Current practices in managing end-of-life existential suffering

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Purpose of review
Within the context of palliative care, existential suffering (ES) can be an exclusive source of suffering or intertwined with physical pain and/or psychological and spiritual suffering. With newly emerging modalities for addressing this phenomenon and its increasing salience given that many patients cite ES as a significant contributing factor to requests for hastened death, a review of recent interventions for addressing ES at the end of life is timely.

Recent findings
This review of newer approaches to dealing with ES in the palliative context suggests some promising new modalities and pharmacological interventions, such as brain stimulation and the use of psychedelics. The use of other pharmacological interventions, such as palliative sedation and lethal injections, solely for the alleviation of existential distress remains ethically controversial and difficult to disentangle from other forms of suffering, not least because a clear clinical definition of ES has yet to emerge in the literature.

Summary
The evaluation of end-of-life (EOL) ES mitigating tools should also consider how broader contexts, such as institutional arrangements and barriers, and cultural factors may influence the optimal management of dying persons' ES in the palliative care setting.

Keywords
end-of-life care, existential suffering, mitigating tools, palliative care

Death and dying is a subject that evokes such deep and disturbing emotions that we usually try to live in denial of death. Yet we could die tomorrow, completely unprepared, and helpless. The time of death is uncertain, but the truth of death is not. All who are born will certainly die.

– Chagdud Tulku Rinpoche (1930–2000).

INTRODUCTION

Benjamin Franklin is famous for saying that 'in this world nothing can be said to be certain, except death and taxes'. [1] And yet this certainty does little to comfort those who experience suffering of an existential nature at the end of life (EOL). Increasingly, attention is being paid to this kind of suffering, despite the lack of consensus in the scholarly literature about what exactly the term connotes [2]. The expansion of the provision of medically assisted death to patients in many jurisdictions, coupled with increasing climate-related existential anxiety at the population level [3], has forced consideration of how to address existential suffering (ES) clinically. Within the context of palliative care, ES can be an exclusive source of suffering or intertwined with physical pain and/or psychological and spiritual suffering. With newly emerging modalities for addressing this phenomenon and its increasing salience given that many patients cite ES as a significant contributing factor to requests for hastened death, a review of recent and dominant interventions for addressing ES at the EOL is timely.

Common existential concerns dying persons can experience are heightened death anxiety, feelings of social, and existential loneliness, and a sense of meaninglessness. Moreover, given the foreshortened time, dying persons are vulnerable to feeling hopeless and may therefore lack the motivation to pursue resources that foster meaning

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KEY POINTS

- The remediation of dying persons' existential issues can present challenges to EOL care clinicians.
- Psychotherapeutic, pharmacological and brain stimulation treatments are options, or emerging options for the treatment of ES.
- Currently pharmacological interventions, such as psychedelic-assisted therapy, PS and MAiD are controversial approaches to managing dying persons' ES.
- Broader contexts, such as institutional and cultural factors (like living in a death-denying culture) can influence the optimal management of dying persons' ES but is a gap in the medical literature needing to be filled.
- The evaluation of EOL ES mitigating tools should also consider proper resources allocation to comprehensive, accessible palliative services that include existential care.

in life and promote coping skills that could help remediate ES [4▪]. The remediation of dying persons' ES can present challenges to EOL care clinicians but has received increasing clinical attention over the past few decades.

REVIEW OF CURRENT END OF LIFE EXISTENTIAL SUFFERING THERAPEUTIC INTERVENTIONS

The review was conducted by searching relevant databases (Medline, Embase, APA PsyInfo, HealthStar, AMED (Allied and Complimentary Medicine), JBI EBP, and Health and Psychosocial Instruments using the key words 'existential'*, 'palliative care', and 'EOL care'. An asterisk followed the word existential to ensure that scholarly works were captured that referred to ES as existential distress, crisis, or existential pain. Inclusion criteria were that papers be published after 2020, be written in English, and that were reporting on empirical studies. It should be noted that while there are other existential interventions within palliative care [5], we also chose to include the dignity therapy (DT) [6] and managing cancer and living meaningfully (CALM) [7] studies even though they fall outside our review timeframe, as these are widely cited ES management approaches within the literature. Papers that pertained to pediatric care or spiritual suffering were excluded, the latter because this form of distress is not synonymous with ES [8]. The literature review yielded eight psychotherapeutic, pharmacological, and medical device interventions that are currently being used or researched to manage dying persons' ES.

