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**Review Article** 

MANAGEMENT OF DEPRESSION IN TERMINALLY ILL PATIENTS - A CRITICAL REVIEW

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# ABSTRACT

Depression is a well-recognized risk factor for shortened life span from cancer. Depression is among the main causes of disability in the world leading to increased suffering and mortality. As per research surveys over the years, prevalence among cancer patients varies widely from 3% to 38% for major depression and 1.5-52% for depression spectrum syndromes. The need of the hour is to effectively treat depression in cancer patients so that the quality of life can be improved and thereby patient survival. Both psychological and pharmacological interventions and the combination of both very much effective in treating depression in cancer patients. A broad range of therapies now exist, and the art of such therapy is the strategic selection of components from several models to best respond to the needs of the individual patient and his/her family in the specific circumstances, whether clinical, psychological, spiritual, or social.

Keywords: Depression, Tricyclic anti-depressants, Psychotherapy, Adverse effects.

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# INTRODUCTION

"Every man has his secret sorrows which the world knows not; and oftentimes we call a man cold when he is only sad." Depression often called the common cold of psychiatry is very common in palliative care. Depression adds to the physical consequence of advanced diseases. Pain, fatigue, and disability usually associate with depression. Evidence says depressed patients have very poor prognosis and incidence of higher mortality in a range of physical illness. Exposure to chronic psychological stressors may lead to the development of either depression or anxiety disorders or both [1]. Terminal illness is accompanied by normal fear and distress making a diagnosis of depression, a hectic task. Furthermore, somatic symptoms of the patients may be due to depression, advanced disease or medical treatment. Cancer accounts for about 14% of death worldwide with numbers increasing up to 25% in western population. The diagnosis of cancer is usually perceived as death sentence by many creating mental distress and feeling of being tortured by nature. Depression is a wellrecognized risk factor for shortened life span from cancer. Hence, the challenge of holistic care has spawned the birth of a new discipline in the field of medicine called the psycho - oncology drawing practitioners from psychiatry, psychology, oncology, social work, and other relevant medical fields to provide great care to cancer patients.

### Depression and its prevalence

Depression is among the main causes of disability in the world leading to increased suffering and mortality. The United States comorbidity survey showed a lifetime prevalence of 16% [2]. When comorbid with medical illness prevalence ranges from 20% to 30% in hospitalized patients [3], with the highest rates noted with endocrine disorders such as Cushing's disease and lowest rate noted with end-stage renal disease.

# Prevalence of depression in cancer patients

As per research surveys over the years, prevalence among cancer patients varies widely from 3% to 38% for major depression and 1.5-52% for depression spectrum syndromes [4]. The prevalence rates reported varies due to the varying conceptualization of depression, difference in diagnostic criteria, methodological approaches to measure depression and also difference in the population studied. The variation in prevalence among different types of cancer patients can be attributed to the pathophysiologic effect of cancer, treatment effects or other unidentifiable factors. Nonetheless, cancer exclusive of the site is associated with depression in rates higher compared to normal population. Cancer types in association with depression include brain (41-93%) [5,6], pancreas (up to 50%) [7], head and neck (42%) [8], breast (4.5-38%) [9,10], lung (11%) [11,27], and gynecological (23%) [12]. High prevalence is associated with stomach, pancreas, breast, and head and neck cancers [13] with lower rates associated with colon cancers (13%)and lymphomas (8%) [14]. Sneed *et al.*, [15] found no gender difference in depression in male and female cancer patients; however, women adjusted more positively than men.

