

Supplementary Material

SUPPLEMENTARY MATERIAL 1

The Mini-Mental State Examination (MMSE) validated for the Spanish population was used as a general cognitive screening test, which is an assessment of general cognitive function. The MMSE is divided into two sections, the first of which requires vocal responses only and covers orientation, memory, and attention, being the maximum score 21. The second part tests the ability to name, follow verbal and written commands, write a sentence spontaneously, and copy a complex polygon similar to a Bender-Gestalt figure, with a maximum possible score of 9. A high MMSE score indicates absence of cognitive decline [1].

The Clock Drawing Test (CDT) was used as a cognitive screening tool and the 7-point version, currently used for elderly Spanish populations, was performed [2]. Higher scores indicate better performance. The CDT assesses visuospatial, visuoconstruction and memory capacities, as well as verbal and numerical knowledge [3].

The Digit Span Test (DST) of the WAIS-III Spanish version measuring attention and memory functions was used [4]. The Digit Span Test forward version (DST-f) requires participants to verbally repeat in the same order as provided, a number sequence, varying from 2 to 9 numbers, being representative of immediate memory. The DST backward version (DST-b) requires participants to verbally repeat in reverse order a number sequence, varying from 2 to 8 numbers, being representative of working memory function [5]. For both tests, the task is finished when the participant fails two attempts consecutively.

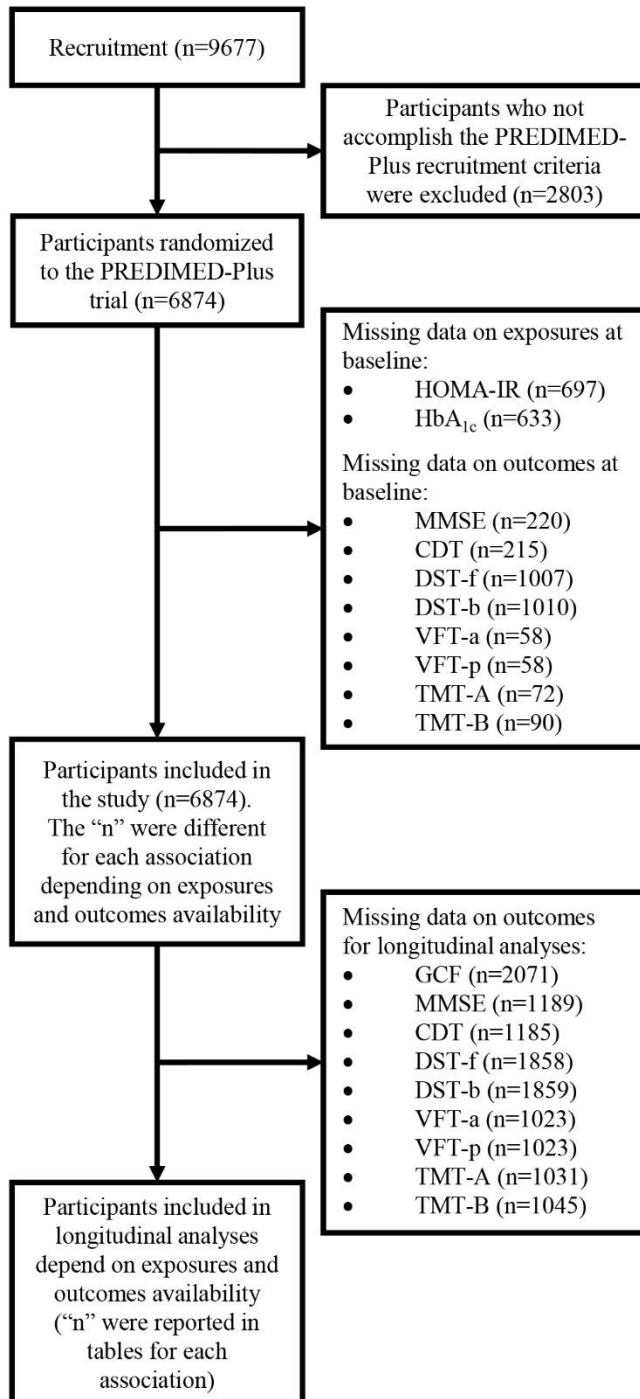
The Spanish Verbal Fluency Tests (VFTs) were used to assess language and executive function [6]. Specifically, we used the semantic VFT animal category version (VFT-a) and the phonemic VFT letter “p” version (VFT-p). Participants were instructed to say the maximum number of words related to the semantic field of animals for VFT-a and the maximum number of words starting with the letter “p” for VFT-p, having a time limit for both tests of 60 seconds. The total score was obtained from the row of properly stated words. The semantic VFT presents more influence on verbal abilities, whereas the phonologic VFT presents more influence on executive control ability [7].

