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Authors: Yi Huang, Yim Onn Siong, Poh San Lai, Rongjun Yu, Soo Hong Chew, Xinyi Gwee, Ma Shwe Zin Nyunt, Qi Gao, Tze Pin Ng, Richard P. Ebstein, Jean-Philippe Gouin

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Successful aging, cognitive function, socioeconomic status, and leukocyte telomere length

Yi Huang [a], Yim Onn Siong [b], Poh San Lai [b], Rongjun Yu [a,c], Soo Hong Chew [d], Xinyi Gwee [e], Ma Shwe Zin Nyunt [e], Qi Gao [e], Tze Pin Ng [e], Richard P. Ebstein [c,f]*, Jean-Philippe Gouin [g]*

[a]. Graduate School for Integrative Sciences and Engineering, National University of Singapore, Singapore.

[b]. Department of Paediatrics, National University of Singapore, Singapore.

[c]. Department of Psychology, National University of Singapore, Singapore.

[d]. Department of Economics, National University of Singapore, Singapore.

[e]. Gerontological Research Programme. Department of Psychological Medicine, National University of Singapore, Singapore.

[f]. China Center for Behavior Economics and Finance, South Western University Finance Economics (SWUFE), Chengdu, China

[g]. Department of Psychology, Concordia University, Montreal, Canada

Corresponding authors:

Jean-Philippe Gouin, Ph.D.

Concordia University

7141, Sherbrooke St. West, PY170-14, Montreal, QC, Canada H4B 1R6

Phone: 514-848-2424 # 7538; Email: jp.gouin@concordia.ca

Richard P. Ebstein, Ph.D.

National University of Singapore and

China Center for Behavior Economics and Finance, South West University Finance Economics (SWUFE), Chengdu, 610052, China

Email:ebstein@swufe.edu.cn and rpebstein@gmail.com

Highlights

- Successful aging mediated the association between chronological age and telomere length
- Lower socioeconomic status was associated with larger age-related decreases in telomere length
- The cognitive functioning dimension of successful aging was uniquely related to telomere length

Abstract

In a rapidly greying world, the notion that some individuals maintain successful aging trajectories, viz. high physical, cognitive, emotional, and social functioning in older age, is increasingly germane. Biomarkers of such successful aging are increasingly sought. Leukocyte telomere length (LTL), an emerging yardstick of cellular aging that is influenced by but distinct from chronological age, may also be associated to successful aging. Furthermore, given that socio-economic status (SES) influences successful aging trajectories, socioeconomic status may also moderate the association between chronological age and LTL. The goals of this study are to examine 1) whether successful aging is associated with LTL; 2) whether successful aging accounts for age-related LTL and 3) whether low SES moderates the effect of age on LTL. Singaporean Chinese (n = 353) aged 65-80 completed a multidimensional assessment of successful aging and provided blood samples for LTL analysis. Results show that LTL negatively correlates with chronological age and positively correlates with successful aging. Successful aging mediates the association between chronological age and LTL. Moderated mediation analyses show that lower SES is associated with stronger negative associations of chronological age with successful aging and LTL. Moreover, the cognitive functioning dimension of successful aging is uniquely associated with LTL and its association with

chronological age is moderated by SES. This study provides evidence that among older Singaporean Chinese with lower SES, declines in successful aging and in cognitive functioning are linked to age-related LTL shortening and hence to accelerated aging at the cellular level.

1. Introduction

Most societies in the world face the challenge of an ever increasing greying population. Increased longevity is often associated with greater time spent in a frail time (Kassebaum et al., 2016). However, there is considerable variability in the rate of decline in physical and cognitive functioning in old age (Christensen et al., 2009; Deary et al., 2009). The notion of successful aging implies that advancing age is not necessarily associated with decline in functioning, but, rather, that some individuals can maintain high levels of functioning and productive life in older age (Rowe and Kahn, 1997). The biological correlates of such successful aging are poorly understood.

