



Remission of Type 2 Diabetes After Total Diet Replacement: Durability, Relapse and the Conversations Nobody Schedules

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Abstract

Remission of type 2 diabetes through weight loss is now an established finding rather than a claim, and the question has moved from whether it happens to how long it lasts. In a randomised trial conducted across 49 general practices, 46 per cent of the intervention group were in remission at 12 months against 4 per cent of controls. At 24 months the figure was 36 per cent, and at five years 10 per cent of the intervention group against 5 per cent of controls. Of the 68 participants in remission at 12 months, 20 (29 per cent) had relapsed by 24 months, having regained 7.1 kg against 4.2 kg among those who did not, a difference that did not reach conventional significance. Remission tracked weight lost rather than anything else: none of the 76 participants who gained weight achieved it, against 34 per cent of the 56 who lost 5 to 10 kg. Among those offered continued support to year five, 34 per cent of recorded visits showed remission against 12 per cent without. This review sets out what the trajectory means for what patients are told at the outset.

Keywords: Type 2 diabetes; Remission; Total diet replacement; Relapse; Weight-loss maintenance

Introduction

Type 2 diabetes was long described as progressive and irreversible, and the demonstration that substantial weight loss can return glucose to a non-diabetic range without medication changed that framing [1,2,3]. Remission is now defined by consensus as an HbA1c below 48 mmol/mol sustained for at least three months after the withdrawal of glucose-lowering therapy [4].

The mechanistic account holds that type 2 diabetes in many people reflects fat accumulation in liver and pancreas beyond what the individual can tolerate, and that removing it restores beta cell function [5,6,7]. That model predicts what the trials found: remission tracks weight lost rather than the method used to lose it [2,8]. Umbrella review of dietary approaches reaches the same conclusion across very different diets [25], and intensive lifestyle programmes in other settings have produced comparable results [16,17,18].

What is less often discussed is the shape of the curve after the first year. This review examines durability, relapse and what the evidence implies for the conversation held when the intervention starts.

Material and Methods

Search strategy: PubMed and the archives of the major diabetes, endocrinology and general medical journals were searched for studies of remission of type 2 diabetes through weight loss. Search terms combined remission, total diet replacement and low-energy diet with type 2 diabetes, relapse, durability, weight regain and maintenance. Reference lists of the principal trial reports [2,9] were screened by hand for related analyses.

Eligibility: Studies were included if they reported remission rates against a defined biochemical threshold, characterised relapse, or examined predictors of either. Mechanistic studies are

cited where they explain the observed pattern and are identified as such.

Data extraction and handling: Design, setting, sample size, the remission definition used and the reported estimate were extracted as published. The time point is stated alongside every remission figure, because the headline result of this literature changes substantially between 12 months and five years. This review describes trial protocols as published and makes no dietary, caloric or exercise recommendations. No pooling or re-analysis was performed. Figures 1 to 6 and Tables 1 to 3 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

The trial: Between July 2014 and August 2017, 306 individuals were recruited from 49 general practices, 23 delivering the intervention and 26 acting as controls, with 149 participants per group in the intention-to-treat population. Participants were aged 20 to 65 years, had been diagnosed with type 2 diabetes within the previous six years, had a body mass index of 27 to 45 kg/m² and were not receiving insulin [2,9]. The intervention withdrew glucose-lowering and antihypertensive drugs at the outset, then proceeded through total diet replacement, stepped food reintroduction and structured maintenance support (Figure 5) [2,10].

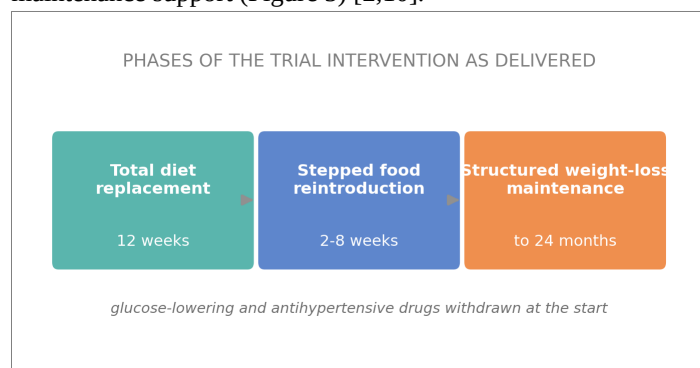


Figure 5: Phases of the trial intervention as delivered [2,10]

Twelve and twenty-four months: Remission was achieved by 68 of 149 intervention participants (46 per cent) against six controls (4 per cent). Weight loss of 15 kg or more occurred in 36 intervention participants (24 per cent) and in none of the controls ($p < 0.0001$). Mean bodyweight fell by 10.0 kg (SD 8.0) against 1.0 kg (3.7), and 74 per cent of the intervention group were taking no glucose-lowering medication at 12 months against 18 per cent of controls [2]. At 24 months remission stood at 36 per cent (Figure 1) [9].

