

POSITION STATEMENT

OCTOBER 2021

Type 2 diabetes remission

About this position statement

The aim of this position statement is to provide up-to-date, practical advice and information to people with diabetes and the community about possible remission of type 2 diabetes. It is not intended to be a scientific or fully detailed report for health professionals.

Introduction

Type 2 diabetes is a condition in which the body becomes resistant to the effects of insulin and the pancreas loses the ability to produce enough insulin. Insulin helps turn glucose into energy for the body and this is essential to maintain health. The inability to process glucose is called glucose intolerance.

One measure for the diagnosis of type 2 diabetes is an HbA1c of 6.5% (48mmol/mol) or greater. HbA1c is a measure of average blood glucose levels over the past three months.

Glucose intolerance starts before type 2 diabetes develops. An estimated 2 million Australians have glucose intolerance, often called 'prediabetes'. People with prediabetes are at high risk of developing type 2 diabetes.¹

The development of type 2 diabetes (and prediabetes) is influenced by a mix of factors including genetics, age, lifestyle factors including food intake and physical activity, weight, use of some medicines, and other medical conditions. These are called risk factors. Some risk factors are modifiable, and some are not.

There is strong evidence that the risk of developing type 2 diabetes can be reduced by up to 58% in people who have prediabetes. This can be achieved through changes to diet and activity levels that result in sustained weight reduction.^{2, 3}

Diabetes Australia recommends that all adults with prediabetes should have access to health

behaviour change programs to support them to prevent type 2 diabetes from developing.

When a person is diagnosed with type 2 diabetes, the first line of treatment should always be healthy behaviour change modifications. Healthy eating (with attention to portion size and kilojoule intake) and regular physical activity are recommended for all people with diabetes. For many people, losing some weight can have a positive impact on glucose levels and other factors such as blood pressure. Even small amounts of weight loss can help.

Historically, type 2 diabetes has been understood as a progressive condition. However, several recent studies have challenged that view. We now understand that, in some cases, progression can be stopped or slowed. Progression generally follows the path of:

- 'normal' glucose tolerance **to**
- 'prediabetes' with glucose intolerance but not sufficient to be diagnosed as type 2 diabetes **to**
- type 2 diabetes.

New research has shown it is possible for some people with type 2 diabetes to reduce their average glucose level to achieve an HbA1c of under 6.5% (48mmol/mol) and sustain them at that level for a prolonged period of time (at least three months) - *without the need for glucose lowering medication*. This is referred to as type 2 diabetes '**remission**'.⁴

1 ADS-ADEA-Dietitians Australia- ESSA- PSA, A Position Statement on Screening and Management of Prediabetes in Adults in Primary Care in Australia; April 2020.
2 Knowler WC, Barret-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; 346: 393-403.
3 Uusitupa M, Lindi V, Louheranta A, et al; Finnish Diabetes Prevention Study Group. Long-term improvement in insulin sensitivity by changing lifestyles of people with impaired glucose tolerance: 4-year results from the Finnish Diabetes Prevention Study. *Diabetes* 2003; 52: 2532-2538.
4 Matthew C. Riddle, William T. Cefalu, Philip H. Evans, et al. Consensus Report: Definition and Interpretation of Remission in Type 2 Diabetes. *Diabetes Care* 2021 Oct; 44 (10): 2438 -2444.

Remission has been achieved following a period of intensive dietary change or by bariatric surgery. Remission is more likely within the first few years of diagnosis with type 2 diabetes.

People who want to pursue diabetes remission should do so in close consultation with their diabetes healthcare team, as intensive dietary and weight changes need careful management, monitoring and support.

It is important to recognise that achieving and sustaining remission may not be possible for everyone. Not everyone living with type 2 diabetes is overweight or obese.