The Trail Making Test (TMT) with normative data provided for the Spanish population was used [8]. The TMT consists of 25 circles spread over a sheet of paper and contains part A (TMT-A) and part B (TMT-B). In TMT-A, participants were asked to connect consecutive numbers (1–2–3–...) in the correct order by drawing a line. In TMT-B, they were asked to connect consecutive numbers and letters in an alternating numeric and alphabetic sequence (1–A–2–B–3–C–...). Each part is scored according to the time taken to complete the task, where more time spent indicates poorer performance. TMTs discriminate cognitive dysfunction [9] and TMT-A assesses attention and processing speed capacities [8] whereas TMT-B requires more executive function abilities such as cognitive flexibility [10].

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Supplementary Figure 1. Flow chart of participant selection for the present study population.



HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; HbA1c, glycated hemoglobin; GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B.

Supplementary Table 1 Association between dichotomized baseline diabetes status and changes in cognitive Z-scores.

Z-scores	Diabetes status	Model 1		Model 2	
		β (95% CI)	P-value	β (95% CI)	P-value
GCF	No-Diabetes (n=3452)	Ref.		Ref.	
	Diabetes (n=1351)	-0.17 (-0.23, -0.11)	<0.001*	-0.07 (-0.10, -0.04)	<0.001*
MMSE	No-Diabetes (n=3973)	Ref.		Ref.	
	Diabetes (n=1712)	-0.09 (-0.14, -0.03)	0.002*	-0.06 (-0.11, -0.01)	0.026*
CDT	No-Diabetes (n=3977)	Ref.		Ref.	
	Diabetes (n=1712)	-0.06 (-0.11, -0.01)	0.048	-0.03 (-0.09, 0.02)	0.234
DST-f	No-Diabetes (n=3598)	Ref.		Ref.	
	Diabetes (n=1418)	-0.08 (-0.14, -0.02)	0.007*	-0.05 (-0.11, 0.01)	0.058
DST-b	No-Diabetes (n=3597)	Ref.		Ref.	
	Diabetes (n=1418)	-0.07 (-0.12, -0.01)	0.022*	-0.03 (-0.09, 0.02)	0.265
VFT-a	No-Diabetes (n=3977)	Ref.		Ref.	
	Diabetes (n=1759)	-0.14 (-0.20, -0.09)	<0.001*	-0.10 (-0.15, -0.05)	<0.001*
VFT-p	No-Diabetes (n=4092)	Ref.		Ref.	
	Diabetes (n=1759)	-0.14 (-0.20, -0.09)	<0.001*	-0.09 (-0.15, -0.04)	<0.001*
TMT-A§	No-Diabetes (n=4088)	Ref.		Ref.	
	Diabetes (n=1755)	0.16 (0.10, 0.21)	<0.001*	0.12 (0.07, 0.17)	<0.001*
TMT-B§	No-Diabetes (n=4080)	Ref.		Ref.	
	Diabetes (n=1749)	0.17 (0.11, 0.22)	<0.001*	0.12 (0.07, 0.17)	<0.001*

GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B.

§ Inverse neuropsychological assessment score.

