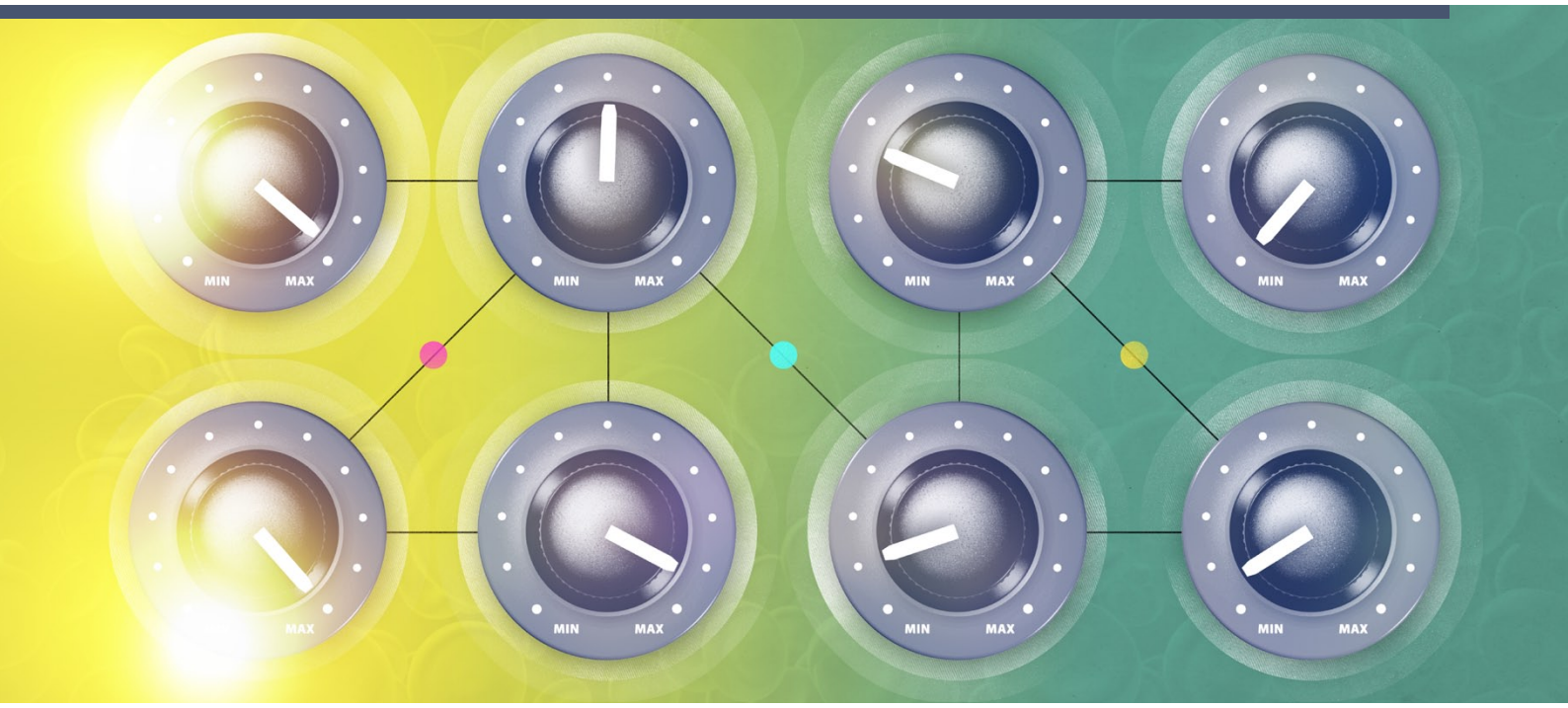


Dialling back treatment intensity for older people with type 2 diabetes

Type 2 diabetes management in older people can be complex due to the wide variations in co-morbidities, physical and cognitive impairment, and life expectancy. HbA_{1c} targets should be reviewed and revised as a patient's health status changes, taking into consideration their preferences and priorities for treatment. Less stringent treatment targets are appropriate when the risks of intensive management outweigh the benefits.

