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In response to enquiry from the Accelerated National Innovation Adoption collaborative

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A review of the clinical and cost effectiveness evidence for a digital type 2 diabetes remission programme in Scotland.

## What were we asked to look at?

We were asked by the Accelerated National Innovation Adoption (ANIA) collaborative to assess the evidence for a digitally delivered type 2 diabetes remission programme. The programme is a weight management intervention comprised of a total diet replacement plan and longer-term support for weight-loss maintenance. A digital delivery model involves the use of videoconferencing and online self-monitoring tools alongside the remote provision of meal replacements; there are no in-person appointments with health professionals unless patients require intervention for other reasons.

## Why is this important?

Type 2 diabetes (T2D) occurs in approximately 88% of all patients with diabetes nationally. Reducing risk factors for developing T2D, and remission of the condition are key indicators in the Scottish Government's T2D prevention, early detection and intervention framework. There is a strong evidence base linking weight reduction with T2D remission. Dietary change based weight management programmes appear to be a scalable and relatively low-cost intervention that can be delivered both remotely and in community healthcare settings. The potential avoidance of diabetes-related complications as a result of disease remission can significantly improve outcomes and quality of life for individuals living with T2D.

## What was our approach?

We conducted a review of the evidence on the clinical effectiveness, cost effectiveness and safety of a digital T2D remission programme.

More information about SHTG Assessments is available on our [website](#).

## What next?

ANIA will use our assessment to inform a value case and subsequent decision making regarding the national implementation of a digital T2D remission programme.

## Key points

1. There is strong evidence demonstrating the effectiveness of weight management based diabetes remission programmes, for example, the Diabetes REmission Clinical Trial (DiRECT).<sup>7,8</sup> Almost half (46%) the participants with T2D who completed an in-person weight management programme were in remission one year later, and 36% were in remission at two years. Recent long-term results show that 23% of participants continue to be in remission at five years with an average weight loss of 8.9 kg.<sup>12</sup>
2. We found no published evidence on the relative effectiveness of digitally delivered remission programmes compared with in-person, face-to-face diabetes remission programmes. We found no published economic studies assessing the cost effectiveness of digital remission programmes. There is evidence from a nationally implemented diabetes prevention (as opposed to remission) programme in England that people using a digital intervention achieved greater levels of weight loss than those using either remote or group-based, face-to-face interventions.<sup>18</sup>
3. Interim results from predominantly remotely delivered remission programmes in England and Wales suggest that participants have been able to achieve levels of remission and weight loss comparable to those observed in DiRECT.<sup>13</sup>
4. An economic evaluation based on the DiRECT study found that the total intervention cost was £1,411 per person.<sup>20</sup> Whilst immediate intervention costs were only partially offset in the short-term, the longer-term benefits of being in remission led to average cost savings to the NHS of £1,337 per person over their lifetime. Longer-term savings accrued from a reduction in medication and need for diabetes-related healthcare with the intervention predicted to be cost saving within six years. Break even analysis found that at levels of remission and relapse observed in the trial, the total intervention cost would need to be in excess of £2,964 per person to cease being cost saving.
5. A comprehensive cost analysis based on registry data for T2D patients in Scotland estimated that on average, diabetes patients used between £2,500 and £6,900 of healthcare resources per year, depending on their risk of developing cardiovascular disease.<sup>21</sup> These figures illustrate the value of a remission programme in terms of the potential reduction in healthcare expenditure arising from diabetes-related complications and comorbidity.

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## Definitions

**Type 2 diabetes** – A chronic disease characterised by high levels of sugar in the blood, either due to the pancreas not producing enough insulin or because the body's cells do not react to insulin. Type 2 diabetes is often linked to being overweight or inactive, or having a family history of the disease. Treatment for type 2 diabetes involves controlling blood sugar levels either through medication or by making changes to a person's diet and activity levels.

**Remission** – Type 2 diabetes is considered to be in remission when blood glucose levels (HbA1c) remain below 48 mmol/mol or 6.5% for at least three months, without the need for diabetes medication.

**Digital service model** – A lifestyle and behaviour change intervention delivered completely online through the use of digital platforms and digital services. This includes mobile apps which allow users to access digital services such as health coaches, online peer support groups, wearable technologies to monitor levels of activity, and the ability to set and monitor goals electronically.

