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Clinical pathway for the screening, assessment and management of anxiety and depression in adult cancer patients: Australian guidelines

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Abstract

***Purpose*: A clinical pathway for anxiety and depression in adult cancer patients was developed to guide best practice in Australia.**

***Methods*: The pathway was based on a rapid review of existing guidelines, systematic reviews and meta-analyses, stakeholder interviews, a Delphi process with 87 multidisciplinary stakeholders and input from a multidisciplinary advisory panel.**

***Results*: The pathway recommends formalized routine screening for anxiety and depression in patients with cancer at key points in the patient's journey. The Edmonton Symptom Assessment System or distress thermometer with problem checklist is recommended as brief screening tools, combined with a more detailed tool, such as the Hospital Anxiety and Depression Scale, to identify possible cases. A structured clinical interview will be required to confirm diagnosis.**

When anxiety or depression is identified, it is recommended that one person in a treating team takes responsibility for coordinating appropriate assessment, referral and follow-up (not necessarily carrying these out themselves).

A stepped care model of intervention is proposed, beginning with the least intensive available that is still likely to provide significant health gain. The exact intervention, treatment length and follow-up timelines, as well as professionals involved, are provided as a guide only. Each service should identify their own referral network based on local resources and current service structure, as well as patient preference.

***Discussion*: This clinical pathway will assist cancer services to design their own systems to detect and manage anxiety and depression in their patients, to improve the quality of care.**

Introduction

Anxiety and depression impact on family and social functioning, work performance, suicidal ideation and survival [1]. The existential turmoil generated by a cancer diagnosis, and its impact on patients' psychological, social and physical functioning, renders these patients vulnerable to anxiety and depression. High levels of these morbidities have been found in cancer patients across demographic backgrounds and cancer types and stages [2–4]. For example, a large ($n = 10\ 153$) Canadian study found that just under a quarter of all cancer patients had clinical or subclinical levels of anxiety, while clinical or subclinical levels of depression were present in up to 16.5% of the sample [5]. Similarly, in a large German study ($n = 4020$) using stratified, purposive sampling, the 4-week prevalence rates for any mental disorder, anxiety and mood disorder were 32%, 12% and 7%, respectively [4]. Even higher rates were reported in a meta-analysis of studies with Chinese adults with cancer [6], while another recent meta-analysis reported some mood disorder in 30–40% of patients [7]. Rates can also be much higher in particular subgroups. For instance, the Canadian study found that more than half of patients who were female and/or aged below 50 years presented with clinical or subclinical anxiety [5].

Despite high acceptance that psychosocial care is integral to quality cancer care, anxiety and depression are often undetected and underestimated in busy cancer services [8], and high unmet need for psychosocial care is persistent in cancer patients [9]. This is despite the large evidence base

that interventions for anxiety and depression in patients with cancer are effective in the short and long terms [10–14].

Because anxiety and depression are often under-detected, routine screening of all cancer patients for psychological distress using validated, reliable, objective measures is internationally endorsed [15]. The International Psycho-Oncology Society and 68 affiliated organizations have set a standard of care involving monitoring distress as the '6th vital sign'.

Screening has been shown to be acceptable and feasible [16]. However, results of trials evaluating the efficacy of distress screening have been mixed. A recent systematic review [16] identified 14 relevant randomized controlled trials (RCTs) and a further 10 non-randomized studies. Only six of the 14 RCTs reported impacts on patient well-being, sometimes only for those initially depressed at baseline. An additional three showed improved secondary outcomes such as communication between clinicians and patients. Five RCTs failed to show any benefits. The majority of these trials have focused on screening in isolation, some adding routine feedback to staff. Comparing successful with unsuccessful trials, it appears that strategies that minimize staff burden and ensure effective follow-up are critical.

A number of guidelines exist internationally for the assessment and management of anxiety and depression in cancer patients [17–24]. However, most have limited guidance on specific timelines, roles and potential content of interventions, which are the hallmarks of effective clinical pathways.

Clinical pathways provide evidence-based recommendations to guide best practice and consistent care for specific patient concerns in homogeneous patient groups. Research has shown that the implementation of clinical pathways significantly increases detection of psychological morbidity and rates of referral for treatment, for example, in heart disease [25]. The provision of clear clinical pathways in the cancer setting, in combination with staff training and effective intervention, should improve patient outcomes [7,25]. The need for such a pathway is underlined by the recent American College of Surgeons patient-centred accreditation standard requiring programmes to implement psychosocial distress screening and referral for psychosocial care [26,27].

Our group aimed to develop clinically relevant, evidence-based and widely endorsed Australian clinical practice pathways for the screening and management of anxiety and depression in the cancer context.

Methods

This clinical pathway was developed based on the following:

1. a rapid review of existing guidelines, systematic reviews and meta-analyses relevant to the screening, assessment and management of anxiety and depression in cancer patients and the general public [10–14,16–24,26–33]. We searched the Cochrane, Google, PubMed, Medline, Psychlit and CINAHL databases;
2. structured interviews with 12 key multidisciplinary staff from different institutions [34];
3. an online Delphi process incorporating two rounds of feedback from 87 stakeholders who are members of the Psycho-Oncology Co-operative Research Group, a national multidisciplinary trials group with over 1000 members and almost complete coverage of Australian clinicians and researchers interested in the psychosocial care of cancer patients [34]. Delphi participants were purposively selected to ensure representation from all clinical stakeholder groups (psychiatry ($n=4$), psychology ($n=16$), social work ($n=14$), other allied health ($n=10$), palliative care ($n=4$), oncology ($n=15$), surgery ($n=8$), nursing ($n=18$) and general practice ($n=1$)); and
4. input from a multidisciplinary advisory panel (10 experts from seven different institutions, selected to ensure representation of all relevant disciplines, with >10 years experience relevant to the treatment of anxiety and depression in cancer patients).

More details about these methods and their results are provided in Shaw *et al*. [34], where possible existing high-quality guidelines were utilized. Where key issues were not present in any guidelines, they were addressed using the best available evidence supported by expert review.

Results

The section below presents a preamble to the pathway, with core principles and issues discussed.

The recommendations made in the clinical pathways are intended as a guide only, and individual centres will need to adapt them to suit their own context and resources. Factors that need to be considered when tailoring the pathways include patient demographics, stage of illness and cancer type.

Professional roles

Possible professional roles are outlined in Table 1. The appropriateness of referral and treatment will depend very much on what is elicited in the initial assessment, so doing this well is crucial. Health professionals carrying out screening and/or follow-up assessment need to have the skills and confidence to comfortably discuss anxiety and depression with patients, and to facilitate referral. They also need to be able to respond with empathy to immediate feelings and concerns. For many patients, it could be the first time they have spoken about anxiety and/or depression, and so screening and assessment need to be conducted in a thoughtful and sensitive way. Individual skills and training within each team will determine who is best placed to undertake specific roles. No professional should take on any role for which they have not received training or which they do not feel competent to undertake.