#### **DEPRESSION BY CANCER TYPE**

#### Depression in breast cancer

Breast cancer is the most studies cancer type in terms of psychological stress. The prevalence of depression ranges from 4.5% to 37%. Studies have assessed the rates of major depression as well duration of depression in breast cancer patients. Morris *et al.* [16] studied 160 women awaiting breast surgery found 22% of patients who had mastectomy for malignant disease had depression for the next 2 years compared to 8% in those with benign disease, similarly Kissane *et al.* [17] Studied 303 early stage and 200 metastatic cancer patients and found prevalence rates of 6.5% and 9.6% among early and malignant groups, respectively. A 5 year observational cohort study of 222 early cancer patients [18] revealed prevalence rates of depression to be 33% at diagnosis of cancer, 15% after 1 year and 45% after recurrence of breast cancer was diagnosed. Independent risk factors for the development of depression among breast cancer patients includes younger age, social status, ethnicity, psychiatric history, comorbidity, alcohol, smoking, and body mass index.

#### Depression in gynecological cancers

A systemic review of 18 studies of psychological distress in ovarian cancer patients by Arden - Close *et al.* [19] found strong evidence for a relationship of younger age, increased physical symptoms, more advanced disease and short time since diagnosis of depression. Gonsalves *et al.* [20] noted that persistence clinical depression was not prevalent (6%) and prevalence was highest at the beginning of treatment. Evans *et al.* [11] reported 23% prevalence of depression among ovarian cancer patients.

#### Depression in head and neck cancers

Head and neck cancers cater high risk of morbidity and mortality with the disease *per se* and treatment factors substantially contributing to disability

and loss of vital functions such as communicating, breathing and eating. A systematic of review of 52 studies found the association of depression with oropharyngeal cancers throughout the trajectory of illness. Depression rates were highest (11-45%) at the time of diagnosis, during treatment and 6 months follow up. The levels came down (9-27%) 3 years after diagnosis [21]. Hammerlid *et al.* [22] studying 357 patients found that those patients having a higher level of mental disability and stress had very low-performance status and more advanced disease.

#### Depression in lung cancer

Lung cancer is usually associated with higher levels of distress when compared to other tumor sites. In a study of depression in 129 patients lung cancer before and after diagnosis Montazeri *et al.* [12] found 12% of patients had depression at the time of presentation and 10% at follow-up. Hopwood and Stephens [10] followed 987 lung cancer patients and found depression was more prevalent in patients with small cell lung cancer than non - small cell cancer.

#### Depression in brain tumors

Psychiatry problems in brain tumors can be mainly due to the disease process itself as well as by treatment including chemotherapy, radiation, and corticosteroids. Arnold *et al.* [6] found 41% of 363 brain tumor patients had depressive symptoms, as assessed by brief patient health questionnaire. Litofsky *et al.* [5] found 93% of 598 high-grade Glioma patients had depression in the early post-operative period compared to 15% recognized by physicians thereby highlighting the underdiagnosis of depression in this population. Depression, emotional distress, and fatigue are interrelated in brain tumor patients, but still depression remains important and is an independent predictor of quality of life, emphasizing in the importance of diagnosing it and treatment.

### Depression in advanced cancer and palliative care

Depression very common among patients with advanced cancer [23], yet it remains underdiagnosed and undertreated [24]. Considerable barriers are faced by health-care professionals in this area. One of them is the common misconception that it is normal for patients with advanced cancer to be sad. Despite such barriers, we must not ignore the fact that depression is an independent predictor of poor survival in advanced cancer. Furthermore, it reduces the quality of life and prolongs hospitalization. Most importantly, depression in advanced cancer is treatable, and validated assessment tools have been developed to facilitate diagnosis. Due to variation in diagnostic criteria, prevalence estimates vary widely from 5% to 26% for major depression and from 7% to 26% for minor depression in those with advanced cancer [6]. The highest prevalence rates of depression have been observed in patients with cancers of the pancreas, head and neck, and breast. Brintzenhofe-Szoc et al. [13] conducted a large cross-sectional study in- and out-patient setting to determine the cancer specific prevalence of both pure depression and mixed anxiety/depression. The highest prevalence of pure depression was seen in patients with pancreatic cancer, whereas the highest prevalence of mixed anxiety/ depression was observed in those with cancer of the stomach. Risk factors for developing major depression in advanced cancer include history of depression, pain, poor functional status, limited social network, and younger age. Psychological concomitants promoting depression include the emotional impact of the advanced disease status, side effects of medications, the progression of cancer with its severe disability, and cerebral dysfunction. Depression in advanced cancer not only reduces the quality of life but also decreases survival time, reduces treatment compliance and prolongs hospital admission with the additional psychological burden on caregivers and family members. It increases the desire to hasten death in terminally ill cancer patients. Recent studies have suggested that depression is associated with interest in physician-assisted suicide. There is also instability of this interest. A request for assisted suicide, when confronted by the patient, the possibility of depression should always be considered. There are no universally accepted criteria for diagnosing depression in the terminally ill patient. As neurovegetative features are associated with advanced cancer, difficulties arise in distinguishing whether the

