Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2019 February 01.

Published in final edited form as:

Int J Obes (Lond). 2018 February ; 42(2): 198–204. doi:10.1038/ijo.2017.202.

Association of Adiposity, Telomere Length and Mortality: Data from the NHANES 1999–2002

John A. Batsis[a,b,c,d,e], **Todd A. Mackenzie**[b,f], **Elizabeth Vasquez**[g], **Cassandra M. Germain**[h], **Rebecca T. Emeny**[b], **Peter Rippberger**[i], **Francisco Lopez-Jimenez**[j], and **Stephen J. Bartels**[b,c,d]

[a]Section of General Internal Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH

[b]Geisel School of Medicine at Dartmouth and The Dartmouth Institute for Health Policy & Clinical

[c]Dartmouth Centers for Health and Aging, Dartmouth College, Hanover, NH

[d]Health Promotion Research Center at Dartmouth, Lebanon, NH

[e]Dartmouth Weight & Wellness Center, Lebanon, NH

[f]Department of Biomedical Data Science, Geisel School of Medicine at Dartmouth Practice, Lebanon, NH

[g]Department of Epidemiology, School of Public Health, SUNY Albany, Albany, NY

[i]University of New England College of Osteopathic Medicine, Biddeford, ME

[j]Division of Cardiovascular Disease, Department of Medicine, Mayo Clinic, Rochester, MN, 55905

Abstract

Corresponding author: John A. Batsis, MD, FACP, AGSF, Section of General Internal Medicine, Dartmouth-Hitchcock Medical Center, 1 Medical Center Drive, Lebanon, NH 03756, Telephone: (603) 653-9500, Facsimile: (603) 650-0915, john.batsis@gmail.com.

Work to be presented in part to the 2017 International Association of Geriatrics and Gerontology, San Francisco, CA, July 2017

There are no conflicts of interest pertaining to this manuscript

CONFLICTS OF INTEREST

NONE

FINANCIAL DISCLOSURE

Dr. Batsis' research reported in this publication was supported in part by the National Institute on Aging of the National Institutes of Health under Award Number K23AG051681. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Support was also provided by the Dartmouth Health Promotion and Disease Prevention Research Center supported by Cooperative Agreement Number U48DP005018 from the Centers for Disease Control and Prevention. The findings and conclusions in this journal article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Dr. Batsis received funding from Health Resources Services Administration (UB4HP19206-01-00) for medical geriatric teaching, the Junior Faculty Career Development Award, the Department of Medicine, Dartmouth-Hitchcock Medical Center, and the Dartmouth Centers for Health and Aging Dr. Bartels receives funding from the National Institute of Mental Health (K12 HS0217695 (AHRQ), NIMH: T32 MH073553, R01 MH078052, R01 MH089811; R24 MH102794 CDC U48DP005018. Dr. Emeny is supported by The Dartmouth Clinical and Translational Science Institute, under award number UL1TR001086 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH).

Dr. Lopez-Jimenez: n/a

Dr. Mackenzie: n/a

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Background/Objectives—Telomere shortening is associated with age and risk of medical co-morbidity. We assessed the relationship between measures of adiposity, leukocyte telomere length, and mortality and whether it is modified by age.

Subjects/Methods—Subjects with dual energy x-ray absorptiometry (DEXA) measures were identified using the National Health and Nutrition Examination Survey 1999–2002. Obesity was categorized using two body fat definitions (BF1%: men≥25%; females ≥35%; BF2% ≥28% and ≥38%, respectively), body mass index (BMI), and waist circumference (WC) (men≥102cm; females≥88cm). Telomere length relative to standard reference DNA (T/S ratio) was assessed using quantitative polymerase chain reaction. Weighted multivariable regression models evaluated the association of telomere length with adiposity, both continuously and categorically (low/normal BF%, low/high WC and standard BMI categories). Differences in telomere length by age and adiposity were ascertained and subsequent models were stratified by age. Proportional hazard models assessed the risk of mortality by adiposity status. A telomere by adiposity interaction was tested in the entire cohort and by age category (<60 vs. ≥60 years; <70 vs. ≥70 years).

Results—We identified 7,827 subjects. Mean age was 46.1 years. Overall telomere length was 1.05±0.01 (SE) that differed by BF1% (low/high:1.12±0.02 vs. 1.03±0.02;p<0.001), BF2% (1.02±0.02 vs. 1.11±0.02;p<0.001), BMI (underweight 1.08±0.03; normal 1.09±0.02; overweight 1.04±0.02; obese 1.03±0.02;p<0.001), and WC (low/high 1.09±0.02 vs. 1.02±0.02;p<0.001). Adjusted β-coefficients evaluating the relationship between telomere length and adiposity (measured continuously) were: BF1% (β=−0.0033 ±0.0008;p<0.001), BF2% (−0.041±0.008;p<0.001), BMI (β=−0.025±0.0008;p=0.005), and WC (β=−0.0011±0.0004;p=0.007). High BF% (BF1%: β=−0.035±0.011;p=0.002; BF2%: β=−0.041±0.008; p<0.001) and WC (β=−0.035±0.011;p=0.008) were inversely related to TL. Stratifying by age, high BF1% (−0.061±0.013), BF2% (−0.065±0.01), BMI-obesity (−0.07±0.015) and high WC (−0.048±0.013) were significant (all p<0.001). This association diminished with increasing age. In older participants, TL was inversely related to mortality (HR 0.36 [0.27,0.49], as were those classified by BF1% (0.68 [0.56,0.81]), BF2% (0.75 [0.65,0.80], BMI (0.50 [0.42,0.60]), and WC (0.72 [0.63,0.83]. No interaction was observed between adiposity status, telomere length and mortality.

Conclusions—Obesity is associated with shorter telomere length in young participants, a relationship that diminishes with increasing age. It does not moderate the relationship with mortality.

Keywords

telomere; obesity; epidemiology; aging

INTRODUCTION

Excess adiposity is associated with an increased risk of medical co-morbidity[1], frailty[2], institutionalization[3] and premature death[4]. One potential mechanism that explains these relationships is a pro-inflammatory state that is observed in both the aging process and in the presence of adiposity[5, 6]. It has been hypothesized that the synergistic interplay between

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

aging and adiposity leads to biological and phenotypic impairments such as inflammatory burden and disability, respectively, in this population of older individuals with obesity.