Model 1: adjusted for sex, age (in years), intervention group, and center size (<250; 250-300, 300-400; \geq 400)

Model 2: further adjusted for baseline education level (primary school; secondary school; college), civil status (single, divorced or separated; married; widower), physical activity (MET min/week), smoking habits (smoker; former smoker; never smoker), alcohol intake (g/day, adding the quadratic term), 17-point Mediterranean diet score, BMI (kg/m²), hypertension (yes/no), hypercholesterolemia (yes/no), and depressive symptomatology (yes/no).

Beta coefficients were estimated using linear regression models with robust standard errors to account for intracluster correlations.

* Significant association after Benjamini-Hochberg correction .

Supplementary Table 2 Longitudinal cognitive impairment incidence in participants with normal cognitive performance at baseline.

Cognitive assessments	Diabetes status	Model 1		Model 2	
		Odds ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
GCF	No-Diabetes (n=3131)	Ref.		Ref.	
	Diabetes (n=1191)	1.43 (1.03, 1.99)	0.031	1.34 (0.96, 1.87)	0.084
MMSE	No-Diabetes (n=3801)	Ref.		Ref.	
	Diabetes (n=1613)	1.44 (0.99, 2.08)	0.054	1.38 (0.95, 2.01)	0.094
CDT	No-Diabetes (n=3558)	Ref.		Ref.	
	Diabetes (n=1510)	1.17 (0.94, 1.44)	0.153	1.11 (0.90, 1.38)	0.331
DST-f	No-Diabetes (n=3403)	Ref.		Ref.	
	Diabetes (n=1328)	0.96 (0.50, 1.87)	0.913	0.88 (0.46, 1.66)	0.688
DST-b	No-Diabetes (n=3570)	Ref.		Ref.	
	Diabetes (n=1409)	1.07 (0.52, 2.17)	0.856	1.04 (0.51, 2.15)	0.909
VFT-a	No-Diabetes (n=3921)	Ref.		Ref.	
	Diabetes (n=1677)	1.39 (1.08, 1.79)	0.011	1.30 (1.01, 1.68)	0.048
VFT-p	No-Diabetes (n=3898)	Ref.		Ref.	
	Diabetes (n=1684)	1.08 (0.80, 1.46)	0.607	1.02 (0.75, 1.39)	0.908
TMT-A§	No-Diabetes (n=3864)	Ref.		Ref.	
	Diabetes (n=1625)	1.30 (0.96, 1.75)	0.090	1.23 (0.91, 1.67)	0.177
TMT-B§	No-Diabetes (n=3676)	Ref.		Ref.	
	Diabetes (n=1492)	1.24 (0.98, 1.58)	0.076	1.19 (0.93, 1.53)	0.170

GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B.

§ Inverse neuropsychological assessment score.

Cognitive impairment was defined by the dichotomization of neuropsychological assessments at respective baseline and follow-up visit (GCF, impaired $\leq 10^{\text{th}}$ percentile; MMSE, impaired ≤ 24 ; CDT, impaired ≤ 4 ; VFT-a, VFT-p, DST-d, DST-b, impaired \leq respective mean - 1.5 SD; TMT-A, TMT-B \geq respective mean + 1.5 SD) Model 1: adjusted for sex, age (in years), intervention group, and center size (<250; 250-300, 300-400; ≥ 400)

Model 2: further adjusted for baseline education level (primary school; secondary school; college), civil status (single, divorced or separated; married; widower), physical activity (MET min/week), smoking habits (smoker; former smoker; never smoker), alcohol intake (g/day, adding the quadratic term), 17-point Mediterranean diet score, BMI (kg/m²), hypertension (yes/no), hypercholesterolemia (yes/no), and depressive symptomatology (yes/no).

Odd ratios were estimated using logistic regression models with robust standard errors to account for intracluster correlations.

Supplementary Table 3 Association between baseline diabetes control and changes in cognitive Z-scores.

