Palliative and end of life care for people with diabetes: a topical issue

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Practice points
• Palliative and end-of-life care are important aspects of the diabetes disease trajectory; proactive end-of-life care planning could be incorporated into the annual diabetes complication screening process.
• The key focus of palliative diabetes care is on undertaking appropriate assessments and monitoring that can guide care decisions, avoid unnecessary burden of care, and manage unpleasant symptoms to promote comfort and quality of life.
• Care, including blood glucose ranges and HbA1c targets, should be individualized and adjusted to suit the individual's health and functional status, end-of-life stage, life expectancy, self-care ability and their end-of-life wishes.
• Hypo- and hyper-glycemia cause distressing symptoms and stress and fear for people with diabetes on glucose-lowering medicines. Symptoms can be atypical and difficult to recognize for the individual and health professionals. Treatment might be delayed or not provided and the health professionals often under-rate the impact of hypo- and hyper-glycemia on the individual's mental and physical wellbeing.
• Regular blood glucose monitoring helps identify hypo- and hyper-glycemia and enables appropriate treatment to be implemented promptly to reduce the metabolic and psychological impact.
• The individual and their families should be involved in care decisions when possible, including proactively planning for end-of-life care.
• It is important to support and educate family and other carers, including health professionals, during the individual's end-of-life journey and often during the bereavement period after death.

SUMMARY Managing diabetes is challenging, especially in palliative and end-of-life situations. The prime focus is usually on safety, comfort and quality of life rather than on achieving 'tight' blood glucose control. Preventing hypo- and hyper-glycemia is an important aspect of comfort and quality of life. The care plan and blood glucose targets need to be personalized to suit the individual's health and functional status, medicine regimen, risk profile and life expectancy, and, importantly, developed with the individual and sometimes their family carers. Once developed, the care plan should be monitored and reviewed regularly to accommodate changing health status and ensure the person's documented wishes are current. Key care challenges include detecting symptoms of hypo- and hyper-glycemia and determining their underlying causes so appropriate care can be initiated. Health professionals often find it difficult to decide on a management plan and when to withdraw treatment in rapidly changing circumstances, especially if the person has not documented their wishes. The paper addresses key palliative and end-of-life care issues relevant to Type 1, Type 2 and corticosteroid-induced diabetes.

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Epidemiological research suggests there is a strong association among obesity, diabetes and other obesity-related diseases including some forms of cancer [1]. Diabetes is an increasingly prevalent disease with a high disease burden due to complications such as cardiovascular and renal disease and the associated effects on quality of life, pain, morbidity and mortality [2]. There is also an association between dementia and diabetes [3] and dementia and hypoglycemia [4,5].

There are two main types of diabetes: Type 1 (T1DM), which is an autoimmune disease that results in destruction of the insulin producing β cells in the pancreas. People with T1DM require insulin injections for life to replace the endogenous insulin they cannot produce. Type 2 diabetes (T2DM), the most common type, is associated with insulin resistance, which means insulin cannot enter body cells to be utilized for energy [6]. People with T2DM often commence treatment with glucose-lowering medicines (GLM) that reduce insulin resistance such as metformin, especially if they are overweight, but other GLMs are also used. Over time the β cells become exhausted and no longer produce enough insulin to control blood glucose; consequently insulin is required in the majority of people with T2DM [7].

Every year 20 million people require palliative care, most in the Western Pacific Region [8]. However, only one in ten people who need or would benefit from palliative care receive such care and 25% of hospital beds are occupied by people who are dying [8]. It is not clear what proportion of these people has diabetes: accurate data about diabetes-related deaths is difficult to obtain because diabetes is not always listed as a contributing cause of death on death certificates [9,10].

However, existing information suggests diabetes is a major cause of mortality in older people with diabetes [11]. In addition, diabetes-related short-term complications such as ketoacidosis (DKA) and hyperosmolar states (HHS) are associated with significant discomfort and morbidity and can be life threatening. Chronic hyperglycemia in the longer term increases the risk of cardiovascular disease including heart failure, sudden death and all-cause mortality among people with T2DM. The mortality risk may be independent of other conventional cardiovascular risk factors [12].