Obesity-associated adipokines and pro-inflammatory cytokines, including IL-6 and TNF-α, are believed to directly lead to oxidative damage to DNA[5, 6]. Telomere segments are non-transcriptional segments of DNA that protect chromosomes from degradation. Yet, telomeres themselves are not invulnerable to such damage, leading to their shortening which is known to be inversely related to longevity and the aging process. Shorter telomeres are associated with an increased risk of developing heart failure[7], osteoporosis[8] and dementia[9], and interventions targeting the management of these underlying disease states have the potential to halt shortening and increase survival.

Both body mass index (BMI) and shorter telomere lengths have also independently observed to be related to mortality[10, 11]. Recently, two meta-analyses demonstrated a weak to moderate inverse correlation between telomere length and BMI[12, 13]. However, in certain populations (e.g. congestive heart failure, hemodialysis, nursing home residents) a mortality benefit is observed with higher BMI, a phenomenon termed ‘obesity paradox[14]. Whether an obesity paradox is observed in older adults with different telomere status is unknown. Such information could provide important information as a biomarker in individuals with obesity that could predict long-term mortality. We hypothesized that telomere length was inversely associated with body-fat defined adiposity, and determined whether it impacted mortality in a large-scale cohort of US adults.

METHODS

Study Design & Population

For this secondary analysis of data, we utilized the 1999–2002 National Health and Nutrition Examination Surveys (NHANES). This cross-sectional survey has been conducted and managed by the Centers for Disease Control since 1971. The survey contents and procedure manuals are available for online access at http://www.cdc.gov/nchs/nhanes.htm (accessed July 2016). The survey oversamples specific groups (race/ethnic minorities and older adults) and uses a multistage, complex, stratified probability sampling design making it representative of the non-institutionalized adult population of the United States. This study was exempt from Institutional Review Board review due to the de-identified nature of the data being analyzed.

Subjects were screened, interviewed, and ultimately examined in a mobile examination center by a licensed physician and staff (n=22,133). Persons aged <18 years (n=6,262) were excluded, in addition to individuals without body composition measures (see below) or telomere data (n=8,044). Our final analytical cohort consisted of 7,827 adults.

Measures of Obesity

Obesity was classified using three methods as the diagnostic accuracy of standard anthropometric measurements differ than gold standard methodologies: body mass index (BMI), waist circumference (WC) and body fat percentage. BMI was calculated as weight (in kilograms) divided by height (in meters) squared. Weight was measured using a

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

calibrated electronic digital scale, and height was measured after deep inhalation using a stadiometer. Subjects were classified using standard BMI categories (underweight ≤18.5kg/m^2; normal 18.5–24.9kg/m^2; overweight 25.0–29.9kg/m^2; obesity ≥30kg/m^2). Waist circumference was measured in centimeters by trained staff measured standing using a tape measure around the trunk, at the iliac crest, crossing at the mid-axillary line. Measurements were all taken on the right side of the body unless amputations, casts or other factors prevented this from occurring. All body composition measures were assessed using dual-energy x-ray absorptiometry (Hologic Scanner, QDR-4500, Bedford, MA), a procedure lasting 3 minutes. Exclusion criteria consisted of height≥192.5cm, weight ≥136.4kg, or any individual with a procedural contraindication. All metal objects were removed (except false teeth or hearing aids). High percent body fat was categorized using sex-specific cutpoints used in our previous studies (males≥25%; females≥35%)[15, 16], but also using ≥28% in men, and ≥38% in females.

Telomere Data

Blood samples were collected by standard protocol. The telomere length assay was performed using polymerase chain reaction at the University of California, San Francisco. Telomere length relative to standard reference DNA (T/S) ratio was measured, with each sample assayed 3 times on 3 different days, on duplicate wells (6 data points). Full details are available at http://cdc.gov/nchs/nhanes under the laboratory section. The interassay coefficient of variation was 6.5%. Values represent the mean (standard deviation) of the T/S ratio.

Co-variates

A self-reported questionnaire assessed race, smoking status (current, former, never) and co-morbid conditions (Have you ever been told by a doctor that you had [medical problem]?). Subjects completed all answers or if they were unable to, their caregiver completed the questions in either English or in Spanish. Age was self-reported from the initial screening questionnaire, and subsequently verified against an age verification chart, with differences reconciled using a standard protocol. Age was also categorized as performed in previous analyses and as outlined by the NHANES sampling domains (https://www.cdc.gov/nchs/data/series/sr_02/sr02_160.pdf) (18–60, 60–69.9, 70–79.9 and ≥80 years). Physical activity was categorized in four levels (sits, walks, light loads, and heavy work) using a self-reported questionnaire that asked participants “Please tell me which of these four sentences best describes your usual daily activities (sits: sits during the day and does not walk about very much; walks – stand or walk about a lot during the day but does not have to carry or lift things very often; light loads – lifts a light load or has to climb stairs or hills often; heavy work – does heavy work or carries heavy loads.

Mortality Data

Mortality data was obtained from the National Death Index, linked to the NHANES data using a unique study identifier. The 2015 public use linked mortality file was current from time of the mobile examination center evaluation through December 31, 2011. Full details are available at https://www.cdc.gov/nchs/ndi/index.htm. Time to death was calculated in days from the examination date of death.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Statistical Analyses

All data was merged into a single dataset according to NHANES protocols. Data was weighted and primary sampling unit and stratum were accounted for in the analysis. Continuous variables are presented as means ± standard errors, and categorical variables as counts (percent). A t-test and chi-square compared continuous and categorical variables. For multi-level variables, an ANOVA was performed. Age was stratified by age ≥60 and <60 years, and by <70 and ≥70 years to reflect the changes observed in body composition observed with the aging process[17–19]. Elevated body fat was categorized by sex (BF1%: males≥25%; females ≥35%; BF2%: males≥28%; females ≥38%) as was waist circumference (males≥102cm; females ≥88cm). Unpaired t-tests compared telomere length between young and older individuals (age <60 vs. ≥60; and age <70 vs. ≥70 years) and as an exploratory analysis among age categories (age 60–69.9, 70–79.9, and ≥80years) for high/low adiposity measure (body fat, BMI, WC). Overall mortality rates were also assessed.