Z-scores	Diabetes control	Model 1		Model 2	
		β (95% CI)	P-value	β (95% CI)	P-value
GCF	Good (n=761)	Ref.		Ref.	
	Poor (n=590)	-0.14 (-0.23, -0.04)	0.006*	-0.07 (-0.16, 0.01)	0.089
MMSE	Good (n=957)	Ref.		Ref.	
	Poor (n=755)	-0.08 (-0.17, 0.01)	0.091	-0.04 (-0.14, 0.05)	0.338
CDT	Good (n=958)	Ref.		Ref.	
	Poor (n=754)	-0.02 (-0.11, 0.07)	0.672	0.01 (-0.09, 0.10)	0.940
DST-f	Good (n=799)	Ref.		Ref.	
	Poor (n=619)	-0.05 (-0.15, 0.05)	0.341	-0.02 (-0.12, 0.07)	0.674
DST-b	Good (n=799)	Ref.		Ref.	
	Poor (n=619)	-0.04 (-0.13, 0.06)	0.480	-0.01 (-0.10, 0.09)	0.939
VFT-a	Good (n=983)	Ref.		Ref.	
	Poor (n=776)	-0.11 (-0.20, -0.02)	0.013	-0.07 (-0.16, 0.01)	0.090
VFT-p	Good (n=983)	Ref.		Ref.	
	Poor (n=776)	-0.18 (-0.27, -0.09)	<0.001*	-0.13 (-0.22, -0.04)	0.003*
TMT-A§	Good (n=982)	Ref.		Ref.	
	Poor (n=773)	0.10 (0.01, 0.20)	0.031	0.06 (-0.03, 0.15)	0.212
TMT-B§	Good (n=981)	Ref.		Ref.	
	Poor (n=768)	0.07 (-0.03, 0.17)	0.136	0.01 (-0.08, 0.10)	0.820

GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B.

§ Inverse neuropsychological assessment score.

Diabetes control was assessed in participants with diabetes.

Good control when HbA1c was ≤ 57 mmol/mol ($\leq 7\%$); Poor control when HbA1c was ≥ 57 mmol/mol ($\geq 7\%$)

Model 1: adjusted for sex, age (in years), intervention group, and center size (<250; 250-300, 300-400; ≥ 400)

Model 2: further adjusted for baseline education level (primary school; secondary school; college), civil status (single, divorced or separated; married; widower), physical activity (MET min/week), smoking habits (smoker; former smoker; never smoker), alcohol intake (g/day, adding the quadratic term), 17-point Mediterranean diet score, BMI (kg/m²), hypertension (yes/no), hypercholesterolemia (yes/no), and depressive symptomatology (yes/no).

Beta coefficients were estimated using linear regression models with robust standard errors to account for intracluster correlations.

* Significant association after Benjamini-Hochberg correction.

Supplementary Table 4 Association between baseline insulin treatment and changes in cognitive Z-scores.

Z-scores	Insulin treatment	Model 1		Model 2		Model 3	
		β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
GCF	No (n=1153)	Ref.		Ref.		Ref.	
	Yes (n=198)	-0.33 (-0.48, -0.18)	<0.001*	-0.31 (-0.44, -0.18)	<0.001*	-0.28 (-0.42, -0.15)	<0.001*
MMSE	No (n=1456)	Ref.		Ref.		Ref.	
	Yes (n=256)	-0.05 (-0.18, 0.09)	0.508	-0.01 (-0.14, 0.13)	0.940	0.01 (-0.13, 0.15)	0.940
CDT	No (n=1456)	Ref.		Ref.		Ref.	
	Yes (n=256)	-0.11 (-0.24, 0.02)	0.102	-0.09 (-0.22, 0.04)	0.177	-0.07 (-0.21, 0.07)	0.299
DST-f	No (n=1211)	Ref.		Ref.		Ref.	
	Yes (n=207)	-0.23 (-0.36, -0.09)	0.001*	-0.23 (-0.35, -0.10)	<0.001*	-0.24 (-0.38, -0.11)	<0.001*
DST-b	No (n=1211)	Ref.		Ref.		Ref.	
	Yes (n=207)	-0.18 (-0.31, -0.04)	0.010*	-0.16 (-0.28, -0.04)	0.011*	-0.17 (-0.30, -0.04)	0.011*
VFT-a	No (n=1495)	Ref.		Ref.		Ref.	
	Yes (n=264)	-0.18 (-0.31, 0.05)	0.005*	-0.15 (-0.27, -0.03)	0.013*	-0.12 (-0.24, 0.01)	0.066
VFT-p	No (n=1495)	Ref.		Ref.		Ref.	
	Yes (n=264)	-0.22 (-0.34, -0.09)	0.001*	-0.19 (-0.31, -0.07)	0.002*	-0.15 (-0.27, -0.02)	0.024*
TMT-A§	No (n=1492)	Ref.		Ref.		Ref.	
	Yes (n=263)	0.25 (0.10, 0.39)	0.001*	0.20 (0.06, 0.34)	0.006*	0.17 (0.02, 0.33)	0.031*
TMT-B§	No (n=1488)	Ref.		Ref.		Ref.	
	Yes (n=261)	0.25 (0.11, 0.39)	<0.001*	0.20 (0.07, 0.33)	0.003*	0.19 (0.05, 0.33)	0.008*

GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B. § Inverse neuropsychological assessment score.

Insulin treatment was assessed in participants with diabetes.

Model 1: adjusted for sex, age (in years), intervention group, and center size (<250; 250-300, 300-400; \geq 400).

Model 2: further adjusted for baseline education level (primary school; secondary school; college), civil status (single, divorced or separated; married; widower), physical activity (MET min/week), smoking habits (smoker; former smoker; never smoker), alcohol intake (g/day, adding the quadratic term), 17-point Mediterranean diet score, BMI (kg/m²), hypertension (yes/no), hypercholesterolemia (yes/no), and depressive symptomatology (yes/no).

Model 3: further adjusted for baseline diabetes control (good; poor); diabetes duration (<5-year diabetes duration; \geq 5-year diabetes duration).

Beta coefficients were estimated using linear regression models with robust standard errors to account for intracluster correlations.

* Significant association after Benjamini-Hochberg correction.

Supplementary Table 5 Association between baseline sulfonylureas treatment and changes in cognitive Z-scores.

Z-scores	Sulfonylureas treatment	Model 1		Model 2		Model 3	
		β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
GCF	No (n=1184)	Ref.		Ref.		Ref.	
	Yes (n=167)	-0.13 (-0.28, 0.02)	0.087	-0.07 (-0.20, 0.06)	0.269	-0.03 (-0.17, 0.10)	0.650
MMSE	No (n=1494)	Ref.		Ref.		Ref.	
	Yes (n=218)	-0.05 (-0.19, 0.09)	0.479	-0.03 (-0.17, 0.10)	0.631	-0.02 (-0.17, 0.12)	0.735
CDT	No (n=1493)	Ref.		Ref.		Ref.	
	Yes (n=219)	-0.09 (-0.23, 0.04)	0.183	-0.08 (-0.22, 0.06)	0.240	-0.07 (-0.21, 0.08)	0.350
DST-f	No (n=1243)	Ref.		Ref.		Ref.	
	Yes (n=175)	-0.06 (-0.21, 0.09)	0.415	-0.02 (-0.16, 0.13)	0.817	-0.01 (-0.16, 0.14)	0.893
DST-b	No (n=1243)	Ref.		Ref.		Ref.	
	Yes (n=175)	-0.01 (-0.15, 0.14)	0.917	0.05 (-0.09, 0.19)	0.504	0.06 (-0.09, 0.20)	0.441
VFT-a	No (n=1534)	Ref.		Ref.		Ref.	
	Yes (n=225)	-0.03 (-0.16, 0.10)	0.649	0.01 (-0.12, 0.14)	0.893	0.05 (-0.08, 0.18)	0.480
VFT-p	No (n=1534)	Ref.		Ref.		Ref.	
	Yes (n=225)	-0.14 (-0.28, -0.01)	0.047	-0.10 (-0.22, 0.03)	0.134	-0.05 (-0.18, 0.07)	0.406
TMT-A§	No (n=1530)	Ref.		Ref.		Ref.	
	Yes (n=225)	0.26 (0.09, 0.43)	0.003	0.22 (0.07, 0.38)	0.005	0.20 (0.04, 0.36)	0.015
TMT-B§	No (n=1525)	Ref.		Ref.		Ref.	
	Yes (n=224)	0.14 (-0.01, 0.28)	0.054	0.09 (-0.03, 0.22)	0.156	0.09 (-0.06, 0.20)	0.280

GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B § Inverse neuropsychological assessment score.

