Recent trends in the management of depression in persons with cancer

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Purpose of review
Depression is a prevalent comorbidity in cancer that significantly increases the risk for numerous negative health outcomes. This review updates the current evidence base for management of depression in cancer, highlighting new research directions based on the inflammatory hypothesis of depression.

Recent findings
Research on pharmacotherapy and psychotherapy for depression in cancer has shown mixed efficacy partly because of methodological issues arising from the phenomenology of depression in cancer. After decades of stagnancy, more recent high-quality clinical trials are beginning to provide an evidence base to guide treatment. Inflammatory cytokine-associated depression is a subtype of depression that may have particular relevance in cancer, opening new avenues to explore therapeutic targets and biobehavioral impacts of interventions, which may improve cancer outcomes.

Summary
The continuum of severity in cancer-related depression is important to consider in management approaches. Choice of treatment should be personalized to the patient and their symptom profile as there is currently insufficient evidence to recommend any particular medication or psychotherapy over another. Psychological interventions should be considered first line for mild-to-moderate depression, and pharmacological treatment added for more severe depression, which can be optimally delivered within a collaborative care model.

Video abstract
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Keywords
cancer, cytokines, depression, pharmacotherapy, psychotherapy

INTRODUCTION

Depression is a common comorbidity in patients with cancer throughout the disease trajectory, requiring treatment both because of the psychological burden that it imposes and its association with numerous negative cancer outcomes. There is limited but growing research evidence to guide treatment for depression in cancer. Expanding research on the inflammatory hypothesis of depression [1] may unearth pathways to develop much needed new treatments for cancer-related depression. The wide range of current pharmacological and psychological treatments for depression should be tailored to the individual and cancer-related needs of the patient. Collaborative care models, which can include support provided by mental health specialists and the front-line oncology team, may enhance the effectiveness of depression interventions in cancer.

PREVALENCE AND CLINICAL SIGNIFICANCE

Cancer is among the most significant global public health challenges, with the number of new cases projected to surpass 27 million by 2040 [2]. Survival rates across many common cancers have improved because of advances in diagnosis and treatment [3], suggesting that people with cancer are living longer,

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KEY POINTS

- Cancer-related depression may have an inflammatory basis, mediated by immune system activation from both psychological and physical stress.
- A nuanced biobehavioural understanding of cytokine associations with depression may lead to more effective psychological and pharmacological interventions for depression in cancer, which may also improve cancer outcomes.
- Psychological interventions should be considered first line for mild-to-moderate depression, and pharmacological treatment added for more severe depression, optimally delivered within a collaborative care model.
- Future work to improve treatment of depression in cancer should focus on better understanding the inflammatory pathways underlying ICAD and high-quality RCTs to strengthen the evidence-base using existing treatments.

albeit with the burden of disease. Across the disease trajectory, patients with cancer experience significant psychosocial challenges, including functional impairment, existential distress, and in some cases, anxiety and mood disorders. Mood-related symptoms in cancer range in severity from nonpathological sadness and grief at one end of the continuum, with subthreshold depression in the middle, and major depression at the other end.

Depression rates in cancer vary across studies, depending on disease and demographic factors (e.g. tumour site, stage, age, sex) and study methodology (e.g. clinician interview versus self-rating scale, diagnostic cut-scores, timing of assessment), but are two to three times higher than in the general population [4–6]. Meta-analytic estimates suggest that the prevalence for major depressive disorder in cancer is 14.9% [7]. However, subthreshold presentations, categorized as minor depression, adjustment disorder or persistent depressive disorder, are even more common. Estimates based on self-report tools capturing subclinical symptoms found pooled prevalence estimates of up to 24% [5].

Both major and subthreshold depression have been linked to significant impairment in wellbeing and quality of life [8,9], greater physical symptoms [10], longer hospital stays and increased readmissions [11,12], delays in treatment and diagnosis [13], nonadherence to medical regimens [14], and disease progression and increased mortality [15▪,16,17]. Psychosocial and pharmacological intervention in individuals with cancer may be associated with decreased recurrence or slower disease progression, presumably through immune-related changes [18,19]. Impacts of depression treatment on cancer-related mortality have been variable [20], with stronger evidence of survival benefits in patients with early-stage disease [21,22].

