

Multidomain Lifestyle Interventions in Older Adults with Type 2 Diabetes: One-stage Individual Participant Data Meta-analysis



Taiki Sugimoto¹, Hisashi Noma², Kazuaki Uchida¹, Yoko Yokoyama¹, Ayaka Onoyama¹, Mio Shinozaki¹, Takuya Omura¹, Hisatomo Kowa³, Toshinari Odawara⁴, Hidenori Arai¹, Takashi Sakurai¹, J-MIND-Diabetes study group, J-MINT study group.
1.National Center for Geriatrics and Gerontology, Obu, Aichi, Japan.; 2. The Institute of Statistical Mathematics, Tokyo, Japan.
3. Kobe University Graduate School of Health Sciences, Kobe, Japan.; 4.Yokohama City University, Yokohama, Japan.



Background

- Type 2 diabetes increases the risk of dementia through multiple diabetes-related and lifestyle factors.
- Multidomain lifestyle interventions are a promising strategy for dementia prevention, but evidence in older adults with type 2 diabetes is limited.
- Previous Japanese multidomain intervention trials (J-MINT, J-MIND-Diabetes) suggested potential benefits, but small sample sizes limited subgroup analyses.
- We conducted an individual participant data (IPD) pooled analysis of four Japanese multidomain intervention trials to evaluate intervention efficacy and identify subgroups most likely to benefit.

