

Guidelines for

MANAGING DIABETES AT THE END OF LIFE

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A DOCUMENT TO ACCOMPANY THE GUIDELINES

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ADEA has reviewed and endorses the use of these Guidelines

Yeah, the patients shouldn't have to worry about it [diabetes care at the end of life] that's the only thing I would say that it's [diabetes] not given as high a priority probably as it should be.

You don't want to go on with endless care... you've got to draw a line somewhere but I think I would like to feel comfortable but not be overactive with treatment and I feel that's not done.

Comments from two people with diabetes receiving palliative care who participated in the interviews.

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List of Abbreviations

ACD	Advanced care directive
AM	Morning
BG	Blood glucose
CAM	Complementary and alternative medicines
CCF	Congestive cardiac failure
DE	Diabetes Educator
DKA	Diabetic ketoacidosis
eGFR	<i>estimated</i> Glomerular filtration rate
GI	Gastrointestinal symptoms
HONK	Hyperosmolar non-ketotic acidosis
Hypo	Hypoglycaemia
ICU	Intensive care unit
IGT	Impaired glucose tolerance/ glucose intolerance
IM	Intramuscular
IRS	Insulin resistance
IV	Intravenous therapy
MI	Myocardial Infarction
OHA	Oral Hypoglycaemic agents
Mmol/L	millimoles/litre – unit for measuring glucose in blood
PCOC	Palliative care outcomes collaboration
PM	Afternoon
QUM	Quality use of medicines
SVC	Superior vena clava syndrome/obstruction
T1	Type 1 Diabetes Mellitus
T2	Type 2 Diabetes Mellitus
TZD	Thiazolidinediones
UTI	Urinary tract infection
WHO	World Health Organisation

DOCUMENT TO ACCOMPANY THE GUIDELINES FOR MANAGING DIABETES AT THE END OF LIFE

Background

The project to develop guidelines for managing diabetes at the end of life originated from collaboration between diabetes and palliative care clinicians. The project was designed to address the critical need for clear guidelines for managing people with diabetes requiring palliative care.

Palliative care is defined as:

An approach that improves the quality of life of patients and their families facing the problem associated with 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.

(World Health Organisation, 2009)

The goal of palliative care is to achieve the best quality of life for patients and their families. Most people gradually deteriorate towards the active dying phase after a period of illness: less than 10% die suddenly or unexpectedly (Emanuel et al. 2008). However, people with chronic diseases such as diabetes may have many episodes of the unstable Palliative Care Outcomes Collaboration (PCOC, 2008) phase before they enter the final end of life stage.

A detailed report about the development of the Guidelines, including a literature and interviews with people with diabetes requiring palliative care and their carers, was prepared. The following sections provide information about the philosophical and theoretical frameworks used to underpin the Guidelines and detailed background information about managing diabetes in people requiring palliative care.

The Palliative Care Outcomes Collaboration framework

The Palliative Care Outcomes Collaboration (PCOC, 2008) palliative care phases and the Quality Use of Medicines (QUM) Framework (PHARM Committee, 2005) were used as the underlying conceptual framework for the Guidelines.

The five palliative care phases are:

1. stable
2. unstable
3. deteriorating
4. terminal
5. bereaved.

The phases are not necessarily sequential and an individual patient can move between the phases (PCOC, 2008). There is no defined duration of the phases or for the entire dying entire process.

Separate Guidelines for managing diabetes are provided for each PCOC phase with the exception of the bereaved phase. In addition, guidelines for managing people, with and without diabetes, who are prescribed corticosteroid medicines are included.

A definition of each phase is presented in the following section based on the PCOC definitions (PCOC, 2008).

Phase 1: STABLE

All people not classified as unstable, deteriorating or terminal.

The person's symptoms are adequately controlled using their established management plan but interventions to maintain symptom control and quality of life have been planned. The family/carers' situation is relatively stable and no new issues are apparent. Any needs are addressed in the established plan of care.

Phase 2: UNSTABLE

The person develops a **new unexpected problem or a rapid increase** in the severity of existing problems, either of which requires an **urgent** change in current management or emergency treatment. The person could restabilise or deteriorate.

The family/carers experience a sudden change in their situation requiring urgent intervention by members of the multidisciplinary team.

Phase 3: DETERIORATING

The person's existing symptoms **gradually worsen** or they develop **new but unexpected problems**. These require specific plans of care and regular review but **not urgent or emergency treatment**.

The family/carers experience gradually worsening distress and other difficulties, including social and practical difficulties, as a result of the illness of the person they are caring for. This requires a planned support program and counselling as necessary.

Phase 4: TERMINAL

Death is likely in a matter of days and no acute intervention is planned or required. However, frequent, usually daily, interventions aimed at physical, emotional and spiritual comfort is required.

The typical features of a person in the terminal phase include some or all of the following:

- profound weakness
- essentially bed bound
- drowsy for extended periods
- disoriented for time and has a severely limited attention span
- increasingly disinterested in food and drink
- finding it difficult to swallow medicines.

The family/carers recognise that death is imminent and care is focussed on ensuring comfort and emotional and spiritual care as a prelude to bereavement.

Phase 5: BEREAVED

The individual died and the carers are grieving. A planned bereavement support program is available in many palliative care services including referral for counselling as necessary.

Diabetes and palliative care

Diabetes is a complex multifaceted disease of disturbed glucose homeostasis. Normal glucose metabolism is finely balanced among glucose uptake and glucose utilisation, production and storage (Table 1 on the next page). However, glucose enters cancer cells down a concentration gradient rather than being insulin-mediated and the metabolism favours lactate production, which is used in the liver for gluconeogenesis, which increases blood glucose levels. Lactate production may also increase the risk of lactic acidosis especially in people with type 2 diabetes taking Metformin. There is an association between some forms of cancer such as breast, pancreas, liver and kidney, and diabetes and obesity. Weight loss associated with cancer often leads to malnutrition, reduced immunity and affects normal cell functioning.

In addition, renal disease is a significant complication of diabetes and influences the choice of medicines, many of which are excreted via the kidney, and care must be taken to protect the kidney if radio-contrast media are used. People with a long duration of diabetes may have autonomic neuropathy, which can lead to unrecognised hypoglycaemia and gastric stasis. The latter can complicate medicine-induced constipation, and nausea and lead to unstable blood glucose levels and nutrient malabsorption, which complicates the nutritional status and contributes to falls.

