**Supplementary Tables**

**Table 1.** **Included Studies Regarding the Effect of Physical Activity on Telomeric Length and Other Factors Associated with Aging.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Study Population Characteristics** | **Study Design** | **Lifestyle** | **Sample and Measurements** | **Aging Biomarker and Measure Method** | **Main Results** |
| Colon et al. [19] | Healthy non-smoking men: 7 triathletes (competition participants in the last 3 years; training at least 10 h/week, average 35.11 ± 5.86 years old) and 7 recreational activity (no participants in any sport; moderate-intense exercise, at least 3 h / week, average 34.14 ± 10.29 years old) | Cross | Physical activity: competitive triathlon training | **Sample:**PBMC | * **Biomarker:** relative telomere length.
* **Method:** PCR
 | * Telomeres significantly shorter in recreationally active men than in triathletes.
* Significant positive relationship between VO2max, lactate threshold velocity and running economy, and relative telomere length.
 |
| **Measurements:*** LTL
* VO2max
* Lactate threshold
* Running economy
 |
| Dimauro et al. [14] | Older subjects (70-75 years) randomized in two groups (10 subjects training for 12 weeks and 10 subjects’ control) | Longitudinal | Physical activity: Resistance training | **Sample:**PBMC | * **Biomarker:** telomere length (in T/S ratio)
* **Method:** qPCR-real time
 | * Statistically higher LTL in the training group regarding control.
* Significantly lower expression of antioxidant proteins after the intervention (MnSOD).
* Significant decrease in the level of global DNA methylation in the training group.
 |
| **Measurements:*** LTL
* Global DNA methylation
* Protein Expression
 |
| Du et al [5] | Cohort of 7813 women from Nurses’ Health Study aged between 35-55 years | Cross-sectionally | * Physical activity
* Sedentary behavior
 | **Sample:**Peripheral Blood | **Biomarker:** relative Telomere length.**Method:** qPCR | * LTL inversely correlated with number of cigarette packages per year and anthropometric measurements.
* Positive relationship between MET-hours / week with LTL. Women with high or moderate activity (moderate or vigorous intensity, 2-4 weeks) have longer LTLs than those less active. Average difference of 4.4 years of aging.
 |
| **Measurements:**LTL |
| Shadyab et al. [16] | Cohort of 1405 older women (45-69 years) Afro-American and white from the Woman’s Health Initiative (WHI) | Cross-sectionally | Physical Activity (Accelerometer Measurement) | **Sample:**Peripheral Blood | * **Biomarker:** Telomere Length: average length of terminal restriction fragments.
* **Method:** Southern Blot
 | * Significant linear association between MVPA (moderate-to-vigorous physical activity) and LTL (MVPA as ≥2.5 h / week).
* LTL on average 80 longer base pairs in women with MVPA ≥2.5 h / week compared to women with MVPA <2.5 h / week.
* Women with greater physical activity have higher LTL, regardless of demographic characteristics and lifestyle factors.
 |
| **Measurements:**LTL |
| Shadyab et al. [17] | 1476 postmenopausal older women (50-79 years) participating in the Woman’s Health Initiative (WHI) study | Cross-sectionally | Physical activity in leisure time | **Sample:**Peripheral Blood | * **Biomarker:** Telomere Length: average length of terminal restriction fragments.
* **Method:** Southern Blot
 | * LTL associated with higher levels of total physical activity in leisure time: telomeres 110 longer base pairs in women with ≥17.00 MET-hours / Week, compared to those with <1.25 MET-hours / Week
* Association between telomere length and MVPA. For every 1 MET-hour / week of MVPA the telomere is 3 bp longer
 |
| **Measurements:**LTL |
| Sousa et al. [20] | Group of Master endurance athletes (between 40-70 years) with at least 15 years of regular competitive activity. Control group matched by age and young people without training. End sample size of 38 subjects. | Cross | Physical activity: Redox balance in runners | **Sample:**Blood | * **Biomarker:** Telomere Length: relative Telomere length (T/S)
* **Method:** qPCR
 | * Lower total antioxidant capacity in endurance race athletes compared to young adults. Athletes and young adults have a better redox balance (antioxidant / prooxidant ratio) compared to adults without training; higher levels of NO in athletes.
* Shorter telomeres in adults without training, respect to athletes and young adults (no significant difference between the latter). Correlation between LTL and NO levels in the corridors.
 |
| **Measurements:**LTLNitric Oxide (NO)Protein peroxidationAntioxidant parameters |
| Tucker [18] | Participants of HNANES. 5823 participants included in the analysis, ages between 20-85 years old. | Cross-sectionally | Physical activity | **Sample:**Blood | * **Biomarker:** Telomere Length: relative Telomere length (T/S)
* **Method:** qPCR
 | * Significantly long telomeres in people with high physical activity (> 1000 MET-minutes / week). Telomere 140 bp longer in this group compared to sedentary people (advantage of biological aging of approximately 9 years) and 137 bp longer compared to less active people (advantage of biological aging of approximately 8.8 years).
 |
| **Measurements:**LTL |

