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## **Supplemental information**

**Plant sterols and cholesterol metabolism are  
associated with five-year cognitive  
decline in the elderly population**

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	Baseline		Five year follow-up		Change
	Mean	SD	Mean	SD	
<b>Endogenous Sterols</b>					
Cholesterol (mg/dL)	0.311	0.100	0.414	0.124	↑
Lathosterol (mg/dL)	0.232	0.124	0.201	0.177	↓
Lanosterol (µg/dL)	23.8	15.6	19.095	6.764	↓
Desmosterol (mg/dL)	0.147	0.133	0.161	0.144	↑
DihydroLanosterol (µg/dL)	3.867	3.26	0.395	0.304	↓
24S-hydroxycholesterol (ng/mL)	55.8	17.1	70.0	20.5	↑
7α-hydroxycholesterol (ng/mL)	152.2	250.1	129.6	79.2	↓
27-hydroxycholesterol (ng/mL)	165.3	51.2	194.9	60.6	↑
Cholesterol (µg/dL)	210.1	40.6	189.0	38.4	↓
HDL-Cholesterol (mg/dL)	65.6	17.8			
Triglycerides (mmol/L)	1.350	0.823			
<b>Phytosterols</b>					
Campesterol (mg/dL)	0.321	0.198	0.290	0.160	↓
Campestanol (µg/dL)	6.03	4.13	3.94	1.43	↓
Stigmasterol (µg/dL)	6.27	3.98	7.90	3.63	↑
Sitosterol (mg/dL)	0.250	0.129	0.249	0.120	=
Sitostanol (µg/dL)	7.23	4.13	4.09	1.85	↓
Brassicasterol (µg/dL)	19.4	10.9	20.7	10.7	↑

**Table S1:** Sterol plasma levels, related to Table 2. Mean baseline and five-year follow-up plasma levels of all cholesterol metabolism intermediates and phytosterols analysed in this study. Arrows indicate a significant increase or decrease in concentration of the designated metabolite at five-year follow up. SD, standard deviation.

	Parsimonious model	Complete Model
<b>Endogenous sterols</b>		
<b>CDR &gt; 0</b>	Lathosterol 0.642 7α-hydroxycholesterol 1.329 Cholesterol 1.434	Lathosterol 0.612 7α-hydroxycholesterol 1.313 Cholesterol 1.492
<b>Phytosterols</b>		
<b>CDR &gt; 0</b>	Stigmasterol 1.292 Sitosterol 0.475	Stigmasterol 1.308 Sitosterol 0.509

**Table S2:** Associations of sterols with baseline cognition, related to Table 2. Binomial regression analysis of the association between baseline cognitive impairment (CDR > 0) and sterol clusters (cholesterol, oxysterol and phytosterols).

	Parsimonious model	Complete Model
<b>Endogenous sterols</b>		
<b>ΔMMSE</b>	Desmosterol 0.076 HDL cholesterol 0.084	Dihydrolanosterol -0.053
<b>ΔCDR-SoB</b>	Dihydrolanosterol: -0.102 24S-OHC -0.119	Dihydrolanosterol: -0.110 24S-OHC -0.113
<b>Phytosterols</b>		
<b>ΔMMSE</b>	Sitosterol* (-0.178)	
<b>ΔCDR-SoB</b>		

**Table S3:** Association of sterols with cognitive decline, related to Table 3. Linear regression analysis of the association between cognitive decline at five years measured using MMSE and CDR-SoB score changes and sterol clusters (cholesterol, endogenous sterols and phytosterols).

	No Statins (n = 592)	Statins (n = 92)	P-Value
Cholestanol mg/dL, mean (S.E)	0.418 (0.122)	0.379 (0.126)	0.002
Lathosterol mg/dL, mean (S.E)	0.207 (0.193)	0.138 (0.095)	< 0.001
Lanosterol μg/dL, mean (S.E)	19,410 (6.586)	15.547 (6.623)	< 0.001
DihydroLanosterol μg/dL, mean (S.E)	0.402 (0.304)	0.273 (0.242)	< 0.001
24S-hydroxycholesterol ng/mL, mean (S.E)	71.054 (19.618)	62.072 (23.106)	< 0.001
7α-hydroxycholesterol ng/mL, mean (S.E)	125.538 (76.420)	146.705 (85.769)	0.007
27-hydroxycholesterol ng/mL, mean (S.E)	197.515 (59.896)	170.146 (52.984)	< 0.001
Cholesterol μg/dL, mean (S.E)	191.025 (37.426)	168.574 (39.275)	< 0.001

**Table S4:** Sterols and statins, related to Table 4. Five-year follow-up plasma levels of cholesterol metabolism intermediates affected by the intake of lipid-lowering medication (statins) at baseline.