Rowe & Kahn (1997) propose that successful aging encompasses three main criteria: low risk of disease and disability, maintenance of high physical and cognitive functioning, and active engagement in social and productive activities. While early attempts to operationalize the concept of successful aging dichotomized individuals based on indicators of physical functioning, recent studies emphasize the importance of conceptualizing successful aging along a continuum based on both physical and psychosocial functioning (Cosco et al., 2013; Depp and Jeste, 2006; Kok et al., 2017; Pruchno et al., 2010). Furthermore, most studies to date have conceptualized successful aging as a static dichotomous classification. However, longitudinal studies indicate that as people age, they are less likely to achieve and maintain successful aging (Depp and Jeste, 2006; Hsu and Jones, 2012; Kok et al., 2017; Pruchno and Wilson-Genderson, 2014). Successful aging should therefore be conceptualized as a dynamic, developmental process that changes over time (Kok et al., 2017).

As our view of successful aging broadens, psychosocial factors contributing to successful aging and health status, especially socioeconomic status (SES), becomes a keen focus of interest.

Socioeconomic status (SES) represents one's relative position in a given society based on social and economic factors (Krieger et al., 1997). Numerous studies illustrate the impact of SES on health status. There is a social gradient in several health outcomes, such that individuals with lower SES are at greater risk for a range of chronic illnesses such as coronary artery diseases, type 2 diabetes, certain cancers (Mackenbach et al., 2008), as well as premature mortality (Signorello et al., 2014). SES is typically assessed by a combination of education, income or wealth, as well as occupational class (Adler and Stewart, 2010) . However, the association of these different indicators of SES with health outcomes varies across populations. Notably, among older adults, indicators reflecting cumulative SES over the life course may show stronger associations with health outcomes than assessments of current SES levels (Chittleborough et al., 2006).

SES influences access to material and social resources, chronic stress exposure, as well as engagement in healthy behaviors over the lifecourse (Adler and Stewart, 2010). The cumulative impact of SES on health outcomes appears to increase as individuals enter older age and become more vulnerable to the development of chronic diseases (House et al., 1994). There is a large literature documenting the impact of SES on age-related declines in physical and cognitive functioning (Lyu and Burr, 2016; Hu et al., 2016). Furthermore, individuals with lower SES are less likely to be categorized as aging successfully (Hsu and Jones, 2012; Kok et al., 2017; Pruchno and Wilson-Genderson, 2014). This suggests that SES is an important predictor of successful aging and that individuals with lower SES may be at greater risk for premature or accelerated aging.

Leukocyte telomere length (LTL) is widely used as a proxy for cellular aging in different tissues (Blackburn et al., 2015). Telomeres are non-coding, tandem repetitive segments

(TTAGGG) and proteins at the ends of human chromosomes that play a key role in genomic integrity and stability (Blackburn et al., 2015). Telomeres are longest at birth and decrease progressively with advancing age (Muezzliner et al., 2013). However, there is considerable inter-individual variability in the rate of age-related decline in LTL (Muezzliner et al., 2013). Prior studies suggest that indicators of successful aging may be associated with LTL. Longer LTL is associated with the absence of illness and disability in old age. Among centenarians, those with good health and no physical functioning limitations have longer telomeres than those with poorer health or disability (Arai et al., 2017). Der and colleagues (2012) report that shorter LTL is related to poor self-rated health, physical functioning, and disability in a cross-sectional study. Furthermore, Njajou et al., (2009) observe that baseline LTL is associated with the number of years with good self-reported health in older adults in a longitudinal study. While these studies focus on the association of LTL with good physical health and the absence of disability, they use a restricted definition of successful aging focusing mostly on physical functioning. To date, no empirical studies have evaluated the association between LTL and a multidimensional definition of successful aging covering physical, cognitive, emotional, and social functioning and whether successful aging may account for age-related changes in LTL.

The goals of the present study are to assess whether successful aging is associated with LTL, whether successful aging accounts for the association between chronological age and LTL, and whether SES moderates age-related decreases in LTL. Given that we use a multidimensional definition of successful aging (Cosco et al., 2013; Pruchno et al., 2010), a secondary goal of this study is to assess whether specific dimensions of successful aging (a compositional measure), are more strongly related to LTL. From a broader perspective, another goal of this study is to investigate LTL and SES in a population of non-European heritage, in East Asia where 22% of

the world's population resides. Asia's elderly population is projected to reach almost a billion people by the middle of this century. Singapore is one of the fastest ageing countries in the Asia-Pacific region, with dementia as a major cause of disability (Phua et al., 2009). Moreover, Singapore has one of the highest rates of income inequality in Asia, with a Gini coefficient of 0.458 in 2016. Additionally, although social class has, for centuries, been implicated as a fundamental cause of health disparity, and the association is thought to cross cultural and geographic boundaries, much less is actually known about the relationship between SES and health outside of the Western developed world. Finally, since LTL may reflect ethnic differences (Brown et al., 2017) and results in Western, educated, industrialized, rich and democratic (WEIRD) (Henrich et al., 2010) populations are not necessarily extended to non-European/North American societies, the current study is salient towards understanding the relationship between successful aging and SES.