**Table 2.** **Included Studies Regarding the Effect of Diet on Telomeric Length and Other Factors Associated with Aging.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Study Population Characteristics** | **Study Design** | **Lifestyle** | **Sample and Measurements** | **Aging Biomarker and Measure Method** | **Main Results** |
| Fretts et al. [9] | Cohort of 2846 Native Americans from Strong Heart Family Stud. Ages between 14.1–93.3 years old. | Cross-sectionally | Food: Processed vs. Unprocessed Meat | **Sample:**Peripheral Blood | * **Biomarker: T**elomere length (in T/S ratio)
* **Method:** qPCR-real time
 | * Processed meat intake related to shorter LTL (shortening of 0.021 shorter T / S units for each additional portion)
* There was no significant association between unprocessed red meat intake with LTL
 |
| **Measurements:**LTL |
| Garcia-Calzon et al. [28] | Children and Adolescents from GENOI study: 287 participants (51% with obesity, 37% with normal weight, 12% with overweight), age between 6-18 years | Cross-sectionally | Diet: Total antioxidant capacity. | **Sample:**Peripheral Blood | * **Biomarker: T**elomere length (in T/S ratio)

**Method:** qPCR-real time | * Positive relationship between TAC and LTL.
* Legume consumption and intake of PUFA associated with longer telomeres.
* Increased consumption of cereal (specifically White Bread) associated with shorter telomeres
* Increase in of 6mmol of Dietary TAC associated with a 70% lower risk of having short telomeres
 |
| **Measurements:**TAC (total antioxidant capacity)LTL |
| Gong et al. [27] | Adults aged between 20-70 years. Cohort of 553 individuals from a prospective study in progress in a population in southeastern China. | Cross | Diet: Dietary pattern. | **Sample:**Peripheral Blood | * **Biomarker:** Telomere Length: average length of terminal restriction fragments.
* **Method:** Southern Blot
 | * There is no significant relationship between dietary patterns and TL in men.
* In women, greater adherence to a diet rich in vegetables related to longer TL.
 |
| **Measurements:**Telomere Length (TL), Dietary Patterns |
| Nonino et al. [23] | Women (27-48 years): 20 in obesity (BMI> 40 kg/m2) and 8 in normal weight (18.5 kg/m2 <BMI <24.9 kg/m2) | Cross interventional | ObesityDiet: supplement with green tea for 8 weeks | **Sample:**Peripheral Blood | * **Biomarker:** relative average of telomeres
* **Method:** qPCR
 | * Significant increase in TL after supplement with green tea.
* There are no significant weight losses or BMI changes with the intervention
* Inverse correlation between BMI and TL.
* Lower TL in patients with obesity.
 |
| **Measurements:**Telomere Length (TL). |
| Tucker [22] | Participants of HNANES (National Health and Nutrition Examination Survey, USA) 5674 participants included in the analysis ages between 20-85 years old. | Cross-sectionally | Food: Fiber consumption | **Sample:**Blood | * **Biomarker:** Relative Telomere length (T/S)
* **Method:** qPCR
 | * Significant linear relationship between fiber consumption and telomere length. For every gram of fiber per 1000Kcal consumed telomeres on average 8.3 bp longer (after adjustment it was still significant with telomeres 6.7 bp longer on average)
* Adults with high fiber consumption have significantly longer telomeres.
 |
| **Measurements:**LTL |