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Table 1. Professional roles[a]

	General practitioner	Treating clinician[b]	Nurse[c]	Social worker	Clinical psychologist	Psychiatrist
Screening	×	×	×	×		
Clinical assessments	×	×	×	×	×	×
Formal diagnosis					×	×
Self-harm risk assessment	×	×			×	×
Supportive care for physical symptoms (e.g. pain and fatigue)	×	×	×			
Psycho-education	×	×	×	×	×	×
Supportive counselling	×	×	×	×	×	×
Referral to psycho-oncology service	×	×	×	×		
Relaxation strategies	×		×	×	×	×
Support group facilitation			×	×	×	
Skills training, e.g. problem solving				×	×	×
Psychological therapy				×	×	×
Psychosocial training for other health profs					×	×
Referral to psychiatrist	×	×			×	
Pharmacotherapy	×	×				×
Follow-up	×	×	×	×	×	×

[a]Developed by the multidisciplinary panel and confirmed by the Delphi process.
[b]Surgeon, medical oncologist, radiation oncologist, haematologist and palliative care physician.
[c]Cancer care coordinator, nurse specialist, clinical nurse specialist, clinical nurse consultant, general cancer nurses and palliative care nurse.

Note that the clinical pathway recommends a high level of involvement for general practitioners (family medicine doctors). While such a high level of involvement is typically the case for general practitioners (GPs) based in rural and remote areas, this is out of necessity, and urban GPs often have limited involvement in care while patients are undergoing active cancer treatment [35].

Screening and assessment

Screening

While staff should always be alert to signs of anxiety or depression, this pathway recommends that formalized routine screening for anxiety and depression in patients with cancer be carried out using validated measures at key points in the patient's journey. There is no established gold standard tool for this purpose. A number of screening tools are available. No screening tool is foolproof; all should be supplemented by clinical interview. Several studies, including a recent meta-analysis by Mitchell *et al*. [36], suggest that a two-step approach is best, where a very short screening tool, followed by a more detailed screening tool, is used to identify possible cases, and a clinical interview used to confirm diagnosis. We recommend using a validated screening measure that is fit for purpose (for comprehensive reviews of screening for distress, see Carlson *et al*. [37], for depression, see Wakefield *et al*. [38]) and for anxiety, see Vodermaier *et al*. [39].

There is merit in consistency of tools used for screening across centres, at least within one country, to allow benchmarking. Following an extensive review of the literature and current approaches to screening, the multidisciplinary panel, supported by Delphi participants, recommends either the Edmonton Symptom Assessment System (ESAS) [40] or distress thermometer (DT) with problem checklist [18], for use as the initial very brief screening tool. If possible anxiety and/or depression is identified by the very brief screening tool, it is recommended that patients complete a more detailed screening tool, such as the Hospital Anxiety and Depression Scale (HADS) [41]. Again, a variety of tools are available for this purpose (for a review, see Luckett *et al*. [42]). On the basis of the literature, the multidisciplinary panel, supported by Delphi participants, recommended the HADS. If either or both the very brief and more detailed screening tools are used, they must be scored and discussed with each patient. A short description of the recommended tools follows, but institutions may choose different measures.

The ESAS [40] consists of nine visual analogue items (0–10), including one for anxiety (ESAS-A) and one for depression (ESAS-D). Recommended cut-offs for the ESAS-A of ≥ 3 and ESAS-D of ≥ 2 ensure that no possible case of anxiety or depression is missed [43]. One advantage of the ESAS is that it also assesses common symptoms (such as pain and fatigue) that may need to be addressed before or alongside anxiety and depression.

The DT is a one-item visual analogue tool (0–10), which should be accompanied by a problem list to identify areas of concern for patients [18]. According to a large ($N=42$), recent meta-analysis of data from 14 808 patients, optimal identification of anxiety and/or depression in a clinical oncology setting can be achieved by using a cut-off score of 4 or more on the DT [44]. An advantage of using the DT in conjunction with a problem list is that it identifies the specific areas of concern to target.

The HADS [41] is a 14-item measure with two subscales. Seven items (rated 0–3) measure anxiety and seven

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items (rated 0–3) measure depression. Items are summed within each subscale. A cut-off of 8 or more on either of the subscales is recommended to ensure that no possible case of anxiety or depression is missed [45]. A score of 11 or more suggests possible moderate to severe anxiety or depression [45]. Clinical interview is recommended to confirm caseness of anxiety or depression.

These tools can be completed by paper and pencil, online or electronically face to face, using tablets. If online, patients can be cued by email to complete the first very short questionnaire; scores can be automatically summed; if above the cut-off, patients can be presented with the more detailed screening tool; and red flags can be sent to responsible staff to initiate contact with patients who score above cut-off. It is recommended that one staff member is nominated to be responsible for ensuring that screening takes place at the appropriate times (see Table 1 for possible staff members to carry out this role). Note also that re-screening is recommended within the pathway at clinically significant time points, such as recurrence.

Assessment

Determining severity of anxiety and depression

At any clinical encounter, staff should be alert to signs of anxiety and depression. If screening or staff observation identifies possible anxiety and/or depression, then a more comprehensive clinical assessment should be conducted. The assessment is typically a semi-structured interview that can be based on standardized diagnostic criteria (Diagnostic and Statistical Manual of Mental Disorders-Fifth edition or International Classification of Diseases-version 10) [46,47] and should aim to identify the nature of the primary problem and its possible causes, and the severity of relevant symptoms.

Note that it is important to first identify any medical conditions that may be contributing to the presentation, such as treatment with steroids, unrelieved pain or withdrawal from drugs or alcohol. Delirium should also be considered, and the cause (such as infection or electrolyte imbalance) identified and treated [17,19]. Some alternative

