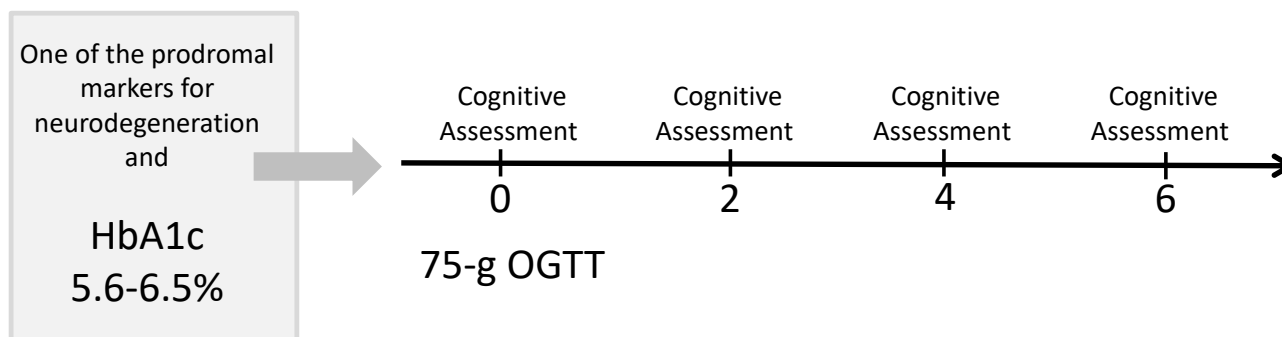


## Supplemental Figure 1



Timeline of the study

**Supplemental Table 1**

	Baseline	After 2 years	After 4 years	After 6 years
N	160	149	78	8
Sex (f/m) (n)	(95/65)	(87/62)	(47/31)	(5/3)
Age (years)	64.3 +/- 5.3	66.1 +/- 5.2	67.6 +/- 5.4	69.1 +/- 4.4
BMI (kg/m <sup>2</sup> )	26.1 +/-3.85	26.1 +/- 3.88	26.4 +/-3.59	25.5 +/-3.12
CERAD sum score	84.9 +/-8.4	85.4 +/- 7.8	84.4 +/-8.0	83.1 +/-10.3
Executive domain	0.58 +/-1.16	0.97 +/-1.14	0.93 +/-1.23	0.73 +/- 0.71
Language domain	0.22 +/- 0.73	0.25 +/- 0.7	0.25 +/- 0.69	0.26 +/- 0.69
Visuspatial domain	-0.5 +/- 1.09	-0.44 +/-1.13	-0.26 +/-1.28	-0.27 +/- 0.97
Memory domain	-0.13 +/- 0.77	0.08 +/- 0.71	0.04 +/- 0.8	0.28 +/- 0.73

*Subjects characteristics and cognitive scores at baseline and follow up. Data are given as mean +/-SD. Shown is the raw data of N, sex, age, BMI, CERAD sum score. Z-scored values are given for the domains.*

**Supplemental Table 2** Predictive strength of ISI Matsuda index vs. HOMA index

Cognitive trait	Metabolic trait	estimate	std.error	p
CERAD sum score	ISI Matsuda index	0.17	0.059	0.0043
	HOMA index	0.13	0.062	0.037
	AUC glucose (0-120min)	-0.064	0.056	0.25
	Fasting glucose	-0.12	0.057	0.035
	AUC insulin (0-120min)	-0.15	0.057	0.01
	Fasting insulin	-0.17	0.059	0.0047
Memory domain	ISI Matsuda index	0.14	0.063	0.025
	HOMA index	0.088	0.068	0.2
	AUC glucose (0-120min)	-0.095	0.06	0.12
	Fasting glucose	-0.14	0.062	0.025
	AUC insulin (0-120min)	-0.13	0.06	0.031
	Fasting insulin	-0.11	0.064	0.091
Word list recall	ISI Matsuda index	0.17	0.055	0.0029
	HOMA index	0.14	0.059	0.018
	AUC glucose (0-120min)	-0.09	0.052	0.086
	Fasting glucose	-0.17	0.053	0.002
	AUC insulin (0-120min)	-0.11	0.053	0.037
	Fasting insulin	-0.15	0.055	0.0069
Word list learn	ISI Matsuda index	0.13	0.059	0.029
	HOMA index	0.1	0.062	0.1
	AUC glucose (0-120min)	0.01	0.055	0.86
	Fasting glucose	-0.082	0.057	0.15
	AUC insulin (0-120min)	-0.12	0.056	0.034
	Fasting insulin	-0.14	0.059	0.016

*The effect size (standardized estimate) was higher for the Matsuda index compared to the HOMA index for the CERAD sum score. It was also higher for the Matsuda index compared to the HOMA index for the other cognitive traits.*