

INVITED COMMENTARY

From evidence to implementation: The global challenge for psychosocial oncology

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Abstract

The human dimensions of medical care were highlighted by such pioneering figures as Cicely Saunders, Elizabeth Kubler-Ross, and Jimmie Holland and their tireless advocacy helped to build an evidence base for psychosocial and palliative interventions. In that spirit, we studied physical and psychological distress in advanced cancer and modeled pathways to distress in this population. We considered acute stress disorder as the prototype for psychological disturbances following the acute onset of life-threatening disorders, showing that it occurred in one-third of patients after the diagnosis of acute leukemia. To treat and prevent these symptoms, we developed Emotion and Symptom-focused Engagement (EASE), an integrated psychotherapeutic and early palliative intervention. We showed that EASE reduced both traumatic stress and physical suffering in these patients and a large multi-center trial is now underway. We also identified symptoms of depression and hopelessness in one quarter of patients with metastatic and advanced cancer, with worsening toward the end of life. To alleviate this distress, we developed a brief supportive-expressive therapy, referred to as Managing Cancer and Living Meaningfully (CALM). We showed in a large RCT that CALM improves depression, distress related to dying and death, and preparation for the end of life. We have now launched a global initiative involving 20 sites to date across North and South America, Europe, Australia, and Asia to have CALM implemented routinely in cancer care. Such initiatives are needed to move psychosocial care in cancer from evidence to implementation and to fulfill the dream of Jimmie Holland that cancer care be as humanistic as it is effective.

KEYWORDS

acute stress disorder, advanced cancer, depression, global health, leukemia, palliative care, psycho-oncology, psychosocial oncology, psychotherapy, traumatic stress-related disorders

1 | INTRODUCTION

Modern systems of health care and innovations in technology and biology have resulted in a doubling of the life span in both high income and low income countries over the past century.¹ However, the

simultaneous neglect of the human dimensions of medical care and of medical illness have left many patients with advanced disease with unnecessary suffering.² Dissatisfaction with this approach was a driving force in the revolution of modern palliative care.³ Led by figures such as Cicely Saunders and Elizabeth Kubler Ross, attention was drawn to the failure of medicine to support the personhood of individuals with advanced and incurable disease and to relieve their pain and suffering. The vision and leadership of Jimmie Holland were

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equally significant in highlighting the importance of psychosocial care in cancer care and in creating the discipline and the field of psychosocial oncology.

It is a tribute to Jimmie Holland that there is now a large evidence base demonstrating the effectiveness of psychosocial interventions for cancer patients and their families at all stages of the disease, utilizing a wide range of modalities.^{4,5} Attention is now much more often paid to the prevalence and responsiveness to treatment of psychological disturbances that occur in cancer patients and their families. Debates about whether psychosocial interventions are feasible, effective, or prolong life are now much more often based on evidence than on rhetoric or personal belief. However, despite the accumulation of this evidence, psychosocial care continues to be under-resourced, compared to other aspects of cancer care, and its application tends to be variable and unstandardized across the world. Although there are well-developed guidelines for the treatment of pain and other physical symptoms, universal guidelines have not been developed or implemented for psychosocial care in oncology or in palliative care. Further, psychosocial oncology is rarely represented at the highest levels of organization and decision-making in cancer centers. This is sometimes the case because of the fragmentation of supportive care services, such that none are then large enough to warrant such representation. It may also be because psychosocial care is still too often regarded as an ancillary or nonessential dimension of cancer care. The consequence of this view has been that proportional funding and resources are typically not allocated to psychosocial care or to research in psychosocial care.

Routine distress screening in cancer clinics has been shown to be feasible in comprehensive cancer centers⁶ although often not implemented.⁷ However, even when such screening is implemented, psychosocial care is still not offered to or accessed by most cancer patients at all stages of the disease.⁸ This limitation in psychosocial care is due to multiple factors, including the lack of consensus about what interventions or support should be available on an urgent or routine basis, the lack of resources in cancer treatment centers, inadequate training of clinic staff and of psychosocial care providers in a range of modalities, and the lack of awareness of patients and of health care professionals about the benefit of psychosocial care.⁶ Psychosocial skills and interventions must be integrated into the cancer treatment system and into palliative care in order for them to be routinely implemented at all stages of disease.