**Remote service model** – A lifestyle and behaviour change intervention delivered through videoconferencing but without additional integrated features and functionality for self-management and support.

## Introduction

Remission from Type 2 diabetes (T2D) can significantly improve outcomes and quality of life for people living with the condition. T2D is often linked to being overweight or obese. Weight-loss interventions using low calorie or low carbohydrate diets can be used to reduce weight and prompt T2D remission. Many people are directed to medication and education to manage their T2D rather than being supported to achieve remission.

In Scotland, an in-person T2D remission programme through the provision of total diet replacement (TDR) products has been implemented on a small scale: Health Boards receive annual funding to use the Counterweight-Plus Remission Programme to treat between 20 to 150 patients per board annually. Currently, health boards have individual contract agreements with Counterweight. There is potential for a Once for Scotland approach to procuring Counterweight (or another commercial programme provider). A digital remission pathway of care offers an alternative to the current face-to-face/in-person mode of programme implementation and may reach more people with the disease.

## Research question

What is the clinical and cost effectiveness of a digital diabetes remission programme?

## Literature search

A literature search of the primary and secondary literature was carried out in September 2022 to identify clinical studies, systematic reviews, meta-analyses, health technology assessments and other evidence-based reports. Databases used included: Medline, Medline in process, Embase, Cochrane and Web of Science.

Our search was targeted to identify evidence pertaining to a digital or remote mode of delivering a diabetes remission programme. As such, this assessment does not provide an exhaustive overview of evidence on the clinical and cost effectiveness of diabetes remission studies delivered in a face-to-face, in-person setting.

## Health technology description

A digital T2D remission programme is a structured dietary and behaviour change intervention for adults recently diagnosed with T2D. The programme includes the provision of low calorie TDR products alongside specialist dietitian and psychologist support via a digital platform. The programme is comprised of three phases: TDR for 12-20 weeks; food reintroduction for 6-12 weeks; and weight-loss maintenance for up to two years.

Digital platforms (online and/or app-based) support the food reintroduction and weight-loss maintenance phases of the programme and include activities such as monitoring, recording and reporting of food and drink intake, body weight, blood pressure, glycaemic control (blood glucose finger prick testing) and daily activities (exercise type/duration/frequency). Digital services include emotional wellbeing tools to support self-management activities, and enable patient feedback and asynchronous communication between patients and care providers.

Anticipated benefits of a digital remission programme over and above an in-person programme are:

- increase in remission rates by virtue of greater access to evidence-based treatment for more people with T2D at the point of diagnosis
- greater convenience for patients, for example, removing the need for travel to appointments
- less scope for patients to experience variations in service and inconsistent quality of care
- greater overall capacity of service provision and a reduction in waiting times.

There are a number of service providers on the market. All providers offer a fully integrated service, which includes the digital platform, TDR products, monitoring equipment, clinical oversight, staffing resource and data reporting functionality. Some providers are also able to support a hybrid model, with the provision of a software as a service (SaaS) solution separate from the supply of TDR products.

Currently, Health Boards have individual contract agreements with Counterweight-Plus to provide the digital platform and TDR products, with administration and in-person support provided by NHS dietitians, psychologists and project support staff.

## Epidemiology

The Scottish Diabetes Survey 2021 is the most recent source of national diabetes epidemiology, based on registry data.<sup>1</sup> According to the survey, there were 287,606 people living with T2D in Scotland at the end of 2021, with 22,221 people newly diagnosed that year. T2D accounts for around 88% of all people with diabetes nationally. Table 1 presents a detailed breakdown of published 5-year incidence figures.