Hypoglycaemia produces unpleasant symptoms and affects cognitive functioning. People with liver disease and limited nutritional reserves are not able to mount an effective counter-regulatory response to hypoglycaemia and glucagon injections may not be effective in these people. In addition, the counter-regulatory response to hypoglycaemia decrease in type 1 diabetes: glucagon and adrenaline secretion diminishes; thus, the early warning signs are lost (Cryer, 1997). Hypoglycaemia can occur when people are on glucose lowering medicines, have renal or liver disease and inadequate carbohydrate intake.

Hyperglycaemia produces unpleasant symptoms, which can be mistaken for other causes. It affects mood, quality of life and cognitive functioning. Significantly, type 2 diabetes is a progressive disease of beta cell decline and insulin is needed in 75% of people to control blood glucose, and thus symptoms.

Table 1. Normal glucose metabolism: a fine balance among glucose uptake, glucose utilisation, production and storage.

Circulating blood glucose (Available fuel)	Hepatic glycogen stores (Stored fuel)	
	After food—the post prandial state	Fasting state and between meals
Glucose enters the bloodstream after food is digested in the GIT and stimulates the pancreas to secrete insulin (glucose-mediated insulin release). The intestinal incretin hormones also play a role in insulin release when the BG rises after food. Insulin attaches to the insulin receptors on the cell membranes (insulin binding). Insulin initiates a cascade of intracellular events that enables glucose to enter the cells. Inside the cell the glucose is used for immediate energy production or stored for longer term use.	Counter-regulatory hormones e.g. glucagon, adrenaline, cortisol, and growth hormone release glucose stores from the liver and muscle between meals, overnight and when fasting. Insulin is required for the glucose to enter the cells. It attaches to the insulin receptors on the cell membranes (insulin binding). Insulin initiates a cascade of intracellular events that enables glucose to enter the cells. Inside the cell the glucose is used for immediate energy production or stored for longer term use	In the longer term glucose is manufactured in the liver from protein and fat stores (gluconeogenesis and glycogenolysis). Thus, protein and fat are important fuel substrates. Insulin is needed for the new glucose to enter the cells. If insulin is lacking or the individual has insulin resistance the glucose does not enter the cells and hyperglycaemia and hyperlipidaemia occur.

A summary of the short and long term complications of diabetes is provided in Table 2. Many of these are present before diabetes is diagnosed thus non-diabetics at risk of type 2 diabetes are likely to have impaired glucose intolerance and complications such as cardiovascular disease.

Table 2. The short term and long term complications of diabetes.

Short term complications	Long term complications
<p>Hypoglycaemia</p> <p>Hyperglycaemia, if not corrected can lead to:</p> <ul style="list-style-type: none"> - ketoacidosis - hyperosmolar states 	<p>(1) <u>Microvascular</u> disease</p> <ul style="list-style-type: none"> - retinopathy - nephropathy (eGFR < 60ml/min) <p>(2) <u>Macrovascular</u> disease</p> <ul style="list-style-type: none"> - cardiovascular disease - cerebrovascular disease - intermittent claudication <p>(3) Neuropathy</p> <ul style="list-style-type: none"> - peripheral - autonomic - responsible for gastroparesis and hypoglycaemia unawareness <p>(4) Periodontal disease</p> <p>(5) Anxiety and depression and burnout</p>
<p>Active infection</p>	

People may already have diabetes when they enter palliative care or may develop diabetes during palliative care, often as a consequence of treatment with diabetogenic medicines. A number of factors are known to increase the risk of people developing diabetes.

Risk factors for type 1 and type 2 diabetes

People most at risk of developing type 2 diabetes:

- family history of diabetes
- have the metabolic syndrome (a cluster of risk factors for cardiovascular disease and type 2 diabetes)
- are aged over 50 years (but prevalence is increasing in younger people)
- have close relatives with type 1 or type 2 diabetes
- are overweight
- are women who had gestational diabetes or gave birth to large babies
- belong to Asian, Pacific Islander or Australian Aboriginal ethnic groups
- have hepatitis C
- have schizophrenia
- have pancreatic cancer
- are using immunosuppressive therapy and/or
- take diabetogenic medicines (Diabetes Australia, 2009b; Dunning, 2009).

People most at risk of developing type 1 diabetes:

- genetic predisposition
- pancreatectomy or other significant pancreatic disease or trauma.

Diagnostic criteria

The criteria for diagnosing diabetes are presented in Figure 1 (next page). Fasting plasma glucose is the preferred diagnostic test, but any of the three tests are acceptable.