2. Materials and Methods

2.1. Participants

Participants (n= 353) are community-dwelling Singaporean Han Chinese elderly aged 65 to 80 that are part of the on-going Singapore Longitudinal Aging Study II (SLASII; Niti et al., 2008). Participants were excluded if they were deemed unable to complete a set of behavioral economics tasks by the research nurses. Eligible participants were invited by telephone to participate in this study during a routine follow-up for the parent study. The study was briefly explained to the participants or their family members prior to their signing the informed consent at the community centre where the testing was conducted. This study was approved by the National University of Singapore Institutional Review Board.

2.2. Procedure

Data was collected over the course of 3 or 4 two-hour study visits in community centres close to participants' homes. During these study visits, a nurse fluent in English, Mandarin, or the local dialect of the participant completed the blood collection, administered interviews (e.g., Activities of Daily Living scale), cognitive testing, (i.e., Mini Mental State Examination), self-reported questionnaires, (e.g. Geriatric Depression Scale) and other behavioral tests unrelated to the present study.

2.3. Measures

2.3.1. Successful aging

A multidimensional assessment reflecting the core dimensions of successful aging as outlined by Rowe & Kahn (1997) was conducted based on our prior work (Ng et al., 2008). The successful aging composite score was created by summing the number of dimensions where the participants were considered to be functioning optimally.

Health status was assessed using a single item self-rated health measure (Idler and Benyamini, 1997). Participants rate their current health status using a 5-point Likert scale ranging from poor (1) to excellent (5). Participants were considered in good health if they endorsed being in good to excellent heath (rating≥3).

Disability was assessed using the Independence in Activities of Daily Living (e.g. feeding, bathing) and Instrumental Activities of Daily Living scales (e.g., preparing meals, travelling) (Lawton and Brody, 1969). Participants were considered free of disability if they reported being independent in all activities of daily living and instrumental activities of daily living (full scores on both subscales).

Cognitive functioning was assessed using the Mini Mental State Examination (MMSE), which consists of 30 questions that assess participants' sense of orientation, attention, immediate and delayed recall, language and construction (Folstein et al., 1975). This cognitive test has been previously validated in China and Singapore (Feng et al., 2012) . Participants are considered to have good functioning if they made no errors on the MMSE (full score of 29 for illiterate participants and 30 for literate participants).

Emotional functioning was assessed using the 15-item Geriatric Depression Scale (GDS) and 20-item Geriatric Anxiety Inventory (GAI). These two instruments have been previously validated for use with older Chinese (Lim et al., 2000). Participants were considered to have good emotional functioning if they reported no depressive or anxiety symptoms (scores of 0 on both scales).

Social engagement was assessed using a scale assessing the frequencies of social (e.g. going to church), productive (e.g., volunteering), and physical activities (e.g., doing taiji) relevant to the populations (Niti et al., 2008). This scale was previously validated in older Singaporeans Chinese (Niti et al., 2008). Participants were considered to be socially engaged if they reported weekly involvement in at least one social, one productive, and one physical activity.

2.3.2. Socio-Economic Status (SES)

Housing type and education level were used as measures of participants' SES. Housing type provides a unique measure of cumulative SES for elderly individuals in Singapore. In 1960, the Singapore government established a large public housing program to improve access to high quality and affordable housing to its citizens. Currently, about 82% of the population own or rent

subsidized public housing, with wealthier families living in larger or more upscale units (Government of Singapore. Housing and Development Board, 2017). For the poorest Singaporeans, the government offers subsidized *rental* housing in the form of 1-2 bedroom apartments. Public housing units of 3-5 bedrooms are *sold* to individuals at subsidized price by the government. Non-public housing units, regardless of their size, tend to be substantially more expensive. Families residing on private properties live in distinct neighborhoods, suggesting that housing type measures aspects of both individual and neighborhood SES in Singapore. Housing type was assessed using a 5-point single item: 1) 1-2 rooms public apartment, 2) 3 rooms public apartment, 3) 4-5 rooms public apartment, 4) executive maisonette public apartment and 5) private condo or landed housing. Education level was assessed using a 5-point single item: 1) no formal education, 2) primary (≤6 years), 3) secondary or Institute of Technical Education (7 to 10 years), 4) pre-university or polytechnic (11 to 12 years) and 5) university (≥13 years). To create a proxy variable for cumulative lifetime SES, we created a composite SES variable by summing education level and housing type.

