UNIVERSITÉ DU QUÉBEC À MONTRÉAL

PREMATURE AGING: ASSOCIATIONS WITH HOSTILITY, DEFENSIVENESS AND EVIDENCE FOR BENEFITS OF STRESS MANAGEMENT

THESIS

PRESENTED

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR

THE DEGREE OF DOCTORATE IN PSYCHOLOGY

BY

LOUISIA STARNINO

OCTOBER 2022

UNIVERSITÉ DU QUÉBEC À MONTRÉAL

VIEILLISSEMENT PRÉCOCE: ASSOCIATIONS AVEC L'HOSTILITÉ, L'ATTITUDE DÉFENSIVE ET BÉNÉFICES DE LA GESTION DU STRESS

THÈSE

PRÉSENTÉE

COMME EXIGENCE PARTIELLE

DU DOCTORAT EN PSYCHOLOGIE

PAR

LOUISIA STARNINO

OCTOBRE 2022

UNIVERSITÉ DU QUÉBEC À MONTRÉAL

Service des bibliothèque

ACKNOWLEDGMENTS

Marathon, the first word that came to mind as I sat down to reminisce about my joumey as a doctoral student. I stepped foot into the unknown and challenged myself to achieve what I had set forth to accomplish: becoming a psychologist. There have been many moments of complete self-doubt, happiness, and vulnerability during my studies. The submission of this document signifies the completion of a period of my life that at times felt would never end. As I say goodbye to a dark cloud of seven years over my head, I realize that the girl who began her doctorate is no longer the same woman who will be completing it, this is without counting the grey hairs. It has taken a village for me to grow as a doctoral student *and* as a person. Here are a few people that I would like to thank from the bottom of my heart.

To *Bianca D'Antono*, I am sincerely grateful for your mentorship. Almost a decade ago, I enrolled in your health psychology class as an undergraduate student and was completely hooked! Over the last few years, you have allowed me to develop better writing skills, methodological rigor, and confidence in research which I thought would never be possible. Thank you for believing in me. Our meetings at the office, in the streets behind the Montreal Heart Institute, in your backyard in the summer time, and more recently over Zoom, are all engraved in my heart forever. You always knew how to motivate and support me , while giving me the chance to succeed at my own pace. Thank you for continuing to inspire me, as a researcher and as a strong female role model.

À *Gilles Dupuis*, je suis sincèrement en admiration avec votre savoir-être qui m'a permis d'acquérir une plus grande perspective face à mon sujet parfois (pour ne pas dire souvent) complexe. Je vous suis particulièrement reconnaissante de m'avoir permis de faire un doctorat à l'UQÀM et de bénéficier de votre savoir, de votre calme et de votre regard humoristique pour la science. Votre philosophie de vie est franchement inspirante et c'est ainsi que je demeure persuadé que vous avez les télomères les plus longs (mais pas trop longs) au monde ! Il sera toujours une grande fierté pour moi de dire que vous avez été mon directeur de thèse. J'espère pouvoir continuer à collaborer avec vous dans le futur. Merci beaucoup!

To the lab coordinators and personnel at the Montreal Heart Institute, thank you for your support and great organizational skills throughout the years! Véronique, je te remercie particulièrement pour ta gentilesse et ta disponibilité! To my other previous and current lab mates at the Montreal Heart Institute, thank you for understanding the hardships of grad school with me. To the participants in our research projects who volunteered their precious time and personal information to make projects like BEL-AGE and MBSR-MS possible, I am forever grateful. To *Anne L.*, thank you for your wonderful MBSR training; you truly have made a difference in our participants'lives throughout the program.

To *Christina G.*, my partner in crime, you have been a true role model for me. I am forever grateful for our friendship and our professional relationship that has grown well beyond the four walls of the lab at the MHI. I could not have done this work without your guidance and it was an absolute pleasure to collaborate with you. Oh and yes, stappling standardized questionnaires for our pilot study is definitely a two person job! I look forward to this next chapter together at the Montreal General Hospital!

Je suis choyée d'avoir retirer des amitiés précieuses grâce à ce parcours à l'UQÀM et au Centre Universitaire de Santé Mcgill. Merci à *Marie-Catherine pour ton âme, tu me fais grandir. Merci à Alexandra, Talina, Emma, Anda, Gabrielle, Cécile et Karine.* Je suis sincèrement reconnaissante de votre soutien, amour et humanité. À *Geneviève*, ta présence en fin de rédaction fut *absolument* nécessaire. Je ne saurais jamais comment te remercier assez pour tes encouragements, ton écoute et nos moments de fous rires qui ont allégé mon anxiété par rapport à la rédaction!

To my clinical supervisors and mentors *Alina K., Jennifer R., Dennis K., Marco S., Wendy W., and Tanya B.*, thank you for letting me find my color as a psychologist—I will hold a little bit of each of your intervention styles forever within my practice. To my favourite author, Irvin Yalom, your words made me feel whole when I felt lost at times during this journey through grad school.

To my patients, thank you for your courage and for trusting me with your process and reminding me of why I fell in love with the art of psychotherapy.

To *Chris,* my best friend of twenty years, from near and far you have been a constant source of encouragement and unconditionnal love, thank you so much. To *Steph,* thank you for your genuine curiosity in my work and noticing when I felt overwhelmed by it all. To *Aya,* thank you for showing me the importance of celebrating every step of this process, not just the end. To my circle of closest friends that have sustained me over the years*: Dyana, Christina, Marla, Bizz, Lanz, Pam, Lina, Lena, Dave, LP, Narek, and Chris* a huge thank you for your support and providing balance in my life.

