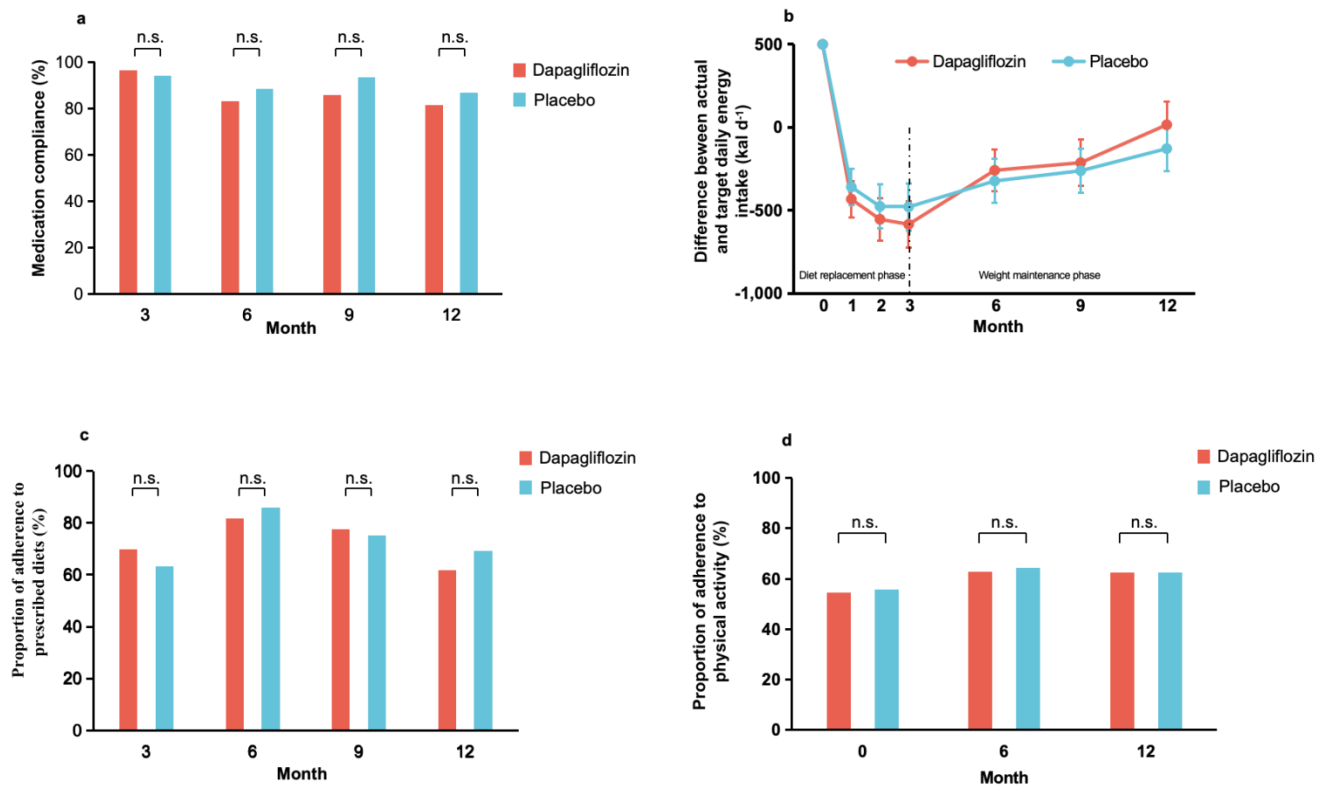


Appendix

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Supplementary figure. Intervention compliance during the 12-month intervention

a, medication compliance over 12 months. Medication compliance was calculated as the percentage of number of drugs distributed minus the number of drugs returned divided by the number of drugs that should be taken. b, daily energy intake target achieved over 12 months. Difference between actual and target daily energy intake was the actual daily energy intake evaluated by dietitian minus the targeted daily energy intake. c, proportion of adherence to prescribed diets over 12 months. Adherence to prescribed diets was defined as average daily energy intake per month achieving the targeted daily energy intake for the time being. d, proportion of adherence to physical activity over 12 months. Adherence to physical activity was defined as actual METs achieving the targeted METs.