*Table 1: Number of new T2D cases by age, Scotland 2017-2021<sup>1</sup>*

Age group	Number of people with T2D diagnosis				2021	
	2017	2018	2019	2020	Cases	Rate (per 100,000)
20–29	205	188	216	254	293	41
30–39	898	884	1,017	977	1,254	175
40–49	2,225	2,169	2,378	2,209	3,010	464
50–59	4,266	4,252	4,872	4,447	5,976	817
60–69	4,331	4,268	4,901	4,264	5,884	1,032
>=70	4,269	4,202	5,123	4,257	5,773	916
<b>Total *</b>	<b>16,216</b>	<b>15,980</b>	<b>18,530</b>	<b>16,430</b>	<b>22,221</b>	<b>432</b>

\*Includes age groups below 20 years not shown in table

A total 9.7% of people with T2D were below the age of 50 and a cumulative 28.9% were below the age of 60. These are the target age groups for a digital diabetes remission programme. In terms of disease duration, approximately 30% of people with T2D had a diagnosis for less than five years (ie new or recently diagnosed), and approximately 25% of people have had T2D for between five to nine years since diagnosis.<sup>1</sup>



In terms of complications, 9.6% of people with T2D were recorded as having had a previous myocardial infarction; 7.5% recorded as having cardiac revascularisation; 5.4% recorded as having had a stroke; 4% recorded as having had a foot ulcer; 0.6% with end stage renal failure and 0.5% with lower limb amputation.

A cross-sectional analysis of The Scottish Care Information-Diabetes (SCI-Diabetes) national registry found that in 2019, 4.8% of people with T2D, aged 30 and over, were in remission (about 1 in 20 people). People in T2D remission tended to be older; had a lower HbA1c at diagnosis; had never taken any glucose lowering medication; had lost weight since the diagnosis of diabetes; or had undergone bariatric surgery.<sup>2</sup>

## Clinical effectiveness

The clinical effectiveness of remission programmes is demonstrated by a large body of published evidence showing a strong association between weight loss and T2D remission. We have summarised key findings from systematic reviews and the DiRECT trial, which showed that sustained remission of T2D in primary care is achievable through weight loss using TDR with continued behavioural support.

Our literature search did not identify any studies on the effectiveness of an entirely digital or remotely delivered diabetes remission programme or protocol, either as a single-arm study or compared with an in-person, face-to-face programme. A plausible reason for this lack of published evidence is the relatively recent development of digital service models in the field of diabetes, and the expected lag in reporting findings from ongoing studies and trials. For this reason, interim and preliminary results from ongoing and recently completed pilot programmes have been included in this assessment.

## Systematic reviews

A 2021 systematic review aimed to identify, characterise and compare existing clinical trials using either low energy diets (LED) or low carbohydrate diets (LCD) to reduce weight and achieve T2D remission.<sup>3</sup> The review found an association across studies (n=15) between average weight loss and reduction in HbA1c at 6, 12 and 24 months, concluding that sustained weight loss is key to T2 diabetes remission. The association was strongest over longer time periods and greater reductions in Hb1Ac were associated with an increased percentage weight loss.

A second systematic review and meta-analysis reviewed the efficacy and safety of low and very LCD for T2 diabetes remission.<sup>4</sup> Twenty-three studies were included in the review, including 14 in which participants were using insulin. Outcomes at 6 months showed that LCDs achieved a higher (32%) rate of remission (defined as HbA1c <6.5 or fasting glucose of <7 mmol/L with or without diabetes medication) compared with control diets (mostly low fat). Studies reporting results at 12 months

were limited and reported only small effects in risks associated with diabetes; clinically important improvements in weight loss, triglycerides and insulin sensitivity at six months diminished at 12 months. Subgroup analysis found that very LCDs were less effective than less restrictive LCDs for weight loss at six months. This effect is explained by improved diet adherence in the LCD group.

Another 2021 systematic review described primary care clinicians' perceptions of dietitians and patient adherence to weight-loss diets.<sup>5</sup> The review contained 14 studies, with five from the UK, dated between 1993 to 2020. Two thirds of the studies were less than ten years old. Participants included 382 nurses, 2,652 general practitioners and 12 other clinicians. A lack of time for staff training and lack of patient education were seen as major constraints to diabetes management in general practice, followed by lack of staff capabilities and knowledge. The review concluded that dietitians were an underutilised resource in primary care, both for patient care and to support primary care staff.

## DiRECT

The DiRECT trial is an influential study that demonstrated that T2D remission following dietary intervention alongside clinical support is possible within a healthcare setting in the UK.

