

## Supplemental materials for

van Wanrooij LL, Richard E, Jongstra S, Moll van Charante EP, van Gool WA. Associations of subjective memory complaints and simple memory task scores with future dementia in the primary care setting. *Ann Fam Med*. 2019;17(5):412-418.

Supplementary table 1. Participants with and without a missing diagnosis of dementia at follow-up

<b>Demographics</b>	<b>Dementia status at follow-up available (N = 3454)</b>	<b>Dementia status at follow-up missing (N = 72)</b>	<b>p-value</b>
Mean age (years) (SD)	74.3 (2.5)	74.0 (2.7)	0.311
Sex male, n (%)	1569 (45%)	38 (53%)	0.263
Educational level			0.154
Low (<7 years), n (%)	822 (24%)	14 (20%)	
Intermediate (7-12 years), n (%)	2140 (63%)	42 (59%)	
High (>12 years), n (%)	458 (13%)	15 (21%)	
Subjective memory complaints	601 (18%)	10 (14%)	0.513
MMSE delayed recall, median (IQR)	2 (2-3)	2 (2-3)	0.483
VAT at baseline, median (IQR)	6 (5-6)	6 (6-6)	0.682

**Supplementary table 2. Risk of dementia for SMC in combination with MMSE-5 and VAT**

	n/N	HR (95% CI)	p-value	Adjusted HR <sup>c</sup> (95% CI) <sup>*</sup>	p-value
No SMC, optimal MMSE-5, optimal VAT <sup>a</sup>	26/921 (3%)	1 (reference)			
No SMC, optimal MMSE-5, imperfect VAT	22/249 (9%)	3.45 (1.95 to 6.09)	<.001	3.51 (1.99 to 6.20)	<.001
No SMC, imperfect MMSE-5, optimal VAT	51/1138 (4%)	1.66 (1.03 to 2.66)	0.036	1.58 (0.98 to 2.55)	0.060
No SMC, imperfect MMSE-5, imperfect VAT	46/500 (9%)	3.61 (2.23 to 5.85)	<.001	3.34 (2.06 to 5.43)	<.001
SMC, optimal MMSE-5, optimal VAT	7/157 (4%)	1 (reference)			
SMC, optimal MMSE-5, imperfect VAT	4/52 (8%)	1.85 (0.54 to 6.32)	0.327	1.57 (0.46 to 5.41)	0.475
SMC, imperfect MMSE-5, optimal VAT	22/216 (10%)	2.54 (1.09 to 5.95)	0.032	2.29 (0.97 to 5.40)	0.058
SMC, imperfect MMSE-5, imperfect VAT	51/171 (30%)	7.77 (3.52 to 17.15)	<.001	6.44 (2.88 to 14.40)	<.001

\* Adjusted for age and educational level

<sup>a</sup> For 50 participants at least one of the following was missing: SMC, MMSE-5, VAT

**Supplementary table 3. Analyses for possible covariates**

	n/N (%)	HR (95% CI)	p-value
Age (continuous)	-	1.14 (1.08-1.20)	< .001

Low education	74/822 (9%)	1 (reference)	
Intermediate education	133/2140 (6%)	0.68 (0.52-0.91)	0.009
High education	22/458 (5%)	0.55 (0.34-0.88)	0.013
Male	100/1569 (6%)	1 (reference)	
Female	133/1885 (7%)	1.03 (0.79-1.33)	0.831

**Supplementary table 4. Sensitivity analyses correcting for randomization group**

	n/N (%)	HR (95% CI)	p-value	Adjusted HR <sup>c</sup> (95% CI) <sup>*</sup>	p-value
No SMC	146/2822 (5%)	1 (reference)			
SMC	86/601 (14%)	3.01 (2.31 to 3.94)	< .001	3.01 (2.32-3.93)	< .001

Optimal MMSE item 5 (3 points)	59/1403 (4%)	1 (reference)			
Imperfect MMSE item 5 (<3 points)	174/2050 (8%)	2.14 (1.59 to 2.87)	< .001	2.14 (1.60-2.88)	0.007
Optimal VAT (6 points)	106/2454 (4%)	1 (reference)			
Imperfect VAT (<6 points)	124/982 (13%)	3.19 (2.46 to 4.13)	< .001	3.19 (2.46-4.13)	< .001

\* Adjusted for randomization group; for easy reference the original estimates from Table 2 are shown on the left

Abbreviations: n = number of dementia cases; N = number at risk; HR = hazard ratio; CI = confidence interval; SMC = subjective memory complaints; MMSE-5 = Mini-Mental State Examination, item 5 (delayed recall); VAT = Visual Association Test

