

**TABLE 2. Final multivariate adjusted<sup>a</sup> models for the association between lifetime hormonal characteristics and poor cognitive function, at baseline.**

	GLOBAL FUNCTION		VERBAL FLUENCY		VISUAL MEMORY		VERBAL MEMORY		PSYCHOMOTOR SPEED		EXECUTIVE FUNCTION	
	OR [95% CI]	$\chi^2$ stat. <sup>d</sup> (p-value)	OR [95% CI]	$\chi^2$ stat. <sup>d</sup> (p-value)	OR [95% CI]	$\chi^2$ stat. <sup>d</sup> (p-value)	OR [95% CI]	$\chi^2$ stat. <sup>d</sup> (p-value)	OR [95% CI]	$\chi^2$ stat. <sup>d</sup> (p-value)	OR [95% CI]	$\chi^2$ stat. <sup>d</sup> (p-value)
<b>Age at 1<sup>st</sup> Menses</b>					1.13 [1.02 - 1.25]	5.5 (0.02*)			1.24 [1.08 - 1.43]	9.3 (0.002*)		
<b>No. reproductive yrs<sup>b</sup></b>			0.96 [0.93 - 0.99]	75.9 (0.005*)								
<b>Age at birth 1<sup>st</sup> child<sup>c</sup></b>												
≤ 20 years old	1.0		1.0		1.0				1.0			
21 - 29 years old	0.55 [0.35 - 0.86]	7.0 (0.008*)	0.39 [0.26 - 0.60]	18.4 (<0.001*)	0.64 [0.42 - 0.96]	4.6 (0.03*)			0.49 [0.27 - 0.87]	5.8 (0.02*)		
≥ 30 years old	0.72 [0.43 - 1.22]	1.5 (0.23)	0.56 [0.34 - 0.94]	4.8 (0.03*)	0.71 [0.43 - 1.17]	1.8 (0.18)			0.81 [0.42 - 1.57]	0.4 (0.53)		
<b>Hormone Therapy</b>												
Never					1.0		1.0		1.0			1.0
Past					1.06 [0.70 - 1.60]	0.1 (0.75)	0.72 [0.48 - 1.08]	3.1 (0.12)	0.78 [0.44 - 1.39]	0.7 (0.40)	1.04 [0.63 - 1.73]	0.1 (0.87)
Current					0.52 [0.29 - 0.93]	4.9 (0.03*)	0.64 [0.38 - 1.06]	2.5 (0.08)	0.49 [0.21 - 1.15]	2.7 (0.10)	0.49 [0.21 - 1.11]	2.9 (0.09)

<sup>a</sup> Hormonal factors are combined together in models that are adjusted for age, educational level, marital status, depressive symptoms (CESD≤16), high caffeine intake, physical incapacities and comorbidity.

<sup>b</sup> Calculated as the difference between the age at menopause and the age at first menses.

<sup>c</sup> Women were excluded from this analysis if they had no children. When the variable for "Age at the birth of the 1<sup>st</sup> child" was excluded from the analysis, similar results were obtained with all 996 women, in relation to the other variables shown.

<sup>d</sup> Test-statistic was compared to a  $\chi^2$  distribution with 1 degree of freedom. \*p<0.05.

**TABLE 3. The association<sup>a</sup> between lifetime hormone-related factors and decline in cognitive performance over the 4-year follow-up period.**