A palliative approach can be integrated with usual diabetes treatment when indicated, for example people on renal dialysis and those with heart failure [13,14]. However, integrated palliative and end-of-life (EoL) care is not included in most 'diabetes guidelines'; consequently there is little guidance to help health professionals plan EoL diabetes care. Two exceptions are Diabetes UK 2012 [14] and Dunning et al. 2010 [15]. It is not clear why EoL care is not included in most diabetes guidelines. One reason could be the lack of level one evidence on which to base recommendations. Dunning et al. [15] and presumably Diabetes UK [14], regarded the lack of guidance about EoL care as a significant care gap that needed to be addressed; although the current authors are not privy to the UK's reasons for developing EoL guidelines.

Dunning et al. [16] adopted recommended guideline development processes that included undertaking a comprehensive literature review to identify the best available evidence, consulting with and expert advisory group, regularly meeting with palliative care clinicians to discuss iterative drafts of the guidelines during routine care planning case discussions. That is, the guidelines were tested in relevant clinical settings before they were released [16].

In addition, Dunning et al. developed a philosophical framework to guide care recommendations and conducted individual interviews with people with diabetes receiving palliative care and their family carers about the way they wanted their diabetes managed at the EoL [17]. The guidelines were subjected to public scrutiny before they were released. Future guideline developers could consider using Dunning et al.'s [16] guideline development method when developing guidelines in situations where there is little available evidence and randomized controlled trials are not feasible. The recommendations in this paper are consistent with Dunning et al. [15] and Diabetes UK's [14] EoL guideline recommendations and encompass Type 1 and 2 diabetes and corticosteroid-induced diabetes.

Palliative & end-of-life care

Palliative care is defined as an approach that improves the quality of life of patients and families living with a life-threatening illness. The focus is on prevention, relieving suffering by identifying problems early by undertaking a through assessment and engaging the individual and family carers in care decisions [18].

EoL care refers to care provided to people likely to die in the next 12 months and includes

imminent death (expected in a few hours to days) and progressive incurable diseases, frailty, acute life-threatening illnesses, and existing diseases that can cause sudden death such as diabetes [19].

EoL has been divided into four inter-related stages that help guide treatment decisions: stable, unstable, deteriorating and terminal [20]. These stages are not linear, especially in people with diabetes who usually encounter many stable/unstable periods before they begin to deteriorate towards the terminal stage [15]. For example, any intercurrent illness or significant life events usually induce glucose variability and hyperglycemia and its related symptoms and can progress to ketoacidosis (DKA) and hyperosmolar states (HHS) [21]. DKA and HHS are generally regarded as periods of unstable diabetes that are usually remediable, including at the EoL.

Management dilemmas

Diabetes and palliative care health professionals (HP) face many clinical ethical dilemmas when managing diabetes in palliative and EoL situations. In the current paper, clinical ethical dilemmas refer to situations involving a choice between two equally unsatisfactory alternatives [22]. Generally, the situation and the context need to be considered together. The following list represents some clinical ethical dilemmas. Making decisions can be especially difficult when the individual's wishes are not documented because they raise concerns about informed consent and vulnerability [23]:

- Balancing risk and benefit considering the pathophysiological differences between T1DM and 2DM diabetes;

- Managing corticosteroid-induced hyperglycemia and their other effects;

- Managing nausea, vomiting, anorexia and the associated consequences such as ineffective hypoglycemia counter-regulatory response, cachexia, weakness and falls risk;

- Detecting and managing hypo- and hyperglycemia, which are life-threatening conditions that compromise comfort and represent unstable diabetes that could be remedial;

- Making appropriate medicine choices;

- Addressing spiritual needs;

- Initiating timely discussion about EoL care with individuals and/or family carers before crises occur and making difficult decisions about terminal care when the individual's wishes are not documented;

- Deciding when to withdraw life-sustaining treatment; that is when it is no longer beneficial and becomes burdensome to the individual/family. Such decisions are more difficult if the individual/family regards treatment withdrawal as 'giving up on them' and do not realize the pain and suffering can still be treated [24].

