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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 Study[4] 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0.001; unpublished data).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

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

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References:

1. 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 high-throughput assay. *Int J Epidemiol* 2009;**38**:1725-34.

2. 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.

3. 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.

4. 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 meta-analysis of clinical trials. *Stat Med* 1994;**13**:293-6.

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