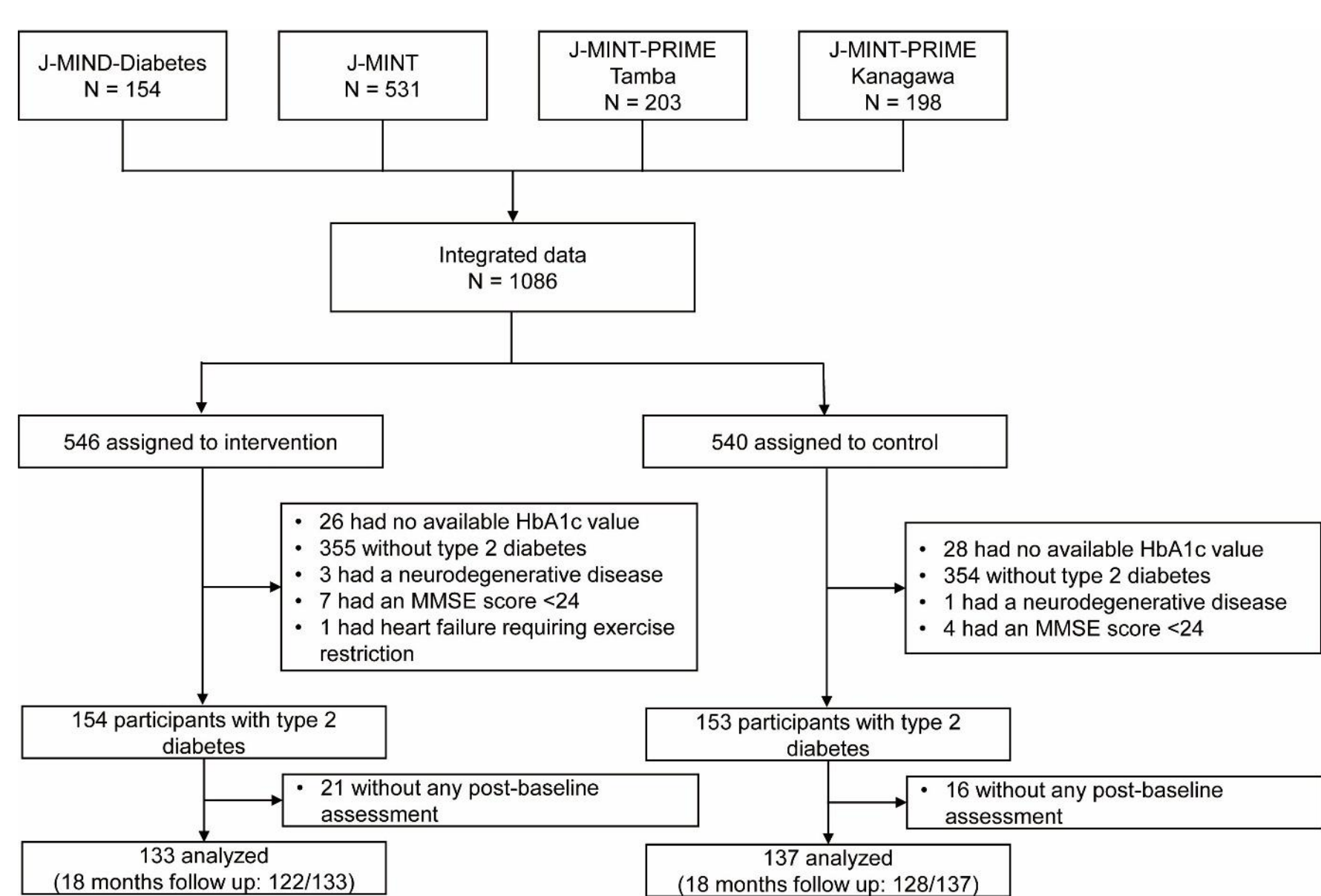
Methods

- Study design:** • Pooled IPD analysis of four Japanese 18-month randomized controlled multidomain intervention trials (J-MIND-Diabetes, J-MINT, J-MINT PRIME Tamba, and J-MINT PRIME Kanagawa).
- Participants:** • Adults aged 65–85 years with type 2 diabetes (diagnosed diabetes, diabetes medication use, or HbA1c ≥6.5%) who completed at least one post-baseline cognitive assessment.
- Outcomes:** • Primary outcome was change in MMSE score over 18 months.
- Statistical analysis:** • Intervention effects were evaluated using mixed-effects models for repeated measures (MMRM), adjusting for demographic and clinical covariates.
• Effect modification was examined by age, sex, BMI, HbA1c, cognitive status, and APOE ε4 genotype.

Trial	N	Key inclusion criteria	Intervention	Control
J-MIND-Diabetes Sugimoto T, et al. 2024	154	• Aged 70–85 years • Outpatients with type 2 diabetes • Mild cognitive impairment (MoCA-J < 26)	• Exercise once every 2 weeks • Nutritional counselling • Promotion of social participation • Management of vascular risks	• Standard diabetes care • General health-related information
J-MINT Sakurai T, et al. 2024	531	• Aged 65–85 years • With age- and education-adjusted cognitive decline	• Exercise once a week • Nutritional counselling • Cognitive training • Management of vascular risks	• General health-related information • Management of vascular risks
J-MINT-PRIME Tamba Oki Y, et al. 2024	203	• Aged 65–85 years • At least one vascular risks: under treatment for diabetes and/or hypertension; SBP ≥ 140 mmHg; DBP ≥ 85 mmHg; HbA1c ≥ 6.0% • Cognitively normal	• Exercise once a week • Nutritional counselling • Cognitive training • Management of vascular risks	• General health-related information • Management of vascular risks
J-MINT-PRIME Kanagawa Ide K, et al. 2025	198	• Aged 65–85 years • With lifestyle-related diseases (hypertension, hyperlipidemia, diabetes, overweight/underweight, and smoking) • Cognitively normal	• Exercise once every 2 weeks • Nutritional counselling • Cognitive training • Management of vascular risks	• General health-related information • Management of vascular risks

Results

Among the 1,086 participants recruited across the four trials, 307 had type 2 diabetes. After excluding 37 participants without post-baseline assessments, 270 were included in the analysis (Figure).



Baseline characteristics	Overall (n = 270)	Intervention (n = 133)	Control (n = 137)
Age	75.7 ± 4.5	75.8 ± 4.5	75.5 ± 4.5
Female sex	126 (46.7%)	61 (45.9%)	65 (47.5%)
Education (years)	12.4 ± 2.5	12.3 ± 2.5	12.5 ± 2.5
Body mass index (kg/m ²)	23.8 ± 3.6	24.0 ± 3.3	23.7 ± 3.9
≥25 kg/m ²	92 (34.1%)	45 (33.8%)	47 (34.1%)
Hypertension	159 (58.9%)	81 (60.9%)	78 (56.9%)
Dyslipidemia	140 (51.9%)	74 (55.6%)	66 (48.2%)
Heart disease	18 (6.8%)	7 (5.3%)	11 (8.0%)
HbA1c (%)	7.0 ± 0.9	7.0 ± 0.9	7.0 ± 0.9
HbA1c (mmol/mol)	53.3 ± 9.6	53.3 ± 10.0	53.4 ± 9.3
Medications for diabetes	211 (78.2%)	103 (77.4%)	108 (78.8%)
Insulin	37 (13.7%)	19 (14.3%)	18 (13.1%)
Sulfonylureas	49 (18.2%)	28 (21.1%)	21 (15.3%)
Glinides	26 (9.6%)	15 (11.3%)	11 (8.0%)
Biguanides	94 (34.8%)	47 (35.3%)	47 (34.3%)
α-Glucosidase inhibitors	47 (17.4%)	23 (17.3%)	24 (17.5%)
Thiazolidinediones	15 (5.6%)	7 (5.3%)	8 (5.8%)
DPP-4 inhibitors	163 (60.4%)	75 (56.4%)	88 (64.2%)
GLP-1 receptor agonists	13 (4.8%)	8 (6.0%)	5 (3.7%)
SGLT2 inhibitors	41 (15.2%)	26 (19.6%)	15 (11.0%)
MMSE	28.1 ± 1.7	28.3 ± 1.7	27.9 ± 1.6
≥1 APOE ε4 alleles*	50/224 (22.3%)	26/109 (23.9%)	24/115 (20.9%)

