

The science of hope

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Hope is a contextual term that has different connotations depending on the setting. We analyse the concept of hope with respect to its applicability for oncology. We review studies that present hope as a direct or secondary mediator of outcome. We posit that an individual's level of hope is often determined by innate personality characteristics and environmental factors, but can also be physiologically influenced by immune modulators, neurotransmitters, affective states, and even the underlying disease process of cancer. We argue that hope can be a therapeutic target and review evidence showing the effects of hope-enhancing therapies. Given the potential for hope to alter oncological outcomes in patients with cancer and the opportunity for improvement in quality of life, we suggest further research directions in this area.

Introduction

Cancer research is scientifically driven and has an unquestionable focus on improving quantifiable parameters of disease, such as survival and functionality. For individuals with cancer, living with the disease is often tortuous, painful, and lonely. Even if their outcome is optimal, the journey to recovery can forever change them psychologically and behaviourally. The way we equip people to cope with cancer might affect not only their quality of life but also survival.

Hope can assist patients through the trajectory of illness spanning diagnosis, treatment, and follow-up.^{1,2} Until the past thirty years, with the advent of empirical hope studies, hope was considered an abstract concept. Often, physicians have the mistaken impression that hope is an innate characteristic that is not affected by external manipulation, and oncologists have been reluctant to embrace hope as a tool to help people living with cancer. However, it is not widely known among physicians that hope is measurable and can be enhanced via therapeutic intervention.

In this article, we define hope, highlight its potential as a tool in cancer care, and emphasise the need for rigorous scientific research on its importance. The physiological basis of hope is explored with specific reference to the emerging research topics of psychoneuroimmunology and psycho-oncology. Finally, ongoing research opportunities are discussed.

Defining hope

The creation of a sufficiently rigorous definition of hope that allows for methodical investigation is difficult. In the vernacular, hope can reflect different connotations; for example, "I hope it will be sunny tomorrow" is different from "I hope to finish my work by tomorrow." For patients with malignant disease, "hoping that my cancer will not return" is not the same as "hoping to see my children before I die". Given the nuances of the word hope, it is important to carefully define the term. Although various models of hope exist in the published medical and social sciences literature,³⁻⁵ Charles Richard Snyder's conceptualisation,^{6,7} known as Hope Theory, has received the most attention among social science researchers in the past 30 years, in part because it lends itself to quantitative measurement and broad application.

Snyder⁷ portrayed hope as a goal-orientated cognitive construct with affective and behavioural implications. Accordingly, a base condition for the presence of hope is to have something for which to hope—ie, a goal or goals. Within this framework, hope has two inter-related components: pathways thinking and agency thinking. A pathway is a strategy for achieving goals.⁸ People engage in pathways thinking whenever they consider mechanisms to reach their goals, and people who have a hopeful outlook tend to create many pathways in order to circumvent possible obstacles.⁷ The second component of hope, agency thinking, consists of "thoughts that people have regarding their ability to begin and continue movement on selected pathways toward those goals".⁹ Such inspiring thoughts motivate individuals to pursue their goals, even in challenging circumstances.

Hope and accomplishment of goals reciprocally affect one another.¹⁰ Hope predicts progress towards goal attainment.^{11,12} However, the degree of progress then affects the subsequent levels of hope for an individual—eg, if a person perceives they are advancing towards a goal, their tendency to engage in pathways and agency thinking readjusts to reflect this goal success.¹¹ Conversely, when people sense that they are not making sufficient progress, their tendency to engage in pathways and agency thinking is commensurately reduced. This process leads to upward and downward spirals of hope, both of which can be relevant in oncological settings in which patient motivation (ie, agency thinking) and adherence to medical regimens (ie, pathways thinking) are necessary to meet treatment goals (figure 1).^{13,14}