Characteristic	GLOBAL FUNCTION		VERBAL FLUENCY		VISUAL MEMORY		VERBAL MEMORY		PSYCHOMOTOR SPEED		EXECUTIVE FUNCTION	
	MMSE <-2		Isaacs ≤-6		Benton ≤-2		Word Recall ≤-2		Trail Making A ≥15		Trail Making B ≥35	
	OR [95% CI]	p	OR [95% CI]	p	OR [95% CI]	p	OR [95% CI]	P	OR [95% CI]	p	OR [95% CI]	P
Age at 1 <sup>st</sup> Menses	1.05 [0.95-1.16]	0.35	0.96 [0.81-1.01]	0.08	0.96 [0.86-1.07]	0.45	1.06 [0.95-1.19]	0.30	1.07 [0.95-1.18]	0.25	1.07 [0.96-1.20]	0.24
Age at Menopause	0.99 [0.96-1.02]	0.41	0.99 [0.96-1.02]	0.38	0.98 [0.95-1.01]	0.29	0.99 [0.95-1.02]	0.37	0.99 [0.96-1.02]	0.36	0.97 [0.94-1.00]	0.05*
No. Reproductive Yrs <sup>b</sup>	0.98 [0.96-1.01]	0.26	0.99 [0.96-1.02]	0.70	0.99 [0.96-1.02]	0.53	0.98 [0.95-1.02]	0.33	0.99 [0.96-1.02]	0.37	0.96 [0.94-0.99]	0.02*
Surgical Menopause	0.95 [0.63-1.45]	0.83	0.74 [0.46-1.17]	0.20	0.79 [0.43-1.17]	0.29	0.81 [0.50-1.32]	0.40	0.89 [0.54-1.42]	0.62	1.24 [0.79-1.93]	0.35
Oral Contraceptive Use	1.46 [0.96-2.23]	0.08	0.79 [0.49-1.27]	0.33	1.06 [0.69-1.63]	0.80	0.69 [0.39-1.20]	0.18	0.62 [0.37-1.05]	0.08	0.71 [0.43-1.20]	0.20
Nulliparous	0.93 [0.56-1.52]	0.76	1.17 [0.71-1.91]	0.54	1.11 [0.68-1.80]	0.68	1.09 [0.64-1.86]	0.76	1.18 [0.70-1.98]	0.53	0.59 [0.32-1.10]	0.10
<b><u>Number of Children</u></b>												
0	1		1		1		1		1		1	
1	1.52 [0.82-2.81]	0.19	0.93 [0.50-1.72]	0.81	0.83 [0.45-1.51]	0.54	0.77 [0.41-1.46]	0.42	0.64 [0.33-1.25]	0.20	1.49 [0.73-3.05]	0.27
2 or 3	1.23 [0.72-2.71]	0.45	0.88 [0.53-1.47]	0.63	0.81 [0.49-1.34]	0.41	0.74 [0.43-1.26]	0.26	0.91 [0.53-1.55]	0.72	1.76 [0.95-3.26]	0.07
>3	1.10 [0.58-2.08]	0.77	0.77 [0.41-1.44]	0.42	0.92 [0.51-1.67]	0.79	0.72 [0.38-1.37]	0.32	0.86 [0.46-1.63]	0.65	0.97 [0.46-2.05]	0.94
<b><u>Age at birth of 1<sup>st</sup> child<sup>c</sup></u></b>												
≤ 20	1		1		1		1		1		1	
21 - 29	0.75 [0.48-1.17]	0.21	0.72 [0.45-1.15]	0.17	0.65 [0.41-1.04]	0.07	0.77 [0.47-1.26]	0.30	1.09 [0.65-1.83]	0.75	0.75 [0.46-1.22]	0.25
≥ 30	0.91 [0.54-1.54]	0.73	1.01 [0.59-1.75]	0.97	0.79 [0.46-1.36]	0.40	0.85 [0.47-1.53]	0.59	1.14 [0.62-2.10]	0.66	0.81 [0.45-1.43]	0.47
<b><u>Hormone Treatment (HT)</u></b>												
Never	1		1		1		1		1		1	
Past	0.93 [0.61-1.43]	0.75	0.96 [0.62-1.50]	0.86	0.81 [0.52-1.27]	0.37	0.92 [0.57-1.50]	0.74	0.82 [0.52-1.29]	0.40	0.74 [0.47-1.19]	0.22
Current	1.08 [0.66-1.76]	0.76	0.80 [0.47-1.38]	0.43	0.98 [0.60-1.61]	0.95	1.20 [0.69-2.08]	0.52	0.65 [0.37-1.16]	0.14	0.81 [0.47-1.41]	0.46
<b><u>Duration of HT</u></b>												
Never	1		1		1		1		1		1	
0 – 9 years of Past use	0.70 [0.40-1.22]	0.20	0.93 [0.53-1.60]	0.78	0.88 [0.52-1.50]	0.64	1.11 [0.63-1.95]	0.72	0.94 [0.55-1.52]	0.66	0.70 [0.39-1.25]	0.23
≥ 10 years of Past use	1.37 [0.77-2.45]	0.28	1.02 [0.54-1.92]	0.95	0.71 [0.36-1.43]	0.34	0.65 [0.29-1.47]	0.30	0.73 [0.36-1.46]	0.37	0.82 [0.41-1.64]	0.57
0 – 9 years of Current use	0.75 [0.28-2.02]	0.57	0.26 [0.06-1.13]	0.07	1.59 [0.72-3.53]	0.25	1.05 [0.39-2.84]	0.92	0.29 [0.07-1.23]	0.09	0.83 [0.31-2.26]	0.72
≥ 10 years of Current use	1.20 [0.70-2.06]	0.51	1.05 [0.59-1.87]	0.87	0.80 [0.45-1.43]	0.46	1.26 [0.68-2.34]	0.47	0.79 [0.43-1.46]	0.46	0.81 [0.43-1.51]	0.50

