

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Intermittent Energy Restriction Example Meal Plan

	<b>500kcal</b>	<b>600kcal</b>
<b>Breakfast</b>	1 serve of fruit (150g) + 1 tub of diet yoghurt	
<b>Lunch</b>	Small tin of tuna in spring water + 1 cup of salad	Add: 1 serve of breads/cereals e.g. 'thin style' wrap
<b>Dinner</b>	100g of cooked chicken breast (1 teaspoon of oil for cooking) + 1.5 cups cooked low carbohydrate vegetables	

Note: 2 litres of fluid was recommended. Diet products were allowed e.g. diet jelly.

**eTable 2.** Initial Medication Protocol

HbA1c	Sulphonylureas	Insulin
<8%	Discontinue at baseline for both groups	<b>CER:</b> Reduce by ~10 units/day <b>IER:</b> Halve insulin dose on intermittent days <i>*If insulin dose before bed was considered to be too high in preparation for an intermittent diet day, before bed dose was also decreased.</i>
>8%	N/A	<b>IER:</b> Reduce by ~10 units on IER days only

Abbreviations: CER, continuous energy restriction; IER, intermittent energy restriction; ~, approximately.

**eTable 3.** Medication Changes Using First Protocol<sup>a</sup>

Grp.	Med. Category	HbA <sub>1c</sub> (%)	Initial Med. Dose	Initial Change	Protocol	Wt loss after first 2wks	Event during first 2wks	Change after first 2wks	Events (3wks-3mths)	Changes before 3mths	Event (3mth-12mths)	Changes after 3mths	Final Med.
CER	OHA	6.2	150mg	Discont.	Yes	Yes	n/a	n/a	n/a	n/a	n/a	n/a	n/a
IER	OHA	6.7	60mg	Discont.	Yes	Yes	n/a	n/a	n/a	n/a	Hypers (non-IER d)	No OHA on IER d	No OHA on IER d
IER	OHA	7.3	60mg	Discont.	Yes	No	n/a	n/a	n/a	Restarted OHA (pt MP)	Hypo (IER d)	Discont. OHA on IER d	No OHA on IER d
IER	OHA	7.5	120mg	Discont.	Yes	Yes	n/a	n/a	Hypers (both d)	Added back half dose (60mg)	Hypo (both d)	Discont. OHA	No OHA
CER	Insulin (LONG + RAPID) + OHA	7.6	LONG 25u, RAPID 12u, OHA 60mg	LONG 12u, RAPID 6u, Discont. OHA	Yes	Yes	Hypers (x3)	LONG 16u, RAPID 7u (pt MP)	n/a	n/a	Hypers	LONG 22u, RAPID 11u (pt MP), LONG 27u, RAPID 8u (pt MP)	LONG 27u, RAPID 8u
CER	Insulin (MIX)	8.6	25/45u	None	Yes	Yes	Hypo (x3)	20/30u	Hypo	20/25u, 20/20u	Hypo	15/25u, 15/30u (levels inc.)	15/30u
CER	Insulin (MIX)	9	88/58u	None	Yes	No	n/a	n/a	W/D				
CER	Insulin	9.7	30/22u	None	Yes	Yes	Hypo (x1)	25/17u	n/a	20/15u (low), 17/10u (low), 20/10u (levels inc.)	n/a	20/5u (low)	20/5u

Grp.	Med. Category	HbA <sub>1c</sub> (%)	Initial Med. Dose	Initial Change	Protocol	Wt loss after first 2wks	Event during first 2wks	Change after first 2wks	Events (3wks-3mths)	Changes before 3mths	Event (3mth-12mths)	Changes after 3mths	Final Med.
IER	Insulin (LONG + RAPID)	7.1	LONG 40u, RAPID 15/15u	LONG 20u, RAPID 7/7u on IER d	Yes	Yes	Hypo (x2) (both d)	LONG 20u on IER d and LONG 30u, RAPID 7/7u on non-IER d	n/a	LONG 30u only on non-IER d (low)	Hypo (both d)	LONG 15u on IER d and 20u on non-IER d, LONG 10u on IER d and 20u non-IER d (low)	LONG 10u on IER d, 20u non-IER d
IER	Insulin (MIX)	7.3	80/75u	40/38u on IER d	Yes	No	Hypo (x3) (IER d)	20/20u on IER d	Hypo (IER d)	20/10u on IER d	W/D		
IER	Insulin	8.8	6/41u	6/20u night before and on IER d	No, > required	Yes	Hypo (x1) (IER d)	0/10u on IER d	n/a	n/a	W/D		
IER	Insulin	8.8	10/50u	10/30u on IER d and 25u night before IER d	No, > required	Yes	n/a	n/a	Hypo (IER d)	10/30u non-IER d, 10/10u night before and IER d	n/a	n/a	10/30u non-IER d, 10/10u night before and IER d
IER	Insulin (LONG + RAPID)	11.5	LONG 28/15/28u, RAPID 28/15/28u	None	Yes	W/D							

<sup>a</sup>Recommendations made by the study's endocrinologist unless otherwise specified. First protocol, eTable 2.