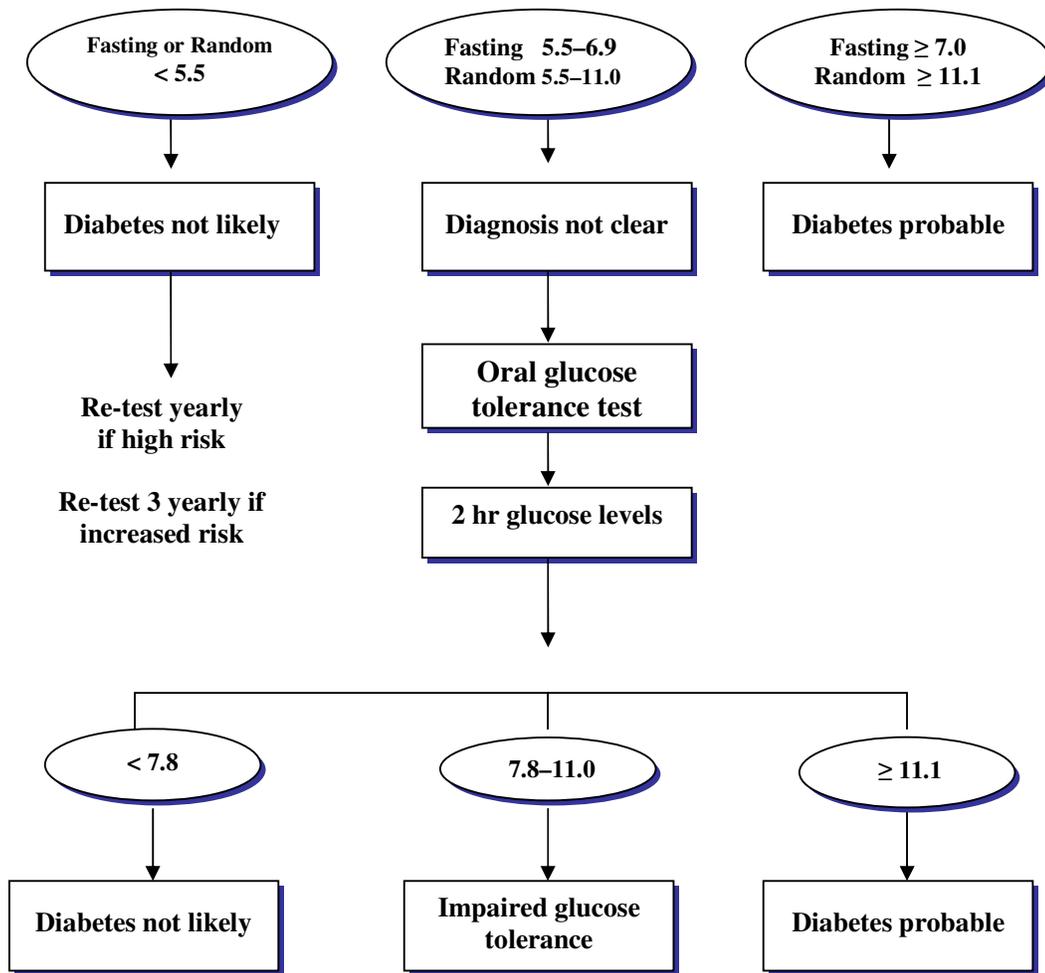


Figure 1. Criteria for diagnosing diabetes (venous plasma glucose levels in mmol/L) (Based on Diabetes Australia, 2009b). The OGTT is rarely required and is contraindicated if the blood glucose is already high.

Overview of diabetes management

In general, diabetes management involves an appropriate diet and activity for both type 1 and type 2 diabetes even when medicines are needed. Managing diabetes involves:

- Lifestyle changes particularly for type 2 diabetes.
- Medicines:
 - Type 1 diabetes – insulin
 - Type 2 diabetes oral hypoglycaemic agents, incretin mimetics and/or insulin.

Note: beta cell function declines over time in type 2 diabetes and approximately 75% eventually need insulin.
- Managing blood glucose, lipids and blood pressure.
- Regular medicines review.
- Regular monitoring by health professionals to identify and manage the short and long term complications of diabetes.
- Diabetes education including educating significant others.
- Self-care by the patient, with support from family/carer.

Hyperglycaemia and hypoglycaemia

Two conditions commonly associated with diabetes are hyperglycaemia, a symptom of uncontrolled diabetes, and hypoglycaemia, a side effect of glucose lowering medicines, especially sulphonylureas and insulin.

Hyperglycaemia

Under usual circumstances, many people with type 2 diabetes do not experience the symptoms of hyperglycaemia until their blood glucose levels are extremely high.

Common symptoms of hyperglycaemia include:

- feeling excessively thirsty
- frequently passing large volumes of urine

- feeling tired
- blurred vision
- infections e.g. thrush, cystitis, wound infections
- lowered mood
- weight loss in the longer term (Diabetes Australia, 2009a).

Hypoglycaemia

Hypoglycaemia, also called a ‘hypo’, low blood glucose, or insulin reaction, occurs when the blood glucose level falls below 4 mmol/L. Symptoms of hypoglycaemia vary from person-to-person, however, common feelings are:

- weakness, trembling or shaking
- sweating
- light headedness
- headache
- dizziness
- difficulty concentrating
- tearful/crying
- behaviour change
- irritability
- hunger
- numbness around the lips and fingers (Diabetes Australia, 2009a).

Hypoglycaemia unawareness may be present especially in people with long-standing type 1 diabetes. This means they may not recognise the early adrenergic symptoms of hypoglycaemia. In addition, symptoms may be masked by analgesia, delirium and other cognitive changes and cancer-related autonomic neuropathy. Significantly, people with diabetes and their family members/carers are often very fearful of hypoglycaemia and the consequences, which includes death.

The Quality Use of Medicines framework

The Quality Use of Medicines (QUM) Framework (PHARM Committee, 2005) is the recommended Australian framework for making medicines-related decisions and was used when formulating these Guidelines (see Figure 2, page 13). The safe and effective use of medicines is extremely important at the end of life (National Prescribing Service Limited and Palliative Care Australia, 2009).

The factors to consider when determining a diabetes medicine regimen for people with diabetes receiving palliative care, if medicines are indicated, are:

- Insulin doses may need to be adjusted frequently.
- Patients on metformin who develop nausea and vomiting especially the elderly, those on diabetogenic medicines, and those with reduced renal function, liver, cardiac and respiratory disease, and people who are not eating, may be at risk of lactic acidosis, a relatively rare but serious adverse event. Significantly, most reported cases of lactic acidosis associated with metformin occurred in people with known contraindications (Australian Adverse Drug Reactions Advisory Committee, 2001). Therefore, metformin may not be the best choice.
- Insulin mimetics can induce weight loss and nausea, therefore, they may be contraindicated.
- Thiazolidinediones contribute to weight gain due to fluid retention and may be contraindicated.
- Diuretics can exacerbate dehydration and increase blood glucose levels.
- Corticosteroids, and atypical antipsychotics are frequently used in palliative care and other disease processes and increase blood glucose levels.
- Glucagon used to treat severe hypoglycaemia usually increases blood glucose quickly. A second dose can induce nausea but may be ineffective in emaciated people with reduced glycogen stores. This means if oral glucose treatment of hypoglycaemia and intramuscular (IM) glucagon are ineffective or contraindicated, intravenous (IV) dextrose may be required.
- Some oral nutrition supplements affect blood glucose levels, often leading to hyperglycaemia.

- The patient may be using complementary medicines (CAM) and other CAM therapies. If so, determine why the person is using CAM, what they are using, and whether CAM is appropriate i.e. the benefits outweigh the risks and there is evidence for its use.
- CAM medicines may interact with conventional medicines. However, some non-medicine CAM therapies can relieve symptoms such as stress and pain and may be safer than medicines.
- CAM use should be included in the management plan and monitored.
- Opioids and other psychoactive medicines can mask hypoglycaemia.