somatic symptoms identified in the DSM-IV criteria are attributable to depression or to cancer [26]. Disclosure of emotional concerns with medical professionals is one of the biggest concerns among patients resulting in depression frequently undetected in advanced cancer. These barriers in diagnosis have led to the development of assessment tools. Such screening instruments are not diagnostic and only serve to identify those patients with symptoms suggestive of depression. After identification of patients by screening, further assessment is warranted before treatment is commenced. The hospital anxiety and depression scale (HADS) devised by Zigmond and Snaith [27] remains one of the most widely used tools. The HADS is a self-reported questionnaire with 14 items and was originally developed as a screening tool for medical patients. Although the HADS appears to perform significantly well in those patients on active anti-cancer treatment, it performs less well in those with progressive disease. So when used alone as a screening tool it has very limited sensitivity and specificity. The Edinburgh depression scale (EDS) originally developed to screen for postnatal depression in the community, has shown much promise [28]. One study of palliative care patients using the EDS found that a cut-off threshold of 13 had a sensitivity of 0.79, a specificity of 0.81 and a positive predictive value of 0.53 using ICD-10 criteria [29] for depression in comparison with a sensitivity of 0.77 and a specificity of 0.85 for the HAD scale [30]. More recently, a brief EDS (BEDS) has been designed, which more is discriminating for depression in patients with advanced cancer. The BEDS has a sensitivity of 0.72, a specificity of 0.83 and a positive predictive value of 0.65 [31]. This tool is now widely used in the palliative care setting for depression screening. Evidence says that depression is not only underdiagnosed but also undertreated in advanced cancer. The single most important barrier to treatment is the common misconception that it is normal for patients with advanced cancer to be sad. Pre-conceived ideas that psychological treatment is better than pharmacological treatment, and attitudes of therapeutic nihilism, that is, nothing works at this stage are some of other barriers for treatment of depression in advanced cancer. In those situations where antidepressant medication is commenced, it is frequently given at inadequate doses or too late for the therapeutic effect of the drug to take place. One survey conducted in the UK palliative care units found that 76% of antidepressants were started in the past 2 weeks of life in patients with advanced cancer [32].

## MANAGEMENT

#### Rationale

The need of the hour is to effectively treat depression in cancer patients and hence that the QOL can be improved and thereby patient survival. Both psychological and pharmacological interventions and the combination of both very much effective in treating depression in cancer patients. Two main class of drugs used in treating depression are Tricyclic anti-depressants (TCA) and serotonin reuptake inhibitors (SSRI) with later being the first-line agent and the former being the second-line agent [33]. The exact mechanism of these drugs has not been established, but they bring adaptive changes in the brain and overtime increase the levels of 5HT levels thereby increasing mood [34]. The first AD's were available 50 years ago, they include TCA's such as amitriptyline and imipramine and monoamine oxidase inhibitors (MAO'S) such as phenelzine. Development of newer AD's over the past two decades has modified the treatment approach to depression. They include SSRIs and SNRIs. Therefore, a good knowledge of the profile of drugs and their side effects are extremely important. Cancer patients usually complaint of constipation, urinary retention, stomatitis, seizures, or cardiac problems such as arrhythmias and orthostatic hypotension which warrants careful selection of AD's. The main characteristics of AD's are summarized in (Table 1). MAOIs are generally contraindicated and not considered safe in cancer patients, because of the high rates of side effects. MAOIs can interact with opioids, sympathomimetics, and procarbazine and can lead to hypertensive crises. In addition, MAOIs interact with some anesthetic drugs when cancer patients undergo surgery. The use of TCAs has been gradually decreasing, because their anti-muscarinic properties may be extremely dangerous for cancer patients (e.g., dry mouth in