METs=metabolic equivalents.

Supplementary table A. Dietary intake, physical activity and quality of life during the 12-month intervention

Variables	Dapagliflozin (n=165)	Placebo (n=163)	P value
Energy intake (kcal/d)			
Baseline	2356.8±883.0	2256.3±775.0	0.28
Month 3	1422.4±281.2	1393.4±253.2	0.36
Month 6	1388.3±273.2	1405.7±271.3	0.62
Final Visit	1443.5±300.1	1403.5±295.4	0.34
Carbohydrate intake (%)			
Baseline	50.1(41.6-57.2)	51.2(42.1-58.3)	0.49
Month 3	40.3(36.3-45.3)	39.8(34.0-43.3)	0.069
Month 6	43.6(37.7-48.3)	41.3(36.3-46.3)	0.081
Final Visit	42.7(37.3-47.0)	41.5(36.0-46.7)	0.79
Protein intake (%)			
Baseline	16.9(14.6-19.0)	16.9(14.4-19.4)	0.55
Month 3	26.0(23.0-29.0)	26.7(24.0-29.5)	0.27
Month 6	20.7(18.7-24.0)	22.0(18.0-25.3)	0.22
Final Visit	21.0(19.0-24.0)	22.0(19.0-25.0)	0.49
Fat intake (%)			
Baseline	33.9(26.8-40.2)	32.5(26.4-39.9)	0.34
Month 3	33.3(28.3-38.0)	33.7(30.0-37.7)	0.18
Month 6	35.3(31.7-39.0)	36.0(32.5-40.7)	0.19
Final Visit	36.3(32.0-39.0)	36.0(31.0-40.0)	0.86
Physical activity (MET hour per week)			
Baseline	11.6(4.4-19.6)	11.6(3.3-17.9)	0.56
Month 6	12.8(7.7-24.5)	13.1(7.3-25.6)	1.00
Final Visit	12.3(7.7-25.6)	11.6(7.7-23.1)	0.098
SF-12 score Physical component summary			
Baseline	50.4(44.8-53.8)	49.9(45.8-53.5)	0.92
Month 6	51.8(47.5-54.2)	51.0(47.5-53.6)	0.22
Final Visit	52.4(48.2-55.3)	51.2(47.3-53.8)	0.37
SF-12 score Mental component summary			
Baseline	56.0(50.0-58.9)	56.0(49.9-58.6)	0.69
Month 6	57.7(52.7-59.9)	56.2(51.9-58.8)	0.33
Final Visit	57.7(52.8-59.8)	56.7(50.5-58.6)	0.36

Data are presented as the mean ± SD or median (IQR).

MET=metabolic equivalents.

Supplementary table B. Adjusted effects of dapagliflozin versus placebo on diabetes remission at request

	Risk ratio (95% CI)	P value
Adjusted for intervention time*	1.63 (1.14-2.31)	0.007
Adjusted for follow-up time**	1.54 (1.11-2.13)	0.009

As requested by *the BMJ* Editorial team, we used a Poisson model with robust variance to estimate the risk ratios and confidence intervals. In this model, log-transformed time variables were treated as offset terms. For log-transformation, the follow-up or intervention time was added by 0.5 to handle the zero value. *The intervention time was the time of dapagliflozin or placebo treatment. **The follow-up time was the time when diabetes remission was determined (i.e. 2 months after either dapagliflozin or placebo was stopped) for participants who reached drug stopping criteria, and the time of final visit for participants who discontinued the trial in advance or did not meet drug stopping criteria.

Supplementary table C. Effects of dapagliflozin versus placebo on diabetes remission in per protocol analysis set

	Dapagliflozin (n=138)	Placebo (n=121)	Risk ratio (95% CI) *	P value
Diabetes remission	73 (52.9%)	45 (37.2%)	1.36 (1.05-1.80)	0.017

Data are presented as the number (percentage) or otherwise stated.

*A cochrane-Mantel-Haenszel (CMH) test, stratified according to whether treated with metformin or not at baseline, was used to estimate risk ratio and corresponding 95% CI.