Abbreviations: Grp, group; Med, medication; HbA<sub>1c</sub>, glycated hemoglobin; Wt, weight; wks, weeks; mths, months; CER, continuous energy restriction; IER, intermittent energy restriction; OHA, oral hypoglycemic agent (gliclazide unless otherwise stated); Discont, discontinue; hypers, hyperglycemia; hypo, hypoglycemia; low, 72-106mg/dL; inc, increasing; W/D, withdrew; d, day/s; pt, participant; MP, medical practitioner; Insulin, long-acting insulin (insulin glargine); LONG, long-acting insulin (insulin glargine); MIX, NovaMix; RAPID, NovaRapid; u, units

**eTable 4.** Medication Changes Using Second Protocol<sup>a</sup>

Grp.	Med. Category	HbA <sub>1c</sub> (%)	Initial Med. Dose	Initial Change	Protocol	Wt loss after first 2wks	Event during first 2wks	Change after first 2wks	Events (3wks-3mths)	Changes before 3mths	Event (3mth-12mths)	Changes after 3mths	Final Med.
CER	OHA	6.1	OHA 120mg	Discont. OHA, pt MP decrease to 60mg	No. At pt MP advice, < required	Yes	n/a	n/a	n/a	n/a	n/a	n/a	60mg OHA
CER	OHA	7.4	OHA 20mg	None	Yes	Yes	n/a	n/a	n/a	n/a	W/D		
CER	OHA	7.7	OHA 80mg	None	Yes	No	n/a	n/a	n/a	n/a	W/D		
CER	OHA	8.3	OHA 60mg	None	Yes	No	n/a	n/a	n/a	n/a	n/a	n/a	n/a
CER	OHA	8.4	OHA 60mg	None	Yes	Yes	n/a	n/a	n/a	n/a	W/D		
CER	OHA	9	OHA 120mg	None	Yes	Yes	n/a	n/a	n/a	60mg OHA (low)	W/D		
CER	OHA	10.9	OHA 80mg	None	Yes	W/D							
IER	OHA (GP)	6	OHA 1mg	Discont. OHA	Yes	Yes	n/a	n/a	n/a	n/a	n/a	n/a	n/a
IER	OHA	6.2	OHA 60mg	Discont. OHA	Yes	Yes	Hypers (x2) (non-IER d)	n/a	n/a	n/a	n/a	n/a	n/a
IER	OHA	7	OHA 60mg	No OHA on IER d	Yes	No	n/a	n/a	Hypos (non-IER d)	30mg OHA on non-IER d	W/D		
IER	OHA (GP)	7	OHA 2mg	No OHA on IER d	Yes	Yes	n/a	n/a	n/a	Discont. OHA (low)	n/a	n/a	No OHA

Grp.	Med. Category	HbA <sub>1c</sub> (%)	Initial Med. Dose	Initial Change	Protocol	Wt loss after first 2wks	Event during first 2wks	Change after first 2wks	Events (3wks-3mths)	Changes before 3mths	Event (3mth-12mths)	Changes after 3mths	Final Med.
IER	OHA	7.3	OHA 60mg	No OHA on IER d	Yes	No	Hypers (x2) (both d)	Restart OHA	W/D				
IER	OHA	7.6	OHA 120mg	No OHA on IER d	Yes	Yes	Hypos (x2) (non-IER d) and Hypers (x5) (non-IER d)	Decrease to 60mg OHA on non-IER d	n/a	n/a	n/a	n/a	60mg OHA on non-IER d
IER	OHA	7.8	OHA 120mg	No OHA on IER d	Yes	No	n/a	n/a	W/D				
IER	OHA	7.9	OHA 120mg	No OHA on IER d	Yes	Yes	n/a	n/a	n/a	n/a	Hypers (both d)	Restart OHA	OHA 120mg
IER	OHA	9.2	OHA 60mg	No OHA on IER d	Yes	Yes	n/a	n/a	n/a	Discont. OHA completely (low)	n/a	n/a	No OHA
IER	OHA	9.5	OHA 60mg	No OHA on IER d	Yes	Yes	n/a	n/a	n/a	n/a	n/a	n/a	No OHA on IER d
CER	Insulin (LONG + RAPID)	6.2	LONG 36u, RAPID 12/12u	LONG 30u, RAPID discont.	No, < required	Yes	n/a	n/a	n/a	LONG 28u (low)	n/a	LONG 22u (low)	22u
CER	Insulin	6.9	20u	None	No, < required	Yes	n/a	n/a	n/a	n/a	n/a	n/a	n/a
CER	Insulin	7.1	12u	10u	No, all pt would agree too, < required	No	n/a	n/a	n/a	9u (low)	n/a	8u (low)	

