

Impact case study (REF3)

Institution: University of Glasgow (UofG)		
Unit of Assessment: UoA1 (Clinical Medicine)		
Title of case study: DiRECT: changing the paradigm for type 2 diabetes remission in the UK		
Period when the underpinning research was undertaken: 2012–2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
(1) Prof. Mike Lean	(1) Chair of Human Nutrition	(1) 1990–present
(2) Prof. Naveed Sattar	(2) Professor of Metabolic Medicine	(2) 1999–present
(3) Dr Paul Welsh	(3) Research Associate; Research Fellow; Lecturer; Reader	(3) 2011–2015; 2015–2016; 2016–2020; 2020–present
(4) Dr Wilma Leslie	(4) Research Nurse	(4) 1997–present
(5) Dr George Thom	(5) Research Associate	(5) 2014–present
(6) Naomi Brosnahan	(6) Research Associate	(6) 2015–present
(7) Louise McCombie	(7) Research Associate	(7) 2016–present
(8) Prof. Ian Ford	(8) Professor of Biostatistics	(8) 1992–2018
(9) Prof. Alex McConnachie	(9) Professor of Clinical Trial Biostatistics	(9) 1996–present
(10) Dr Yiqiao Xin	(10) Research Associate	(10) 2013–present
(11) Prof. Andrew Briggs	(11) Chair in Health Economics	(11) 2005–2019
Period when the claimed impact occurred: 2015–2020		
Is this case study continued from a case study submitted in 2014? No		
1. Summary of the impact		
<p>Type 2 diabetes (T2D) was traditionally considered permanent and inevitably progressive. However, in 2018, the Diabetes Remission Clinical Trial (DiRECT) validated a primary care approach to achieve remission. UK diabetes professional bodies and treatment guidelines have now designated remission as a treatment target, with remission a core strategy of Diabetes UK. The landmark DiRECT findings have changed NHS practice and policy, and the approach has been implemented in Scotland and England. DiRECT-based remission clinics are being implemented in Qatar, and have entered international clinical guidelines. Multiple commercial providers now deliver T2D remission programmes based on DiRECT.</p>		
2. Underpinning research		
<p>Prof. Mike Lean's team has been developing evidence-based primary care interventions to manage obesity since 2000. For example, as a principal investigator Lean led development and evaluations of a weight management programme, 'Counterweight', to incorporate behaviour change among clinicians and patients, with a food-based diet designed to achieve moderate (5%) weight loss (2000–2012; originally coordinated by Robert Gordon University, the work led to a spin-out company in 2011, Counterweight Ltd., to deliver this weight loss intervention).</p> <p>In 2010, Lean's team modified Counterweight to reach individuals with medically complicated obesity, targeting 15% weight loss in patients unwilling or unable to access bariatric surgery. The approach involved 'total diet replacement' over ~12 weeks using a nutritionally complete formula diet, followed by phased food re-introduction and weight loss maintenance, supported by a trained practice nurse or dietitian. The UofG team led a feasibility study of this approach among 91 severely obese patients at 25 general practices across seven NHS Scotland health boards (2010–11), in collaboration with Counterweight dietitians based at Robert Gordon University [1]. Weight loss of ≥15 kg (sufficient to put T2D into remission) was achieved and maintained at 12 months by 30 participants [1]. The liquid-formula diet was highly acceptable to both clinicians and obese patients within primary care; people with rapid weight loss did best at sustaining weight-loss at 12 months, countering the long-held and widespread belief that such weight loss is inevitably reversed after transitioning to a food-based diet. Importantly, weight loss using this approach was equally achievable for the subset of patients with T2D.</p> <p>This study formed the clinical basis of the DiRECT trial (2014–2018). DiRECT was designed and co-directed <u>jointly</u> by Prof. Lean and Prof. Roy Taylor (Newcastle University), with funding from Diabetes UK (GBP2.8 million; 62% to UofG). DiRECT aimed to determine whether T2D remission could be predictably and sustainably achieved using a pragmatic approach, when delivered in primary care. The intervention involved an 825 kcal/day 'total diet replacement' for</p>		

~12 weeks, followed by phased food re-introduction (2–8 weeks) accompanied by withdrawal of all antidiabetic and antihypertensive drugs. DiRECT-trained practitioners supported food re-introduction and long-term weight loss maintenance through 'Counterweight-Plus', a structured programme of direct engagement and tailored workbooks. Remission was defined as an HbA_{1c} level <48 mmol/mol (6.5%) and being off all antidiabetic medicines for at least 3 months. All UofG researchers named above coordinated the DiRECT study, including overall clinical aspects and biochemistry; all statistical analyses; economic and cost-effectiveness evaluation; and delivery, fidelity checking and support for practitioners delivering Counterweight-Plus.