Key management strategies

Generally, care should be personalized according to the individual's needs and desires, their EoL stage, the benefit and risk of any treatment options and life expectancy. Care planning encompasses deciding suitable glycemic targets to prevent hypo- and hyper-glycemia, managing medicines and deciding when to stop medicines and withdraw other treatment [14,15].

Glycemic targets

Cardiovascular and renal diseases are leading causes of death in people with diabetes [2]. Maintaining blood glucose and blood pressure close to the normal ranges helps prevent cardiovascular disease and other diabetes complications when people have a longer life expectancy. Preventing long-term diabetes complications is not a priority of EoL care.

However, managing existing complications to promote comfort and quality of life, relieve pain and prevent unnecessary admission to hospital, is important, especially during the stable/unstable EoL phases where recovery is likely [2,15,17].

There is no consensus about the optimal HbA1c and blood glucose ranges or the frequency of blood glucose monitoring (BGM) at the EoL. As indicated, many guideline developers and other diabetes experts agree that these targets must to be individualized. Recent blood glucose target recommendations are 6–11 mmol/l [15], avoiding levels <6 mmol/l and >15 mmol/l [2,14], and HbA1c up to 8%. However, there is very little evidence to support these recommendations and they most likely do not apply in the deteriorating and terminal stages. Preventing hyperglycemia in the deteriorating stage is relevant because it exacerbates pain and causes discomfort that could be alleviated.

Blood glucose monitoring

The value of BGM in T2DM is debated, regardless of the person's health status. However, BGM

is important to detect hypo- and hyper-glycemia, which can be difficult at the EoL because symptoms are often atypical and/or attributed to other causes and not treated. BGM helps detect high and low BG excursions. Our research suggests many people with diabetes and their families want BGM to continue at the EoL because BGM represents stability/familiarity during a frightening, uncertain time and helps them interpret symptoms [15,17]. Some people with diabetes and/or their families feel abandoned if BGM is discontinued and may think staff 'gave up on them.'

Research also suggests palliative care staff regard BG monitoring as painful and, unnecessary [25], which is interesting, considering other very invasive and painful treatments that are often used in palliative care. Like all care, BG monitoring frequency should be decided in consultation with the individual considering their EoL stage, life expectancy, medicine regimen including diabetogenic medicines such as corticosteroids, and the individual's hypo- and hyper-glycemia risk profile.

Hyperglycemia

Hyperglycemia is not a benign condition. It causes distressing osmotic symptoms such as thirst, urinary frequency and lethargy, exacerbates pain, contributes to delirium and confusion, reduces mood, and affects problem solving, coping ability and quality of life [17]. Significantly, hyperglycemia can be present without significant symptoms; consequently, it can be missed and go untreated and progress to DKA or HHS, which are life-threatening situations and require urgent care. Dying from DKA or HHS is uncomfortable and unnecessary.

As indicated, people with T1DM require insulin and T2DM is associated with progressive loss of β-cell function and declining insulin production: >50% people with T2DM eventually need insulin [7]. The need for insulin may be greater in palliative and EoL care when diabetogenic medicines and other factors such as pain contribute to hyperglycemia. Managing hyperglycemia enhances comfort and might include more frequent BG testing, fluid replacement and insulin. Ketone testing should be part of the care plan for T1DM and very ill people with T2DM.

Families/carers may need support, frequent explanations and education about how to recognize and manage hyperglycemia and what BG levels and symptoms should trigger them to seek health professional advice [17].

• Hypoglycemia

Hypoglycemia is a significant issue risk for many people, see **Box 1**. It is important to realize that hypoglycemic risk can change and needs to be assessed regularly. Hypoglycemia affects delayed and working memory in the short term and affects decision-making and problem solving [5,26] and can trigger myocardial infarction [24]. In the longer term it is associated with dementia [27].

As indicated, regular BGM is important to detect hypoglycemia in people at high risk of hypoglycemia. Symptoms can differ from 'text book' symptoms, especially in older people and those with long-standing diabetes when neuroglycopenic symptoms usually predominate because of the changed counter-regulatory response to falling BG levels. Over time, glucagon, cortisol and growth hormone production diminishes [5,29]. It is important that health professionals learn to recognize the neuroglycopenic signs and help people with diabetes and their families learn to recognize other relevant body cues.