PHENOMENOLOGY AND AETIOLOGY

Despite the burden of depression in oncological populations, it remains underdiagnosed and undertreated in medical settings [23]. Providers experience difficulty differentiating between nonpathological sadness and depression, as well as the somatic symptom overlap between depression and cancer. Primary depression, or depression arising from no known cause, may be phenomenologically similar to – but distinct from – cancer-related depression. The neurovegetative features of depression (i.e. psychomotor slowing, weight loss, sleep disturbance, cognitive difficulties) are both more prevalent in cancer-related depression and challenging to disentangle from symptoms resulting from cancer or its treatment [24]. The core psychological symptoms of depression, which include excessive guilt or feelings of failure and worthlessness, are less frequently observed in cancer-related depression [7]. Moreover, the desire to hasten death from demoralization in cancer populations [25–27] can be difficult to distinguish from depressive suicidality. These distinctions may reflect etiological differences between primary and cancer-related depression.

The development and maintenance of depression in cancer is multifactorial, resulting from the interaction of multiple psychosocial, iatrogenic, and biological factors [9,23,28]. The risk factors for primary depression, including female gender, family or individual history of depression, social isolation, and maladaptive coping strategies, are also seen in cancer-related depression. Cancer-specific risk factors include poor communication with health providers, particular cancer types (e.g. pancreatic and head and neck cancers [6,29]), severity of pain and physical symptoms, and proximity to death [9,30]. Unlike primary depression, research has found an absence of sex differences in the prevalence of depression in advanced cancer [31], suggesting that medical factors may overwhelm gender effects in cancer. Due to these distinctions from primary depression, cancer-related depression is posited to have an inflammatory basis, mediated by immune system activation [32▪,33].

Meta-analyses and reviews support the presence of elevated inflammatory biomarkers among patients with primary depression, although there is substantial heterogeneity partly related to the absence of a clear inflammatory stimulus in this

population [34–36]. One possibility is that only a subset of primary depression has an inflammatory basis. A recent meta-analysis of 44 studies demonstrated that individuals who respond to antidepressant treatment had lower baseline interleukin 8 (IL-8) levels and significant declines in TNF-α levels after treatment [37]. Some studies have also suggested that antidepressants have anti-inflammatory properties [38], as evidenced by the recent association between antidepressant use and reduced risk of intubation or death in patients hospitalized for coronavirus disease 2019 (COVID-19) infection [39▪].

Inflammatory cytokine-associated depression (ICAD) has been conceptualized as a subtype of depression, marked by more neurovegetative and fewer core psychological symptoms [40]. Inflammation can cause lassitude, fatigue, pain, and hypersensitivity to pain, typically considered 'sickness behaviours' [41,42], which may lead to depression characterized by more persistent symptoms, decreased motivation, and poorer treatment response [43–45]. This pathophysiology likely contributes to the treatment-resistant nature of depression in cancer [46].

INFLAMMATION AND DEPRESSION IN CANCER

ICAD occurs in patients undergoing cytokine-based cancer treatments, as seen in up to 50% of patients with melanoma or renal cell carcinoma treated with interferon (IFN)-alpha [47,48]. Cancer presents a clear inflammatory stimulus in the form of tumour cell burden, infection, or treatment-induced tissue destruction. Psychological stress has also been invoked in the inflammation–depression relationship in cancer [49]. There have been at least 16 studies in cancer populations identifying associations between depression and inflammatory cytokines, such as IL-10, IL-8, IL-6, IL-4, TNF-α, and C-reactive protein (CRP) [32▪,50–52]. Depression has long been speculated to precede a pancreatic cancer, the idea later strengthened by the association of both conditions with IL-6 [53,54]. However, recent evidence suggests that IL-6 more strongly predicts sickness behaviours heralding a pancreatic cancer diagnosis rather than depression [52,55▪].

The discovery of such associations has inspired biobehavioural research in psychoneuroimmunology, focusing on the impact of stress (e.g. depression) on cancer and progression. Emerging preclinical and clinical work has demonstrated the impact of chronic stress on impairing protective immunity in tumour-infiltrating lymphocytes, tumour-associated macrophages, and stromal cells in the tumour microenvironment through inflammatory pathways [18]. A nuanced biobehavioural understanding of cytokine associations with depression will be required to develop better psychological and pharmacological interventions for depression in cancer, which may also improve cancer outcomes [52,56].

