human reproduction

SUPPLEMENTARY DATA

		Beta estima	te (95% CI)	
		Unstandardized	Unstandardized Standardized P-value	
		outcomes4	outcomes ⁵	
Mothers ¹				
Non-ART	(n=881) vs Endometriosis (n=73)			
	Age-adjusted DunedinPoAm	0.014 [-0.005, 0.032]	0.162 [-0.059, 0.384]	0.15021
	PhenoAgeAccel by Levine et al.	0.073 [-1.263, 1.408]	0.013 [-0.229, 0.255]	0.91499
	-Age-adjusted DNAmTL by Lu et al.3	-0.019 [-0.058, 0.02]	-0.118 [-0.359, 0.123]	0.33728
	DNAmAgeAccel by Horvath	0.297 [-0.87, 1.463]	0.06 [-0.176, 0.297]	0.61785
	DNAmAgeAccel by Hannum et al.	-0.19 [-0.916, 0.536]	-0.063 [-0.306, 0.179]	0.60782
Non-ART	(n=881) vs Tubal factor (n=124)			
	Age-adjusted DunedinPoAm	0.033 [0.019, 0.048]	0.39 [0.22, 0.56]	7.88E-06
	PhenoAgeAccel by Levine et al.	0.991 [-0.031, 2.012]	0.183 [-0.006, 0.371]	0.05743
	-Age-adjusted DNAmTL by Lu et al.3	0.009 [-0.021, 0.039]	0.057 [-0.129, 0.244]	0.54726
	DNAmAgeAccel by Horvath	0.091 [-0.811, 0.994]	0.019 [-0.164, 0.201]	0.84236
	DNAmAgeAccel by Hannum et al.	0.087 [-0.486, 0.661]	0.029 [-0.16, 0.217]	0.76550
Non-ART	(n=881) vs Ovulation factor (n=94)			
	Age-adjusted DunedinPoAm	0.023 [0.006, 0.04]	0.274 [0.076, 0.472]	0.00684
	PhenoAgeAccel by Levine et al.	0.181 [-1.011, 1.374]	0.033 [-0.184, 0.25]	0.76553
	-Age-adjusted DNAmTL by Lu et al.3	-0.024 [-0.059, 0.011]	-0.147 [-0.363, 0.069]	0.18264
	DNAmAgeAccel by Horvath	-0.517 [-1.557, 0.524]	-0.104 [-0.314, 0.106]	0.33012
	DNAmAgeAccel by Hannum et al.	0.182 [-0.471, 0.836]	0.061 [-0.156, 0.277]	0.58385
Non-ART	(n=881) vs Unexplained infertility (n	=201)		
	Age-adjusted DunedinPoAm	0.021 [0.009, 0.033]	0.245 [0.102, 0.388]	7.95E-04
	PhenoAgeAccel by Levine et al.	-0.084 [-0.964, 0.795]	-0.015 [-0.173, 0.143]	0.85108
	-Age-adjusted DNAmTL by Lu et al.3	-0.01 [-0.036, 0.015]	-0.064 [-0.222, 0.093]	0.42224
	DNAmAgeAccel by Horvath	-0.181 [-0.949, 0.587]	-0.036 [-0.191, 0.118]	0.64415
	DNAmAgeAccel by Hannum et al.	0.012 [-0.465, 0.489]	0.004 [-0.154, 0.162]	0.96117
Fathers ²				
Non-ART	(n=864) vs Sperm factor (n=292)			
	Age-adjusted DunedinPoAm	0.001 [-0.009, 0.011]	0.009 [-0.105, 0.123]	0.87283
	PhenoAgeAccel by Levine et al.	-0.095 [-0.958, 0.767]	-0.015 [-0.149, 0.119]	0.82846
	-Age-adjusted DNAmTL by Lu et al.3	-0.003 [-0.029, 0.023]	-0.015 [-0.148, 0.119]	0.83047
	DNAmAgeAccel by Horvath	-0.561 [-1.199, 0.077]	-0.114 [-0.243, 0.016]	0.08463
	DNAmAgeAccel by Hannum et al.	-0.225 [-0.708, 0.257]	-0.062 [-0.196, 0.071]	0.35982
Non-ART	(n=864) vs Unexplained infertility (n	=206)		
	Age-adjusted DunedinPoAm	0.01 [-0.001, 0.021]	0.117 [-0.014, 0.247]	0.08065
	PhenoAgeAccel by Levine et al.	-0.236 [-1.241, 0.768]	-0.037 [-0.192, 0.119]	0.64434
	-Age-adjusted DNAmTL by Lu et al.3	-0.008 [-0.037, 0.021]	-0.043 [-0.198, 0.112]	0.58637
	DNAmAgeAccel by Horvath		-0.112 [-0.264, 0.039]	
	DNAmAgeAccel by Hannum et al.	0.007 [-0.546, 0.56]	0.002 [-0.153, 0.156]	0.98148

Supplementary Figure S3. Association between epigenetic age accelerations and main causes of infertility. ¹In mothers, the associations were adjusted for smoking (pre-pregnancy), alcohol intake (pre-pregnancy), BMI (pre-pregnancy), education, parity and plate. ²In fathers, the associations were adjusted for smoking, alcohol intake, BMI, education, partner's parity and plate. ³Age-adjusted DNAmTL by Lu *et al.* was multiplied by -1. DNAmTL declines with advanced chronological age. ⁴The epigenetic age accelerations as outcome variables were not standardized. ⁵The epigenetic age accelerations as outcome variables were standardized.