**Table 3. Included Studies Regarding the Effect of Techniques for Stress Control and Comprehensive Lifestyle Changes on Telomeric Length and Other Factors Associated with Aging.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Study Population Characteristics** | **Study Design** | **Lifestyle** | **Sample and Measurements** | **Aging Biomarker and Measure Method** | **Main Results** |
| Conklin et al. [34] | Healthy people from the Spirit Rock Meditation Center (28 recruited from a group of candidates pre-registered for retreats, and 34 from the local community who will not participate in retirement at least 4 weeks before the study). Mean age 50.74 years) | Longitudinal | Stress Control: Insight Meditation (1-month withdrawal) | **Sample:**PBMC | * **Biomarker:** telomere length (in T / S ratio)
* **Method:** qPCR-real time.
 | * Increase in TL observed in the group of meditation retreat participants of on average 104.2 bp (equivalent to reduction of 4 years of aging) there were no changes in controls.
* Slightly higher levels of TA in the controls, although not significant.
* Significant changes in gene expression in the withdrawal group (*Atrip, Cct1, Cct6, Gar1 and Hnrnpa1* with the highest levels of expression)
 |
| **Measurements:*** Telomere Length (TL)
* Telomerase Activity (TA)
* Expression of telomere related genes (TRG).
 |
| Dada et al. [31] | Cohort of Fathers of children diagnosed with retinoblastoma (56 of 131 included, mean age 33.17±11.2 years). Control group of 50 parents (mean age 32.5±4.5 years) of children born healthy in the last year | Longitudinal | Stress Control: Yoga and Meditation(6-month intervention) | **Sample:**Sperm | * **Biomarker:** telomere length (in T / S ratio)
* **Method:** qPCR-real time.
 | * Higher seminal levels of ROS, DFI, and 8-OHdG levels in Fathers of children with retinoblastoma
* Shorter telomeres in parents of children with retinoblastoma (non-significant difference)
* Gradual reduction of DFI, rapid decrease of ROS and 8-OHdG after the intervention.
 |
| **Measurements:*** 8-OHdG,
* Telomere Length
* ROS
* DFI
 |
| Duan et al. [29] | Men and women aged 55-65 randomized in two groups (intervention with Tai Chi, Control). 96 subjects included. | Longitudinal randomized | Physical Activity-Stress Control: Tai Chi (6-months of intervention) | **Sample:**PBMC | **TE-ELISA** (immunosorbent assay linked to the human telomerase enzyme) | * Telomerase activity significantly increased in the Tai chi group after the intervention (from 23.75 ± 3.78 u/mmol to 26.31 ± 2.93 u/mmol after 6 months)
* The control group showed no significant changes
 |
| **Measurements:**Telomerase Activity (TA) |
| Hoge et al. [33] | Individuals over 18 years of age or older: group of individuals with extensive training in LKM (50 partitioners), and control group of individuals without experience in meditation practices (22 partitioners) | Cross | Stress Control: Metta or Love-Kindness Meditation (LKM) Practice | **Sample:**Peripheral Blood | * **Biomarker:** Relativetelomere length
* **Method:** qPCR
 | * Longer telomere lengths in LKM practitioners than in controls (significant relationship in women, but not in men)
 |
| **Measurements:**Relative Telomere Length (rTL) |
| Krishna et al. [30] | Healthy Yoga Practitioners, age between 30-40 years and minimum 2 years of practice (n=15). Control (n=18): healthy non-practicing physical activity people matched in age, gender and BMI. | Prospective case-control study | Stress Control: yoga practice | **Sample:**Blood | * **Biomarker:** telomere length (in T / S ratio)
* **Method:** qPCR-real time.
 | * LTL significantly shorter in the control group than in yoga practitioners
* Higher levels of TAOS, MDA and homocysteine lower in yoga practitioners.
* LTL positively correlated with TAOS, but negatively correlated with MDA and Homocysteine levels.
 |
| **Measurements:**LTL, oxidative stress: TAOS, MDA, Homocysteine |
| Ornish et al. [13] | Men with low-risk prostate cancer who chose active surveillance instead of conventional treatment. 30 enrolled patients aged 49-80 years. | Longitudinal | Comprehensive lifestyle change: diet, physical activity, stress management and social support | **Sample:**PBMC | * **Biomarker:** telomere length (in T / S ratio)
* **Method:** qPCR-real time.
 | * Increase in rTL in the lifestyle intervention group and decrease in rTL in the control group.
* Correlation between adherence to change in lifestyle and rTL.
 |
| **Measurements:**Relative Telomere Length (rTL), Telomerase Activity  |
| Tolahunase et al. [32] | 96 Men and women (30-65 years) leading the modern unhealthy lifestyle. | 12-week prospective exploratory study | Stress control: Yoga-Meditation intervention (YMLI) | **Sample:**Blood | **Biomarkers:*** Relative telomere length
* 8-OH2dG
* TAC.

