Underwriting the Applicant With Diabetes: How Important Is Glycemic Control?

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Increasingly, living insurance benefits policies (Critical Illness, Income Protection and TPD) are being offered for those with diabetes mellitus. Both type 1 and type 2 diabetes are predisposed to microvascular disease complications (retinopathy, nephropathy and neuropathy) and macrovascular disease complications (heart attack, stroke, peripheral vascular disease and gangrene).

Recent studies have addressed particularly the relationship between glycemic control (typically measured using HbA1c) and complications of type 2 diabetes mellitus. Those findings are reviewed in this article in the context of underwriting and risk management.

Classification of diabetes

Type 1 diabetes is an autoimmune disease typically presenting acutely in genetically susceptible individuals with virtually total insulin deficiency. Insulin therapy is almost universally required from the outset. The disease presents in the young (childhood to early adulthood) who have healthy arteries at onset of disease.

Type 2 diabetes, however, is typically a disease of insulin resistance (hence higher insulin levels are detectable); it also has a genetic link with a key risk factor being central obesity. The lifetime risk for a first-degree relative of a patient with type 2 diabetes is 5 to 10 times higher than that of age- and weight-matched subjects without a family history of diabetes. This disease typically does not have the classical symptoms of thirst, weight loss and polyuria (due to some preservation of insulin function albeit at a higher level) and is therefore often “picked up” on a blood test performed for other reasons, e.g., health screening. Self-monitoring of blood glucose levels should be considered in all people with type 2 diabetes. The illness occurs typically after age 40 at presentation. Because age is one of the strongest risk factors for atherosclerosis, at the time of presentation many people with type 2 diabetes already have silent but established arterial disease. It is known that disordered glycemic control is present for years before a diagnosis of diabetes is made, and many with type 2 diabetes have established microvascular disease at the time of diagnosis.
Gestational diabetes (diabetes that is first identified during pregnancy) and diabetes due to other causes — for example, genetic defects in β-cell function and genetic defects in insulin action — are not discussed in this article.

The diagnostic cutoff point for diabetes is a fasting plasma glucose level of 126 mg per decilitre (7.0 mmol per litre) or greater, or a glycated hemoglobin level of 6.5% or more; the diagnosis requires confirmation by the same or the other test. A fasting glucose level of 100 to 125 mg per decilitre (5.6 to 6.9 mmol per litre) is consistent with pre-diabetes; the range of glycated hemoglobin levels that are diagnostic of pre-diabetes is controversial, but the American Diabetes Association recommends a range of 5.7% to 6.4%.3

Diabetes in Australia
In 2012 approximately 1 million Australians were diagnosed with diabetes. It has been estimated that, in Australia, for every five diagnosed cases of diabetes, there are four undiagnosed cases. If diabetes incidence continues to rise at the current rates, up to 3 million Australians over the age of 25 years will have diabetes by 2025. For type 2 diabetes, this estimate is likely driven by rising obesity, the ageing population, dietary changes and sedentary lifestyles. Obesity is a major contributor to type 2 diabetes, with estimates showing that eliminating obesity from the population could potentially reduce the incidence of type 2 diabetes by over 40%. In children aged 0 - 14 years, Australia is ranked seventh highest in the world for prevalence and sixth highest for incidence of type 1 diabetes. The prevalence of type 1 diabetes is predicted to increase by 10% between 2008 and 2013. Data from 2010 show that only about half of the Australian population with diabetes is reaching the glycemic target of HbA1c <7% (HbA1c <53mmol/mol). Those individuals not reaching the <7% target are at higher risk of diabetic complications. The percentage of the population that reaches glycemic targets increases with age. Only around 36% of those aged <40 years meet the target in contrast to 61% of those >80 years.7

Glycated haemoglobin measurement (HbA1c) – Usefulness and limitations
The best measure of long-term glycemic control is the HbA1c, which has now been standardised internationally. Red blood cells are continuously being made by long bones and released into the blood stream. When these cells are released, they pick up glucose in the blood stream. HbA1c is a measure of glucose binding to one of the hemoglobin moieties in red blood cells. This is a reasonable measure as glucose permeates freely into red blood cells – which have minimal glucose on first entering the blood stream. Whilst this is quite a good measure of glycemic over the life of a red blood cell (120 days), in reality it best measures glycemic control over the previous 8 - 12 weeks. HbA1c is reported as a percentage or mmol/mol. According to guidelines by the National Health and Medical Research Council, glycated haemoglobin should be measured at least twice a year in people with type 2 diabetes and stable blood glucose control. More frequent testing is required in people with sub-optimal control and following changes to therapy.5

The HbA1c becomes less accurate with aberrations in red cell composition (e.g., Thalassaemia) or survival (e.g., longer survival with iron deficiency, shorter survival with those treated for B12 deficiency) and finally inaccuracies with chronic renal failure have been documented. The HbA1c will also be in the non-diabetic range (i.e. <6.5 mmol/L) with impaired fasting glucose or impaired glucose tolerance, and it is important to note that even impaired glucose metabolism (the “pre-diabetic”) have increased risk of macrovascular events. There appears to be a graded rise in cardiovascular risk with increasing degrees of glucose intolerance whilst still below the definition of overt diabetes.6