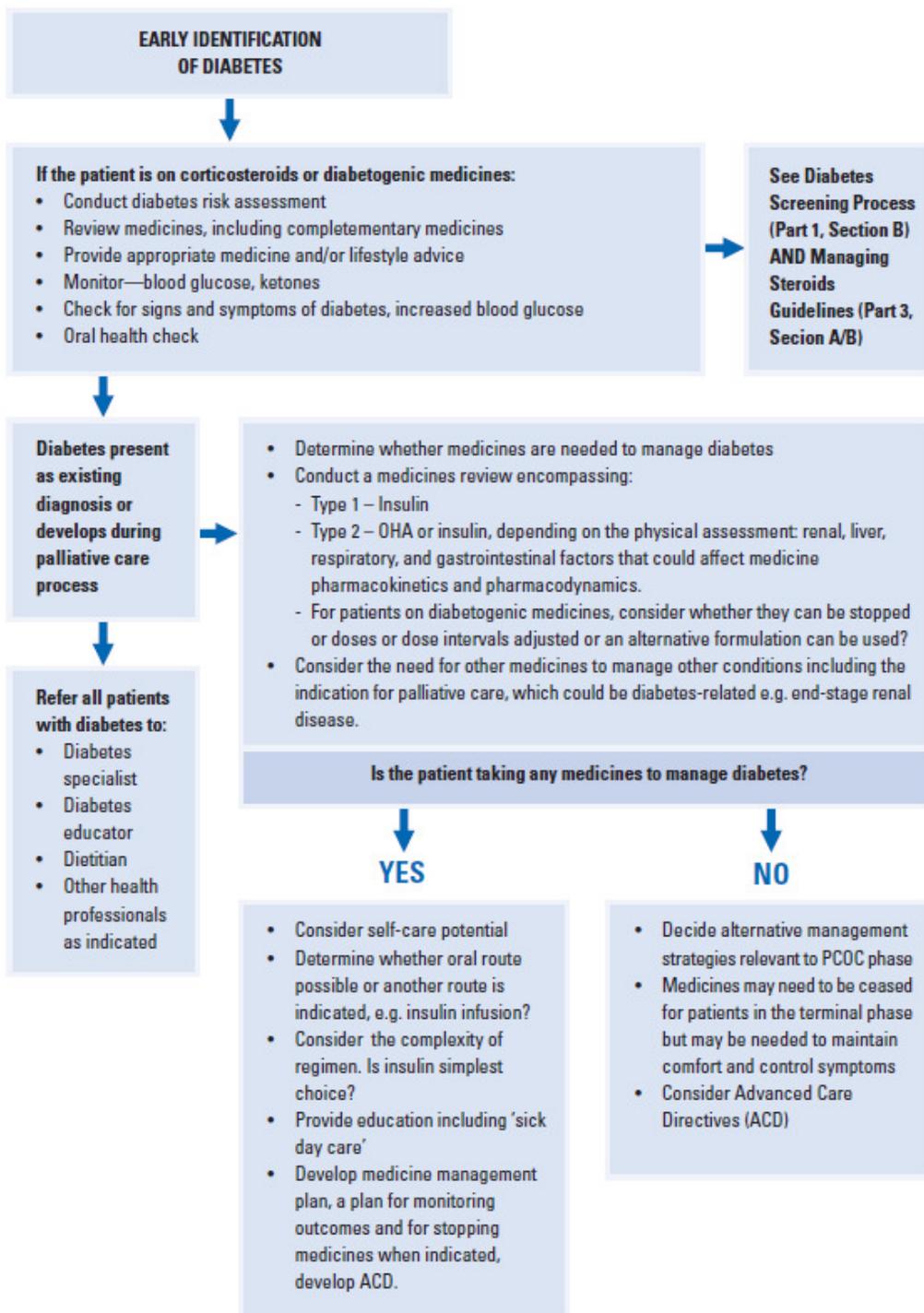


Figure 2. Quality Use of Medicines Framework for managing diabetes at the end of life.

Corticosteroid medicines

Corticosteroid medicines are an essential part of the management of several disease processes such as haematological malignancies, inflammatory diseases, allergies and shock. However, long term use and high doses predispose people to insulin resistance (IRS), glucose intolerance (IGT) and steroid-induced diabetes; and causes hyperglycaemia and the resultant symptoms in people with diagnosed diabetes. IRS and IGT can occur within 48 hours of commencing steroids, especially in at-risk individuals and those with diabetes. People should be informed they could develop diabetes when diabetogenic medicines are prescribed.

Several mechanisms have been proposed for the diabetogenic effects of steroids.

These include:

- Enhancing gluconeogenesis by upregulating key regulatory hormones that contribute to hyperglycaemia such as glucose-6-phosphatase and phosphoenolpyruvate carboxylase.
- Suppressing insulin release from the beta cells.
- Inducing peripheral insulin resistance by inhibiting production of glucose transporters in adipose and skeletal muscle cells.

Both fasting and post prandial blood glucose levels are affected.

These proposed mechanisms of action suggest the key areas to target when developing strategies to manage IGT, IRS, and steroid-induced diabetes. However, the effect on blood glucose depends on the biological action of the specific corticosteroid medicine and the period of time it is used for as well as the individual's personal risk of developing diabetes. Hyperglycaemia usually occurs when doses of Prednisolone or equivalent medicines exceeds 7.5 mg/day. In contrast, short courses may not cause hyperglycaemia or only have a short term effect on the blood glucose.

Corticosteroids can also mask the signs and symptoms of infections, which often do not present in the usual way in people with diabetes and can be difficult to detect. The skin can become thin and fragile and prone to tears. If not managed, these effects can cause considerable discomfort and distress. Corticosteroids also have variable effects on bone formation and reduce calcium absorption from the intestine, which predisposes susceptible individuals to osteoporotic fractures and pain.

Mental changes can also occur ranging from mild psychosis to significant pathology. These effects can be distressing for the individual and carers.

Managing medicine-induced diabetes in palliative care patients

Balancing the need for corticosteroid medicines with their effects on glucose homeostasis is multifactorial and challenging and is affected by individual susceptibility, meal schedules, whether dosing is intermittent or continuous and the diabetogenic effects of the individual medicines. Table 3 (next page) outlines an appropriate diabetes management strategy for people with medicine-induced diabetes.

Table 3. Managing medicine-induced diabetes.