Sulfonylureas treatment was assessed in participants with diabetes.

Model 1: adjusted for sex, age (in years), intervention group, and center size (<250; 250-300, 300-400; \geq 400).

Model 2: further adjusted for baseline education level (primary school; secondary school; college), civil status (single, divorced or separated; married; widower), physical activity (MET min/week), smoking habits (smoker; former smoker; never smoker), alcohol intake (g/day, adding the quadratic term), 17-point Mediterranean diet score, BMI (kg/m²), hypertension (yes/no), hypercholesterolemia (yes/no), and depressive symptomatology (yes/no).

Model 3: further adjusted for baseline diabetes control (good; poor); diabetes duration (<5-year diabetes duration; \geq 5-year diabetes duration).

Beta coefficients were estimated using linear regression models with robust standard errors to account for intracluster correlations.

Supplementary Table 6 Association between baseline metformin treatment and changes in cognitive Z-scores.

Z-scores	Metformin treatment	Model 1		Model 2		Model 3	
		β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
GCF	No (n=313)	Ref.		Ref.		Ref.	
	Yes (n=1038)	0.03 (-0.09, 0.15)	0.615	0.04 (-0.06, 0.15)	0.441	0.07 (-0.04, 0.18)	0.202
MMSE	No (n=400)	Ref.		Ref.		Ref.	
	Yes (n=1312)	-0.02 (-0.13, 0.09)	0.701	-0.02 (-0.13, 0.09)	0.718	-0.02 (-0.13, 0.09)	0.764
CDT	No (n=398)	Ref.		Ref.		Ref.	
	Yes (n=1314)	0.04 (-0.07, 0.15)	0.466	0.05 (-0.06, 0.16)	0.374	0.07 (-0.05, 0.18)	0.245
DST-f	No (n=322)	Ref.		Ref.		Ref.	
	Yes (n=1096)	-0.03 (-0.14, 0.09)	0.674	-0.01 (-0.12, 0.11)	0.902	-0.01 (-0.12, 0.11)	0.950
DST-b	No (n=322)	Ref.		Ref.		Ref.	
	Yes (n=1096)	0.05 (-0.07, 0.16)	0.425	0.07 (-0.04, 0.18)	0.185	0.08 (-0.03, 0.19)	0.159
VFT-a	No (n=403)	Ref.		Ref.		Ref.	
	Yes (n=1356)	-0.07 (-0.17, 0.04)	0.208	-0.06 (-0.15, 0.04)	0.261	-0.04 (-0.14, 0.06)	0.453
VFT-p	No (n=403)	Ref.		Ref.		Ref.	
	Yes (n=1356)	-0.04 (-0.15, 0.07)	0.517	-0.03 (-0.13, 0.07)	0.557	-0.01 (-0.11, 0.09)	0.862
TMT-A§	No (n=403)	Ref.		Ref.		Ref.	
	Yes (n=1352)	0.01 (-0.11, 0.12)	0.919	0.01 (-0.11, 0.12)	0.924	-0.02 (-0.14, 0.10)	0.785
TMT-B§	No (n=401)	Ref.		Ref.		Ref.	
	Yes (n=1348)	-0.01 (-0.12, 0.11)	0.904	-0.01 (-0.12, 0.10)	0.845	-0.03 (-0.14, 0.08)	0.587

GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B § Inverse neuropsychological assessment score.

Metformin treatment was assessed in participants with diabetes.

Model 1: adjusted for sex, age (in years), intervention group, and center size (<250; 250-300, 300-400; \geq 400).

Model 2: further adjusted for baseline education level (primary school; secondary school; college), civil status (single, divorced or separated; married; widower), physical activity (MET min/week), smoking habits (smoker; former smoker; never smoker), alcohol intake (g/day, adding the quadratic term), 17-point Mediterranean diet score, BMI (kg/m²), hypertension (yes/no), hypercholesterolemia (yes/no), and depressive symptomatology (yes/no).