**Method:*** qPCR (telomere length)
* Cayman’s EIA kit (8-OH2dG)
* ELISA kits (TAC)
 | * Significant decrease in levels of 8-OH2dG and ROS and increase and TAC of telomerase activity after 12 weeks of YMLI
* Increase in telomere length after 12 weeks of YMLI, but not significant.
* Decrease in cortisol and IL-6 levels and increase in β-endorphin BDNF and sirtuine-1, after 12 weeks of YMLI
 |
| **Measurements:**LTL, Telomerase Activity (TAC), 8-OH2dG (DNA damage), ROS |

**Table 4.** **Included Studies Regarding the Effect of Unhealthy Lifestyles and Psychological Stress on Telomeric Length and Other Factors Associated with Aging.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Study Population Characteristics** | **Study Design** | **Lifestyle** | **Sample and Measurements** | **Aging Biomarker and Measure Method** | **Main Results** |
| Chen et al. [43] | Adult people: 20 with a diagnosis of MDD (depressive disorder) and 20 healthy controls matched by age, sex and ethnicity. | Cross | Psychological stress related to ACEs, and MDD | **Sample:**PBMC | * **Biomarker:** telomere length (in T / S ratio)

**Method:** qPCR | * People with MDD have greater telomerase activity than controls. They had no significantly shorter telomeres
* ACEs showed a significant inverse relationship with LTL, but showed no significant relationship with telomerase activity, in the controls.
* ACEs had no significant relationship with LTL, but a positive relationship with telomerase activity in people with MDD.
 |
| **Measurements:*** LTL
* Telomerase Activity
 |
| Grun et al. [42] | 66 subjects between 18-65 years, classified according to BMI in 2 groups: people with obesity and Control of healthy individuals. | Cross-sectionally | Obesity | **Sample:**PBMC | * **Biomarker:** telomere length (in T / S ratio)
* **Method:** qPCR-real time.
 | * TL significantly shorter in obese individuals; also, on gene expression of components of the Shelterin complex (*TRF1, TRF2, POT1 and DKC1*) and increased oxidative damage of molecules and non-enzymatic antioxidant systems.
* Expression levels of TRF1 as the main contributor to telomere shortening in people with obesity.
 |
| **Measurements:**Telomere Length (TL)Determinants of oxidative damageNon-enzymatic antioxidant systems |
| Huzen et al. [39] | Cohorts of 8592 individuals aged between 28-75 years participating in the PREVEND (Prevention of Renal and Vascular End-stage Disease) study at three moments of follow-up. | Longitudinal | * Smoking
* Metabolic traits
 | **Sample:**Peripheral Blood | * **Biomarker:** telomere length (in T / S ratio)
* **Method:** qPCR-real time.
 | * Changes in RTL associated with age, gender, glucose levels, waist-hip ratio, HDL cholesterol and smoking, the latter with a dose-dependent association (baseline measures).
* High systolic and diastolic pressure, triglyceride levels, diabetes, high waist hip ratio and smoking actively related to increased shortening of telomeres (under follow-up).
 |
| **Measurements:**Relative Telomere Length (RTL) |
| Joshu et al [41] | 596 men treated surgically for prostate cancer (40-75 years), participants of the HPFS (Health Professionals Follow-up Study) | Cross Prospective Study | * Obesity
* Physical inactivity
 | **Sample:**Prostatectomy tissue, by cancer diagnosis (cell culture) | * **Biomarker:** telomere length
* **Method:** FISH test (telomere-specific)
 | * TL significantly shorter in men with: overweight/obese, greater waist circumference, greater weight gain from 21 years (> 25 pounds), and lower physical activity (in stromal cells).
* No significant differences were found in telomere length in epithelial and luminal cells or in cancer cells.
 |
| **Measurements:**Telomere Length (TL), Cell type |
| Latifovic et al. [35] | 678 healthy volunteers (men and women) aged between 20-50 years (final sample of 477 individuals) | Cross-sectionally | * Alcohol consumption