Our primary outcome was to ascertain the association between each body composition measure (predictor) and telomere length (outcome). Separate models were created for each body fat definition (referent=low), BMI (referent=normal); WC (referent=low). Each adiposity measure was also assessed as a continuous variable. B-coefficients ± standard errors with associated p-values are presented. Model was 1 was unadjusted; Model 2 was adjusted for age, race, education, smoking; Model 3 was further adjusted for diabetes mellitus, congestive heart failure, non-skin cancer, coronary artery disease, arthritis, physical activity, and smoking status. Interactions between age category (cutpoint of 60 or 70 years) and each adiposity measure (BF1%, BF2%, BMI or WC) were assessed. We created cox proportional hazard models to separately assess the risk of death by adiposity measure, TL and death. A separate model assessed telomere length and mortality with a telomere * adiposity category interaction term. We also stratified by age with a similar interaction term. As an ancillary analysis, separate interaction terms for age category * telomere length was assessed within each adiposity category (high vs. low). All analyses were performed using STATA v.13 (College Station, TX). A p-value <0.05 was considered statistically significant.

RESULTS

We identified 7,827 individuals who met our inclusion criteria that were part of the analytical cohort. Baseline characteristics are represented in Table 1. Mean age was 46.1±0.37 years (51.4 % female). Differences were observed in race, comorbidity, smoking status, physical activity level and body fat and waist circumference. Telomere length was 1.05±0.01 in the overall cohort but was shorter in the older compared to the younger cohorts (<60 years: 0.91±0.02 vs. 1.10±0.01;p<0.001; age 70 years: 0.87±0.02 vs. 1.08±0.01;p<0.001). Telomere length was higher in younger participants independent of body fat status. In older adults, telomere length shortened between ages 60–69.9, 70–79.9 and ≥80 years in the overall cohort (0.96±0.02, 0.88±0.02, and 0.84±0.02; p<0.001). This decrease in telomere length with age was also observed across BF and WC categories (Table 2).

We observed consistent relationships with additional covariate adjustment (Table 3). High BF1% or BF2% and WC were strongly associated with lower telomere length (β=

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

−0.035±0.011, p=0.002, β=−0.041±0.008, p<0.001 and β=−0.032±0.011, p=0.008). Testing the interactive effect between body fat, BMI, and waist circumference as continuous variables with age on telomere length demonstrated p-values of <0.001, <0.001 and 0.007, respectively. High BF, BMI-obesity and high WC were all inversely associated with telomere length (Table 4), a trend that dissipated with increasing age. The analysis was subsequently stratified by age and suggested that adiposity is associated with reduced telomere length but disappears with increasing age. This is most clear with BF% and less clear for BMI and WC. Multivariable mortality analyses of age category, telomere length and mortality are noted in Table 5. High BF, BMI and WC were protective in older adults but led to a higher mortality risk in younger adults. TL was inversely associated with mortality risk in older adults. We did not observe an interaction between adiposity category, telomere length and mortality. This was also not observed between high/low age categories. Our ancillary analyses (Appendix 2 and 3) demonstrate that in low adiposity categories there is an interaction between telomere length and age on mortality.

DISCUSSION

With an increased interest in the contribution of telomere length in the aging process, this study suggests an inverse association between shorter telomere length and increased adiposity. However, our mortality results suggest that with increasing age, there is an attenuation in the association of adiposity on TL and mortality. The results also imply that among the very old, for those with obesity, irrespective of how it is defined, telomere length compared to individuals with normal body composition may not have a significant impact on important outcomes.

We observed a consistent inverse relationship between high body fat and WC on length of telomeres in the entire adult population examined. Our results may provide biological insight to the associations of both body fat and WC with disability and mortality in large, population-based studies[20, 21]. When our analyses were stratified by age, the association between adiposity and telomere length was only observed in younger adults and diminished in older adults. A few potential explanations could exist. First, age-associated body composition changes (fat and muscle) between the ages and 60–70 may impact peripheral blood telomere length, and could provide some potential mechanistic explanation to our findings. Whether and how adipose tissue modifies the effect of telomere repair mechanisms, for example reduced expression of telomerase[22, 23], is unclear but could play a role. Our results may parallel the findings, in part, to those of Bischoff et al who found that with increasing age, the relationship between telomere length and age lessened[24], yet contrasts to the findings by Lee[25]. Only with longitudinal data could the relationship between adiposity and telomere length be confirmed. As such, our findings should be considered exploratory.

The cross-sectional associations and mortality estimates became non-significant in older adults, a phenomenon that has been observed with the obesity paradox in certain populations[14], where obesity can be ‘protective’ on longer term outcomes in older adults. By deliberately stratifying by age, we assessed the relationship of telomere length with aging. Telomere length in younger individuals with obesity is lower, suggesting a higher-risk

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

population. Yet, this relationship appears to be non-significant across all older age groups. We evaluated the interaction of adiposity on telomere length on mortality and found that it did not modify its risk. In older adults with adiposity, there appeared to be a protective effect of adiposity on death, results which were non-significant after incorporating telomere length in the analysis. Those with adiposity may have died earlier and those remaining in older age may have had a slower rate of accumulation of subcutaneous and visceral adiposity, both of which can have a negative impact on telomere length. Previous studies have demonstrated that duration of adiposity is a negative prognostic factor in health outcomes[26]. In certain individuals, this shorter timeframe prevents the accumulation of inflammatory and co-morbid factors that could contribute to disease. Factors such as fat-free mass, nutritional status or cardiorespiratory fitness may also play a role.

These findings can add to the growing and disparate literature of how obesity can potentially moderate telomere length through inflammatory and oxidative stress mechanisms. A possible hypothesis to explain the lack of association between adiposity and TL on mortality in the oldest old, is that accumulated exposures from obesity (e.g. cardiometabolic, musculoskeletal or organ-speciifc harms) could plateau and not result in additional problems. Senescence could be prematurely triggered by obesity[27–29]. In vitro studies have demonstrated that weight changes may be implicated in this process as well. Adipose tissue changes with age which may reflect underlying genetic changes, and hence telomere alterations. Future work should focus on understanding more thoroughly these mechanistic changes as it has implications on other telomere-related diseases of aging.