Hope differs from other future-focused expectancy constructs such as self-efficacy, locus of control, and optimism. Snyder observed that self-efficacy is principally concerned with the belief that an individual can do a behaviour, whereas locus of control involves the belief that an individual's behaviours will lead to desired outcomes.⁷ Neither of these constructs specifically addresses goal-directed planning, whereas hope focuses on both the elements of planning (pathways) and motivation (agency). Also different from hope, optimism is a highly generalised expectation of a positive future. Optimism is the belief that positive outcomes will occur without regard to a person's actions, whereas hope

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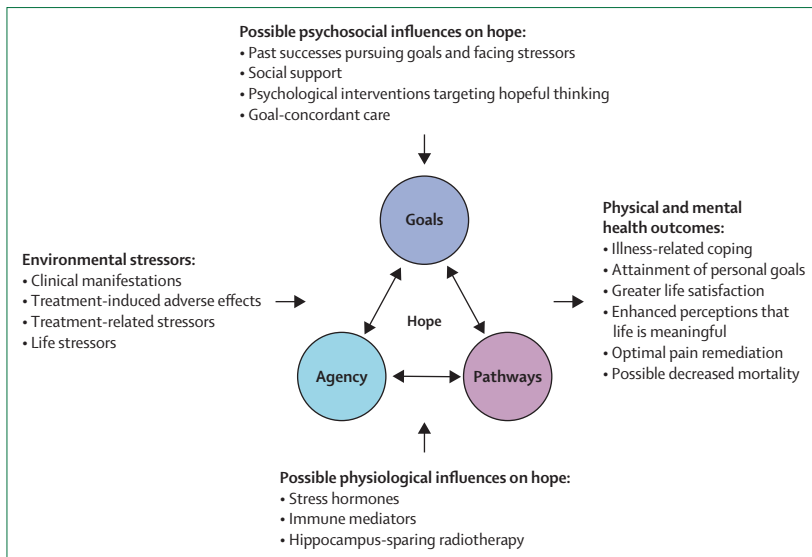


Figure 1: The hope construct
 Graphic depiction of the central components of Hope Theory^{6,7} (ie, goals, pathways, and agency), which are influenced by physiological, psychosocial, and environmental inputs. Potential downstream implications are shown.

explicitly involves expectancies that positive outcomes will occur through a person’s pathways and agency. Scheier and colleagues,¹⁵ creators of the most widely used measure of optimism (the Life Regard Index), define optimism as “expectancies that are generalised—expectancies that pertain more or less to the individual’s entire life space”.¹⁵ This difference in emphasis on personal involvement led Rand and colleagues¹⁶ to observe that, in situations in which individuals can exercise some measure of control, hope seems to be a stronger predictor of behavioural and affective outcomes than optimism. In regression analyses, hope has been shown to account for variance in pain tolerance,¹⁷ coping,¹⁰ mental health symptoms,¹⁸ and quality of life¹⁹ in various populations, even after statistically controlling for variables like self-efficacy, locus of control, and optimism. Moreover, using both exploratory and confirmatory factor analysis, hope has been shown to be statistically and conceptually distinct from these other constructs.^{20–22}

Hope Theory is not the only perspective on hope that has been proposed. Herth’s hope construct represents another common model.^{3,23} Similar to Snyder, Herth defines hope as “a motivational and cognitive attribute that is theoretically necessary to initiate and sustain action toward goal attainment”.²⁴ However, the measure most commonly used to assess this version of hope, the Herth Hope Index, contains a variety of items that seem to assess other constructs besides hope, including loneliness, positive memories, and religiosity. These additions create psychometric difficulties for the Herth Hope Index, potentially confounding hope with other aspects of psychological wellbeing. Indeed, previous research shows inconsistent results regarding the index’s

factor structure, variably finding one, two (including a religiosity factor), or three factors (including an interconnectedness factor).²⁵ We believe that the most direct operationalisation of hope is Snyder’s model; therefore, we will primarily focus on this construct, although we do include research using the Herth Hope Index where appropriate.

Measuring hope

After defining hope, the next challenge is to find tools for measurement that are simple to administer and sufficiently versatile for a variety of settings. Various valid and reliable methods have been developed to assess hope.⁸ These scales consist of between six and 12 items and can be completed by the respondent or administered verbally in 5–7 min.