Treating hypoglycemia is difficult when people have anorexia and nausea and/or vomiting because of the low glucose stores in muscle and liver and the changed counter-regulatory response to the falling blood glucose level [30,31]. GLMs are often stopped in people who have frequent severe hypoglycemic episodes. However, stopping GLMs might not be appropriate, except in the deteriorating and terminal stages because of the likelihood of hyperglycemia and its adverse effects, especially people with T1DM and insulin-requiring T2DM.

It is essential to undertake a comprehensive medicine review and identify and manage other hypoglycemia risk factors. The choice of GLM/s, dose and dose frequency needs to be carefully considered to maintain BG >6 mmol/l to reduce the hypoglycemia risk [2,14,15]. Educating the individual and family/carers and sometimes health professionals about how to recognize hypoglycemia and any changes to the medicine regimen might be required.

Dietetic advice can help health professionals and family/carers plan an acceptable diet and provide supplements if necessary to minimize the effects of malnutrition, and minimize weight loss and it consequences; loss of muscle mass in the stable and unstable EoL stages. Reversible causes of anorexia and weight loss such as dysphagia, depression, nausea and malabsorption need to be addressed [32].

Box 1. Common risk factors for hypoglycemia in people with diabetes on palliative care and at the end of life. The more risk factors present the greater the risk of hypoglycemia.

- Prescribed GLM especially sulphonylureas and insulin
- Using medicines that interact with GLMs including some herbal GLMs
- Prescribed medicines that affect appetite
- Weight loss, malnourishment and cachexia, which affects glucose stores and the ability to mount a counter-regulatory response and which occurs in 40–90% of the cancer palliative care population [5]
- Renal disease, which is a common complication of diabetes and affects medicine excretion and may require dialysis. End-stage renal disease is an indicator for palliative end-of-life care. Macroalbuminuria predicts hypoglycemia [28]
- Liver disease, which affect medicine metabolism
- Hypoglycemia unawareness, which is common in older people and those with Type 1 diabetes mellius due to autonomic neuropathy and inability to mount a suitable counter-regulatory response due to deficient secretion of key counter regulatory hormones such as glucagon [5,26]. Severe hypoglycemia is a cause of hospital admission in people >80 years with Type 2 diabetes mellius [19]
- Cognitive impairment and delirium, which could be from chronic hypoglycemia, hyperglycemia, medicines or dementia
- Unmanaged pain, which affects appetite. Adequate pain management is essential and is generally well documented in palliative care plans
- Fasting for procedures or surgical interventions
- Health professionals and family carers mistakenly attributing hypo- or hyper-glycemic coma to other causes, such as the dying process

GLM: Glucose-lowering medicine.

However, the metabolic processes involved in wasting due to cachexia and sarcopenia that arise in palliative care situations are complex, vary among different disease processes, and differ from cancer-related cachexia and are generally irreversible in advanced disease [32]. Cachexia and sarcopenia also affect muscle glucose stores and reduce the individual's capacity to mount a counter-regulatory response to hypoglycemia.

Medicine management

Quality use of medicines [33] is essential to achieve acceptable glycemic control and minimize hypoglycemia and other medicine-related risks. QUM encompasses deciding whether a medicine is needed; selecting appropriate medicine/s if a medicine is required, proactively monitoring medicines effectiveness and stopping medicines (deprescribing) where possible [33,34]. Medicine choices are influenced by their availability and cost, the person's prognosis, health status, oral intake, medicine risk profile, comorbidities and the type of diabetes: T1DM or T2DM.

Type 1 diabetes

People with T1DM in the stable phase could continue their usual insulin regimen. The dose might need to be adjusted when the person develops renal and liver disease, to accommodate weight loss and food intake to avoid hypo- and hyper-glycemia. Medicines are usually ceased in the terminal stage. Most people with T1DM use basal (long/intermediate acting)/bolus (rapid acting) insulin regimens. Insulin analogs are often used. Basal bolus regimens enable insulin doses to be adjusted to accommodate people's eating pattern (give a bolus dose when they eat) and can be particularly useful in the unstable and deteriorating stages and when nausea, vomiting and anorexia are present and to prevent hyperglycemia.