2.3.3. Leukocyte Telomere length (LTL)

Blood samples were collected by venipuncture in EDTA-coated tubes. DNA was extracted from the blood sample using the QIAamp DNA Blood Midi Kit (Qiagen, catalog number 51185), per the manufacturer instructions. DNA is stored in a -20°C freezer until analysis.

The methodology for relative telomere length (LTL) measurement is adapted from Cawthon (Cawthon, 2009). Forty samples are selected at random from the pool of samples and diluted to 80 ng/µl concentration. These samples are then pooled to form the first standard,

which is then serially diluted to produce standards of 40, 20, 10, 5, 2.5, and 1.25 ng/µl concentrations. The PCR assays consist of real-time quantitative amplifications with both telomere and reference gene primers in the same reaction. SYBR Green provides the fluorescence. The telomere-specific primer used are 5'-ACACTAAGTTTGGGTTTGGGTTTGGGTTTGGGTTAGTGT-3' and 5'-TGTTAGGTATCCCTATCCCTATCCCTATCCCTATCCCTAACA-3', while 5'-CGGCGGCGGGCGGCGCGGGCTGGGCGGCTTCATCCACGTTCACCTTG-3' and 5'-GCCCGGCCCGCCGCGCCCGTCCCGCCGGAGGAGAAGTCTGCCGTT-3' are used for the haemoglobin β reference gene. Each individual reaction uses 8 µl of 2x QuantiFast SYBR Green PCR Master Mix (Qiagen, Catalog number 204054), 1.4 µl of each 10 µM telomere primer, 0.8 µl of each 10 µM reference primer, 40 ng of genomic DNA, 0.08 µl of 1 M Dithiothreitol, and sterile water to a total volume of 16 µl. The following PCR protocol is used: 15 minutes at 95°C, 2 cycles of 15 seconds at 94°C followed by 15 seconds at 52°C, 32 cycles of 15 seconds at 94°C, 10 seconds at 62°C, 15 seconds at 74C° with fluorescent signal acquisition (for telomere amplicons), 10 seconds at 84°C, and finally 15 seconds at 88°C with signal acquisition (for reference amplicons). PCR is performed on a CFX96 Real-Time PCR Detection System (Bio-Rad), and the C_q values are calculated by the operating software after the threshold is manually determined for each run.

Assays are conducted in triplicate for each DNA sample on 96-well plates with opaque wells (Bio-Rad, Catalog number HSP9665). Standards are run in every plate. The means of the triplicate readings are used to determine the starting quantity of telomere and reference gene, and the LTL of each sample is calculated as the ratio of the telomere to the reference gene. The average inter-assay coefficient of variation was 4.1%. A coefficient of variation (CV) cut-off of

<10.0% was applied to filter the triplicate results by removing samples which gave poorly consistent triplicate measurements even after repeated assays. A <5.0% CV threshold for duplicate readings is then utilized to evaluate the quality of these samples on a second tier. One sample from our dataset which failed both tiers of quality evaluation is dropped from analyses.

2.4. Statistical analysis

Both the successful aging and LTL scores are normally distributed in the present sample. However, one outlier LTL value greater than 4 standard deviations above the mean is removed from the data. Twenty participants have missing data on the successful aging scores. Following recommendations of Cosco et al. (2013), we use the full successful aging score as a continuous variable rather than as a dichotomous variable. Gender, smoking status (current smoker or not), and presence of any major disease (excluding hypertension, high cholesterol) are included as covariates in all following analyses, given that these factors could confound the relationships among the key variables (Hsu and Jones, 2012) . Mediation and moderation analyses are conducted in different models using the Process macro (Hayes, 2017) in SPSS v.21. Bootstrapping analysis using 5000 resamples tested the hypothesized indirect effects.

