



# Psychological stress and melanoma: Are we meeting our patients' psychological needs?

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**Abstract** Approximately 30% of all patients diagnosed with melanoma report levels of psychological distress indicative of the need for clinical intervention. Despite this, the psychological and emotional needs of patients frequently go undetected and unmet. This contribution aims to provide clinicians and researchers with a succinct update on our understanding of the psychosocial challenges faced by individuals with melanoma. There is now strong evidence that psychological interventions can improve psychosocial outcomes for patients with melanoma, including reductions in general mood disturbance, depression, and anxiety. Further prospective cohort studies are required for a better understanding of the impact of psychological stress on melanoma survival and recurrence, as well as the potential psychoneuro-immunological mechanisms involved.

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We cannot continue to ignore the large volume of evidence originating from basic and clinical studies that supports the notion that biopsychosocial issues are closely associated with the well-being and prognosis of our patients with cancer.<sup>1</sup>

In recent decades, there has been much debate about whether psychological stress may be associated with the development and progression of malignant disease, including melanoma. In an excellent commentary on this debate, Smith et al<sup>1</sup> argue that the time has come to incorporate psychological principles within traditional cancer treatment regimes. Twenty years earlier, in the *Handbook of Psycho-Oncology*, Lewis Thomas waged a similar debate, arguing for the influential role of psychological factors in affecting individual susceptibility and adaptation to cancer, as well as the course and outcome of cancer treatment.<sup>2</sup> The lengthy time span between these theses begs the question: How far have we come in integrating psychological principles into the care of individuals with (or at risk of) malignant melanoma?

What achievements have been made and what challenges lie ahead? This paper aims to provide clinicians with a succinct update on our understanding of the psychosocial difficulties faced by patients with melanoma. It is hoped that this overview will facilitate awareness of these issues, as well as stimulate research into the improvement of psychological care for those affected by this disease.

## Psychological stress

By definition, psychological stress refers to the emotional, cognitive, behavioral, and physiological reactions experienced when a person confronts a situation (real or imagined) in which the demands exceed their coping resources. Stress responses are dependent on a range of factors, including the nature of the stressor, as well as the individual's physical and emotional capabilities, early life experiences, learned behaviors, social environment, coping skills, resources, and genetics. In most circumstances, the response depends on the person's interpretation of the meaning of the stressor, as well as his or her perceived

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ability to cope or enlist the help of others.<sup>3</sup> In all life situations, a moderate amount of stress can be useful and can enhance performance. For patients with melanoma, moderate stress levels may motivate participation in treatment decision making, as well as compliance with clinical management recommendations.<sup>4</sup> Episodes of intense, unpleasant, and distressing emotions, such as fear, sadness, and anger, are part of the normal spectrum of responses to a stressful event. These reactions are common, rarely last more than a day or two, and are not indicative of a psychological disorder; however, an individual may exceed an “optimum” level of stress, such that the effects become immobilizing and destructive. Persistent stress that is not resolved through coping or adaptation may lead to psychological distress, which may manifest as excessive worry or rumination, heightened irritability, difficulties with concentration, insomnia, anhedonia, social withdrawal, feelings of loneliness and helplessness, appetite disturbances, increased use of medication, use of illicit drugs or alcohol, and increased somatic complaints, such as headaches, nausea, heart palpitations, and diarrhea or constipation.

### Prevalence and predictors of psychological stress in individuals affected by melanoma

For many people, there are significant emotional, social, and psychological consequences to having melanoma. A diagnosis of melanoma may change many aspects of an individual’s life from self-identity, self-esteem, body image, and perceived well-being, to family roles and relationships, lifestyle behaviors, sexuality, career opportunities, friendships, and finances. Patients often experience shock, fear, sadness, anger, and sometimes guilt at the time of diagnosis, and some will also have to face progressive illness and approaching death. The stress evoked by these transitions, and the associated uncertainty of outcome, may not only cause immediate suffering, but may also impact adversely on a wide range of patient behaviors. Psychological distress has been associated with patient delay in seeking medical advice,<sup>5,6</sup> decreased adherence to treatment regimes,<sup>7</sup> lower quality of life,<sup>8</sup> greater medical costs,<sup>9,10</sup> and reduced engagement in posttreatment screening and preventive behaviors.<sup>11</sup>