Specific management in the unstable stage depends on whether the individual is likely to return to stable state or deteriorate and progress to the terminal stage. If recovery is likely, an intravenous insulin infusion might be indicated during acute illnesses and surgical procedures. Blood ketone tests should be performed if the blood glucose is >15 mmol/l, especially if the individual has nausea, vomiting and signs of dehydration, which could indicate remediable ketoacidosis [2,15].

Insulin pumps are increasingly popular, especially among young people with T1DM. Pumps deliver a constant small basal dose of insulin and bolus doses when indicated, for example, with meals, which enables flexible insulin dosing in changing situations such as palliative and EoL care [14]. It is essential that HPs understand that

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insulin pumps only supply rapid-acting insulin: if the pump is turned off or malfunctions the BG can rise very quickly.

Generally people who use insulin pumps are very knowledgeable about and competent to manage their pumps, but may need help during periods of instability. HPs must have the technical expertise and competence to manage insulin pumps and seek expert advice early when such knowledge is lacking.

Type 2 diabetes

The individual's usual GLM regimen can usually be continued in the stable phase but doses may need to be reduced or insulin initiated to simplify the medicine regimen and/or reduce the risk of hypoglycemia, especially in the unstable and deteriorating EoL stages. The choice of GLM or GLM combinations should suit the individual's health status, BG pattern, life expectancy, self-care capacity and hypoglycemia and medicine adverse event risk profile. Gastrointestinal problems such as autonomic neuropathy and malabsorption syndromes can inhibit absorption of oral GLMs and gastrointestinal prokinetic medicines and reduce their effectiveness [28]. Gastrointestinal stasis can also delay glucose absorption, which prolongs hypoglycemia [28]. Approximately 75% of people with diabetes have gastrointestinal problems.

Most people with diabetes are prescribed a range of other medicines such as antihypertensive and lipid lowering medicines, anticoagulants for comorbidities and the benefits and risks of continuing these medicines: the doses and dose intervals need to be considered with a view to reducing polypharmacy and the medicine burden where possible and safe [35,36]. The unwanted gastrointestinal effects of nonsteroidal anti-inflammatory medicines need to be considered when the individual is anorexic or using corticosteroids [37]. **Table 1** outlines some commonly used GLMs and relevant issues to consider before prescribing.

Complementary & alternative therapies

Complementary refers to integrating complementary and alternative therapies (CAM) and conventional treatments/medicines; an alternative is used when CAM is used instead of conventional treatment/medicines [38].

People with diabetes are high CAM users [39,40]. In addition, people receiving palliative and EoL often use CAM to relieve pain, maintain comfort and quality of life and manage the spiritual aspects of dying to achieve a 'good death' [41,42]. CAM is also used to reduce restlessness, agitation and mental stress [43]. Horowitz [43] suggested people receiving palliative or EoL care often self-prescribe or are prescribed the following CAM:

- Massage, with and without essential oils;
- Music therapy including thanatology;
- Guided imagery;
- Essential oils administered in vapourizers, baths or massage;
- Acupuncture;
- Pet therapy; the book *Making Rounds with Oscar* [44] demonstrates the power of pets at the end of life;
- Meditation;
- Art therapy;
- Reflexology.

Some herbal medicines can interact with conventional medicines. If herbal medicines are used they should be monitored as part of the overall care plan [45].

Nutrition & hydration

Anorexia, cachexia and dysphagia are common in people receiving palliative care [46]. In addition people with diabetes are often deficient in essential nutrients and are often anemic, especially if they have renal disease and are on metformin, which inhibits absorption of vitamin B_{12}, thus may require supplementary nutrients including protein in the stable and unstable EoL stages [47]. When people can no longer consume adequate food and fluids orally, enteral feeds may be required to sustain energy reserves and provide essential nutrition and fluids.

However, the risks and benefits, including the risk of accelerating death, and the individual's EoL stage must be considered before enteral feeds are commenced. For example, people in the stable phase with significant hypoglycemia risk and renal disease might benefit from extra calories to minimize the hypoglycemia risk. However, enteral feeding may not benefit people with advanced disease where it is unlikely to improve nutritional or functional status,

Table 1. Commonly prescribed glucose-lowering medicine classes and some issues to consider when prescribing and monitoring glucose-lowering medicines.

