NINTH EDITION

The Palliative Care Handbook

Guidelines for clinical management and symptom control

Featuring extensive support for advanced dementia

ROD MACLEOD ● STEPHEN MACFARLANE

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Guidelines for clinical management and symptom control

This edition by Rod MacLeod and Steve Macfarlane has been revised and adapted to include the care of people with dementia and is based on previous editions written by Rod MacLeod, Jane Vella-Brincat and Sandy Macleod

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Champion Life

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Many of the medications listed are being used outside their product licence. Prescription of a drug (whether licensed use/route or not) requires the prescriber, in the light of published evidence, to balance both the potential good and the potential harm which might ensue. Prescribers have a duty to act with reasonable care and skill in a manner consistent with the practice of professional colleagues of similar standing. Thus, when prescribing outside the terms of the licence, prescribers must be fully informed about the actions and uses of the drug, and be assured of the quality of the particular product (www.palliativedrugs.com/ using-licensed-drugs-for-unlicensed-purposes). Prescribers also have a duty to inform patients that drugs are being used outside their licence and to inform them of any expected effects and side effects. Care has been taken to ensure accuracy of information at time of printing. This information may change and final responsibility lies with the prescriber. Some medication will incur a cost to the user, it is important to consider this before prescribing

This Handbook should be used in conjunction with Therapeutic Guidelines – Palliative Care – version 3 (Therapeutic Guidelines Limited, Melbourne) where possible

Throughout the book, drugs that are either not available or not funded in New Zealand are marked with *

Abbreviations

subcut	subcutaneous	CNS	central nervous system
bd	twice daily	LFTs	liver function tests
tds	three times daily	MAOIs	monoamine oxidase inhibitors
qid	four times daily	NSAIDs	nonsteroidal anti-inflammatory drugs

Foreword

Palliative care has come a long way from the beginnings of the modern hospice movement in the 1960s and is now widely understood as an essential part of care for the whole person during life-limiting illness and at end-of-life.

Increasingly we are aware of the importance of being able to provide palliative care when and where it is needed and this often means involving palliative care earlier in the course of illness and not just in hospital or hospice, but at home and in residential care.

Alongside these developments, dementia has become a leading cause of death in many nations, something which is still relatively new to our experience, but which can be expected to increase.

As a result, the interaction of palliative care with the end-of-life needs of a person with dementia has never been more important or prevalent and yet this is not widely addressed in literature and clinical support.

As the authors of *The Palliative Care Handbook* (ninth edition) point out, too often people with dementia miss out on palliative care referrals and treatments that could make such a difference for them in their final days.

Which is why this new edition is so vital. Not only have the highly regarded clinical and pharmacological guidelines been fully updated, extensive notes and advice have been included for the first time specifically addressing the end-of-life needs of people with dementia.

To accomplish this, original author, Prof Rod MacLeod and new author, Dr Stephen Macfarlane, have used their extensive expertise and experience to add many important insights and guidelines for palliative care in the context of dementia.

There is no doubt that this new edition of *The Palliative Care Handbook* will continue to support excellence in palliative care around the world and now also support a growing awareness of the palliative needs of people with dementia.

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Introduction

Welcome to the ninth edition of *The Palliative Care Handbook.* This edition has been extensively revised and for the first time includes specific guidelines to inform management of the provision of palliative care services to those living with dementia.

Dementia is now the leading cause of death for women in Australia (second leading cause overall) and a number of other Western countries. Yet the rates of referral of those with dementia to palliative care or hospice services remain very low, with most dying either in hospital wards or in aged care homes. Even when it has been recognised that a person with dementia has entered the dying phase, those with dementia are significantly less likely to receive palliative medications, including analgesia.

It is unclear whether this data reflects a lack of comfort that palliative care professionals have in working with people with dementia, or ignorance around the issues that those dying with dementia might face – research in the area is sorely lacking. What is known, however, is that the health needs at the end-of-life for those with dementia are comparable to the needs of those dying from cancer.

Part of the problem may lie in the difficulties health professionals experience in determining the prognosis of a person with dementia. The average duration between the diagnosis of dementia and dying from dementia is around 10 years, and even people with advanced dementia might, by the time they enter this stage of illness, survive another 2 or 3 years. In one study, only 1.1% of residents with advanced dementia were perceived to have a life expectancy of 6 months or less, yet 71% died within this time. A failure to recognise the onset of the dying process in a person with dementia exposes them to unnecessary investigations, hospital admissions, medical procedures and prescription of psychotropic drugs, whilst depriving them of more appropriate palliative interventions.

Regardless of the low rates of referral to palliative care of those with a primary diagnosis of dementia it is undeniable that, as the population ages, palliative care services will increasingly encounter patients for whom dementia is a significant comorbidity that will impact upon their management in a palliative care setting.