		Estimated mean changes from baseline to 18-month follow-up				
	N	Intervention (n = 133)	Control (n = 137)	MD between groups	P	P for interaction
Overall	270	-0.63 (-1.13 to -0.13)	-1.13 (-1.62 to -0.64)	0.50 (0.01 to 0.99)	0.046	NA
Age						
65–74 years	110	-1.05 (-1.37 to -0.34)	-1.58 (-2.26 to -0.89)	0.52 (-0.24 to 1.29)	0.179	0.903
≥75 years	160	-0.29 (-0.91 to 0.34)	-0.75 (-1.37 to 0.34)	0.46 (-0.19 to 1.11)	0.162	
Sex						
Male	144	-0.43 (-1.02 to 0.15)	-1.18 (-1.77 to -0.59)	0.75 (0.08 to 1.41)	0.029	0.286
Female	126	-0.87 (-1.51 to -0.23)	-1.08 (-1.69 to -0.47)	0.21 (-0.51 to 0.93)	0.565	
Body mass index						
<25 kg/m ²	178	-0.67 (-1.24 to -0.11)	-1.29 (-1.85 to -0.74)	0.62 (0.01 to 1.24)	0.046	0.515
≥25 kg/m ²	92	-0.61 (-1.31 to 0.09)	-0.89 (-1.56 to 0.23)	0.28 (-0.55 to 1.11)	0.506	
HbA1c						
<7.0%	146	-0.66 (-1.29 to -0.02)	-0.67 (-1.28 to -0.06)	0.01 (-0.65 to 0.67)	0.966	0.029
≥7.0%	124	-0.58 (-1.24 to 0.08)	-1.68 (-2.33 to -1.02)	1.10 (0.38 to 1.81)	0.003	
Cognitive status						
Cognitively normal	86	-0.43 (-1.37 to 0.28)	-0.46 (-1.16 to 0.25)	0.03 (-0.84 to 0.89)	0.949	0.206
MCI	184	-0.81 (-1.37 to -0.26)	-1.51 (-2.05 to -0.97)	0.70 (0.11 to 1.28)	0.020	
APOE						
0 APOE ε4 allele	174	-0.39 (-1.00 to 0.03)	-1.06 (-1.66 to -0.46)	0.67 (0.02 to 1.32)	0.043	0.390
≥1 APOE ε4 allele	50	-0.91 (-1.84 to 0.03)	-0.97 (-1.96 to 0.01)	0.07 (-1.14 to 1.28)	0.912	

- The mean difference (MD) in the change in MMSE score was significant (MD = 0.50, 95% confidence interval [CI] = 0.01 to 0.99, $P = 0.046$). No heterogeneity was observed across the four trials ($I^2 = 0.0\%$, $P = 0.42$).
- Interaction analyses revealed a significant interaction between intervention allocation and HbA1c (P for interaction = 0.029). Participants with HbA1c ≥ 7.0% ($n = 124$) showed a significant cognitive benefit, whereas no significant effect was observed among those with HbA1c < 7.0%.

Conclusion

Multidomain lifestyle interventions were associated with a modest attenuation of cognitive decline in older adults with type 2 diabetes, with potentially greater effects among individuals with HbA1c ≥7.0%. However, given the limited sample size and exploratory nature of the subgroup analyses, these findings should be considered hypothesis-generating and require confirmation in larger, multinational RCTs and meta-analyses.