**Supplementary table 5. Sensitivity analyses using a less strict cut-off for the MMSE-5**

	n/N (%)	HR (95% CI)	p-value	Adjusted HR <sup>c</sup> (95% CI) <sup>*</sup>	p-value
High MMSE-5 (2-3 points)	150/2778 (5%)	1 (reference)			
Low MMSE-5 (0-1 points)	83/675 (12%)	2.47 (1.89 to 3.23)	<.001	2.39 (1.82 to 3.13)	<.001
No SMC & high MMSE-5 (2-3 points) <sup>a</sup>	102/2308 (4%)	1 (reference)			
No SMC & low MMSE-5 (0-1 points)	44/513 (9%)	2.02 (1.42 to 2.88)	<.001	1.97 (1.37 to 2.82)	<.001

SMC & high MMSE-5 (2-3 points)	48/444 (11%)	2.56 (1.82 to 3.62)	<.001	2.56 (1.81 to 3.62)	<.001
SMC & low MMSE-5 (0-1 points)	38/157 (24%)	6.93 (4.77 to 10.07)	<.001	6.52 (4.46 to 9.54)	<.001

\* Adjusted for age and educational level

<sup>a</sup> For 32 participants SMC and/or MMSE-5 was missing

### Supplementary table 6. Sensitivity analyses using a less strict cut-off for the VAT

	n/N (%)	HR (95% CI)	p-value	Adjusted HR <sup>c</sup> (95% CI) <sup>*</sup>	p-value
High VAT (5-6 points)	156/3058 (5%)	1 (reference)			
Low VAT (0-4 points)	74/378 (20%)	4.40 (3.34 to 5.81)	<.001	4.12 (3.11 to 5.45)	<.001
No SMC & high VAT (5-6 points) <sup>a</sup>	77/2060 (4%)	1 (reference)			
No SMC & low VAT (0-4 points)	68/749 (9%)	2.62 (1.89 to 3.63)	<.001	2.56 (1.84 to 3.57)	<.001
SMC & high VAT (5-6 points)	29/373 (8%)	2.25 (1.47 to 3.44)	<.001	2.33 (1.52 to 3.58)	<.001
SMC & low VAT (0-4 points)	55/223 (25%)	7.74 (5.47 to 10.94)	<.001	7.15 (5.01 to 10.19)	<.001

\* Adjusted for age and educational level

<sup>a</sup> For 49 participants SMC and/or VAT was missing

**Supplementary table 7. Sensitivity analysis using less strict cut-offs for MMSE-5 and the VAT in combination with SMC**

	n/N	HR (95% CI)	p-value	Adjusted HR <sup>c</sup> (95% CI) <sup>*</sup>	p-value
No SMC, high MMSE-5, high VAT <sup>a</sup>	76/2106 (4%)	1 (reference)			
No SMC, high MMSE-5, low VAT	25/191 (13%)	3.97 (2.53 to 6.24)	<.001	3.80 (2.41 to 5.98)	<.001
No SMC, low MMSE-5, high VAT	29/432 (7%)	1.92 (1.25 to 2.94)	0.003	1.88 (1.22 to 2.91)	0.005
No SMC, low MMSE-5, low VAT	15/79 (19%)	6.00 (3.45 to 10.45)	<.001	6.18 (3.54 to 10.78)	<.001
SMC, high MMSE-5, high VAT	31/379 (8%)	1 (reference)			
SMC, high MMSE-5, low VAT	16/61 (26%)	3.98 (2.17 to 7.31)	<.001	3.21 (1.70 to 6.06)	<.001
SMC, low MMSE-5, high VAT	20/117 (17%)	2.54 (1.44 to 4.48)	0.001	2.22 (1.25 to 3.94)	0.007
SMC, low MMSE-5, low VAT	17/39 (44%)	7.30 (4.02 to 13.28)	<.001	6.22 (3.38 to 11.47)	<.001

\* Adjusted for age and educational level

<sup>a</sup> For 50 participants at least one of the following was missing: SMC, MMSE-5, VAT