It is timely, then, for issues related to dementia to assume a greater importance within the palliative care sphere. It is hoped that this edition of *The Palliative Care Handbook* might be a step towards this.

The first section of this book is a set of guidelines for the alleviation of symptoms commonly encountered in palliative care. Drug therapy is included.

The second section (the pharmacopoeia) contains drug information:

- It is in alphabetical order by generic drug name.
- The interactions listed include discussion about enzymes responsible for drug metabolism commonly known as Cytochrome P450 (CYP) enzymes. There are many CYP enzymes some of which are genetically controlled. The interactions listed are based mainly on theory, are subject to change as more is learnt about the CYP enzyme system and are meant to be used as a guide only to potential interactions. Only commonly used palliative care drugs have been included but interactions with other drugs may also occur.
- There is also information about the use of syringe drivers.

While drug information in this book relates primarily to availability in Australia and New Zealand, the medications will generally be available in the UK, US and internationally. Where needed, further information is available from your nation's regulatory agency e.g. the UK Medicines and Healthcare Products Regulatory Agency and the US Food and Drug Administration.

Palliative care aims

- to achieve the best possible quality of life for patients and their families
- to understand and address patients' physical, psychological, social and spiritual suffering
- to be applicable from early on in the course of the illness

The World Health Organisation defines palliative care as:

'An approach that improves the quality of life of patients and their families facing the problems associated with a life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.'

Palliative care:

- provides relief from pain and other distressing symptoms
- affirms life and regards dying as a normal process
- intends neither to hasten or postpone death
- integrates the psychological and spiritual aspects of patient care
- provides support to help patients live as actively as possible
- provides support to the family during the illness and bereavement
- uses a multidisciplinary team approach
- enhances quality of life and influences the course of the illness
- is applicable early in the course of illness alongside therapies that are intended to prolong life (e.g. chemotherapy, radiotherapy) and diagnostic investigations

General symptom management principles

- accurate and meticulous assessment is essential
- assess and address non-physical as well as physical issues
- difficult to control symptoms may require several different approaches
- aim for highest possible quality of life
- use risk versus benefit assessments when side effects of therapy occur
- explain issues as much as possible to the patient and their carers
- use a multidisciplinary approach
- reassess continuously

Central nervous system

Dementia

Dementia is an insidious, global deterioration of cognition without impairment of consciousness. More than 100 causes are recognised, though most of these are exceedingly rare:

- a terminal disease (albeit slow) with a median survival of 7 to 10 years post-diagnosis
- prevalence of 10% in over 65-year-olds, 20% in over 80-year-olds, 40% in 90-year-olds, and for indigenous Australians the prevalence is 3 to 5 times that of non-indigenous Australians
- About 1% of all dementia is considered early-onset (age < 65). In indigenous Australians, early-onset disease is defined by an age of onset <50 years

Types

- Alzheimer's is the most common (70% of all dementias)
  - predominant early deficits are episodic memory and orientation to time.
- vascular (30% of all dementias)
  - accompanies a history of cardiovascular events (CVA/TIA)
  - islets of retained functioning
  - language is preserved
  - dysexecutive syndrome
  - gait disturbance
  - subcortical signs
- frontotemporal (FTD – 10% of all dementias; commonest cause of early-onset disease)
  - can occur in those with Motor Neurone Disease (10 to 15%)
  - disinhibition, apathy and loss of empathy
  - hyperorality, lability, poor insight and compulsive, perseverative behaviours
- Lewy body dementia (LBD)
  - Parkinsonism
  - visual hallucinations and cognitive fluctuations
  - cognitive fluctuations typically marked
  - REM-Sleep behaviour disorder
  - vulnerability to delirium
  - extreme sensitivity to antipsychotics – quetiapine is the agent of choice.
- treatable causes
  - depressive pseudodementia
  - subdural and hypothyroidism
  - B_{12}/folate deficiency
  - syphilis

- others
  - Parkinson's disease (essentially very similar to Lewy body dementia), Huntington's, alcoholic, post traumatic brain injury, paraneoplastic, post encephalitic

Note that mixed types of dementia become increasingly common with age, and that end-stage dementia (regardless of cause) tends to assume a common phenotype. With the exception of Lewy body dementia, determining the exact type of dementia in a palliative/end-stage setting is much less important than recognition and appropriate treatment of a behavioural syndrome.