The multivariable modeling deliberately adjusted for a number of sociodemographic and comorbidities that could impact both obesity and telomere lengthening. After model adjustment, the strength of association did not markedly change. These findings implicate high adiposity and possible adipokines could be the main toxic exposure impacting telomere length. We would have expected that the relationship would weaken our estimates after adding covariates representing inflammatory mediators yet the dataset did not have such information. Other pro-inflammatory and/or lipid-mediating hormones that were unmeasured likely influence this relationship[30]. The relationship between adipose-associated factors such as the adipokines leptin and adiponectin with telomere length or telomerase activity is not entirely clear. Similar positive associations were observed between telomere length and insulin-like growth factor in a study of elderly men[31]. Another cross sectional study found no significant association between telomere activity and adiposity, BMI, visceral fat, adiponectin or leptin in a smaller cohort of healthy adults (n=317, age 40–64) recruited from a health center[30]. The one prospective study that has reported telomere length change over time among individuals with stable coronary disease, demonstrated 3 trajectories of individuals whose leukocyte telomere length shortened, lengthened or remained stable[32]. Abdominal obesity (WHR) was independently predictive of increased risk of shorter telomeres over a 5 year follow-up, along with the other independent predictors, baseline telomere length, age and male sex, even when controlling for BMI, adipokines (adiponectin, leptin) and inflammatory markers (CRP, IL-6 and TNFa). Thus specific strata such as sex or age, as demonstrated in the current study, may influence associations and explain discrepant findings when analyses do not account for these moderators.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

The results from a recent systematic review and meta-analysis demonstrated that the association between telomere length and BMI was weak to moderate in nature[12, 13]. Our study indicated that the standard BMI categories were not related to telomere length and did not impact risk of death. A potential explanation could be that BMI is known to be a poor marker of general adiposity, missing 50% of those with obesity in a general population[33] but also having a poor sensitivity in an older population[34]. This ubiquitous measure incorporates both fat and muscle mass, while DEXA-measured body fat ascertains overall fat mass, and waist circumference is a surrogate for central adiposity. Our results may explain the inconsistent results observed with relationships between adiposity and telomere length, when using BMI as a surrogate for adiposity, as described by An et al[35] and Njajou et al[36].

A disadvantage of categorizing a continuous variable into categories is not only the loss of study power, but values slightly above the threshold may have only incremental and modest long-term risk, potentially resulting in overdiagnosis[37]. Misclassification is possible as well, and this has implications for public health in the identification and management of higher risk populations. We deliberately used each of these anthropometric measures in our modeling as a continuous variable to circumvent this issue and to demonstrate that our results were consistent.

The study has a number of limitations inherent to NHANES such as the use of community-dwelling adults and self-reported bias. As older adulthood generally is considered 65 years and older, we deliberately created two dichotomous cutpoints to assess changes in these age groups; however, we recognize that our sample size in those aged ≥70 years may limit our ability to make generalizations. Other biomarkers, including inflammatory cytokines could be helpful to explain this phenomenon between increased adiposity and decreased telomere length and their interplay should be considered in further studies. Lifespan changes of adiposity are not accounted for in this analysis including weight change and weight cycling. Importantly, alterations in physical function that could impact morbidity, mortality and quality of life should be considered.

Implications

In an era of individualized medicine, our results provide some helpful guidance for clinical practice. First, using telomere length to predict outcomes on disease states in populations with obesity may only reveal associations in younger as compared to older adults. Second, the use of biological data in obesity medicine, while still in its infancy, may explain a number of the relationships that are observed in large-scale epidemiological studies. This translational approach can help clarify relationships that are inconclusive. Third, our results further suggest the need to move away from traditional measures of adiposity (ie: BMI) and move towards body fat percent, which has increased ability to predict long-term outcomes. In low-tech settings, at least waist circumference or WHR should be considered. Fourth, our results provide evidence for an independent effect of obesity on telomere length specifically in younger adults. Yet, we did not observe any interactive effects, specifically in older adults. Engaging in healthy lifestyle measures improves one’s chances of preventing disability[38], enhancing quality of life, and reducing disease burden, all important tenants in old age. Yet, our results prompt the need for further evaluation of longitudinal datasets with repeated

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

measures to assess whether reduced adiposity in earlier geriatric years can restore telomerase activity, and thus telomere length. This reversal may be beneficial in this population.

CONCLUSIONS

Shorter telomere length is inversely related to higher percent body fat and waist circumference but becomes non-significant in adults over the age of 60 years. Adiposity does not appear to modify the relationship between telomere length and mortality in community-dwelling adults.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

NONE

ABBREVIATIONS

BMI	body mass index
BF	body fat
DEXA	dual energy x-ray absorptiometry
NHANES	National Health and Nutrition Examination Survey
WC	waist circumference

References

1. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005; 293(15):1868–74. [PubMed: 15840861]
2. Blaum CS, Xue QL, Michelon E, Semba RD, Fried LP. The association between obesity and the frailty syndrome in older women: the Women's Health and Aging Studies. J Am Geriatr Soc. 2005; 53(6):927–34. [PubMed: 15935013]
3. Zizza CA, Herring A, Stevens J, Popkin BM. Obesity affects nursing-care facility admission among whites but not blacks. Obes Res. 2002; 10(8):816–23. [PubMed: 12181391]
4. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. JAMA. 2005; 293(15):1861–7. [PubMed: 15840860]
5. Forsythe LK, Wallace JM, Livingstone MB. Obesity and inflammation: the effects of weight loss. Nutr Res Rev. 2008; 21(2):117–33. [PubMed: 19087366]
6. Schrager MA, Metter EJ, Simonsick E, Ble A, Bandinelli S, Lauretani F, et al. Sarcopenic obesity and inflammation in the InCHIANTI study. J Appl Physiol (1985). 2007; 102(3):919–25. [PubMed: 17095641]
7. Haver VG, Mateo Leach I, Kjekshus J, Fox JC, Wedel H, Wikstrand J, et al. Telomere length and outcomes in ischaemic heart failure: data from the COntrolled ROsuvastatin multiNAtional Trial in Heart Failure (CORONA). Eur J Heart Fail. 2015; 17(3):313–9. [PubMed: 25639660]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