3. Results

Descriptive statistics are shown in Table 1. 69.41% of the participants are females. There is no significant difference in successful aging between women (M=3.71, SD=1.00) and men (M=3.55, SD=0.98), t(325)=1.34, p=0.18. Women (M=0.83, SD=0.22) have longer LTL than men (M=0.77, SD=0.21), t(346)=2.03, p=0.04. Bivariate correlations indicate that older age is

associated with shorter LTL, while better cognitive functioning and greater successful aging are associated with longer LTL (see Table 1).

3.1. Chronological Age, Successful Aging and LTL

We hypothesize that successful aging partially accounts for the association between chronological age and LTL. A mediation analysis is conducted with age as the independent variable, successful aging as a mediator, LTL as the dependent variable, and sex, smoking status, and the presence of chronic medical conditions as covariates (see Figure 1A). Results show that older age is significantly associated with shorter LTL (path c'), B = -0.0072, SE = 0.0032, t = -2.26, p = 0.02. Increasing chronological age is also significantly related to lower successful aging (path a), B = -0.0475, SE = 0.0137, t = -3.46, p = 0.001. Furthermore, successful aging is positively associated with LTL (path b), B = 0.0306, SE = 0.0128, t = 2.39, p = 0.017. This indicates that after controlling for age and other covariates, greater successful aging is independently associated with longer LTL. A bootstrapping analysis indicates that there is a significant indirect effect of age on LTL through successful aging, with a point estimate of -0.0015 (SE = 0.0007) and a 95% bias-corrected CI of (-0.0034, -0.0004). The association between older age and shorter LTL is partially explained by a decline in successful aging with increasing chronological age. This indirect effect accounts for 16.80% of the total variance of age on LTL.

Bivariate correlations indicate that cognitive functioning is the only successful aging component that is independently associated with LTL (See Table 1). A successful aging score that excluded cognitive functioning (i.e., included only self-rated health, disability, emotion functioning, and social activity) was also significantly correlated with LTL, r = .13, p = .02, suggesting that above

and beyond the individual components, the successful aging composite as a whole is related to LTL. However, given its stronger bivariate association with LTL, cognitive functioning may uniquely contribute to the association between successful aging and LTL. A mediation analysis (Figure 1B) indicates that age is negatively correlated with cognitive functioning (path a), B = -0.0842, SE = 0.0187, t = -4.52, $p < 0.001$. Better cognitive functioning is significantly associated with longer LTL, (path b), B = 0.0175, SE = 0.0088, t = 1.98, p = 0.048. A bootstrapping analysis indicates a significant indirect effect of cognitive function on the association between age and LTL, with a point estimate of -0.0015 (SE = 0.0007) and a 95% bias-corrected CI of (-0.0031, -0.0002). These results suggest that cognitive functioning is a key dimension of successful aging explaining age-related declines in LTL.

3.2. SES as a moderator of the effect of age on LTL

Moderation analysis using age as the independent variable, LTL as the dependent variable and SES as a moderator demonstrates that SES significantly moderates the relationship between age and LTL, B = 0.0042, SE = 0.0021, F(1, 339) = 3.97, p = 0.047, $\Delta R^2 = 0.011$. Specifically, among older adults with lower and mean SES levels, there is a significant age-related decline in LTL. In contrast, there is no significant association between age and LTL among individuals with higher SES (See Figure 2). These results suggest that the age-associated declines in LTL are buffered by higher SES, viz. higher SES somehow reduces the age-related 'wear and tear' on cellular aging.

3.3. SES moderates the indirect effect of age on LTL via successful aging

We carry out a moderated mediation analysis to examine whether SES moderates the indirect effect of age on LTL through successful aging (Figure 3A, B). Results show that the interaction between age and SES on successful aging is marginally significant, B = 0.0169, SE = 0.0093, t = 1.81, p = 0.071. Older chronological age is associated with lower successful aging among participants with lower or mean SES levels. In contrast, there is no significant association between age and successful aging among participants with higher SES. A bootstrapping analysis indicates that the indirect effect of age on LTL through successful aging depends on SES levels. The indirect effect is significant among older adults with lower (B = -0.0017, SE = 0.0010, 95% CI: -0.0045, -0.0002) and mean SES (B = -0.0009, SE = 0.0006, CI: -0.0026, -0.0001), but not among participants with higher SES (B = -0.0002, SE = 0.0007, CI: -0.0022, 0.0007). Age-related declines in successful aging thus explain part of the age-associated shorter telomeres among older adults with lower SES, but not among participants with higher SES who show no significant decline in successful aging with increasing chronological age.