Data on nearly 400,000 people with diabetes in 2010 show that only around half of the Australian population with diabetes is reaching the glycemic target of HbA1c <7% (HbA1c <53mmol/mol). Those individuals not reaching the <7% target are at higher risk of diabetic complications. The percentage of the population that reaches glycemic targets increases with age. Only around 36% of those aged <40 years meet the target in contrast to 61% of those >80 years.7

Complications of diabetes mellitus
Serious complications can result from elevated blood glucose. These are largely preventable, and can be delayed with early and effective treatment.
Hyperglycemia impacts multiple metabolic pathways with the end result being oxidative stress and the accumulation of reactive oxygen species, which contributes to plaque formation.

Individuals with diabetes have an increased risk for atherosclerosis due both to diabetes and to the frequent presence of other vascular risk factors. Almost 29% of people with known diabetes and 16% of those with undiagnosed diabetes reported a previous cardiovascular disease (CVD) event (angina, coronary heart disease or stroke), while 11% of those with pre-diabetes reported a previous CVD event. There is also a greater than twofold increased risk of CVD mortality in those with diabetes and those with pre-diabetes, compared to those with normal blood glucose levels.8

Nerve damage (peripheral neuropathy) affects the legs and feet of approximately 13% of Australians with known diabetes and 7% of those with undiagnosed diabetes, while the prevalence of poor circulation (peripheral arterial disease) in the legs and feet is almost 14% in those with known diabetes and 7% in those with undiagnosed diabetes. Risk factors for these forms of nerve damage and poor circulation include duration of diabetes, age, blood pressure, blood glucose levels and smoking.9

A condition affecting the blood vessels at the back of the eye (diabetic retinopathy) is found in over 15% of Australians with diabetes.10

Furthermore, diabetic patients with CHD are more likely to be asymptomatic or have atypical symptoms than nondiabetic patients with CHD. At the time of diagnosis of type 2 diabetes, many patients already have one or more risk factors for macrovascular disease (hypertension, dyslipidemia, smoking) and many have evidence of overt atherosclerosis (past myocardial infarction, ischemic changes on electrocardiogram, or peripheral vascular disease).

Compared with nondiabetics, men and women with diabetes have decreased life expectancy (six to eight years less). When diabetes is listed as the underlying cause of death, coronary heart disease is listed as an associated cause in 67% of deaths, kidney-related disease in 30% of deaths and heart failure in 20% of deaths.11

Regarding kidney disease, within Australia the annual number of people with diabetes, who began dialysis or have had a kidney transplant since 1980, has risen dramatically, with almost all the rise being due to type 2 diabetes. Diabetes is now the single most common cause of end-stage kidney disease.12

Glycemic control and complications (vascular and microvascular) in type 1 diabetics

The prospective Diabetes Control and Complications Trial (DCCT) demonstrated that intensive therapy aimed at lower levels of glycemia results in decreased rates of retinopathy, nephropathy, and neuropathy in type 1 diabetes patients.13

Long-term follow up of the DCCT groups also showed a 42% decrease in any cardiovascular event, and there was a 57% reduction in serious cardiovascular events, with a mean duration of intensive treatment of 6.5 years.14

The results are supported by similar findings from a cohort study of 879 individuals with type 1 diabetes, followed for 20 years. In this study individuals in the highest quartile of A1c (≥12 percent) had increased all-cause (relative risk [RR] 2.4) and cardiovascular (RR 3.3) mortality compared with individuals in the lowest quartile (≤9.4 percent).15
The above findings provide conclusive evidence that strict glycemic control (HbA1c), if achieved before irreversible end-organ damage has occurred, reduces the incidence of microvascular disease, neurologic dysfunction, and cardiovascular disease in patients with type 1 diabetes.

Glycemic control and complications (vascular and microvascular) in type 2 diabetics

Whereas the importance of tight glycemic control for protection against microvascular and cardiovascular disease in diabetes was established in the DCCT/EDIC study for type 1 diabetes, the same has not been proven for macrovascular prevention for type 2 diabetes.

It may also be important to establish good control quickly upon diagnosis of type 2 diabetes due to the “metabolic memory effect”. Results of the post-trial monitoring phase of the United Kingdom Prospective Diabetes Study (UKPDS) showed that a sustained period of good glycemic control in newly diagnosed patients with type 2 diabetes has long lasting benefits in reducing microvascular disease.16

In addition this study demonstrated that good glycemic control reduced microvascular disease in type 2 diabetes. The overall microvascular (retinopathy, nephropathy, and possibly neuropathy) complication rate was decreased by 25% in type 2 diabetes with intensive therapy, which achieved a median HbA1c of 7.0% compared with conventional therapy with a median HbA1c of 7.9%. For every percentage point decrease in HbA1c (e.g., 9% to 8%), there was a 35% reduction in the risk of complications.17

However, unlike in type 1 diabetes, the role of good glycemic control in reducing cardiovascular (macrovascular disease) risk has not been established as clearly for type 2 diabetes. The UKPDS showed no beneficial effect of lowering blood glucose on cardiovascular complications but did demonstrate that lowering blood pressure to a mean of 144/82 mmHg significantly reduced strokes, diabetes-related deaths, heart failure, microvascular complications and visual loss.