EVIDENCE-BASED TREATMENT

Despite over 35 years of psychosocial oncology research, there has been a surprising paucity of research to guide the treatment of depression in patients with cancer. Systematic reviews over the last decade have identified few high-quality clinical trials and multiple meta-analyses have been unable to conclude the superiority of any specific treatment [57,58]. Tables 1 and 2 provide a narrative review synthesizing the recent evidence regarding efficacy of depression treatment according to GRADE guidelines, which consider the direction and strength of recommendations based on the strength of trial evidence, as well as risks, generalizability, and resource use [59].

Currently available antidepressants achieve remission of primary depression in fewer than 40% of patients [60], as also reflected in the recent Cochrane systematic review of pharmacotherapy for depression in cancer [61]. This review identified only 10 randomized controlled trials (RCTs) for depression to 2017, with meta-analyses demonstrating no significant effect of antidepressants above placebo (SMD = −0.45 [95% confidence interval – CI −1.01 to −0.11]). When restricted to threshold depression, a meta-analysis of five placebo-controlled trials to 2015 found modest benefit in the treatment groups (SMD = −0.58 [95% CI −1.09 to −0.07]) [58].

More recent trials are beginning to demonstrate efficacy of pharmacotherapy (Table 1), but few are placebo-controlled or designed with depression as the primary outcome. Strikingly, there is no high-quality evidence for the efficacy of antidepressants in cancer; consequently, clinical practice is largely extrapolated from treatment of primary depression. Stimulants, oft-proposed as acute antidepressants in palliative care, are more likely improving the sickness behaviour of fatigue rather than depression. Stimulants have not demonstrated efficacy for depression in meta-analyses of patients with cancer-related fatigue [62]. Barriers to this research in cancer include difficulties recruiting highly burdened patients to placebo-controlled trials for medications that are already in widespread clinical use.

Compared with pharmacotherapy trials, there have been considerably more psychological

Table 1. Pharmacologic efficacy in reducing depression among patients with cancer

Medications	Trials		[a]Depression severity	Recommendation GRADE
	Positive	**Negative**		
Antidepressants				
Fluoxetine	Holland *et al.* [63]	Razavi *et al.* [64]	Threshold	Strong recommendation moderate quality
	Navari *et al.* [65]; Pirzadeh *et al.* [66]		Subthreshold	
Citalopram	Nikbakhsh *et al.* [67]		Threshold	Strong recommendation low quality
	Capozzo *et al.* [68]		Subthreshold	
Bupropion	Salehifar *et al.* [69]	Nunez *et al.* [70]; Ashrafi *et al.* [71]	Subthreshold	Strong recommendation low quality
Escitalopram	Rodriguez Vega *et al.* [72]; Biglia *et al.* [73]		Threshold	Strong recommendation low quality
Duloxetine	Torta *et al.* [74]; Biglia *et al.* [73]		Threshold	Strong recommendation very low quality
Mirtazapine	Ersoy *et al.* [75]; Kim *et al.* [76]; Cankurtaran *et al.* [77]; Ng *et al.* [78]		Threshold	Strong recommendation very low quality
	Theobald *et al.* [79]		Subthreshold	
Sertraline	Torta *et al.* [80]; Schillani *et al.* [81]; Li *et al.* [82]		Threshold	Strong recommendation very low quality
Venlafaxine	Bovero *et al.* [83]		Threshold	Strong recommendation very low quality
	Walker *et al.* [84]	Boekhout *et al.* [85]	Subthreshold	
Mianserin	Costa *et al.* [86]; van Heeringen [87]		Threshold	Weak recommendation moderate quality
Paroxetine	Pezzella *et al.* [88]	Musselman *et al.* [89]	Threshold	Weak recommendation moderate quality
	Morrow *et al.* [90]		Subthreshold	
Amitriptyline	Pezzella *et al.* [88]		Threshold	Weak recommendation low quality
	Di and Xu [91]		Subthreshold	
Desipramine	Holland *et al.* [63]	Musselman *et al.* [89]	Threshold	Weak recommendation low quality
Reboxetine	Grassi *et al.* [92]		Threshold	Weak recommendation very low quality
Stimulants				
Methylphenidate	Homsi *et al.* [93]; Ng *et al.* [78]	Sullivan *et al.* [94]	Threshold	Weak recommendation low quality
	Olin and Masand [95]	Butler *et al.* [96]; Centeno *et al.* [97]; Bruera *et al.* [98]	Subthreshold	
Modafinil	Lundorff *et al.* [99]	Jean-Pierre *et al.* [100]; Boele *et al.* [101]; Spathis *et al.* [102]; Conley *et al.* [103]	Subthreshold	Weak recommendation very low quality
Mazindol		Bruera *et al.* [104]	Subthreshold	Weak recommendation Insufficient evidence
Anti-inflammatory agents				
Prednisone	Bruera *et al.* [105]		Subthreshold	Weak recommendation low quality
Celecoxib	Alamdarsaravi *et al.* [196]		Threshold	Weak recommendation low quality

