SUPPLEMENTARY APPENDIX

Figure S1: Primary outcomes and remission of diabetes in relation to weight loss at 12 months.
A: First co-primary outcome, achievement of ≥15kg weight loss at 12 months, by randomised group. **B:** Second co- primary outcome, remission of diabetes (HbA_{1c} <48mmol/mol, off anti-diabetic medication for 2 months), by randomised group.
C: Remission of diabetes, in relation to weight loss achieved at 12 months (both randomised groups combined).

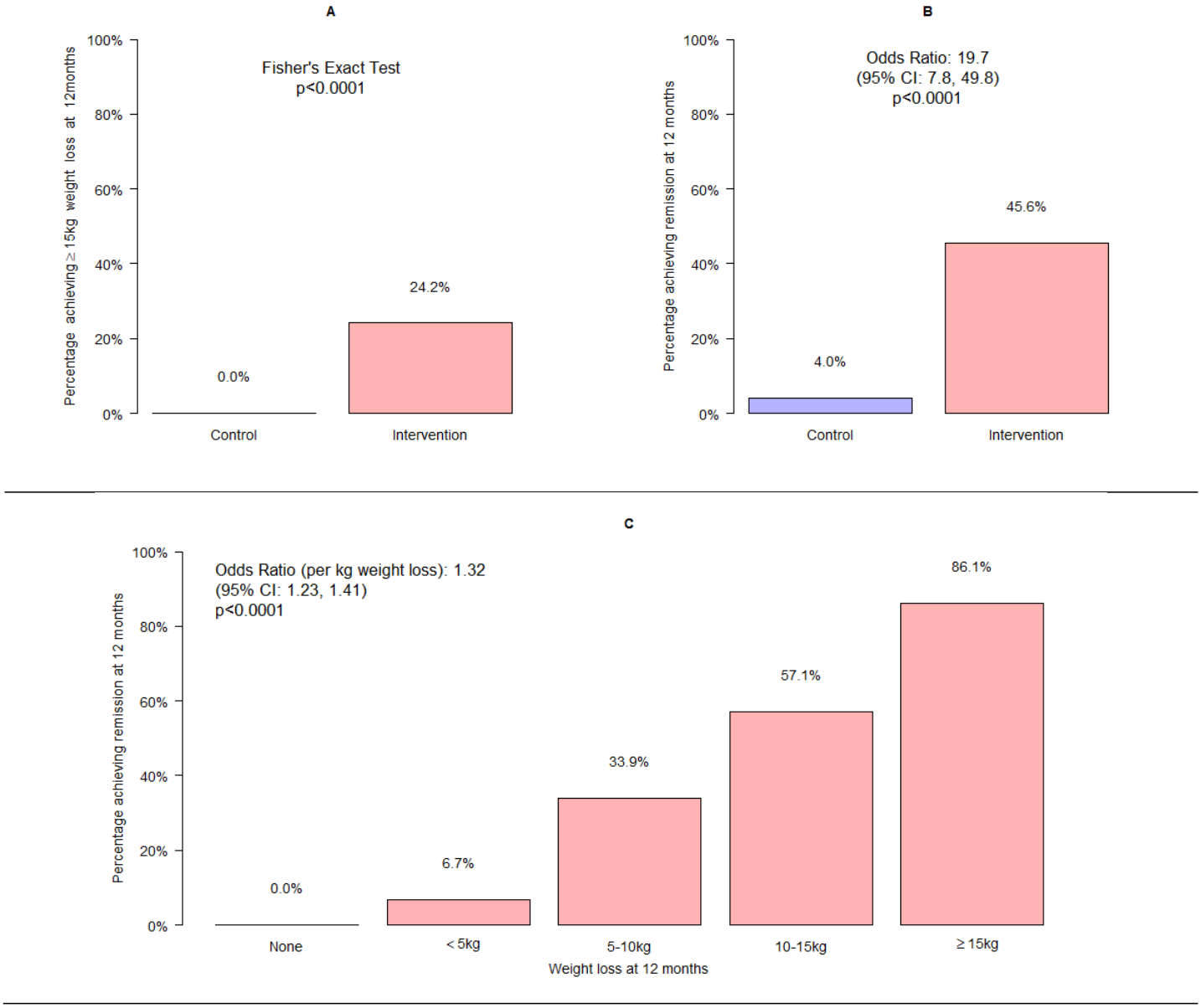

Table S1: Further analyses of secondary outcome measures and other outcomes in the intervention and control groups at baseline and 12 months