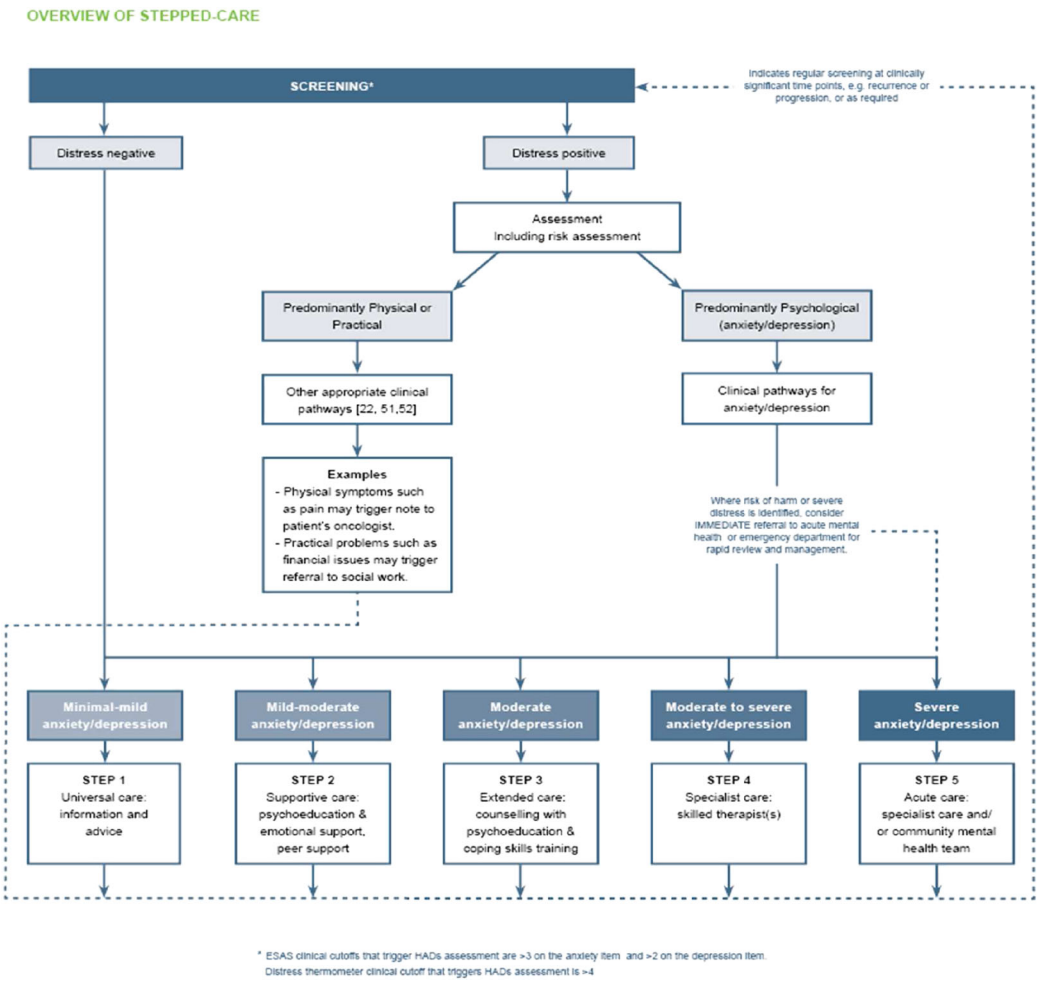

Figure 1. Overview of the pathway and stepped care

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guidelines for such issues are provided in Figure 1 [22,48–50]. Once these are resolved, re-screening for anxiety and depression should take place to determine if these are independently troublesome.

Symptoms and severity

The signs and categorization of different levels of anxiety and depression according to severity are shown in Tables 2 and 3. Symptoms of anxiety in cancer patients are difficult to classify because they can be a normative or excessive reaction to cancer threats, a response to poor symptom control, an adverse effect of certain treatments or drug interactions, a clinical anxiety disorder or a combination of these factors [51]. Level of anxiety or depression will ultimately be decided based on clinical judgment.

It is recommended that one person takes responsibility for ensuring that appropriate assessment, referral and follow-up are undertaken (but does not necessarily carry these out themselves). See Table 1 for appropriate personnel to carry out assessment and referral. Every health service with which a patient comes into contact (including general practice and surgery) will need to identify who are the most appropriately trained and supported staff members to (a) coordinate screening, assessment and referral and (b) carry out these processes. In some centres, a different staff member may be identified within each tumour stream to coordinate and/or carry out this process.

Table 2. Signs and symptoms of anxiety and depression[a]

Anxiety	Depression
• Autonomic arousal (e.g. accelerated heart rate, sweating, trembling and dry mouth)	• Lowered mood
• Symptoms of chest and abdomen (difficulty breathing, feeling of choking, chest pain and nausea)	• Decreased energy and activity
• Symptoms of brain and mind (feeling dizzy, unsteady, faint or light headed, feeling objects are unreal, depersonalization, fear of losing control or dying, difficulty concentrating, mind going blank and irritability)	• Marked tiredness after activity
• General symptoms (hot flushes or cold chills and numbness or tingling)	• Diminished pleasure, interest and concentration
• Symptoms of tension (muscle tension or aches and pains, restlessness, inability to relax, difficulty swallowing and lump in throat)	• Loss of libido
• Difficulty getting to sleep because of worrying	• Significant change in appetite and sleep patterns (loss of appetite and early wakening)
	• Reduced self-esteem and self-confidence
	• Feelings of worthlessness or excessive, inappropriate guilt
	• Recurrent thoughts of death or suicide

[a]Based on International Classification of Diseases-version 10 [47].

Table 3. Characteristics of mild, moderate and severe anxiety and depression[a]

	Anxiety	Depression
Mild	• Has two or three of the previous symptoms, proportion to stressors, e.g. worry, uncertainty about future and concerns regarding illness	• Has two or three of previous symptoms
	• Person is distressed but can continue with activities	• Person is distressed but can continue with most activities
Moderate	• Four or more of previous symptoms	• Four or more of previous symptoms
	• Cancer-related worries shift from one topic to another, including both major and minor concerns and difficult to control	• Person is distressed and having great difficulty continuing normal activities
	• Person is very distressed and having great difficulty continuing usual activities	
Severe	• Four or more of previous symptoms consistent with a diagnosed anxiety disorder (e.g. phobia, generalized anxiety disorder, panic, post-traumatic stress disorder and obsessive–compulsive disorder)	• Four or more of previous symptoms consistent with a diagnosed depression
		• Symptoms are severe and distressing and the person is unable to continue usual activities
	• Symptoms are severe and distressing, and the person is unable to continue usual activities and may be housebound	• Loss of self-esteem, worthlessness and guilt
	• Co-morbidity may be present	• Suicide ideation
		• May have some psychotic elements (hallucinations, delusions and psychomotor retardation)

Note that symptoms of anxiety in cancer patients are difficult to classify because they can be a normative or excessive reaction to cancer threats, a response to poor symptom control, an adverse effect of certain treatments or drug interactions, a clinical anxiety disorder or a combination of these factors.
Risk factors for anxiety and depression in cancer patients include the following [32]:

- recurrent, advanced, progressive disease (i.e. disease-induced vulnerability) or presence of chronic illnesses in addition to cancer;
- history of depression, substance use of abuse and other mental health problems;
- perceived lack of social support; and
- other factors (e.g. younger age, female, living alone, dependent children and financial problems).

[a]Based on International Classification of Diseases-version 10 [47].

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Suicide/self-harm risk assessment

For patients with moderate or severe anxiety and/or depression, a formal risk assessment for suicide and self-harm should be conducted to assess previous history, strength of intent, means and capacity. Table 4 provides risk factors and scoping questions that can be used for this purpose.

