

Web Table 1. Baseline Characteristics in the Overall Sample and in the Telomere Subsample of ESTHER (2000-2015)

	Categories	Overall sample (n=9,949)		Telomere subsample (n=3,566)	
		n	Mean/%	n	Mean/%
Age (years)	Mean ± SD	9,949	62.1 ± 6.6	3,566	61.9 ± 6.6
Sex	Women	5,467	55.0	1,977	55.4
	Men	4,482	45.0	1,589	44.6
Education	≤ 9 years	7,242	74.7	2,575	74.0
	10-11 years	1,373	14.2	532	15.3
	≥12 years	1,082	11.1	373	10.7
All-cause mortality	Dead	1,832	18.4	733	20.6
	Alive	8,116	81.6	2,833	79.4
CVD mortality	CVD-death	584	5.9	232	6.5
	No CVD-death	9364	94.1	3,334	93.5
Cancer mortality	Cancer death	640	6.4	253	7.1
	No cancer death	9308	93.6	3,313	92.9

Web Table 2. Association of LTL with All-cause Mortality in the Nurses' Health Study (1989-2010) and ESTHER (2000-2015)

Nurses' Health Study									
Telomere Length	N/Cases	HR^a	95% CI	HR^b	95% CI	HR^c	95% CI	HR^d	95% CI
Quintiles of z-score									
1 (shortest)	1725/494	1.37	1.20, 1.56	1.17	1.02, 1.33	1.09	0.95, 1.25	1.00	0.85, 1.18
2	1728/447	1.21	1.05, 1.38	1.08	0.94, 1.24	1.01	0.87, 1.16	0.95	0.80, 1.19
3	1721/418	1.12	0.97, 1.28	1.03	0.90, 1.19	0.98	0.85, 1.13	1.01	0.85, 1.20
4	1726/410	1.12	0.97, 1.29	1.07	0.93, 1.23	1.05	0.90, 1.21	1.01	0.85, 1.20
5 (longest)	1733/380	Ref.		Ref.		Ref.		Ref.	
z-score (continuous)	8633/2149	0.90	0.86, 0.94	0.95	0.91, 0.99	0.97	0.93, 1.01	0.99	0.94, 1.05
z-score < median	4316/1125	1.12	1.03, 1.22	1.03	0.94, 1.12	0.98	0.90, 1.08	0.94	0.84, 1.04
z-score ≥ median	4317/1024	Ref.		Ref.		Ref.		Ref.	
ESTHER									
Telomere Length	N/Cases	HR^a	95% CI	HR^b	95% CI	HR^c	95% CI	HR^d	95% CI
Quintiles of z-score									
1 (shortest)	700/133	2.11	1.55, 2.87	1.43	1.05, 1.95	1.14	0.81, 1.61	1.17	0.81, 1.69
2	734/169	1.92	1.46, 2.51	1.37	1.04, 1.80	1.28	0.95, 1.72	1.33	0.97, 1.83
3	693/150	1.49	1.14, 1.93	1.18	0.91, 1.54	1.16	0.87, 1.54	1.20	0.89, 1.63
4	744/162	1.31	1.02, 1.68	1.11	0.87, 1.43	1.11	0.85, 1.45	1.14	0.86, 1.52
5 (longest)	694/119	Ref.		Ref.		Ref.		Ref.	
z-score (continuous)	3566/733	0.74	0.67, 0.83	0.87	0.78, 0.97	0.92	0.82, 1.03	0.93	0.82, 1.05
z-score < median	1790/383	1.48	1.25, 1.76	1.21	1.02, 1.45	1.15	0.95, 1.39	1.17	0.95, 1.43
z-score ≥ median	1776/350	Ref.		Ref.		Ref.		Ref.	

HR, hazard ratio; 95% CI, 95% confidence interval; Ref., reference category

^a crude model, only adjusted for batch effect (random effect)

^b like model 1, but additionally adjusted for age (and sex in ESTHER)

^c like model 2, but additionally adjusted for smoking status, body mass index, physical activity, alcohol consumption and education

^d like model 3, but additionally adjusted for systolic blood pressure, total cholesterol, history of diabetes, cancer, stroke and coronary heart disease.

Web Table 3. Association of LTL with CVD Mortality in the Nurses' Health Study (1989-2010) and ESTHER (2000-2015)