KEY PRACTICE POINTS:

- Diabetes management in older people should aim to maintain quality of life and minimise the risks associated with achieving stringent glycaemic targets, e.g. hypoglycaemia, while also avoiding the symptoms and adverse consequences of hyperglycaemia
- The benefits of intensive glycaemic control for the prevention of microvascular complications are less clear as a person's health status becomes more complex and their life expectancy is reduced
- Most randomised clinical trials including middle-aged and older people with longstanding type 2 diabetes have not shown any benefit of intensive glycaemic control for the prevention of CVD-related or all-cause mortality
- Less stringent HbA_{1c} targets, e.g. 58–64 mmol/mol or higher, are recommended for older people with diabetes; higher targets, e.g. 70 mmol/mol, are likely to be appropriate for those with very poor health, e.g. due to co-morbidities or frailty, those who have limited life expectancy or experience severe or recurrent hypoglycaemia
- Continue to recommend lifestyle interventions, i.e. diet and exercise, to help manage diabetes in all patients, particularly those who are overweight, but goals should be tailored to the individual's physical capabilities and fitness level

The burden of diabetes among older people in New Zealand

The prevalence of type 2 diabetes increases markedly with age. In 2017, 16% of people in New Zealand aged ≥ 65 years were estimated to have diabetes,* compared to 8% of people aged 45–64 years and 1.3% of people aged < 45 years.[1] The association of type 2 diabetes with ageing is likely due to the combined effects of lifestyle, genetics and age-related changes in physiology on pancreatic beta cell function and insulin resistance.[2]

There are significant ethnic disparities in the prevalence of diabetes among older adults in New Zealand; the highest rates are observed in Pacific peoples (50%), followed by Asian (29%), Māori (26%) and European/Other (13%).[1]

* Data are for type 1 and type 2 diabetes combined, however the significant majority (> 90%) of older people have type 2 diabetes[1]

The challenges of treating diabetes in older people

The health status of people with type 2 diabetes often becomes more complex over time and can lead to a shift in the balance between the benefits and harms of maintaining very stringent glycaemic targets, e.g. HbA_{1c} 48–53 mmol/mol or lower,

particularly in those with limited life expectancy. In addition, there are limited data available to inform evidence-based targets for older people and/or people with complex health needs as these groups are often excluded from clinical trials.

Factors such as the onset or worsening of co-morbidities, physical and cognitive impairment, frailty, age-related physiological changes, social isolation, loss of independence and depression can affect diabetes management in various ways, including:

Reducing the ability to self-manage a complex regimen: cognitive impairment and poor dexterity and/or vision may limit the ability of a patient to manage a complex medicine regimen, e.g. multiple oral glucose-lowering medicines, monitoring blood glucose levels, adjusting insulin doses, administering insulin injections.

Reducing the ability to engage in lifestyle interventions: physical disability, frailty or depression may prevent people from undertaking the recommended lifestyle interventions for weight loss, e.g. exercise, preparation of healthy meals. These physical limitations also increase vulnerability to the adverse effects of glucose-lowering medicines, e.g. falls due to hypoglycaemia.

Impairing the ability to achieve glycaemic control: co-morbidities may interfere with achieving glycaemic control, e.g. renal impairment may mean the required dose of a medicine to achieve the agreed target is contraindicated. Some medicines, e.g. corticosteroids, may worsen glycaemic control in people with diabetes. Co-morbidities may also increase the complexity of the medicine regimen resulting in poor adherence.

Increasing the risk of hypoglycaemia: age-related physiological decline in renal function can affect the clearance of sulphonylureas, insulin and metformin,* leading to increased concentrations. Age-related weight loss can affect insulin requirements, such that a previously suitable dose becomes inappropriate in an older person, particularly if they have accelerated weight loss due to frailty.

For information on diagnosing and managing frailty in primary care, see: **www.bpac.org.nz/2018/frailty.aspx**

* While metformin alone does not cause hypoglycaemia, it can worsen hypoglycaemia when used in combination with sulphonylureas or insulin

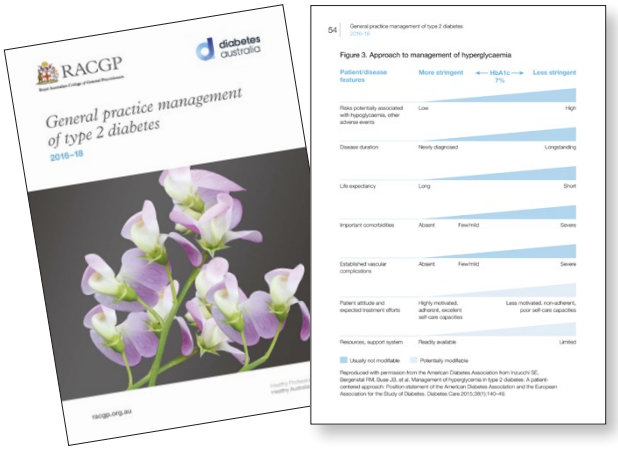
When to consider dialling back HbA_{1c} targets