1. Pre-prescription evaluation	<ul style="list-style-type: none">• Screen for diabetes risk factors.• Complete assessment and medical history.• Undertake a comprehensive medicine review including self-prescribed and complementary medicines.• Provide education and counselling about weight, diet and activity.• Select the most appropriate medicine and use the least diabetogenic medicine for shortest duration, if possible (Quality Use of Medicines principles).• Monitor blood glucose regularly.
2. Individualise therapy	<ul style="list-style-type: none">• Choose an appropriate medicine (as above).• Reduce diabetogenic medicine doses as soon as possible.• Set blood glucose target and commence relevant oral hypoglycaemic agents (OHAs) or insulin, if indicated e.g. blood glucose consistently > 7 mmol/L.• Target post-prandial blood glucose levels, use long acting insulin analogue. Add prandial insulin (meal time) use rapid acting analogue if indicated.
3. Monitor	<ul style="list-style-type: none">• Self-blood glucose testing regularly.• Test ketones if person has type 1 and blood glucose is high.• The need to continue corticosteroids.• Reduce OHA/insulin doses as steroid doses are reduced.• Monitor physical and mental status.

Palliative care symptoms and diabetes

Sub-optimal symptom control can be due to the diabetes or the life-threatening primary illness or both. Distinguishing between cause and effect can be difficult. Symptoms not caused by diabetes can have significant effects on diabetes management. Table 4 (pages 17–19) outlines the relationships between common palliative care symptoms and diabetes.

Table 4. The relationship between common palliative care symptoms and diabetes. (Table continues over 3 pages)

Common palliative care symptoms	Impact on diabetes management	May be diabetes-related
Pain (acute/chronic)	<p>Increased:</p> <ul style="list-style-type: none"> - somnolence or confusion/cognitive impairment due to pain/analgesia - risk of hyperventilation - hyperglycaemia <p>Reduced:</p> <ul style="list-style-type: none"> - intake - mobility - sleep - self-care ability - quality of life 	<ul style="list-style-type: none"> - Peripheral vascular disease - Amyotrophy - Peripheral neuropathy - Myocardial Infarction (MI) - Tissue glycosylation (e.g. carpal tunnel syndrome) - Ketoacidosis (abdominal pain)
Depression/ anxiety	<p>Increased:</p> <ul style="list-style-type: none"> - fatigue - lethargy, change in performance status - risk of DKA, HONK - social isolation <p>Reduced:</p> <ul style="list-style-type: none"> - self-care ability, disinterest increased risk of hyperglycaemia - confidence - inadequate nutrition increased risk of hypoglycaemia - effects on communication and self-care 	<ul style="list-style-type: none"> - Associated with diabetes especially hyperglycaemia - Renal disease - Corticosteroid medicines - Hypoglycaemia symptoms can be mistaken for anxiety
Oral Pathology (oral and maxillofacial pathology) Mucositis, ulcers, dry mouth	<p>Increased:</p> <ul style="list-style-type: none"> - pain - dry mouth - inadequate nutrition, inappropriate weight loss, cachexia, hypoglycaemia if on OHA/insulin <p>Reduced:</p> <ul style="list-style-type: none"> - intake - self-care deficits - mood 	<ul style="list-style-type: none"> - Diabetic ketoacidosis (DKA), hyperosmolar states (HONK) may lead to dry mouth, thirst and clinical dehydration - Risk of dental caries and oral pathology - Risk of hypoglycaemia if on OHAs or insulin
Sepsis		<ul style="list-style-type: none"> - May be silent in diabetes (urinary tract infection (UTI), MI) - May precipitate DKA, HONK

Common palliative care symptoms	Impact on diabetes management	May be diabetes-related
Nausea/vomiting	<p>Increased:</p> <ul style="list-style-type: none"> - confusion - lethargy - disinterest - pain/discomfort - inadequate nutrition → weight loss, cachexia, hyperglycaemia - hypoglycaemia if on OHA/insulin - dehydration and electrolyte imbalance - risk of ketoacidosis <p>Reduced:</p> <ul style="list-style-type: none"> - intake - energy, depleted energy stores 	<ul style="list-style-type: none"> - May be due to gastric autonomic neuropathy - Renal disease - Hyperglycaemia – DKA, HONK - Medicines: <ul style="list-style-type: none"> - Metformin - Byetta
Delirium	<p>Increased:</p> <ul style="list-style-type: none"> - cognitive impairment <p>Reduced:</p> <ul style="list-style-type: none"> - ability to communicate and detect signs/symptoms of hypo/hyperglycaemia - self-care ability 	<ul style="list-style-type: none"> - May be due to many factors including hyper and hypoglycaemia
Acute Dyspnoea	<p>Increased:</p> <ul style="list-style-type: none"> - hypoxia contributing to confusion <p>Reduced:</p> <ul style="list-style-type: none"> - self-management capacity <p>Note: MI often silent in diabetes</p>	<p>Increased:</p> <ul style="list-style-type: none"> - confusion - energy requirements - pain - difficulty interpreting elevated white cell count, which could be caused by hyperglycaemia, sepsis, or other factors - bone marrow failure <p>Reduced:</p> <ul style="list-style-type: none"> - intake increased DKA, HONK risk - quality of life - wound healing

Common palliative care symptoms	Impact on diabetes management	May be diabetes-related
Diabetes Emergencies	Examples: <ul style="list-style-type: none"> - Hypoglycaemia - Hyperglycaemia - MI 	<ul style="list-style-type: none"> - Hypoglycaemia - DKA, HONK, Lactic acidosis
Oncology Emergencies	Examples: <ul style="list-style-type: none"> - Spinal Cord Compression (corticosteroids) and acute immobility - Superior vena clava (SVC) obstruction (acute dyspnoea and delirium) – high dose of corticosteroids - Febrile neutropenia - Major bronchial obstruction (dyspnoea and use of corticosteroids) 	<ul style="list-style-type: none"> - Hypoglycaemia - DKA, HONK, Lactic acidosis

Considerations when using the Guidelines

The key themes that emerged from the interviews with patients and their family members/carers that were conducted to ensure the guideline development process was consistent with NHMRC (1999) recommendations and people with diabetes and their relatives' voices were heard, follow. Importantly, these themes are consistent with the guiding principles developed as the conceptual framework for the Guidelines development project.

- Care should be individualised for each patient because the situation, diagnosis and responses of each individual are unique.
- Patients want a consistent approach to their diabetes management. When they are cared for by health professionals they want their diabetes management to be consistent with their usual self-management practices, and they want different health professionals to be consistent in how they manage the patient's diabetes.
- Comfort is very important to patients and interview participants stressed that they want their diabetes managed to prevent unpleasant symptoms of hypoglycaemia and hyperglycaemia.