		N	Mean (SD)			Intervention Effect (Relative)			ICC
			Baseline	12months	Change	Estimate	95% CI	p-value	
Percentage weight change from baseline[(a)]	Intervention	137		-9·9 (7·6)		-8·8	(-10·2, -7·3)	p<0·0001	0·01
	Control	148		-1·1 (3·8)					
BMI (kg/m^2)	Intervention	137	35·0 (4·5)	31·5 (4.9)	-3·5 (2.8)	-3·0	(-3·5, -2·5)	p<0·0001	0·01
	Control	148	34·2 (4·3)	33·8 (4·5)	-0·4 (1.3)				
Number of other prescribed medications (not oral antidiabetic or antihypertensive)	Intervention	148	3·5 (3·0)	4·0 (3·9)	0·5 (2·0)	-0·08	(-0·49, 0·33)	p=0·7036[(b)]	<0·01
	Control	148	3·6 (3·4)	4·2 (3·7)	0·6 (1·4)				
Diastolic blood pressure (mmHg)	Intervention	128	84·8 (10·2)	83·5 (9·5)	-1·3 (10·3)	-0·4	(-2·5, 1·6)	p=0·6863	<0·01
	Control	147	85·5 (8·8)	84·5 (8·9)	-1·1 (10·1)				
Quality of Life EQ-5D health utility score	Intervention	125	0·806 (0·279)	0·793 (0·278)	-0·013 (0·211)	0·025	(-0·023, 0·073)	p=0·3146[(c)]	<0·01
	Control	147	0·799 (0·282)	0·759 (0·302)	-0·040 (0·203)				

Intervention effects reported as estimated mean differences (Intervention-Control), based on mixed effects linear regression model, adjusted for randomised group, baseline value[(a)], study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.

N refers to number of participants with data available at baseline and 12 months for each outcome. ICC: Intraclass Correlation Coefficient.

(a): Effect estimate for percentage weight change includes adjustment for baseline weight

Some model residuals showed signs of non-Normal distribution:

(b): Results confirmed using non-parametric test of 12 month values (p=0.37) and change from baseline (p=0.053)

(c): Results confirmed using non-parametric test of 12 month values (p=0.33) and change from baseline (p=0.39)

Table S2: Weight at baseline and 12 months, under alternative assumptions regarding missing data

		N	Mean (SD)			Intervention Effect			ICC
			Baseline	12months	Change	Estimate	95% CI	p-value	
Complete Data (as in Table 2)	Intervention	137	100·4 (16·5)	90·4 (16·4)	-10·0 (8·0)	-8·8	(-10·3, -7·3)	p<0·0001	<0·01
	Control	148	98·7 (16·1)	97·7 (16·4)	-1·0 (3·7)				
IMPUTATION OF MISSING WEIGHTS									
Conservative (Return to Baseline)	Intervention	149	101·0 (16·7)	91·8 (17·1)	-9·2 (8·1)	-8·0	(-9·5, -6·5)	p<0·0001	<0·01
	Control	149	98·8 (16·1)	97·8 (16·4)	-1·0 (3·7)				
Optimistic (Last Observation Carried Forward)	Intervention	149	101·0 (16·7)	91·3 (16·8)	-9.7 (8·0)	-8·4	(-9·9, -6·9)	p<0·0001	<0·01
	Control	149	98·8 (16.1)	97.8 (16·4)	-1.0 (3·7)				
Realistic (see below)	Intervention	149	101·0 (16.7)	91·6 (17·0)	-9·4 (8·0)	-8·2	(-9·6, -6·7)	p<0·0001	<0·01
	Control	149	98·8 (16.1)	97·8 (16.4)	-1·0 (3·7)				

Intervention effects reported as estimated mean differences (Intervention-Control), based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.