Assessment

- Take an extensive history (in end-stage dementia this will invariably need to be from a family member or close caregiver).
- Formally assess mental state, including the use of cognitive screening tools e.g. Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) - where the patient retains verbal skills. (see 'Useful resources' p. 162)
- In many cases a formal cognitive evaluation will not be possible in advanced dementia, but the broader mental status examination remains invaluable, particularly in relation to:
  - General appearance and behaviour. Is the patient agitated, distressed, vocalising? Are there any signs of drug side effects (Parkinsonian facies, resting tremor, dyskinetic movements - oro-lingual dyskinesias are particularly common), dystonic reactions, motor tics or perseveration?
  - Affect - does the patient's expression reflect sadness, anxiety, anger? Are they guarded and suspicious? Lability may reflect frontal involvement, and should be differentiated from depression.
  - Perception. Does the person appear to be responding to external stimuli?

Behavioural and Psychological Symptoms of Dementia (BPSD)

- delirium
  - a careful history is vital. The biggest single risk factor for delirium is the presence of pre-existing cognitive impairment, so those with dementia are at vastly increased risk. Reduced cognitive reserve lowers delirium threshold.
  - A history of acute deterioration (cognitive, functional, behavioural) in the setting of previously stable impairments should always suggest delirium, and should be treated as such.
- depression (treat early initially with a SSRI or mirtazapine)
  - this is a difficult diagnosis to make in the presence of advanced dementia, where the patient's ability to report symptoms accurately is compromised
  - clinicians are advised to fall back on the presence of 'hard-core' biological symptoms of depression in this setting (recent change in sleep or appetite patterns, complete anhedonia, self-harm behaviour)
  - if there is any doubt, erring on the side of a trial of treatment is often advisable. Depression should be on the list of differential diagnoses for most behavioural disturbances in dementia, and modern antidepressants are much less toxic than the antipsychotic drugs that might otherwise be prescribed

  - Mirtazapine is a useful drug in this patient group. It has beneficial effects on sleep, appetite and anxiety that occur early in the course of treatment and which are independent of its antidepressant effects
  - The minimum antidepressant dose of mirtazapine is 30mg. If treating depression there is generally no advantage to commencing at a lower dose (often justified on the basis of minimising sedation…mirtazapine is an inverse agonist at the histamine receptor, however, and thus is more sedating at lower doses)
- agitation/aggression (consider low dose short term antipsychotics, benzodiazepines)
  - identify precipitants (can be difficult)
  - avoid confrontation
  - if the issue is agitation alone, antipsychotics hold no advantage over benzodiazepines, and are considerably more toxic
  - an intermediate half-life benzodiazepine with no active metabolites (e.g. oxazepam 7.5-15mg, temazepam 10mg) is the safest choice
  - there is evidence for the use of low-dose risperidone in the management of aggression, but the effect size is small (~0.2)
- anxiety
  - peaks in early/mid stages
- delusions (treat with antipsychotic)
  - particularly paranoid
  - beware 'delusions of theft' and 'misidentification delusions.' These may well be beliefs that have arisen as the artefact of cognitive impairment and/or to reflect neurological impairment (e.g. prosopagnosia) and are not likely to be antipsychotic responsive
- hallucinations
  - visual (up to 50% in LBD, although 20% of Alzheimer's patients will hallucinate at some stage during the course of the disease)
- sleep/wake cycle reversal/sundowning
- loss of insight/judgement
- wandering (60% of patients)
  - pacing and lapping (exclude akathisia)
  - (dangerous) eloping i.e. getting lost, accidents
- rejection of care
  - of food, hydration (consider artificial hydration) and hygiene

Complications

- eating and swallowing difficulties, cachexia
- infections – pneumonia, urinary tract
  - in pneumonias, the mortality is sevenfold that of a non-dementia patient
  - treat if symptomatic, antibiotics have limited efficacy
- falls – due to impulsivity, frailty, benzodiazepines and other sedatives
- pain – common in very elderly (50%)
  - may present behaviourally (non-verbally, crying, irritability)

  - roughly 70% of patients with significant BPSD are likely to have under-treated or unrecognised pain as a contributing factor
- adverse reactions to drugs
  - antipsychotics – sensitivity (Lewy body disease), parkinsonism, akathisia, acute dystonic reactions, sedation, peripheral oedema, chest infections, accelerated cognitive decline, stroke risk (3 fold that of non-dementia patients, 1.5 fold mortality), hypotension
  - benzodiazepines – sedation, falls

Treatment

As curative treatment does not exist, ensure that end-of-life discussions/advance directives/appointment of enduring power of attorney all happen early before loss of capacity. The environment of care is important – it should be simple, safe, involve attentive and patient staff, include support and education for family and carers, person-centred, proactive, include distractions, activities, routine, memory cues and benign paternalism.

- Mild – cholinesterase inhibitors may have temporary cognitive benefit
- Moderate – focus on quality of life and maintenance of function
- Severe – maximise comfort, avoid aggressive, burdensome or futile treatments, avoid enteral tube nutrition, consider a secure facility, allow a natural death (AND)

Depression

In end-of-life care it is important to distinguish between clinical depression and profound sadness.