In a recent systematic review of published studies, we found that approximately 30% of all patients diagnosed with melanoma report levels of psychological distress indicative of the need for clinical intervention.<sup>12</sup> This level of clinical distress is equivalent to that identified in patients with breast and colon cancer.<sup>13</sup> The most commonly reported psychological disorders are anxiety and depression,<sup>13-15</sup> typically arising in reaction to the diagnosis or treatment of melanoma. Symptoms of anxiety appear to be more prevalent than depression during both

the diagnostic and treatment phases, with studies reporting the proportion of participants within the clinical range for anxiety and depression to be approximately 23% and 11%, respectively.<sup>16-18</sup> Subjective beliefs about melanoma, its treatment, prognosis, and likelihood of recurrence may play a greater role in determining stress responses than the clinical characteristics of the disease, such as disease stage and time since diagnosis.<sup>19</sup> There are, however, some data disputing the thesis that disease factors have a limited influence on psychological distress.<sup>16,17</sup> Overall, a variety of measurable and in some cases relatively stable variables may be predictive of psychological distress in people with melanoma. These include younger age, female gender, lower education, unemployment, previous mental health problems, and limited social support, as well as perceptions of melanoma as threatening, passive or avoidant coping styles, and a lack of confidence in one’s ability to cope with the situation.<sup>12,19,20</sup>

### Psychological stress responses throughout the disease trajectory

Psychological responses to melanoma may vary substantially over time and according to specific aspects of the clinical care process. Throughout the diagnostic process, patients with melanoma report significant reductions in emotional functioning and quality of life, including greater pain and fatigue, insomnia, and greater interference of stressors (physical and emotional) on social activities.<sup>18,21</sup> During the immediate period following diagnosis, patients tend to give worse evaluations of overall personal health,<sup>21</sup> and express fears about death and suffering, as well as concerns about the emotional well-being of significant others such as family and friends. Many patients experience the period between detection of a suspicious lesion and skin biopsy as the most stressful time in the diagnostic process, likely indicating anxiety about the prospect of surgery or poor prognosis.<sup>18</sup> Some patients experience fear of disfigurement caused by surgery, and report that the visibility of treatment-related scarring can form a constant reminder of the cancer experience.<sup>22</sup> The degree of surgical indentation, the use of skin graft rather than primary closure, and discrepancy between the actual size of a scar and presurgery expectations may all contribute to emotional distress,<sup>23</sup> especially in women and younger patients. For example, in a surgical randomized controlled trial of high-risk patients with melanoma, patients with a 3-cm excision margin reported significantly poorer mental and physical functioning compared with those with a 1-cm excision margin.<sup>24</sup> Within 6 months, the difference in impact on health-related quality of life between the 2 groups was no longer significant, except for persisting concern about the scar in the 3-cm excision group.

Once the acute risk phase is over, psychological responses may dissipate<sup>18,24,25</sup> but may be reactivated at

particular periods in the clinical care process. Regular clinical skin examinations may provide a sense of safety and reassurance for patients<sup>26</sup>; however, these consultations may also serve as a reminder of past threats and can activate fears of cancer recurrence or the possibility of new primary disease. In a study of 331 patients with Stage I disease, more than half of the patients reported anxiety before attending follow-up clinical consultations.<sup>27</sup> Although most individuals affected by melanoma perceive follow-up surveillance as worthwhile, many also indicate that little attention is paid to their emotional well-being during consultations.<sup>28</sup>

### Unmet information needs of patients with melanoma

Information needs are one of the greatest areas of unmet psychosocial need for patients with cancer.<sup>29</sup> Research has consistently demonstrated that patients who receive information according to their preferences report greater emotional, social, and physical well-being.<sup>30</sup> It has long been established, however, that patients are often dissatisfied with the quality and quantity of cancer-related information they receive.<sup>31</sup> For example, 3 months after surgical treatment, 46% of patients with early-stage melanoma reported dissatisfaction with the amount and nature of information they received during clinical care. Compared with those who were satisfied, dissatisfied patients reported significantly higher levels of psychological and psychosomatic problems, including anxiety, depression, sleeping difficulties, and somatic complaints.<sup>32</sup> An Australian survey assessed the needs of outpatients attending a melanoma clinic and found that 6 of the 10 highest ranked needs concerned health information.<sup>33</sup> In our own research, we have found that doubts about the efficacy of treatment for advanced melanoma underscore some patients' desire to receive up-to-date information on the latest clinical research findings.<sup>34</sup> Melanoma survivors also report misconceptions about cancer risk and recurrence, and may have questions about how their prognosis will change over time.<sup>34</sup> In terms of doctor-patient communication about melanoma, patients had strong preferences for receiving full and clear information, discussing their prognosis, and receiving emotional support from their doctor at the time of diagnosis.<sup>35</sup> These factors were also found to influence patients' psychosocial outcomes.