Psychotherapeutic interventions

Four psychotherapeutic interventions have been recently examined to determine their effectiveness in managing dying persons' ES. These psychotherapeutic interventions focus on developing the patient's sense of meaning, dignity, legacy, and social relatedness to address death anxiety and are based on different approaches to psychotherapy. DT [6] is a well-known psychotherapeutic intervention grounded on an empirically based model of dignity built on the notion that illness and experiences with the healthcare system can be damaging to one's sense of self. DT is administered by EOL care clinicians who use the DT interview guide to prompt dying persons to discuss their life history and how they most want to be remembered by their loved ones. The therapeutic sessions are recorded and transcribed, and a 'generativity document' is created to bequeath to a family member or friend. DT's therapeutic goal is to reinforce dying persons' sense of meaning and purpose, helping them to identify their legacy, and in doing so, contribute to preserving their dignity [9]. See Table 1 to review the findings on the effectiveness of DT in patients who have been diagnosed with a terminal condition [6].

CALM [7] is a tailored, semistructured psychotherapeutic intervention for patients with advanced cancer to relieve distress and promote psychological well-being and growth. CALM is a three-to-eight session intervention grounded in existential, attachment, and relational theory [10–12]. CALM builds the therapeutic relationship and creates reflective space to focus on the following domains: symptom management and communication with EOL care clinicians; changes in self and relations with close others; spiritual well-being and the sense of meaning and purpose; and mortality and future-oriented concerns [7]. The CALM program enables EOL care clinicians to identify dying persons' existential concerns, optimally engage in supportive existential conversations, and promote connected personal caregiver relationships that foster dying persons' ES coping skills. See Table 1 for a review of the findings on the effectiveness of CALM in patients with terminal cancer [7].

Logotherapy is a meaning-oriented psychotherapeutic intervention that aims to help individuals obtain a greater sense of meaning in their lives by enhancing their motivation for change. Holocaust survivor Viktor Frankl is the founder of logotherapy, which is based on the belief that a person could transcend suffering if he or she had a reason to live. According to Frankl, 'he who has a *why* to live for can bear any *how*' [13]. While individual logotherapy has been shown to be relatively effective in managing death anxiety and existential loneliness, group logotherapy fosters a shared meaning of common hardship and allows each member of the group to feel less alone and more connected to the world

Table 1. Psychotherapeutic interventions

Author	Psychotherapeutic intervention	Sample size	Study design	Participating countries	Findings
Chochinov *et al.* [6]	DT	441	RCT Dignity Therapy Standard Palliative Care Client-Center Care	Canada USA Australia	No significant difference in distress levels before and after the completion of the study between the different groups DT was significantly more likely to improve QoL and increase a sense of dignity DT was significantly better than client-centered care in improving spiritual well-being and was significantly better than standard palliative care in lessening sadness or depression
Rodin *et al.* [7]	CALM	305	RCT CALM Usual Care	Canada	CALM participants reported less severe depressive symptoms than usual care at 3 months and at 6 months Significant findings for greater EOL preparation at 6 months There were no differences in anxiety, spiritual well-being, or death anxiety between the two groups
Heidary *et al.* [4]	Group logotherapy	63	RCT Logotherapy Usual Care	Iran	Patients in the logotherapy group reported a significant decrease in death anxiety and existential loneliness
Grassi *et al.* [14▪]	RET	29	Exploratory	Italy	RET provided a sense of togetherness and a sense of acknowledgment of the support coming from other participants, and thereby confirming the importance of perceived relatedness when coping with existential distress and of strengthening interpersonal relationships within psychosocial interventions. Themes were found in the meaning of the group experience in the 'good bye letters', namely 'togetherness and gratitude', 'legacy', and 'acceptance'.

DT, dignity therapy; CALM, managing cancer and living meaningfully; QoL, quality of life; RCT, randomized controlled trial; RET, reorientation existential therapy.

around them. Heidary *et al.* [4▪] tested group logotherapy which was comprised of 10 weekly sessions, and each therapeutic session lasted about 2 h. See Table 1 to review Heidary and colleagues findings on the effectiveness of group logotherapy in patients with terminal cancer.

Similar to group logotherapy, reorientation existential therapy (RET) [14] is a group psychotherapeutic intervention that is based on the meaning-centered psychotherapy existential framework [15]. RET is an eight sessions 90-min weekly intervention with six to eight patients per group. RET also has a background in cognitive analytic therapy (CAT) which has substantial roots in Mikhail Bakhtin's dialogic self and meaning in interpersonal relationships [16]. The concepts of sequential reformulation of significant interpersonal relationships, significant life events, and the reciprocal roles played by the person were taken from CAT and transformed, in RET, as a written diagrammatic 'route existential map' [14]. Moreover, the 'goodbye letter' was taken from CAT and is used as a narrative approach to summarize the patient's meaning of the experience of therapy. See Table 1 to review Grassi and colleagues exploratory findings on the effectiveness of RET in breast cancer patients.

