

Tailor treatment in the older patient with type 2 diabetes

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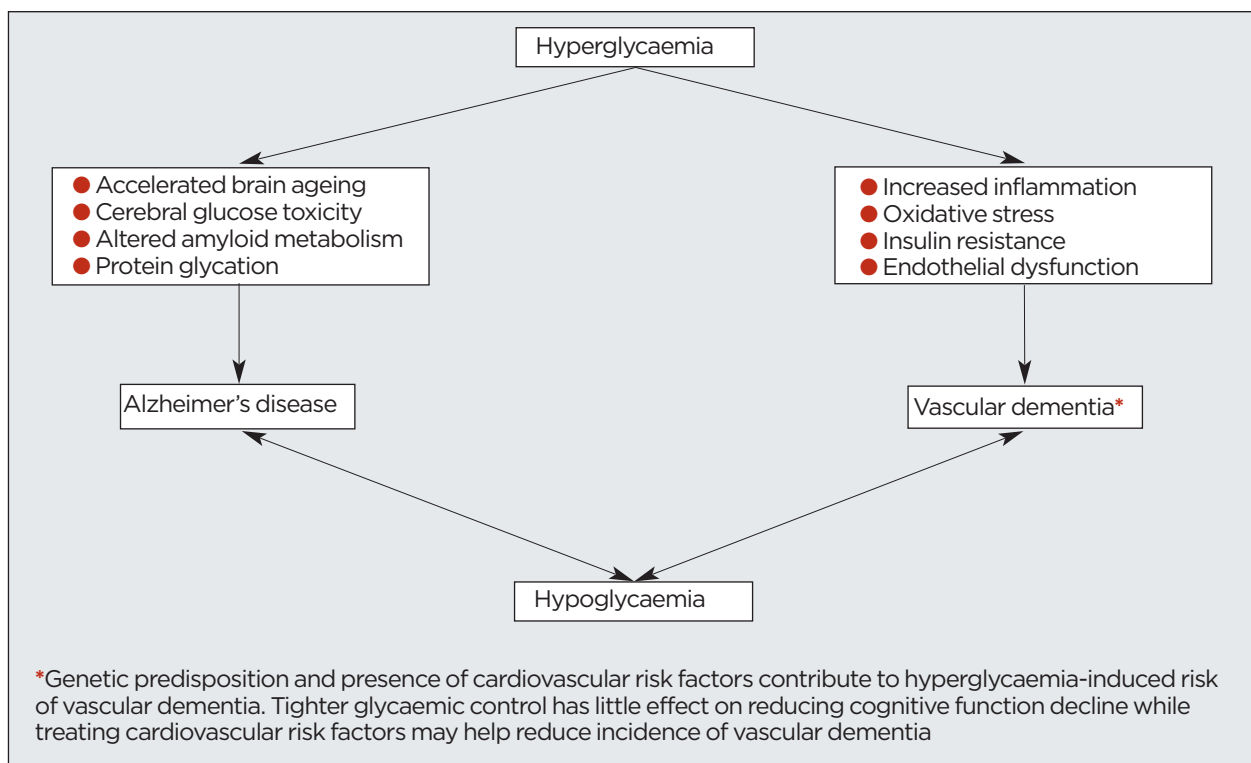
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FIGURE 1

Relationship of hyperglycaemia and hypoglycaemia with the development of dementia in older people with diabetes



How do older patients with diabetes present?



IN OLDER PEOPLE, DIABETES IS A DISABLING DISEASE DUE TO THE ASSOCIATED VASCULAR COMPLICATIONS,

multiple comorbidities and the increased prevalence of geriatric syndromes. Because of the complexity of diabetes in old age a comprehensive assessment is important at initial diagnosis, with the aim of preventing loss of autonomy and preserving independence.

CLINICAL PRESENTATION

Around 50% of older people with diabetes are asymptomatic.¹ When symptoms are present they are often nonspecific, patients may feel generally unwell, tired or lethargic. Symptoms may be atypical such as anorexia rather than the typical polyphagia. Classic

What are the common complications?

osmotic symptoms are usually less prominent in older age because of an increased renal threshold for glucose, resulting in reduced polyuria, and impairment of thirst sensation, resulting in reduced polydipsia. Diabetes complications such as nonketotic hyperosmolar coma may be the presenting symptom or diabetes may be first diagnosed during an acute illness or routine screening.