DiRECT showed for the first time, in a **real-world UK primary care setting, that sustainable remission of T2D can be attained through weight loss**. Remission in the first 12 months was achieved in 68 of 149 T2D patients (46%) receiving the intervention [2], with 53 (36%) showing sustained remission at 24 months versus six (3%) in the control arm [3]. With weight loss >10kg, about two-thirds of patients were in remission at both 1 and 2 years. Weight loss >15kg generated remission rates of 86% at 1 year and 82% at 2 years [3]. The intervention was associated with statistically significant secondary benefits at 2 years, including lower HbA_{1c} level with fewer anti-diabetic drugs; reduced blood pressure, despite reduced use of antihypertensive drugs; reduced cardiovascular risk score; and improved quality of life, with fewer serious adverse events [3]. UofG researchers also contributed to the design and interpretation of a DiRECT sub-study on mechanisms of remission, showing that loss of ectopic fat in liver and pancreas was key to remission, and insulin-producing β cells retain the ability to recover long-term function. This changed the paradigm that T2D causes irreversible loss of β -cell function [4].

A UofG-led cost-effectiveness study funded as part of DiRECT showed an incremental within-trial cost of GBP616 for the intervention compared with the control group (standard care), and a cost per remission of GBP1,907. Lifetime horizon projections indicated the intervention was both more effective (a per-patient gain of 0.06 quality-of-life-years, QALY) and cost-saving (mean total lifetime cost saving per patient of GBP1,337) in adults with T2D than standard care, with the intervention expected to become cost-neutral, with improved health outcomes after 5–6 years [5].

3. References to the research

1. **Lean M, et al.** (2013) Feasibility and indicative results from a 12-month low-energy liquid diet treatment and maintenance programme for severe obesity. *Br. J. Gen. Pract.* 2013; 63 (607): e115-e124. (doi: [10.3399/bjgp13X663073](https://doi.org/10.3399/bjgp13X663073)).
2. **Lean MEJ, et al.** (2018) [Primary care-led weight management for remission of type 2 diabetes \(DiRECT\): an open-label, cluster-randomised trial](#). *Lancet*, 391(10120), 541-551. (doi:[10.1016/S0140-6736\(17\)33102-1](https://doi.org/10.1016/S0140-6736(17)33102-1)) [citations: 451; FWCI: 97.08 (Scopus)]
3. **Lean MEJ, et al.** (2019) [Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial](#). *Lancet Diabetes Endocrinol.* pii: S2213-8587(19)30068-3. (doi: [10.1016/S2213-8587\(19\)30068-3](https://doi.org/10.1016/S2213-8587(19)30068-3))
4. Taylor R. et al. [...] **Sattar N, Lean MEJ** (2018) Remission of human type 2 diabetes requires decrease in liver and pancreas fat content but is dependent upon capacity for β cell recovery. *Cell Metab.* 28(4):547-556.e3. (doi: [10.1016/j.cmet.2018.07.003](https://doi.org/10.1016/j.cmet.2018.07.003))
5. **Xin, Y., et al.** [...] **Lean MEJ.** (2020). Type 2 diabetes remission: 2 year within-trial and lifetime-horizon cost-effectiveness of the Diabetes Remission Clinical Trial (DiRECT)/Counterweight-Plus weight management programme. *Diabetologia*, 63: 2112–2122 (doi: [10.1007/s00125-020-05220-6](https://doi.org/10.1007/s00125-020-05220-6))

4. Details of the impact

NHS data indicate that 3.4 million people in the UK have T2D; for Scotland alone, there are ~260,000 affected individuals, with 17,000 new cases diagnosed annually. T2D was traditionally considered permanent and inevitably progressive; however, DiRECT showed that sustainable remission can be achieved through a weight-loss intervention delivered within primary care [3.2]. **Within 1 year of the primary results, DiRECT had changed understanding, practice and policy at national and international levels.**

