

## Primary Care-Led Weight Management for Remission of Type 2 Diabetes (DiRECT): An Open-label, Cluster-Randomised Trial.

Lean MEJ, et al. *Lancet*. 2017:Published online Dec 5, 2017. ([http://dx.doi.org/10.1016/S0140-6736\(17\)33102-1](http://dx.doi.org/10.1016/S0140-6736(17)33102-1))

### Introduction:

A UK research team conducted a trial to assess whether intensive weight management with a total diet replacement (TDR) within routine primary care in the UK, would achieve remission of Type 2 diabetes (T2D). In the UK, remission is defined as HbA1c <6.5% after at least 2 months off all antidiabetes medications. It is important to note, in the US, remission is defined as normoglycemia for at least 1 year (HbA1c in normal range (<5.7%; fasting glucose <117 mg/dL) without active pharmacological therapies or procedures.\* Co-primary outcomes were weight loss of 15 kg (33 lbs) or more and remission of diabetes, defined as HbA1c <6.5% after at least 2 months off all antidiabetes medications.

\*Buse JB, et al. *Diabetes Care*. 2009;32:2133–2135.

### Methods:

- Open-label, cluster-randomized trial
- 49 primary care centers in Scotland and England
- n=149 for intervention group (TDR)
- n=149 for active control group (best-practice care with a food-based diet)
- 20-65 years old
- Inclusion Criteria:
  - Diagnosed with T2D within the previous 6 years
  - BMI of 27-45 kg/m<sup>2</sup>
  - Not on insulin therapy
  - HbA1c ≥6% (125 mg/dL) and ≤12%. Those with HbA1c <6.5% had to be on at least 1 antidiabetes medication
- Primary Outcomes:
  - Weight loss of 15 kg (33 lbs) or more
  - Remission of diabetes, defined as an HbA1c <6.5% after at least 2 months off all antidiabetes medications, from baseline to 1 year
- Secondary Outcomes:
  - Quality of life (as measured by the EuroQol 5 Dimensions (EQ-5D) visual analog scale
  - Reflects participants judgement of their: 1. Mobility; 2. Self-Care; 3. Usual Activities; 4. Pain and Discomfort; 5. Anxiety and Depression
  - Serum lipids
  - Physical activity

### Interventions:

#### Intervention Group

- Discontinue antidiabetes and antihypertensive medications
  - If HbA1c ≤6.5% (140 mg/dL), participants remained on antidiabetes medication

- TDR formula (26% Protein, 59% CHO, 13% Fat, 2% Fiber) provided 825-853 kcal/day for 3-5 months
- Structured food reintroduction for 2-8 weeks (15% Protein, 50% CHO, 35% Fat)
- Structured monthly support for long-term weight-loss maintenance
- Participants were encouraged to continue typical physical activity level during the active-weight loss phase and to increase steps to 15,000/day during food reintroduction and weight maintenance phases

#### Control Group

- Best practice care as provided in each country's current diabetes guidelines and standards

Outcomes	Results (at 1 Year)	
	Intervention Group	Control Group
Completed study	86% (n=128)	99% (n=147)
Achieved study weight loss goal of >15 kg (33 lbs)	24% (n=36) Mean weight loss was 10 kg (22 lbs)	0 participants Mean weight loss was 1 kg (2.2 lbs)
Achieved diabetes remission	46% (n=68)	0
HbA1c	Decreased by 0.9% (21 mg/dL)	Increased by 0.1% (44 mg/dL)
Discontinued antidiabetes medication	74% (n=109) Mean HbA1c 6.4% (137 mg/dL)	18% (n=27) Mean HbA1c 7.2% (160 mg/dL)
Discontinued antihypertensive medication	48%	0
Quality of Life (EQ-5D visual analogue scale)	Improved 7.2 points	Declined -2.9 points

### Conclusion

Outcomes and remission of diabetes in the UK was related to the amount of weight lost. Diabetes remission was achieved in 86% of patients with weight loss of 15% or more and in 57% of patients with weight loss of 10% to 15%.

The investigators concluded, "our results should pave the way for this type of intervention to be considered in the routine care of patients with type 2 diabetes who wish to attain diabetes remission." The DiRECT study shows that, in the UK, to achieve the degree of weight loss required for significant improvements and remission in those recently diagnosed with diabetes (<6 years) a total meal replacement program is superior to standard treatment for people with diabetes.