DIAGNOSIS

Diabetes should be diagnosed if fasting plasma glucose is ≥ 7 mmol/L or two hour postprandial glucose ≥ 11.1 mmol/L.²

Normal glycaemia is defined as fasting plasma glucose < 6.1 mmol/L or two hour postprandial glucose

What are the goals of treatment?

< 7.8 mmol/L. Therefore, there are two categories between normal glycaemia and diabetes:

- Impaired fasting glycaemia when plasma fasting glucose is ≥ 6.1 but < 7 mmol/L
- Impaired glucose tolerance when two hour postprandial glucose is ≥ 7.8 but < 11.1 mmol/L

Patients in these two categories are at high risk of developing diabetes and vascular complications.³ HbA_{1c} can be used as a diagnostic test with a cut-off ≥ 48 mmol/mol (6.5%) for a diagnosis of diabetes. The advantages of testing for HbA_{1c} are: convenience to patients, less day to day variability, and international standardisation. However, HbA_{1c} has high specificity (98.7%) for diagnosing diabetes but low sensitivity (46.8%) which means

SYMPOSIUM CARE OF THE ELDERLY

DIABETES

that more than 50% of individuals with diabetes may be missed.⁴

ASSESSMENT

In addition to traditional micro- and macrovascular complications seen in younger people, older people with diabetes are at risk of developing atypical complications or geriatric syndromes such as cognitive dysfunction, depression, disability, falls, persistent pain and urinary incontinence. Therefore, older people with diabetes should have a comprehensive assessment on diagnosis, see table 1, right.

MANAGEMENT

Lifestyle modification and drug therapy

Adopting a healthy lifestyle, such as weight reduction in overweight patients, regular exercise and smoking cessation, is beneficial across all age groups.

However, special considerations should be undertaken when making decisions about drug therapy in older people with diabetes, see table 2, below.

Glycaemic targets

These should be individualised taking into consideration the patient's overall health and life expectancy. Both hyperglycaemia, which causes dehydration, visual impairment,

infections and lethargy, and hypoglycaemia, which causes confusion and falls, need to be avoided. It is important to remember

that older people may tolerate higher levels of blood glucose before they develop osmotic symptoms because of a higher renal threshold for glucose

Table 1

Comprehensive assessment to optimise care for older patients with diabetes

A Screening for microvascular complications

- **Retinopathy:** Cataracts, glaucoma and macular degeneration are common in older people with diabetes in addition to diabetic retinopathy. Preservation of vision could prevent social isolation, reduce incidence of falls and maintain independence particularly for self-medication with insulin
- **Nephropathy:** Renal insufficiency is common in older people with diabetes. Therefore, renal function monitoring is essential for adjustment of medications as well as screening for microalbuminuria, considering the use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers, as appropriate
- **Neuropathy:** Prevalence of diabetic peripheral neuropathy increases with age. Regular foot examination is essential as many older people may not be able to care for their feet because of disability

B Screening for cardiovascular risk factors

Cardiovascular disease remains the most common cause of mortality in older people with diabetes. Therefore, screening and management of cardiovascular risk factors is important. Lifestyle modification with weight reduction, regular exercise and smoking cessation is recommended. Achieving blood pressure and blood glucose control is essential along with treatment of dyslipidaemia and the use of antiplatelet drugs as secondary prevention

C Screening for geriatric syndromes

- Cognitive function
- Depression
- Physical function including mobility, gait, balance and activities of daily living
- Nutritional status including oral health, hydration and swallowing
- Comorbidity burden
- Medication review to reduce polypharmacy
- Assessment of neuropathic and non-neuropathic pain
- Urinary incontinence
- Social status