Class of drugs	Disadvantages	Advantages
A. TCA's e.g., Imipramine, desipramine, clomipramine and amitriptyline	Constipation, dry mouth, drowsiness, postural hypotension reflex tachycardia	Action on pain
B. SSRI's e.g., fluvoxamine, paroxetine, sertraline, citalopram, escitalopram	Sexual dysfunction, gastrointestinal side effects	Action on sleep
C. SNRI's e.g., reboxetine	Decreased blood pressure Dizziness, dry mouth, urinary retention	Some more sedative
D. SSNRI's e.g., Venlafaxine, desvenlafaxine, duloxetine, milnacipram	Hypotension	Improved drive and cognitive functions
E. Selective dopamine and noradrenaline reuptake inhibitors e.g., Bupropion	Anxiety, psychomotor activation	Decrease fatigue, increased attention
F. Noradrenergic and specific serotonergic reuptake inhibitors e.g., mirtazapine	Drowsiness	Drowsiness (helpful in insomnia)
G. Serotonin antagonists and reuptake inhibitors e.g., trazodone, nefazodone	NIL	Rapid effect
H. Psychostimulants dextro-amphetamine, methylphenidate, modafinil	Restlessness, agitation, insomnia, nightmares, anorexia, arrhythmia, tachycardia, tolerance, dependence, seizures	Action on pain

Table 1: Characteristics of anti-depressants

TCA: Tricyclic anti-depressants, SSRI: Serotonin reuptake inhibitors, SNRI: Serotonin norepinephrine reuptake inhibitors, SSNRI: Selective serotonin norepinephrine reuptake inhibitors

patients with mucositis due to chemotherapy, reduction of bowel peristalsis in patients receiving opioids for pain, confusional states, and delirium in debilitated cancer patients). In contrast, the use of SSRIs and SNRIs has increased because of higher safety profile [35,36], although cardiovascular adverse effects, abnormal bleeding, hyponatremia, seizures, and agranulocytosis should be kept in mind while treating cancer patients [37]. Psychostimulants (e.g., methylphenidate, pemoline, d-amphetamine) are useful in the treatment of depression in cancer, in terminally ill patients, because of their rapid onset of action and effect concentration and attention problems and also on fatigue [38]. ADs usually start working within 2 weeks, but other medications in cancer patients may have an impact on antidepressant metabolisms, such as steroids, anti-emetics, and narcotics. Usually, patients are started off on low dosages of ADs to check for any side effects such as rash, or adverse drug-drug interactions, and then escalated to full dosage. The full benefit is seen by patients in 4-6 weeks or maybe even longer.

Neutropenia is a one among the possible complication of the use of TCAs [39] mianserin [40] and mirtazapine [41] with data also for fluoxetine, trazodone, nefazodone, and sertraline [42]. Examination of white cell count is extremely important in cancer patients receiving chemotherapy. Patients with lung cancer often have dyspnea, anxiety, pain and, in about 25% of the cases, clinically significant depressive states [42]. Whereas, the use of ADs is not generally contraindicated, benzodiazepines should be generally avoided. Although they may provide short-term relief of anxiety, they, in fact, exacerbate breathing difficulties and, in combination with opioids, causing detrimental effect on pulmonary function. Bowel obstruction is very common in patients with ovarian cancer. Anti-cholinergic should be avoided in these patients as it reduces bowel movements ADs should also be carefully when used in cancer patients receiving opioids for pain in view of their own peristalsis. Since these drugs are metabolized by the liver, they should be carefully used in patients with compromised liver function as well in those patients with liver tumors receiving treatment. Hence, baseline and periodic liver function tests are warranted. Among ADs, nefazodone may cause fatal hepatotoxicity and should not be used in patients with liver dysfunction. It is necessary to avoid anticholinergic medications, such as the TCAs, in patients with delirium [43].