Stepped care

Stepped care has proven to be an effective model of healthcare delivery, including the treatment of anxiety and depression [52,53]. In stepped care, the *first* intervention should be the *least intensive* of those currently available, which is still likely to be effective [50]. More intensive interventions are reserved for patients who do not benefit from simpler first-line treatments [53]. Stepped care is self-correcting in that the outcomes of interventions are monitored systematically, and care is stepped up if current interventions are not achieving significant health gain. For example, psycho-education can be delivered via self-help materials with GP support accessed according to need. If this appears not to be meeting the patient's needs and reducing morbidity, a referral to a psychologist should be considered.

Patient preferences are critical in determining the most appropriate intervention, the intervention setting and the intervention provider. Given that the prevalence of anxiety and depression in the general community is quite high, patients may have an existing relationship with a mental health professional. Cancer diagnosis and treatment can often exacerbate pre-existing psychological issues. When referring for intervention, it is important to establish patient preferences for treatment through existing mental healthcare professionals or psycho-oncology services.

The section below presents the pathway itself. Figure 1 below provides an overview of the clinical pathway for identifying and managing anxiety and depression, utilizing the stepped care approach.

The five steps of the clinical pathway are summarized in Figures 2–5 later, which detail recommended interventions, intervention duration, review periods, maintenance and continuation phases (where appropriate) and health professionals involved at each stage. Descriptions of each intervention and their evidence base are provided in Appendix A. Note that interventions listed could be used individually or concurrently. For example, for moderate to severe depression or anxiety, cognitive–behaviour therapy is often combined with pharmacotherapy for optimal outcomes.

The exact nature of each step, the professionals involved and the interventions provided will depend on local resources and current service structure, as well as patient preference. Each service should identify its own referral network. Recommendations for treatment length are a guide only and will ultimately be determined by clinical need, patient situation and patient preference.

Note that patients may not accept a referral or complete treatment that is offered. The American Society of Clinical Oncology guidelines [17] recommend that health professionals providing psychosocial care regularly monitor clinical progress, side effects and satisfaction with care, the frequency depending on the severity of the individual's condition. If there is limited improvement in anxiety and/or depression, low satisfaction or difficulties with adherence to treatment, the health professional and patient should review the treatment plan making adjustments as necessary. Changes to the treatment plan may include the addition of pharmacotherapy, moving from group to individual therapy or moving up to the next step.

It is difficult to say with any certainty how many patients are likely to enter at each step because this can vary according to gender, cancer type, stage of disease, time since treatment, demographic variables and the measurement instrument used [3–5]. However, based on past research, it could be expected that most patients will experience minimal to mild depression and/or anxiety, with 20–30% experiencing moderate to severe depression and/or anxiety [3–5].

Education (face to face and online) and brief emotional support from the whole team are recommended to respond to minimal to mild anxiety and/or depression (universal

Table 4. Assessment for suicide risk[a]

Risk factors	Scoping questions
Suicidal ideation Suicidal plan Access to means Prior attempts High levels of anger/hostility/impulsivity Current depression Current anxiety Disorientation/disorganization Hopelessness Identifiable stressors Substance abuse Psychosis Poor medical status Withdrawal from others Expressed communication Psychiatric service history Poor coping strategies Lack of supportive others (connectedness) High carer/family/significant other perception of risk History of violence/aggression/self-harm Family history of mental illness or suicide	❖ Have things been so bad lately that you have thought you would rather not be here? ❖ Have you had any thoughts of harming yourself? ❖ Are you thinking of suicide? ❖ Have you ever tried to harm yourself? ❖ Have you made any current plans? ❖ Do you have access to a firearm or other ways of harming yourself?

[a]Based on the Australian Psychological Society Suicide Risk Assessment Tool https://www.psychology.org.au/Assets/Files/Risk%20assessment%20guide.pdf

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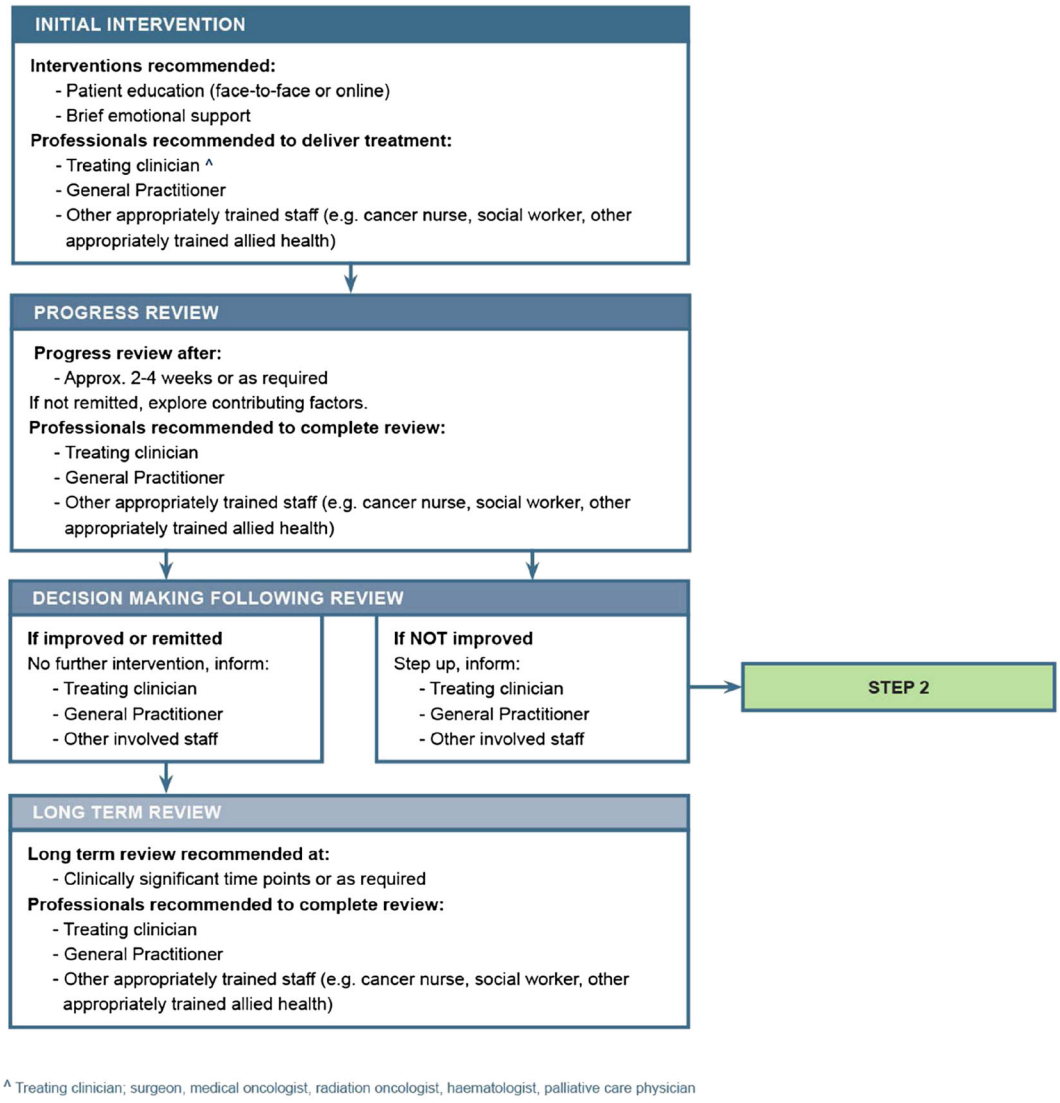