<sup>a</sup> Adjusted for age, educational level and baseline cognitive test score. <sup>b</sup> Calculated as the difference between the age at menopause and age at first menses. <sup>c</sup> Women were excluded from this analysis if they had no children.

**SUPPLEMENTARY TABLE 1. The age and education adjusted association between lifetime hormone-related factors and poor cognitive performance, at baseline.**

Characteristic	GLOBAL FUNCTION		VERBAL FLUENCY		VISUAL MEMORY		VERBAL MEMORY		PSYCHOMOTOR SPEED		EXECUTIVE FUNCTION	
	MMSE <26		Isaacs ≤40		Benton ≤10		Word Recall ≤3		Trail Making A ≥69		Trail Making B ≥137	
	OR [95% CI]	p	OR [95% CI]	p	OR [95% CI]	p	OR [95% CI]	P	OR [95% CI]	p	OR [95% CI]	P
Age at 1 <sup>st</sup> Menses	1.00 [0.90-1.11]	0.99	1.08 [0.97-1.19]	0.15	1.10 [1.00-1.21]	0.05*	1.04 [0.95-1.14]	0.40	1.16 [1.02-1.32]	0.03*	0.98 [0.86-1.12]	0.82
Age at Menopause	1.00 [0.97-1.04]	0.83	0.96 [0.94-1.00]	0.04*	1.01 [0.98-1.04]	0.64	0.99 [0.96-1.01]	0.30	0.99 [0.95-1.03]	0.28	0.98 [0.95-1.02]	0.41
No. Reproductive Yrs <sup>a</sup>	1.00 [0.97-1.03]	0.86	0.97 [0.94-0.99]	0.01*	1.00 [0.97-1.03]	0.88	0.98 [0.96-1.01]	0.19	0.98 [0.95-1.02]	0.62	0.99 [0.95-1.02]	0.47
Surgical Menopause	0.72 [0.45-1.15]	0.17	0.90 [0.59-1.38]	0.62	0.85 [0.57-1.28]	0.44	1.02 [0.70-1.50]	0.90	0.78 [0.44-1.38]	0.39	0.91 [0.53-1.56]	0.72
Oral Contraceptive Use	0.93 [0.58-1.47]	0.75	0.72 [0.44-1.17]	0.19	0.84 [0.54-1.30]	0.43	0.95 [0.63-1.44]	0.82	0.68 [0.35-1.31]	0.25	0.72 [0.38-1.35]	0.30
Nulliparous	0.89 [0.52-1.56]	0.70	0.96 [0.58-1.61]	0.88	0.56 [0.32-0.98]	0.04*	0.91 [0.58-1.44]	0.69	0.61 [0.28-1.31]	0.20	0.72 [0.36-1.45]	0.35
<b><u>Number of Children</u></b>												
0	1		1		1		1		1		1	
1	1.10 [0.58-2.11]	0.77	1.49 [0.80-2.77]	0.21	1.30 [0.70-2.43]	0.41	0.88 [0.50-1.56]	0.67	1.81 [0.75-4.38]	0.19	1.51 [0.68-3.33]	0.31
