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#### Review

# Systematic review of the association between chronic social stress and telomere length: A life course perspective



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#### ABSTRACT

Our aim was to examine whether chronic social stress is associated with telomere length throughout the life course, following our protocol published in 2014. Structured searches were conducted in MED-LINE (PubMed interface), EMBASE (OVID interface), Cochrane Central (OVID interface) and grey from their start date onwards. Reference lists of retrieved citations were hand searched for relevant studies. Eighteen studies published until May 1, 2015 investigating the association between chronic social stress (as defined by poverty, exposure to violence, or family caregiving) and telomere length in healthy or diseased adults and children were independently selected by 2 reviewers. Sixteen of those studies were cross-sectional and two had a longitudinal design. Studies differed in type of stress exposure, method to measure telomere length and cell type. As meta-analysis could not be conducted, the data were synthesized as a narrative review. Based on this comprehensive review, chronic social stress accompanies telomere shortening in both early and adult exposures, with most eligible studies showing a significant relationship. We discuss the significance of chronic stress of social origin and the potential for social interventions through public policies and we recommend methodological improvements that would allow for future meta-analysis.

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#### 1. Introduction

Telomere length (TL) has become a popular subject among scientists who conduct research on how biomarkers are linked with chronic conditions, stress and mortality. During the last decade, a large number of scientific papers on the effects of stress on TL have been published (Price et al., 2013; Starkweather et al., 2014). This research provides evidence for the link between stress and cellular aging through pathways of chronic diseases and inflammation (O'Donovan et al., 2012). Most of this literature is based on observational studies of volunteers and selected samples of people who have been subjected to stressful experiences and trauma, and it suggests that exposure to chronic stress leads to telomere attrition. While this research has been reviewed, including the relationship with perceived stress (Schutte and Malouff, 2014), there has not yet been a systematic analysis of stress exposures because there is a large range of stressor types. Such a review would be helpful to see if different types of stressor, or timing of the stressor (childhood vs adulthood) has a relationship with TL.

Social gradients of education and income in TL attrition have been examined, arguing that since there is a steep social gradient of mortality and disease going from the least educated (less affluent) to the most educated (most affluent) individuals within a given society (Marmot and Allen, 2014), TL should closely follow this social gradient since TL predicts mortality. Conclusions of these studies are conflicting, as most studies do not find a linear gradient between education or income and TL. Socioeconomic gradients may not have consistent effects on TL and may differ by race/ethnicity, cultural and chronic stress exposures. We suggest that living in poverty and not low socioeconomic status should be considered as a strong chronic stressor leading to telomere attrition. Poverty could be defined as an economic stress since it threatens the satisfaction of basic needs (food, housing, clothing), according to what is expected in a given society. In most high and middle income countries, definitions of poverty are relative and based on cut off points to distinguish those living under the poverty threshold. This threshold is usually established in terms of family income, number of people in the household and context (metropolitan, urban or rural).

Second, stress of social origin must typically be embodied as perceived psychological stress activating a stress response in order to acts on TL, although behavioural pathways, as life style may have important effects as well. Most studies measure perceived stress (Schutte and Malouff, 2014), although this is typically measured only over the past month, thus not counting as chronic stress. Chronic or severe stress exposures have been studied in several ways, most commonly as exposures to violence, to an ongoing situation like family caregiving, and to a lesser extent, poverty. Early life experiences and caregiving for a disabled relative have a huge impact on response to stress (Heim and Nemeroff, 2001; Sansoni et al., 2013). Also, living in extreme poverty implies exposure to severe circumstances of economic disadvantage threatening survival or adequate food, housing and clothing necessary for survival. (Palomar-Lever and Victorio-Estrada, 2012). Here we define chronic stress as stressful situations that originate from one's social environment (or social stressors); such as chronic exposure to poverty and violence, and to a different extent, long term caregiving of children or adults with disability or disruptive behaviors, as sources of chronic social stress extending over long periods of time throughout the life course.

Studies focusing on the experience of violence at different stages of the life course, during childhood (physical and emotional maltreatment in childhood) or adulthood (intimate partner violence), conclude that individuals who have been exposed to violence have shorter TL than comparable individuals of the same age. And lastly, some recent research has examined the links between violence and TL in some populations with mood disorders (Simon et al., 2006), more specifically PTSD, proposing that people who have suffered both childhood trauma and adult exposure to trauma will be more likely to have accelerated telomere shortening than those having only PTSD but not having experienced childhood trauma.

With a few exceptions, these studies are cross-sectional on selected samples and mostly without adequate control for potential confounders. With very few exceptions, these studies have been conducted in high income countries, mostly in the United States and Northern Europe.

Our objectives are to assess whether chronic social stress is associated with telomere length over the life course of human populations. We aimed to assess the available evidence on the asso-

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