To my brother *Mario*, thank you for your encouragement and always teaching me new ways of looking at things. To my sister *Victoria*, thank you for inspiring me with your knowledge and always giving me something to think about.To my sister-in-law *Melissa*, thank you for your compassion and doing « tomatoes » with me. Being a PhD student yourself, you fully understood my struggle and more! To my grandfather Arne , thank you for always taking interest in my work and supporting me through it all, I will be celebrating the end of this process on September 7th in your honour! Per i miei nonni, siete stati li con me durante l'intero processo. Mi manchi.To my extended family *Ari, Sabrina, Oria, Roni*, *Michelle, Kayla, Yoni, Gavin, and Niaira,* our dinners and trips have kept me sane! To *Sab*, thank you for being there, even when I did not know how to ask for help. To *Ari*, thank you for reminding me of what it's like to have a balanced life and for always making me laugh. You both have helped me to keep it all together! To my aunts, uncles, and cousins, I could not have finished this process without your endless love and encouragement, and for supporting me through thick and thin!

To my partner *Dani,* thank you for your incredible patience throughout this grad school journey and reminding me that what I do *is* enough. You have brought so much light into my life; I don't feel like I am the same person that you met at the beginning of this doctoral degree. I love you and I cannot wait to see what the next chapter of our life will be about!

To my parents, thank you for supporting me in my life choices that make me who I am today. *Mom,* thank you for teaching me about sacrifice, you are a symbol of poise and resilience for all women. *Dad*, thank you for always being there and most of all for telling me *to let go* of this process when I needed to hear it the most…

Finally, thank you to the Fonds de recherche en santé du Québec (FRQS) grants for financially supporting through this work. I wish all doctoral students could be as fortunate.

DEDICATION

This thesis is dedicated to my inner critic who I continuously learn to embrace. To my magnificent mother for her endless love. To my fearless father who has brought so much meaning to this work and whose perseverance inspired me to never give up.

FOREWORD

The author of this dissertation was involved in various steps of a larger ongoing longitudinal study on psychological factors associated with premature aging (Bel-Age) from Dr. Bianca D'Antono's at the Montreal Heart Institute. First, discussions with Dr. D'Antono and Dr. Dupuis enabled her to clarify her research interests based on the Bel-Age project and raise questions regarding the association between personality traits and biological aging. She analyzed the scientific writings related to this subject which led to research objectives, making it possible to respond to some of the various gaps present in the field. For her first study, the author participated in the recruitment, participant testing at the Montreal Heart Institute, collaborated with other healthcare professionals, and later trained other research assistants who contributed to the recruitment and testing of participants. She developed the databases (Excel and SPSS), entered and verified data, and performed the statistical analyses. For her second study (MBSR-MS), she participated in the study design, recruitment process, project coordination, and assisted the MBSR sessions, as well as created the databases and performed the statistical analyses. Moreover, she was the co-first author with Christina Gentile for the article based on the feasibility and acceptability of a Mindfulness-Based Stress Reduction pilot randomized controlled trial (Annex A) prior to examining her own thesis objectives.

TABLE OF CONTENTS

LIST OF FIGURES

Chapter I : Introduction

Figure

Chapter II: Article 1

Figure

Annex A

Figure

LIST OF TABLES

Chapter II : Article 1

Table

Chapter II: Article 2

Table

Annex 1

Table

LIST OF ABBREVIATIONS AND ACRONYMS

ANCOVA: analysis of covariance

ANOVA: analysis of variance

ANS : autonomic nervous system

BP: blood pressure

BMI: body mass index

CAD: coronary artery disease

CI: confidence interval

CMHo: Cook-Medley Hostility Scale

CRP: C-reactive protein

CVD: cardiovascular disease

DBP: diastolic blood pressure

ES: effect size

HF: high frequency

HDL: high-density lipoprotein

HPA: Hypothalamic- Pituitary-Adrenal axis

HR: hazard ratio

HRQOL: health-related quality of life

HRV: heart rate variability

LF : low frequency

LDL : low-density lipoprotein

MBI: mindfulness-based interventions

MBSR : Mindfulness-Based Stress Reduction

MCDS: Marlowe-Crowne Social Desirability Scale

MetS: metabolic syndrome

MHI: Montreal Heart Institute

MMPI: Minnesota Multiphasic Personality Inventory

OR: odds ratio

RCT: randomized-controlled trial

SBP: systolic blood pressure

SCL-90: Symptom Checklist-90

SD: standard deviation

STAXI: State-Trait Anger Expression Inventory

TA: telomerase activity

TL: telomere length

T/S ratio: the relative amount of telomeric DNA (T) to the beta-globin single copy gene (S)

QLSI: Quality of Life Systemic Inventory

QoL: quality of life

qPCR: quantitative polymerase chain reaction

RÉSUMÉ

Les maladies coronariennes (MAC) sont l'une des causes majeures de décès chez les personnes âgées. L'allongement de l'espérance de vie pourrait entraîner un risque d'augmentation du nombre d'individus atteints de MAC dans le futur. La question qui se pose est : est-ce que certains individus seraient à risque de vieillir plus rapidement que d'autres à cause de certains traits de personnalité ? L'hostilité et l'attitude défensive sont des traits associés à la mortalité précoce entre autres, chez des patients avec une MAC. L'hostilité se manifeste par une attitude cynique, de la colère extériorisée ou des comportements interpersonnels plus querelleurs. L'attitude défensive est notamment caractérisée par la répression de sentiments/émotions socialement indésirables découlant d'un fort besoin d'affiliation et /ou le besoin de maintenir une bonne estime de soi. Plusieurs études ont porté sur le lien entre la personnalité et la maladie, alors que très peu ont regardé la relation entre la personnalité et les télomères. Le raccourcissement de la longueur des télomères (LT) et la diminution de l'activité de la télomérase (AT) qui sert à conserver la LT, peuvent indiquer un vieillissement cellulaire prématuré et un risque accru de MAC et de mortalité. Bien qu'il existe des données sur la LT dans les troubles psychiatriques, ce n'est pas le cas pour les traits de personnalité inadaptés liés aux MAC.