A narrative review of select studies updating an earlier version by Li *et al.* 2012 [30] using GRADE recommendations [59] is presented.
[a]Threshold depression severity denotes either study eligibility criteria including diagnosed major depression, reporting of subgroups with major depression or scoring above a validated cut-score for significant depressive symptoms on a depression-rating scale.

intervention studies. These studies have been similarly hampered by difficulties establishing appropriate control groups in a population with both depression and cancer as well as the presence of strong placebo effects in control groups. The effectiveness of psychotherapies in alleviating depression in cancer has yielded mixed findings because of the heterogeneity in modality of therapy and treatment

Table 2. Psychological efficacy in reducing depression among patients with cancer

Disease status	Trials		[a]Depression Severity	Recommendation GRADE
	Positive	Negative		
Mindfulness or relaxation-based stress reduction				
Newly diagnosed/postsurgery	Henderson *et al.* [112]; Wurtzen *et al.* [113]; Gudenkauf *et al.* [114]; Shao *et al.* [115]	Janusek 2019 [116]	Subthreshold	Strong recommendation moderate quality
Mixed sample		Bränström *et al.* [117]	Subthreshold	Weak recommendation low quality
Undergoing treatment		Loi *et al.* [118]	Threshold	Weak recommendation high quality
		Hoogland *et al.* [119]	Subthreshold	
Posttreatment or survivorship		Sarenmalm *et al.* [120]	Threshold	
		Bower *et al.* [121]; Cramer *et al.* [122]; Lengacher *et al.* [123]; Ho *et al.* [124]; Johannsen *et al.* [125]	Subthreshold	Weak recommendation high quality
Metastatic or advanced	Mosher *et al.* [121]; Milbury *et al.* [127]		Subthreshold	Weak recommendation low quality
Psychoeducation or self-management				
Newly diagnosed/postsurgery	McArdle *et al.* [128]	Gudenkauf *et al.* [114]; Stevenson *et al.* [129]	Threshold	
	Rawl *et al.* [130]; Bredal *et al.* [131]; Lally *et al.* [132]		Subthreshold	Strong recommendation low quality
Undergoing treatment	Schofield *et al.* [133]	Halkett *et al.* [134]; Badr *et al.* [135]	Subthreshold	Strong recommendation moderate quality
Mixed sample		Dieng *et al.* [136]	Subthreshold	No evidence of efficacy
Posttreatment or survivorship	Ashing and Rosales [137]; Willems *et al.* [138]; McCusker *et al.* [139▪]	Johns *et al.* [140]	Subthreshold	Strong recommendation high quality
Metastatic or advanced	Mosher *et al.* [126]; Greer *et al.* [141]		Threshold	Weak recommendation very low quality
Cognitive behavioural therapies				
Newly diagnosed/postsurgery	Nezu *et al.* [142]		Threshold	Strong recommendation moderate quality
	Gudenkauf *et al.* [114]		Subthreshold	
Undergoing treatment	Evans and Connis [143]; Kangas *et al.* [144]		Threshold	Strong recommendation moderate quality
	Zhang *et al.* [145]		Subthreshold	
Posttreatment or survivorship	Qiu *et al.* [146]		Threshold	Strong recommendation high quality
	Stagl *et al.* [147]; Peoples *et al.* [148]; Fenlon *et al.* [149]		Subthreshold	
Mixed sample	Hopko *et al.* [150]; Watson *et al.* [151]		Subthreshold	Strong recommendation high quality

Table 2 (*Continued*)