The most widely used measure of hope, the Adult Hope Scale, was developed to assess hope as a stable characteristic of a person, rather than a fleeting psychological state.¹⁰ Its scores are thus relatively insensitive to daily events, instead capturing the degree to which hopefulness is part of an individual’s personality. Examples include “there are lots of ways around any problem” (pathways) and “I energetically pursue my goals” (agency), which participants rate on a scale of 1 (definitely false) to 8 (definitely true). A second measurement, the State Hope Scale, was developed to capture fluctuations in hope, allowing researchers to assess changes in agency and pathways over hours, days, weeks, or months.²⁶ In addition to these more general measures of hopefulness, the Goal-Specific Hope Scale¹¹ monitors hope for a particular goal that has been nominated by a researcher, clinician, or patient (eg, in a hope enhancement intervention) and the Domain-Specific Hope Scale²⁷ contains subscales assessing hope in six life areas: social, academic, family home, romantic, work, and leisure. Finally, the Children’s Hope Scale²⁸ was developed for use in individuals aged 8–16 years.

Hope as a predictive factor

Several studies show the connection between having a high level of hope and health-promoting behaviour, including being a non-smoker,²⁹ undertaking regular physical activity,^{30,31} and salutary dietary behaviours.^{32,33} This association can have particular relevance for patients with cancer. For example, Guericco and colleagues³⁴ showed longer progression-free survival in people with advanced colorectal cancer who reported greater physical activity than in those who exercised less.³⁴ In one study, women with high hope had greater knowledge about breast cancer than women with low hope and could identify a larger number of behavioural strategies for addressing the disease.³⁵ Building on the conclusions of these studies, if hope predicts health-promoting behaviours, hope could ultimately be a predictor of survival as mediated by these behaviours.

Another area of study relevant to oncologists involves the connection between hope and pain. In a laboratory

study, Snyder and colleagues³⁷ found that healthy adults with high hope were able to submerge their hands in freezing water for longer than low-hope participants were. This effect seems to be due to high-hope participants perceiving the onset of this pain significantly later than their low-hope counterparts. Additionally, interventions based on Hope Theory have been shown to reduce perceptions of pain in patients with chronic pain.³⁶ This connection between hope and pain perception is likely to be mediated by so-called pain catastrophisation, with research showing that higher-hope people spend less time ruminating on their pain than lower-hope individuals.³⁷

Research is increasingly exploring the role that hope has in coping with cancer. Ho and colleagues³⁸ found that high hope was associated with increased psychological resilience following genetic testing for colorectal cancer. In a longitudinal study of women with breast cancer, Stanton and colleagues³⁹ observed that participants reporting higher levels of hope were more likely to engage in healthy emotionally-expressive coping, more likely to report positive perceptions of their physical health, and had higher levels of positive emotions at 3 months post-treatment than low-hope participants. These investigators also noted an interaction between hope and coping, such that participants who used more emotionally expressive coping experienced less emotional distress and required fewer cancer-related medical visits than those who used less emotionally expressive coping, but only when they were also high in hope. Similarly, Jafari and colleagues⁴⁰ determined that hope was associated with life satisfaction in adults seeking treatment for various types of cancer. A connection also seems to exist between higher levels of hope and greater psychological growth in individuals with cancer diagnoses.⁴¹ That is, higher-hope individuals are more likely than their lower-hope counterparts to report positive psychological changes in response to their cancer treatment, including discovering new friendships, deepening spirituality, and embracing gratifying activities.

Psychoneuroimmunological basis of hope

Although there is no debate that hope is predictive of various aspects of psychobehavioural wellbeing, the question remains of whether or not hope can have a disease-modifying effect in patients with cancer.

Although there have been few studies on the role of hope itself in disease modification, a huge amount of research exists regarding the association between cognitive and affective states and physiological outcomes. Psychoneuroimmunology developed as a discipline to address this issue.