# OPTIFAST® Studies that Support the Results of the DiRECT Trial:

In general, Optifast® programs, both low calorie diets (LCD) and very low calorie diets (VLCD), as practiced in several countries (Australia, Canada, Germany, USA) have demonstrated the ability to reduce body weight and improve glycemic control as evidenced through controlled calorie intake aided by total meal replacement, behavioral modification, and lifestyle counselling.

These studies support and reinforce the important role of full meal replacement (FMR) to achieve significant weight loss.

Citation	Conclusion
<b>Steven S, et al.</b> Very-low-calorie diet and 6 months of weight stability in type 2 diabetes: pathophysiologic changes in responders and nonresponders. <i>Diabetes Care</i> . 2016;39(5):808-815.	In patients with obesity and T2DM, VLCD can reduce HbA1c to <6.5% (48 mmol/mol) and fasting plasma glucose (FPG) to <126 mg/dL (7.0 mmol/L) in the absence of pharmacological therapy.
<b>Shiau JY, et al</b> Effects on diabetes medications, weight and A1C among patients with obesity and diabetes: 6-month observations from a full meal replacement, low-calorie diet weight management program. <i>Can J Diabetes</i> . 2017;Jun 6. pii: S1499-2671(17)30045-X.	Utilizing OPTIFAST® LCD (900 kcal) for 8 to 12 weeks has shown significant weight loss in patients with diabetes, significantly reducing HbA1c and antidiabetic medication. 30% of subjects remained without antidiabetic medication at 6 months follow-up.
<b>Bischoff SC, et al.</b> Multicenter evaluation of an interdisciplinary 52-week weight loss program for obesity with regard to body weight, comorbidities, and quality of life: a prospective study. <i>Int J Obesity</i> . 2012;36(4):614-624.	A large prospective cohort study showed a 50% reduction in the prevalence of metabolic syndrome after completion of the OPTIFAST® Program (800 kcal). Diabetes prevalence was also significantly reduced (11% to 4%).
<b>Ard J, et al.</b> Practical application of a comprehensive weight management program in patients with and without metabolic syndrome. <i>J Obes Wt Loss Ther</i> . 2014;S4:007.	Patients with metabolic syndrome showed significantly greater reductions in fasting plasma glucose, triglycerides, waist circumference and LDL-C after completion of an OPTIFAST® 800 program.
<b>Gow MI, et al.</b> Reversal of type 2 diabetes in youth who adhere to a very-low-energy diet: a pilot study. <i>Diabetologia</i> . 2017;60:406-415.	A pilot study in eight (8) children and adolescents with obesity and T2DM showed significant weight reduction and improvements in HbA1c, and 2 h OGTT. Increased weight loss is associated with improvements in fasting insulin and insulin sensitivity.

## Benefits of the OPTIFAST® Program

Patients who actively participate in a 26-week OPTIFAST® Program typically lose approximately 50 pounds with weight loss-related improvements in blood pressure and cholesterol levels, which is similar to the results found in the DiRECT trial.

A full meal replacements program, such as the OPTIFAST® Program, is an effective weight management plan to help people lose significant amounts of weight and manage their weight for the long-term.

The OPTIFAST® Program is a clinically proven program including a full meal replacement phase that helps patients control the amount and type of food they eat while providing stimulus control (decreasing environmental food cues) and complete nutrition.

In addition to the overall program, the OPTIFAST® products are a suitable choice for patients with diabetes.

Results of a recent study presented as a late breaking abstract and poster at the 2017 Obesity Week Conference (T-P-LB-3681. Periman S, et al. Consumption of High Protein Meal Replacements Improves Glycemic Response in Type 2 Diabetic Adults):

- Participants with T2DM had a better glycemic response after consumption of any of the four (4) OPTIFAST® meal replacements tested, compared to control products.
- After consuming OPTIFAST® products, participants had a smaller spike in blood glucose, lower peak concentration of blood glucose, and lower blood glucose levels over time, as compared to control products.
- Study suggests that in addition to benefits seen within a medically-supervised weight-management program, the use of high-protein meal replacements may also acutely assist with glucose management in patients with T2DM.

Access the full DiRECT trial, listen to a summary of the results presented by Roy Taylor, MD, Newcastle University, and view the complete BBC news story at [www.bbc.com/news/health-42154666](http://www.bbc.com/news/health-42154666).