8. Nielsen BR, Linneberg A, Bendix L, Harboe M, Christensen K, Schwarz P. Association between leukocyte telomere length and bone mineral density in women 25–93 years of age. Exp Gerontol. 2015; 66:25–31. [PubMed: 25868397]
9. Liu M, Huo YR, Wang J, Wang C, Liu S, Liu S, et al. Telomere Shortening in Alzheimer's Disease Patients. Ann Clin Lab Sci. 2016; 46(3):260–5. [PubMed: 27312549]
10. Cawthon RM, Smith KR, O'Brien E, Sivatchenko A, Kerber RA. Association between telomere length in blood and mortality in people aged 60 years or older. Lancet. 2003; 361(9355):393–5. [PubMed: 12573379]
11. Collaborators GBDO, Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, et al. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. N Engl J Med. 2017; 377(1): 13–27. [PubMed: 28604169]
12. Muezzinler A, Zaineddin AK, Brenner H. Body mass index and leukocyte telomere length in adults: a systematic review and meta-analysis. Obes Rev. 2014; 15(3):192–201. [PubMed: 24165286]
13. Mundstock E, Sarria EE, Zatti H, Mattos Louzada F, Kich Grun L, Herbert Jones M, et al. Effect of obesity on telomere length: Systematic review and meta-analysis. Obesity (Silver Spring). 2015; 23(11):2165–74. [PubMed: 26407932]
14. McAuley PA, Artero EG, Sui X, Lee DC, Church TS, Lavie CJ, et al. The obesity paradox, cardiorespiratory fitness, and coronary heart disease. Mayo Clin Proc. 2012; 87(5):443–51. [PubMed: 22503065]
15. Batsis JA, Mackenzie TA, Barre LK, Lopez-Jimenez F, Bartels SJ. Sarcopenia, sarcopenic obesity and mortality in older adults: results from the National Health and Nutrition Examination Survey III. Eur J Clin Nutr. 2014; 68(9):1001–7. [PubMed: 24961545]
16. Dickey R, Bartuska C, Bray G, Callaway W, Davidson E, Feld S, et al. AACE/ACE Position statement on the prevention, diagnosis, and treatment of obesity (1998 revision). Endocr Pract. 1998; 4(5):300.
17. Baumgartner RN. Body composition in healthy aging. Ann N Y Acad Sci. 2000; 904:437–48. [PubMed: 10865787]
18. Hughes VA, Frontera WR, Roubenoff R, Evans WJ, Singh MA. Longitudinal changes in body composition in older men and women: role of body weight change and physical activity. Am J Clin Nutr. 2002; 76(2):473–81. [PubMed: 12145025]
19. Tian S, Morio B, Denis JB, Mioche L. Age-Related Changes in Segmental Body Composition by Ethnicity and History of Weight Change across the Adult Lifespan. Int J Environ Res Public Health. 2016; 13(8)
20. Angleman SB, Harris TB, Melzer D. The role of waist circumference in predicting disability in periretirement age adults. Int J Obes (Lond). 2006; 30(2):364–73. [PubMed: 16231023]
21. Cerhan JR, Moore SC, Jacobs EJ, Kitahara CM, Rosenberg PS, Adami HO, et al. A pooled analysis of waist circumference and mortality in 650,000 adults. Mayo Clin Proc. 2014; 89(3): 335–45. [PubMed: 24582192]
22. Jun ES, Lee TH, Cho HH, Suh SY, Jung JS. Expression of telomerase extends longevity and enhances differentiation in human adipose tissue-derived stromal cells. Cell Physiol Biochem. 2004; 14(4–6):261–8. [PubMed: 15319529]
23. Ogura F, Wakao S, Kuroda Y, Tsuchiyama K, Bagheri M, Heneidi S, et al. Human adipose tissue possesses a unique population of pluripotent stem cells with nontumorigenic and low telomerase activities: potential implications in regenerative medicine. Stem Cells Dev. 2014; 23(7):717–28. [PubMed: 24256547]
24. Bischoff C, Petersen HC, Graakjaer J, Andersen-Ranberg K, Vaupel JW, Bohr VA, et al. No association between telomere length and survival among the elderly and oldest old. Epidemiology. 2006; 17(2):190–4. [PubMed: 16477260]
25. Lee M, Martin H, Firpo MA, Demerath EW. Inverse association between adiposity and telomere length: The Fels Longitudinal Study. Am J Hum Biol. 2011; 23(1):100–6. [PubMed: 21080476]
26. Houston DK, Ding J, Nicklas BJ, Harris TB, Lee JS, Nevitt MC, et al. Overweight and obesity over the adult life course and incident mobility limitation in older adults: the health, aging and body composition study. Am J Epidemiol. 2009; 169(8):927–36. [PubMed: 19270048]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

27. Herbert KE, Mistry Y, Hastings R, Poolman T, Niklason L, Williams B. Angiotensin II-mediated oxidative DNA damage accelerates cellular senescence in cultured human vascular smooth muscle cells via telomere-dependent and independent pathways. Circ Res. 2008; 102(2):201–8. [PubMed: 17991883]

28. Newsholme P, de Bittencourt PI Jr. The fat cell senescence hypothesis: a mechanism responsible for abrogating the resolution of inflammation in chronic disease. Curr Opin Clin Nutr Metab Care. 2014; 17(4):295–305. [PubMed: 24878874]

29. Ottinger MA. Mechanisms of reproductive aging: conserved mechanisms and environmental factors. Ann N Y Acad Sci. 2010; 1204:73–81. [PubMed: 20738277]

30. Diaz VA, Mainous AG, Player MS, Everett CJ. Telomere length and adiposity in a racially diverse sample. Int J Obes (Lond). 2010; 34(2):261–5. [PubMed: 19773737]

31. Moverare-Skrtic S, Svensson J, Karlsson MK, Orwoll E, Ljunggren O, Mellstrom D, et al. Serum insulin-like growth factor-I concentration is associated with leukocyte telomere length in a population-based cohort of elderly men. J Clin Endocrinol Metab. 2009; 94(12):5078–84. [PubMed: 19846733]