- Most patients want some say in how their diabetes is managed, but are happy for experienced health professionals to work with their family/carers to make decisions when they are no longer able to do so, if they have not communicated their wishes in an Advanced Care Directive.
- Family members/carers need education about managing diabetes as the patient's health deteriorates and the family member/carer takes on new responsibilities.

General considerations—diabetes and all palliative care phases

Goal of care

- Symptom management and support for the patient. Manage diabetes using the Guidelines for each PCOC phase in people diagnosed with diabetes. Identify diabetes or impaired glucose tolerance in non-diabetics for example, those on corticosteroids to enable appropriate timely care and symptom control.
- Consider the patient's wishes and choices when making decisions about diabetes management.
- Discuss changes in diabetes management with other relevant health professionals, the patient and family members/carers.
- Include diabetes management in care plans and advanced care planning directives.
- Provide education to the patient and their family members or carers concerning the focus of care, which focuses on preventing symptoms of hypo/hyperglycaemia and their consequences and enhancing quality of life. However, long term diabetes complications may be present and affect palliation, general care plan, medicine choice, and contribute to or be the cause of symptoms. Therefore, they must be identified and managed.
- Involve an interdisciplinary health team to foster inclusive, collaborative goals of care (endocrinologist, diabetes educator, palliative care specialists—medical/nursing; psychologist; social worker; occupational therapist; physiotherapist; pastoral care worker) and communication.
- In addition to the tools already used to assess patients, assess whether the patient has diabetes and/or the signs and symptoms of diabetes.
- Blood glucose monitoring is an important decision-making tool rather than an unnecessary intervention.

- Admissions may be needed for acute illnesses.

General considerations and case studies—individual palliative care phases

Stable phase

General considerations

- The goals of care are symptom management and support for the patient and carers to maintain independence and self-care capacity as long as possible.
- Determine the cause of the symptoms and whether diabetes is causing or exacerbating symptoms.
- The stable phase represents a ‘window of opportunity’ to identify, acknowledge and document patient’s wishes for current and future diabetes management. Initiate Advanced Care Planning including preferences for future diabetes management
- Assess carer’s capacity to provide care and their need for diabetes education.
- Management begins with a thorough clinical assessment and medicines review during which the patient’s and carer’s level of understanding and current treatment regimen is evaluated.
- If the patient’s blood glucose pattern is stable and in an acceptable range (4-8 mmol/L) continue current treatment regimen. The assessment should include documenting the presence of long term complications and a medication review. Liver/renal disease may mean OHAs and some other medicines are contraindicated. Determine whether the patient is using complementary medicines (CAM) or other CAM therapies and their safety and efficacy and potential interactions with conventional medicines.
- The patient’s diet may need to be revised and supplements may be needed particularly if anorexia or cachexia is present. The patient and carers may need significant explanation and education if the diet changes significantly from the diet they have been familiar with for many years.
- Glucocorticoids induce glucose intolerance and insulin resistance and may cause blood glucose levels to rise. People prescribed these medicines often need insulin to control blood glucose levels and diabetes symptoms. The

effect of corticosteroids on glycaemic control varies with individual corticosteroid medicines and among individuals.

- Other medications can cause hyperglycaemia, for example, atypical antipsychotics, thiazide diuretics and octreotide (a somastatin analogue).
- Blood glucose monitoring is advisable to identify hyperglycaemia early and manage it to reduce the impact of diabetes-related symptoms on pain, mood and quality of life and prevent consequences such as DKA, HONK and lactic acidosis.
- Blood glucose testing for patients who are not on corticosteroids could be once to twice a day. Increase the frequency of blood glucose monitoring if symptoms develop or the patient becomes ill. In the stable phase this might be every 2–4 hours depending on the type of diabetes. Patients with type 1 diabetes should also be tested for ketones.
- If the patient is on corticosteroids refer to Part 3 of the Guidelines.

Case study

“A” is a 78-year-old woman with severe dementia and type 2 diabetes. She lives in a residential aged care facility and requires full nursing care including continence management. She has no Advanced Care Plan. She previously had very limited intake, which became much worse in the last three months, and her family have requested a palliative approach.

- Ascertain whether there is an Enduring Medical Power of Attorney (EMPOA) or limitation of treatment order. An Advanced Care Plan is vital to establish the boundaries of care and help health professionals respect the individual’s wishes.
- “A” may need insulin to prevent hyperglycaemia if oral medicines are stopped. Insulin should be considered with the other ‘core’ out-of-hours emergency medicines to ensure it is available as part of the contingency plan as part of the discussion with other health professionals, in particular with her General Practitioner. Including insulin in the ‘core’ medicines list should minimise the risk of an inappropriate/unwanted out-of-hours admission to hospital.

Unstable phase

General considerations

- The goal of care is to rapidly identify the cause/causes of the instability, treat the cause/s if possible, manage symptoms and support the patient and his or her carers.
- Consider whether the phase is likely to revert to stable or continue to the deteriorating or terminal phases.
- Determine the cause of symptoms and whether hypo/hyperglycaemia could be causing or exacerbating symptoms. Monitor BGLs regularly for example every four hours while her condition is unstable.
- Provide education to the patient and his or her family members or carers about the focus of care, which should be on preventing symptoms of hypo/hyperglycaemia and their consequences and enhancing quality of life. However, short and/or long term complications may be present and affect palliative care, medicine choice and contribute to or be the cause of symptoms. Therefore, ideally, they should be identified and managed.
- Review her medicines regimen, including any CAM treatments and self-prescribed medicines she might be using, considering her complication status and BGL pattern, and potential medicine interactions.
- Several symptoms of advanced cancer are similar to those of hyperglycaemia. It is important to consider diabetes as a possible cause of symptoms. Blood glucose monitoring is important to determine whether diabetes is involved.
- If changes in symptoms are due to intercurrent illness, treat the cause and/or consider whether an emergency department or hospital admission is needed. Consider the possibility that DKA could occur in type 1 diabetes and test for ketones. Blood ketone testing is preferred over urine ketone testing.
- The patient's diet may need to be revised and supplements may be needed particularly if anorexia or cachexia is present. The patient and carers may need significant explanation and education if this is a radical change from the diet they have been familiar with for many years.
- Ascertaining the patient's and family's wishes is vital to determine the boundaries of investigating the primary disease and progressive co-morbidities. Using disease-specific prognostic tools when they are available,

these tools can also assist health professionals obtain informed consent from the patient or carers. General prognostication such as functional status prior to the period of instability might help determine the appropriate approach.