The DiRECT trial is an open-label, cluster randomised controlled study with 306 participants (157 intervention participants, 149 control participants) recruited from 49 GP practices in Scotland and Tyneside.<sup>6</sup> The intervention consisted of withdrawal of antidiabetes and antihypertensive drugs, TDR (825–853 kcal per day formula diet for 12–20 weeks), stepped food reintroduction (2–8 weeks), and then structured support for weight-loss maintenance.

The intention-to-treat population consisted of 149 participants per group. The 12-month primary outcome results showed 46% of intervention group participants achieved remission compared with 4% of control group. Almost 90% of intervention participants achieved remissions if they lost 15 kg or more in weight.<sup>7</sup>

At 24 months, weight loss of 15 kg or more was observed in 17/149 (11%) intervention group participants, and by 3/149 (2%) participants in the control group. In the intervention group 24.2% (36/149) maintained  $\geq 10$  kg weight loss at 24 months. At 24 months, 36% of intervention group participants and 3% control group participants had remission of diabetes.<sup>8</sup> The results showed that 70% of remissions could be sustained for 24 months, provided an average weight loss of 10 kg was maintained. Weight loss (either in kilograms or percentage loss) was the strongest predictor of remission at 12 months and 24 months.<sup>9</sup>

A post-hoc analysis of the DiRECT dataset was used to assess changes in the pancreas created by weight loss.<sup>10</sup> The change in pancreas volume and fractional dimension for both the intervention and control group were measured. Findings showed that changes in the gross morphology of the pancreas volume was significant for those in the intervention group who had achieved remission through weight loss, even after adjusting for body weight, age, diabetes duration and gender. After



24 months of remission, the pancreas had increased in volume to 89% of that of a matched group without diabetes. The increase in volume was associated with a complete return to normal of the irregularity of the pancreas. In contrast, there were no changes in the pancreas of those in the control group.

A second post-hoc evaluation looked at the weight-loss management (WLM) component of the DiRECT trial.<sup>11</sup> 83% of DiRECT intervention participants commenced the WLM phase, with 80% gaining over 2 kg. Of the 99 participants with weight gain, 61% used relapse treatment (RT). At two years, those regaining >2 kg and using RT had mean (SD) weight losses of 7.4 (6.1) kg, with 25 (42%) remissions and seven (12%) programme withdrawals. Those not using RT had weight losses of 8.8 (6.0) kg, with 21 (54%) remissions and four (10%) programme withdrawals. The evaluation concluded that most people regained more than 2 kg during the two years following substantial initial weight loss from a LCD with only one third managing to correct their weight gain during the maintenance phase. There was similar weight loss, remission and programme withdrawal at two years compared with those not using a RT.

Five-year results from a longer-term, extension study of DiRECT are available.<sup>12</sup> In the extension study, 95 participants from the original intervention group who had received the weight management programme continued to receive support and advice from their GP surgery to help them maintain weight loss over the next three years. Participants who regained more than 2 kg during the three years were offered an additional package of support consisting of a LCD for four weeks and support to reintroduce normal meals. Data from the extension study revealed an average 5-year weight loss of 6.1 kg in the intervention group, with 13% in remission. Forty-eight out of 85 people from the intervention group were in remission at the start of the three-year extension study. 11 out of 48 (23%) were still in remission at five years, and their average weight loss was 8.9 kg. This compares with an average 5-year weight loss of 4.6 kg, with 3.4% remaining in remission, for those in the control group.

## Real-world evidence

The NHS LCD pilot in England was launched in September 2020 with 10 integrated care systems (ICSs) testing, in real-world settings and at scale, TDR approaches to achieving clinically significant weight loss to help people achieve T2D remission. The pilot was expanded in early 2022 to include an additional 11 ICSs with plans for further expansion to full national coverage by 2023/24.

The NHS LCD Programme has been primarily delivered as a remote service model because of the COVID-19 pandemic. This differs from a digital service, which is remotely delivered to participants, but with additional features and functionality for self management and support being integrated within the service platform. The real-world findings from this pilot, and its subsequent expansion using a fully digital model, are relevant to our research question.



