Cancer patients experience a range of challenges that can encompass: psychological distress; difficulties communicating with health providers, family and friends; obtaining the required health information; physical changes in body functioning and appearance; sexual dysfunction; and disruption to family functioning and occupation.1-3 These challenges are exacerbated as the disease progresses.4 Moreover, there can be vast variations in the prognosis of individuals with advanced disease. The length of survival time between different disease types can vary from expectation of years, such as for locally advanced prostate cancer, to an expectation of a few months, such as for metastasised small cell lung cancer. These factors have implications for the types of psychosocial or supportive care interventions that will be effective in ameliorating suffering. This paper describes the impact of advanced cancer on the person and the issues associated with the development and testing of appropriate psychosocial and supportive care interventions.

Impact of the ‘bad news’ about advanced cancer

While the news of an advanced cancer diagnosis has many similarities to earlier bad news episodes, it also has some unique characteristics. Understandably, most people rate this news as more devastating than the initial diagnosis of localised disease.5 The challenges for patients and their families on hearing that their cancer is not curable are multifaceted. They face worsening quality of life (QoL) and having to confront existential and spiritual questions, which in addition to increasing physical symptoms, cause significant psychological distress.6

A high proportion (61%) of Australian women with advanced breast cancer indicate that they would like changes to the way their diagnosis of advanced disease was communicated to them.7 While there is research on preferences for prognostic information among patients with advanced cancer,8-9 there have been no empirical studies evaluating ways of communicating ‘bad news’ to patients with advanced disease.

Impact on physical functioning and quality of life

Physical functioning, emotional functioning and general QoL are all intimately connected. Fatigue in advanced disease is the most common symptom and the most challenging to manage.10 Indeed, dealing with a lack of energy and tiredness is rated by patients with advanced cancer as their top unmet need.11 Severe fatigue has been associated with higher levels of depression and increased pain.12 Effective management options are limited, however there is evidence that exercise programs can reduce cancer-related fatigue in patients with early cancer.12 Pain, both neuropathic and nociceptive, is critical to control. It is arguably a more important symptom than fatigue because it can be debilitating and is likely to lead to loss of activity, which in turn exacerbates fatigue. Patients also see pain as a sign of advancing disease and this contributes to psychological symptoms of fear, depression and anxiety.13

Dyspnea is also highly prevalent among those with advanced cancer, especially lung cancer.14 It is a highly distressing symptom, which restricts all activity and causes anxiety, panic, depression and fear of impending death.14 Nausea, vomiting and constipation are often poorly controlled and can also adversely affect a patient’s QoL.15 Optimising QoL is not only an important outcome in itself, but it is also associated with longer survival and lower levels of depression among patients with advanced cancer.16-17 These studies highlight the importance of controlling symptoms, especially fatigue and pain, however, research into effective interventions for people with advanced cancer is scarce.

Impact on psychosocial functioning

People with advanced cancer often experience high levels of psychological distress, with as many as a third meeting diagnostic criteria for psychiatric disorders.18-20
Distress has been linked to prognostic awareness. Depression among people receiving palliative care who did not acknowledge their prognosis has been found at rates almost three times that of those who demonstrated partial or complete conscious acknowledgement of their condition.20 Patients’ social interactions also suffer, as symptoms restrict functioning in social and work-related roles.21 In comparison to others, people with advanced disease report higher levels of unmet needs in most domains, but especially in the psychological, physical and daily living domains.2,22

In a recent systematic review of 329 trials of psychological interventions for cancer patients, it was concluded that group-based therapies require further research before recommendations can be made about their use to reduce anxiety and depression, improve general affect and coping and increase survival time. Informational and educational interventions also warrant further research for their role in reducing depression, improving QoL and increasing survival time. The involvement of significant others in psychosocial interventions for cancer patients reduces their anxiety and distress and enhances their QoL.23 The review also showed that only 15% of the 329 trials reviewed examined psycho-educational intervention oriented to patients with advanced disease. Disturbingly, only one trial of the 329 was judged methodologically adequate; consequently only tentative recommendations could be made about the effectiveness of interventions on patient outcomes.

**Impact on family functioning**

Many people with advanced cancer experience guilt as a result of the burden they perceive being placed on their caregivers.11 Family physical and emotional distress increases as the cancer advances, peaking during the terminal phase of the illness.24-25 Children of parents with advanced cancer experience significant psychological distress, particularly adolescent daughters of ill mothers, and parents may not be aware of this distress.26-27 Given the impact advanced illness has on family functioning, it has been recommended that the patient and their family should be recognised as the “unit of care”.28 Carers of people with advanced disease also have significant unmet informational needs and experience high levels of distress.29 As Australian palliative services are predominantly community-based, family caregivers are required to assess and monitor the patients’ needs and then deliver the required therapeutic intervention for symptom control at home.29 Pain management can be particularly challenging and many carers experience difficulties performing these activities.3,30

**Existential issues**

A person with incurable cancer is likely to face important existential questions related to the meaning of life and the prospect of facing death. “Uncertainty about the future” was described as an unmet need by a majority of women (61%) with advanced breast cancer.7 These existential concerns can cover a range of issues including isolation, loss of control, burden on others, uncompleted life tasks, hope, hopelessness and preparation for death.31 Using the construct of demoralisation syndrome, Kissane and colleagues32 have attempted to incorporate the idea of existential distress into palliative care. They argue that the concept of demoralisation provides clinicians with a framework for identifying the deep emotional pain and existential distress that accompanies loss of hope and social isolation in the terminally ill.