Case study

“B” is a 60-year-old woman with renal failure, cardiovascular disease (NYHA stage IV) and type 1 diabetes. Her weight has decreased from 80 kg to 65 kg over the last six months. B is unstable due to increasing dyspnoea at rest, a prolonged episode of chest pain, and delirium. She has been taking regular long acting opioids (morphine). B has an Advanced Care Plan (ACP).

- Consider what symptoms represent and what can and cannot be controlled or reversed. There are many causes of delirium.
- Determine whether the ACP covers her diabetes management preferences or the contingency that this may represent acute on chronic renal impairment?
- B’s symptoms, including delirium, may be due to hyperglycaemia leading to dehydration, or hypoglycaemia including nocturnal hypoglycaemia, and she may need acute complex management.
- B’s dose or choice of opioid may change depending on the degree and rapidity of her renal function decline and further renal impairment.
- Her 19% recent weight loss is a very significant prognostic factor and needs to be considered when formulating a management plan as well as considering her pre-existing diabetes and renal impairment.
- If renal and diabetic causes are excluded, a host of other factors that could cause or contribute to the presenting picture including opioid toxicity, hypoxia, stroke, thromboembolism and ketoacidosis need to be considered.
- Determining the venue of immediate care and the degree of intervention is complex and may require a senior clinician’s guidance.

Deteriorating phase

General considerations

- The goal of the deteriorating phase is to support and comfort the patient and carers, maintain comfort, dignity and autonomy as long as possible and maximum comfort.
- Generally, do not cease insulin for patients with type 1 diabetes in this phase but dose reductions may be indicated.
- Check the patient's Advance Care Plan if they have one. If not, ascertain their wishes *as a matter of urgency*.
- Provide education for the patient and their family members or carers about the focus of care, which should be on preventing symptoms of hypo/hyperglycaemia and their consequences and enhancing quality of life. However, short and long term diabetes complications may be present and affect palliative care and medicine choice and contribute to or be the cause of symptoms. Therefore, ideally they should be identified and managed.
- Weight loss, lack of appetite and decreasing performance status are the main expected issues in this phase. Maximising and maintaining as much function as possible may require a multimodality approach including nutritional supplements, exercise including resistance training and orexigenic medications that can alter glucose metabolism and diabetes management. Examples include glucocorticoids and agents such as megestrol acetate. The diabetes management plan will need to be revised if these interventions are used.
- The patient's diet may need to be revised and supplements may be needed particularly if anorexia or cachexia is present. The patient and carers may need significant explanation and education if this is a radical change from the diet they have been familiar with for many years.
- Several symptoms of advanced cancer such as dry mouth and polydipsia are similar to the symptoms of hyperglycaemia. It is important to consider diabetes as a possible cause of symptoms, which, if corrected will enhance comfort. Blood glucose monitoring is important to determine whether diabetes is involved.
- If changes in symptoms are due to intercurrent illness, consider whether treatment and/or an emergency department or hospital admission is needed.

- A patient with diabetic ketoacidosis (DKA) or hyperosmolar non-ketotic (HONK) coma may not actually be in a coma. If these conditions are present insulin is generally needed.
- Ketone testing is important in type 1 diabetes during illness and hyperglycaemia to detect DKA early. DKA can contribute to pain and cognitive changes. Insulin doses may need to be increased to manage ketosis.

Case study

“C” is a 65-year-old male with metastatic non-small cell lung cancer. He has cachexia and is taking dexamethasone. He has steroid-induced diabetes. C has no Advanced Care Plan.

- Determine the patient’s wishes and suggest he develops an ACP.
- C may need insulin when on high dose Dexamethasone. Note the syndrome of cancer cachexia may increase insulin resistance.
- C’s insulin doses and dose frequency will need to be carefully titrated when his Dexamethasone dose is weaned or increased.
- Regular blood glucose monitoring will provide important information on which to base insulin dose adjustments.
- The patient and carers may need diabetes education because Mr C’s diabetes is a very ‘new’ diagnosis. Education should include blood glucose testing and medicines management. They may be distressed at dealing with a new illness in addition to the primary lung cancer. It may all feel ‘too much;’ support and counselling may be needed.

Terminal phase

General considerations

- The goal of the terminal phase is to maximise comfort and ensure a peaceful transition to death.
- Very limited or no oral intake is often a sign that death may be close. Providing mouth care may be the major comfort measure.

- Decisions should be made about which medicines can be stopped and whether blood glucose testing should be continued or stopped, explored. Check the patient's Advance Care Plan if they have one. If not, ascertain their wishes as soon as possible.
- A patient with diabetic ketoacidosis (DKA) or hyperosmolar non-ketotic (HONK) coma may have an impaired conscious state. These states should be excluded as the cause of 'the terminal phase' and treated to manage symptoms.
- Glucocorticoids may no longer confer any symptom or quality of life benefit and could be ceased.

Case study

"D" is a 40-year-old woman with breast cancer and depression. D has type 1 diabetes and no Advanced Care Plan.

- Determining D's judgement regarding the boundaries of care may be difficult due to her depression and no pre-morbid ACP.
- The duration of the terminal phase may influence the approach to managing her diabetes care. If she dies in a matter of a few hours the issue may not arise, but some people can remain in the terminal phase for days and insulin or other interventions may be needed to promote comfort. The ethical considerations may be complex and need a multi-disciplinary approach and senior clinicians discussing the issues with her family so they can make a substituted judgement.
- Consider whether D's depression can be treated in the timeframes indicated by your prognostication, or whether it is caused or affected by her blood glucose levels.
- Her insulin requirements may change dramatically and she may need a more flexible dose regimen.
- Blood glucose and ketones monitoring will help plan care to prevent short-term symptoms and ease her discomfort.
- All oral medicines may need to be rationalised with a view to stopping them.

Full case study

“E” is a 55-year-old male with colorectal cancer and long standing type 2 diabetes

E lives alone with his dog. He is Italian and has limited English. He presented with rectal bleeding and was diagnosed with metastatic colorectal cancer (bulky liver metastases) following palliative bypass surgery during which widespread peritoneal seeding was noted. He often experiences nausea and vomiting, he has had peripheral diabetic neuropathy (PDN) for over 20 years. He has episodes of angina and erectile dysfunction.