Whilst epidemiologic analyses suggest a correlation between higher rates of cardiovascular disease (CVD) and chronic hyperglycemia,18,19 a reduction in HbA1c with intensive control has not uniformly demonstrated a reduction in heart attack and stroke risk or mortality.

The VADT20, ACCORD21 and ADVANCE22 trials were designed to study the effects of intensive versus conventional therapy on cardiovascular outcomes in subjects with long-standing diabetes (duration 8 to 12 years). None show a benefit of intensive control, and surprisingly, results from ACCORD showed a significant increase in total and CVD mortality with intensive therapy. Surprisingly, all three trials consistently show that over the time period studied (3.5 to 6 years), near-normal glycemic control (A1c 6.4% to 6.9%) did not reduce cardiovascular events in patients with longstanding diabetes.

The clinical approach for cardiovascular risk reduction in type 2 diabetes appears therefore to be multifactorial risk factor reduction (glycemic control, stopping smoking, aggressive blood pressure control, treatment of dyslipidemia). The American Diabetic Association recommends lifestyle intervention (diet, weight loss, increased physical activity) to improve the lipid profile in all patients with diabetes.23

In patients with clinical cardiovascular disease (CVD) or over age 40 years with other CVD risk factors, statin therapy should be added to lifestyle intervention regardless of baseline lipid levels. For patients without clinical CVD and under age 40 years, statin therapy can be considered in addition to lifestyle intervention if LDL cholesterol remains above 100 mg/dL (2.6 mmol/L), or in those with multiple CVD risk factors. In individuals without overt cardiovascular disease, the goal LDL is <100 mg/dL (2.6 mmol/L), whereas in patients with overt CVD, a lower LDL goal (<70 mg/dL [1.8 mmol/L]) is an option. Triglyceride levels <150 mg/dL (1.7 mmol/L) and HDL levels >40 mg/dL (1.0 mmol/L) for men and >50 mg/dL (1.3 mmol/L) for women are preferable.

Blood pressure should be at least <140/80 and in certain individuals (e.g., younger patients) even tighter control.
Regarding the HbA1c, the American Diabetic Association recommends aiming to achieve normal or near normal glycemia with an A1c goal of <7%. More stringent goals (i.e., a normal A1c, <6.5%) can be considered in individual patients. Less stringent treatment goals (e.g., <8%) may be appropriate for older patients, those with a history of severe hypoglycemia, limited life expectancies, older adults and individuals with comorbid conditions.

Most type 2 diabetics will require insulin – insulin therapy is not a marker of severity of diabetes. It is almost irrelevant what treatment the diabetic is on (even “diet controlled”); the critical question is “Is he or she reaching risk factor targets?”

Insurance underwriting
The above data is helpful in determining guidelines for offering insurance to those individuals with diabetes. Some examples may be helpful. A 60-year-old diagnosed with type 2 diabetes 12 months prior, with excellent lipid, blood pressure and HbA1c management, as evidenced by achieving the best practice guidelines/goals described above, is a much better risk and may be considered for living insurance benefits in addition to life cover. A recent diagnosis (implying less duration exposure to the complications of diabetes) and a short remaining term of living insurance cover (most trauma policies expire before age 70) are favourable rating factors.

It is critical to ensure that the traditional risk factors of BP and lipid control are ideal as they are strong influencers of heart attack and stroke in addition to the HbA1c level.

This hypothetical case is in contrast to a 45-year-old type 2 diabetic diagnosed perhaps 15 years before his application (thereby having significantly more time with an “unhealthy” inner arterial environment), with either borderline or substandard traditional risk factors, not on a statin, whose risk of an event is clearly much higher and would likely not be offered living insurance benefits. Any life cover would be offered at very substandard terms.

Health behaviour of diabetes is also critical. Lack of compliance with medications, persistent smoking, increasing weight gain over time, persistently high HbA1c, lipids or BP would all be extremely unfavourable features.

Conclusion
Cardiovascular disease, a more common cause of death in populations with diabetes than microvascular complications, is less clearly impacted by levels of hyperglycemia or the intensity of glycemic control.

Tight glycemic control appears to protect against both microvascular and cardiovascular disease in type 1 diabetes and against microvascular disease in type 2 diabetes. However, its role in reducing cardiovascular risk has not been established as clearly for type 2 diabetes.

From an underwriting perspective, especially in type 2 diabetes, blood pressure and lipid control as well as the absence of smoking are probably just as important as the HbA1c in the risk of heart attack and stroke claims.

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Endnotes
7 Michaelides, C et al. An HbA1c mapping tool helps identify where interventions and strategies for change need to be targeted. ADS 2008 poster.
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