L'objectif global de cette thèse a été d'améliorer la compréhension des mécanismes potentiels sous-jacents par lesquels les traits psychologiques pourraient contribuer à la morbidité et à la mortalité cardiovasculaires et de déterminer si ces mécanismes sont susceptibles de changer via une intervention en gestion du stress de type pleine conscience. La première étude de cette thèse a visé à mieux comprendre le lien qu'a l'hostilité et l'attitude défensive avec la LT chez 1 036 individus, âgé entre 30-70 ans, avec ou sans MAC recrutés à partir de la cohorte hospitalière de l'Institut de Cardiologie de Montréal. Puis, les effets modérateurs du sexe (hommes et femmes) et du statut de santé (MAC vs maladies chroniques non-cardiovasculaires) ont été examinés (Article 1). Les résultats de l'étude 1 ont démontré qu'un niveau plus élevé d'hostilité est associé à des télomères plus courts chez les femmes uniquement, indépendamment de l'état du statut de santé. L'inverse fut observé chez les hommes en santé plus hostile. La relation entre l'attitude défensive et la LT, quant à elle, est influencée à la fois par le sexe et le statut MAC, de sorte que les patients coronariens plus défensifs avaient des télomères plus longs, alors que les hommes en santé plus défensifs présentaient des télomères plus courts.

D'autre part, l'hostilité et l'attitude défensive, ainsi que la qualité de vie (QV) basée sur l'atteinte des objectifs de vie, représentent des dimensions psychologiques moins étudiées que la dépression, l'anxiété, ou la QV reliée à la santé, en lien avec diverses interventions complémentaires visant les télomères. Des programmes de réduction du stress, tel que « Mindfulness-Based Stress Reduction » (MBSR), intégrés dans les centres hospitaliers, pourraient venir influencer ces traits de personnalité, ainsi que leur effet sur la régulation des LT. Cette thèse a permis la réalisation d'un essai pilote innovant chez des participants âgés de l'étude 1 ayant un syndrome métabolique avec réponses non-normatives au stress représentant ainsi un risque accru pour les MAC et un prognostic appauvri. Ces patients ont été randomisés dans un programme MBSR de 9 semaines ou dans un groupe témoin liste d'attente. L'étude visait à obtenir des données préliminaires sur l'effet d'un programme de MBSR sur l'hostilité, l'attitude défensive, la QV, la LT et l'AT, après l'intervention et deux mois plus tard (Article 2). Les résultats concernant la faisabilité, l'acceptabilité et les paramètres métaboliques de l'étude sont présentés dans un 3e article à l'annexe A. Les résultats de l'article 2 ont démontré que le programme de MBSR a engendré une réduction de l'AT par rapport au groupe témoin. Les analyses intra-sujets montrent une diminution de l'hostilité et une amélioration de la QV, des réductions dans l'AT, et un maintien de la LT au suivi. La pratique de la MBSR à domicile était associée à des changements du niveau d'hostilité et de QV, au suivi de deux mois.

Les retombées cliniques de ces résultats préliminaires sont difficiles à prévoir, mais suggèrent une avenue intéressante pour éclairer comment les traits de personnalité inadaptés peuvent contribuer aux MAC. De plus, les effets du MBSR sur l'hostilité et la QV sont encourageants. Les résultats ambigus au niveau de la LT et de l'AT justifient des recherches supplémentaires pour mieux comprendre ces résultats inattendus. Les implications théoriques et cliniques de ces résultats ainsi que des suggestions de recherches et des stratégies de transfert de connaissances sont également fournies dans la discussion finale.

Mots clés : télomères, hostilité, attitude defensive, maladies coronariennes, réduction du stress par la pleine conscience, qualité de vie

ABSTRACT

Coronary artery disease (CAD) is one of the leading causes of mortality worldwide in the elderly. Increased life expectancy could increase risk for CAD in the future. The following question remains: are certain individuals at risk of aging faster than others based on their personality traits? Hostility and defensiveness are traits associated with early mortality, among others, in patients with CAD. Hostility is characterised by a cynical attitude, externalized anger, or more quarrelsome interpersonal behavior. Defensiveness refers to the repression of socially undesirable negative feelings/emotions arising from a strong need for affiliation and/or a need to maintain a vulnerable self-esteem. Several studies have looked at the link between personality and disease, while very few have looked at the association between personality and telomeres. Shortening of telomere length (TL) and decreased telomerase activity (TA), an enzyme which maintains TL, may indicate premature cell aging and an increased risk for CAD and mortality. Although there is some evidence for shorter TL in psychiatric disorders, data is limited for the maladaptive personality traits associated with CAD.

The overall objective of this thesis was to improve the understanding of the potential underlying mechanisms by which psychological traits could contribute to cardiovascular morbidity and mortality and to determine whether these mechanisms are likely to change via meditation type intervention. First, this thesis aimed to better understand the link between hostility and defensiveness with TL in 1,036 individuals, aged between 30-70 years old, with or without CAD and recruited from the Montreal Heart Institute's Hospital Cohort. In addition, the moderating effects of sex (men and women) and health status (CAD vs. Chronic non-cardiovascular diseases) were examined (*Article 1*). The results of Study 1 reveal that a higher level of hostility is associated with shorter telomeres in women, but with longer telomeres in healthy men. An interaction between defensiveness and CAD status was found to be significant. Defensive cardiac patients had longer telomeres, while healthy defensive men had shorter telomeres.