E has not told his health care professionals that he takes some complementary medicines (CAM). He consumes 10–20 standard units of alcohol per day and probably drank more in the past.

Shortly after being admitted to a community palliative care program he phoned complaining of severe abdominal pain associated with nausea and vomiting. He has been reluctant to monitor his blood glucose in the past and is reluctant to do it now. He does not want to come into hospital, which was suggested by the community nurse. He is drowsy and relatively immobile.

Unstable phase

Key issues:

- Exclude hyperglycaemia as a cause of his symptoms.
- Determine what his current diabetes medicine regimen is and whether he takes his medicines. There could be interactions with his CAM medicines. Some OHA may be contraindicated given his alcohol intake.
- The long standing alcohol intake may have caused liver disease and nutritional deficiencies.
- His social isolation means that supporting his care requirements or new diabetes regimen will be very difficult even with frequent community nursing visits.
- Clinically, he appears to have a sub-acute bowel obstruction. He is not able to take any oral intake. E thinks he is dying.

- After explaining that his symptoms might improve with simple non-surgical approach he agrees to a hospital admission if his dog can be cared for. His PDN has worsened with recent (weeks) of non-adherence to his adjuvant analgesics. He will need:
 - IV fluids.
 - Intravenous infusions to deliver analgesics and anti-emetics.
 - He may be prescribed high dose corticosteroids.
 - He may need an insulin infusion and then regular insulin doses while he is on glucocorticoids.
 - Medicines to prevent alcohol withdrawal symptoms.

E's symptoms settle with the regimen described above and after five days he insists on returning home on BD insulin after meeting the diabetes team once and the diabetes educator once more.

Stable Phase

Once home he is well supported by the community care team and a further outpatient visit to the diabetes educator. He is able to stop his dexamethasone and his OHAs and regular analgesia for PDN are recommenced. He admits the major reason he wants to return home is his dog.

Key issues:

- Careful monitoring during corticosteroid dose titration.
- Significant education was required when he commenced insulin
- It is important to explore his wishes in general and that an ACP is started.
- Social work involvement is important to help address social interventions and to discuss his preferences for his pet's care into the future.
- Contingency medications, care plans, and orders need to be in place.

He remains well for three months following an endocrinology review and his cancer is relatively indolent, with stable liver disease and no major episodes of obstruction, on an oral chemotherapy regimen.

Deteriorating phase

Over the next few months E complains of increasing abdominal distension and becomes jaundiced. He notes his muscles are wasted. His nausea increases in frequency and his appetite diminishes. He is re-commenced on Dexamethasone to improve his appetite, wellbeing and nausea. He is given some nutritional supplements. His alcohol intake reduces dramatically. He admits he feels depressed. He finally agrees to complete his advanced care plan.

Key issues:

- His weight is unlikely to reflect his muscle mass due to probable ascites.
- His caloric intake may be dramatically reduced (alcohol and general intake).
- BGL monitoring is required when he commences glucocorticoids.
- Insulin may be required when on glucocorticoids but the doses may be lower than before due to his weight loss and other factors.
- Contingency plans that reflect his ACP should be in place.
- Consider the effects of acute alcohol withdrawal.
- An appetite stimulating antidepressant (many suppress appetite) may be part of a treatment plan for his depression.
- Discussion regarding his preferences for venue of terminal care should be finalised and the timing of when his dog should be moved to the home that agreed to adopt it, explored.
- If the decision is to treat his anorexia/cachexia, the ramifications for his diabetes management should be considered.
- If he is deemed to be clinically depressed this may effect whether his ACP was based on informed consent from a competent individual.

Terminal Phase

A few weeks later E becomes drowsy, bed-bound, confused and is noted to be much more jaundiced with obvious hepatic asterixis (liver flap). He outlined in his ACP (he was not thought to be clinically depressed when he made it) that when this occurred he wished to be admitted to the local palliative care unit for terminal care and that his dog should go to the home that agreed to adopt it. He confessed he has an estranged son and asks to see the priest despite letting his faith lapse.

Key issues:

- Oral medications should be rationalised and it is likely that most, if not all, oral medicines could be stopped.
- Routine blood tests may indicate whether this is truly a terminal event and exclude reversible causes.
- Blood glucose monitoring will guide what type of insulin regimen he will need, although his ACP stated that in the terminal stages he wanted comfort measures only.
- Regular antipsychotic medicines may help control the symptoms of delirium.
- He may need higher doses of sedatives to reduce terminal restlessness based on his long standing alcohol history.
- His estranged family should be contacted and supported as needed.
- His spiritual requests should be respected and the priest contacted.
- Symptoms of alcohol withdrawal should be monitored and PRN medications to reduce the discomfort provided if needed.

E dies 36 hours later in the company of his adult son having required medicines through a syringe driver to manage his agitation.

References

Australian Drug Reactions Bulletin (ADRAC). (2001). *Incidence of lactic acidosis between 1985–2001*, from www.tga.gov.au/aarb/aadr9505/htm (accessed December 2007).

Cryer, P. (1997). *Hypoglycaemia, Pathophysiology, Diagnosis and Treatment*. New York: Oxford University Press.

Diabetes Australia (2009a). What is diabetes? Diabetes Australia, Canberra.

Diabetes Australia. (2009b). *Diabetes Management in General Practice, 15th Ed.*: Diabetes Australia.

Dunning, T. (2009). *Care of people with diabetes. A manual of nursing practice* (3rd ed.). Chichester: Wiley Blackwell.

Emanuel, L., Alexander, C., Arnold, R. M., Bernstein, R., Dart, R., Dellasantina, C., et al. (2004). Integrating palliative care into disease management guidelines. *Journal of Palliative Medicine*, 7(6), 774–783.

National Health and Medical Research Council. (1999). *A guide to the development, implementation and evaluation of clinical practice guidelines*. Canberra: National Health and Medical Research Council.

National Prescribing Service Ltd and Palliative Care Australia. (2009). *Achieving quality use of medicines in the community for palliative and end of life care: A consultation report*. Sydney: National Prescribing Service Ltd.

Palliative Care Outcomes Collaboration (PCOC) (2008): PCOC Assessment tool definitions: Phase V 1.2.

Pharmaceutical Health and Rational use of Medicines (PHARM) Committee (2005) The quality use of medicines in diabetes. PHARM.

World Health Organization. (2009). *WHO definition of palliative care, 2009*, from www.who.int/cancer/palliative/definition/en