The DiRECT intervention is adopted into UK policy and strategy

Following the DiRECT 1-year results [3.2], the Scottish Government recommended that Counterweight-Plus be implemented within NHS Scotland as a core intervention for T2D remission (July 2018). This position is reflected both within the national obesity strategy delivery plan and the national T2D prevention, early detection and early intervention framework ('the Framework') [5.A]. The Framework was allocated GBP42 million to improve weight management services, offering Counterweight-Plus as 'level 3' (T2D patients) and 'level 4' (complex case management) interventions. The Framework also introduces and promotes the term 'diabetes remission' throughout its messaging. The Professional Advisor (Programme Lead) to the Framework said, "**DiRECT ... has been one of the single most influential pieces of research to change and enhance dietetic practice and the weight management options/services in NHS Scotland for people with Type 2 Diabetes over the last decade**" [5.B]. By April 2019, **all 14 NHS Scotland health boards were approved to implement this intervention among eligible patients over the next 5 years**. Across Scotland, 500 patients were anticipated to begin in 2019–2020, supported by a GBP3 million budget and Scottish Government guidance that is wholly underpinned by the DiRECT studies [3.2,3.3] [5.B]. As a result, General Practitioners (GP) and other healthcare providers in Scotland can now refer newly diagnosed T2D patients to dietitians within local Weight Management Teams for assessment, which then support eligible patients on the Counterweight-Plus intervention [5.B].

In England, **the NHS Long Term Plan launched in January 2019 used DiRECT [3.2] as sole evidence that T2D remission is achievable** [5.C]. This pledged to implement an initial 2-year programme supporting low-calorie diets for obese people with T2D [5.C]. Following delay due to Covid-19 disruption, in September 2020, NHS England / NHS Improvement launched the NHS Low Calorie Diet (LCD) programme for 5,000 patients across ten large English Health and Social Care Partnership regions, citing the DiRECT trial and economic analysis [3.5] [5.D]. Independent of this programme, several other regions have trialled Counterweight-Plus for T2D, including North Tyneside, East Berkshire, Homerton (London), and a pilot in Wales with 90 places [5.O].

DiRECT is the largest research study ever supported by Diabetes UK, with T2D remission now representing a major strategic shift for the charity, as noted by the Director of Research: "**The results of the DiRECT study have resulted in a step-change in the understanding of type 2 diabetes and its treatment**" [5.E1]. Remission is now one of four cross-organisational priorities for its 2020–2025 strategy [5.E2]. The charity has produced three remission resources web-pages for people with T2D and healthcare professionals (380,000 unique views, Jan 2019–Jun 2020) [5.E1] and an 'information prescription' for primary care staff to use with patients [5.E3].

The cost savings from national programmes are estimated to be considerable given that 28% of people with T2D who were approached about DiRECT opted to participate, with ~33% free of T2D and off all medications at 2 years. Antidiabetic drugs represent a fraction of the total healthcare costs of T2D, with inpatient care and medications for complications dominating the average per-patient costs. A revised calculation, based on health economic data [3.5], indicates a net monetary benefit per person of GBP2,517, based on a willingness to pay value of £20,000 per QALY [5.F]. For the 1,500 patients estimated to have been supported on the Counterweight-Plus intervention between 2018–2020, as provided by Counterweight Ltd alone [5.O], this delivers population health impact valued at GBP3.78 million.

Diabetes remission is recognised in practice and perception in the UK and internationally

While DiRECT was aimed at delivery in a UK primary care context, the intervention has been recognised, replicated and adopted internationally. T2D remission is now validated as a treatment endpoint internationally on the basis of DiRECT. The President of the International Diabetes Federation (IDF) said, "*the results of this study [DiRECT] are in my view one of the most important reports regarding management of type 2 diabetes in the last decade...As President of IDF, I travel frequently and speak at international conferences and in the last few months have spoken at meetings in the Middle East, South East Asia, India and also the World Diabetes Congress in Busan, South Korea. At each of these meetings, the topic of the DiRECT study and its seminal results has been a focus of wide interest and discussion*" [5.G].