Figure 2. Step 1: universal care – minimal to mild anxiety/depression

care) [54,55]. For mild to moderate anxiety or depression, telephone helplines and peer support groups or group therapy are recommended in addition [56–61]. Patients diagnosed with localized cancer identified as having moderate anxiety or depression may benefit from relaxation and stress management training [62–66], problem-solving approaches [67] and cognitive behavioural therapy [10–12]. Patients with advanced disease may be more likely to benefit from approaches that facilitate the processing of existential concerns and fear of mortality, such as mindfulness training, acceptance and commitment therapy and supportive–expressive psychotherapy [68–72]. However, treatment should always be tailored to the individual, and many patients with localized disease also struggle with existential issues and may benefit from therapies addressing this also. Internet-based treatments have also been proven effective for people with moderate anxiety and depression in the general population, and there is emerging evidence for their efficacy in cancer populations also [73,74]. Patients with severe disease will need face-to-face interventions and may require pharmacotherapy.

Pharmacologic interventions for mood and adjustment disorders

Depending on the severity of symptoms, pharmacotherapy may be indicated. A summary outlining the key principles underpinning pharmacological management of anxiety and depression is provided in Appendix B. For detailed information about specific drugs, readers are referred to the Therapeutic Guidelines that are available online in most public hospitals. The *Therapeutic Guidelines*: *psychotropic*. *Version 7*, *2013* [75] provides comprehensive evidence-based information about specific drugs to treat

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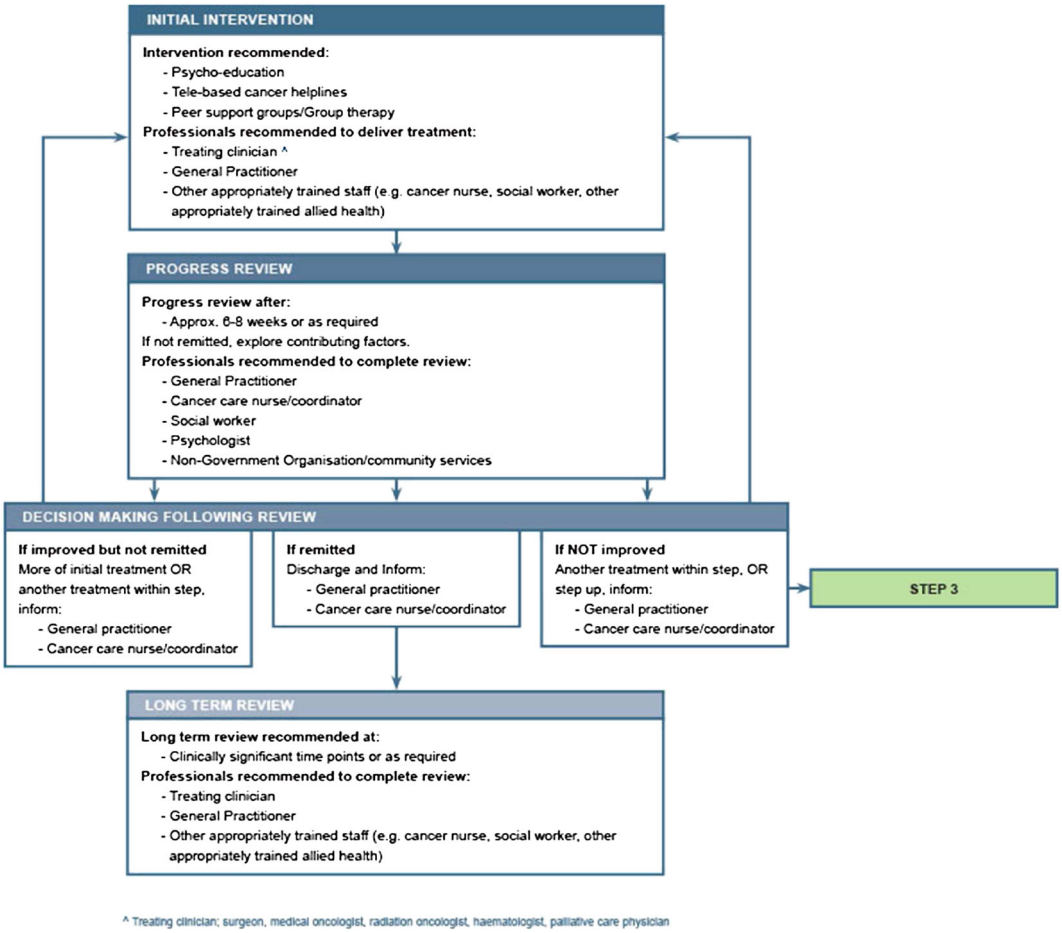

Figure 3. Step 2: supportive care – mild to moderate anxiety/depression. Note that health professionals reviewing progress would be expected to have seen the patient before. The majority of cancer patients might be expected to enter the stepped care model at step 2

anxiety and depression, their side-effect profiles and drug interactions. The *Palliative Care Expert Group Therapeutic guidelines*: *palliative care*. *Version 3* is also helpful [76].

Suicidal thoughts and self-harm

For patients with moderate or severe anxiety and/or depression, a formal risk assessment for suicide and self-harm should also be conducted to assess previous history, strength of intent, means and capacity. If a patient is found to be at risk of suicide or self-harm, contact or escort the patient to the emergency department or acute mental health team for rapid review and management, and psychiatric intervention as appropriate. Discuss with the patient's treating team. Suicidal thoughts have been identified in 6–11% of cancer patients [77–79], although only around 10% of these individuals express actual suicidal intent [79]. The presence of other symptoms, such as psychosis, severe agitation and confusion (delirium) warrant referral to appropriate services for emergency evaluation [19].

Discussion

The clinical pathway presented earlier comprises the first attempt internationally to develop a comprehensive pathway for managing anxiety and depression in the cancer context that provides guidance regarding staffing, timing and potential content of interventions, to facilitate implementation into routine practice. We believe the pathway provides a further step, beyond guidelines, in assisting oncology services to put into place and sustain services that not only identify patients who are suffering from anxiety and depression but also optimize the chances that they receive appropriate care.