Disease status	Trials: Positive	Trials: Negative	[a]Depression Severity	Recommendation GRADE
Metastatic or advanced	Savard *et al.* [152]	Serfaty *et al.* [153▪▪]	Threshold	Weak recommendation high quality
	Yanez *et al.* [154]; Greer *et al.* [141]		Subthreshold	
Third-wave psychotherapies				
Posttreatment or survivorship	Johns *et al.* [140]; Fernandez-Rodriguez *et al.* [155]	Nissen *et al.* [156]	Subthreshold	Strong recommendation moderate quality
Mixed sample	Compen *et al.* [157]		Threshold	Strong recommendation low quality
Metastatic or advanced	Wells-Di Grigorio *et al.* [158]		Threshold	Weak recommendation low quality
	Rost *et al.* [159]; Cheung *et al.* [160]; Mosher *et al.* [126]		Subthreshold	Strong recommendation moderate quality
Supportive-expressive/humanistic-existential interventions				
Newly diagnosed/postsurgery		Rodriguez Vega *et al.* [72]	Threshold	Strong recommendation moderate quality
	Goerling *et al.* [161]; Bredal 2014 [131]; Peng 2019 [162]	Classen *et al.* [163]; Boesen *et al.* [164]; Ludwig *et al.* [165]	Subthreshold	
Undergoing treatment	Kangas *et al.* [144]; Beutel *et al.* [166]		Threshold	Strong recommendation moderate quality
Posttreatment or survivorship	Schellekens *et al.* [167]; van der Spek *et al.* [168]	Chochinov *et al.* [169]; Ho *et al.* [124]	Threshold	Strong recommendation moderate quality
Metastatic or advanced	Kissane *et al.* [170]; Rodin *et al.* [171]		Threshold	
	Lo *et al.* [172]; Breitbart *et al.* [173]; Badr *et al.* [174]; Ye *et al.* [175]; Fraguell-Hernando *et al.* [176]	Breitbart *et al.* [177]	Subthreshold	Strong recommendation high quality
Care delivery interventions				
Newly diagnosed	Arving *et al.* [178]; Hauffman *et al.* [179▪]		Threshold	Strong recommendation high quality
Mixed sample	Sharpe *et al.* [180]; Krebber *et al.* [181]		Threshold	Strong recommendation high quality
	Ell *et al.* [182]; Strong *et al.* [183]; Fann *et al.* [184]; Kroenke *et al.* [185]		Subthreshold	
Metastatic or advanced		Schuurhuizen *et al.* [186]; Woo *et al.* [187]	Threshold	Weak recommendation moderate quality

A narrative review of select randomized controlled trials (RCTs) examining the effects of psychological interventions on depressive symptoms using grade recommendations [59] is presented. Due to the large number of studies in this area, we focused on RCTs after 2010, except for threshold depression or care delivery interventions as there are fewer studies in these areas.
[a]Threshold depression severity denotes either study eligibility criteria including diagnosed major depression, reporting of subgroups with major depression or scoring above a validated cut-score for significant depressive symptoms on a depression-rating scale.

phase of cancer. A major challenge has been floor effects from including participants without clinically significant levels of depression at baseline [23]. Meta-analyses of mindfulness-based interventions in cancer demonstrate only small effects on depression, less than the minimum clinically important difference (MCID) for depression measures [106,107▪▪]. In contrast, recent meta-analyses found that cognitive behavioural interventions produced large effect sizes in reducing depressive symptoms in patients with breast cancer (SMD = −1.11 [95% CI −1.28 to -0.94) [108], and moderate-to-large effects sizes (SMD = −0.67 [95% CI −1.06 to −0.29] [109]; −0.82 [95% CI −1.02 to −0.62] [110]) for psychotherapeutic interventions in palliative cancer. For threshold depression, a meta-analysis to 2015 of six psychological therapies found moderate benefit for the experimental groups (SMD = –1.40 [95% CI –2.50 to –0.29]) [58].

Although criticized for being disproportionately focused on breast cancer [111], the evidence base for psychological therapies can be pragmatically presented based on the number of positive trials per intervention type and disease or treatment status (Table 2). Although the research evidence is based on modalities that can be quantified and standardized, in practice, psychosocial clinicians most often employ an integrative approach, incorporating strategies from varying modalities and tailoring to the clinical needs and psychological traits of the individual with cancer [188].