Stress reduction programs, such as "Mindfulness-Based Stress Reduction" (MBSR), have been shown to improve symptoms of depressive and anxiety as well as health-related quality of life, however personality traits such as hostiltiy, defensiveness, and specifically quality of life base on life goals (QoL), as well as on the regulation of TL have been less of the focus in hospital settings. An innovative pilot randomized controlled trial in older participants of study 1 presenting with metabolic syndrome and non-normative responses to stress were recruited. These patients were randomized to a 9-week MBSR program or to a waitlist control group. The study aimed to obtain preliminary data on the effect of an MBSR program on hostility, defensiveness, QoL, TL and TA, after the intervention and two months later *(Article 2).* The results concerning the feasibility, acceptability and metabolic parameters of the study are presented in a third article in Annex A. The results of article 2 revealed that the MBSR program reduced TA compared to the control group. Within-subject analyses show decreased hostility and improvement in QOL, reductions in TA, and maintenance of TL at follow-up. Practice of MBSR at home was associated with changes in hostility level and QoL at the two-month follow-up.

The clinical outcomes from these preliminary results are difficult to predict but suggest an interesting avenue for shedding light on how maladaptive personality traits may contribute to CAD. In addition, the effects of MBSR on hostility and QoL are encouraging. The results on TL and TA warrant further research to better understand these unexpected results. Lastly, theoretical and clinical implications of these results, as well as research suggestions and knowledge transfer strategies are also provided.

Keywords : telomere, hostility, defensiveness, coronary artery disease, Mindfulness-Based Stress Reduction, quality of life

CHAPTER I : GENERAL INTRODUCTION

"It is not by the gray of the hair that one knows the age of the heart".

—Edward Bulwer-Lytton, 1853

1.1 Introduction

Aging, or the process of growing older, is often characterized by an intrinsic and progressive decline in function, and for better or for worse, is accompanied by various physiological, cognitive, psychological, and social changes over time. Physiologically, these changes often include declines in function, marked by a decrease in the capacity and ability for the body to adapt sufficiently to stressors in order to maintain homeostasis (Pomatto & Davies, 2017). Underlying this biological aging is cellular degeneration, which increases risk for development of age-related diseases (Liguori et al., 2018). Changes that happen at the molecular and cellular levels, such as those proposed for telomere length (TL), a known biomarker for aging, may contribute to many of the changes that we associate with older age.

This said, considerable variability exists regarding the rate of such biological aging and in one's susceptibility to diseases of aging. Environmental or psychological factors may contribute to observed variability in biological aging. Over the last several years, the attention has turned to the possibility that psychological risk factors, such as stress, depression, pessimism, and possibly malaptative traits result in premature cellular aging and thus increase vulnerability to diseases of aging (Brydon et al., 2010; Epel et al., 2004; O'Donovan et al., 2009; Simon et al., 2006, Starnino et al., 2016; Vakonaki et al., 2018).

Indeed, one's personality may influence one's choice of lifestyle (and associated health habits), and hence one's health and well-being. However, it may also directly influence or be associated with biological processes that contribute to premature aging. Of particular interest for this thesis are hostility and defensiveness, enduring personality traits that have been associated with increased morbidity and mortality (Chida & Steptoe, 2009; Friedman et al., 2010; Helmers et al., 1995; Kriegbaum et al., 2019; Miller et al., 1996; Rafanelli et al., 2015; Rutledge et al., 2000; Sahoo et al., 2018).

A small body of research suggests that underlying personality traits are associated with shorter TL but there is some heterogeneity across results. If such associations are confirmed, this may reflect one pathway by which personality may increase vulnerability for early aging. This thesis seeks to investigate the link between maladaptive traits (hostility and defensiveness) and TL within a large sample size of men and women with and without CAD, while elucidating any sex (male/female) and/or health status differences in this regard.

Furthermore, unprecedented changes are occurring as the world's population is aging and life expectancy is augmenting. Longer lives must be planned for. Statistics Canada (2019) reports that almost one in five people in Canada are aged 65 years and older. By 2068, it is expected to be one in four Canadians that will be aged over 65 years old. Given that older adults have a greater prevalence of CVD and other chronic illnesses, it is critical to implement changes in lifestyle (e.g., stress management, mindfulness), that may minimize the impact of maladaptive traits and related cell senescence, which in turn can contribute to improved QoL and better autonomy with aging (Epel et al., 2009; Ryan, 2010). In respect to this, we aimed to obtain preliminary data, in a small pilot randomised controlled trial (RCT), on the effects of an established stress reduction intervention (Mindfulness-Based Stress Reduction) on one's restorative biological processes associated with aging (as measured here by TL and telomerase activity levels), in addition to, quality of life, hostility and defensiveness. The thesis will consist of two articles addressing these objectives. A third article on the feasibility and acceptability of the pilot RCT can be found in Annex A.

Before turning to the details of the two studies, several aspects of hostility and defensiveness as potential risks factors for CVD and other diseases will be examined. Next, the role of TL as a marker of biological aging will be presented as well as its association with CAD, hostility, and defensiveness. This will be followed by a brief review of the existing literature on mind-body interventions, and their effects on maladaptive traits associated with CAD, telomere biology, and quality of life.

1.2 Personality traits and Cardiovascular Disease

Cardiovascular disease remains the number one cause of death around the world for both men and women (WHO, 2019). Coronary artery disease (CAD) in particular, accounts for roughly fifty percent of these deaths. In addition to the well-known risk factors such as age, smoking, obesity, lack of physical activity, dysregulation of the autonomic nervous system, diabetes, hypertension, and hypercholesterolemia, results from meta-analyses have shown that psychosocial risk factors such as depression, social isolation, perceived stress, and anxiety, may impact cardiovascular health (incidence and progression) and increase the risk for mortality by 21 to 46% (Barth et al., 2004; Celano et al., 2015; Holt-Lunstad et al., 2015; Levine et al., 2021; Richardson et al., 2012; Vahedian-Azemi & Moayed, 2019) . Meta-analyses and independent studies have shown that these behavioral, medical, physiological, and psychosocial risk factors may be more present in those with certain personality traits (Bird et al., 2018; Chida & Steptoe, 2009; Denollet et al., 2006; Guerrero Rodriguez et al., 2018; Lévesque et al., 2010). Personality is typically defined as a relatively stable pattern of traits and unique characteristics that give both consistency and individuality to a person's pattern of thoughts, feelings, motives, behaviors and perceptions exhibited across situations (Carver et al., 1996; McCrae & Costa, 2003, p.20). Personality traits or dispositions differ in dimensions or degree that influence behavior. For instance, someone who is agreeable or socially desirable (trait) may be disposed to act overtly pleasing and cooperative towards others. As such, a personality trait may be quantified as a continuous variable, such that the degree of presence versus absence of the characteristic is distributed across a population (Carver & Sheier, 1996).