3.4. SES moderates the indirect effect of age on LTL via cognitive functioning

There is also a significant interaction between age and SES predicting cognitive functioning (MMSE score), B = 0.0339, SE = 0.0123, t = 2.75, p = 0.006. Among older adults with lower or mean SES levels, there is a significant negative association between age and cognitive functioning. In contrast, there is no association between age and MMSE scores among individuals with high SES. High SES appears to protect individuals from age-related declines in cognitive function. To test a moderated mediation, a bootstrapping procedure shows that there is a significant indirect effect for lower (-1SD) SES (B = -0.0014, SE = 0.001; CI: -0.0042, -0.0003) and mean SES older adults (B = -0.0008, SE = 0.0005; CI: -0.0022, -0.0001), but not for

higher SES participants (B=-0.0001, SE=0.0005; CI: -0.0009, 0.0008). Specifically, older adults with lower SES experience large age-related decreases in cognitive functioning, which are then associated with shorter LTL. In contrast, participants with higher SES maintain higher cognitive functioning despite increasing age, which in turn is related to greater LTL. Cognitive functioning as assessed by the MMSE appears to be a key dimension of successful aging that is related to LTL and whose association with chronological age is moderated by SES (Figure 3C, D).

4. Discussion

In this sample of elderly Singaporean-Chinese, a multidimensional successful aging composite is associated with longer LTL. The negative correlation between chronological age and LTL is partially mediated by a decrease in successful aging with advancing age. Moreover, individuals with lower SES exhibited greater age-related LTL shortening and declines in successful aging, compared to participants with higher SES for which the negative correlation between chronological age and successful aging was not statistically significant. Secondary analyses indicated that the cognitive functioning dimension of successful aging is independently associated with LTL and that its association with chronological age is also moderated by SES. Collectively, these results suggest that successful aging is a key process associated with telomere length among older adults. However, successful aging is itself sensitive to SES; the lowest SES group shows the sharpest decline in successful aging and shorter LTL.

Individuals characterized by higher scores on our successful aging measure, have longer LTL. Prior studies also show that low risk of illness and disability is related to longer LTL among older adults (Der et al., 2012; Terry et al., 2008). Additionally, longer LTL is associated with high cognitive functioning, low psychological distress, and high social support among

elderly individuals (Carroll et al., 2013; Darrow et al., 2016; Martin-Ruiz et al., 2006; Yaffe et al., 2011). The current study extends these prior findings by showing that the maintenance of high functioning across physical, cognitive, emotional, and social domains in old age is related to longer LTL. Furthermore, it shows that the cognitive functioning dimension of successful aging is uniquely associated with LTL. Notably, declines in normal cognitive functioning, considered well within the normal range, are indexed by LTL. LTL appears, at least in elderly Chinese, to be a very sensitive measure of cognitive decline. These results accord with epidemiological studies documenting an association between cognitive functioning and LTL in older age (Der et al., 2012; Harris et al., 2012; Martin-Ruiz et al., 2006; Rask et al., 2016; Valdes et al., 2010; Yaffe et al., 2011). Furthermore, in prior studies there is some indication of causality since baseline LTL prospectively predicted decline in cognitive functioning in old age (Martin-Ruiz et al., 2006; Yaffe et al., 2011). Interestingly, in a lifestyle intervention trial with participants at risk for cognitive impairment, participants with lower baseline LTL showed the largest improvement in cognitive functioning over time (Sindi et al., 2017). However, a caveat is in place since some studies have failed to find an association between cognitive functioning and LTL (e.g., Insel et al., 2012), perhaps due to differences in sample composition (e.g. percentage of women) and in the cognitive assessment battery employed.

In the present sample, socioeconomic factors are shown to play an overarching role in moderating the association of chronological age with successful aging and LTL. Specifically, individuals with lower SES show the steepest age-related declines in successful aging and LTL, while individuals with higher SES did not exhibit significant age-associated decreases in successful aging or LTL. Relatedly, successful aging mediated the association between chronological age and LTL only among participants with lower or average SES levels. These

findings are consistent with the larger epidemiological literature showing that lower SES is associated with greater age-related declines in functioning and greater risk for chronic diseases in older age (Shalev et al., 2013).