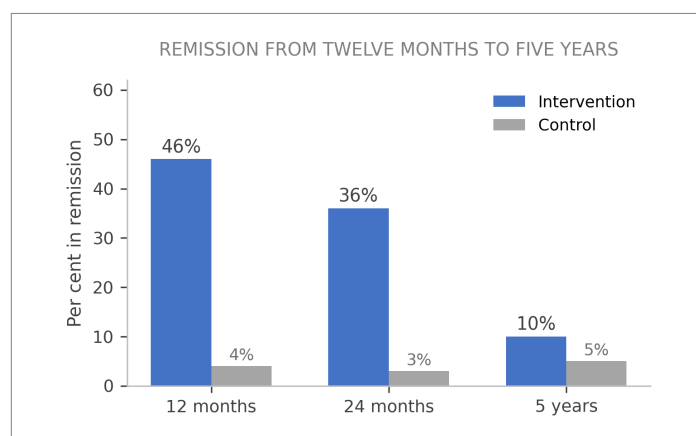


Figure 1: Remission from twelve months to five years [2,9,11]

Remission follows weight lost: Across the whole study population, remission was achieved by none of the 76 participants who gained weight, by six of 89 (7 per cent) who maintained a loss of 0 to 5 kg, and by 19 of 56 (34 per cent) who lost 5 to 10 kg (Figure 4) [2]. This gradient is the central mechanistic observation and it is why sustained weight loss, rather than any particular dietary composition, is the operative variable [5,8,31]. Bariatric surgery achieves remission by the same route and sustains it longer [19,20].

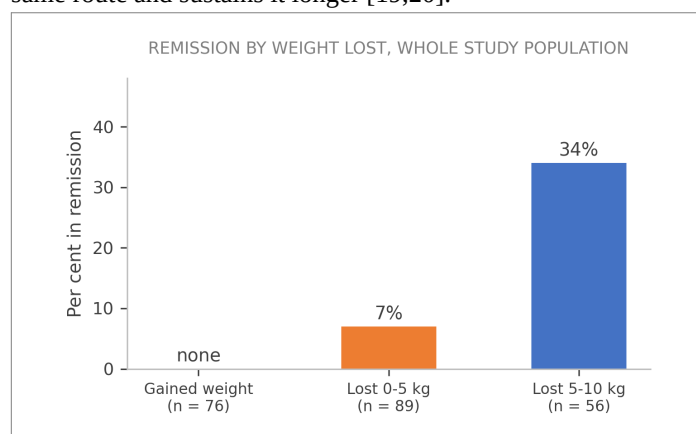


Figure 4: Remission by weight lost across the whole study population [2]

Relapse: Of the 68 participants in remission at 12 months, 20 (29 per cent) had relapsed by 24 months (Figure 2). Those who relapsed had regained a mean of 7.1 kg (SD 5.4) against 4.2 kg (SD 3.7) among those who maintained remission, a difference that did not reach conventional statistical significance ($p = 0.073$) (Figure 3) [12].

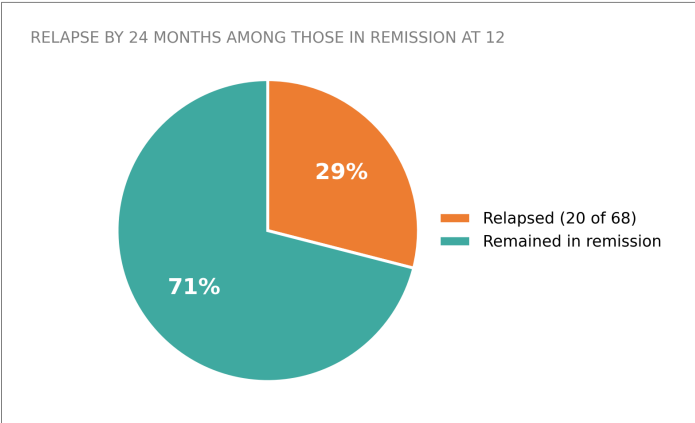


Figure 2: Relapse by 24 months among those in remission at 12 months [12]