Table 2

Hypoglycaemic medications in older people with diabetes

Medication	Advantage	Disadvantage
Metformin	First-line therapy, less risk of hypoglycaemia, weight neutral	Conditions that increase risk of lactic acidosis are common in older people e.g. renal impairment, heart failure, dehydration and acute illness. So metformin therapy should be carefully monitored
Sulfonylureas	First-line, if metformin is not tolerated, or add-on therapy	Increased risk of hypoglycaemia and weight gain. Long-acting sulfonylureas e.g. chlorpropamide should not be used in older people
Pioglitazone	First-line or add-on therapy, less risk of hypoglycaemia, can be used in patients with renal impairment	Fluid retention, not suitable in patients with heart failure and volume overload. Increases risk of fractures and possibly bladder cancer
Meglitinides	Short-acting insulin secretors, suitable for patients with irregular eating patterns	Risk of hypoglycaemia and weight gain but less than that with sulfonylureas
Alpha-glucosidase inhibitors	Low risk of hypoglycaemia	Less effective, gastrointestinal side effects e.g. flatulence and diarrhoea
DPP-IV inhibitors*	Weight neutral, low risk of hypoglycaemia	Dose needs to be adjusted with renal impairment
GLP-1 mimetics**	Weight loss in obese patients, low risk of hypoglycaemia	Injectable, weight loss in frail patients, not suitable in renal impairment, nausea is common and possible risk of pancreatitis
Insulin	Suitable when drug therapy fails. Long-acting insulin analogues are easy to use with lower risk of hypoglycaemia	Injectable, weight gain, high hypoglycaemia risk, needs close blood glucose monitoring

*DPP-IV= dipeptidyl peptidase IV, ** GLP-1= glucagon like peptide-1

Table 3**Common symptoms of hypoglycaemia in the elderly**^{9,10}

- Visual disturbances
- Slurring of speech
- Pallor
- Falls
- Drowsiness
- Poor coordination
- Seizures
- Confusion
- Coma
- Tiredness
- Sweating
- Dizziness
- Trembling
- Weakness
- Faintness
- Inappropriate behaviour

with increasing age. On the other hand, they may appear to tolerate lower levels of blood glucose because of diminished autonomic symptoms of hypoglycaemia with increasing age. Targets are day to day or long term:

Day to day: A comfortable daily target of random blood glucose > 4 but < 15 mmol/L seems suitable to avoid development of symptoms as blood glucose outside this range is likely to be symptomatic and results in cognitive changes.⁵ Maintaining blood glucose in this 'comfort zone' especially in frail patients may ensure 'comfort care' avoiding extreme blood glucose levels to maintain mental function and general wellbeing.⁶

'Older people with diabetes have been found to be twice as likely to develop Alzheimer's disease or vascular dementia'

Long term: Long-term targets are based on HbA_{1c} levels which should be around 53 mmol/mol (7%) for the fit elderly in the community with new onset diabetes, similar to that for younger patients.

However, for older people with established cardiovascular disease and long-standing diabetes a safer

Table 4**Risk factors for hypoglycaemia**^{9,11,12}

- Older age
- Insulin or sulfonylurea use
- Recent hospitalisation
- Hypoglycaemia unawareness
- Chronic renal or hepatic dysfunction
- Acute illness
- Multiple medications (≥ 5)
- Dementia
- Social isolation
- History of hypoglycaemia
- Multiple comorbidities
- Malnutrition
- Blunted counter-regulatory responses
- Heart failure
- Depression
- Stroke or transient ischaemic attack

target around 58 mmol/mol (7.5%) is appropriate. In frail older people with multiple comorbidities a target around 64 mmol/mol (8%) is suitable. Targets could be even higher for more frail elderly patients especially those in nursing homes with a very short life expectancy where day to day glucose levels are more important than the long term HbA_{1c} value to avoid symptoms and preserve quality of life.⁷

Special considerations in older people

Reducing hypoglycaemia: The increased risk of hypoglycaemia in older people with diabetes is not only related to tight glycaemic control but also to overall health and associated multiple comorbidities.⁸

Older patients are at an increased risk of hypoglycaemia even at a comparable level of glycaemic control to younger patients. The use of sulfonylureas, stroke, transient ischaemic attack, heart failure and depression have been shown to predict an increased risk for hypoglycaemia in older people.⁹ Recognising symptoms and risk factors for hypoglycaemia is important, see tables 3 and 4, above.¹⁰⁻¹³

Medications should be reviewed, and patients taking longer acting sulfonylureas switched to shorter acting agents. In insulin-treated patients the new class of long-acting insulin analogues may be a good option as they reduce the risk of hypoglycaemia.