UK: In 2019, the UK Primary Care Diabetes Society and the Association of British Clinical Diabetologists issued a joint position statement emphasising the evidence to support achieving T2D remission and agree criteria for remission (based around the DiRECT criteria) [5.H1]. Primary care physicians now have a route to offer this as a treatment target. This position was also endorsed by DESMOND, the most widely used UK programme providing structured behavioural education to T2D patients [5.H2]. The DiRECT trial is also featured in ‘Hot Topics’ ([NB Medical Education](#)) the leading UK provider of healthcare continuing professional development courses—widely delivered for annual GP updating in the UK and Australia. In 2019, the Medical Director, NB Medical Education, said “...since the publication of the DiRECT trial and the BMJ paper on diabetes remission, we will have taught approx. 20,000 GPs and practice nurses this topic in the UK alone, and it has been extremely well received as a topic” [5.I].

Qatar: Building on the success of DiRECT, in 2018 the [DIADEM-1 study replicated DiRECT](#) in 13 Middle Eastern and North African countries (61% remission rate at 12 months) [5.J1]. Qatar subsequently revised its T2D treatment strategy to include remission clinics. The Director of the Qatar National Obesity Treatment Centre said, “*This initiative, supported by evidence from DiRECT and DIADEM-1, will be linked to the national diabetes screening programme in Qatar... Seeing DiRECT findings translated into the UK NHS has supported the plans for establishment of clinics in Qatar. It is expected that the clinics will be fully operational by May 2021*”. The DiRECT and DIADEM-1 findings and interventions formed the basis of the Qatar National Diabetes Prevention Programme, which has been awarded USD25 million to address different stages of T2D [5.J2]

US and Europe: In 2018, the DiRECT trial was described in detail in the Consensus Report of the American Diabetes Association and the European Association for the Study of Diabetes, which identified, for the first time, remission of T2D as a clinical management target [5.K].

Australia: The Vice President of the IDF (Australia) said, “*The DiRECT study has already impacted clinical advice in Australia*” [5.L]. The Australian Diabetes Society updated its T2D management algorithm to include intensive weight loss for remission (2020), with DiRECT referred to in the 2020 edition of the Royal Australian College of General Practitioners (RACGP) handbook. In September 2020, the University of Sydney began a DiRECT replication study. “*We expect to observe similar results which in turn will lead to this intervention becoming standard practice for newly diagnosed T2D and inclusion in national management guidelines*” [5.L].

Improved patient health and wellbeing

Within the DiRECT study, patients on the intervention reported a greater improvement in quality of life at 12 and 24 months than those on standard care [3.2, 3.3]. Patients also described that the intervention had transformed their lives. For example: “*When doctors told me that my pancreas was working again, it felt fantastic, absolutely amazing! I don’t think of myself as a diabetic anymore. I get all my diabetes checks done, but I don’t feel like a diabetic. I am one of the lucky ones to have gone into remission*” – Isobel, the first participant in DiRECT; “*By the end of it, my 16 tablets a day went down to zero, my blood pressure which was sky high went back to normal. I felt 10 years younger*” – Tony, in remission following Counterweight-Plus [5.M].

The outcomes of implementation are yet to be fully realised due to the 12-month timeframe of the intervention and pause of national services during the 2020 Covid-19 pandemic. An outcomes dataset has yet to be integrated across the Scottish Framework; however, early data from the East of Scotland Partnership (NHS boards Fife, Borders and Lothian) indicate that in Fife 77 people had enrolled, with median weight loss of 17.3 kg (15% body weight) in women and 22.9 kg (17.9% body weight) in men, sufficient to induce T2D remission [5.N1]. The number of Scottish patients coded as in **T2D remission in the [Scottish SCI-Diabetes registry](#) was 245 in 2017 when DiRECT completed [5.N2]; however, by October 2020 remissions had risen to 2,321 [5.N2]**. Outcome data are not yet available for the NHS England LCD programme, but 500 people had been referred to the programme by 31 December 2020 [5.D]. East Berkshire’s small pilot, completed in 2020, saw an average weight loss of 11.5 kg and half of participants achieving T2D remission [5.O].

New commercial benefits

[Counterweight Ltd.](#) has been a key partner in delivering Counterweight-Plus. The DiRECT results led to a new investor purchasing the rights to Counterweight Ltd., and incorporating a new company in March 2018, re-structured around Counterweight-Plus for T2D remission. The new CEO of the company said, “**Without DiRECT, Counterweight Ltd would not now exist, nor would we have been in a position to raise any funds**” [5.O]. Counterweight Ltd. has seven employees and outsources services to a network of Counterweight-trained dietitians; during the DiRECT trial, 70 dietitians and nurses were trained to support patients on Counterweight-Plus, with a further 150 trained since 2018. Counterweight have increased sales fivefold, from <100 Counterweight-Plus users per year prior to DiRECT (as a weight-loss plan) to ~500 per year since DiRECT (as a T2D remission plan), including patients in NHS Scotland, dietetic services in England and Wales, and those working with independent dietitians [5.O].