Medicine class	Issues to consider
Metformin	Metformin is the most commonly used oral GLM especially in overweight people. Renal function needs to be monitored and metformin doses adjusted or the medicine ceased if renal function declines (creatinine >150 mmol/l or eGFR <30 ml/min/1.73 m^2). Metformin may also be contraindicated it the person has risk factors for lactic acidosis, distressing gastrointestinal symptoms such as nausea and flatulence and significant weight loss
Sulphonylureas	Sulphonylureas may be contraindicated if renal and/or liver disease is present and when there is a high risk of hypoglycemia
Thiazolididones	Thiazolididones are not indicated if liver and/or congestive heart failure is present. They cause edema, which can cause discomfort and uncomfortable symptoms. Pioglitazone is contraindicated in people at risk of bladder cancer and people who already have bladder cancer
Incretins	GLP-1 and DPP-4 analogs may be an alternative depending on prescribing indications in the relevant country. GLP-1 and sulphonylurea combination increases the risk of hypoglycemia. GLP-1 often cause nausea and weight loss and may be contraindicated. Both GLP-1 and DPP-4 have been associated with pancreatitis. Thus, they may not be the best choice in people with pancreatic disease and should be stopped if they cause abdominal pain
SGLT-2	There is not enough clinical experience with the SGLT-2 medicines to recommend their use in palliative care situations and they are not approved for use in many countries. They are associated with urinary tract and genital infections and polyuria
Insulin	As indicated, the majority of people with Type 2 diabetes eventually require insulin and may already be on insulin when they commence palliative care. Insulin doses are easier to adjust than oral GLMs. Initiating insulin can reduce the tablet burden and simplify the medicine regimen

GLM: Glucose-measuring medicine; SGLT-2: Sodium-glucose cotransporter-2 inhibitor.

quality of life or survival [48,32]. Risks associated with enteral feeding include, nausea, bloating and diarrhea, which compromise comfort and quality of life [48].

People who are actively dying do not experience hunger due to ketone production that accompanies starvation; although they may experience thirst, but thirst is not quenched by artificial hydration [49]. Mouth care should be provided to alleviate dry mouth [49].

Diabetogenic medicines

Some medicines affect glucose homeostasis and cause/exacerbate hyperglycemia in people with diagnosed diabetes and predispose people at risk of diabetes to corticosteroid-induced diabetes [50,51]. The degree of hyperglycemia is proportional to the dose, dose formulation, dose regimen and duration of treatment [14,36]. Short courses may not cause hyperglycemia or only have a short-term effect on the blood glucose.

Commonly prescribed diabetogenic medicines include antipsychotic medicines, thiazide diuretics and corticosteroids such as dexamethasone or prednisolone. Corticosteroids are indicated in conditions such as hematological malignancies, inflammatory diseases, chronic constructive pulmonary disease, allergies, shock and to manage symptoms in palliative care.

Screening people for diabetes risk factors before commencing corticosteroids helps identify the likelihood the individual will develop corticosteroid-induced hyperglycemia. Educating people with diabetes about the effect corticosteroids could have on their BG and an appropriate BG monitoring regimen enables treatment to be initiated early to reduce the impact of hyperglycemia on comfort, cognitive function and other symptoms. **Box 2** outlines some of the proposed mechanisms for the diabetogenic effects of corticosteroids,

In addition, corticosteroids can mask the signs and symptoms of infections, which can compound the fact that signs and symptoms of infections are often atypical in people with diabetes. The skin can become thin and fragile and prone to tears, especially in older people, which cause considerable discomfort and distress. Corticosteroids also have variable effects on bone formation and reduce calcium absorption,

> **Box 2. Some proposed mechanisms that could explain the diabetogenic effects of corticosteroids.**
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> - Enhancing hepatic gluconeogenesis by upregulating key regulatory hormones that contribute to hyperglycemia such as glucose-6-phoshatase and phosphoenolpyruvate carboxylase
> - Suppressing insulin release from the β cells
> - Inducing peripheral insulin resistance by inhibiting production of glucose transporters in adipose and skeletal muscle cells. Insulin resistance and impaired glucose tolerance can occur within 48 h of commencing corticosteroids
> - Corticosteroids appear to cause both fasting and postprandial hyperglycemia. However, a morning daily dose tends to cause hyperglycemia in the late afternoon or early evening

which increases the risk of osteoporotic fractures and pain [52]. Mental changes range from mild psychosis to significant psychiatric pathology and might be difficult to distinguish from delirium and other cognitive changes [53].