Patients who have erratic eating patterns and unpredictable caloric intake could be managed with a regimen where short-acting insulin

analogues are administered only after meals, thus preventing insulin-induced hypoglycaemia if a meal is missed or only partly consumed.

Dementia: Older people with diabetes have been found to be twice as likely to develop Alzheimer's disease or vascular dementia as age-matched controls without diabetes.¹⁴

Persistent hyperglycaemia may play a part in increasing cerebrovascular disease by inducing inflammation, endothelial dysfunction, oxidative stress and insulin resistance. These cerebrovascular changes may explain the increased incidence of vascular dementia.¹⁵

'Cognitive dysfunction increases risk of hypoglycaemia and a history of severe hypoglycaemia increases risk of cognitive dysfunction'

Accelerated brain ageing due to insulin dysregulation, altered amyloid metabolism, protein glycation and direct cerebral glucose toxicity may explain the increased incidence of Alzheimer's disease.¹⁶

Hypoglycaemia, on the other hand, is related to cognitive dysfunction in a mutual way. Cognitive dysfunction increases risk of hypoglycaemia¹⁷ and a history of severe hypoglycaemia increases risk of cognitive dysfunction,¹⁸ see figure 1, p21.

Structural changes in the brain have been noted to be associated with diabetes. Cerebral atrophy and lacunar infarctions are reported more frequently in older people with diabetes and contribute to cognitive dysfunction. Hippocampal atrophy has also been observed and correlated with impairment in immediate memory. The hippocampus is susceptible to acute metabolic changes suggesting that it might be susceptible to diabetes-related metabolic complications such as hypoglycaemia.¹⁹

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key points

SELECTED BY

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Around 50% of older people with diabetes are asymptomatic.

When symptoms are present they are often nonspecific, patients may feel generally unwell, tired or lethargic. Classic osmotic symptoms are usually less prominent in older age because of an increased renal threshold for glucose, resulting in reduced polyuria, and impairment of thirst sensation, resulting in reduced polydipsia. Because of the complexity of diabetes in old age a comprehensive assessment is important at initial diagnosis, with the aim of preventing loss of autonomy and preserving independence.

Diabetes should be diagnosed if fasting plasma glucose is ≥ 7 mmol/L or two hour postprandial glucose ≥ 11.1 mmol/L.

In addition to traditional micro- and macrovascular complications seen in younger people, older people with diabetes are at risk of developing atypical complications or geriatric syndromes such as cognitive dysfunction, depression, disability, falls, persistent pain and urinary incontinence.

Glycaemic targets should be individualised taking into

consideration the patient's overall health and life expectancy. Older people may tolerate higher levels of blood glucose before they develop osmotic symptoms because of a higher renal threshold for glucose with increasing age. On the other hand, they may appear to tolerate lower levels of blood glucose because of diminished autonomic symptoms of hypoglycaemia.

HbA_{1c} levels should be around 53 mmol/mol (7%) for

the fit elderly, in the community with new onset diabetes. However, for older people with established cardiovascular disease and long-standing diabetes a safer target around 58 mmol/mol (7.5%) is appropriate. In frail older people with multiple comorbidities a target around 64 mmol/mol (8%) is suitable. Targets could be even higher for more frail elderly patients.

Elderly patients are at an increased risk of hypoglycaemia

even at a comparable level of glycaemic control to younger patients. Patients taking longer acting sulfonylureas should be switched to shorter acting agents. In insulin-treated patients long-acting insulin analogues may be a good option as they reduce the risk of hypoglycaemia.

Older people with diabetes are twice as likely to develop

Alzheimer's disease or vascular dementia as age-matched controls without diabetes. Persistent hyperglycaemia may play a part in increasing cerebrovascular disease by inducing inflammation, endothelial dysfunction, oxidative stress and insulin resistance. These cerebrovascular changes may explain the increased incidence of vascular dementia. Accelerated brain ageing due to insulin dysregulation, altered amyloid metabolism, protein glycation and direct cerebral glucose toxicity may explain the increased incidence of Alzheimer's type dementia.