The focus of my work and that of my research team over the past two decades has been on improving the psychological wellbeing of patients with life-threatening, advanced, and progressive disease and their families and caregivers. I will describe here the trajectory of this research, the evidence that we have accumulated and the initiatives that we have undertaken in order for standardized psychosocial interventions to be incorporated into routine cancer care. We have identified acute stress disorder (ASD) and posttraumatic stress disorder (PTSD) as prototypical psychological disturbances that occur at the time of disease onset and recurrence, and depression, demoralization and loss of the will to live as those that occur with the more gradual and progressive course of metastatic and advanced disease. We have developed psychological interventions to address these states and have embarked on knowledge translation strategies for them to

become implemented as part of routine care. We will describe here the process, the evidence, the interventions, and the knowledge translation strategies that we have undertaken. The time, effort, resources and collaborative relationships that were required to gather evidence about these clinical problems, to develop and test interventions, to conduct pilot studies and more formal randomized controlled trials, and then to undertake the process of knowledge translation are much more difficult to describe.

2 | THE TRAUMA OF LIFE-THREATENING DISEASE OF ACUTE ONSET

There is an enormous body of research on the psychological effects of trauma, largely focused on the sequelae of physical and sexual assault, natural catastrophes and war zones.⁹ These are all circumstances in which the profound psychological impact of trauma has been demonstrated. By contrast, there has been relative neglect of the psychological trauma of serious medical illness, even though this may be the most common and universal trauma that humans experience. This oversight may be because trauma is typically conceptualized as the impact of an injury or threat that is externally imposed, while the trauma of diseases such as cancer is internal.¹⁰ However, the internal and therefore inescapable nature of medical illness may contribute to its uniquely distressing quality. With cancer, the course of the disease and treatment frequently means that the trauma is repetitive and cumulative, perhaps similar in that respect to the experience of individuals living in abusive home environments or in zones of war or natural catastrophe.

The research on traumatic stress, ASD and PTSD in cancer and other medical populations has been limited by the extraordinary difficulty of recruiting into research patients who have been recently diagnosed or who have suffered from recurrence or progression of their disease. Such individuals, who are often overwhelmingly anxious about the implications of their diagnosis and preoccupied with treatment decisions, may be unwilling or unable to consider participation in a research project or even to provide informed consent at such a time of personal upheaval. In research that has been conducted to investigate the frequency of traumatic stress disorders in cancer patients, ASD was identified in approximately one quarter of patients with brain cancer,¹¹ localized breast cancer,¹² and first-onset head and neck, or lung cancers.¹³ The adverse effects of full and threshold ASD and PTSD on health outcomes, quality of life, and survival in other populations^{14,15} highlight the clinical relevance of these findings. Recent research has also shown that ASD is associated with an increased risk of cardiac mortality,¹⁶ a subsequent risk of suicide that is 10 times that in the general population,¹⁷ and an increased risk for the chronicity of traumatic stress symptoms.¹⁸

We first examined traumatic stress in the cancer setting in a study of women with and without a history of breast cancer undergoing mammography screening.¹⁹ Not surprisingly, we found that those with a past history of breast cancer and those who had previously received treatment with psychotropic medication reported higher levels of traumatic stress. However, we were also intrigued to find that perceived physician engagement and support were also linked to

occurrence of traumatic stress. The observation that the perceived support of health care providers at the time of trauma protects patients from traumatic stress is consistent with research demonstrating the protective effects of perceived support for other trauma victims.^{20,21} These findings suggested to us that inpatient medical settings, where supportive care can be mobilized, might provide a unique opportunity and responsibility to intervene to prevent and treat traumatic stress in individuals hospitalized with the recent onset of a life-threatening illness.

We identified acute leukemia (AL) as a prototype for a disease in which ASD and PTSD would be likely to occur because of its acute onset, the immediate requirement for hospitalization and intensive treatment, and the high risk of death due either to AL or to the treatment.²²⁻²⁴ Although treatment settings for adults with AL are often characterized by a "culture of cure,"²⁵ the mortality rate in this population remains high, particularly in older adults.²⁶ The prolonged initial hospitalization for the treatment of AL is disruptive to the lives of these patients²⁷ but it also provides a unique opportunity to investigate the impact of the disease and treatment and to implement therapeutic interventions. However, there has been virtually no evidence base to support the value of specialized psychosocial and palliative interventions in this population. Referral rates for both specialized psychosocial and palliative care tend to be low,^{28,29} and it has not been clear to what extent such interventions could relieve physical and psychological distress in patients newly diagnosed or relapsed with AL.

In the context of uncertainty and debate regarding the value of proactive specialized supportive care in AL, we established a collaborative research group to address this question. We brought together the disciplines of oncology, psychosocial oncology, and palliative care to construct an integrated psychosocial and palliative intervention for this population and to build an evidence base regarding its value. Such interventions have been lacking in the care of patients with solid tumors, as well as in those with hematological malignancies. Although there has been much recent attention to the integration of palliative care with oncology,³⁰ there has been much less consideration of the need to integrate specialized psychosocial care in oncology.