Supplementary table 8. Analyses repeated with MMSE sum scores replacing MMSE-5 scores

	n/N (%)	HR (95% CI)	p-value	Adjusted HR <sup>c</sup> (95% CI)*	p-value
MMSE Sum $\geq$ 28 <sup>a</sup>	117/2489 (5%)	1 (reference)			
MMSE Sum < 28	115/959 (12%)	2.74 (2.12 to 3.55)	<.001	2.64 (2.03 to 3.45)	<.001
No SMC & MMSE Sum $\geq$ 28 <sup>b</sup>	85/2099 (4%)	1 (reference)			
No SMC & MMSE Sum < 28	61/718 (8%)	2.18 (1.57 to 3.03)	<.001	2.10 (1.50 to 2.94)	<.001
SMC & MMSE Sum $\geq$ 28	32/364 (9%)	2.25 (1.50 to 3.38)	<.001	2.23 (1.47 to 3.37)	<.001
SMC & MMSE Sum < 28	53/236 (22%)	6.74 (4.78 to 9.49)	<.001	6.49 (4.56 to 9.23)	<.001
No SMC, optimal MMSE Sum, optimal VAT <sup>c</sup>	50/1590 (3%)	1 (reference)			
No SMC, optimal MMSE Sum, imperfect VAT	35/500 (7%)	2.38 (1.54 to 3.66)	<.001	2.32 (1.50 to 3.59)	<.001
No SMC, imperfect MMSE Sum, optimal VAT	27/467 (6%)	1.88 (1.18 to 3.00)	0.008	1.87 (1.16 to 3.02)	0.011
No SMC, imperfect MMSE Sum, imperfect VAT	33/248 (13%)	4.77 (3.08 to 7.41)	<.001	4.69 (3.00 to 7.33)	<.001
SMC, optimal MMSE Sum, optimal VAT	14/252 (6%)	1 (reference)			
SMC, optimal MMSE Sum, imperfect VAT	17/108 (16%)	2.66 (1.30 to 5.45)	0.008	2.27 (1.09 to 4.73)	0.029
SMC, imperfect MMSE Sum, optimal VAT	15/121 (12%)	2.37 (1.14 to 4.90)	0.021	2.12 (1.02 to 4.43)	0.045
SMC, imperfect MMSE, imperfect VAT	38/115 (33%)	7.39 (4.00 to 13.65)	<.001	6.18 (3.29 to 11.60)	<.001

\* Adjusted for age and educational level

<sup>a</sup> For 6 participants MMSE Sum score was missing

<sup>b</sup> For 37 participants SMC and/or MMSE Sum score was missing

<sup>c</sup> For 53 participants SMC and/or MMSE Sum score and/or VAT was missing

Supplementary table 9. Sensitivity analyses using a less strict cut-off for the MMSE sum score and the VAT

	n/N (%)	HR (95% CI)	p-value	Adjusted HR <sup>c</sup> (95% CI)*	p-value
MMSE Sum >= 27	153/2959 (5%)	1 (reference)			
MMSE Sum < 27	79/489 (16%)	3.41 (2.60 to 4.47)	<.001	3.24 (2.44 to 4.30)	<.001
No SMC & MMSE Sum >= 27 <sup>b</sup>	108/2459 (4%)	1 (reference)			
No SMC & MMSE Sum < 27	38/358 (11%)	2.53 (1.75 to 3.66)	<.001	2.42 (1.66 to 3.54)	<.001
SMC & MMSE Sum >= 27	44/471 (9%)	2.24 (1.58 to 3.18)	<.001	2.23 (1.57 to 3.19)	<.001
SMC & MMSE Sum < 27	41/129 (32%)	9.29 (6.48 to 13.32)	<.001	8.76 (6.04 to 12.72)	<.001



No SMC, high MMSE Sum, high VAT <sup>c</sup>	85/2237 (4%)	1 (reference)			
No SMC, high MMSE Sum, low VAT	22/211 (10%)	2.93 (1.84 to 4.69)	<.001	2.80 (1.75 to 4.49)	<.001
No SMC, low MMSE Sum, high VAT	20/298 (7%)	1.79 (1.10 to 2.91)	0.019	1.73 (1.05 to 2.87)	0.033
No SMC, low MMSE Sum, low VAT	18/59 (31%)	10.07 (6.05 to 16.77)	<.001	10.62 (6.34 to 17.80)	<.001
SMC, high MMSE Sum, high VAT	30/409 (7%)	1 (reference)			
SMC, high MMSE Sum, low VAT	13/58 (22%)	3.62 (1.88 to 6.97)	<.001	2.97 (1.50 to 5.91)	0.002
SMC, low MMSE Sum, high VAT	21/87 (24%)	3.87 (2.20 to 6.78)	<.001	3.35 (1.87 to 5.97)	<.001
SMC, low MMSE, low VAT	20/42 (48%)	9.17 (5.17 to 16.26)	<.001	7.76 (4.31 to 13.97)	<.001

\* Adjusted for age and educational level

<sup>a</sup> For 6 participants MMSE Sum score was missing

<sup>b</sup> For 37 participants SMC and/or MMSE Sum score was missing

<sup>c</sup> For 53 participants SMC and/or MMSE Sum score and/or VAT was missing