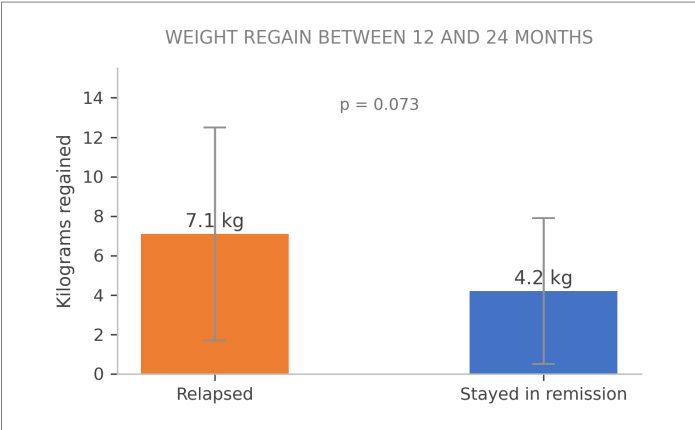


Figure 3: Weight regain between 12 and 24 months by remission status [12]

Predictors: Weight loss achieved as early as four weeks predicted remission at both 12 and 24 months, and higher programme attendance was associated with achieving it [12]. The investigators noted that attendance may be partly a consequence rather than a cause, since those regaining weight are less likely to attend and success promotes engagement. Of the 28 participants (19 per cent) who had not achieved a 6 kg loss by eight weeks, six had never started the intervention and 11 of the remaining 22 withdrew before the end of the first phase; six nonetheless went on to achieve remission, giving the eight-week threshold 89 per cent sensitivity but only 23 per cent specificity for predicting it [12].

Time point	Intervention	Control	Source
12 months	46% (68 of 149)	4% (6)	Main trial [2]
24 months	36%	3%	Two-year report [9]
5 years	10% (12 of 118)	5% (5 of 93)	Extension study [11]
5 years, continued support	13% (11 of 85)	—	Extension study [11]

Table 1: Remission over time, as reported by the original investigators

Five years: After the two-year results were shared with all participants, national health service data were collected annually to year five. Remission data were available for 118 of the

original intervention group and 93 controls: 12 of 118 (10 per cent) were in remission against five of 93 (5 per cent). Among the 85 who had continued to receive support from their general practice through years three to five, 11 (13 per cent) remained in remission [11]. Participants in the extension had more recorded visits with an HbA1c below 48 mmol/mol (36 against 17 per cent, $p = 0.0004$), more visits without glucose-lowering medication (62 against 30 per cent, $p < 0.0001$) and more visits in remission (34 against 12 per cent, $p < 0.0001$) (Figure 6) [11].

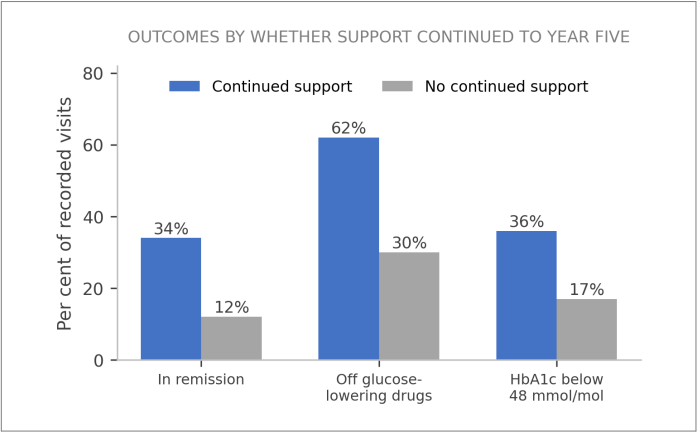


Figure 6: Outcomes by whether structured support continued to year five [11]

Study or analysis	Design	Principal reported finding
Main trial [2]	Cluster RCT, 306 recruited, 49 practices	46% remission at 12 months against 4% in controls
Two-year report [9]	Same cohort at 24 months	Remission 36%; weight loss remained the driver
Predictors analysis [12]	Intervention arm	29% of those in remission at 12 months relapsed by 24
Extension study [11]	Annual follow-up to year 5	10% in remission against 5% of controls
Extension study [11]	Continued support subgroup	34% of visits in remission against 12% without
Cost analysis [13]	Within-trial economic evaluation	Programme judged cost-effective in primary care

Table 2: Principal studies reviewed, with the finding as reported by the original investigators

Discussion

The trajectory is the finding. Forty-six per cent at one year is a striking result for a condition previously described as progressive, and 10 per cent at five years is a different statement about the same intervention [2,11]. Both numbers are correct, and which one a patient hears depends entirely on when the conversation happens.