Nurses' Health Study									
Telomere Length	N/Cases	HR^a	95% CI	HR^b	95% CI	HR^c	95% CI	HR^d	95% CI
Quintiles of z-score									
1 (shortest)	1725/139	1.29	1.01, 1.66	1.09	0.85, 1.39	1.00	0.76, 1.30	0.85	0.62, 1.16
2	1728/105	0.94	0.72, 1.23	0.84	0.64, 1.09	0.78	0.59, 1.04	0.64	0.46, 0.89
3	1721/99	0.90	0.69, 1.18	0.84	0.64, 1.11	0.76	0.57, 1.02	0.75	0.54, 1.05
4	1726/114	1.06	0.81, 1.37	1.01	0.78, 1.32	0.93	0.70, 1.23	0.78	0.57, 1.09
5 (longest)	1733/111	Ref.		Ref.		Ref.		Ref.	
z-score (continuous)	8633/568	0.93	0.86, 1.01	0.99	0.92, 1.08	1.01	0.92, 1.11	1.08	0.97, 1.20
z-score < median	4316/282	0.99	0.84, 1.17	0.90	0.76, 1.06	0.88	0.74, 1.05	0.79	0.64, 0.97
z-score ≥ median	4317/286	Ref.		Ref.		Ref.		Ref.	
ESTHER									
Telomere Length	N/Cases	HR^a	95% CI	HR^b	95% CI	HR^c	95% CI	HR^d	95% CI
Quintiles of z-score									
1 (shortest)	700/43	2.84	1.64, 4.91	1.74	1.01, 3.02	1.32	0.73, 2.40	1.16	0.61, 2.18
2	734/48	2.15	1.32, 3.53	1.46	0.89, 2.41	1.24	0.73, 2.12	1.07	0.59, 1.92
3	693/53	1.98	1.24, 3.15	1.49	0.93, 2.39	1.45	0.87, 2.41	1.33	0.78, 2.27
4	744/55	1.62	1.03, 2.53	1.33	0.85, 2.08	1.30	0.80, 2.11	1.27	0.76, 2.13
5 (longest)	694/33	Ref.		Ref.		Ref.		Ref.	
z-score (continuous)	3566/232	0.70	0.59, 0.85	0.85	0.71, 1.02	0.92	0.76, 1.11	0.97	0.79, 1.19
z-score < median	1790/120	1.56	1.15, 2.10	1.22	0.90, 1.65	1.15	0.83, 1.59	1.09	0.76, 1.56
z-score ≥ median	1776/112	Ref.		Ref.		Ref.		Ref.	

HR, hazard ratio; 95% CI, 95% confidence interval; Ref., reference category

^a crude model, only adjusted for batch effect (random effect)

^b like model 1, but additionally adjusted for age (and sex in ESTHER)

^c like model 2, but additionally adjusted for smoking status, body mass index, physical activity, alcohol consumption and education

^d like model 3, but additionally adjusted for systolic blood pressure, total cholesterol, history of diabetes, cancer, stroke and coronary heart disease.

Web Table 4. Association of LTL with Cancer Mortality in the Nurses' Health Study (1989-2010) and ESTHER (2000-2015)

Nurses' Health Study									
Telomere Length	N/Cases	HR^a	95% CI	HR^b	95% CI	HR^c	95% CI	HR^d	95% CI
Quintiles of z-score									
1 (shortest)	1725/183	1.17	0.95, 1.45	1.04	0.84, 1.28	1.01	0.81, 1.26	0.95	0.73, 1.24
2	1728/169	1.08	0.87, 1.34	0.99	0.80, 1.23	0.93	0.74, 1.17	0.90	0.69, 1.18
3	1721/184	1.15	0.93, 1.42	1.09	0.88, 1.32	1.05	0.84, 1.31	1.09	0.84, 1.41
4	1726/158	1.02	0.82, 1.27	0.99	0.79, 1.23	1.00	0.80, 1.26	1.00	0.76, 1.31
5 (longest)	1733/164	Ref.		Ref.		Ref.		Ref.	
z-score (continuous)	8633/858	0.95	0.89, 1.01	0.99	0.93, 1.06	1.00	0.93, 1.08	1.03	0.94, 1.13
z-score < median	4316/437	1.05	0.92, 1.21	0.99	0.86, 1.13	0.94	0.82, 1.08	0.91	0.77, 1.08
z-score ≥ median	4317/421	Ref.		Ref.		Ref.		Ref.	
ESTHER									
Telomere Length	N/Cases	HR^a	95% CI	HR^b	95% CI	HR^c	95% CI	HR^d	95% CI
Quintiles of z-score									
1 (shortest)	700/50	1.92	1.15, 3.18	1.40	0.84, 2.33	1.21	0.70, 2.09	1.52	0.85, 2.72
2	734/56	1.65	1.05, 2.61	1.26	0.79, 2.00	1.27	0.78, 2.07	1.56	0.93, 2.62
3	693/51	1.37	0.88, 2.13	1.14	0.73, 1.78	1.25	0.79, 1.99	1.50	0.91, 2.47
4	744/53	1.18	0.78, 1.80	1.04	0.69, 1.59	1.03	0.66, 1.61	1.27	0.79, 2.04
5 (longest)	694/43	Ref.		Ref.		Ref.		Ref.	
z-score (continuous)	3566/253	0.79	0.67, 0.94	0.90	0.75, 1.07	0.93	0.78, 1.12	0.89	0.73, 1.09
z-score < median	1790/136	1.50	1.12, 2.01	1.28	0.95, 1.73	1.27	0.92, 1.74	1.31	0.93, 1.84
z-score ≥ median	1776/117	Ref.		Ref.		Ref.		Ref.	