Guidelines generally recommend less stringent HbA_{1c} targets for older people, however, there is some variability in the exact targets due to the lack of clinical trial data.[3–5] HbA_{1c} targets in the range of 58–64 mmol/mol, or higher, are likely to be appropriate for most older adults; the target should be individualised and focus on the risks and benefits of maintaining a particular target according to the health status of the patient rather than their chronological age.[3–5]

There will be older people with diabetes who maintain otherwise good health, e.g. have few co-morbidities and good physical and cognitive function, for whom lower treatment targets, e.g. ≤ 53–58 mmol/mol, remain appropriate.[6] Higher targets, e.g. 58–64 mmol/mol, should be considered for those with co-morbidities, mild frailty or cognitive impairment, complex medicines regimens or who at risk of hypoglycaemia.[6] For people with very poor health, such as those who have moderate to severe frailty or cognitive impairment, those in long-term residential care or who have end-stage chronic disease, treatment should aim to avoid symptomatic hyperglycaemia and HbA_{1c} targets in the region of 70 mmol/mol are appropriate.[6]

N.B. HbA_{1c} targets > 70 mmol/mol are associated with an increased risk of symptomatic hyperglycaemia, i.e. glycosuria, dehydration, hyperglycaemic hyperosmolar syndrome, candidiasis, urinary tract infections and poor wound healing.[6] Glycaemic targets should aim to avoid these outcomes.[6]

For a diagrammatic representation of patient characteristics and how they affect the selection of glycaemic targets, see: **www.racgp.org.au/FSDEDEV/media/documents/Clinical%20Resources/Guidelines/Diabetes/General-practice-management-of-type-2-diabetes_1.pdf** (Page 54)



Reviewing the benefits and risks of stringent glycaemic targets in older people with diabetes

The benefits of glycaemic control for preventing microvascular complications

The microvascular complications of diabetes, e.g. retinopathy, nephropathy and neuropathy, develop over many years; long-term glycaemic control prevents the onset and slows the progression of these complications.[6] Over time, however, the balance of benefits and harms associated with maintaining stringent glycaemic targets can change. For example, someone with limited life expectancy is unlikely to live long enough to benefit from the prevention of microvascular complications

by treating to a stringent target, however, a hypoglycaemia-related fall could accelerate their functional decline and loss of independence (see: "Intensive glycaemic control increases the risk of hypoglycaemia"). In addition, there are some clinical trial data showing that the protection against microvascular complications* for patients who have maintained stringent targets may continue even after the target is dialled back.[6]

N.B. There is no evidence that maintaining stringent targets will improve renal outcomes in people with established diabetic kidney disease.[7]

* Defined as vitreous haemorrhage, retinal photocoagulation or renal failure in the follow-up of the UKPDS trial.[8]

Further information on the renal complications of diabetes is available from: "Slowing progression of renal dysfunction in patients with diabetes", see: **www.bpac.org.nz/2019/renal.aspx**

Intensive glycaemic control is unlikely to prevent the major macrovascular complications of diabetes

The three major clinical trials* investigating the effects of intensive glycaemic control (achieved HbA_{1c} levels of 46–53 mmol/mol)† in people with longstanding type 2 diabetes (mean age of 60–66 years; mean duration of diabetes of eight to 12 years) on the risk of macrovascular complications found no benefit of intensive treatment for reducing all-cause mortality and CVD-related mortality.[6, 9] Furthermore, one of these trials, the ACCORD study, found that the risk of all-cause and CVD-related mortality was significantly higher in the intensive treatment arm (achieved HbA_{1c} levels of 46 mmol/mol); the reason for this outcome is not completely clear but may relate to hypoglycaemia triggering CVD events.[6, 9, 10] For patients with established CVD or high CVD risk, the benefits of addressing non-glycaemic factors, i.e. blood pressure control, lipid-lowering with statin treatment, aspirin for secondary prevention, and lifestyle modifications, are likely to be greater than any potential benefits of glucose-lowering with medicines currently funded in New Zealand for reducing CVD risk.[11]