While remission may not be possible for everyone with type 2 diabetes, for most people, reducing both weight and HbA1c offers great improvements for health and wellbeing. Indeed, there would likely be far greater health benefit for a person with type 2 diabetes who reduced their HbA1c from 10% (86 mmol/mol) to 8% (64 mmol/mol) through healthy behaviour change (not remission) than for a person who reduced their HbA1c from 6.9% (52 mmol/mol) to 6.4% (64 mmol/mol) (remission).

This position statement sets out the evidence for type 2 diabetes remission, how it is defined and potential issues for further consideration. We acknowledge the recently published statements from Diabetes UK, the American Diabetes Association and European Association for the Study of Diabetes, as well as evidence reviews.

Key points

1. Type 2 diabetes remission is defined as a sustained improvement in blood glucose where HbA1c levels remain below 6.5% (48mmol/mol) for at least 3 months in the absence of glucose-lowering medications.
2. Type 2 diabetes remission is possible through weight loss achieved following intensive dietary changes or bariatric surgery.
3. Remission is the best term to use – it does not mean that type 2 diabetes is cured or reversed. The underlying glucose intolerance may persist, an increased cardiovascular health risk may persist and, over time, glucose levels may return to levels indicating type 2 diabetes.
4. Type 2 diabetes remission, as defined in this position statement, is not realistic for everyone. Nor is it desirable for some people to stop taking certain glucose-lowering medications, as they have benefits beyond the management of blood glucose levels. It should be noted that some people may prefer to continue with medications to manage their diabetes.
5. People with type 2 diabetes who want to attempt diabetes remission need to do so in close consultation with their diabetes healthcare team, as intensive dietary and weight changes need careful management, monitoring and support.
6. Remission of type 2 diabetes is more likely in people with a shorter duration of diabetes (less than five years), a lower HbA1c when attempting remission, and those not requiring insulin therapy.
7. It is likely that less than half of all people with type 2 diabetes who attempt remission through intensive dietary changes will achieve it at one year, and only one third will sustain it over two years. It takes considerable clinical and psychosocial support.
8. People who do not achieve or sustain remission should not feel that they have 'failed'. The health benefits of weight loss and a reduction in HbA1c are significant even if remission does not occur, as these reduce the risk of developing diabetes-related complications and may lead to reducing or stopping glucose-lowering medications.
9. As there is insufficient evidence on the impact of remission on diabetes complications, everyone who is in remission should continue to receive regular diabetes monitoring at least annually and keep up their Annual Cycle of Care health care checks. This includes timely diabetes eye checks and ongoing support for self-management tailored to their needs.
10. People who achieve type 2 diabetes remission should remain registered with the National Diabetes Services Scheme so that they can access the same support and resources as those who are not in remission.

11. Bariatric surgery should be more widely available for people with type 2 diabetes who meet recommended criteria.
12. More research is needed to understand the 'real world' achievement of remission of type 2 diabetes, the different means of going into remission and maintaining it, the long-term impact of remission on complications, and remission in different population groups including children and young people with type 2 diabetes, First Nations peoples and people from culturally and linguistically diverse backgrounds.

Defining type 2 diabetes remission

Type 2 diabetes remission is defined as a HbA1c of less than 6.5% (48mmol/mol) for at least three months after stopping glucose-lowering medication.

It is important to note that remission may not be a permanent state and a person with type 2 diabetes who is in remission still requires ongoing diabetes management and regular diabetes healthcare checks as outlined in the Annual Cycle of Care.

Remission, reversal or cure? – a note on language

The language used to talk about type 2 diabetes remission is very important. The term remission has been carefully chosen over alternatives including 'cure' and 'reversal'.

Remission is a term commonly used in relation to cancer treatment. It describes a decrease in, or disappearance of, the signs and symptoms of a disease. In type 2 diabetes remission, while an elevated glucose level may no longer be present, the underlying tendency towards diabetes remains. Ongoing monitoring is required because glucose levels may increase again in people who are in remission.