N refers to number of participants with data available at baseline and 12 months for each outcome. ICC: Intraclass Correlation Coefficient.

Imputation options:

- Conservative (Return to Baseline): missing 12 month weights imputed as the baseline value
- Optimistic (LOCF): missing 12 month weights imputed as the last recorded weight. For intervention patients, this could be during a treatment visit; for control patients, this will be the baseline value
- Realistic: missing 12 month weights imputed as the mean value from other patients in the same randomised group who did not attend the 12 month visit, but for whom the weight was obtained from GP records

Table S3: Changes in weight during each treatment phase. Data during TDR phase reported for all participants who started TDR; data during FR phase reported for all participants who successfully completed TDR; data during WLM phase reported for all participants who successfully completed FR (plus one patient who progressed directly from TDR to WLM). ”End of TDR” and “End of FR” weights refer to the final weight recorded at a study treatment visit during each phase.

		Completed Phase	Not Completed Phase	Difference[(a)] (95% CI), p-value
Weight During TDR Phase (for those who started TDR phase)				
	N	128	15	
Baseline	Mean (SD)	100·9 (16·7)	101·6 (18·4)	-0·7 (-9·7, 8·3), p=0·8797
End of TDR	Mean (SD)	86·4 (15·6)	98·6 (17.9)	-12·1 (-20·6, -3·7), p=0·0050
Change during TDR	Mean (SD) [95% CI]	-14·5 (6·0) [-15·5, -13·4]	-3·0 (3·6) [-5·0, -1·0]	-11·5 (-14·5, -8·6), p<0·0001
Weight During FR Phase (for those who progressed from TDR to FR)				
	N	107	20	
End of TDR	Mean (SD)	85·2 (15·0)	92·0 (17·7)	-5.5 (-13·4, 2·5), p=0·1779
End of FR	Mean (SD)	86·2 (15·4)	95·2 (17·1)	-8.1 (-16·2, 0·0), p=0·0488
Change during FR	Mean (SD) [95% CI]	1·0 (3·2) [0·3, 1·6]	3·2 (2·3) [2·1, 4·3]	-2·7 (-4·3, -1.1), p=0·0010
Weight During WLM Phase (for those who progressed from TDR to FR to WLM, or directly from TDR to WLM)				
	N	78	30	
End of FR	Mean (SD)	85·1 (14·6)	89·5 (17·0)	-4·4 (-10·8, 2·1), p=0·1851
12 Months	Mean (SD)	87·0 (15·1)	92·0 (17·2)	-5·0 (-11·6, 1·7), p=0·1424
Change during WLM	Mean (SD) [95% CI]	1·9 (2·9) [1·2, 2·5]	2·4 (3·0) [1·3, 3·5]	-0·6 (-1·8, 0·7), p=0·3809

(a): Difference (Completed – Not Completed) derived from two-sample t-test for differences at the start and end of each treatment phase. Differences in the change during each phase derived from a linear regression model of the change in weight, adjusted for weight at the start of the phase

Table S4: Secondary outcomes: binary outcomes in the intervention and control groups at baseline and 12 months