* The ACCORD, ADVANCE and VADT studies; for further information on these trials, see: **www.bpac.org.nz/bpj/2010/august/HbA1c.aspx**

† The HbA_{1c} levels in the standard treatment groups ranged from 56 mmol/mol to 68 mmol/mol

Intensive glycaemic control increases the risk of hypoglycaemia

Intensive glycaemic control is associated with a significantly increased risk of hypoglycaemia.[9, 12] Age-related physiological changes make older people susceptible to hypoglycaemia and more vulnerable to the adverse outcomes associated with hypoglycaemia-related falls, e.g. fractures, head injuries, hospital admissions, need for long-term residential care.[13] Hypoglycaemia also increases the risk of cognitive decline, dementia, myocardial infarction, stroke and death.[14, 15] Fear of hypoglycaemia can cause significant anxiety (e.g. worrying about not waking up in the morning) and lead to or worsen social isolation and/or depression in older people by affecting their confidence to leave the house to engage in social activities, exercise or travel.

Hypoglycaemia in older people can manifest as non-specific neurological symptoms, e.g. confusion, dizziness, weakness, visual disturbances, rather than adrenergic symptoms, e.g. tremors, sweating. Repeated hypoglycaemic episodes can lead to hypoglycaemia unawareness, which in turn increases the risk of hypoglycaemia-related mortality.[14] Clinicians should have a low threshold of suspicion for hypoglycaemia in older patients if they or their caregivers report any possible symptoms.[16]

It is also important to ensure that patients and their family/whānau understand "sick day" management and how to adjust regimens to accommodate any missed meals or changes in activity to reduce the risk of hypoglycaemia.

Stringent HbA_{1c} targets increase the risk of polypharmacy

HbA_{1c} levels often increase over time and intensification of treatment is needed to achieve an agreed target. For many patients this means using multiple glucose-lowering medicines. If other co-morbidities are present, the risk of polypharmacy and associated adverse outcomes, e.g. poor adherence, medicine-medicine interactions, medicine-disease interactions, is increased. Selecting a less stringent HbA_{1c} target requiring fewer medicines or a simplified regimen (e.g. switching to a combined metformin + vildagliptin tablet) while still maintaining reasonable glycaemic control can help to minimise the adverse outcomes associated with polypharmacy.

Discussing regimen changes with patients and their whānau

Patients and their family/whānau or caregivers may perceive that relaxing glycaemic targets and any accompanying changes to the treatment regimen signifies the clinician "giving up" on them. Decision-making should be shared with the patient and their caregivers, family/whānau if appropriate and incorporate their preferences and priorities for treatment. Provide reassurance that any changes to the regimen are about providing the best balance of benefits and risks for them. On the contrary, some patients may think that reducing their medicines means that their condition is improving, and they no longer need to maintain a healthy diet and lifestyle, therefore it is important to effectively communicate the goals of treatment.

For further information on how to approach the conversation of stopping medicines in older people, see: **www.bpac.org.nz/2018/stopping.aspx**

Individualising glycaemic control in older people

Strategies to dial back HbA_{1c} targets

A less stringent HbA_{1c} target may be achieved by:

- De-intensifying treatment, e.g. reducing the dose or withdrawing an add-on oral glucose-lowering treatment or insulin
- Not intensifying treatment, e.g. by not adding a second or third oral glucose-lowering medicine or initiating insulin treatment when HbA_{1c} levels increase

Oral glucose-lowering medicines

Metformin remains the first-line treatment option for older people with type 2 diabetes due to its effectiveness for lowering blood glucose levels and low risk of hypoglycaemia, however, it is contraindicated in people with advanced renal impairment (creatinine clearance < 15 mL/min) and maximum doses should be lowered as renal function declines, i.e. once creatinine clearance is < 60 mL/min.[6, 17]

As sulphonylureas are associated with a greater risk of hypoglycaemia, where possible, patients at high risk of hypoglycaemia should be switched to an alternative, e.g. vildagliptin.[6] If a sulphonylurea is used, a formulation with a shorter duration of action, e.g. gliclazide or glipizide, is preferred over one with a longer duration, e.g. glibenclamide, due to the increased risk of hypoglycaemia with longer acting sulphonylureas.[6]

Stopping an oral glucose-lowering medicine or switching to another type does not usually require tapering of the medicine before it is discontinued.