Of course, it is up to individual patients to decide whether or not they wish to accept services offered, and many patients access help outside of oncology services or refuse help because of stigma, fear, passivity or a desire to help themselves [80]. To increase the chances of the pathway producing improved outcomes and to optimize informed consent, it is critical to provide education and resources to patients to normalize anxiety and depression in the context of a cancer diagnosis and aid their understanding of

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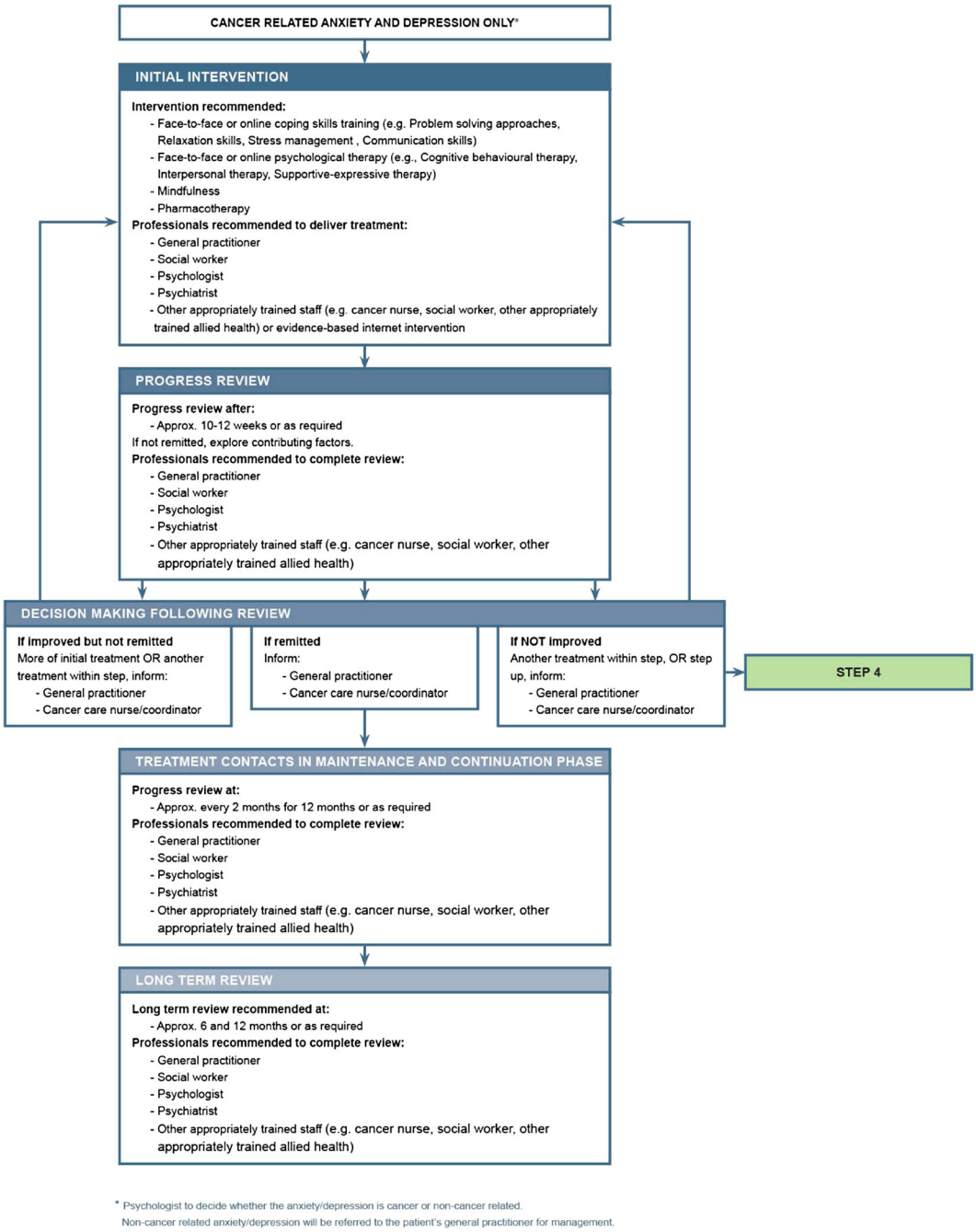

Figure 4. Step 3: extended care – moderate anxiety/depression

treatment options and their likely benefits and costs. Furthermore, it is important to address perceived barriers from the patients' perspective. Thus, in the pathway earlier, we have included online interventions for those with moderate to severe anxiety or depression. Web-based interventions, because they allow privacy, some degree of anonymity and increased access, overcome many of the barriers known to prevent people accessing mental health services. Furthermore, they have been shown in numerous trials to be as effective as face-to-face treatment [73,74].

Another advantage of online interventions is that they require minimal staff time, freeing psychosocial staff to see the more serious cases that can most benefit from expert face-to-face contact. Concern about added time requirements is the primary barrier endorsed by clinical staff when considering routine screening for anxiety and depression [80]. Hence, in addition to addressing patient barriers in implementation plans, clinical pathways must be designed to be acceptable to staff and feasible to implement.