Although SES was not directly associated with LTL, SES moderated the link between age and LTL such that lower SES is associated with a stronger negative correlation between chronological age and LTL. Extending Shiels et al., (2011) findings, this moderation effect of SES on healthful aging is observed among elderly individuals who tend to experience greater age-related telomere attrition (Yaffe et al., 2011). Multiple mechanisms may underlie this relationship. Individuals with lower SES may have less access to health care services, greater exposure to hazardous environments, lower capacity to engage and access to environments that promote healthy behaviors, and they may face greater chronic stress exposure over their life course due to the challenging social and material disadvantages they experience (Adler and Stewart, 2010). Such SES-related stress exposure is thought to lead to a gradual physiological wear and tear (Adler and Stewart, 2010). In particular, lower SES has been associated with greater oxidative stress and inflammation (Gruenewald et al., 2009; Janicki-Deverts et al., 2009). These effects might be compounded in old age when natural age-related increases in inflammation are occurring (Maggio et al., 2006), thereby promoting accelerated biological and psychological aging.

Given the cross-sectional design of the study, it is not clear whether longer telomeres facilitate successful aging or whether successful aging promotes longer telomeres. LTL predicted risk for disease, disability and cognitive function in longitudinal studies (Martin-Ruiz et al., 2006; Njajou et al., 2009), but change in cognitive functioning during adulthood also predicted LTL later in life (Rask et al., 2016). Furthermore, some interventions promoting successful aging

increased or maintained LTL over time (Carlson et al., 2015; Ornish et al., 2013), highlighting the potential influence of behavioral interventions to alter LTL. Longitudinal studies along with intervention studies aimed at enhancing or maintaining cognitive functioning in old age are needed to better tease apart the directionality of the association between successful aging and LTL.

One of the strengths of our study is the use of a truly multidimensional operationalization of successful aging that includes both subjective and objective components (Cosco et al., 2013). Furthermore, community-dwelling older adults in the present study were, on average, high functioning, socially active, and in good health. Indeed, a relatively small proportion of participants reported poor health or disability in the present samples. Even in this sample of high functioning older adults with a restricted range of illness and disability, there was an association between the multidimensional criteria of successful aging and LTL. These findings should be replicated in samples with wider ranges of poor health and disability, where we can expect to find a stronger association between successful aging and cell aging. In the present study, LTL was assessed from circulating leukocytes. While leukocyte LTL provides a general assessment of immune cell aging, there is evidence that certain lymphocyte subsets show differential telomere attrition over time (Lin et al., 2016). Future studies should thus assess the association between successful aging and LTL within different cell types. Moreover, it would be of interest in future studies to assess telomerase activity, an enzyme that can promote telomere maintenance and elongation.

In conclusion, this study shows that a multidimensional definition of successful aging mediated the relationship between chronological age and LTL as well as cognitive function and LTL among elderly Singaporean-Chinese. Furthermore, this effect was moderated by SES, such

that greater age-related declines in successful aging and LTL were observed among individuals with lower SES. To examine the causal association between successful aging and LTL, future studies should test whether promoting successful aging and, specifically, enhancing cognitive functioning, may delay telomere decline among older adults from a less advantaged SES background.

Conflict of Interests

Declarations of interest: none

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Table 1. Descriptive statistics and bivariate correlations among study variables.

	Age	SES	Health status	Disability	Cognitive functioning	Emotional functioning	Social engagement	Successful aging score	Telomere length
Mean (SD)	71.73 (3.93)	4.94 (1.37)	3.16 (0.64)	35.96 (0.41)	28.79 (1.36)	0.38 (0.94)	12.09 (3.84)	3.66 (0.99)	0.81 (0.22)
Successful aging (%)	-	-	90.37	98.02	40.23	66.01	67.71	-	-
Age									
SES	-0.27***								
Health status	-0.06	0.04							
Disability	-0.04	0.02	0.07						
Cognitive functioning	-0.24***	0.34***	-0.03	0.10					
Emotional functioning	0.05	-0.02	-0.11*	0.03	-0.09				
Social engagement	-0.19***	0.16**	0.14**	0.13*	0.12*	-0.21***			
Successful aging score	-0.22***	0.24***	0.35***	0.20***	0.46***	-0.38***	0.47***		
Telomere length	-0.18***	0.10	-0.000	0.08	0.15**	-0.04	0.01	0.17**	

Note. Continuous variables are used for each successful aging dimension. The Emotional Functioning variable is the mean score on the GDS and GAI *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$. Successful aging (%) indicates the percentage of participants who fulfilled the successful aging criteria for a particular dimension.