Insulin

Many older people with type 2 diabetes will be using insulin to maintain glycaemic control. However, insulin is the glucose-lowering medicine most associated with hypoglycaemia and older people are particularly vulnerable to this adverse effect. In addition, older people with cognitive or physical impairment may have difficulty maintaining adherence to blood glucose monitoring and insulin injection regimens. It may be necessary to simplify the insulin regimen, e.g. switch from basal-bolus or biphasic regimen to a once daily injection of basal insulin, reduce the dose and/or switch from evening to morning dosing. It may be appropriate to withdraw insulin completely for some older people.

If continuing insulin treatment, patients (or their caregivers) should maintain once daily self-monitoring of blood glucose levels, preferably before breakfast; a higher fasting blood glucose target than usually recommended, e.g. 8–10 mmol/L, may be appropriate depending on the patient's health status.[6]

For further information on the pharmacological treatment of diabetes, see: **www.bpac.org.nz/2019/hba1c.aspx**

Individualising lifestyle modifications

Lifestyle modifications to improve cardiovascular health and glycaemic control, i.e. diet and exercise, are recommended for all people with diabetes, including older adults.[18] Clinicians should tailor the recommended modifications to reflect any changes in the patient's physical and cognitive abilities and circumstances.

Weight loss should be managed carefully in overweight older people; ensure that patients understand what constitutes a balanced diet, including adequate levels of protein to combat the loss of muscle mass and strength associated with both diabetes and frailty, even in those who are overweight.[18] Patients who require additional support can be referred to local services, e.g. cooking courses or Meals on Wheels. If the patient has more complex health needs, e.g. requires assistance with shopping, preparing meals or access to a dietitian, referral for a needs assessment may be appropriate.

Patients who are underweight or malnourished and cannot meet their nutritional needs through diet alone can be prescribed a nutritionally complete food supplement formulated for people with diabetes, e.g. Diasip, Glucerna Select and Nutrison Advanced Diason are fully subsidised with Special Authority approval (see the NZF for further information).

Nutritional status can be assessed using the following validated tools: the Mini Nutritional Assessment, available here: **www.mna-elderly.com/forms/MNA_english.pdf** and the Short Nutritional Assessment Questionnaire, available here: **www.fightmalnutrition.eu/toolkits/summary-screening-tools**

Exercise recommendations should be appropriate for the patient's level of mobility, strength and aerobic fitness. Some patients may be able to undertake moderate-intensity exercise several times per week, and for others, recommendations may need to focus on strategies to avoid sedentary behaviour.[18] Chair-based exercises can be recommended to those who have limited mobility. Ideally, all older people should do a combination of resistance-based, balance and flexibility exercises, to reduce the risk of frailty and falls.[10] Patients can be referred to falls prevention classes or in-home services, if available locally.

Examples of exercises suitable for people with limited mobility are available here: **www.diabetes.org.nz/type-2-diabetes-physical-activities**

Older people are at risk for depression, particularly if they are socially isolated and/or have limited mobility. Depression may impact upon adherence to diabetes treatment regimens and lifestyle interventions and therefore worsen glycaemic control. Depression can be identified using the Geriatric Depression Scale, a 15-part questionnaire where a score of more than ten is indicative of depression.

The Geriatric Depression Scale is available here: **www.bpac.org.nz/BPJ/2011/July/appendices.aspx**

Additional resources

- For further information on weight loss, see: **www.bpac.org.nz/2019/weight-loss.aspx**
- For further information on nutritional and exercise interventions to prevent the progression of frailty, see: **www.bpac.org.nz/2018/frailty.aspx**
- For further information on preventing falls, see: **www.bpac.org.nz/BPJ/2015/August/falls.aspx**
- The Stay independent falls prevention toolkit for clinicians, which includes assessments for estimating risk of falling, is available here: **www.hqsc.govt.nz/our-programmes/reducing-harm-from-falls/publications-and-resources/publication/2232/**
- For information on locally available falls prevention classes, see: **www.livestronger.org.nz/**
- Nutritional information for patients is available in a variety of languages is available from: **www.healthnavigator.org.nz/healthy-living/eating-drinking/n/nutrients/**
- For further information on funded services providing dietary advice or assistance with cooking, meals or grocery shopping, see: **www.govt.nz/browse/health/help-in-your-home/cooking-and-meals/**
- For further information on support services available locally for older people, see: **www.ageconcern.org.nz/ACNZPublic/Local_Age_Concerns/ACNZ_Public/AroundNZ.aspx?hkey=189abbc5-0199-4204-b7f6-582dc8804305**

Acknowledgement: Thank you to **Dr Catherine McNamara**, Consultant in Diabetes, Endocrinology and General Medicine, Waitemata DHB for expert review of this article.