Meta-analyses and longitudinal studies have repeatedly shown that behavioral risk factors for CAD and mortality, including smoking, diet, exercise, alcohol use, and risk-taking are all related to personality dispositions (Bunde & Suls, 2006; Turiano et al., 2015). This is further described by the transactional stress moderation model which suggests that individuals with certain personality dispositions may have tendencies toward using particular coping strategies when stressed and that maladaptive coping styles may lead to adverse physiological and behavioral consequences (Lazarus & Folman, 1984). Less obvious factors such as health decision making styles (Flynn & Smith, 2007) and health risk evaluation (Hampson et al., 2006) have also been linked to personality.

Personality traits appear to influence health through biological pathways as well. Psychological patterns on a cognitive, behavioral and emotional level, such as those seen in hostile individuals, have been linked to physiological alterations involving platelet reactivity (Shimbo et al., 2009 ; Markovitz et al., 1996), inflammation (Girard et al., 2016; Hackett et al., 2015 ; Janicki-Deverts et al., 2010; Ranjitt et al, 2007), autonomic nervous system (sympathetic and parasympathetic) (Lin et al., 2015), the hypothalamic-pituitary-adrenal (HPA) (Wasserman et al., 2007) and the sympatho-adrenomedulary axes (Peters et al., 2018), and as we will discuss below, more recently to telomere length (TL) (Brydon et al., 2012 ; Schoormans et al., 2018 ; Starnino et al., 2016). While personality traits are considered both genetically and environmentally influenced and are relatively stable across time, changes can occur over the long term as of result of developmental changes, life experiences, or following psychosocial intervention (Roberts et al., 2006). These changes may occur even in middle and old age (Roberts & Mroczek, 2008). Moreover, important gender differences amongst traits exist, including across more egalitarian cultures (Schmitt et al., 2017). Therefore, it is important that a personality approach is taken in identifying those patients who are at increased risk for cardiac events.

Among the personality traits that may increase risk or worsen the prognosis for CAD and other non-cardiovascular health issues are hostility and defensiveness (Chida & Steptoe, 2009; Denollet et al., 2008; Pragodpol & Ryan, 2013; Rafanelli et al., 2016; Sahoo et al., 2018). These traits and their association with biological processes related to aging will be the focus of this dissertation. The following section will define the specific behavioral and personality characteristics of hostility and defensiveness. This will be followed by a review of selected studies regarding the relationship between hostility, defensiveness and cardiovascular disease. Before turning to evidence in regard to a biological marker for aging, a theoretical model relating hostility and defensiveness to CAD will be provided.

1.2.1 Defining Trait Hostility

> If you are pained by external things, it is not they that disturb you, but your own judgement of them...
>
> –Marcus Aurelius (AD 161-180)

Hostility is one of the most well-studied personality factors in the health psychology literature, particularly as pertains to hypertension and CVD. Buss (1961) conceptualised hostility as holding negative attitudes towards the other, anger as negative emotional responses, and aggression as verbal or physical behavioral responses directed toward the other. These characteristics of hostility have also been identified in several personality constructs, such as Type A behavior, (high) neuroticism and (low) agreeableness Five-Factor Model dimensions, and trait anger (Sahoo et al., 2018).

These hostile behavioral and emotional responses may be in response to potential stressors (i.e., life events or social interactions) (Sahoo et al., 2018). Most researchers today would agree that hostility, in fact, represents a broad multidimensional psychological construct, encompassing affective, behavioral, and cognitive components of an individual's negative orientation toward interpersonal interaction (Barefoot et al., 1989; Smith, 1994; Van Teffelen et al., 2020). The affective component of hostility is described as the tendency to recurrently experience anger, that may vary in intensity from mild irritability to full blown rage and may be accompanied by other closely related unpleasant emotions including resentment, hate, disgust, and envy. Such trait tendencies to experience anger frequently must be distinguished from the occasional experience of anger, as measured by state measures of anger. Indeed, state anger and hostility are only moderately correlated in clinic and non-clinical samples, sharing less than 50% of their variance (Miller et al., 1995). The behavioral component of hostility refers to overt aggressive or quarrelsome behavior, including violent acts, or more passive aggressive behaviors (e.g., withholding important information, ignoring, or stonewalling the other person) (Smith, 1994). For example, verbally aggressive individuals may use rudeness, sarcasm, overt derogation (e.g., snide comments), or insults to show aggression. They may act in a competitive manner during conversations by frequently cutting others off or raising the volume of their speech. The cognitive component refers to cynicism, social mistrust, or a hostile attributional style which is the tendency to interpret others' behaviors as having aggressive intent, even when the behavior is ambiguous or benign (Smith, 1994). Although clear theoretical distinctions exist between the cognitive, affective, and behavioural dimensions of hostility, there is great deal of overlap among these components. They frequently co-occur and can affect each other in a multidirectional manner.

Moreover, the trait is typically operationalized as a continuous variable, ranging from very high to very low hostility. Operationalizing traits as dimensions provide more nuanced information about people rather than a crude present/absent membership (Strong et al., 2005). Given the substantial history of associations with negative psychological sequelae in a variety of populations (Albanese et al., 2016; Mathes et al., 2020; Wang, 2021), it is apparent that hostility must be assessed reliably, not only for accurate contributions to the scientific literature, but ultimately for the purposes of valid assessment in populations served by health-care practitioners across.