		N/Total (%)	Odds Ratio		
			Estimate	95% CI	p-value
Prescribed oral anti-diabetic medications	Intervention	39/148 (26·4%)	0·07	(0·03, 0·14)	p<0·0001
	Control	121/148 (81·8%)			
All Patients					
HbA_{1c} <48mmol/mol	Intervention	71/138 (48·6%)	7·02	(3·66, 13·46)	p<0·0001
	Control	23/148 (15·5%)			
HbA_{1c} <42mmol/mol	Intervention	40/138 (29·0%)	8·38	(3·49, 20·14)	p<0·0001
	Control	7/148 (4·7%)			
For those patients prescribed oral anti-diabetic medication at 12 months					
HbA_{1c} <48mmol/mol	Intervention	3/35 (8.6%)	0·55	(0·14, 2·09)	p=0·3797
	Control	17/121 (14.0%)			
HbA_{1c} <42mmol/mol	Intervention	1/35 (2.9%)	0·46	(0·05, 4·28)	p=0·4941
	Control	6/121 (5.0%)			
For those patients NOT prescribed oral anti-diabetic medication at 12 months					
HbA_{1c} <48mmol/mol	Intervention	68/103 (66.0%)	7·51	(2·40, 23·48)	p=0·0005
	Control	6/27 (22.2%)			
HbA_{1c} <42mmol/mol	Intervention	39/103 (37·9%)	15·40	(1·98, 120·12)	p=0·0091
	Control	1/27 (3.7%)			

Intervention effects reported as estimated odds ratios (Intervention:Control), based on mixed effects logistic regression model, adjusted for randomised group, study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.
Total N varies by outcome depending on data availability

Table S5: Secondary outcomes: physical activity, sleep duration and efficiency in intervention and control groups at baseline and 12 months

		N	Mean (SD)			Intervention Effect (Intervention:Control)			Intra-class coefficient
			Baseline	12months	Change	Estimate	95% CI	p-value	
Sleep duration (minutes/day)	Intervention	73	421·4 (77·1)	423·1 (74·8)	2 (86)	8.2	(-13·2, 29.5)	p=0.4522[(a)]	0.02
	Control	74	441·7 (64.5)	427·8 (61·8	-14 (63)				
Sleep efficiency (%)	Intervention	73	72·7 (10.7)	71·9 (11·9)	-0.8 (13.8)	-1.21	(-4.76, 2.35	p=0.5066[(b)]	0.03
	Control	74	74·5 (9.0)	74·1 (9.3)	-0.3 (10.4)				
Sedentary time (minutes/day)	Intervention	73	188·3 (63·2)	180·6 (67·3)	-8 (71)	-5·9	(-25·7, 13·9)	p=0·5587	<0·01
	Control	77	177·5 (65·2)	180·8 (69·9)	3 (63)				
Light activity (minutes/day)	Intervention	73	117·5 (39·2)	117·9 (42·9)	0 (42)	3·0	(-8·8, 14·8)	p=0·6184	<0·01
	Control	77	109·6 (46·6)	110·8 (44·7)	1 (37)				
Moderate activity (minutes/day)	Intervention	73	51·0 (21·3)	51·2 (23·1)	0·1 (22·3)	0·81	(-5·80, 7·42)	p=0·8110	<0·01
	Control	77	48·1 (26·5)	48·9 (26·5)	0·7 (21·4)				
Vigorous activity (minutes/day)	Intervention	73	0·9 (0·7)	0·8 (0·9	-0·03 (0·91)	0·03	(-0·23, 0·28)	p=0·8402[(c)]	0·05
	Control	77	0·7 (0·6)	0·7 (0·7)	0·01 (0·64)				

Intervention effects reported as estimated mean differences (Intervention-Control), based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.

N refers to number of participants with data available at baseline and 12 months for each outcome.

Some model residuals showed signs of non-Normal distribution:

(a): Results confirmed using non-parametric test of 12 month values (p=0.81) and change from baseline (p=0.23)

(b): Results confirmed using non-parametric test of 12 month values (p=0.47) and change from baseline (p=0.77)

(c): Results confirmed using non-parametric test of 12 month values (p=0.32) and change from baseline (p=0.55)

Table S6: Withdrawal from Treatment in Year 1 for those who commenced treatment (ITT population)

	Control (n=115)	Intervention (143)
Reason for withdrawal	0	26 (0)
No remission; patient decision	0	1 (3.8%)
Medical reasons	0	2 (7.7%)
Social reasons	0	8 (30.8%)
Limited weight loss	0	3 (11.5%)
Weight regain	0	1 (3.8%)
Other	0	6 (23.1%)
Not Known	0	5 (19.2%)

