

## Supplementary Online Content

Honig LS, Kang MS, Schupf N, Lee JH, Mayeux R. Association of shorter leukocyte telomere repeat length with dementia and mortality. *Arch Neurol*. 2012. doi:10.1001/archneurol.2012.1541.

eTable 1. Literature relating telomeres to dementia and mortality

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Literature relating telomeres to dementia and mortality

Study <sup>a</sup>	Subjects	Material	Method	Results
<b>Dementia</b>				
Panosian et al, <sup>1</sup> 2003	n=15 AD; n=15 NC	T cells	TRF	TL shorter in AD
Honig et al, <sup>2</sup> 2006	n=125 dementia; n=127 no dementia	PBL	PCR	TL shorter in dementia
Martin-Ruiz et al, <sup>3</sup> 2006	n=195 no dementia, stroke survivors	PBMC	PCR	TL shorter in dementia
Grodstein et al, <sup>4</sup> 2008	n=5 dementia; n=8 MCI; n=49 NC nurses	PBL	PCR	TL shorter in MCI and dementia
Thomas et al, <sup>5</sup> 2008	n=54 AD; n=56 NC	PBL	PCR	TL shorter in AD
Thomas et al, <sup>5</sup> 2008	n=54 AD; n=56 NC	Buccal cells	PCR	TL shorter in AD
Thomas et al, <sup>5</sup> 2008	n=13 AD; n=9 NC	Brain tissue	PCR	TL longer in AD
Njajou et al, <sup>6</sup> 2009	n=2721 NC age 70-79 y	PBL	PCR	TL not different for dementia (but only 43 cases of dementia)
Fitzpatrick et al, <sup>7</sup> 2011	n=1136	PBL	TRF	TL not different for dementia (but only 53 dementia events)
<b>Mortality</b>				
Cawthon et al, <sup>8</sup> 2003	n=143 NC age ≥60 y	PBL	PCR	TL shorter with mortality
Honig et al, <sup>2</sup> 2006	n=125 dementia; n=127 no dementia age ≥65 y	PBL	PCR	TL shorter with mortality
Martin-Ruiz et al, <sup>3</sup> 2006	n=195 no dementia, stroke survivors	PBMC	PCR	TL shorter with mortality
Fitzpatrick et al, <sup>7</sup> 2011	n=1136	PBL	TRF	TL shorter with mortality
Kimura et al, <sup>9</sup> 2008	n=179 NC	PBL	TRF	TL not clearly related to successful aging
Njajou et al, <sup>6</sup> 2009	n=2721 NC age 70-79 y	PBL	PCR	TL unrelated to mortality, but related to more years of healthy living
Martin-Ruiz et al, <sup>10</sup> 2005	n=598 age>85 y	PBMC	PCR	TL not related to mortality
Bischoff et al, <sup>11</sup> 2006	n=825, including 752 twins; age≥ 73 y	PBL	TRF	TL not related to mortality

<sup>a</sup>Includes studies investigating relationship of TL to dementia and mortality.

Abbreviations: AD, Alzheimer disease; MCI, mild cognitive impairment; NC, normal controls; PBL, peripheral blood leukocytes; PBMC, peripheral blood mononuclear cells; PCR, polymerase chain reaction; TL, telomere length; TRF restriction fragment method.

e-Table 2. Association of TL with mortality by dementia status<sup>a</sup>

	No. of Participants	Mortality	HR	95% CI	P Value
<b>No Dementia</b>					
TL (shortest) Q1	329	44.1%	1.63	1.26-2.11	<.001
TL Q2	355	41.7%	1.61	1.25-2.07	<.001
TL Q3	379	35.6%	1.34	1.04-1.72	.02
TL (longest) Q4	406	27.3%	1.00	1.00 [Reference]	
<b>Incident Dementia</b>					
TL (shortest) Q1	52	67.3%	2.00	1.09-3.67	.02
TL Q2	48	52.1%	1.24	0.65-2.35	NS
TL Q3	47	44.7%	1.06	0.55-2.04	NS
TL (longest) Q4	43	41.9%	1.00	1.00 [Reference]	
<b>Prevalent Dementia</b>					
TL (shortest) Q1	109	75.2%	1.98	1.23-3.18	.004
TL Q2	92	75.0%	1.56	0.97-2.53	.07
TL Q3	69	68.1%	1.58	0.95-2.61	.08
TL (longest) Q4	44	54.5%	1.00	1.00 [Reference]	

<sup>a</sup>Calculated as Cox regression analysis, with mortality as outcome variable, TL quartile as independent variable, stratified on dementia status. Covariates (and significances) include age at blood draw (increased age:  $P < .00001$ ,  $P < .0005$ ,  $P < .00001$ ), sex (men:  $P < .0001$ ,  $P = .002$ , NS), ethnicity (Hispanic compared with white:  $P = .02$ , NS,  $P < .01$ ), education (decreased years: NS, NS, NS), and apolipoprotein E  $\epsilon 4$  carrier status (NS, NS, NS).

Abbreviations: HR, hazard ratio; NS, not significant; Q, quartile; TL, telomere length.

eTable 3. Association of TL with mortality by *APOE*  $\epsilon 4$  status

	No. of Participants	Mortality	HR	95% CI	P Value
<b>All Cases</b>					
TL (shortest) Q1	494	53.6%	1.72	1.40-2.11	<.0001
TL Q2	495	48.9%	1.57	1.28-1.94	<.0001
TL Q3	495	41.0%	1.35	1.09-1.67	.005
TL (longest) Q4	494	31.0%	1.00	1.00 [Reference]	
<b><i>APOE</i> <math>\epsilon 4</math> Positive</b>					
TL (shortest) Q1	133	51.9%	1.90	1.21-2.97	.005
TL Q2	134	53.7%	2.21	1.42-3.42	.0004
TL Q3	143	49.7%	2.15	1.39-3.33	.0005
TL (longest) Q4	119	24.4%	1.00	1.00 [Reference]	
<b><i>APOE</i> <math>\epsilon 4</math> Negative</b>					
TL (shortest) Q1	347	55.0%	1.68	1.33-2.13	<.0001
TL Q2	358	47.3%	1.41	1.11-1.79	.005
TL Q3	351	37.6%	1.14	0.89-1.46	NS
TL (longest) Q4	366	32.8%	1.00	1.00 [Reference]	

<sup>a</sup>Calculated as Cox regression analysis, with mortality as outcome variable, TL quartile as independent variable, stratified on *APOE*  $\epsilon 4$  status. A small number of cases (2%) have missing values for *APOE* status. Covariates (and significances) include age at blood draw (increased age:  $P < .00001$ ,  $P < .00001$ ,  $P < .00001$ ), sex (men:  $P < .00001$ ,  $P < .003$ ,  $P < .0001$ ), ethnicity (Hispanic compared with white:  $P = .06$ , NS,  $P = .05$ ), and education (decreased years: NS, NS, NS).

Abbreviations: *APOE*, apolipoprotein E; HR, hazard ratio; NS, not significant; Q, quartile; TL, telomere length.

## eReferences

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