Table 5

Screening and referral for cognitive dysfunction in older patients with diabetes

A Screening

- Screening for cognitive dysfunction should be part of the annual review or carried out sooner if patients show signs of noncompliance with medication, diet or frequent hypoglycaemia
- Screening and treating cardiovascular risk factors may reduce cerebrovascular disease and risk of cognitive dysfunction
- The time frame of benefit for blood pressure and lipid lowering is short (around 1-2 years) unlike that of blood glucose control which is longer (around 10 years). Therefore, patients with limited life expectancy (< 5 years) may still benefit from blood pressure and lipid lowering to reduce cognitive decline when the benefit from tight glycaemic control is limited

B Referral

- Mild cognitive dysfunction can mostly be managed in primary care
- Referral to a psychogeriatrician should be considered if the patient has a low score on mental function assessment (e.g. ≤ 7 in abbreviated mental test)
- Referral should also be considered if patients develop significant difficulties in activities of daily living or performing tasks necessary to maintain their diabetes management because of a decline in cognitive function

Although there is an association between hyperglycaemia and cognitive dysfunction, it has been shown that intensive glycaemic control is not able to prevent a decline in mental function.²⁰

In a community-based study of 1,398 older patients with diabetes, mean (SD) age 70 (7.4) years, adherence to diabetes self-care tasks (taking diabetes medication, performing regular exercise, following a recommended eating plan, undertaking blood glucose monitoring and foot inspection) decreased as cognitive impairment increased. Specific self-care tasks of exercise and diet adherence were the most strongly associated with cognitive impairment.²¹

The findings of this study may alert clinicians to the importance of screening for cognitive dysfunction if noncompliance with self-care tasks is observed, see table 5, above.

Care home residents: Around one in four residents in care homes has diabetes. Comorbidity burden is high in this population especially with regard to continence, feeding, mobility and communication. In one study, patients had a mean of four comorbidities (range 1-8) in addition to diabetes.²² Therefore, diabetes management in these settings should take into account patients' frail condition and complex needs.

Quality of life should be maintained without subjecting residents to unnecessary therapeutic interventions. Tight glycaemic control including

dietary restriction, frequent blood testing, insulin injections and polypharmacy may be a burden leading to additional complications. For example, dietary restriction may cause weight loss, frequent finger pricks and insulin injections may lead to agitation especially in cognitively impaired patients and polypharmacy may increase risk of falls.

Hydration should be maintained because of impaired thirst sensation particularly in patients with dementia to avoid risk of volume depletion and hyperglycaemic crises.

Individualised vs disease oriented models of care: The individualised care model covers a holistic approach to address the complex needs of the individual rather than focusing on a single disease. The health status of older people with diabetes is too heterogeneous to develop a single intervention strategy to fit all. Therefore, educational programmes should be adapted to patients' abilities. Each individual should have their own care plan — taking into consideration their wishes and preferences, functional status and life expectancy — putting quality of life at the heart of therapeutic goals.

CONCLUSION

Older patients with diabetes are a heterogeneous group with varying health status. The management of diabetes in older people poses unique challenges. The increased prevalence of comorbidities associated with

ageing combined with the increased prevalence of geriatric syndromes contributes to the complexity of managing diabetes in older people.

'Each individual should have their own care plan putting quality of life at the heart of therapeutic goals'

The diagnosis of diabetes in older people also presents challenges as symptoms may be less prominent or atypical in old age. When diabetes is first diagnosed older patients should have a comprehensive assessment to screen for microvascular complications, screen and treat cardiovascular risk factors and screen for geriatric syndromes. Clinicians should adopt an individualised rather than a disease-orientated approach to care focused on maintaining and improving quality of life.

Cognitive and physical dysfunction are common in older people with diabetes which may affect health outcomes and quality of life. Individual therapeutic targets should take into consideration functional status, life expectancy and patient preferences.