Cognitive and affective states are not completely reducible to neurochemical and neurophysiological processes; however, they have reciprocal associations and one can affect the other.^{42–44} A major question is the directionality of such associations. Do mental states, such as stress, contribute to the oncological disease

process by mediating changes in the immune system or do alterations in the immune system affect cognitive and affective states? Of course, a synthesis of these two dynamics might well exist. Answering these questions is an important clinical challenge because they determine treatment targeting.

There is ample research postulating that depression and stress increase the incidence of cancer and worsen prognosis in malignant disease. This association is based on the effects that stress and affective disorders have on the inflammatory response and the link between inflammatory mediators and cancer. Several studies have proposed that pro-inflammatory cytokines and other markers of inflammation increase with depression.^{45,46} A meta-analysis of 76 studies⁴⁷ showed that higher levels of depressive symptomatology predicted an increased risk for developing cancer and mortality. Pro-inflammatory cytokines have been proposed to induce so-called sickness behaviour, which includes manifestations of depression, somnolence, anorexia, anergia, and hyperalgesia.^{48,49} Robust associations between hope and depressive symptoms have been shown in studies, pointing to a possible mediating role for hope.^{7,18} Furthermore, hope-based therapy interventions have been shown to reduce depressive symptoms.^{7,50}

Krizanova and colleagues⁵¹ have reviewed the effects of stress on cancer. Stress increases concentrations of catecholamines, which in turn modulate immune mediators. In breast cancer, Obeid and Conzen⁵² reviewed how catecholamine concentrations affect progression of breast cancer by reducing the efficacy of chemotherapeutic drugs, thereby increasing cancer cell proliferation. There were also alterations in the tumour microenvironment in terms of inflammatory response and angiogenesis that facilitate tumour growth.⁵³ β -Adrenergic blockers have been used to try to mitigate the effects of catecholamines, but the results have not been encouraging.⁵⁴

The most obvious relation between affective states and tumours is that some affective states, such as depression and anxiety, might deleteriously affect survival.⁵⁵ However, animal studies have shown that the opposite can occur, with tumours inducing negative affective states, creating a possible cycle.⁵⁶ Tumour-related elevation of cytokines can activate anorexia and cachexia, and it would not be surprising that the same would be true for depression.⁵⁷ For example, there is documented linkage between pancreatic cancer and pre-morbid affective disorders occurring in the year before diagnosis,⁵⁸ but whether depression was a factor in tumorigenesis or resulted from the presence of an undetected malignancy remains unclear.

This potential role of affective states raises the question of whether psychosocial interventions can have a positive effect on cancer prognosis. If the affective state is the independent variable affecting cytokines and neural pathways associated with tumour proliferation, then it would be reasonable to consider such therapy. However,

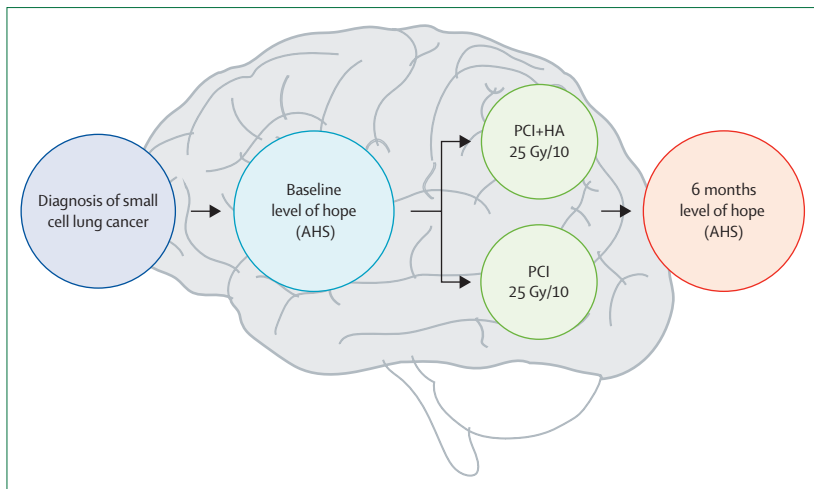


Figure 2: Schematic depicting the approach used in the ongoing NRG Oncology CC-003 trial for patients with small cell lung cancer (NCT02635009). Hopefulness is measured before and after the interventions. If hopefulness is retained when the hippocampus is spared, then that structure might be implicated in the genesis of hope. AHS=Adult Hope Scale. HA=hippocampal avoidance. PCI=prophylactic cranial irradiation.

