

Spurious association between telomere length reduction over time and baseline telomere length

Erik J. Giltay, Geja J. Hageman, Daan Kromhout

▶ To cite this version:

Erik J. Giltay, Geja J. Hageman, Daan Kromhout. Spurious association between telomere length reduction over time and baseline telomere length. International Journal of Epidemiology, 2010, 10.1093/ije/DYQ235 . hal-00650657

HAL Id: hal-00650657 https://hal.science/hal-00650657

Submitted on 12 Dec 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



International Journal of Epidemiology

Spurious association between telomere length reduction over time and baseline telomere length

Journal:	International Journal of Epidemiology
Manuscript ID:	IJE-2010-08-0807
Manuscript Type:	Letter to the Editor
Date Submitted by the Author:	05-Aug-2010
Complete List of Authors:	Giltay, Erik; Leiden University Medical Center (LUMC), Psychiatry Hageman, Geja; NUTRIM, Maastricht University, Health Risk Analysis and Toxicology Kromhout, Daan; Wageningen University
Key Words:	telomere length, epidemiology, prospective study



Spurious association between telomere length reduction over time and baseline telomere length

Ehrlenbach and co-workers found a linear relationship between baseline relative telomere length (RTL) and the decrease of RTL over 10 years (r=0.674; P<0.001).¹ Similarly, others have reported on this relationship between the telomere attrition rate and the baseline telomere length and found largely similar associations.^{2,3} Likewise, when we correlated the RTL and delta RTL during 7 years of follow-up in 75 men from the Zutphen Elderly Study⁴ with an age range of 70 to 91 years we found a largely identical association (r=0.733; P<0.001; unpublished data).

We question whether this association is trivial. We used a random number generator to produce 510 baseline RTL values, similar to the number of pairs in the study of Ehrlenbach *et al.*¹ A mean of 1.49 was aimed at for baseline values and 1.05 at 10-years follow-up, with distributions comparable to those presented in Table 1.¹ Using these random numbers, we found a beta coefficient that was nearly similar to the beta coefficient that was presented in Table 2 (0.557 as compared to 0.589, respectively). Because baseline RTL (X) was used to calculate the RTL shortening rate (X-Y), the 'dependent' and 'independent' variables were functionally related.⁵ Pearson's correlation coefficients using randomly generated factors can be estimated to be around $1/\sqrt{2}$, if baseline and outcome have equal variances.⁵ Therefore, it was to be expected that a linear regression model would best fit the data (as X was regressed on X-Y) and that an exceptional *P*-value of 2.3×10^{-90} was found (Table 2).¹ We think that the slope of the regression line should have been tested against the slope of a no-effect line, instead of zero (i.e., a horizontal line).

We therefore think that the reported association is not explained by older cells having lower division rates nor by telomerase that acts preferentially on short telomeres as a special protection mechanism, as was suggested as potential explanations,^{1,2} but is merely a

consequence of mathematical coupling. It seems more likely that the attrition rate of RTL is biologically independent of baseline RTL.

Erik J. Giltay¹, MD, PhD, Geja J. Hageman², PhD, Daan Kromhout³, PhD, MPH

- Leiden University Medical Center, Department of Psychiatry, Leiden, The Netherlands
- Department of Health Risk Analysis and Toxicology, NUTRIM, Maastricht University, Maastricht, The Netherlands
- 3. Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands

Corresponding author: Dr. E.J. Giltay, Leiden University Medical Center, Department of Psychiatry, Leiden, P.O.Box 9600, 2300 RC, Leiden, The Netherlands; Tel: +31-(0)71-5263784, Fax: +31-(0)71-5248156, e-mail: giltay@dds.nl

Conflict of interest: None declared.

References:

- Ehrlenbach S, Willeit P, Kiechl S, Willeit J, Reindl M, Schanda K, Kronenberg F, Brandstätter A. Influences on the reduction of relative telomere length over 10 years in the population-based Bruneck Study: introduction of a well-controlled highthroughput assay. *Int J Epidemiol* 2009;**38**:1725-34.
- Nordfjäll K, Svenson U, Norrback KF, Adolfsson R, Lenner P, Roos G. The individual blood cell telomere attrition rate is telomere length dependent. *PLoS Genet* 2009;5:e1000375.
- Aviv A, Chen W, Gardner JP et al. Leukocyte telomere DYNAMICS: longitudinal findings in young adults of the Bogalusa Heart Study. *Am J Epidemiol* 2009;**169**:323–29.
- Giltay EJ, Zitman FG, Kromhout D. Cardiovascular risk profile and subsequent disability and mental well-being: the Zutphen Elderly Study. *Am J Geriatr Psychiatry* 2008;**16**:874-82.
- **5.** Senn S. Importance of trends in the interpretation of an overall odds ratio in the metaanalysis of clinical trials. *Stat Med* 1994;**13**:293-6.