Managing corticosteroid-induced diabetes in palliative & EoL care

The aim is to balance the benefits of using corticosteroid medicines with their effects on glucose homeostasis by assessing:

- Individual susceptibility to hyperglycemia and psychological effects;

- Meal times;

- Proposed dose schedule: intermittent or continuous;

- The diabetogenic effects of individual medicines: choose the least diabetogenetic medicine and use it for the shortest time to limit the effects on glucose variability, prevent DKA and HHS and limit the care burden on the individual and their family/carer;

- When to cease the corticosteroid by slowly reducing doses and adjusting insulin and other GLM doses to prevent hypoglycemia [19,36].

Management consists of BGM, especially in the afternoon, but more frequently if insulin is prescribed and proactively adjusting insulin doses to reduce hyperglycemia. People managed using diet may require medicines when they are prescribed corticosteroids; others not on insulin may require insulin to manage fasting and/or postprandial hyperglycemia and the related symptoms. The choice of GLM depends on the person's health status, corticosteroid regimen and relevant medicine precautions and contraindications [15,35,54]. Target BG range is fasting approximately 6 mmol/l and postprandial <11 mmol/l [55].

Large doses of corticosteroid for more than 2 weeks can induce adrenal insufficiency, which dramatically reduces insulin requirements. The signs of adrenal insufficiency are similar to other palliative care symptoms: increased fatigue, weight loss, nausea and diarrhea [54].

Supporting family/carers

Family and other carers must be informed about and in some cases involved in developing a care plan for the person with diabetes. Some family/carers may require education about diabetes self-care tasks such as BG monitoring and administering insulin to enable them to support the person with diabetes [17]. The stress of witnessing a loved one suffer can be significant, thus it is essential to consider carers' health status and wellbeing, including after their loved one dies [56]. Significantly, the severity of the individual's distress is the strongest predictor of EoL family/carer distress [57]. Men are less likely to report caregiver strain than women and use fewer words to describe their stain and distress. Significantly, caring is associated with increased risk of myocardial infarction in the months after a loved one dies [58].

Consequently, HPs need to watch for signs of stress and use appropriate probing questions. In addition, the Caregiver Strain Index [59] might be useful to monitor family/carer strain. HPs can involve family/carers in palliative and EoL care; for example helping with feeds, providing CAM and other treatment, and scheduling rounds to coincide with family/carer visits if possible. The caregiver Strain Index is used in a variety of different disease states and in different countries to screen for carer strain in long-term caring relationships and can be used with carers of any age. The Carer Strain Index has good internal validity: alphas range from 0.86–0.91 and test-retest reliability coefficient is 0.88 [59]. A positive response (seven or more items scoring positive) indicates the need to undertake in-depth assessment and follow-up.

Withdrawing treatment

Ethical issues are associated with decisions about withdrawing treatment, even at the end of life [60]. Such decisions are more difficult when people's desired EoL care, including withdrawing or not instigating treatment, is not documented. Health professionals have a responsibility to discuss such issues with people with diabetes and their family members and inform them that they have the right to stop treatment when it is no longer beneficial and when it becomes burdensome [24]. However, health professionals should ask the person with diabetes which aspects of care they regard as burdensome and no longer useful. Savage *et al.* [17] found people with diabetes want blood glucose testing and GLM medicines continued until the terminal stage because testing is a familiar routine in a changing world and GLMs contribute to comfort by preventing hyperglycemia. Proactively discussing EoL care with people with diabetes and their families in the stable stage and clearly documenting and communicating the information to the care team is essential to effective EoL care. However, decisions people make when they are relatively well may change at a later date, consequently the EoL plan should be reassessed, for example during the annual health check and during periods of unstable disease.