# Some guidelines for the use of ADs in cancer patients

- Treatment initiation at low doses and then followed dose titration to achieve an optimum response to avoid side effects.
- Inform patients of latency period and possible side effects to avoid premature drop-out, inpatients receiving other medications.

- Treat the patient for 4-6 months to avoid relapses or new episodes of depression after remission.
- Regular monitoring of the physical variables and other medications used for cancer (for example, steroids, antiemetic's, antibiotics, antiestrogen, and chemotherapy agents).
- By tapering the dose by 50% over a couple of weeks to reduce the risk of withdrawal drugs should be discontinued.
- Education and proper reassurance of the patients are extremely important in oncology settings.

## Psychotherapy for depression in cancer and palliative care

Evidence-based medicine warrants the use of effective interventions ahead of non-efficacious treatment. Jacobsen and Jim suggest that psychosocial cancer care that is ineffective is worse than not caring at all. It is highly pertinent to assess intervention's impact rather than relying on good intentions alone. We begin with individually-focused therapies for patients with early stage cancer, move to systemic therapies (couple, group, and family) that bridge across all stages of cancer and then psychotherapy for advanced cancer, including patients receiving palliative care.

# PSYCHOTHERAPIES IN EARLY STAGE CANCER

#### Individually-focused psychotherapies

### Issues and symptoms

As depression phenotype is heterogeneous in cancer it is of high importance to formulate the case with differential diagnosis before the start of psychotherapy. Depression must be viewed within the bio-psychosocial context of the person, rather than as an isolated symptom cluster. The differential diagnosis for major depression includes mood disorder due to a medical condition, substance induced mood disorder, dementia, delirium, and bipolar disorder. In these cases, the primary treatment should be underlying condition and not necessarily on psychotherapy. Even though it requires a temporal association between the onset and course of the medical condition and depression, psychiatric symptoms of a medical illness may antedate its clinical recognition. Correction of the medical illness may not eliminate the depressive symptoms since depression is often multicentered. Comorbid substance abuse may also benefit from specific drug treatments, inpatient detoxification, or psychotherapies [44].

## Cognitive therapy (CT)

CT or cognitive-behavioral therapy (CBT) is based on the hypothesis that it is not the situation that causes an emotional reaction but rather how a person perceives that situation [45]. Triggering a situation

leads to an "automatic thought" which then generates a response that can be emotional (e.g., worry), behavioral (e.g., withdrawal), or physiological (e.g., gastrointestinal discomfort). Important component of CT is reframing of dysfunctional automatic thoughts. The main aim is to moderate the intensity of cognitive thinking biases by engaging the patient in a consideration of more reasonable alternatives. Evidence supporting the efficacy of CBT for depression can be found in meta-analyses of multiple randomized controlled trials in cancer survivors [46]. A newer paradigm recommends the use of a psychotherapy intervention to prevent distress among patients at high risk for depression. Pitceathly et al. [47]. Demonstrated that a short course of CBT intervention (three sessions), administered by trained nurses, significantly reduced the rate of depression in high-risk patients but not depressed at baseline. The first session was conducted face to face, but subsequent sessions were conducted by phone. Significant effects were noted up to 6 months after the intervention. Team of well -trained nurse therapists is another welcome improvement to allow more patients access to depression treatment.

#### Problem-solving therapy

It is based on the hypothesis that more efficient problem solving or improved coping results in less psychological distress. The standard 90 minutes\*10 sessions trains patients to define the problem, evaluate possible options, brainstorm potential solutions, monitor success, and refine them. A family member can be designated the team leader, as cancer affects whole family and people collaborate in solving it [48]. In a randomized controlled study, problem solving was effective in reducing depressive symptoms (p<0.05) versus a waiting list control, a benefit that was still robust at 1 year [49].