Remission in type 2 diabetes is not a cure and there is not necessarily permanent reversal of the underlying cause or pathology. Remission simply means that the person has a HbA1c less than 6.5% (48mmol/mol), which they are currently achieving with intensive health behaviour changes rather than glucose-lowering medication. The challenge of managing diabetes in this way should not be underestimated.

The evidence to date shows a gradual return to increased glucose levels in many people, including after bariatric surgery. However, even when this happens, the time spent in remission is still of long-term health benefit. Some increased risk of complications such as heart attacks and stroke, eye damage and kidney failure may continue – so it is important that people with type 2 diabetes in remission maintain regular contact with their diabetes care team. This includes at least annual HbA1c checks to determine whether a person is still in remission.

How is remission achieved

For people who have overweight or obesity, remission of type 2 diabetes usually requires substantial weight loss. While any amount of weight loss is usually beneficial, people are more likely to achieve remission if they lose around 10% - 15% of their body weight. Weight loss may be achieved through intensive dietary change (e.g. very low energy diet) and other healthy behaviour modification, or bariatric surgery.

Intensive dietary changes

While several approaches to weight loss may help a person with type 2 diabetes achieve remission, there has been considerable recent focus on particular dietary interventions including very low energy and ketogenic diets. The major studies investigating intensive dietary interventions include DiRECT, DIADEM-1 and a study by technology company Virta Health (see *table below*).

Defining dietary approaches

- A very low energy diet
 - » Consuming 3,300 kJ per day or less. This is often achieved through total meal replacements (shakes, soups, or bars).
- A ketogenic diet
 - » Primarily high in fats, very low in carbohydrates, with moderate intake of proteins. The dietary macronutrients are divided into approximately 55% to 60% fat, 30% to 35% protein, and 5% to 10% carbohydrates.

Major studies investigating dietary interventions

Study	Intervention	Remission Definition	Remission at 1 year	Remission at 2 year
DiRECT Study (United Kingdom) N=306	Meal replacement (e.g. shakes) – followed by a gradual reintroduction of food before entering a weight maintenance phase.	No glucose-lowering medication HbA1c <6.5% Duration ≥ 2 months	I: 46% ⁵ C: 4%	I: 36% ⁶ C: 3%
DIADEM Study (Qatar – involving people from the Middle East and North Africa) N=147	Meal replacement (e.g. shakes) - followed by a gradual reintroduction of food before entering a weight maintenance phase.	No glucose-lowering medication HbA1c <6.5% Duration ≥ 3 months	I: 61% ⁷ C: 12%	-
Virta Health (United States) N=349	Ketogenic ('keto') diet	No glucose-lowering medication HbA1c <6.5% Duration not stated	25% (I) ⁸	17.6% (I) ⁹ 2.4% (C)

I = Intervention group; C = Control group

A recent systematic review and meta-analysis reported that rates of people achieving type 2 diabetes remission (HbA1c less than 6.5% (48mmol/mol) with no glucose-lowering medications) by following a low or very low carbohydrate diet were not higher than the rate of remission achieved by people following other dietary approaches.¹⁰

5 Lean M, Leslie W, Barnes A, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *The Lancet*, 2018; 391(10120): 541-551.

6 Ibid.

7 Taheri S, Zaghoul H, Chagoury O, et al. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-1): an open-label, parallel-group, randomised controlled trial. *Lancet Diabetes Endocrinol* 2020; 8: 477-489.

8 Hallberg S, McKenzie A, Williams P, et al. Effectiveness and safety of a novel care model for the management of type 2 diabetes at 1 year: an open-label, non-randomized, controlled study. *Diabetes Therapy*, 2018 9(2): 583-612.

9 Athinarayanan SJ, Adams RN, Hallberg SJ, et al. Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial. *Frontiers in Endocrinology*, 2019; 10: 348. doi: 10.3389/fendo/2019/00348.