[REDACTED]

Early outcomes from an observational cohort study of this population assessing interim weight change at 6-months are available.<sup>13</sup> By September 2021, 2,162 people had been referred to the programme and 1,362 (63%) had started TDR. For people with six months follow-up data (N = 619), 77% were still active on the programme. Mean weight change was 13.2 kg (-13.9 kg to -12.4 kg) which equates to a mean percentage weight change of -11.8% (95% CI: -12.4% to -11.2%); 87% of participants lost ≥5% of baseline weight, 63% lost ≥10% of baseline weight and 32% lost ≥15% of baseline weight. People of white ethnicity lost more weight than people of Asian ethnicity, -12.7% (-13.4% to -12.0%) versus -7.4% (-8.9% to -5.9%) respectively. Weight losses observed in the NHS LCD programme are similar to those seen in the DiRECT trial at six months<sup>7</sup> [REDACTED]

[REDACTED]

In January 2020 following the publication of the DiRECT study results, dietetics departments within four university health boards worked with NHS Wales, to implement an All Wales pilot to test the delivery of a TDR based intervention in 90 patients with T2D to achieve remission through weight loss. 42 patients completed the 12-month intervention. For patients with two HbA1c results available at 12 months, 62% successfully achieved remission and 79% had an improvement in their diabetes control from baseline.<sup>14</sup>

### Digital diabetes remission service models

The evidence base for the clinical effectiveness of LCD/LED weight-loss programmes in diabetes remission comes largely from in-person models delivered through face-to-face appointments. Our literature search did not identify any systematic reviews or clinical trials which evaluated the effectiveness of a digitally delivered programme. The only available evidence on digital service models for diabetes remission were interim results from ongoing or recently completed programmes for targeted populations.

One conference poster presentation reported uptake and retention rates for a digital LCD programme delivered to an ethnically diverse population with T2D.<sup>15</sup> In addition to 12-weeks of TDR, patients had access to a smartphone app for self monitoring and coach support. Preliminary six-month data from 37 adults with T2D, found 81% of participants completed the 12-week TDR phase and 90% completed six months on the programme. Average 12-week weight loss was 10.9 kg (n=30), and 11 kg (n=27) at six months. For those who had reached 12 months, average weight loss was 11.5 kg (n=11). An average of 2.2 prescriptions for diabetes medication were stopped per patient.

Another conference poster reporting on a service evaluation of a digital LCD programme delivered to a geographically remote population with T2D was also presented at the 2022 Diabetes UK conference.<sup>16</sup> Of 28 patients who started the programme 26 (93%) completed the TDR phase, 68% completed the 12 month programme, and 29% regained 2 kg during the maintenance phase and commenced a refocus phase. Remission was achieved in 62.5% of patients. An average of 3.3 prescriptions for diabetes medication were stopped per patient.

### Learning from digital diabetes prevention programmes

While published evidence on digital diabetes remission programmes is lacking, there is evidence on the effectiveness of digital diabetes prevention programmes which may be insightful. In 2016, the NHS in England established The Healthier You: NHS Diabetes Prevention Programme to prevent or delay the onset of T2D in adults identified with non-diabetic hyperglycaemia (also termed prediabetes), through group-based face-to-face (F2F) structured lifestyle interventions. In 2017, a pilot digital diabetes prevention programme (DDPP) was commissioned, which was expanded to full national coverage in 2020, alongside remote delivery via video conferencing (due to the COVID-19 pandemic). The DDPP offers similar support, assistance and guidance as the F2F programme but through the use of digital platforms such as mobile apps that allow users to access health coaches, online peer support groups, wearable technologies that monitor levels of exercise, and the ability to set and monitor goals electronically.

A first service evaluation across nine pilot areas showed participation in the DDPP was associated with clinically significant reductions in weight and HbA1c.<sup>17</sup> Final 12 month data were available for 50% of 3,623 registered participants. Mean weight reduction at 12 months was  $-3.1$  kg (SD $-3.4$  to  $-2.8$  kg;  $p < 0.001$ ) with HbA1c reduction of  $-1.6$  mmol/mol (SD $-1.8$  to  $-1.4$  mmol/mol;  $p < 0.001$ ). These outcomes were comparable to the outcomes for patients receiving the F2F intervention.

Access to peer support, a website and a telephone service was associated with significantly greater reductions in HbA1c and weight loss at six and 12 months. Whether or not participants had access to wearables had no differential impact on 12-month HbA1c change. Demographic characteristics that were associated with greater weight loss included those who are older, had been through higher education, and were from the second least deprived socioeconomic group. Greater reductions in HbA1c were associated with people from mainly rural areas.