- depression is a pervasive sense of misery
- sadness is a normal response to loss which waxes and wanes but enjoyment and future planning are retained
- most terminally ill patients do not become clinically depressed
- prevalence is about 15% (compared with 5 to 10% in the general population), most commonly in the early cancer stages
- reaching a diagnosis of depression in terminal patients is difficult as the usual physical symptoms of depression in the otherwise well such as anorexia, weight loss, sleep disturbance are often already present in patients with malignant disease whether they are depressed or not
- the psychological symptoms are more discriminative
- asking 'Are you depressed?' provides a bed-side assessment of mood
- suicide is rare, however, fleeting suicidal thoughts and fluctuating 'will to live' in cancer patients are common and not necessarily pathological
- requests for euthanasia and/or physician assisted suicide are more common although, as for suicide, this is not limited to depressed patients
- clinical depression is under-recognised and under-treated yet it is generally very responsive to treatment
- the cause of depression is unknown but imbalances in neurotransmitters, especially serotonin, in the brain may play a part

Psychological symptoms of major depression may include

- hopelessness
- anhedonia (loss of pleasure)
- morbid guilt and shame
- worthlessness and low self esteem
- request for physician assisted euthanasia
- persisting suicidal ideation
- lowered pain threshold
- decreased attention and concentration
- cognitive slowing
- impaired memory
- indecisiveness
- early morning wakening
- ruminative negative thoughts
- nihilistic and depressive delusions
- feeling of unreality

Depression in older people and people with dementia

It is worth noting that the 'textbook' symptoms of major depression as they appear in references such as DSM-V have not been validated in older persons. Many older people with depression will not use the word 'depression' to describe their feeling state, but will instead use terms such as 'anxiety,' or 'I'm just worried, doctor.' Taking these terms at face value may lead to the inappropriate prescription of anxiolytics. Older persons also tend to express their depression more frequently in terms of somatic symptoms than younger persons do, which can clearly present diagnostic difficulties in a setting where palliative care is being provided.

Similarly, the diagnosis of depression in the setting of dementia is fraught. In cognitively intact populations, the diagnosis is made on the basis of symptom self-report. In advanced dementia, however, most patients will be unable to reliably verbalise their symptoms. The psychological distress that depression causes may instead be expressed in terms of externalising behaviours, which may include agitation, aggression, pacing and calling out, themselves common behavioural and psychological symptoms of dementia (BPSD). Two of the more reliable 'biological' symptoms of depression in the setting of dementia are recent worsening in sleep or appetite.

SSRI antidepressants are considered first-line pharmacological management for symptoms of BPSD. One of the likely reasons for their apparent success in controlling BPSD is that many cases labelled as BPSD are, in fact, cases of depression manifesting as disturbed behaviour. In a similar vein, while drug treatment trials of depression in the setting of dementia have been disappointing/contradictory, part of the problem inherent in such trials is a lack of certainty around diagnosis. In other words, these trials may well have included persons with undifferentiated BPSD, rather than depression.

A number of screening tools for depression in dementia exist. Perhaps the most commonly used tool is the Cornell Scale for Depression in Dementia. Clinicians should be wary of placing too much faith in the Cornell, however, as it has not been validated in patients with an MMSE of 10 or less, nor in patients with significant BPSD.

The role of antidepressants in treating depression in advanced dementia is controversial, and is likely to remain so, given the methodological problems in 'true case' ascertainment. When in doubt, however, clinicians are advised to err on the side of a trial of treatment.

Risk factors

- inadequate symptom control - unrelieved pain, nausea
- poor quality of life
- lack of social support
- past and/or family history of depression
- older age
- substance abuse
- misinformed prognosis
- polypharmacy
- specific drugs
  - steroids, cytotoxics, antibiotics, anti-hypertensives, neuroleptics, sedatives, beta-blockers, opioids
- immobility
- advanced malignant disease

Differential diagnosis

- adjustment/grief reaction (sadness)
- 'vital (physiological) exhaustion'
- demoralisation (a state of existential despair, meaninglessness and hopelessness but not of anhedonia and joylessness)
- delirium/sedation
- detachment (the terminal shedding of attachments)
- 'giving up' (affect neutral, rational, decisive)

Management

- mild to moderate depression
  - support, empathy, clarification of stressors or precipitators, explanation, cognitive therapy, symptomatic relief
- severe depression
  - supportive psychotherapy plus drug therapy
  - drug therapy - antidepressants are effective in 50 to 70% of cases
    - > a therapeutic trial is usually appropriate
    - > if in doubt, refer to a specialist psychiatrist
    - > SSRI e.g. escitalopram, sertraline, fluoxetine