## Psycho-educational interventions

Psycho-educational interventions orients patients to novel oncology situations by providing verbal, visual, and written help to patients. Acquisition of new knowledge is essential to help patients learn new medical systems. Devine and Westlake's meta-analysis of 116 psycho-educational studies [50] reported a moderate effect size (d=0.54, 95% CI=0.43-0.65) for the amelioration of depression, and a positive result was found in a systematic qualitative analysis of 63% of studies reviewed [50]. The fact that better orientation and support in unfamiliar medical situations can reduce demoralization and helplessness and can shape better expectations.

#### **Relaxation therapies**

It is one among the most widely used psychosocial services offered to cancer patients and are particularly useful for managing "here and now" behaviors or distress associated with cancer treatments. Luebbert's meta-analysis [51] estimated a moderate effect size of relaxation on depression (d=0.54, 95% CI=0.30-0.78). Jacobsen *et al.* [52] developed a self-administered stress management intervention for chemotherapy self-administered, using print, and audio instructions. Using three techniques (paced abdominal breathing, progressive muscle relaxation with guided imagery, and coping self-statements), depression, and anxiety symptoms were significantly less than in the control group after two, three, and four cycles of chemotherapy.

#### Interpersonal therapy (IPT)

IPT focus on interpersonal conflicts, life transitions, grief, losses, and social isolation, all of which are pertinent contextual issues for the depressed cancer patient. In a meta-analysis, IPT was superior to placebo in 8 out of 13 studies [53], but unlike CBT, it had no documented additive effect when given together with an antidepressant [53]. Specific psycho-oncology data are lacking at this time.

# Systemic psychotherapies

#### Issues and settings

The distress of cancer reverberates through couples, families, and communities. Higher rates of depression have been observed in the spouses of patients with prostate cancer [54] and with non-gender based metastatic cancers [55]. Hence, there is a need for models

of psychotherapy within oncology that target couples and families, especially in the setting of advanced disease. For isolated people, a group approach can be crucial as a primary means to foster social support.

# **Couple therapy**

Main targets of couple therapy are Relationship enhancement and protection against relational distress. Fostering open communication promotes mastery, while using the relationship as a key source of mutual support [56]. In the breast cancer setting, a randomized controlled trial of an active coping intervention for couples relative to usual care showed a reduction in women's depressive symptoms up to 6 months post-treatment [57]. Couple therapy in prostate cancer is illustrated by the FOCUS intervention, which targets family involvement, optimistic attitude, coping effectiveness, uncertainty reduction and symptom management couple therapy in the setting of advanced cancer shifts the emphasis to anticipated loss, caregiving, and existential concerns [58]. Emotion-focused couple therapy addresses threats to emotional engagement by recognizing distancing interactions and promoting closeness and thereby reducing depression. Effective mutual support results when couples are securely attached to each other. Couple therapy that identifies existential fears and supports intimacy in the face of death to protect against demoralization and depression.

#### Group therapy

Supportive-expressive group therapy (SEGT) [59] is efficacious in relieving distress, and successfully helps in the treatment of depression, as well as preventing its onset in the advanced cancer setting. In cognitive-existential group therapy (CEGT), therapists aim to promote a supportive environment, facilitate grief work over the multiple losses, alter maladaptive cognitive patterns, improve problem solving and coping skills, foster a sense of mastery and encourage review of lifestyle priorities for the future [60]. Clear focus is emphasized on (a) the cancer journey, (b) its existential challenges, (c) coping with anti-cancer treatments, (d) supporting adherence to the medical regimen, (e) cognitive strategies to counter fear of recurrence and living with uncertainty, (f) optimizing relationships with physicians, partners, families and friends, and (g) meaning-making through recognition of what is fulfilling, creative and purposeful in life. The goals of SEGT are to build bonds, express emotions, detoxify death, redefine life's priorities, fortify families and friends, enhance doctor-patient relationships and improve coping. With such extraordinary influence on the cancer patient's life, SEGT actually protects cancer patients from developing new cases of clinical depression compared to those receiving usual cancer care [61].