2 or 3	1.04 [0.60-1.81]	0.89	1.15 [0.66-1.99]	0.62	1.48 [0.86-2.53]	0.16	1.00 [0.62-1.62]	0.99	1.63 [0.74-3.59]	0.22	1.22 [0.61-2.45]	0.58
>3	0.99 [0.51-1.91]	0.97	1.26 [0.66-2.38]	0.48	1.45 [0.78-2.69]	0.25	0.94 [0.53-1.65]	0.83	2.02 [0.84-4.86]	0.12	1.32 [0.59-2.96]	0.50
<b><u>Age at birth of 1<sup>st</sup> child<sup>b</sup></u></b>												
≤ 20	1		1		1		1		1		1	
21 - 29	0.55 [0.36-0.85]	0.008*	0.40 [0.26-0.61]	<0.001*	0.67 [0.45-1.00]	0.05*	0.74 [0.50-1.11]	0.14	0.55 [0.31-0.95]	0.03*	1.15 [0.64-2.07]	0.64
≥ 30	0.71 [0.42-1.21]	0.21	0.56 [0.34-0.93]	0.03*	0.78 [0.48-1.27]	0.31	0.76 [0.47-1.23]	0.27	0.97 [0.52-1.83]	0.93	1.02 [0.50-2.06]	0.96
<b><u>Hormone Treatment (HT)</u></b>												
Never	1		1		1		1		1		1	
Past	0.73 [0.46-1.16]	0.19	1.02 [0.67-1.55]	0.93	1.04 [0.70-1.54]	0.86	0.73 [0.49-1.10]	0.13	0.82 [0.48-1.40]	0.46	1.13 [0.69-1.85]	0.64
Current	0.87 [0.51-1.47]	0.60	0.75 [0.43-1.31]	0.32	0.67 [0.39-1.13]	0.13	0.63 [0.38-1.03]	0.06	0.46 [0.20-1.06]	0.07	0.48 [0.21-1.09]	0.08
<b><u>Duration of HT</u></b>												
Never	1		1		1		1		1		1	
0 – 9 years of Past use	0.71 [0.40-1.26]	0.24	1.18 [0.72-1.96]	0.51	1.09 [0.68-1.76]	0.71	0.63 [0.38-1.06]	0.08	0.99 [0.54-1.83]	0.97	1.17 [0.65-2.11]	0.60
≥ 10 years of Past use	0.76 [0.38-1.53]	0.44	0.77 [0.39-1.53]	0.46	0.94 [0.52-1.73]	0.85	0.91 [0.51-1.61]	0.74	0.54 [0.21-1.40]	0.21	1.06 [0.49-2.26]	0.89
0 – 9 years of Current use	1.90 [0.90-4.02]	0.09	0.83 [0.33-2.06]	0.68	0.69 [0.28-1.70]	0.42	0.71 [0.30-1.66]	0.43	0.45 [0.10-1.94]	0.28	0.72 [0.21-2.49]	0.61
≥ 10 years of Current use	0.54 [0.27-1.09]	0.09	0.72 [0.37-1.40]	0.33	0.66 [0.36-1.21]	0.18	0.59 [0.33-1.07]	0.08	0.47 [0.18-1.23]	0.13	0.38 [0.13-1.09]	0.07

<sup>a</sup> Calculated as the difference between the age at menopause and age at first menses. <sup>b</sup> Women were excluded from this analysis if they had no children. \*p<0.05.