

TABLE 2. Final multivariate adjusted^a models for the association between lifetime hormonal characteristics and poor cognitive function, at baseline.

	GLOBAL FUNCTION MMSE <26		VERBAL FLUENCY Isaacs ≤40		VISUAL MEMORY Benton ≤10		VERBAL MEMORY Word Recall ≤8		PSYCHOMOTOR SPEED Trail Making A ≥69		EXECUTIVE FUNCTION Trail Making B ≥137	
	OR [95% CI]	χ ² stat. ^d , (p-value)	OR [95% CI]	χ ² stat. ^d , (p-value)	OR [95% CI]	χ ² stat. ^d , (p-value)	OR [95% CI]	χ ² stat. ^d , (p-value)	OR [95% CI]	χ ² stat. ^d , (p-value)	OR [95% CI]	χ ² stat. ^d , (p-value)
Age at 1st Menses					1.13 [1.02 - 1.25]	5.5 (0.02*)			1.24 [1.08 - 1.43]	9.3 (0.002*)		
No. reproductive yrs^b			0.96 [0.93 - 0.99]	75.9 (0.005*)								
Age at birth 1st child^c												
≤ 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)		
Hormone Therapy												
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)

^a 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.

^b Calculated as the difference between the age at menopause and the age at first menses.

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

^d Test-statistic was compared to a χ² distribution with 1 degree of freedom. *p<0.05.

TABLE 3. The association^a 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 st 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 ^b	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
<u>Number of Children</u>												
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
<u>Age at birth of 1st child^c</u>												
≤ 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
<u>Hormone Treatment (HT)</u>												
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
<u>Duration of HT</u>												
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

^a Adjusted for age, educational level and baseline cognitive test score. ^b Calculated as the difference between the age at menopause and age at first menses. ^c 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 st 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 ^a	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
<u>Number of Children</u>												
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
<u>Age at birth of 1st child^b</u>												
≤ 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
<u>Hormone Treatment (HT)</u>												
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
<u>Duration of HT</u>												
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

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