32. Farzaneh-Far R, Lin J, Epel E, Lapham K, Blackburn E, Whooley MA. Telomere length trajectory and its determinants in persons with coronary artery disease: longitudinal findings from the heart and soul study. PLoS One. 2010; 5(1):e8612. [PubMed: 20072607]

33. Romero-Corral A, Somers VK, Sierra-Johnson J, Thomas RJ, Collazo-Clavell ML, Korinek J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. Int J Obes (Lond). 2008; 32(6):959–66. [PubMed: 18283284]

34. Batsis JA, Mackenzie TA, Bartels SJ, Sahakyan KR, Somers VK, Lopez-Jimenez F. Diagnostic accuracy of body mass index to identify obesity in older adults: NHANES 1999–2004. Int J Obes (Lond). 2016; 40(5):761–7. [PubMed: 26620887]

35. An R, Yan H. Body weight status and telomere length in U.S. middle-aged and older adults. Obes Res Clin Pract. 2017; 11(1):51–62. [PubMed: 26895795]

36. Njajou OT, Cawthon RM, Blackburn EH, Harris TB, Li R, Sanders JL, et al. Shorter telomeres are associated with obesity and weight gain in the elderly. Int J Obes (Lond). 2012; 36(9):1176–9. [PubMed: 22005719]

37. Batsis JA, Lopez-Jimenez F. Cardiovascular risk assessment--from individual risk prediction to estimation of global risk and change in risk in the population. BMC Med. 2010; 8:29. [PubMed: 20500815]

38. Pahor M, Guralnik JM, Ambrosius WT, Blair S, Bonds DE, Church TS, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA. 2014; 311(23):2387–96. [PubMed: 24866862]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1

Baseline Characteristics of Subjects NHANES 1999–2002 Cohort

		Age	Cohort	
	Overall	**<60 years**	**≥60 years**	**p-value**
	N=7,827	**N=5,155**	**N=2,672**	
Age, years ± s.e.	46.1±0.37	38.9±0.26	70.9±0.28	<0.001
Female sex (%)	4,056 (51.4)	2,744 (50.2)	1,312 (55.5)	<0.001
Weight, kg	80.3±0.39	81.1±0.46	77.5±0.40	<0.001
Race				<0.001
Hispanic American	2,293 (13.8)	1,629 (15.5)	664 (7.8)	
Non-Hispanic White	3,965 (72.9)	2,408 (70.1)	1,557 (82.7)	
Non-Hispanic Black	1,333 (9.3)	936 (10.0)	397 (6.9)	
Other	236 (4.0)	182 (4.4)	54 (2.7)	
Co-Morbid Conditions				
Hypertension	1,922 (82.7)	730 (78.2)	1,192 (88.5)	<0.001
Diabetes Mellitus	840 (7.7)	303 (5.1)	537 (16.9)	<0.001
Congestive Heart Failure	230 (2.2)	55 (1.1)	175 (6.2)	<0.001
Non-skin cancer	644 (7.8)	173 (4.1)	471 (20.6)	<0.001
Stroke	237(2.3)	51 (0.99)	186 (6.7)	<0.001
COPD	542 (7.7)	290 (6.5)	252 (11.6)	<0.001
Osteoporosis	96 (0.85)	36 (0.51)	60 (2.0)	<0.001
Kidney Disease	108 (2.4)	47 (1.9)	61 (4.0)	0.002
Coronary Artery Disease	578 (6.1)	134 (2.7)	444 (18.0)	<0.001
Arthritis	1,895 (21.6)	654 (13.5)	1,241 (49.2)	<0.001
Current Smoker				<0.001
Current	1,695 (24.4)	1,369 (28.0)	326 (12.2)	
Never	4,016 (50.1)	2,763 (50.9)	1,253 (47.0)	
Former	2,101 (25.5)	1,014 (21.1)	1,087 (40.8)	
Physical Activity Level				<0.001
Sits	1,964 (24.6)	1,184 (23.7)	780 (27.8)	
Walks	4,137 (50.3)	2,616 (48.6)	1,521 (56.4)	
Light Loads	1,212 (17.7)	912 (18.9)	300 (13.8)	
Heavy Work	505 (7.3)	442 (8.9)	63 (2.1)	
Anthropometric Measures				
% Body Fat	33.9±0.15	33.0±0.16	36.9±0.15	<0.001
BMI, kg/m^2	28.1±0.14	28.1±0.16	28.2±0.14	0.30
WC, cm	96.0±0.35	95.0±0.39	99.6±0.29	<0.001
Body Mass Index Categories				

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

		Age	Cohort	
	Overall	**<60 years**	**≥60 years**	**p-value**
	N=7,827	**N=5,155**	**N=2,672**	
Underweight	111 (1.8)	79 (1.8)	32 (1.5)	
Normal	2,291 (32.9)	1,605 (34.2)	686 (32.4)	
Overweight	2,756 (35.0)	1,757 (34.1)	999 (31.9)	0.003
Obesity	2,420 (30.4)	1,624 (29.9)	796 (27.7)	

Data are mean ± standard errors or counts (%). Data are weighted according to the National Health and Nutrition Examination Survey protocol

Abbreviations: BMI – body mass index; COPD – chronic obstructive pulmonary disease; WC – waist circumference

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2019 February 01.