The tested psychotherapeutic interventions noted above encouraged dying individuals to engage in supportive existential conversations with professional caregivers and to remain socially connected to others. While these psychotherapeutic practices had beneficial effects on terminal patients' existential distress, the interventions did not apply consistent terminology in evaluating existential issues, nor was there a consistent approach to how clinicians provided existential care. These findings are not surprising because the psychotherapeutic interventions were based on different theoretical approaches. Chochinov and colleagues and Rodin and colleagues studies also reported how the psychotherapeutic interventional management tools impacted dying persons' depressive symptoms,

indicating some EOL care researchers may associate dying persons' existential distress with psychiatric illness, while others resist identifying ES as pathological. Last, it is worth noting that although many of the above EOL ES mitigating tools promote dignity, meaning, and social connectedness with personal and professional caregivers, the literature does not discuss or address how broader contexts, such as institutional arrangements and cultural factors (i.e. cost and/or time to implement psychotherapeutic interventions, inequitable access to comprehensive palliative care services, and Western society's death denying culture), can negatively impact the optimal management of dying persons' ES.

Emerging psychopharmacological interventions

Three pharmacological interventions have recently been considered in managing dying persons' ES. Psilocybin is a naturally occurring psychedelic drug that induces altered states of consciousness that are associated with enduring positive changes in cognition, affect, behavior, and spirituality, including increased feelings of connectedness, a heightened perception of life as meaningful, and the emotion of awe [17,18]. Patchett-Marble *et al.* [19▪▪] published a case report that detailed how one psilocybin session occasioned an experience of a mystical nature that the terminal patient with substantial ES would later describe as the single-most personally meaningful experience in their life. This patient reported that this experience led to immediate, substantial, and sustained improvements in her ES and quality of life. Agin-Liebes *et al.* [20] also reported that psilocybin-assisted psychotherapy holds promise in promoting long-term relief from cancer-related ES after performing a follow-up to Ross and colleagues parent study that demonstrated a single dose of psilocybin led to decreases in cancer-related demoralization, and hopelessness as well as improved spiritual well-being. See Table 2 to review the findings on psilocybin's effectiveness in managing dying persons' ES.

Palliative sedation (PS) and medical assistance in dying (MAiD) are two controversial pharmacologic interventions used to manage or end a dying person's refractory existential distress. PS, defined as 'the act of purposely inducing and maintaining a pharmacologically sedated and unconscious state without the intent to cause death' [21] has been used to alleviate not only physical refractory symptoms and psychological distress (e.g. anxiety and depression), but also ES (e.g. hopelessness, meaninglessness, and fear) [22]. According to Rodrigues and colleagues, there is a lack of consensus for the clinical practice of PS to counteract ES

Table 2. Emerging psychopharmacologic interventions

References	Pharmacologic intervention	Sample size	Study design	Participating countries	Findings
Patchett-Marble *et al.* [19▪▪]	Psilocybin mushrooms	1	Case report	Canada	Patient-reported marked improvements in mood, anxiety, and quality of life 1 day, 1 week and monthly there after the psilocybin session. The results were sustained at 4 months at which time the patient rated the experience as the single-most 'personally meaningful', 'psychological insightful', and 'psychologically challenging' experience of her life Patient said that the experience served as a daily 'spiritual anchor' for her during their cancer journey
Ross *et al.* [17] (Parent study)	Psilocybin mushrooms	29 (RCT)	RCT LTFU Psilocybin on the first medication session followed by niacin on the second session	USA	Psilocybin led to decreases in cancer-related demoralization and hopelessness as well as improved spiritual well-being at 2 and 26 weeks postdose
Agin-Liebes [20] (LTFU)		15 (LTFU)	Niacin on the first medication session followed by psilocybin on the second session		Reductions in anxiety, depression, hopelessness, demoralization, and death anxiety were sustained at the first and second follow-ups (average of 3.2 and 4.5 years following psilocybin administration)

RCT, randomized controlled trial; LTFU, long-term follow-up.