A second service evaluation found that during the COVID-19 pandemic, weight loss achieved using remote and digital interventions was greater than losses previously achieved through group-based F2F interventions, and was greater for people using digital than remote interventions.<sup>18</sup> Data from three groups of participants starting the Healthier You programme was analysed: participants who attended at least one remote intervention session; participants who engaged with at least one digital intervention session; and participants who attended their first F2F intervention session between June 2016 and February 2019.

Results for those who completed the programme showed mean weight changes of  $-3.24$  (SD  $-3.30$  to  $-3.19$ ) kg for participants taking part remotely,  $-4.76$  (SD  $-4.92$  to  $-4.60$ ) kg for participants taking part digitally and  $-3.04$  (SD  $-3.07$  to  $-3.00$ ) kg for participants taking part F2F. Linear regression analysis showed that after adjustment, remote participants lost  $0.31$  ( $0.25$ – $0.37$ ) kg more weight and digital participants lost  $2.26$  ( $2.11$ – $2.41$ ) kg more weight than F2F participants. Remote and digital participants were significantly younger (60 and 56 versus 65 years) and heavier (86.1 kg and 91.0 kg versus 84.1 kg) compared with F2F. All results were statistically significant.

The findings of this service evaluation illustrate that the effectiveness of remote and digital service models for diabetes prevention offered during the COVID-19 pandemic was greater than F2F interventions pre-pandemic, with no evidence of adverse impacts on health inequalities. This is consistent with findings of a recent systematic review of eight clinical trials of diabetes prevention, six of which reported significant reductions in weight and/or glycaemic parameters in comparison with control groups, with results comparable to, or in some cases more effective than, in-person delivery.<sup>19</sup>

## Safety

One systematic review of randomised trials of very LCD programmes reported that participants experienced no significant difference in quality of life at six months but did experience clinically important, but not statistically significant, worsening of quality of life and low density lipoprotein cholesterol at 12 months.<sup>8</sup> Otherwise, no significant or clinically important between group differences were found in terms of adverse events or blood lipids at six and 12 months.

In the DiRECT trial, there were no differences in serious adverse events (SAE) between patients receiving LCD diet versus control diet reported at 12 months. In the second year of the study, there were fewer SAEs in the intervention group than in the control group (nine versus 22).<sup>8</sup>

## Patient and social aspects

There may be concerns about the potential for certain population groups to experience exclusion arising from a digital delivery model. The main factors that influence this “digital divide” in the UK include age, region, socioeconomic status and whether a person has a disability. Older individuals might not be familiar with, or have access to, a smart device to access the web app. This is particularly relevant for the digital remission programme where the target population is anticipated to be individuals aged 65 years or below.

Service evaluations of the remote and digital models of the NHS England diabetes prevention programme did not observe any effects of the digital divide with regard to age or ethnicity, and found no association with exacerbation of health inequalities compared with a face-to-face approach.<sup>17,18</sup> Older participants on the digital programme achieved greater weight loss at 12 months than younger participants.<sup>17</sup> Remote delivery was associated with improved retention of

those of Asian, Black, mixed and other ethnicities, whereas these groups had greater attrition rates in the face-to-face programme.<sup>18</sup>

## Cost effectiveness

### Literature review

The only published economic evaluation on the use of LED based weight-loss programmes for T2D remission is a trial-based cost-effectiveness analysis of the DiRECT study. An economic model was developed to estimate the within-trial and lifetime cost effectiveness of the Counterweight-Plus weight management programme utilised in DiRECT.<sup>20</sup>

The lifetime cost-effectiveness analysis of the Counterweight-Plus intervention was based on costs and resource use measured in DiRECT over two years, and projected longer-term cost and quality-adjusted life-years (QALYs) based on duration of diabetes remission. DiRECT intervention costs over the two years included costs for training dietitians/practitioners, LED formula sachets, practitioner appointments, primary and secondary care visits, hospitalisation and medication use.