if the tumour is causing a pro-inflammatory response that is inducing depression, then psychosocial interventions will be less effective.

Several studies—covering a variety of conditions, including cancer—have assessed the effect of psychological interventions on different biomarkers of inflammation. Two meta-analyses reviewing a variety of diseases showed that there was an attenuating effect but it was not retained and was limited to specific biomarkers such as C-reactive protein.^{59,60} It is difficult to draw conclusions from these studies—especially in terms of relevance to cancer—because a range of interventions of varying intensities and durations were analysed and the selection and timing for measuring inflammatory markers varied greatly. Despite these limitations, several reports provide evidence that a biobehavioural approach might be instrumental in modulating pro-inflammatory mediators and even in prolonging survival. First, in women with non-metastatic breast cancer, microarray analysis of leucocytes showed that social wellbeing was associated with reduced levels of pro-metastatic gene expression.⁶¹ This association confirmed findings from an earlier study⁶² concerning early-stage breast cancer. Second, a cognitive-behavioural stress management intervention lasting 10 weeks reversed elevated expression of anxiety-related pro-inflammatory genes in circulating leucocytes.⁶³ Long-term follow-up by this group showed the retained effect of cognitive-behavioural stress management up to 15 years in terms of quality of life. Finally, in a randomised trial,⁶⁴ the effect of an 8-week mindfulness-based stress-reduction programme in 192 patients with breast cancer was tested. In the intervention group, participants received standardised instructions on meditation, breathing awareness, and mindful yoga. The control group attended educational seminars pertinent to their disease or lifestyle.

The intervention resulted in improved levels of stress, reduced depression, and enhanced sleep quality. Concomitantly, concentrations of tumour necrosis factor α and interleukin-6 decreased and interferon- γ production increased.

The potential for including biobehavioural interventions in cancer treatments has been discussed in a 2015 review,⁶⁵ which highlighted studies showing possible effects of such interventions on the biological tumour-associated changes and long-term outcomes. The authors advocated for more studies and discussed methodological challenges for designing experiments that would provide meaningful data.

In the context of hope-based psychosocial intervention and cancer progression, a multistage analysis will be needed that measures the effect of the intervention on specific biobehavioural states, then assesses the effects on markers related to pro-inflammatory cytokines and other factors associated with tumour proliferation and progression. Such studies will require relatively large numbers of participants to ensure that intervening biological and psychosocial factors are controlled for.

Ongoing studies to assess hopefulness

The National Cancer Treatment Network is sponsoring several assessments of hopefulness. Hope is a cognitive state; therefore, there is great interest in identifying neuroanatomic correlates of hope. The clinical importance of this research question has been related to radiation oncology because specific patterns of radiation dose deposition are associated with neurocognitive deficits.

Investigators from NRG Oncology have surmised that the hippocampus could be a central mediator of hopefulness.^{66,67} In one study (CC-003), patients with small cell lung cancer are being randomly assigned to prophylactic cranial irradiation with or without hippocampal avoidance (trial number NCT02635009). By using the Adult Hope Scale to assess levels of hopefulness before and following treatment, it will be possible to determine if baseline levels of hopefulness can be maintained in those who have the hippocampus spared as opposed to patients who received a full dose of radiation to all brain regions (figure 2). As such, it could be possible to infer that the hippocampus is implicated in central pathways promoting hopefulness.