There have been a variety of instruments developed to measure the various components of hostility. The most popular appear to be the Cook Medley Hostility Scale (Cook-Medley Hostility Scale (CMHo; Cook &Medley, 1954), the State-Trait Anger Expression Inventory (STAXI; Spielberger et al., 1983), and the Buss Durkee Hostility Inventory (BDHI; Buss & Durkee, 1957). Of these, the BDHI, comprised of 75 true–false items, is frequently administered to measure anger expression in violence research (Lange et al., 1995; Vassar & Hale, 2008) and to a lesser extent in health psychology such as psycho-oncology research (Lemogne et al., 2013). However, it is lengthy and important concerns regarding the reliability, especially the internal consistency of the BDHI subscales have been raised (Vassar & Hale, 2008).

Another measure of the affective and behavioral components of hostility that is widely used in the literature is Spielberger's Trait Anger and Anger Expression Scale (STAXI; Spielberger, 1983). In this measure, individuals report their proneness to experiencing anger (Trait Anger), their typical style of anger expression: either outwardly expressing their emotion (Anger-Out), actively inhibiting the expression of their anger while continuing to experience these feelings (Anger-In), or successfully regulating the emotional response (Anger- Control) (Spielberger, 1983). Trait anger can also be broken down into two elements: 1. Anger temperament, a general tendency to experience anger without provocation, and 2. Anger Reactions, a general tendency to feel anger when criticized or being mistreated (Spielberger, 1983). It should be noted that this affective response measure also contains items assessing behavioral and cognitive elements (Miller et al., 1995). For example, anger-out contains items that reflect a tendency to display aggressive behaviors, while anger-in also includes aspects of hostile cognitions such as brooding, cynicism, and mistrust (Miller et al., 1995).

However, the measure of hostility most commonly used in the CVD literature is the Cook-Medley Hostility Scale (CMHo), originally a 50-item true/false questionnaire derived from the Minnesota Multiphasic Personality Inventory (MMPI), which is divisible into cognitive, affective, and behavioral subscales. The cognitive relate to hostile attribution bias (i.e. the tendency to interpret others' behaviors as having hostile intent) and cynicism (i.e. a general mistrust of others' motives) subscales; the affective component represents anger affect (i.e., general irritation towards others); and the behavioral component is composed of items which display aggressive responding (i.e., being verbally or physically aggressive in social interactions) and social avoidance (i.e., the tendency to avoid social contact) (Barefoot et al., 1989). Higher scores indicate greater hostility. Reliability of the CMHo Scale is very good with internal consistency coefficients of 0.84-0.86 (Cook & Medley, 1954; (Barefoot, et al., 1983; Shekelle et al., 1983). Although the BDHI, AQ, STAXI, and CMHo scales have some construct overlap and high internal consistency (Bishop & Quah, 1998), there are clear differences between the dimensions of hostility they are measuring. Moreover, there is some evidence that these dimensions differentially predict CAD morbidity and mortality. Hostility, as measured with the CMHo, has been more consistently observed to predict CAD morbidity and mortality and was also found to predict the severity of CAD in cardiac patients (Chida & Steptoe, 2009) as well as all-cause mortality (Kriegbaum et al., 2019).

As the original CMHo can be lengthy for administration in epidemiological studies, shorter versions have been devised with the goal of more efficiently defining the hostility domains measured (Barefoot, et al., 1989; Willams, et al., 1980; Greenglass & Julkunen, 1989; Short et al., 2005; Wong et al., 2014). For example, Barefoot (Barefoot et al. 1989) used an a priori analysis of the content of the CMHo to distinguish the following subscales: hostile attributions, cynicism, hostile affect, aggressive responding, and social avoidance. They found that cynicism, hostile affect, and aggressive responding were all predictive of mortality, and that the combination of these three subscales (27 items) appeared to be more predictive than any individual subscale or the entire 50-item CMHo. Many investigators have used only Barefoot's 13-item cynicism subscale. For example, Chaput et al. (2002) found that the association between cynicism subscale and CAD events was as strong as the entire CMHo measure, but other investigators failed to find this association (Siegman et al., 1989). Other researchers have also used a 39-item composite of the CMHo that includes the hostile attributions, cynicism, hostile affect, and aggressive responding subscales (Barefoot et al., 1995; Boyle et al. 2004, 2005; Brydon et al., 2010). In a more recent five-year prospective study of 1024 CAD patients, the 39-item version of the CMHo predicted increased mortality more frequently than the other CMHo versions (Wong et al., 2014). Hence, hostility will be operationalized using this 39-item version in the current thesis.

1.2.2 Defining Defensiveness

> As long as you keep secrets and suppress information, you are fundamentally at war with yourself…The critical issue is allowing yourself to know what you know. That takes an enormous amount of courage.
>
> — Bessel A. Van der Kolk, 2015

Sigmund Freud (1894) was the first to formally speak of defense mechanisms, such as suppression and repression. The former was defined as a conscious mechanism intended to eliminate undesirable psychical content (i.e., anxiety-provoking thoughts, fantasies, memories, emotions) out of awareness. The difference between suppression and repression lies in the fact that this latter defense mechanism is unconscious and under its influence repressed content becomes or remains unconscious (as distinguished by Anna Freud, 1946). More commonly today, though subject to debate, repression is the general term that is used to describe the unconscious style of coping to inhibit the experience and the expression of negative feelings or unpleasant cognitions to protect the ego from being threatened, as compared to suppression where the person is partly aware of their emotional inhibition (Garssen, 2007). In the field of health psychology, numerous concepts akin or related to that of repression or suppression have been of interest, such as emotional control, emotional inhibition, concealment, defensiveness, Type C response style, Type D personality, and alexithymia (please refer to Garssen (2007)'s diagram on defensiveness and overlapping constructs below). Of interest to this thesis, is the defensiveness construct which is a concept dominating and including all other constructs (e.g., social desirability, repression, self and other-deception). Defensiveness stems from the tendency to avoid reporting socially undesirable aspects of oneself and the need to be viewed in a positive manner by others, otherwise originally known as impression management (Crowne & Marlowe, 1964; Paulhus, 1984).