10 Goldenberg J, Day A, Brinkworth G, et al. Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of published and unpublished randomized trial data. *BMJ*, 2021; 372 m4743 doi: 10.1136/bmj.m4743.

Bariatric surgery

Bariatric surgery refers to several surgical procedures designed to reduce the size of a person's stomach and the amount they need to eat to feel full. A range of studies have shown that people with type 2 diabetes have achieved remission following bariatric surgery with the median duration of remission being about eight years.¹¹

Remission from bariatric surgery occurs more often in younger people and in people recently diagnosed with type 2 diabetes.

The largest studies that have looked at the impact of bariatric surgery on type 2 diabetes remission include the Swedish Obesity Study (SOS)¹², the Longitudinal Assessment of Surgery-2 (LABS-2)¹³ and the Scandinavian Obesity Surgery Registry.¹⁴ All three studies show a significant percentage of people achieved long-term type 2 diabetes remission. In particular in the SOS study, 38% of participants were still in remission after 10 years, while in LABS-2 46% of participants were in remission after seven years.

Bariatric surgery is a significant commitment. Once the surgical procedure has been completed, it cannot be undone easily. Despite significant weight loss and improvements in physical health, research shows that emotional and mental health problems may remain.¹⁵

Diabetes Australia supports bariatric surgery as a treatment option for people with type 2 diabetes with a body mass index of at least 30, where dietary, physical activity and medical interventions for obesity or diabetes have not been successful.¹⁶ Appropriate clinical and psychological support needs to be made available.

Defining surgical procedures

- Gastric band (or lap band)
 - » A small silicon device is surgically implanted around the top portion of the stomach creating a small pouch that can only hold a small amount of food.
- Gastric sleeve
 - » Some of the stomach is removed including the part of the stomach that makes the hormone that makes you hungry.
- Roux-en-Y bypass (RYGB) or gastric bypass
 - » A pouch is created from the stomach and then connected directly to the small intestine.

11 Rubino, F, Nathan D, Eckel R, et al Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations. *Diabetes Care*, 2016; 39(6): 861-877.

12 Sjöström L, Peltonen M, Jacobson P, et al. Association of Bariatric Surgery With Long-term Remission of Type 2 Diabetes and with Microvascular and Macrovascular Complications. *JAMA*, 2014; 311(22): 2297.

13 Purnell J, Dewey E, Laferrère B, et al. Diabetes Remission Status During Seven-year Follow-up of the Longitudinal Assessment of Bariatric Surgery Study. *The Journal of Clinical Endocrinology & Metabolism*, 2021; 106(3):774-788.

14 Jans A, Näslund, I, Ottosson, J, Duration of type 2 diabetes and remission rates after bariatric surgery in Sweden 2007–2015: A registry-based cohort study. *PLOS Medicine*, 2019; 16(11): .e1002985.

15 Jumble S, Hamlet C and Meyrick J. Psychological Aspects of Bariatric Surgery as a Treatment for Obesity. *Current Obesity Reports*, 2017; 6(1): 71-78.

16 Australian Diabetes Society. (2016) The Australian Obesity Management Algorithm. Retrieved (11 October 2021) from <https://diabetessociety.com.au/documents/ObesityManagementAlgorithm18.10.2016FINAL.pdf>

Who could benefit from type 2 diabetes remission?

People with type 2 diabetes most likely to achieve remission include those who have overweight or obesity and those who have lived with type 2 diabetes for less than five years.

It is important to remember that not everyone living with type 2 diabetes has overweight or obesity.

Even if diabetes remission is not possible there may be important benefits of significant weight loss for people with longer standing type 2 diabetes.

What are the key issues with remission?