*Table 2: Key base case values applied in the DiRECT economic model<sup>20</sup>*

Variable	Value	95% CI
Male %	59 %	
Remission (year 1): intervention group	45.6%	37.6, 53.0
Remission (year 2): intervention group	35.6%	28.2, 43.0
Remission (year 1): control group	4.0%	1.3, 7.4
Remission (year 2): control group	3.4%	0.7, 6.7
Relapse (year 2)	28.4%	18.7, 38.6
Annual cost of diabetes: year 1	£1,250	-
Annual cost of diabetes: % increase per annum	6.7%	-
Health state utility multiplier for diabetes	0.925	0.87, 0.96

Long-term outcomes were projected for each treatment arm in DiRECT using a three-state model (remission, diabetes, death). Individuals entered the model with existing diabetes. After 1 year a proportion achieved remission but were subject to relapse in future years. The proportion remaining



in remission over time was estimated based on the rate of relapse observed in year 2; however, all participants were assumed to relapse after a maximum period of 10 years of remission in the base case. QALYs were calculated by applying standard UK age-dependent health state utility population norms. For people not in remission, including those who had relapsed, these age-dependent health state utilities were reduced using a constant multiplier of 0.925 to reflect a decrement associated with living with diabetes.

The lifetime healthcare costs associated with diabetes were compiled first from the measured costs for the first two years of DiRECT; further costs were included for ongoing weight management for participants remaining in remission and long-term healthcare costs associated with diabetes. Long-term diabetes-related healthcare costs were assumed to increase linearly with duration of diabetes (that is, time since relapse), over 15 years, from £1,250 in the year of diagnosis to £3,117 after 15 years, based on a UK cost of diabetes study.

Key results are presented in Table 3. The cost of formula diet and practice visits together was £1,364 per participant over 2 years, and total intervention costs, including amortised clinic set-up costs, amounted to £1,411 per participant. Lower use of glucose lowering and antihypertensive medications, combined with fewer healthcare contacts, provided total savings in the intervention arm over two years of £796 per participant. This cost saving in routine (non-trial) resource use offset 56% of the two year intervention costs, leaving a two year incremental cost for the intervention of £616 per participant. The net difference in remission rates between groups was 32.3% and the cost per two year remission was £1,907.

*Table 3: DiRECT Cost-effectiveness model results*<sup>20</sup>

	Intervention	Control	Difference
Total intervention cost per participant*	£1,411	£0	£1,411
Total cost of medications (2 years)	£105	£362	- £257
Total cost of other resource use (2 years)	£1,519	£2,058	- £539
Total 2 year cost	£3,036	£2,420	£616
Proportion in remission (2 years)	35.6%	3.4%	32.3%
Cost per 2 year remission	-	-	£1,907
Lifetime QALYs	11.27	11.22	0.06
Lifetime costs	£32,947	£34,283	- £1,337

\* Cumulative of intervention set-up costs, TDR products and dietitian visits.

In terms of long-term cost effectiveness, the intervention was predicted to generate an additional 0.06 QALYs per participant. After accounting for diabetes management costs and time to relapse



(maximum 10 years), the intervention was projected to generate savings of £1,337 per participant. The intervention therefore dominated standard care and had the probability of being both cost-saving and cost-effective at a threshold of £20,000 per QALY. The model predicted the intervention would become cost saving overall after a period of 5–6 years under base case assumptions for relapse. Sensitivity analysis showed that the intervention remained cost saving even if participants who achieved remission relapsed after a maximum of three years.

In the case of a national digital diabetes remission service in Scotland, the intervention is likely to cost more than the trial estimate of £1,411 per person. This is because of inflation, greater staffing resource and added digital platform requirements. SHTG requested further scenario analysis from the authors of the DiRECT model to estimate potential cost savings at a higher intervention cost. Results of additional scenarios are presented in Table 4.

At a total cost per participant of £1,800 or £2,200, the intervention generates cost savings of £1,164 and £764 respectively (scenarios 1 and 4). We also tested the impact of applying a more conservative remission and relapse rate to account for the possibility of lower real-world efficacy compared with trial conditions. Results showed that the intervention continued to be cost saving even with a 20% decrease in remission and a 20% increase in relapse (scenarios 2 and 4). Break even analysis shows that at base case DiRECT levels of remission and relapse, the total intervention cost would need to be in excess of £2,964 per participant to cease being cost saving (scenario 7).