The NHS LCD programme has commissioned four UK-based commercial operators to deliver the programme across the 10 sites in England: [ICS Health](#); [Oviva UK](#); [Momenta](#); and [Reed Wellbeing](#) [5.D]. Oviva UK (a digital health provider) and ICS Health had pre-existing programmes to support T2D remission, based on DiRECT. In 2019, Oviva UK launched a low-calorie TDR-based 12-month intervention with digital delivery through an NHS Digital approved smart-phone app (Oviva Diabetes 800), available through GP referral. Their Clinical Director said, “*Oviva have taken all of the research from the DiRECT trial, and similar research across the world, and built a year-long intervention called Oviva Diabetes 800*”. Following a pilot, since January 2020 the programme has supported 52 people [5.P1]. ICS Health supported NHS North West London to deliver their ‘Diabetes REWIND’ programme, created in response to DiRECT findings, which launched in February 2020 with capacity for 350 participants per month [5.P2].

5. Sources to corroborate the impact (PDFs uploaded for all listed items)

- A. Scotland policy: (1) Diabetes Prevention Framework: ‘[A Healthier Future – type 2 diabetes prevention, early detection and intervention: framework](#)’ (July 2018) cites DiRECT: ref.12 p.6, ref. 52 p.30–3; (2) National obesity strategy: [A Healthier Future – Scotland’s Diet & Healthy Weight Delivery Plan](#) (July 2018) Scottish Government: DiRECT study cited on p.22 (ref. 51)
- B. Testimony, Scottish Government Professional Advisor to the Diabetes Framework
- C. NHS England: (1) NHS Long Term Plan: Chapter 2, More NHS action on prevention and health inequalities ([Obesity, section 2.17](#), citing DiRECT as ref.37); (2) LCD programme [announcement \(Nov 2018\)](#) (describing DiRECT in context) and [launch \(Sept 2020\)](#)
- D. Testimony from the National Clinical Director for Diabetes and Obesity, NHS England
- E. Diabetes UK: (1) Testimony from Director of Research; (2) [Diabetes UK Strategy 2020–2025](#) (see Outcome 2, p.24–27); (3) Diabetes UK information prescription for GPs
- F. Bouttell, Grieve, Xin & Wu (2020) Modelling to support DiRECT impact case study for REF2021, Health Economics & Health Technology Assessment team, UofG
- G. Testimony from President of the IDF
- H. UK recognition of T2D remission: (1) Nagi *et al.* (2019) *Br J Diabetes*, 19: 73–76 (doi: [10.15277/bjd.2019.221](#)); (2) DESMOND Project: [Remission Position Statement](#) (June, 2019)
- I. GP education: (1) Email from CEO of NB medical Education (October, 2019), see p.2; (2) Example GP education workbook material
- J. Qatar testimony: Chair, National Diabetes Research Strategy Committee, Qatar; Prof. Medicine, Weill Cornell Medicine Qatar
- K. [Management of Hyperglycemia in Type 2 Diabetes, 2018](#). ([3.2] cited as ref.75 on p.2479)
- L. Australia data: (1) Testimony from VP of the IDF; (2) [Australian Diabetes Society management algorithm](#) (top-right of page); (3) 2020 RACGP [Management of type 2 diabetes](#) (see p.42, lifestyle interventions)
- M. Example patient testimonials collected by: (1) Diabetes UK and (2) Counterweight Ltd.
- N. NHS Scotland data: (1) Health board data on Counterweight-Plus; (2) 2017 data: [McCombie et al. \(2017\)](#); (3) 2020 SCI-diabetes registry data via National Lead for Diabetes
- O. Testimony from CEO, Counterweight Ltd.
- P. Other commercial providers: (1) Oviva ([Diabetes 800](#); [Clinical Director video](#) (DiRECT quote at [02:03 mins in video](#)); Testimony from Oviva Clinical Research Lead); (2) ICS Health (Testimony from lead dietitian; [REWIND launch](#); [REWIND](#) info).