Table 2

Mean Telomere Length Ratio by Obesity Measure

	Overall Cohort	<60 years	≥60 years	p-value[#]	<70 years	≥70 years	p-value[#]	60–70 years	70–80 years	80+ years	p-value
	n= 7,827	n= 5,155	n= 2,672		n=6364	N=1463		N=1209	N=877	N=586	
Overall Cohort	1.05±0.01	1.10±0.01	0.91±0.02	<0.001	1.08±0.01	0.87±0.02	<0.001	0.96±0.02	0.88±0.02	0.84±0.02	<0.001
Body Fat, %											
High (n=5,532)	1.03±0.01	1.08±0.02	0.91±0.02	<0.001	1.06±0.02	0.86±0.02	<0.001	0.96±0.02	0.87±0.02	0.84±0.02	<0.001
Low (n=1,689)	1.12±0.02	1.15±0.02	0.92±0.02	<0.001	1.14±0.02	0.88±0.02	<0.001	0.97±0.03	0.91±0.03	0.85±0.87	<0.001
p-value[†]	<0.001	<0.001	0.61	---	<0.001	0.31		0.80	0.27	0.72	---
Body Fat-2, %											
High (n=5,532)	1.02±0.02	1.06±0.02	0.91±0.02	<0.001	1.05±0.02	0.87±0.02	<0.001	0.95±0.02	0.88±0.02	0.84±0.02	<0.001
Low (n=1,689)	1.11±0.02	1.14±0.02	0.91±0.02	<0.001	1.12±0.02	0.86±0.02	<0.001	0.97±0.02	0.87±0.02	0.84±0.02	<0.001
p-value[†]	<0.001	<0.001	0.99		<0.001	0.52		0.40	0.56	0.93	
Body Mass Index, kg/m^2											
Underweight (n=111)	1.08±0.03	1.12±0.03	0.92±0.05	0.001	1.12±0.03	0.86±0.03	<0.001	0.95±0.02	0.90±0.02	0.83±0.03	0.04
Normal (n=2,291)	1.09±0.02	1.14±0.02	0.90±0.02	<0.001	1.12±0.02	0.87±0.02	<0.001	1.14±0.11	0.87±0.03	0.83±0.04	0.26
Overweight (n=2,756)	1.04±0.02	1.09±0.02	0.91±0.02	<0.001	1.07±0.02	0.87±0.02	<0.001	0.95±0.02	0.89±0.02	0.84±0.02	0.56
Obesity (n=2,420)	1.03±0.02	1.07±0.02	0.92±0.02	<0.001	1.05±0.02	0.85±0.02	<0.001	0.97±0.02	0.84±0.02	0.87±0.03	<0.001
p-value[†]	<0.001	<0.001	0.65	---	<0.001	0.59		0.29	0.20	0.58	---
Waist Circumference, cm											
High (n=3987)	1.02±0.02	1.07±0.02	0.91±0.02	0.08	1.05±0.02	0.87±0.02	<0.001	0.95±0.02	0.87±0.02	0.85±0.02	<0.001
Low (n=3577)	1.09±0.02	1.12±0.02	0.92±0.02	<0.001	1.11±0.02	0.87±0.02	<0.001	0.97±0.02	0.90±0.02	0.83±0.03	<0.001
p-value[†]	<0.001	<0.001	0.59	---	<0.001	0.53		0.42	0.18	0.51	----

Values represented are means ± standard error

High body fat is categorized in males as ≥25% and in females as ≥35%

BMI categories: underweight (<18.5kg/m^2), normal (18.5–24.9kg/m^2), overweight (25.0–29.9kg/m^2), obesity (≥30kg/m^2)

High waist circumference is categorized in males as ≥102cm in males, and ≥88cm in females

[#]-p-value represents difference in telomere length between individuals aged <60 years and >60years.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

† -p-value represents the difference between high/low body fat, BMI or waist circumference within the overall cohort, and stratified by age 60

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2019 February 01.

Table 3

Association of Mean Telomere Length with Anthropometric Measures

	Model 1		Model 2		Model 3	
	β± standard error	**p-value**	**β ± standard error**	**p-value**	**β± standard error**	**p-value**
Body Fat-1, %	−0.00374±0.00054	<0.001	−0.0033±0.00077	<0.001	−0.0033±0.0008	<0.001
High	−0.09 ± 0.011	<0.001	−0.036±0.01	0.001	−0.035±0.011	0.002
Low	Referent		Referent		Referent	
Body Fat-2, %						
High	−0.0862±0.009	<0.001	−0.0412±0.0083	<0.001	−0.041±0.008	<0.001
Low	Referent		Referent		Referent	
Body Mass Index, kg/m^2	−0.0032±0.0008	0.001	−0.0025±0.00083	0.005	−0.0025±0.00081	0.005
Underweight	0.013±0.024	0.60	0.032±0.02	0.14	0.039±0.019	0.05
Normal	Referent		Referent		Referent	
Overweight	−0.037±0.022	0.10	0.004±0.019	0.84	0.010±0.020	0.61
Obese	−0.047±0.024	0.06	−0.011±0.020	0.59	−0.004±0.02	0.86
Waist Circumference, cm	−0.0024±0.00037	<0.001	−0.0011±0.00037	0.006	−0.0011±0.00037	0.007
High	−0.068±0.010	<0.001	−0.032±0.011	0.006	−0.032±0.011	0.008
Low	Referent		Referent		Referent	

All values represented are β coefficient ± standard error

Each anthropometric measure represents a separate model (both continuous and categorical)

Model 1: no adjustment

Model 2: Model 1 adjusted for age, sex race, education, smoking

Model 3: Model 2 adjusted for diabetes mellitus, congestive heart failure, non-skin cancer, coronary artery disease, arthritis, physical activity

High body fat-1 is categorized in males as ≥25% and in females as ≥35%

High body fat-2 is categorized in males as ≥28% and in females as ≥38%

High waist circumference is categorized in males as ≥102cm in males, and ≥88cm in females

BMI categories: underweight (<18.5kg/m^2), normal (18.5–24.9kg/m^2), overweight (25.0–29.9kg/m^2), obesity (≥30kg/m^2)

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2019 February 01.