*Table 4: Additional scenario analysis*

Scenario	Cost per participant	Remission (yr 1)	Remission (yr 2)	Relapse	Cost saving per participant
1	£1,800	45.60%	35.60%	28.40%	- £1,164
2	£1,800	36.48%	28.48%	34.08%	-£521
3	£1,800	54.72%	42.72%	22.72%	-£1,989
4	£2,200	45.60%	35.60%	28.40%	-£764
5	£2,200	36.48%	28.48%	34.08%	-£121
6	£2,200	54.72%	42.72%	22.72%	-£1,589
7	£2,964	45.60%	35.60%	28.40%	0

### Costs of T2D associated cardiovascular disease

People with T2D are at increased risk of developing cardiovascular disease (CVD), which is the leading cause of comorbidity and death within this population. In addition to reduction in quality of life and life expectancy, CVD associated morbidity places significant burden on health services. Our search identified one comprehensive costing study which estimates the cost of prevalent and incident CVD in people with T2D in Scotland.<sup>21</sup>

The analysis compared costs for three groups of people with T2D: those at high risk of future CVD, those without CVD and those with established CVD. It also compared costs incurred by people with T2D who have an incident CVD event with those remaining event-free for three years.

Data was obtained from the SCI-Diabetes registry and included all people with T2D alive on 1<sup>st</sup> July 2015 to assess prevalence. Classification of people into the three groups mentioned above was based on a 10-year lookback period of linked individual patient data on healthcare utilisation and mortality. Incidence was based on people in the registry from January 2010 to June 2015, who were followed up for a maximum of three years, during which occurrence of the first CVD event was recorded. The cost of inpatient stays, prescriptions, primary care visits and care home use was accounted for. Productivity losses were also included by applying a weekly cost of £560 for the period that working age patients were unable to work.

Results of mean annual cost per patient based on prevalence data (for year 2015/16) are presented in Table 5. Of 244,752 people alive with T2D, approximately 30% had established CVD at a mean cost of £6,900. Approximately 58% were at high risk of future CVD at a mean cost of £3,300. The remaining 12% had no CVD and were not high risk with a mean cost of £2,500. Mean costs were lower for people in the cohort in the target age range for a digital remission programme (that is, 65 years or younger).

*Table 5: Total mean cost by CVD status and age<sup>21</sup>*

Category	Annual cost per patient	Annual cost per patient <60 years	Annual cost per patient 60-69 years
<i>Cohort size</i>	244,752	72,055	70,631
Established CVD	£6,900	£3,800	£5,000
High risk of CVD	£3,300	£1,800	£2,800
No CVD, low risk of CVD	£2,500	£1,300	£2,300

\* Non-indexed costs at 2015/16 levels.

The costs identified in this analysis provide an indication of the potential reduction in levels of diabetes-related healthcare utilisation and expenditure achievable with the implementation of a remission service.

The incidence analysis offers insight into how costs develop over time after an incident CVD event. The mean cost per person three years after an incident CVD event was £25,000 compared with £5,900 for those remaining CVD event-free. Cerebrovascular events were associated with the highest cost over three years (£37,900) and revascularisation procedures were associated with the lowest cost (£17,500).

## Conclusion

Evidence shows that a low energy diet-based diabetes remission programme, delivered in-person, is both a clinically and cost-effective service to implement. Currently, there is no published evidence on a remote or digitally delivered diabetes remission programme which allows for a direct or indirect comparison of the relative effectiveness of different service models.

Emerging findings from pilot studies suggests that a digital service model will produce equivalent, and potentially superior outcomes to an in-person, face-to-face service model. Interim analysis of data from a large-scale pilot in England suggests that a remote service (rather than purely digital) model is able to achieve levels of remission and weight loss in participants comparable to those observed in face-to-face clinical trials. Additionally, parallel evidence from a nationally implemented diabetes prevention programme in England shows that people using the digital intervention achieved greater levels of weight loss than those using either the remote or face-to-face interventions.

## Identified research gaps

The relative effectiveness of different diabetes remission service models (that is, digital vs face-to-face) has not been formally investigated as part of a research study by design.

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