The deteriorating and terminal phases are often key decision points for withdrawing treatment. Most people with diabetes do not want unnecessary treatment continued in the terminal phase but they want to be comfortable and die with dignity [17,61–62].

Knowing the prognosis helps HPs, people with diabetes and their carers make decisions about withdraw treatment. It is difficult to predict prognosis, however The Gold Standard Prognostic Indicator [19] and the EoL stages [20] can be helpful. Factors that suggest the individual has a short prognosis include:

- Presence of multiple comorbidities;

- Weight loss >10% in a short period of time;

- 'Failure to thrive' and/or general decline;

- Serum albumin <25 g/l;

- Declining performance such as a Karnofsky Performance Status scale <50% [63];

- Needing significant help to perform usual activities of daily living and diabetes self-care tasks;

- Will to live. The will to live is a strong predictor of survival in older people regardless of their age, gender and comorbidities [64]. Social factors such as satisfaction, support from family, friends and HPs are important to the will to live.

GLMs should be stopped when risks outweigh the benefits: that is, they cause frequent, severe hypoglycemia, and other associated risks such as falls, especially in the deteriorating and terminal phases. However, the discomfort and risks associated with hyperglycemia need to be considered in light of the likely prognosis. Significantly, some CAM is effective nonmedicine options [38,42].

Diabetes education

Education and support, including bereavement support is essential for individuals with diabetes, their families and often health professional carers. Sensitive discussion about the need to adjust medicines and other changes to established self-management routines is essential. In addition, diabetes specialists are in an ideal position to take opportunities during consultations to begin discussing palliative care and other end-of-life issues, for example during annual complication screening programs and when a life-threatening complication such as a myocardial infarction occurs.

However, there is limited evidence about how often such discussion actually occurs or what factors facilitate or inhibit such discussion. Many health professionals are not comfortable discussing emotive issues such as death and/or do not want to distress patients by raising such issues. The current focus on respecting patient choices initiatives, which include planning EoL care and the recent publication of the Diabetes UK [14] and Dunning *et al.*'s [15] EoL guidelines may lead to change in the future.

Spiritual needs

It is essential that care plans encompass spiritual needs and make provision to assist the individual and their families find meaning and purpose in EoL and the individual has a peaceful, dignified death. It is essential that health professionals realize that personal growth can occur up to the moment of death and that spirituality does not necessarily involve religion [65,66]. However, religious and cultural care of the body after death should be known and in some cases documented in the care plan.

Conclusion

Key EOL care points were presented at the beginning of the paper and highlight significant issues in EoL care for people with diabetes. Essentially, EoL care should be individualized, holistic, and adopt early detection, and risk assessment and risk minimization strategies to support comfort and quality of life relevant to the EoL stage and life expectancy. That is, appropriate care will differ among the EoL stages, stable, unstable, deteriorating and terminal, depending on the health status and needs and wishes of the individual concerned. The individual and their family carers should be involved in care decisions whenever possible, including plans to withdraw treatment, which must be clearly documented. Where possible, people with diabetes should be encouraged to document their EoL wishes and complete appropriate documentation when they are well enough to make such decisions.

Future perspective

Diabetes UK [14] and Dunning et al.'s [15] innovative guidelines have paved the way for more clinical research in the area. For example, health professionals could evaluate the impact of the recommendations in the Guidelines in other palliative care settings. Strategies to help diabetes health professionals understand the need to discuss EoL care and to document and monitor people's EoL need to be developed. Collaborative endeavours with other specialty areas such as renal and cardiac specialities could result in a consistent approach to EoL care and reduce the number of guidelines that health professionals need to consider and ensure guidelines are incorporated into relevant policies and procedures. Future guideline developers could consider using Dunning et al.'s [16,23] guideline development method that blended evidence, consensus, patient experience and engaged stakeholders throughout the development process when developing guidelines where there is little available evidence. In the future it would be useful to determine the utility of EoL clinical guidelines in practice and how they are used to add to the body of evidence concerning palliative and EoL care and to inform future guidelines development or revision of current guidelines.

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