Table S7: Secondary outcomes: other binary outcomes in the intervention and control groups at 12 months

		N/Total (%)	Odds Ratio		
			Estimate	95% CI	p-value
	Control	121/148 (81.8%)			
Prescribed antihypertensive medications	Intervention	47/148 (31.8%)	0.30	(0.16, 0.54)	p=0.0001
	Control	91/148 (61.5%)			
Prescribed antidepressants	Intervention	40/148 (27.0%)	1.40	(0.79, 2.49)	p=0.2506
	Control	31/148 (20.9%)			
SBP >130mmHg	Intervention	67/128 (52.3%)	0.66	(0.37, 1.19)	p=0.1683
	Control	95/147 (64.6%)			
DBP >80mmHg	Intervention	80/128 (62.5%)	0.77	(0.46, 1.31)	p=0.3356
	Control	103/147 (70.1%)			

Intervention effects reported as estimated odds ratios (Intervention:Control), based on mixed effects logistic regression model, adjusted for randomised group, study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.
Total N varies by outcome depending on data availability.

Table S8: Secondary outcomes: serum lipids in the intervention and control groups at baseline and 12 months

		N	Mean (SD)			Intervention Effect (Intervention:Control)			ICC
			Baseline	12months	Change	Estimate	95% CI	p-value	
Total cholesterol (mmol/l)	Intervention	121	4·3 (1·1)	4·5 (1·3)	0·23 (1·36)	1·03	(0·97, 1·10)	p=0·2874	0·05
	Control	147	4·3 (1·1)	4·3 (1·1)	0·07 (0·87)				
HDL-cholesterol (mmol/l)	Intervention	121	1·1 (0·3)	1·2 (0·4)	0·13 (0·25)	1·06	(1·00, 1·13)	p=0·0563	0·15
	Control	147	1·2 (0·3)	1·2 (0·3)	0·04 (0·21)				
Triglycerides (mmol/l)	Intervention	121	2·1 (1·4)	1·7 (1·4)	-0·31 (1·33)	0·80	(0·72, 0·89)	p<0·0001	<0·01
	Control	147	1·9 (0·9)	2·0 (1·2)	0·09 (0·92)				

Intervention effects reported as estimated relative differences (Intervention:Control), based on mixed effects linear regression model of log-transformed lipid measures, adjusted for randomised group, baseline value (log-transformed), study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.

N refers to number of participants with data available at baseline and 12 months for each outcome. ICC: Intraclass Correlation Coefficient.

Table S9: Adverse effects identified a priori as relevant to the intervention treatment, experienced by intervention group participants during year one at study visits in each phase of the weight management programme. The usual-care control group was seen only at baseline and 12 months.