Recently, a dignity therapy intervention designed to improve psychosocial and existential distress among terminally ill patients was evaluated using a pre/post design.33 Post-intervention measures indicated reductions in suffering and depression among participants. Despite a short follow-up, only 7-10 days after baseline, there was a 22% dropout rate, primarily due to death or deterioration. This illustrates one of the many difficulties with conducting psychosocial research with people with advanced disease.

**Conducting psychosocial research in the advanced cancer setting**

In order to address the psychosocial issues facing people with advanced cancer and their significant others, we need a repertoire of effective interventions that have been demonstrated to improve patient outcomes in the clinical setting. Hence, it is imperative that targeted, rigorous research is conducted. The highest level evidence for the effectiveness of an intervention is a series of well-conducted randomised control trials.34 However, very few randomised control trials are conducted in the advanced cancer setting.35 The primary reason is most likely the difficulties encountered in implementing a randomised trial with this population.

The most serious difficulty is recruitment and attrition rates. The pool of potential recruits may be smaller than anticipated because: patients may fail to meet eligibility criteria because they are judged to be unable to complete the study requirements due to low performance status; cognitive dysfunction resulting from brain metastases or treatment side-effects; or poor prognosis. Further impacting on recruitment rates, there is a comparatively higher refusal rate by eligible patients and greater professional gate-keeping of access to patients because advanced cancer frequently makes people feel unwell or distressed.36 With randomised control studies, issues may arise for the treatment team about withholding supportive interventions that may be reasonably expected to benefit patients who have a shortened life expectancy.37 Moreover, higher refusal rates increase the probability of sample bias that can limit the generalisation of the findings. Some of these difficulties can be addressed by: broadening the inclusion criteria; conducting bias analyses; working closely with the treatment team to reduce gate-keeping; and ensuring that study burden is kept to a minimum, for example, by reducing the length of the questionnaire.

The high level of attrition results from the unpredictable health of people with advanced cancer who can quickly become too sick to complete the study requirements, or...
die unexpectedly. The estimation of prognosis is known to be inaccurate. Christakis and Lamont\textsuperscript{37} have shown that the life expectancy estimates for individual palliative patients by the treating physician are frequently wrong, on average by a factor of five, usually overestimating survival time. Reducing the length of follow-up can ameliorate the problem of attrition. However, when follow-up assessments are close together, outcome measures need to be chosen carefully. For example, it is recommended that some QoL measures are not repeated within 30 days as more frequent administrations may affect the validity of scores.\textsuperscript{38}

Participant engagement in the intervention as specified by the protocol is another problem. Fluctuating health may mean that patients do not receive the intervention or receive only part of it. Conducting ‘intention to treat’ analysis as recommended by the CONSORT criteria for randomised control trials\textsuperscript{39} means that if a sizeable proportion of intervention patients do not receive the entire intervention, this will dilute the impact of the intervention on outcome measures. Hence, it is critical to consider carefully practical issues when conducting this type of research. Certain intervention modalities may be tricky to implement in practice, such as group sessions, as it may be difficult for participants all to attend at the same time. One study examining a group intervention for carers of palliative care patients found that for elderly carers, the provision of a transport service assisted with uptake of the intervention.\textsuperscript{40}

The evaluation of supportive care interventions for the family members of people with advanced disease poses additional challenges, including the design of studies that do not place too great a time burden on family members who may already have many competing demands. Achieving adequate study retention may also be difficult, especially if the study has follow-ups planned for during bereavement. Other difficulties relate to rapid fluctuations in patients’ health and the reliability of data where carers are asked to make assessments on patients’ behalf.\textsuperscript{41}

The challenges associated with conducting supportive care research in this area may account for why there are considerable gaps in our knowledge about optimal supportive care interventions for people with advanced cancer. The care of people with advanced cancer will only be improved by the conduct of high quality research to inform practice change. The research challenges with this population are greater than with other groups, but many difficulties are able to be ameliorated if not overcome, by various mechanisms such as broadening inclusion criteria, careful consideration of intervention delivery, reducing length of follow-up, shorter questionnaires and data collection by telephone. Higher levels of attrition and lower recruitment rates may also need to be accepted as features of this research. However, eschewing this work on the basis that it is too hard or that it is unfair or inappropriate to ask people with advanced disease to take part in research is unacceptable. It is paternalistic to assume that people with advanced disease do not wish to be involved in research because they are unwell or have limited time left. As researchers, we need to rise to this challenge and not subscribe to the excuses that are proffered to avoid working with this worthy group.

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**References**