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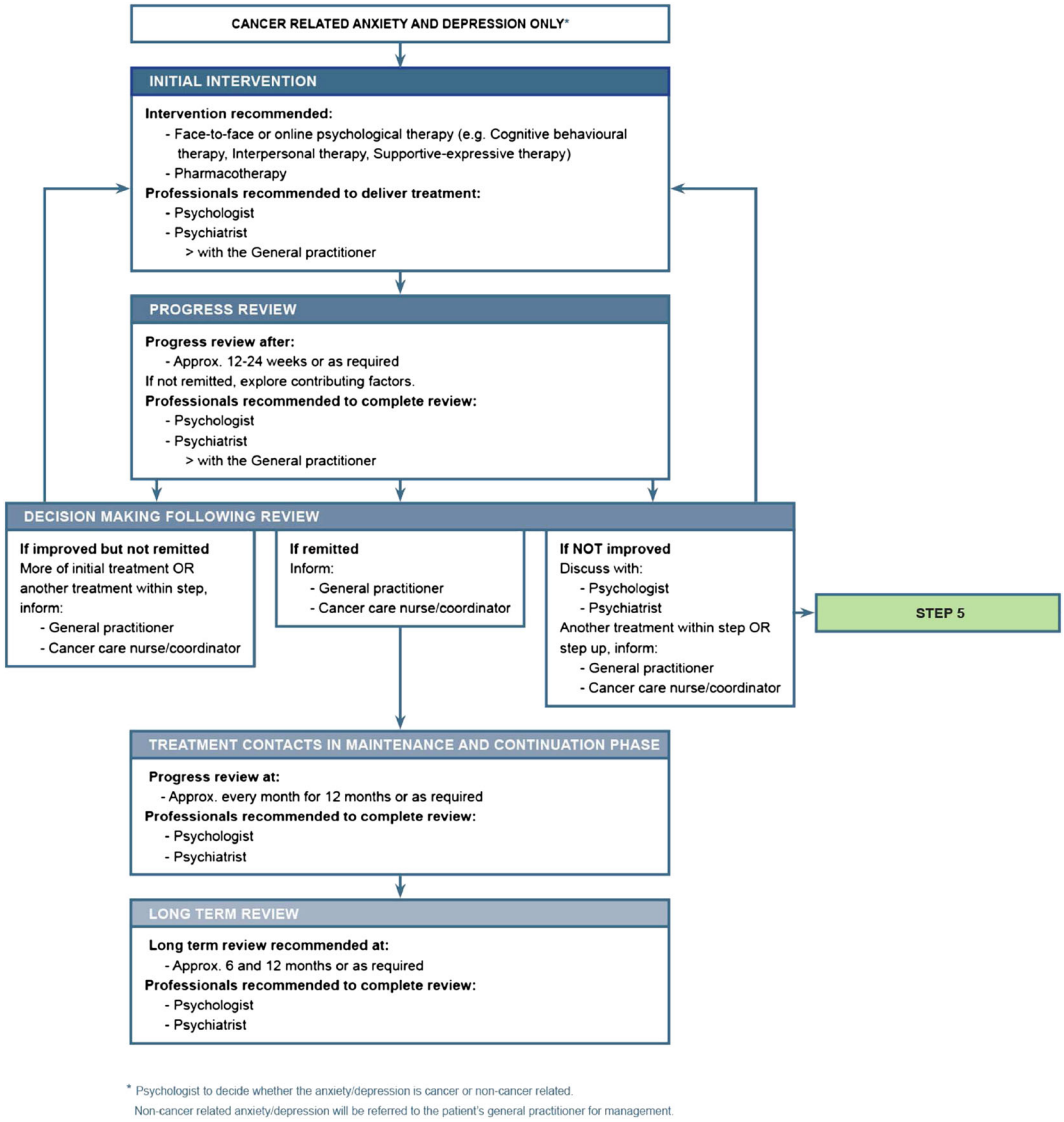

Figure 5. Steps 4 and 5: specialist care – moderate to severe anxiety/depression

Another way to minimize demands on staff time is adoption of electronic patient-reported outcome (ePRO) systems, increasingly used in cancer clinical care settings [81]. These are superior to paper-based PRO assessments in their potential to reduce staff time in overseeing the screening process, accessibility in a range of languages, completion in the clinic or remotely, automated scoring of assessments, generation of real-time feedback reports to the care team and linkage into existing patient records hence integrating psychosocial information with other clinical information. Such systems can be adapted to incorporate clinical pathways such as this one, to provide electronic prompts for re-screening, review and discharge summaries, as well as links to recommended management and resources. In our own barrier analysis for the current pathway [80], participants in structured interviews emphasized the importance of being able to track referrals and demonstrate outcomes to ensure high quality care and evaluate services. ePRO systems are likely to be utilized in the future to enable such processes and facilitate incorporation of pathways into clinical care.

Another oft-cited barrier to screening and management of anxiety and depression is lack of staff training and education. Education is needed to target screening, assessing, making a referral – particularly when patients are reluctant – and empathic communication. It is also critical that cancer services staff understand each other's roles and responsibilities in order to integrate processes for screening, referral and providing aftercare for patients [81]. Such training and support is already available online, through the Canadian Association of Psycho-Oncology IPODE website at http://www.capo.ca/ipode-project/screening-for-distress and is delivered face to face in many other sites. Materials such as these, adapted for the local context, will facilitate uptake of the pathway.

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It is important that pathways like this one are empirically tested to ensure that they are feasible and acceptable to health services, are actually implemented and lead to improved patient care. We are currently undertaking such an evaluation in Australia.

Limitations

This pathway was developed in the Australian context and may not be applicable to all health systems, particularly those of low-income countries where some resources may be unavailable. Even in developed countries, these resources are all too frequently not integrated or available.

Furthermore, this pathway is general and does not detail how to respond to issues that may be specific to particular disease sites, disease stages, cultures, sexes, ages, and so on nor does it address the needs of the family who may have distress as great as, or greater than, the patient themselves.

We were not able to find enough evidence to guide us, or to gain consensus from our Delphi panel, regarding the optimal timing for re-screening and assessment. Panel members felt this was a very individual decision, based on client needs. Further clarity on this issue would be beneficial to explore both in research and in future guidelines.

New evidence is always emerging, and the pathway will need to be periodically updated. However, the structure and content of the pathway were developed to allow this to occur easily. We suggest updating at five yearly intervals to incorporate new and emerging data.

In summary, we hope the pathway for anxiety and depression in the cancer context will facilitate fully integrated and effective screening, detection and management of anxiety and depression in cancer services and aid in reducing the enormous burden of suffering that patients with these psychological morbidities experience, as well as reducing the economic costs to services that are incurred when anxiety and depression are not adequately treated. While clearly delineated pathways such as these facilitate implementation, careful attention to patient, health professional and system barriers will optimize chances of success.

Appendix A: Description and evidence base for interventions for anxiety and depression

Patient education/psycho-education: the formal or informal provision of information, delivered through informal discussion, brochures, formal educational sessions, and video, audio and online resources, to improve knowledge and reduce uncertainty and improve physical side effects such as pain [54].

Brief emotional support: healthcare professionals confidently and comfortably discussing anxiety and depression with patients. It can help to prevent the emergence of anxiety and depression and/or identify it early [55].

Tele-based cancer helplines: offer emotional support for people with cancer in addition to providing psycho-educational materials and referral to further psychosocial services, if needed over the phone [56–58], particularly helpful for geographically isolated patients and have been shown to reduce levels of anxiety and depression [56–58].

Internet-based interventions: provide psychological therapies online. As effective as face-to-face care for mild to moderate anxiety and depression [73,74].

Peer support groups/group therapy: facilitates mutual support between people and provides opportunities to learn coping skills in a non-judgmental and caring environment. It is effective in reducing anxiety and depression [59–61].

Problem-solving approaches: focus on generating, applying and evaluating solutions to identified problems [67]. These are effective in reducing anxiety and depression [67].

Relaxation skills: techniques designed to induce physical and mental relaxation, including progressive muscle relaxation, guided imagery and hypnosis. These are effective in reducing anxiety and depression [65,66].

Stress management: provides training in anxiety-reduction skills, increased awareness of sources of stress and indicators of stress, and noticing and replacing negative thoughts to improve the ways patients manage stressors [62]. Stress management has been shown to improve emotional well-being and positive affect [62–64].