Recent trends in treatment have focused on collaborative models of care, prevention of depression in cancer, and psychedelic interventions in cancer. Collaborative care combines pharmacologic and psychological treatment utilizing an integrated management team, including a dedicated care manager, consulting psychiatrist, and oncologist. Meta-analyses have shown collaborative care to be significantly more effective than placebo at remitting and maintaining remission of depression in cancer (12-month SMD = –0.49 [95% CI –0.81 to –0.16]) [58]. However, the required systemic reorganization of mental healthcare delivery can be challenging [189], making it only feasible to provide for depression of greater severity rather than subthreshold depression, which is more prevalent in cancer. For the range of depression severity, principles of stepped care suggest lower intensity interventions (i.e. self-management, peer support) for mild-to-moderate depression, stepping up to higher intensity interventions for persisting (i.e. individual psychotherapy) or severe (i.e. medications) depression [190].

Prophylactic intervention may be another way to address depression. Meta-analytic evidence of pharmacotherapy and psychotherapy trials for depression prevention in cancer identified 18 studies, finding small positive prophylactic effects in 7 of them [191]. A notable interest in psychedelics in palliative cancer, particularly ketamine [191] and psilocybin [192], has reemerged, and although both have shown rapid and robust mood effects, the specificity for depression versus existential distress is unclear. Whenever used in microdosing protocols, both drugs are frequently delivered within a calming environment as part of psychedelic-assisted psychotherapy, obscuring identification of the active agent. Moreover, recent studies have demonstrated large placebo effects [193▪,194].

NEW DIRECTIONS FOR TREATMENT

Future work to improve treatment of depression in cancer should focus on two streams: conducting basic research in psychoneuroimmunology to better understand the inflammatory pathways underlying ICAD; and developing high-quality randomized controlled trials (RCTs) to develop a stronger evidence-base to inform practice using existing treatments. A meta-analysis of existing anti-inflammatory drugs in primary depression demonstrated antidepressant effects either as add-on or monotherapy, although there was a trend towards increased infections [195]. To date, there has been one RCT of celecoxib monotherapy for depression in colorectal cancer demonstrating improvement in mild-to-moderate depression after 6 weeks [196]. Although promising, the positive effect of the intervention over the placebo was less than the MCID for the primary depression measure [197] and no difference between groups in depression remission was observed at study endpoint. Broad steroidal and nonsteroidal anti-inflammatory agents are routinely used during cancer treatment. However, because of the risk of unintended impacts on chemotherapy or immunotherapy response, targeted cytokine inhibitor trials in cancer may be premature until researchers have a better understanding of ICAD.

ICAD studies would benefit from longitudinal study designs to demonstrate causal biomarker relationships and bioinformatics analyses of interacting cytokine networks with back translation into animal models to dissect central nervous system pathways and impacts on the tumour microenvironment. The growing biobehavioural research on the impact of psychological interventions on cancer progression and survival [198,199] should consider biological plausibility in their study designs. Early research in this field failed to demonstrate survival benefits in metastatic cancer populations treated for existential distress. The reasonable effect size of a psychological intervention on immune function in the face

of advanced disease burden would be biologically implausible. Later longitudinal research in early breast cancer populations has shown decreased cancer recurrence, associated with activation of innate immune function. Future clinical trials should recruit patients with elevated levels of depression in nonmetastatic populations, with short-term outcomes related to the adaptive immune system and immunosurveillance.

To inform research and current guidelines on the management of depression in cancer, large randomized intervention trials for major depression are needed. Trial designs that overcome the barrier of placebo controls in cancer might include restriction to moderate severity depression, comparisons between two antidepressant medications or psychotherapies, psychotherapy versus medication trials, or add-on designs with psychotherapies or medications. Research should focus on tailoring clinical interventions to the biology (e.g. patients with high or low inflammation) and psychology (e.g. patient's reflective capacity, coping resources, social support, preference for individual or group therapy formats) of individual patients to increase efficacy.

CONCLUSION

The emerging evidence base supporting effective interventions for depression in cancer supports the use of antidepressant medications for more severe depression, and psychological therapies for mild-to-moderate depression across various stages of the cancer trajectory [200,201]. Recent research is focused on developing effective models of interprofessional collaborative care delivery, combining psychological and pharmacological management using stepped-care delivery. Further exploring the inflammatory hypothesis of depression may lead to novel, more effective interventions for depression in cancer [202]. High-quality, pragmatic clinical trials targeting interventions to those patients most likely to respond will support the move towards precision psychiatry. Empathic communication by healthcare providers combined with a high index of suspicion for depression in patients undergoing burdensome and highly inflammatory cancer treatments are essential components of depression management in patients with cancer.

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Conflicts of interest

There are no conflicts of interest.

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- ■ of special interest
- ■■ of outstanding interest

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