* Smoking
* Physical Activity
 | **Sample:**Blood | * **Biomarker:** Relative length of telomere (T/S)
* **Method:** qPCR multiplex monochrome
 | * No significant association was observed between rLTL and alcohol consumption.
* Shorter rLTL associated with current daily smokers, compared to people who never smoked (rLTL 0.096 shorter relative units).
* Longer rLTL with increase in total physical activity (not significant) and positive relationship of rLTL with vigorous physical activity.
 |
| **Measurements:**Relative Telomere Length (rLTL) |
| Muezzinler et al., [36] | 3600 men and women aged 50-70 years. Subsample of ESTHER study participants | Longitudinal (with cross sectional analysis) | Smoking | **Sample:**Peripheral Blood | * **Biomarker:** Relative telomere length
* **Method:**
* **qPCR (**Relative Telomere length T/S)
* **Southern Blot** (average length of terminal restriction fragments)
 | * LTL inversely associated with smoking (the greater the intensity of the minor LTL habit); but associated with lower rates of telomere shortening in 8 years of follow-up.
* Longer telomeres in people who never smoked than in current smokers and smokers. Higher LTL in ex-smokers than in current smokers, positive time to quit smoking and LTL.
 |
| **Measurements:**LTL |
| Puterman et al. [44] | 263 middle-aged women. Age range between 50-65 years old | Longitudinal (with cross sectional analysis) | * Psychological stress
* Healthy behaviors
 | **Sample:**Blood | * **Biomarker:** Relative length of telomere (T/S)
* **Method:** qPCR
 | * Stable trend of telomeric length change in 1 year of follow-up.
* Main stressors during the year of follow-up related to accelerated telomere shortening (for each event there is a decrease in the telomere of 34.7 bp).
* Moderating effect of healthy behaviors (physical activity, sleep quality, and diet) on shortening due to stressors (these were not related to telomere shortening in women with high levels of healthy behavior).
 |
| **Measurements:**LTL |
| Revesz et al [38] | Longitudinal cohort of 2936 adults (18-65 years) participating in the Dutch Depression and Anxiety Study (NESDA). 6-year follow-up. | Longitudinal (with cross sectional analysis) | Biopsychosocial determinants (socio-demography, lifestyle psychosocial stressors and biological stress markers) | **Sample:**Peripheral Blood | * **Biomarker:** Relative length of telomere (T/S)

**Method:** qPCR | * Short LTL associated with high alcohol consumption (>14 and >21 drinks per week in women and men, respectively), high number of cigarettes per day, presence of gastrointestinal disease, two or more recent stressors, depressive or anxiety disorder, high hip circumference, triglycerides, glucose CRP, PEP, and low levels of HDL cholesterol.
* Sleep duration> 9 hours, gastrointestinal disease, childhood trauma and couple status as predictors of telomere shortening in 6 years of follow-up
 |
| **Measurements:**LTL, Markers of metabolic and physiological stress (MetS, HPA, ANS, basal inflammation) |
| Verhoeven et al. [45] | 2,936 participants (18-65 years) of the Dutch Study of Depression and Anxiety (NESDA) ages between. | Cross | Psychological stress: early psychosocial stress (childhood adversity) and recent | **Sample:**Blood | * **Biomarker:** Relative telomere length
* **Method:**
* **qPCR (**LTL in T/S ratio)

**Southern Blot** (average length of terminal restriction fragments) | * TL negatively associated with alcohol consumption, smoking status and BMI.
* There is no relationship between early life events or childhood trauma with TL
* Relationship between TL and the number of life events experienced in the last year and stressful events in the last 5 years (shorter telomeres). Reduced relationship by lifestyle.
 |
| **Measurements:**Telomere Length (TL) |