Table 4

Multivariable Fully Adjusted Model by Age Category

	Age <60 years		Age >60 years		Interaction term	Age <70 years		Age >70 years		Interaction term
	β± standard error	p-value	β ± standard error	p-value	p-value	β± standard error	p-value	β ± standard error	p-value	p-value
Body Fat-1, %	−0.053±0.0009	<0.001	−0.00062±0.001	0.55	<0.001	−0.0055±0.0009	<0.001	−0.00078±0.001	0.56	0.001
High	−0.061±0.013	<0.001	−0.0076±0.019	0.70	0.012	−0.065±0.012	<0.001	−0.016±0.02	0.45	0.048
Low	Referent	---	Referent	---	---	Referent	---	Referent	---	---
Body Fat-2, %										
High	−0.065±0.01	<0.001	−0.0032±0.012	0.78	<0.001	−0.067±0.009	<0.001	0.0081±0.16	0.61	<0.001
Low	Referent	---	Referent	---	---	Referent	---	Referent	---	---
Body Mass Index, kg/m^2	−0.0032±0.000094	0.002	0.00074±0.0011	0.53	0.001	−0.0029±0.001	0.002	−0.0013±0.002	0.48	0.16
Underweight	−0.0175±0.03	0.55	0.0087±0.053	0.87	0.52	−0.0022±0.028	0.94	−0.022±0.032	0.50	0.93
Normal	Referent	---	Referent	---	---	Referent	---	Referent	---	---
Overweight	−0.0486±0.02	0.004	0.0043±0.014	0.76	0.01	−0.049±0.012	0.003	0.0045±0.018	0.80	0.06
Obese	−0.070±0.015	<0.001	0.010±0.012	0.41	<0.001	−0.067±0.013	<0.001	−0.026±0.022	0.25	0.15
Waist Circumference, cm	−0.0016±0.0004	0.001	−0.0002±0.0005	0.68	0.004	−0.0016±0.0004	<0.001	−0.00062±0.0008	0.46	0.18
High	−0.048±0.013	0.001	−0.017±0.014	0.25	0.006	−0.05±0.012	<0.001	−0.02±0.017	0.26	0.01
Low	Referent	---	Referent	---	---	Referent	---	Referent	---	---

All values represented are β coefficient ± standard error

Model adjusts for age, sex race, education, smoking, diabetes mellitus, congestive heart failure, non-skin cancer, coronary artery disease, arthritis, physical activity.

High body fat-1 is categorized in males as ≥25% and in females as ≥35%

High body fat-2 is categorized in males as ≥28% and in females as ≥38%

High waist circumference is categorized in males as ≥102cm in males, and ≥88cm in females

BMI categories: underweight (<18.5kg/m^2), normal (18.5–24.9kg/m^2), overweight (25.0–29.9kg/m^2), obese (≥30kg/m^2)

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2019 February 01.

Table 5

Multivariable Analyses – Overall, Age, Telomere, Anthropometry and Mortality Status

		Ix	Age <60	Ix	Age>60	Ix	Age<70	Ix	Age<70	Ix
	Model 3	**p-value**	**Model 3**		**Model 3**		**Model 3**		**Model 3**	
Body Fat-1, %	**0.99 [0.98,1.00]**	---	**1.04 [1.01,1.06]**	---	**0.96 [0.95,0.98]**	---	**1.02 [1.01,1.04]**	---	**0.97 [0.95,0.98]**	---
High	**0.78 [0.67,0.92]**	0.47	1.18 [0.86,1.62]	0.17	**0.68 [0.56,0.81]**	0.06	1.20 [0.95,1.52]	0.80	**0.71 [0.58,0.88]**	0.25
Low	Referent	---	Referent	---	Referent	---	Referent	---	Referent	---
Body Fat-2, %										
High	0.89 [0.78,1.01]	0.55	**1.56 [1.16,2.09]**	0.94	**0.75 [0.65,0.86]**	0.62	**1.30 [1.06,1.60]**	0.54	**0.79 [0.67,0.93]**	0.97
Low	Referent	---	Referent		Referent	---	Referent	---	Referent	---
Body Mass Index, kg/m^2	**0.98 [0.97,0.99]**		1.01 [0.99,1.03]	---	**0.94 [0.93,0.95]**		0.99 [0.98,1.01]		**0.95 [0.94,0.97**]	
Underweight	**1.61 [1.06,2.45]**	0.12	1.08 [0.34,3.47]	0.71	1.70 [1.08,2.66]	0.06	2.03 [1.06,3.89]	0.33	1.16 [0.67,2.01]	0.74
Normal	Referent	---	Referent	---	Referent	Ref	Referent	Ref	Referent	Ref
Overweight	**0.80 [0.69,0.92]**	0.34	0.89 [0.63,1.27]	0.43	**0.68 [0.58,0.79]**	0.08	0.85 [0.66,1.08]	0.87	**0.74 [0.62,0.89]**	0.40
Obese	**0.80 [0.69,0.94]**	0.75	1.18 [0.84,1.66]	0.35	**0.50 [0.42,0.60]**	0.28	0.86 [0.67,1.10]	0.21	**0.63 [0.51,0.77]**	0.62
Waist Circumference, cm	1.00 [0.99,1.00]	---	**1.01 [1.00,1.02]**	---	**0.98 [0.98,0.99]**	---	**1.00 [1.00,1.01]**	---	**0.99 [0.98,0.99]**	---
High	0.93 [0.83,1.06]	0.73	1.50 [1.12,2.01]	0.69	**0.72 [0.63,0.83]**	0.19	1.16 [0.95,1.42]	0.57	**0.81 [0.69,0.95]**	0.36
Low	Referent	---	Referent	---	Referent		Referent	---	Referent	
Mean Telomere Length	0.79 [0.61,1.02]	---	0.65 [0.38,1.11]	---	**0.36 [0.27,0.49]**	---	**0.33 [0.22,0.49]**	---	**0.61 [0.43,0.87**]	---

Each vertical column represents a separate multivariable model; bold indicates statistically significant

Ix: Interaction between anthropometric term x telomere status on mortality

All values represented are β coefficient ± standard error for continuous variables (Body Fat, body mass index, waist circumference and mean telomere length). Categorical variables (high/low body fat-1/2, BMI categories, and high/low waist circumference are represented as Hazard ratios [95% confidence intervals]

All models represented are fully adjust for age (where appropriate, sex, race, education, smoking status, diabetes mellitus, congestive heart failure, non-skin cancer, coronary artery disease, arthritis, physical activity

High body fat-1 is categorized in males as ≥25% and in females as ≥35%

High body fat-2 is categorized in males as ≥28% and in females as ≥38%

High waist circumference is categorized in males as ≥102cm in males, and ≥88cm in females

BMI categories: underweight (<18.5kg/m^2), normal (18.5–24.9kg/m^2), overweight (25.0–29.9kg/m^2), obesity (≥30kg/m^2)