Supplementary table D. Effects of dapagliflozin versus placebo on long-term diabetes remission

	Dapagliflozin (n=165)	Placebo (n=163)	Risk ratio (95% CI) *	P value
3 month remission†	55 (33.3%)	33 (20.2%)	1.64 (1.14-2.37)	0.007
4 month remission‡	53 (32.1%)	30 (18.4%)	1.74 (1.18-2.56)	0.004

Data are presented as the number (percentage) or otherwise stated.

*A cochrane-Mantel-Haenszel (CMH) test, stratified according to whether treated with metformin or not at baseline, was used to estimate risk ratio and corresponding 95% CI.

† Diabetes remission was defined as HbA1c<6.5% and FPG<126 mg/dl in the absence of any anti-diabetic medication for at least 3 months

‡ Diabetes remission was defined as HbA1c<6.5% and FPG<126 mg/dl in the absence of any anti-diabetic medication for at least 4 months.

Supplementary table E. Effects of dapagliflozin versus placebo on metabolic risk factors after multiple imputations. †

Variables	Dapagliflozin (n=165)	Placebo (n=163)	Mean difference (95% CI)	P value
Change in body weight (kg)	-4.2 (-4.8 to -3.6)	-2.6 (-3.2 to -1.9)	-1.6 (-2.2 to -1.0)	<0.001
Change in waist circumference (cm)	-4.0 (-4.7 to -3.4)	-3.5 (-4.1 to -2.8)	-0.6 (-1.2 to 0.1)	0.084
Change in fat mass (%)	-1.4 (-1.8 to -1.1)	-1.0 (-1.3 to -0.6)	-0.5 (-1.0 to 0)	0.06
Change in lean mass (%)	1.4 (0.8 to 2.0)	1.3 (0.7 to 1.9)	0.1 (-0.5 to 0.7)	0.81
Change in systolic blood pressure (mmHg)	-4.6 (-6.2 to -3.0)	-2.8 (-4.3 to -1.2)	-1.8 (-3.5 to -0.2)	0.027
Change in diastolic blood pressure (mmHg)	-1.5 (-2.6 to -0.4)	-1.4 (-2.5 to -0.2)	-0.2 (-1.4 to 1.0)	0.77
Change in fasting plasma glucose (mg/dl)	-24.8 (-27.4 to -22.1)	-14.3 (-17.0 to -11.6)	-10.4 (-13.5 to -7.3)	<0.001
Change in HbA _{1c} (%)	-1.0 (-1.1 to -1.0)	-0.9 (-1.0 to -0.9)	-0.1 (-0.2 to -0.1)	0.001
Change in HOMA-IR	-1.6 (-1.9 to -1.4)	-0.7 (-1.0 to -0.4)	-0.9 (-1.3 to -0.6)	<0.001
Change in HOMA- β (%)	6.5 (-0.6 to 13.5)	9.5 (2.3 to 16.7)	-3.1 (-13.0 to 6.9)	0.55
Change in total cholesterol (mg/dl)	0.8 (-2.4 to 4.0)	-1.1 (-4.4 to 2.1)	2.0 (-1.7 to 5.7)	0.30
Change in low-density lipoprotein cholesterol (mg/dl)	0.9 (-2.5 to 4.2)	-1.3 (-4.7 to 2.1)	2.2 (-1.2 to 5.5)	0.20
Change in high-density lipoprotein cholesterol (mg/dl)	2.8 (2.1 to 3.5)	1.4 (0.7 to 2.1)	1.5 (0.5 to 2.4)	0.003
Change in triglycerides (mg/dl)	-24.3 (-35.0 to -13.6)	-7.9 (-18.8 to 2.9)	-16.4 (-31.6 to -1.2)	0.034

Multiple imputations were conducted using Markov Chain Monte Carlo method. † Changes of variables are presented as least-square mean changes (95% CI); differences are reported as estimated mean differences, i.e. effect of dapagliflozin minus that of placebo, based on a mixed-effects linear regression model with study centers as random effects, stratification of treatments, baseline value, treatment group, time, and their interaction as fixed effects. CI, confidence interval; HbA_{1c}, glycated haemoglobin; HOMA-IR, homeostatic model assessment of insulin resistance; HOMA- β , homeostatic model assessment of β -cell function.