The first researchers to formulate a theoretical argument about the nature of individual differences in impression management were Crowne and Marlowe (1964). They argued that styles of responses to questionnaires simply represent expressions of behavior derived from a deeper approval motive. Contexts in which social evaluation elicit this motive enhance individuals' tendency to adopt obedient, conformist, and socially approved behaviors and to avoid socially undesirable behaviors. Ironically (given their wish to avoid undesirable behaviors to gain the approval of others), individuals scoring high on an impression management scale are willing to lie in self-descriptions. Later research by Crowne (1979) allowed for an additional meaning to impression management which is more related to self-deception: defensiveness of the self.

The defensiveness trait is a personality trait characterized by avoidance, denial, or repression of information perceived as threatening by the individual (Crowne & Marlowe, 1960; Paulhus, 1984). The motivation that drives defensive individuals is not social approval, but rather the avoidance of social disapproval, which in itself, serves a more basic goal of protecting a vulnerable (i.e., low and insecure) self-esteem (Crowne, 1979). Such vulnerability may lead to cognitively depleting anxiety in social contexts, which carries a myriad of negative consequences, such as being anxious, stressed, emotionally drained, cognitively preoccupied, and, in the long run, socially maladjusted in order to achieve their interpersonal goals (Uziel, 2010). It is known that individuals with higher levels of defensiveness tend to divert their attention from non-socially desirable states (Bonanno et al. 1991) and may resist exploration of negative affective reactions to symptoms and lifestyle (Burns, 2000) and these behaviors may have damaging effects on their health. One of the defining characteristics of defensive individuals is that when they are put in potentially stressful situations, they may report low levels of distress but are physiologically very reactive (e.g., increased heart rate, raised blood pressure) (Myers et al., 2008; Myers, 2010). This will be further visited in the following sections.

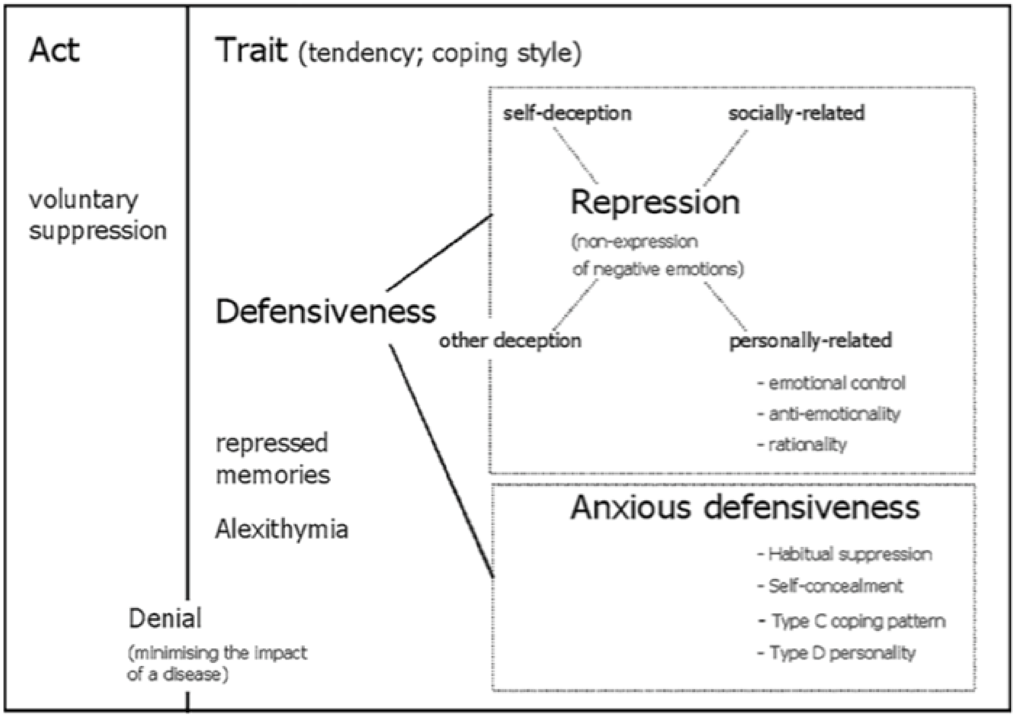


Figure 1.1 Garssen (2007). Concepts which are associated, yet theoretically different from defensiveness

The most popular measure of defensiveness used in the health psychology literature is the Marlowe-Crowne Social Desirability Scale (MCSD). The MCSD scale was originally developed to measure social desirability. Social desirability is defined as an individual's need to "obtain approval by responding in a culturally appropriate and acceptable manner" (Crowne & Marlowe, 1960, p. 353). Before the MCSDS was developed, social desirability was measured by Edwards Social Desirability Scale (ESDS; Edwards, 1957). A problem with the ESDS was that there was a high correlation between the ESDS and the scales of Minnesota Multiphasic Personality Inventory (MMPI) F, L, and K scales (Hathaway & Mckinlet, 1951). The high correlation between the scales suggested that the ESDS is a measure of psychopathology rather than social desirability. Therefore, to not confound social desirability with psychopathology, the MCSD was developed with non-MMPI items. The MCSD excludes any items that are pathologically-relevant or indicative of abnormalcy.