With funding from the Canadian Institutes of Health Research (CIHR), Camilla Zimmermann and I co-led a five-year longitudinal study of the psychological and physical impact of AL. With the support of a large research team and the leukemia program at the Princess Margaret Cancer Centre, we demonstrated that ASD could be identified in about one third of patients with AL in the first month following the diagnosis or relapse of the disease, and that these symptoms persisted or recurred in more than half of these cases at 3 months.²⁴ In qualitative studies led by Rinat Nissim, these patients described the experience of diagnosis and treatment as being "abducted by the illness"²³ and after discharge they reported struggling to construct a new sense of identity.³¹ Physical distress was also common in these patients, with more than 90% reporting more than five concurrent physical symptoms, including pain in 49%.²⁸ The symptoms of ASD were as common as those reported following major physical trauma²² and the physical suffering that they reported was as great as that reported by patients with metastatic and advanced cancer.²⁸

In order to alleviate and prevent the psychological and physical distress that we consistently identified in patients with AL, we developed

an integrated psychological and palliative intervention that we called Emotion and Symptom-focused Engagement (EASE).^{32,33} The psychological component of the intervention (EASE-psy) was based on trauma-focused cognitive behavioral strategies that have been shown to be effective in the management of anxiety associated with PTSD^{34,35} and on the principles of relational support and empathic understanding that we have shown to be effective in the psychotherapeutic treatment of patients with advanced cancer.³⁶ EASE-psy was paired with systematic screening of physical symptoms, with scores of 4 or greater on any item on the Edmonton Symptom Assessment System (ESAS)³⁷ (modified for AL) triggering a referral to early palliative care (EASE-phys). In a Canadian Cancer Society (CCS) funded pilot study of EASE, we demonstrated its feasibility and preliminary efficacy. Although the study was powered only to detect medium to large effects, we found reductions in traumatic stress and in physical symptoms in the EASE group, compared to usual care.³² Funded in part by the CCS, we are now beginning a multi-center national study to establish the efficacy of EASE and the generalizability of these findings.

3 | THE BURDEN OF ADVANCED AND PROGRESSIVE DISEASE

The field of palliative care was initially focused on the end of life, and many of the early observational studies were undertaken with patients in palliative care units.^{38,39} However, over the past decade there has been growing interest in early palliative care and in the psychological and physical well-being of cancer patients from the time of diagnosis.⁴⁰⁻⁴² With this focus, we undertook a large CIHR-funded longitudinal study of patients with metastatic cancer attending ambulatory oncology clinics at the Princess Margaret Cancer Centre. In the so-called Will to Live Study, we assessed approximately 700 patients with metastatic cancer at baseline⁴³ and followed more than 400 of them longitudinally or until the end of life.^{44,45} We found that more than 20% of these patients reported significant symptoms of depression and hopelessness⁴⁵ and that, without intervention, this distress became 2 to 3 times more common near the end of life.⁴⁴ Further, the rates of depression in spouses were almost twice as high as those in patients with advanced cancer.⁴⁶ Remarkably, the desire for hastened death was extremely uncommon in this population, with elevated scores reported by only 1.5% of the sample.⁴⁷ Although medically assisted dying has received a great deal of recent attention,⁴⁸⁻⁵⁰ patients receiving care at a comprehensive cancer center overwhelmingly report a strong will to live.⁴⁷

In the large sample of patients with metastatic and advanced cancer in the Will to Live Study, we were able to test a model for the emergence of depression and hopelessness (Figure 1),⁴⁵ consistent with terror management theory.⁵¹ We found that the degree of physical suffering was one of the strongest predictors of depression and that protective factors included attachment security, self-esteem, and the sense of personal meaning. These findings informed the subsequent development of a tailored supportive-expressive intervention for this population. This intervention built on the work of others in cancer and palliative care, including that of Irvin Yalom,⁵² David Spiegel,⁵³ William Breitbart,⁵⁴ David Kissane,⁵⁵ and Harvey Chochinov⁵⁶

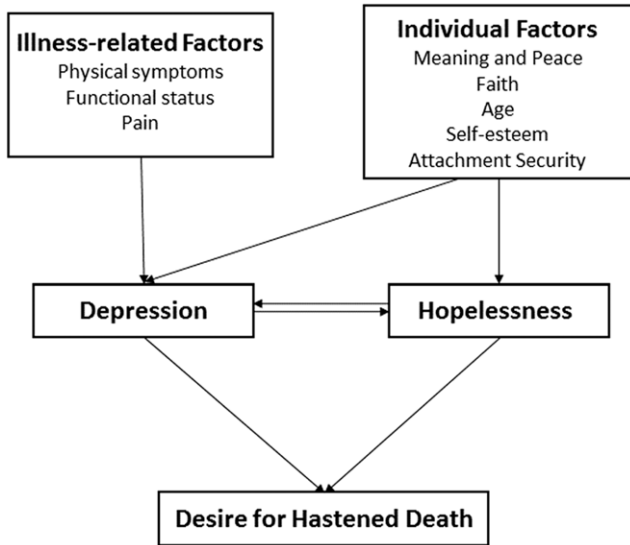


FIGURE 1 Heuristic model of the associations between illness-related factors, individual factors, psychological distress, and the desire for hastened death in individuals with advanced cancer. Adapted with permission from Figure 1 in Rodin et al. (2009) "Pathways to distress: The multiple determinants of depression, hopelessness, and the desire for hastened death in metastatic cancer patients" *Social Science and Medicine*, 68(3), p. 562

and of psychoanalytic theorists in relational and attachment theory,^{57,58} self-psychology, and mentalization-based therapy.⁵⁹