The mechanism explains why. Remission tracks sustained weight loss with a clear gradient, from none among those who gained weight to 34 per cent among those who lost 5 to 10 kg [2]. If remission depends on maintained loss, then relapse is not a failure of the remission but the expected consequence of regain, and weight regain after substantial loss is the norm rather than the exception. The relapse analysis is consistent with that: those who relapsed had regained more, 7.1 against 4.2 kg,

though with 68 participants the comparison did not reach significance and should be read as suggestive [12].

The extension data carry the most practical message and also the greatest risk of over-reading. Participants who continued to receive support had markedly better outcomes at year five, 34 against 12 per cent of visits in remission [11]. That looks like evidence that continued support works, and it may be, but the extension group was not randomised. People who opt into three further years of appointments differ systematically from those who do not, and the same investigators observed in the two-year analysis that success promotes engagement rather than only the reverse [11,12]. The honest reading is that continued support is associated with durability and that the size of any causal contribution is unknown.

This bears directly on what is said at the outset. A patient beginning the programme is not being offered a cure, and the evidence does not support describing it as one. What the evidence supports is that roughly half will reach remission within a year, that most of those will have relapsed within five, that the determinant throughout is whether weight loss is maintained, and that maintaining it is difficult in a way the first twelve weeks are not. None of that argues against offering the intervention, which is effective and was judged cost-effective in primary care [13]. Similar programmes delivered by referral from general practice have randomised support [24], and population data show remission occurring outside trials as well [26,29]. It argues against a framing that treats month twelve as the endpoint.

There is also a specific clinical hazard worth naming. Glucose-lowering and antihypertensive drugs are withdrawn at the start of the intervention [2,10]. A person who relapses without follow-up is therefore a person with type 2 diabetes and no treatment, and the relapse is biochemical before it is symptomatic. Antihypertensive requirements also change with weight loss and were formally examined in the same trial [33]. Brief formula-based relapse management has been described as one response [10]. Structured monitoring after the programme ends is not an optional refinement; it is what prevents an intervention designed to improve control from producing a period of untreated hyperglycaemia [4,11].

A further point concerns what remission is taken to mean. The consensus definition is biochemical: an HbA1c below 48 mmol/mol sustained for three months off glucose-lowering therapy [4]. It does not assert that the underlying tendency has been removed, and the relapse data confirm it has not. Describing a patient as cured, or as no longer having diabetes, goes beyond what the definition supports and beyond what the five-year figures show [4,11].

It is also worth setting these results against the alternatives. Bariatric surgery achieves remission in a larger proportion and sustains it for longer, with ten-year randomised follow-up available [19,20]. Intensive lifestyle intervention in a larger and

less selected population produced far lower remission rates, which is consistent with the weight-loss gradient rather than contradicting it [17,18]. The intervention reviewed here occupies a middle position: more effective than routine lifestyle advice, less durable than surgery, and considerably less invasive than either comparison implies.

Study limitations

The limitations belong to the underlying literature. The trial recruited people aged 20 to 65 diagnosed within six years and not on insulin, so the results do not extend to longer-duration or insulin-treated diabetes [2]. It was open-label, as any dietary intervention must be, with blinding confined to the statisticians. The five-year extension is not randomised: participants elected whether to continue, so the comparison between extension and non-extension groups is confounded by the characteristics that drive that choice [11]. Attrition by year five left remission data for 118 of 149 intervention participants, and those lost are plausibly those who did worse [11]. The relapse comparison rests on 68 participants and did not reach significance [12]. Remission was defined biochemically, and an HbA1c below 48 mmol/mol off medication does not mean the underlying tendency has been removed [4]. The trial was conducted in Scotland and northeast England in a predominantly white population, and acceptability in populations with different food cultures has been examined separately and is not established [14]. And the intensity of dietetic and behavioural support provided exceeds what is routinely available in general practice [13,15,34]. Alternative delivery models, including remotely supervised and exercise-based programmes, report varying results and are not directly comparable [27,28,30,32].

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Conclusion

Remission of type 2 diabetes after substantial weight loss is real, reproducible and achieved by roughly half of participants within a year. It is also, for most of them, temporary: 36 per cent remained in remission at two years and 10 per cent at five, with relapse tracking weight regained rather than anything intrinsic to the diabetes. That makes the durability question a weight-maintenance question, and weight maintenance is the part of this pathway with the weakest supporting infrastructure. The biology works against it: hormonal adaptations to weight loss persist for years and favour regain [21,22,23]. The conversation that is missing is not the one at the start, which happens, but the one at eighteen months about what happens when the weight returns and the medications have already been stopped.

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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