N.B. Expert reviewers do not write the articles and are not responsible for the final content.

References

1. Health Quality & Safety Commission New Zealand. Atlas of healthcare variation: diabetes. 2019. Available from: https://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/diabetes/ (Accessed Mar, 2019).
2. Lee PG, Halter JB. The pathophysiology of hyperglycemia in older adults: clinical considerations. Diabetes Care 2017;40:444–52. doi:10.2337/dc16-1732
3. American Diabetes Association. 12. Older Adults: standards of medical care in diabetes – 2019. Diabetes Care 2019;42:S139–47. doi:10.2337/dc19-S012
4. Ministry of Health. Cardiovascular disease risk assessment and management for primary care. 2018. Available from: https://www.health.govt.nz/system/files/documents/publications/cardiovascular-disease-risk-assessment-management-primary-care-feb18-v4_0.pdf (Accessed April, 2019).
5. Royal Australian College of General Practitioners (RACGP). General practice management of type 2 diabetes 2016-2018. 2016. Available from: www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/management-of-type-2-diabetes (Accessed Apr, 2019).
6. American Diabetes Association. Standards of medical care in diabetes — 2019. Diabetes Care 2019;42:S61–70. doi:10.2337/dc19-S006
7. Delanaye P, Scheen AJ. Preventing and treating kidney disease in patients with type 2 diabetes. Expert Opin Pharmacother 2019;20:277–94. doi:10.1080/14656566.2018.1551362
8. Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359:1577–89. doi:10.1056/NEJMoa0806470
9. Lipska KJ, Krumholz H, Soones T, et al. Polypharmacy in the aging patient: a review of glycemic control in older adults with type 2 diabetes. JAMA 2016;315:1034. doi:10.1001/jama.2016.0299
10. Hanefeld M, Frier BM, Pistrosch F. Hypoglycemia and cardiovascular risk: is there a major link? Dia Care 2016;39:S205–9. doi:10.2337/dcS15-3014
11. Skyler JS, Bergenstal R, Bonow RO, et al. Intensive glycemic control and the prevention of cardiovascular events: implications of the ACCORD, ADVANCE, and VA Diabetes Trials: a position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association. Circulation 2009;119:351–7. doi:10.1161/CIRCULATIONAHA.108.191305
12. Miller ME, Bonds DE, Gerstein HC, et al. The effects of baseline characteristics, glycaemia treatment approach, and glycated haemoglobin concentration on the risk of severe hypoglycaemia: post hoc epidemiological analysis of the ACCORD study. BMJ 2010;340:b5444–b5444. doi:10.1136/bmj.b5444
13. Kachroo S, Kawabata H, Colilla S, et al. Association between hypoglycemia and fall-related events in type 2 diabetes mellitus: analysis of a U.S. commercial database. J Manag Care Spec Pharm 2015;21:243–53. doi:10.18553/jmcp.2015.21.3.243
14. Freeman J. Management of hypoglycemia in older adults with type 2 diabetes. Postgraduate Medicine 2019;:1–10. doi:10.1080/00325481.2019.1578590
15. Mattishent K, Loke YK. Bi-directional interaction between hypoglycaemia and cognitive impairment in elderly patients treated with glucose-lowering agents: a systematic review and meta-analysis. Diabetes, Obesity and Metabolism 2016;18:135–41. doi:10.1111/dom.12587
16. Kezerle L, Shalev L, Barski L. Treating the elderly diabetic patient: special considerations. Diabetes Metab Syndr Obes 2014;7:391–400. doi:10.2147/DMSO.S48898
17. New Zealand Formulary (NZF). NZF v83. 2019. Available from: www.nzf.org.nz (Accessed Apr, 2019).
18. LeRoith D, Biessels GJ, Braithwaite SS, et al. Treatment of diabetes in older adults: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2019;104:1520–74. doi:10.1210/jc.2019-00198

This article is available online at: **www.bpac.org.nz/2019/diabetes-elderly.aspx**