In a clinical research program with Sarah Hales and Chris Lo, we developed an intervention to address the practical and profound problems that face patients with advanced cancer and their caregivers. Referred to as Managing Cancer and Living Meaningfully (CALM), this three-to-six session intervention with patients and, when possible, with caregivers, was intended to provide reflective space and to be integrated with cancer care and early palliative care. It aims to help patients with advanced disease to (1) attend to the practical problems and treatment decisions that they face, and to their relationships with health care providers; (2) adjust to disruptions in attachment security and the renegotiation of attachment relationships that is often required in this circumstance; (3) reconsider and reframe their life priorities; and (4) face fears and make plans for the progression of disease and the end of life (Figure 2). The reflective space and the curiosity and interest of the therapist can help patients to recover the capacity to mentalize and to reimagine possibilities for living in the face of their disease. Such imagination or "double awareness"⁶⁰ is easily lost in the face of the dominating singular reality of advanced disease. CALM provides a framework that helps to guide both clinicians and patients in an intervention that is relatively brief and can be implemented as part of standard cancer care.

We conducted phase 1 and phase 2 qualitative and quantitative studies⁶¹⁻⁶³ and then a large CIHR-funded phase 3 randomized controlled trial evaluating the effect of CALM on the primary outcome of depression at the primary endpoint of 3 months.⁶⁴ We found that patients who participated in CALM reported less depression and greater death preparation at the primary end point and at 6 months and that there was a significant reduction in distress about death and dying at these endpoints in those who reported moderate distress



FIGURE 2 The four domains of CALM

of this kind at baseline.³⁶ CALM also had a significant effect on the prevention of depression in those who were not depressed at baseline. In our qualitative studies, patients described experiencing CALM as a "safe place" to discuss their feelings, and said that participation in it made them feel treated as "a whole person" in the cancer system and that they would be now able to "face death in a peaceful way".⁶³

We began a knowledge translation activities from the beginning of our CALM research program and have now trained more than one thousand clinicians from more than 20 countries. Research studies on CALM have been conducted in Germany, led by Anja Mehnert^{65,66} and in Italy led by Luigi Grassi and Rosangela Caruso.⁶⁷ The Global Institute of Psychosocial, Palliative and End-of-Life Care (GIPPEC) at the University of Toronto and the global agency Movember, based in Melbourne, Australia, are now coordinating and supporting a global CALM implementation project that involves 20 sites to date. With the support of Lili Tang, the Peking University Cancer Hospital and the Chinese Psycho-Oncology Society have been early adopters of CALM, providing encouraging support for the universality of this intervention. Psychosocial and palliative care leads at cancer centers in other countries, including Australia, Japan, South Korea, Hong Kong, Portugal, the Netherlands, the United Kingdom, Switzerland, Chile, Malaysia, the United States, and Canada, have enlisted in this global project, beginning at different stages of development (Figure 3). We hope that this can be a vehicle to structure training, clinical implementation, and research and to facilitate the routine implementation of psychosocial interventions of this kind in cancer care.

4 | THE FUTURE

The field of psychosocial oncology has made enormous advances since Jimmie Holland established the International Psycho-Oncology Society more than three decades ago. The number of clinicians, educators, and researchers in the field and national psycho-oncology societies has grown exponentially. There is now a large body of research demonstrating the effectiveness of psychosocial interventions at all stages



FIGURE 3 Global CALM levels of development

of disease. However, psychosocial care for treatment and prevention of psychological distress and for the promotion of psychological well-being is not yet a routine standard of care for all patients at most cancer centers in the world. I have described here two approaches from our research team, one more recent than the other, to move from observation to intervention to global knowledge translation. Others have also been engaged in projects of this kind involving a variety of interventions at all stages of cancer. The success of these projects remains to be determined, but they are attempts to carry forward the dream of Jimmie Holland that psychosocial oncology contribute substantially to “the humanism that is increasingly being attached to care of patients with cancer, especially during palliative care”.⁶⁸ Collaborative efforts now being undertaken in our global community may help to ensure that this dream becomes a consistent and universal reality in cancer care.

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