REFERENCES

- 1 Meneilly GS, Tessier D. Diabetes in the elderly. In: Morley JE, van den Berg L. Eds. Contemporary Endocrinology, Endocrinology of Aging. Humana Press. Totowa, NJ. 2000
- 2 American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 2002;25(suppl 1):S5-S20
- 3 Barzilay JL, Spiekerman CF, Wahl PW et al. Cardiovascular disease in older adults with glucose disorders: comparison of American Diabetes Association criteria for diabetes mellitus with WHO criteria. *Lancet* 1999;354:622-5
- 4 Peter A, Fritsche A, Stefan N et al. Diagnostic value of hemoglobin A1c for type 2 diabetes mellitus in a population at risk. *Exp Clin Endocrinol Diabetes* 2011;119:234-7
- 5 Cox DJ, Kovatchev BP, Gonder-Frederick LA et al. Relationships between hyperglycemia and cognitive performance among adults with type 1 and type 2 diabetes. *Diabetes Care* 2005;28:71-7
- 6 Lee SJ, Eng C. Goals of glycemic control in frail older patients with diabetes. *JAMA* 2011; 305:1350-1
- 7 Sinclair AJ, Paolisso G, Castro M et al. European Diabetes Working Party for Older People 2011 Clinical Guidelines for Type 2 Diabetes Mellitus. (EDWPOP). *Diabetes Metab* 2011; 37:S27-S38
- 8 Abdelhafiz AH, Sinclair AJ. Hypoglycemia in residential care homes. *Br J Gen Pract* 2009; 59:49-50
- 9 Bramlage P, Gitt AK, Binz C et al. Oral antidiabetic treatment in type-2 diabetes in the elderly: balancing the need for glucose control and the risk of

hypoglycaemia. *Cardiovasc Diabetol* 2012; 11: 122. doi:10.1186/1475-2840-11-122

10 Childs BP, Clark NG, Cox DJ et al. Defining and reporting hypoglycaemia in diabetes: A report from the American Diabetes Association Workgroup on Hypoglycaemia. *Diabetes Care* 2005;28:1245-50

11 Jaap AJ, Jones GC, McCrimmon RJ et al. Perceived symptoms of hypoglycaemia in elderly type 2 diabetic patients treated with insulin. *Diabet Med* 1998;15:398-401

12 Chelliah A, Burge MR. Hypoglycaemia in elderly patients with diabetes mellitus: causes and strategies for prevention. *Drugs & Aging* 2004;21:511-30

13 Bruce DG, Davis WA, Casey GP et al. Severe hypoglycaemia and cognitive impairment in older patients with diabetes: the Fremantle Diabetes Study. *Diabetologia* 2009;52:1808-15

14 Lu FP, Lin KP, Kuo HK. Diabetes and the risk of multi-system aging phenotypes: a systematic review and meta-analysis. *PLoS ONE* 2009; 4: e4144. doi:10.1371/journal.pone.0004144

15 Middleton LE, Affe K. Promising strategies for the prevention of dementia. *Arch Neurol* 2009;66:1210-5

16 Biessels GJ, Staekenborg S, Brunner E et al. Risk of dementia in diabetes mellitus: A systematic review. *Lancet Neurol* 2006;5:64-74

17 Punthakee Z, Miller ME, Launer LJ et al.; ACCORD Group of Investigators; ACCORD-MIND Investigators. Poor cognitive function and risk of severe hypoglycaemia in type 2 diabetes: post hoc epidemiologic analysis of the ACCORD trial. *Diabetes Care* 2012;35: 787-93

18 Whitmer RA, Karter AJ, Yaffe K et al. Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. *JAMA* 2009;301:1565-72

19 McCrimmon RJ, Ryan CM, Frier BM. Diabetes and cognitive dysfunction. *Lancet* 2012; 379:2291-9

20 Launer LJ, Miller ME, Williamson JD et al. ACCORD MIND investigators. Effects of intensive glucose lowering on brain structure and function in people with type 2 diabetes (ACCORD MIND): a randomised open-label substudy. *Lancet Neurol* 2011;10:969-77

21 Feil DG, Zhu CW, Sultzer DL. The relationship between cognitive impairment and diabetes self-management in a population-based community sample of older adults with type 2 diabetes. *J Behav Med* 2012;35:190-9

22 Gadsby R, Barker P, Sinclair A. People living with diabetes resident in nursing homes: assessing levels of disability and nursing needs. *Diabet Med* 2011; 28:778-80

Useful information

Diabetes UK

For healthcare professionals
Good Clinical Practice Guidelines for Care Home Residents with Diabetes available on the website

For patients

The charity also provides information and advice for patients and carers

www.diabetes.org.uk

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