### Impact of psychological stress on melanoma survival and recurrence

Over the past 25 years, a small number of studies have examined the association between psychological stress, coping responses, and melanoma survival or recurrence.

At present, there is inconclusive evidence that psychosocial factors influence outcome in melanoma. Although some studies have found no association between psychosocial variables and disease outcomes,<sup>14,36,37</sup> others have reported weak<sup>26,38,39</sup> or moderate effects.<sup>8,40-42</sup> These studies vary in the length of patient follow-up, the psychological constructs measured, and the potential confounders controlled for in analyses. Only one of these studies examined outcomes in patients with metastatic melanoma.<sup>8</sup> In this study, which followed 125 patients with metastatic melanoma for 6 years, Butow et al<sup>8</sup> found that after controlling for other prognostic factors, patients who survived longer were more likely to perceive the aim of treatment to be cure ( $P < .001$ ), minimize their illness ( $P < .05$ ), express their feelings of anger ( $P < .05$ ), be married ( $P < .01$ ), and report better quality of life ( $P < .05$ ). Patients who believed treatment would lead to a cure (average survival 10.6 months) survived on average about 5 months longer than those who did not (average survival 5.6 months).

Most recently, baseline psychosocial predictors of survival were examined in 59 patients with localized melanoma. After controlling for age, sex, and Breslow thickness, this prospective study found that anger suppression ( $P < .05$ ), hopelessness ( $P < .01$ ), and over-positive reporting of quality of life ( $P < .05$ ) predicted reduced survival up to 10 years after diagnosis.<sup>42</sup> These findings are consistent with the notion of the cancer-prone "Type C" personality originally proposed by Temoshok<sup>43</sup> and Temoshok et al,<sup>44</sup> which is characterized by introversion, a need to please others, and the internalization of anger. In addition, a cognitive escape-avoidance coping style (whereby individuals tend to minimize cognitive responses to the diagnosis) strongly predicted longer survival ( $P = .001$ ). These findings bear similarity to those found by Butow et al<sup>8</sup> in patients with advanced melanoma.

It should be kept in mind, however, that many of the studies examining the association between psychosocial factors, including stress, and melanoma outcomes suffer from methodological limitations, such as inadequate power and failure to control for somatic risk factors. Only rigorous prospective studies can provide definitive data on the impact of stress on melanoma outcome, and these studies are needed to further our understanding of the psychological processes and psycho-neuro-immunological mechanisms involved. Also, although there are benefits to achieving a better understanding of the mechanisms underlying melanoma survival, it is vital that great care is taken when communicating such findings to patients and their families, as well as the wider community. Patients with melanoma should not be pressured to adopt a particular coping style or use specific coping strategies in an attempt to improve their chances of survival or prevent a recurrence of their cancer. Indeed, health professionals can play an important role in relieving patients from the burden or responsibility they may feel to "cope better" so as to improve treatment outcomes.

## Psychological care for individuals with melanoma

Psychological interventions, when evaluated for use in the cancer setting, have by and large been reported as having positive effects on the emotional well-being and quality of life of patients with cancer (see recent reviews<sup>45-50</sup>). Broadly, there are 4 main approaches to the provision of supportive care for patients with cancer: (1) educational techniques,<sup>51,52</sup> (2) behavioral or skills training,<sup>53,54</sup> (3) social support,<sup>55</sup> and (4) psychotherapy.<sup>56</sup> A supportive care program for patients with melanoma may feature one or a combination of these approaches, and may be tailored to the specific needs of the individual and his or her family. Within these approaches, patients may be offered variations on psychotherapeutic modalities, such as psychodynamic, cognitive-behavioral, supportive-expressive, and dialectical behavioral therapies, and support may be delivered via a variety of formats, including face-to-face interaction, written materials, Web-based or multimedia resources, or telephone-based support. Excellent examples of noncommercially sponsored educational resources designed specifically for patients with melanoma can be found at [www.genomel.org](http://www.genomel.org), the Web site of the melanoma genetics consortium (GenoMEL). These resources cover topics such as coping with melanoma diagnosis and treatment, skin self-examination, and genetic risk assessment for melanoma. The Web site also features plain language summaries of recent melanoma research findings.