Figure Captions

Figure 1. Path model of a mediation analysis linking age and telomere length via successful aging (A) and cognitive functioning (B). Unstandardized regression coefficients are presented along with their corresponding standard errors in parenthesis. *$p < 0.05$, **$p < 0.01$, *** $p < 0.001$.

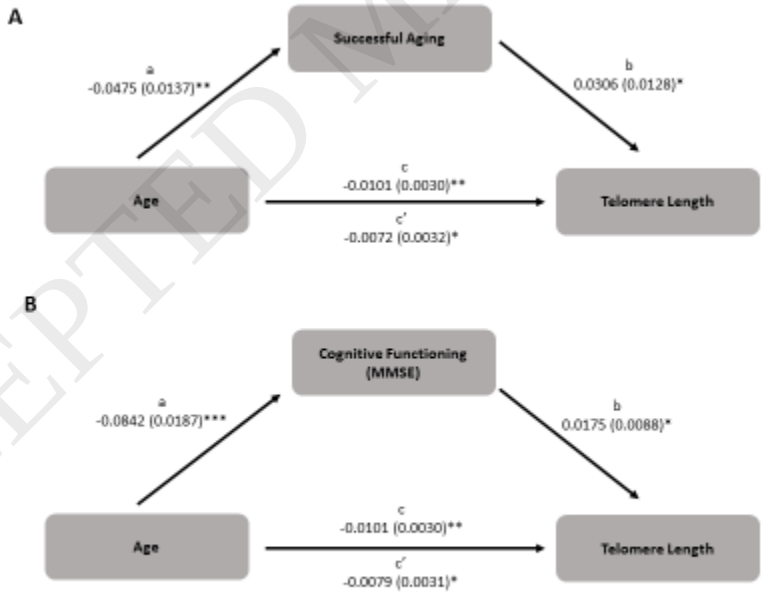

Figure 2. The association of age with leukocyte telomere is moderated by socio-economic status (SES). The analyses were run using a continuous variable. SES groups (mean±1SD) were created for illustration purposes only.

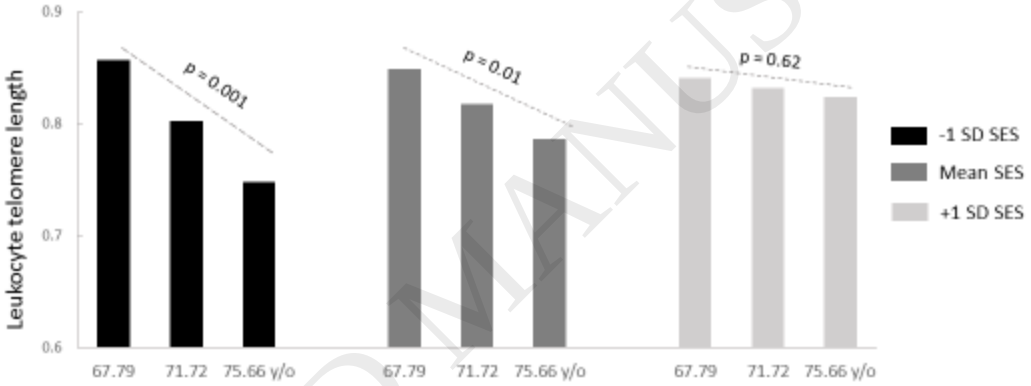

Figure 3. SES moderates the mediating effect of age on leukocyte telomere length via successful aging (A, B) and cognitive functioning (C, D). Numbers in B and D refer to unstandardized regression coefficients and their corresponding standard errors in parenthesis. # $p = 0.07$, ** $p < 0.01$. The analyses were run using a continuous variable. SES groups (mean±1SD) were created for illustration purposes only.