	TDR phase (12-20 weeks)				FR phase (2-8 weeks)				WLM phase (up to 52 weeks)			
	Total (n=139)	Mild	Moderate	Severe	Total (n=124)	Mild	Moderate	Severe	Total (n=94)	Mild	Moderate	Severe
Constipation	65 (46·8)	30 (21·6)	24 (17·3)	11 (7·9)	18 (14·5)	14 (11·3)	4 (3·2)	0 (0·0)	6 (6·4)	2 (2·1)	2 (2·1)	2 (2·1)
Sensitivity to cold	57 (41·0)	37 (26·6)	12 (8·6)	8 (5·8)	30 (24·2)	19 (15·3)	6 (4·8)	5 (4·0)	13 (13·8)	7 (7·4)	2 (2·1)	4 (4·3)
Headache	53 (38·1)	31 (22·3)	13 (9·4)	9 (6·5)	15 (12·1)	10 (8·1)	3 (2·4%)	2 (1·6)	8 (8·5)	5 (5·3)	2 (2·1)	1 (1·1)
Dizziness	49 (35·3)	40 (28·8)	7 (5·0)	2 (1·4)	11 (8·9)	3 (2·4)	6 (4·8)	2 (1·6)	7 (7·4)	4 (4·3)	3 (3·2)	0 (0·0)
Fatigue	45 (32·4)	24 (17·3)	11 (7·9)	10 (7·2)	18 (14·5)	10 (8·1)	3 (2·4)	5 (4·0)	8 (8·5)	2 (2·1)	0 (0·0)	6 (6·4)
Mood change	35 (25·2)	16 (11·5)	12 (8·6)	7 (5·0)	10 (8·1)	4 (3·2)	4 (3·2)	2 (1·6)	4 (4·3)	1 (1·1)	2 (2·1)	1 (1·1)
Nausea	25 (18·0)	15 (10·8)	4 (2·9)	6 (4·3)	3 (2·4)	3 (2·4)	0 (0·0)	0 (0·0)	1 (1·1)	1 (1·1)	0 (0·0)	0 (0·0)
Diarrhoea	23 (16·5)	11 (7·9)	10 (7·2)	2 (1·4)	5 (4·0)	4 (3·2)	1 (0·8)	0 (0·0)	1 (1·1)	1 (1·1)	0 (0·0)	0 (0·0)
Indigestion	20 (14·4)	15 (10·8)	3 (2·2)	2 (1·4)	4 (3·2)	2 (1·6)	2 (1·6)	0 (0·0)	1 (1·1)	1 (1·1)	0 (0·0)	0 (0·0)
Hair Loss	19 (13·7)	10 (7·2)	7 (5·0)	2 (1·4)	13 (10·5)	3 (2·4)	6 (4·8)	4 (3·2)	8 (8·5)	4 (4·3)	3 (3·2)	1 (1·1)

Data reported as N(%)

Table S10: Per-protocol analysis of primary outcomes

		N/Total (%)	Odds Ratio		
			Estimate	95% CI	p-value
Weight loss ≥15kg at 12 months	Intervention	36/128 (28·1%)	-	-	p<0·0001[(a)]
	Control	0/147 (0·0%)			
Diabetes remission (HbA_{1c} <48mmol/mol, off diabetic medication of ≥2 months)	Intervention	65/127[(b)] (51·2%)	23·8	(9·60, 58·8)	p<0·0001
	Control	6/147 (4·1%)			

Intervention effects reported as estimated odds ratios (Intervention:Control), based on mixed effects logistic regression model, adjusted for randomised group, study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect. For per protocol analyses, no assumptions were made about missing values.

(a) regression model could not be fitted for weight loss outcome; p-value from Fisher's Exact Test

(b) remission outcome missing for one subject in Intervention group due to blood sample not being obtained at 12 month visit, and no HbA_{1c} record being available in GP notes

Table S11: Subgroup analyses of primary outcomes: weight loss ≥15kg at 12 months. Given that none of the control group achieved this outcome, the planned analyses using logistic regression models with interaction terms were not possible, so the odds ratios presented here relate to achievement of the outcome in the Intervention group only, for each subgroup relative to the reference group

		Control	Intervention	Odds Ratio (within Intervention group)		
		N/Total (%)	N/Total (%)	Estimate	95% CI	p-value
Age at baseline (years)	<50	0/30 (0·0%)	9/52 (17·3%)	reference		
	50-54	0/31 (0·0%)	9/32 (28·1%)	1·78	(0·62, 5·17)	p=0·29
	55-59	0/31 (0·0%)	10/34 (29·4%)	2·14	(0·75, 6·07)	p=0·15
	≥60	0/57 (0·0%)	8/31 (25·8%)	1·64	(0·55, 4·86))	p=0·37
Sex	Male	0/93 (0·0%)	27/83 (32·5%)	reference		
	Female	0/56 (0·0%)	9/66 (13·6%)	0·32	(0·14, 0·76)	p=0·0094
Duration of diabetes (years)	<2	0/60 (0·0%)	6/50 (12·0%)	reference		
	≥2, <4	0/39 (0·0%)	13/47 (27·7%)	2·93	(1·00, 8·65)	p=0·051
	≥4, <6	0/50 (0·0%)	17/52 (32·7%)	3·82	(1·34, 10·85)	p=0·012
Baseline HbA_{1c} (%)	<7·0	0/50 (0·0%)	7/44 (15·9%)	reference		
	≥7·0, <8·0	0/66 (0·0%)	19/65 (29·2%)	2·10	(0·79, 5·60)	p=0·14
	≥8·0	0/33 (0·0%)	10/40 (25·0%)	1·92	(0·64, 5·77)	p=0·24
Baseline weight (kg)	<90	0/48 (0·0%)	3/40 (7·5%)	reference		
	≥90, <110	0/68 (0·0%)	18/71 (25·4%)	4·46	(1·21, 16·4)	p=0·024
	≥110	0/33 (0·0%)	15/38 (39·5%)	8·28	(2·13, 32·1)	p=0·0022
Number of oral anti-diabetic medications at baseline	None	0/34 (0·0%)	9/38 (23·7%)	reference		
	1	0/79 (0·0%)	14/65 (21·5%)	0·97	(0·36, 2·60)	p=0·96
	2+	0/36 (0·0%)	13/46 (28·3%)	1·37	(0·50, 3·73)	p=0·54