Five randomized controlled trials (RCTs) have been conducted to evaluate psychological interventions for patients with melanoma; 2 of high quality<sup>39,57-59</sup> and 3 of medium quality,<sup>60-62</sup> according to the evidence rating system of the National Health and Medical Research Council of Australia.<sup>63</sup> All of these studies have produced evidence that such interventions can improve psychosocial outcomes for patients with melanoma, including reductions in general mood disturbance, depression, and anxiety. The first and most well-known of these interventions was developed by Fawzy et al<sup>39,57,58</sup> and later replicated by Boesen et al.<sup>59</sup> These studies demonstrated that brief, structured psychological interventions incorporating health education, stress reduction techniques, illness-related coping skills, and psychotherapy can be effective in reducing distress, as well as increasing patients' use of active coping strategies. Fawzy et al<sup>58</sup> also demonstrated beneficial effects of psychological intervention on immune function, including significant increases in large granular lymphocytes and natural killer cell function compared with matched controls; moreover, at 5-year follow-up, superior survival and recurrence rates were observed in patients with melanoma who had received psychological care.<sup>39</sup>

As evidence for the clinical effectiveness of psychological programs continues to grow, studies evaluating the fiscal cost associated with providing supportive care are

also necessary to allow for adequate allocation of limited resources. Bares et al<sup>61</sup> conducted a small RCT of cognitive-behavioral therapy (CBT) for patients with heterogeneous melanomas who were reporting clinically significant levels of distress. The study aimed to evaluate the cost-effectiveness of the intervention above standard care. CBT was found to be marginally more expensive (49¢ per minute) than the cost to nursing staff of dealing with distress-driven telephone calls during standard care (41¢ per minute); however, the cost/benefit ratio (total costs/change in distress) was significantly lower for CBT. The cost to change distress in standard care was more than \$402 for a 1-point change in distress, versus \$7.66 for CBT. Including reimbursement for services in the analysis, CBT would generate \$1.16 per minute, whereas standard care would cost the hospital \$0.40. Thus, CBT was found to be cost-effective.

## Future directions and challenges

It is clear from this growing body of work that a biopsychosocial approach is needed to improve the care provided to individuals affected by melanoma. Despite this, the psychological and emotional needs of patients are often overlooked. The reasons for this vary and may include underrecognition of the need for psychological care by the treatment team, difficulties in doctor-patient communication about psychosocial issues, an absence of clear referral pathways, inadequate funding and resources, difficulties experienced by patients attempting to access support, and the perceived stigma associated with uptake of psychological services. Clinical practice guidelines for the management of melanoma consistently recommend that structured psychosocial interventions and psycho-education be made available to all patients.<sup>64</sup> According to the National Institutes of Health, however, some of the most basic psychological and social issues affecting patients with cancer are often not adequately addressed.<sup>65</sup> Indeed, research suggests that there is a large discrepancy between the recommendations for psychosocial care and what is implemented in the clinical setting.<sup>66</sup> One of the greatest challenges we currently face is the timely translation of evidence into sustainable clinical practice. It is startling to think that in the context of primary care, it is estimated to take an average of 17 years to turn 14% of original research into improvements in patient care.<sup>67</sup> Strategies for more successfully navigating our way through the "translational highway"<sup>68</sup> from research bench to bedside are urgently needed. This work will rely heavily on multi-disciplinary collaborations spanning the disciplines of medicine, basic science, psychology, nursing, social work, public health, health economics, and health policy. Each discipline will have unique insights into the challenges our patients face, and possible ways to improve the care we provide.

All patients with melanoma who show emotional distress, low social support, or tumor-related difficulties in various

aspects of daily life should be offered psychological support, irrespective of whether they meet the criteria for psychiatric disorder. Routine psychological screening of patients with melanoma is widely recommended as standard practice in many countries, including Australia, the United States, and the United Kingdom<sup>64</sup>; however, the barriers (structural, economic, or motivational) to integrating such screening into clinical care are rarely discussed. Accurate detection of distress, or identification of those most vulnerable to developing maladaptive psychological responses, can enable clinicians to initiate early intervention, tailor assistance to meet individual needs, and effectively target limited health care resources to reduce patient suffering and potentially increase the chances of survival.<sup>60,69</sup> Standard psychological screening measures may have limited sensitivity and specificity; thus, the development of a brief, valid, and reliable screening tool incorporating empirically supported risk factors (such as those identified in a recent systematic review<sup>12</sup>) is recommended to improve the timely identification and support of those patients with melanoma who are most vulnerable to adverse psychological outcomes. Clinical trials to assess the efficacy and cost-effectiveness of such a tool are needed. There is also evidence to suggest that patients might benefit from increased emotional support and information at the time of initial clinic attendance (before biopsy), as the uncertainty associated with this period has been recognized to be particularly stressful for some patients.<sup>18</sup> There is still much work to be done, both in developing a better understanding of the role of psychological factors in melanoma onset and survival, as well as how to implement effective and sustainable psychological care that is tailored to the unique emotional experiences of the individual. It is hoped that this overview provides guidance on the directions such work could take.

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