## Family therapy

Family-centered care harness areas of competence, affirm skills and promote hope and reintegration when cancer experiences can contribute to hopeless feeling among family members. There is a correlation between poor family support and recurrence of depression resulting in devastating complications [62]. In a randomized controlled trial targeting 'at risk' families, family therapy that was designed to provide effective communication, enhanced cohesion and was found to reduce depression and mourning from family loss due to cancer. In general, mild family dysfunction needs four to six sessions in comparison to 10-12 sessions for families with pronounced dysfunction. Circular questions to unravel family dynamics and offering regular summaries to help families integrate [63]. Couple and group models are important in early stage while family therapy comes to play mainly with advanced cancers.

### PSYCHOTHERAPIES IN ADVANCED CANCER AND PALLIATIVE CARE

The inevitable challenge in individuals with advanced disease is the psychological well-being, because of the extreme stress and burden that comes with it which includes physical suffering and disability, the threat of impending doom, alterations of support and personal relationships, the challenge of making correct treatment decisions that have life and death implications. Early interventions to treat depressive symptoms may help to protect or improve emotional well-being and quality of life. Unfortunately, however, the majority of patients at this stage of disease are not referred for psychosocial or psychiatric care and most of those referred do not receive adequate treatment for depression [64]. Although routine distress screening is now regarded as a standard in cancer care at all stages of the disease, its benefit is always limited due to failure of treatment centers to provide effective interventions that follow screening. Therefore an integrated approach is needed, which includes symptom control, the social environment and the psychological disturbance itself. Psychological treatments for depression are preferred when compared to pharmacological care and the type of psychotherapy often becomes most appropriate as the disease progresses. Individual sessions permit the therapy to be flexibly tailored to individual needs and also the timing of the sessions can be easily adjusted to take into account other clinic appointments, investigations and treatments, and the fluctuating trajectory in health status at this stage of disease [65]. Psychotherapy should be advocated before debilitating physical symptoms and also before impairment in cognition limits the capacity for self-reflection. Models of therapy include logo-therapy, existential psychotherapy, grief therapy, life review, life narrative, and IPT. The investigational research carried out so far to investigate the effectiveness of individual psychotherapies in terminally ill patients so far has been limited by the absence of appropriate inclusion criteria for the severity of depression and inadequate randomization [66]. Several psychotherapy interventions are currently being investigated to determine their effectiveness. These treatments can be broadly categorized into those that promote active coping strategies and those that emphasize the communication and understanding of emotional experience and the joint creation of meaning, usually described as supportive-expressive therapies.

#### CONCLUSION

Depression is very common in cancer patients. It results in significant morbidity and mortality. Although the prevalence of depression varies ranging between 1.5% and 52%, there should be no doubt that cancer is associated with a high degree of depression. There is much to do to enhance the quality of life of patients with cancer and prevent the onset of depression. Further research evidence is needed on the efficacy, effectiveness and safety of ADs in the different settings of oncology (inpatient units, outpatient clinics and palliative care units) and types of cancer. More information is needed about the interactions between ADs and the variety of drugs, especially chemotherapeutic agents, cancer patients receive. Depression increases suffering in the oncology setting. A broad range of therapies now exist and the art of such therapy is the strategic selection of components from several models to best respond to the needs of the individual patient and his/her family in the specific circumstances, whether clinical, psychological, spiritual, or social. Although we have pragmatically placed more emphasis on CBT in early cancer and supportive- expressive therapies in advanced cancer, a wise therapist selects whatever model offers most to the needs of the patient at that time. Existential, spiritual, and meaning-based themes are commonly met and dealt with in the early stage patient with cancer. Furthermore, many of these therapies are appropriately combined with psychotropic medication.

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