Estimated odds ratios based on mixed effects logistic regression model, adjusted for study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.

Table S12: Subgroup analyses of primary outcomes: remission of diabetes (HbA_{1c} <48mmol/mol, off anti-diabetic medication for 2 months) at 12 months. Given that few in the control group achieved this outcome, the planned analyses using logistic regression models with interaction terms were highly underpowered, so the odds ratios presented here relate to achievement of the outcome in the Intervention group only, for each subgroup relative to the reference group

		Control	Intervention	Odds Ratio (within Intervention group)		
		N/Total (%)	N/Total (%)	Estimate	95% CI	p-value
Age at baseline (years)	<50	1/30 (3·3%)	17/52 (32·7%)	reference		
	50-54	1/31 (3·2%)	14/32 (43·8%)	1·53	(0·61, 3·83)	p=0·36
	55-59	1/31 (3·2%)	18/34 (52·9%)	2·47	(1·00, 6·09)	p=0·049
	≥60	3/57 (5·3%)	19/31 (61·3%)	3·27	(1·28, 8·31))	p=0·.013
Sex	Male	4/93 (4·3%)	27/83 (49·4%)	reference		
	Female	2/56 (3·6%)	9/66 (40·9%)	0·70	(0·36, 1·36)	p=0·29
Duration of diabetes (years)	<2	6/60 (10·0%)	22/50 (44·0%)	reference		
	≥2, <4	0/39 (0·0%)	24/47 (51·1%)	1·38	(0·61, 3·09)	p=0·44
	≥4, <6	0/50 (0·0%)	33/52 (42·3%)	0·97	(0·44, 2·13)	p=0·93
Baseline HbA_{1c} (%)	<7·0	5/50 (10·0%)	25/44 (56·8%)	reference		
	≥7·0, <8·0	1/66 (1·5%)	32/65 (49·2%)	0·68	(0·31, 1·53)	p=0·35
	≥8·0	0/33 (0·0%)	11/40 (27·5%)	0·28	(0·10, 0·73)	p=0·0099
Baseline weight (kg)	<90	3/48 (6·2%)	19/40 (47·5%)	reference		
	≥90, <110	1/68 (1·5%)	31/71 (43·7%)	2·10	(0·79, 5·60)	p=0·14
	≥110	2/33 (6·1%)	18/38 (47·4%)	1·92	(0·64, 5·77)	p=0·24
Number of oral anti-diabetic medications at baseline	None	6/34 (17·6%)	26/38 (68·4%)	reference		
	1	0/79 (0·0%)	30/65 (46·2%)	0·42	(0·18, 1·01)	p=0·053
	2+	0/36 (0·0%)	12/46 (26·1%)	0·17	(0·06, 0·45)	p=0·0004

Estimated odds ratios based on mixed effects logistic regression model, adjusted for study centre (Tyneside, Scotland), and practice list size (≤5700, >5700) as fixed effects, and GP practice as a random effect.