of depressive symptoms in palliative care: A systematic review. *Brazilian Journal of Psychiatry*, 182–195. https://doi.org/10.47626/1516-4446-2022-2876
67. Goldman, N., Frankenthaler, M., & Klepacz, L. (2019). The efficacy of ketamine in the palliative care setting: A comprehensive review of the literature. *Journal of Palliative Medicine, 22*(9), 1154–1161. https://doi.org/10.1089/jpm.2018.0627

68. Fan, W., Yang, H., Sun, Y., Zhang, J., Li, G., Zheng, Y., & Liu, Y. (2017). Ketamine rapidly relieves acute suicidal ideation in cancer patients: A randomized controlled clinical trial. *Oncotarget, 8*(2), 2356–2360. https://doi.org/10.18632/oncotarget.13743
69. Falk, E., Schlieper, D., Van Caster, P., Lutterbeck, M. J., Schwartz, J., Cordes, J., Grau, I., Kienbaum, P., & Neukirchen, M. (2020). A rapid positive influence of S-ketamine on the anxiety of patients in palliative care: A retrospective pilot study. *BMC Palliative Care, 19*(1). https://doi.org/10.1186/s12904-019-0499-1
70. Sumner, R. L., Chacko, E., McMillan, R., Spriggs, M. J., Anderson, C., Chen, J., French, A., Jung, S. H., Rajan, A., Malpas, G., Hay, J., Ponton, R., Muthukumaraswamy, S. D., & Sundram, F. (2021). A qualitative and quantitative account of patient's experiences of ketamine and its antidepressant properties. *Journal of Psychopharmacology, 35*(8), 946–961. https://doi.org/10.1177/0269881121998321
71. Schimmel, N., Breeksema, J. J., Smith-Apeldoorn, S. Y., Veraart, J., van den Brink, W., & Schoevers, R. A. (2022). Psychedelics for the treatment of depression, anxiety, and existential distress in patients with a terminal illness: A systematic review. *Psychopharmacology, 239*(1), 15–33. https://doi.org/10.1007/s00213-021-06027-y
72. Rosenbaum, D., Boyle, A. B., Rosenblum, A. M., Ziai, S., & Chasen, M. R. (2019). Psychedelics for psychological and existential distress in palliative and cancer care. *Current Oncology, 26*(4), 225–226. https://doi.org/10.3747/co.26.5009
73. Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., Cosimano, M. P., & Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of Psychopharmacology, 30*(12), 1181–1197. https://doi.org/10.1177/0269881116675513
74. Reiche, S., Hermle, L., Gutwinski, S., Jungaberle, H., Gasser, P., & Majić, T. (2018). Serotonergic hallucinogens in the treatment of anxiety and depression in patients suffering from a life-threatening disease: A systematic review. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 81*, 1–10. https://doi.org/10.1016/j.pnpbp.2017.09.012