Remission offers hope

The emerging evidence for type 2 diabetes remission enables healthcare professionals to offer a greater range of approaches to managing type 2 diabetes, especially for those people with a recent diagnosis. For the person with type 2 diabetes, the possibility of remission offers the opportunity to aim for intensive weight loss to achieve remission. From a psychological perspective this offers hope, which is important, as low levels of hope are associated with depression.¹⁷ Depression is twice as common in people with type 2 diabetes compared to the general population¹⁸ and increases a person's risk for diabetes-related complications.¹⁹

However, expectations need to be realistic. It is important that people with type 2 diabetes do not experience remission as 'more hype than hope'.

Remission requires support

The changes that a person needs to make to achieve and sustain type 2 diabetes remission are considerable. These include several long-term changes to health behaviours and changes in people's relationship with food, which may significantly impact on their social behaviours and relationships.²⁰

The studies that have shown remission to be possible have ensured that participants have access to considerable medical, dietary and psychological resources. Most people with type 2 diabetes will not necessarily have access to such intensive resources.

People also often need intensive support from their families and friends. Some family and friends will be supportive, but others may resist or sabotage the person's efforts to make these changes. For some people, it will be important to seek out support from other people who are also attempting to achieve or sustain remission.

Remission is not achievable for everyone

While type 2 diabetes remission through intensive dietary change is possible for some people, the evidence shows that only around 50% of people will be able to achieve it. The best results were achieved in the DIADEM-1 study, with 61% of participants in remission after one year. However, 39% of participants were not in remission after one year. The best results over a two-year period were seen in the DiRECT study with 36% of participants in remission after two years. That is 64% of participants were not in remission after two years. These studies show that, even with the best resources, remission is not sustainable for two thirds of people who attempt it.

17 Leite A, de Medeiros AGAP, Rolim C, et al. Hope theory and its relation to depression: a systematic review. *Annals of Psychiatry and Clinical Neuroscience*, 2019; 2(2): 1014.

18 Pouwer F, Schram MT, Iversen A, et al. How 25 years of psychosocial research has contributed to a better understanding of the links between depression and diabetes. *Diabetic Medicine*, 2020; 37(3): 383-392.

19 Nouwen A, Adriaanse MC, van Dam K, et al. Longitudinal associations between depression and diabetes complications: a systematic review and meta-analysis. *Diabetic Medicine*, 2019; 36(12): 1562-1572.

20 Rehackova L, Rodrigues AM, Thom G et al. Participant experiences in the Diabetes REmission Clinical Trial (DiRECT). *Diabetic Medicine*, 2021; e14689. doi: 10.1111/dme.14689.

Intensive dietary change is not appropriate for everyone

There are several situations where intensive dietary changes could be dangerous for a person's health. These include people taking certain medications, or if they have other health issues including kidney and heart disease.

We strongly recommend that intensive dietary changes for people with type 2 diabetes need to be undertaken in consultation with a person's diabetes healthcare team.

Diabetes complications can still develop

People living with type 2 diabetes are at risk of a range of diabetes-related complications including eye damage and blindness, heart disease and stroke, foot problems and limb amputation, kidney failure, and mental health challenges including diabetes-related distress, depression and anxiety. It may seem logical to think that risk of these complications will be lower in remission. However, it is not yet known whether the risk of these complications reduces enough after remission to remove the need for regular ongoing health checks.

It is important that people who achieve type 2 diabetes remission continue the regular diabetes checks that form the Annual Cycle of Care. This includes regular HbA1c blood, kidney, diabetes eye, and blood pressure and cholesterol checks. People with type 2 diabetes should also have their diabetes status reassessed annually.²¹

Optimal diabetes management is about success, not failure

A treatment goal of remission of type 2 diabetes may be very useful and positive for some people.

However, not everyone with type 2 diabetes will be able to achieve remission. By making remission a treatment goal, those who cannot achieve remission may feel like they have failed – or they may be judged harshly by others who assume they have not tried hard enough. This may increase the mental and emotional health

burden of people living with type 2 diabetes. Research suggests that more than 80% of people living with diabetes have experienced feelings of blame and shame for living with the condition.²² Making remission a treatment goal for everyone with type 2 diabetes may add to this burden.