HR, hazard ratio; 95% CI, 95% confidence interval; Ref., reference category

^a crude model, only adjusted for batch effect (random effect)

^b like model 1, but additionally adjusted for age (and sex in ESTHER)

^c like model 2, but additionally adjusted for smoking status, body mass index, physical activity, alcohol consumption and education

^d like model 3, but additionally adjusted for systolic blood pressure, total cholesterol, history of diabetes, cancer, stroke and coronary heart disease.

Web Table 5. Summary Estimates of Association of LTL with Mortality From Fixed-Effects Meta-Analysis (Nurses' Health Study (1989-2010) and ESTHER (2000-2015))

All-cause mortality											
Telomere Length	n	Cases	HR^a	95% CI	P value	HR^b	95% CI	P value	HR^d	95% CI	P value
Quintiles of z-score											
1 (shortest)	2425	627	1.46	1.30, 1.65	<0.001	1.21	1.07, 1.37	0.003	1.10	0.97, 1.25	0.156
2	2462	616	1.33	1.18, 1.50	<0.001	1.13	1.00, 1.28	0.047	1.06	0.93, 1.20	0.405
3	2414	568	1.19	1.05, 1.35	0.005	1.06	0.94, 1.20	0.345	1.01	0.89, 1.15	0.837
4	2470	572	1.16	1.03, 1.32	0.016	1.08	0.96, 1.22	0.219	1.06	0.93, 1.21	0.349
5 (longest)	2427	499	Ref.			Ref.			Ref.		
z-score (continuous)	12199	2882	0.87	0.84, 0.91	<0.001	0.94	0.90, 0.98	0.002	0.96	0.93, 1.00	0.065
z-score < median	6106	1508	1.18	1.10, 1.28	<0.001	1.06	0.98, 1.15	0.124	1.01	0.93, 1.10	0.818
z-score ≥ median	6093	1374	Ref.			Ref.			Ref.		
CVD mortality											
Telomere Length	n	Cases	HR^a	95% CI	P value	HR^b	95% CI	P value	HR^d	95% CI	P value
Quintiles of z-score											
1 (shortest)	2374	182	1.48	1.18, 1.85	0.001	1.18	0.94, 1.48	0.150	1.05	0.82, 1.34	0.707
2	2411	153	1.14	0.90, 1.44	0.289	0.95	0.75, 1.20	0.667	0.86	0.67, 1.11	0.252
3	2371	137	1.10	0.87, 1.38	0.444	0.94	0.76, 1.17	0.590	0.89	0.69, 1.15	0.370
4	2415	152	1.18	0.94, 1.48	0.151	1.08	0.86, 1.36	0.486	1.01	0.79, 1.29	0.923
5 (longest)	2390	144	Ref.			Ref.			Ref.		
z-score (continuous)	11962	800	0.89	0.83, 0.96	0.002	0.97	0.90, 1.04	0.349	0.99	0.91, 1.08	0.844
z-score < median	5984	402	1.10	0.95, 1.27	0.197	0.97	0.83, 1.12	0.639	0.93	0.80, 1.09	0.389
z-score ≥ median	5978	398	Ref.			Ref.			Ref.		

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Cancer mortality											
Telomere Length	n	Cases	HR ^a	95% CI	P value	HR ^b	95% CI	P value	HR ^d	95% CI	P value
Quintiles of z-score											
1 (shortest)	2345	233	1.26	1.04, 1.53	0.021	1.09	0.89, 1.32	0.406	1.04	0.84, 1.27	0.736
2	2370	225	1.17	0.96, 1.42	0.120	1.03	0.85, 1.26	0.744	0.98	0.80, 1.21	0.877
3	2334	235	1.19	0.98, 1.44	0.078	1.10	0.91, 1.32	0.319	1.08	0.89, 1.33	0.425
4	2375	211	1.05	0.87, 1.28	0.605	1.00	0.82, 1.22	0.994	1.01	0.82, 1.23	0.953
5 (longest)	2358	207	Ref.			Ref.			Ref.		
z-score (continuous)	11783	1111	0.93	0.88, 0.99	0.015	0.98	0.92, 1.04	0.494	0.99	0.92, 1.06	0.764
z-score < median	5900	573	1.12	0.99, 1.23	0.074	1.03	0.91, 1.17	0.591	0.99	0.87, 1.12	0.822
z-score ≥ median	5883	538	Ref.			Ref.			Ref.		

HR, hazard ratio; 95% CI, 95% confidence interval; Ref., reference category

^a crude model, only adjusted for batch effect (random effect)

^b like model 1, but additionally adjusted for age (and sex in ESTHER)

^c like model 2, but additionally adjusted for smoking status, body mass index, physical activity, alcohol consumption and education

^d like model 3, but additionally adjusted for systolic blood pressure, total cholesterol, history of diabetes, cancer, stroke and coronary heart disease.