Grp.	Med. Category	HbA <sub>1c</sub> (%)	Initial Med. Dose	Initial Change	Protocol	Wt loss after first 2wks	Event during first 2wks	Change after first 2wks	Events (3wks-3mths)	Changes before 3mths	Event (3mth-12mths)	Changes after 3mths	Final Med.
CER	Insulin (MIX) + OHA	7.5	22/30u, OHA 120mg	15/20u, Discont. OHA	No, > required	Yes	n/a	n/a	Hyper	15/25u	Hypers	17/27u	17/27u
CER	Insulin + OHA (GP)	7.8	26u, OHA 4mg	None	No, < required	Yes	n/a	n/a	Hypo	20u, 18u, 16u	n/a	14u, 12u, 10u (low)	10u
CER	Insulin	8.3	36u	None	Yes	W/D							
CER	Insulin	8.5	80/34u	None	Yes	Yes	Hypers (x5)	n/a (pt MP advice)	Hypers	n/a (pt MP advice)	Hypers	n/a (pt MP advice)	n/a (pt MP advice)
CER	Insulin	8.8	30u	None	Yes	No	Hypers (x4)	n/a	n/a	n/a	Hypers	35u, 38u, 40u	40u
CER	Insulin	9.3	75/75u	None	Yes	Yes	n/a	n/a	n/a	n/a	n/a	70/70u (low)	70/70u
CER	Insulin + OHA (GP)	10	25u, OHA 4mg	None	Yes	Yes	n/a	n/a	Low	20u	W/D		
IER	Insulin (MIX) + OHA	5.7	45/45u, OHA 60mg	10/10u, no OHA on IER d, 25/25u on non-IER d	No, < required	Yes	n/a	n/a	Hyper	25/30 non-IER d	Hypers	10/15u on IER d, 15/30u on non-IER d	10/15u on IER d, 15/30u on non-IER d
IER	Insulin + OHA	7.5	16u, OHA 60mg	No insulin the night before or on IER d, no OHA on IER d	Yes	Yes	Hypers (x4) (non-IER d)	18u non-IER d	n/a	n/a	n/a	16u non-IER d (low)	16u non-IER d



Grp.	Med. Category	HbA <sub>1c</sub> (%)	Initial Med. Dose	Initial Change	Protocol	Wt loss after first 2wks	Event during first 2wks	Change after first 2wks	Events (3wks-3mths)	Changes before 3mths	Event (3mth-12mths)	Changes after 3mths	Final Med.
IER	Insulin + OHA	7.6	70/70u, OHA 60mg	10/10u, no OHA on IER d and 10u the night before on IER d	No, all pt would agree too, < required	Yes	Hypos (x6) (both d), Hypers (x2) (non-IER d)	50/50u non-IER d	Hypos (both d)	40/40u non-IER d and no insulin night before IER d or on IER d	Hypos (non-IER d)	30/30u on non-IER d and no insulin night before IER d or on IER d, 20/20u	20/20u non-IER d
IER	Insulin	7.7	40u	30u on IER d	No. Pts MP, < required	Yes	n/a	n/a	n/a	n/a	n/a	n/a	30u
IER	Insulin (MIX)	7.8	40/40u	No insulin on IER d	Yes	No	n/a	n/a	n/a	n/a	Hypers (non-IER d)	65/65u on non-IER d, 30/30u on non-IER d (low)	30/30u
IER	Insulin (MIX + RAPID)	7.9	44/24u MIX, 6u RAPID as req.	No MIX night before or on IER d	Yes	No	Hypers (x14) (both d)	10u of RAPID on IER d as req.	n/a	n/a	n/a	n/a	n/a
IER	Insulin	8.7	32u	No insulin night before or on IER d	Yes	Yes	Hypo (x1) (non-IER d)	25u on non-IER d	Hypo (non-IER d)	20u on non-IER d	W/D		
IER	Insulin + OHA (GP)	9	26u, OHA 4mg	5u night before IER d and none on IER d	No, < required	Yes	Hypers (x12) (both d)	10u night before IER d	Hypo (IER d)	Decrease to 5u night before IER d	Hypers (both d)	10u night before IER d, 20u on non-IER d (low)	20u non-IER d, 10u night before and none on IER d
IER	Insulin + OHA (GP)	9.8	34u, OHA 4mg	22u on IER d	No, < required	Yes	n/a	17u on IER d (low)	n/a	15u on IER d (low)	n/a	12u on IER d (low)	12u

<sup>a</sup>Recommendations made by the study's endocrinologist unless otherwise specified. Second protocol detailed in manuscript.