Taking a different approach, in 2019, the Southwest Oncology Group (SWOG) approved a survey of levels of hopefulness among SWOG investigators. Although oncology researchers and clinicians are hypothesised to be classified as high-hope people, this specific hypothesis has never formally been tested or documented. The study will test for associations between characteristics of the investigators (eg, age, gender, and specialty) and levels of hopefulness. As SWOG considers the integration of hope enhancement techniques into its protocol design, it will be important to ascertain whether there is discordance in

	Study population	Design	Treatment	Results
Rustøen et al ⁶⁹	Patients with breast cancer (n=195)	Single group longitudinal study	Eight weekly sessions teaching cognitive coping techniques	Increased hopefulness at 1 week and 3 months
Duggleby et al ⁷⁰	Patients with terminal cancer (n=60)	Randomised trial (treatment group and control group)	1 week of "hope activities"	Increased hopefulness at 1 week
Thornton et al ⁷¹	People with recurrence of gynaecological cancers (n=32)	Single group longitudinal study	20 weekly sessions emphasising goal pursuit	Increased hope and quality of life, and decreased anxiety at 6 months
Rosenberg et al ⁷²	Adolescents and young adults (n=92) with cancer (mostly leukaemia or lymphoma)	Randomised trial (treatment group and control group)	PRISM	Increased hopefulness at 6 months
Breitbart et al ⁷³	Patients with advanced cancer (n=273)	Randomised trial (treatment group and control group)	Eight sessions once a week of MCGP	Decreased hopelessness at 6 months (hopefulness not measured)
Herth ⁷⁴	Patients with recurrent disease (n=115)	Randomised trial (treatment group and two control groups)	7 weekly sessions using cognitive reframing	Increased hopefulness at 1 week

PRISM=Promoting Resilience In Stress Management. MCGP=meaning-centred group psychotherapy.

Table: Studies of hope interventions for patients with cancer

hopefulness between the investigators and the patients they recruit for studies. If such discordance can be anticipated, it might prove prudent to create dyads (eg, high-hope investigators with high-hope study participants) that would theoretically increase the likelihood of adherence to protocol guidelines.

Clinical maintenance and enhancement of hope

The value of hope in oncology seems to be independent of the patient's clinical state and prognosis. Smith and colleagues⁶⁸ measured hopefulness using the Herth Hope Index in 27 patients diagnosed with advanced cancer who were about to receive bad news. There was no change in this metric of hopefulness when it was measured after bad news was delivered in comparison with baseline levels of hopefulness. These results showed that hope can be maintained when patients with advanced cancer are given such news provided that the information is conveyed in an authentic and truthful manner.

Several investigators have tried to enhance levels of hopefulness in patients already diagnosed with cancer (table). Such efforts were inspired by interventions in populations including students with learning disabilities, prisoners, and even athletes.⁶ Among athletes, sports psychologists have harnessed the benefits of temporal framing to underscore the worth of competing in individual matches even when a league championship is unachievable.^{14,75} This example is analogous to the value of encouraging patients with disseminated malignancies to hope for short-term goals despite a bleak prognosis.

Rustøen and colleagues⁶⁹ enrolled 195 patients with breast cancer in a programme that included eight weekly sessions that isolated one characteristic per session (eg, belief in oneself, trust, and future orientation). The intervention succeeded in promoting hope at 3 months as measured by the Herth Hope Index. Herth used the index to document enhanced hopefulness among 115 patients who had a first recurrence of cancer.⁷⁴ In a three-group trial,⁷⁴ patients were randomly assigned to

the intervention (treatment group), attention control (informational group), and control group (usual treatment). The intervention focused on connecting with others, expanding boundaries to include spiritual issues, and using rational thought processes to build hopefulness. The treatment consisted of weekly sessions for 7 consecutive weeks and significantly increased hopefulness was documented in the experimental group at 3-month, 6-month, and 9-month intervals, albeit with a waning effect size over time.⁷⁴

Similarly, Duggleby and colleagues⁷⁰ reported results of the Living with Hope programme, which involved 60 patients with terminal cancer. This programme included a video on hope and a choice of three hope activities that were implemented during a 1-week period. At the end of the week, there was increased hopefulness documented by the Herth Hope Index. Thornton and colleagues⁷¹ offered an intervention of 20 sessions, including hope-based techniques, to 32 women with recurrence from breast or ovarian cancers. Although the study did not include a control group, results showed that stress, anxiety, and general negative affect decreased, whereas hopefulness, positive affect, and quality of life increased at the 6-month follow-up assessment.