Table 3. Brain stimulation therapy

References	Pharmacologic intervention	Sample size	Study design	Participating countries	Findings
Watt *et al.* [26▪▪]	rTMS	2	Case report	Canada	Both patients exhibited marked improvements in depression, anxiety symptoms over the 5-day treatment course With respect to symptoms of existential distress, patient A reported full resolution of feelings of despair, showing no further crying episodes, markedly increased sociability, and goal-oriented behavior. Patient B demonstrated marked reduction in panic attack symptoms, improved motivation and appetite and reported a renewed sense of control in his life

because the definition and terminology for ES are unclear and ambiguous. Furthermore, these researchers state that 'the assessment of ES is a difficult and controversial issue as subjectivity is involved in the patient's narrative of his or her suffering and in the physician's interpretation of it' [22]. Due to the impossibility of obtaining feedback from terminal patients who are unconscious, no empirical studies have been carried out to test the effectiveness of PS in easing existential issues in dying persons.

Unlike PS, MAiD is designed to relieve dying persons' unbearable suffering with the intent of causing death. Following the decriminalization of assisted dying in Canada (February 2016), Li *et al.* [23] reported that the common reasons terminal patients requested an assisted death were related to the loss of autonomy, to avoid burdening others or losing dignity, and to the intolerability of not being able to enjoy one's life. The authors also emphasized that few terminal patients cited refractory pain or other symptoms as reasons to request MAiD [23]. These findings suggest that terminal patients commonly request MAiD to alleviate symptoms often seen to be related to intolerable ES. In contrast, when interviewing employees from the Swiss 'right-to-die organization' (EXIT Suisse Romande), Gaignard and Hurst [24] found that assisted death requests motivated by 'pure' existential reasons were uncommon. The authors rationalize that these requests to manage intolerable ES are rare in Switzerland because, according to the Swiss Academy of Medical Sciences dying and death guidelines, terminal patients are only eligible for an assisted death if the assisting persons can verify that 'symptoms of disease and/or functional impairments are the source of intolerable suffering' (as cited in Gaignard and Hurst 2019, p. 7) [24]. However, other studies suggest a more complicated relationship between physician pain and psychological and existential forms of suffering.

The pharmacological approaches used to manage dying persons' ES are considered controversial. Although the use of psilocybin has been shown to mitigate dying persons' ES and produce salutary effects that persist after the patient has stopped taking the therapy, the research is still in its early stages, and researchers have noted that a historical stigma remains with psychedelic-assisted therapy [25]. Moreover, study participants from the Ross *et al.* [17] study also received psychotherapy, and it is therefore not possible to separate the effects of psilocybin from those of the psychotherapeutic sessions. Last, it is worth noting from an ethical perspective that timely and effective palliative care and/or psychotherapeutic interventions should be made accessible prior to a dying person opting for PS or MAiD to alleviate refractory existential concerns.

Brain stimulation therapy

Increasingly, newer brain stimulation therapies are being used to treat mental disorders. Similar to electric convulsive therapy, these therapies involve activating or inhibiting the brain with electricity and include vagus nerve stimulation, repetitive transcranial magnetic stimulation (rTMS), magnetic seizure therapy, and deep brain stimulation. Only one study to date reports using brain stimulation therapy to specifically treat ES in a palliative care setting using rTMS, and it involved a 5-day course of eight sessions per day delivered at 45-min intervals with 600 pulses of intermittent theta-burst stimulation per 3-min session, at 80% of resting motor threshold, targeting the left dorsolateral prefrontal cortex [26▪▪]. See Table 3 to review case reports on accelerated rTMS's effectiveness in managing dying persons' ES. It is worth noting that the expanding use of these therapies in other contexts to treat

depression, post-traumatic stress disorder, and obsessive-compulsive disorder that do not respond to more conventional psychotherapeutic interventions suggests that we should expect an expansion of their use in the context of treating ES in the palliative care setting in the future.

CONCLUSION

The remediation of dying persons' existential issues can present challenges to EOL care clinicians because of a lack of clarity around its definition and because its treatment can often take time. This review of newer approaches to dealing with ES in the palliative context suggests some promising new modalities and pharmacological interventions, such as brain stimulation and the use of psychedelics. Both require further, rigorous study. The use of other pharmacological interventions, such as PS and lethal injections, solely for the alleviation of existential distress remains ethically controversial and difficult to disentangle from other forms of suffering, not least because a clear clinical definition of ES has yet to emerge in the literature.

The evaluation of EOL ES mitigating tools should also consider how broader contexts, such as institutional arrangements and barriers, and cultural factors may influence the optimal management of dying persons' ES in the palliative care setting. From an institutional arrangement perspective, these considerations include proper resource allocation to comprehensive and accessible palliative services that include time and resources for addressing ES [2]. Lastly, the training of clinicians charged with managing ES at the EOL will need to include critical appraisal skills for emerging modalities.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:
- ■ of special interest
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