Abbreviations: Grp, group; Med, medication; HbA<sub>1c</sub>, glycated hemoglobin; Wt, weight; wks, weeks; mths, months; CER, continuous energy restriction; IER, intermittent energy restriction; OHA, oral hypoglycemic agent (gliclazide unless otherwise stated); GP, glimepiride; Discont, discontinue; hypers, hyperglycemia; hypo, hypoglycemia; low, 72-106mg/dL; d, day/s; W/D, withdrew; pt, participant; MP, medical practitioner; Insulin, long-acting insulin (insulin glargine); LONG, long-acting insulin (insulin glargine); MIX, NovaMix; RAPID, NovaRapid; u, units

**eTable 5.** Primary, Secondary and Exploratory Outcomes From Baseline to 12 Months for Intermittent vs Continuous Groups (Completers Analysis)<sup>a</sup>

Variable	Mean (SEM) [95% CI]				
	All Participants (n = 97)	P Value for Time	Continuous	Intermittent	P Value for Diet by Time
<b>Primary Outcome</b>					
HbA1c, %	-0.4 (0.09) [-0.6 to -0.1]	<.001	-0.4 (0.2) [-0.8 to -0.05]	-0.3 (0.1) [-0.6 to -0.01]	.62
<b>Secondary Outcomes</b>					
Weight, kg <sup>b</sup>	-6.1 (0.7) [-7.8 to -4.3]	<.001	-5.0 (0.8) [-7.0 to -3.0]	-7.1 (1.1) [-9.9 to -4.4]	.15
BMI, kg/m <sup>2</sup>	-2.1 (0.2) [-2.7 to -1.5]	<.001	-1.8 (0.3) [-2.5 to -1.1]	-2.5 (0.4) [-3.4 to -1.6]	.19
Total Body Fat, % <sup>c</sup>	-2.2 (0.4) [-3.3 to -1.1]	<.001	-1.7 (0.4) [-2.7 to -0.6]	-2.8 (0.8) [-4.7 to -0.9]	.21
Total Fat Mass, kg <sup>c</sup>	-4.4 (0.6) [-5.9 to -3.0]	<.001	-3.7 (0.7) [-5.4 to -1.9]	-5.2 (0.9) [-7.5 to -2.9]	.22
Total FF Mass, kg <sup>c</sup>	-1.8 (0.2) [-2.3 to -1.3]	<.001	-1.3 (0.3) [-2.1 to -0.5]	-2.2 (0.3) [-2.9 to -1.5]	.02
Android Fat, % <sup>c</sup>	-3.3 (0.7) [-5.0 to -1.6]	<.001	-2.1 (0.5) [-3.4 to -0.8]	-4.5 (1.2) [-7.6 to -1.4]	.07
Android Fat Mass, kg <sup>c</sup>	-0.7 (0.1) [-0.9 to -0.5]	<.001	-0.6 (0.1) [-0.9 to -0.3]	-0.9 (0.1) [-1.2 to -0.5]	.14
Android FF Mass, kg <sup>c</sup>	-0.2 (0.04) [-0.3 to -0.1]	<.001	-0.3 (0.05) [-0.2 to 0.1]	-0.2 (0.06) [-0.2 to 0.1]	.80
VAT, kg <sup>c</sup>	-0.2 (0.07) [-0.4 to -0.1]	<.001	-0.2 (0.09) [-0.4 to -0.05]	-0.3 (0.1) [-0.5 to -0.05]	.38

Abbreviations: HbA<sub>1c</sub>, glycated hemoglobin; BMI, body mass index; FF, fat free; VAT, visceral adipose tissue.

<sup>a</sup>Data were included for 97 participants (CER group: n=46; IER group: n=51) unless otherwise stated: mean (SEM) and [95% CI] were estimated with repeated-measures ANOVA.

<sup>b</sup>Total analysed: n=94 (CER group: n=44; IER group: n=50) 3 participants did not attend final appointment, GP sent HbA<sub>1c</sub> results.

<sup>c</sup>Total analysed: n=81 (CER group: n=39; IER group: n=42) weight >130kg or declined DEXA scan.