The results of two prospective randomised trials with implications for hope (although not necessarily specifically targeting hope), have also been published in the past five years.^{72,73} These phase 3 trials are encouraging; however, they are limited by small sample sizes and short-term follow-up. In a trial designed for adolescents and young adults (aged 13–25 years) with leukaemia or lymphoma, investigators at the Seattle Children's Hospital (WA, USA) randomly assigned 92 patients to stress management (Promoting Resilience In Stress Management [PRISM]) techniques or usual care.⁷² The stress management techniques of PRISM are predicated on goal-setting ability and the development of skills for finding meaning in the disease journey. Using Snyder's hope scale, a significantly greater increase in hope at

Search strategy and selection criteria

We searched the National Library of Medicine MEDLINE database and the American Psychological Association PsycInfo database using a variety of search terms, including "hope", "optimism", "resilience", "goals", "well-being", and "health-promoting behavior". These terms were then linked to different pro-inflammatory cytokines, given their purported role in the psychoneuroimmunological basis of hope. The results were then linked to those related to oncology, and narrowed to specific cancer types. The search was limited to studies in the English language that have been published since 1990.

6-month follow-up was recorded in the PRISM group than in the usual care group.

Breitbart and colleagues⁷³ developed meaning-centred group psychotherapy (MCGP) for patients with advanced cancer. The intervention incorporates existential concepts (eg, building identity, freedom, and coping with life challenges) taught by trained psychotherapists over eight weekly, 2-h sessions. In 273 patients randomly assigned to either MCGP or supportive group psychotherapy, there was a statistically significant decrease in hopelessness associated with the intervention group. Although intuitive, whether analogous benefits would be achievable when hopefulness (rather than hopelessness) is measured remains unclear from this study. Moreover, the combination of the need for a trained psychotherapist and the coalescence of a group meeting for 8 weeks could make this intervention impractical in many settings.

Conclusion

The studies discussed suggest that health-care providers can modulate hopefulness. However, we have concerns about the robustness of some of the tools used to measure hope and feel that only highly motivated individuals could invest the time needed to do the respective interventions described. Accordingly, we are currently testing short (2-h) workshops based on the work of Feldman and Dreher¹² that are administered on a single occasion. Separate tracks have been created to determine whether hopefulness can be enhanced for patients (eg, with stage IV breast cancer) and oncologists (clinical trial: NCT03074071). In the case of oncologists, the effect of the intervention, not only on hopefulness but also on burnout, will be gauged.

Additionally, SWOG is considering inserting hope measurements into many studies assessing new oncological treatments (O'Rourke M, co-chair of the SWOG Palliative and End-of-Life Care Committee, personal communication). Should those investigations find an effect of naturally occurring hopefulness on classic oncological endpoints, an attempt will be made to determine whether a similar effect prevails in patients who become more hopeful after participating in hope enhancement workshops.

Cancer has often been equated with hopelessness.¹ As an outgrowth of major advances in oncology, that perception has now changed; however, patients still face challenges related to coping with life as cancer survivors.⁷⁶ Oncological care is a complex and sophisticated endeavour. It is easy for oncologists to neglect attending to the dynamics of hope as part of disease management. Emerging research in psychoneuroimmunology is consistent with the notion that hope could have clinical implications for prognosis. Therefore, hope might be an effective construct for professionals in oncological disciplines who seek to help patients live with cancer or cope with a difficult prognosis. We propose that hope enhancement techniques could be an important tool for oncologists, health-care providers, and patients.

Contributors

All authors contributed equally to this manuscript.

Declaration of interests

We declare no competing interests.

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