Model 3: further adjusted for baseline diabetes control (good; poor); diabetes duration (<5-year diabetes duration; \geq 5-year diabetes duration).

Beta coefficients were estimated using linear regression models with robust standard errors to account for intracluster correlations.

Supplementary Table 7 Association between baseline IDPP-4 treatment and changes in cognitive Z-scores.

Z-scores	IDPP4 treatment	Model 1		Model 2		Model 3	
		β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
GCF	No (n=1010)	Ref.		Ref.		Ref.	
	Yes (n=341)	-0.05 (-0.16, 0.07)	0.434	-0.03 (-0.13, 0.07)	0.565	0.01 (-0.10, 0.12)	0.827
MMSE	No (n=1296)	Ref.		Ref.		Ref.	
	Yes (n=416)	0.01 (-0.11, 0.11)	0.961	0.01 (-0.09, 0.12)	0.814	0.02 (-0.09, 0.13)	0.704
CDT	No (n=1297)	Ref.		Ref.		Ref.	
	Yes (n=415)	-0.05 (-0.17, 0.06)	0.361	-0.05 (-0.17, 0.06)	0.353	-0.04 (-0.16, 0.08)	0.551
DST-f	No (n=1062)	Ref.		Ref.		Ref.	
	Yes (n=356)	0.06 (-0.06, 0.18)	0.327	0.06 (-0.05, 0.18)	0.280	0.08 (-0.04, 0.20)	0.214
DST-b	No (n=1062)	Ref.		Ref.		Ref.	
	Yes (n=356)	0.07 (-0.05, 0.19)	0.266	0.08 (-0.04, 0.19)	0.193	0.09 (-0.03, 0.20)	0.130
VFT-a	No (n=1336)	Ref.		Ref.		Ref.	
	Yes (n=423)	-0.05 (-0.15, 0.05)	0.341	-0.04 (-0.14, 0.05)	0.391	-0.01 (-0.11, 0.09)	0.792
VFT-p	No (n=1336)	Ref.		Ref.		Ref.	
	Yes (n=423)	-0.05 (-0.16, 0.06)	0.365	-0.04 (-0.15, 0.06)	0.423	-0.01 (-0.11, 0.10)	0.910
TMT-A§	No (n=1333)	Ref.		Ref.		Ref.	
	Yes (n=422)	0.05 (-0.05, 0.16)	0.341	0.04 (-0.06, 0.14)	0.459	0.01 (-0.10, 0.11)	0.889
TMT-B§	No (n=1327)	Ref.		Ref.		Ref.	
	Yes (n=422)	0.02 (-0.09, 0.13)	0.702	0.01 (-0.10, 0.11)	0.928	-0.02 (-0.13, 0.08)	0.692

IDPP-4, dipeptidyl peptidase-4 inhibitors; GCF, Global Cognitive Function; MMSE, Mini-Mental State Examination; CDT, Clock Drawing Test; DST-f, Digit Span Test forward section; DST-b, Digit Span Test backward section; VFT-a, Verbal Fluency Test animal category; VFT-p, Verbal Fluency Test letter “p”; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B.

§ Inverse neuropsychological assessment score.

IDDP-4 treatment was assessed in participants with diabetes.

Model 1: adjusted for sex, age (in years), intervention group, and center size (<250; 250-300, 300-400; \geq 400).

Model 2: further adjusted for baseline education level (primary school; secondary school; college), civil status (single, divorced or separated; married; widower), physical activity (MET min/week), smoking habits (smoker; former smoker; never smoker), alcohol intake (g/day, adding the quadratic term), 17-point Mediterranean diet score, BMI (kg/m²), hypertension (yes/no), hypercholesterolemia (yes/no), and depressive symptomatology (yes/no).

Model 3: further adjusted for baseline diabetes control (good; poor); diabetes duration (<5-year diabetes duration; \geq 5-year diabetes duration).

Beta coefficients were estimated using linear regression models with robust standard errors to account for intracluster correlations.

APPENDIX

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