People who feel stigmatised, blamed or shamed for living with diabetes face more challenges with managing the condition and can have poorer long-term outcomes and a higher risk of diabetes-related complications.

Remission and type 1 diabetes

There is no evidence that people living with type 1 diabetes can achieve remission.

Children with type 2 diabetes

There is currently no evidence of remission of type 2 diabetes in children. Intensive dietary changes in children must only be done with medical supervision.

First Nations peoples and culturally and linguistically diverse communities

While the DIADEM-1 study focused on people from Middle Eastern and North African backgrounds, there is limited evidence specifically on remission among other culturally diverse communities.

21 Riddle MC, Cefalu WT, Evans PH, Consensus report: definition and interpretation of remission in type 2 diabetes. *Diabetes Care*, 2021; dci210034. doi: 10.2337/dci21-0034.

22 Speight J, Holmes-Truscott E, Scibilia R, Black T (2021). Diabetes: Stigma, blame and shame. Diabetes Australia, Canberra. Retrieved (11 Oct 2021) from: https://headsupdiabetes.com.au/wp-content/uploads/sites/4/2021/07/DIAA0039-StigmaReport_17sp_20210711.pdf

Talking to people about type 2 diabetes remission

When talking to people with type 2 diabetes about remission, it is important to be realistic. Around 50% of people with type 2 diabetes who attempt remission may not achieve it. Two thirds of people cannot sustain it at two years. Remission does not need to be the main or only goal. The benefits of sustained reduction in glucose levels and/or weight loss in people with type 2 diabetes who do not achieve remission is still very positive and has significant health benefits. People with type 2 diabetes who do not achieve remission have not 'failed', and the impact on their emotional and mental health should be considered carefully.

Communications in clinical practice, in public health and in the media need to portray remission as a worthwhile yet challenging goal. People with type 2 diabetes do not need false hope. They need to feel confident about attempting remission and be well supported to achieve it.

Importantly, communications must not stigmatise the vast majority who cannot achieve or sustain type 2 diabetes remission, or for whom it is not an appropriate therapeutic option.

Long-term outlook

There is currently little evidence about how long remission lasts, or the impact on risk of diabetes-related complications. Best estimates show one third of people are in remission at two years following intensive dietary changes, and up to half of people who have had bariatric surgery remain in remission seven to 10 years later.

The future

Diabetes Australia encourages further research to better understand the real-world implementation of programs to support remission of type 2 diabetes and intensive dietary changes. We also need research to understand which people with type 2 diabetes are most likely to achieve remission, what real-world challenges they face in attempting to achieve it, and how it impacts on their emotional well-being and quality of life. We also need research to show how people with and without type 2 diabetes perceive the term 'remission' and what it means for them. More information on the impact of remission on diabetes-related complications is important.

Diabetes Australia is currently supporting the DiRECT Australia Study in NSW, which is aiming to replicate the UK's DiRECT study in an Australian context.

Further Information

Diabetes UK Position Statement – Remission in Adults with Type 2 Diabetes

<https://www.diabetes.org.uk/professionals/position-statements-reports/statement-remission-type2>

Consensus Report: Definition and Interpretation of Remission in Type 2 Diabetes (American Diabetes Association, Endocrine Society, European Association for the Study of Diabetes and Diabetes UK)

<https://care.diabetesjournals.org/content/early/2021/08/17/dci21-0034>

DiRECT Diabetes Remission Clinical Trial

<https://www.directclinicaltrial.org.uk/>

DiRECT-Aus and Type 2 Diabetes Remission

<https://diabetesnsw.com.au/directaus/>

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The members of the Expert Advisory Group include:

- Professor Stephen Colagiuri, University of Sydney
- Professor Jonathan Shaw, Baker Heart and Diabetes Institute
- Dr Gary Deed, GP and Chair of the Royal Australian College of General Practice Specific Interests – Diabetes network
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