Mindfulness: teach patients to increase awareness of thoughts and the impact they can have on symptoms of anxiety and depression, with the aim of interrupting these automatic processes and facilitating non-judgmental awareness of thoughts [68]; include mindfulness-based stress reduction, mindfulness-based cognitive therapy and acceptance commitment therapy; and effectively reduce anxiety and depression [68,71].

Cognitive behavioural therapy: focuses on identifying, challenging and changing maladaptive thoughts and behaviours to reduce negative emotions and promote psychologic adjustment [10]. It is one of the most common therapies used, with proven effectiveness in anxiety and depression [10–12].

Supportive–expressive therapy/supportive psychotherapy: 'focuses on the communication and processing of subjective experience and on the joint creation of meaning within a therapeutic relationship to reduce distress' [69]. Targeted and manualized psychotherapies, particularly for those with advanced illness, have recently been developed, including meaning-centred group therapy, dignity therapy, mindfulness-based meditation therapy and a brief supportive–expressive intervention referred to as Managing Cancer and Living Meaningfully [72]. Supportive–expressive therapy is effective against depression and cancer-related distress [69,70].

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Appendix B: Pharmacologic interventions for mood and adjustment disorders

Depending on the severity of symptoms, pharmacotherapy may be indicated. The aim of this section of the document is to outline the key principles underpinning pharmacological management of anxiety and depression. For detailed information about specific drugs, readers are referred to the Therapeutic Guidelines that are available online in most public hospitals. These guidelines are developed by an expert group and are regularly updated. The general information later is based on information in Therapeutic Guidelines referenced later unless stated otherwise.

Depression

There is strong evidence that antidepressants effectively treat clinical depression [82].

No particular class of antidepressants has been shown to be more effective than another in the treatment of depression [68], with direct comparison between classical tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) in a number of head-to-head trials showing no differences [83].

Compared with the general adult population, prescription of antidepressant medication for patients with cancer is more complex, and a number of factors must be taken into account in both selection of a particular drug and the dose, including the following:

- side-effect profile – for example, there is potential for initial exacerbation of nausea and sleep disturbance, and some drugs can lower seizure threshold;
- potential for drug interactions – for example, SSRIs may interact with anticonvulsants, anticoagulant therapy and tamoxifen. Some SSRIs have a long half-life with active metabolites meaning that the potential for ongoing interactions increases. Some drugs when prescribed with SSRIs will increase the risk of serious adverse serotonin-related toxicity;
- patient response to previous treatments;
- family history of response to treatments;
- patient co-morbidities – for example, elderly patients are vulnerable to exacerbation of pre-existing cognitive deficits and the development of confusion, and in patients with pre-existing heart disease, renal impairment or liver disease, the choice of drug is affected, and dose reduction will commonly be required; and
- the potential for beneficial impact on other symptoms – for example, improvement in sleep, treatment of hot flushes or as an adjunct to treatments for pain.

In the general adult population, the first-line pharmacological treatment of depression will most commonly be an SSRI or serotonin–norepinephrine reuptake inhibitor, mainly because of their more favourable side-effect profile compared with the older drugs such as tricyclic antidepressants (TCAs).

In patients with cancer, TCAs may have a valuable role even in low dose to relieve sleep disturbance and assist with pain management. However, their side-effect profile (especially anticholinergic effects) may limit treatment, and their use can be associated with troubling side effects including constipation, urinary retention and postural hypotension. *Note that TCAs are lethal in overdose and should not be prescribed for patients for whom suicide is considered a risk.*

Stimulants such as methylphenidate and dexamethasone have been used in a palliative setting because of their rapid onset of action and their effect on other symptoms such as attention and concentration. However, there is a lack of evidence, and recent European Guidelines on the management of depression in a palliative setting do not recommend the use of psychostimulants [82]. The *Therapeutic Guidelines Version 7, 2013* provides comprehensive evidence-based information about specific drugs to treat depression and anxiety, their side-effect profiles and drug interactions.

Resistant depression

It may take 2 to 4 weeks before an improvement in mood is evident after initiation of antidepressant treatment. It is important to remember that when using antidepressant medication, the patient continues to require frequent and regular contact with and psychological support from their treating clinician to promote full recovery. Failure to respond to treatment should lead to a systematic approach comprising the following:

- review of the diagnosis – for example, is this really depression rather than grief? Delirium should always be considered as a possible underlying condition in a medically ill person with sudden onset of mood disturbance;
- exclusion of any other contributory condition (for example, identification of unaddressed alcohol abuse or other causes of a depressive syndrome such as hypothyroidism, metabolic disturbance such as hypercalcaemia or central nervous system disease);
- review of any problems with adherence to medication;
- review of psychosocial and personality factors, and adequacy of concurrent psychological support/intervention;
- review of drug interactions (including depressive syndromes secondary to other medications such as corticosteroids and antihypertensive agents); and

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- finally, review and titration of the dose. The Therapeutic Guidelines lists dose ranges for antidepressants.

If the person's mood fails to improve with the previous steps, specialist review is recommended. Augmentation with other medications may be appropriate, and in some instances, electroconvulsive therapy may be considered as the safest and most effective treatment option.

Anxiety

Psychological interventions that might include a combination of cognitive behavioural therapy, relaxation training and guided imagery are the first-line therapy for generalized anxiety. Pharmacotherapy will be indicated if psychological interventions do not provide sufficient improvement in symptoms, or when relief of anxiety is required urgently, for example, in order for a patient to complete a course of radiotherapy.

Selective serotonin reuptake inhibitors are the first line choice of medication for treatment of anxiety requiring pharmacotherapy [51]. Patients who are anxious may be highly sensitive to the side effects of medication, which can include an initial exacerbation of anxiety and sleep disturbance. For this reason, some clinicians may choose to commence drug treatment with a lower dose than usual and increase the dose as the person adjusts to side effects.

Benzodiazepines have a limited role in the treatment of anxiety disorders and are *not* first-line treatment except in a short-term crisis situation (for example, a patient who requires fitting of a face mask for radiotherapy or in palliative care settings). Use of benzodiazepines is associated with significant morbidities including confusion, ataxia and falls in the elderly. Development of dependence and tolerance can occur within 1 month of regular consumption. Use of benzodiazepines with a short half-life can lead to rebound anxiety and a cycle of dosage escalation as the person interprets their symptoms as requiring more medication.

Antipsychotic medication for the treatment of anxiety is not recommended. Older persons are especially vulnerable to the side effects of antipsychotic medication, and there are reports of increased risk of cardiac events and stroke associated with their use in this population. The following guidelines provide useful overviews.

Psychotropic Expert Groups. *Therapeutic Guidelines*: *psychotropic*. *Version 7*. *Melbourne*: *Therapeutic Guidelines Limited*; 2013. ISBN 978-9808253-9-8.

Palliative Care Expert Group. *Therapeutic Guidelines*: *palliative care*. *Version 3*. *Melbourne: Therapeutic Guidelines Limited*; 2010. ISBN: 97809804764.

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