While the MCSD scores are often negatively correlated with scores on distress questionnaires (Boden et al., 2005; Izawa et al., 2005; Mann et al., 1998), several reviews have concluded that measurements of socially desirable response style actually refer to a personality trait with clear behavioral correlates and not to a simple response bias (Jorgensen & Thibodeau, 2007; Garssen, 2010). Weinberger (1990) makes a distinction between two types of defensiveness: he defines repression as scoring high on defensiveness but low on anxiety, and anxious defensiveness as scoring high on both defensiveness and distress self-report scales combined. However, we and others have found that higher levels of defensiveness on its own, measured by the MCSD, has been associated with physiological processes and increased health risks (Denollet et al., 2008 ; Lévesque et al., 2010 ; Starnino et al., 2016).

In conclusion, the reliability and validity of the MCSD scale have been confirmed in many studies, and this scale appears to contribute to the most favourable understanding of the defensiveness construct. The next section will briefly review past studies that have focused on these traits and cardiovascular health.

1.2.3 Hostility and Cardiovascular Health

A large body of evidence supports associations between hostility, as separate from state anger, in the prediction of CVD development, progression, and mortality (Chen et al., 2019; Chida & Steptoe, 2009; Everson-Rose et al., 2014; Keith et al., 2017; Klabbers et al., 2013).

Hostility increases risk of coronary events in relatively healthy individuals. For example, in a meta-analysis of 21 large prospective studies from across the world, Chida and Steptoe (2009) estimated that hostility alone significantly increased the risk of CAD events among healthy individuals by 20% (95% CI [1.01 to 1.42]). In addition, their analysis of 18 studies involving individuals with established CAD found that hostility increased by 21% (95% CI [1.03

to 1.43]) the risk of CAD recurrence and by 18% (95% CI [1.05 to 1.35]) the risk of mortality (after controlling for baseline health status) (Chida & Steptoe, 2009). Increased risk for CVD events, or mortality in more hostile individuals is partly explained by their greater propensity to engage in negative health behaviours (Appleton et al., 2016; Chida & Steptoe, 2009; Wong et al, 2013). For example, while Wong and colleagues (2013) showed that in a predominately older male sample with stable CAD, mortality risk and the risk of secondary cardiovascular events were 50% and 49% greater respectively among those with the highest levels of cynical hostility (CMHo cynicism subscale), this association was no longer significant after adjustment for behavioral factors such as physical activity and smoking (Wong et al., 2013). This finding corroborates those of Chida and Steptoe's meta-analysis (Chida and Steptoe, 2009). Nonetheless, several other investigations reported a significant relationship between hostility and CAD and CAD-mortality, that was independent of lifestyle (Niaura et al., 2002; Tindle et al., 2009; Todaro et al., 2005). For example, in 754 middle-aged men without CVD followed over 13 years, those who presented with both metabolic syndrome[1] and high levels of hostility (measured by the CMHo) were more likely to develop myocardial infarction in comparison to patients who only had metabolic syndrome, a relationship that remained robust even after adjustment for sociodemographic and behavioral characteristics (Odds ratio (OR)1.59, 95% CI [1.29 to 1.96])(Todaro et al., 2005).

Moreover, hostility appears to be related to all-cause mortality Miller et al., 1996; Tindle et al., 2009; Vitori et al., 2021). For example, Vitori and colleagues (2021) reported that in a study of 193 CAD patients, 38 patients died during the 24-month follow-up and the presence of hostility was an independent predictor for all-cause mortality, after controlling for important covariates (i.e., age, sex, ethnicity, prior cardiac events, diabetes, hypertension, and smoking). In conclusion, hostility appears to increase risk for CAD, CAD events, and mortality. While

[1] Metabolic syndrome affects 40% of adults over age 60 and doubles risk for cardiovascular disease (CVD)(Alberti et al., 2009; Riediger & Clara, 2011). Metabolic syndrome typically refers to the presence of at least three of the following interconnected factors: central adiposity, high blood pressure (BP), elevated triglycerides, increased fasting blood glucose, and low levels of high-density lipoprotein (HDL) cholesterol (Alberti et al., 2009) (refer to Appendix A for metabolic syndrome parameters and cut-off values).

increased behavioral risk factors in more hostile individuals may be partly responsible, other biological processes may also be involved. One such process will be discussed in greater detail later.

1.2.4 Defensiveness and Cardiovascular Health

Defensiveness is commonly observed in those suffering from asthma (e.g., Cooke, et al., 2003; Feldman, et al., 2002) cancer (e.g., Jensen, 1987; Petersen & Zacharia, 2010), and cardiovascular diseases and related risk factors (e.g., hypertension) (Mund & Mitte, 2012). The latter being of interest to this thesis. An impressive collection of past studies exists to support defensive traits as predictors of a variety of physiological processes linked to cardiovascular development and prognosis (Denollet et al., 1996; Denollet et al., 2008; Lévesque et al., 2009; Rutledge et al., 2003). Defensiveness is significantly greater amongst populations with chronic illnesses and in elderly individuals (Cooke et al., 2003; Erskine et al., 2007; Erskine et al., 2016; Mund & Mitte, 2012; Soubelet & Salthouse, 2011), compared to non-clinical populations (Contrada et al., 1997; Jorgensen & Zachariae, 2006; Myers & Reynolds, 2000). According to a meta-analysis (k=4), higher levels of defensiveness was associated with an increased risk by 80% of suffering from high blood pressure compared to those with lower defensiveness (Mund & Mitte , 2012).

Higher levels of defensiveness, typically assessed using the MCSD (Crowne & Marlowe, 1960), have been associated with cardiovascular-related morbidity (Helmers et al., 1995; Jorgensen al., 2001) and mortality (Denollet, 1991) in some but not all research (Ginzburg et al., 2002; Shapiro et al., 1995). For instance, Jorgensen and colleagues (1996), in a meta-analysis of 19 studies involving healthy (generally younger) men and women, as well as 19 other studies involving hypertensive patients, found that greater defensiveness was associated with increases in blood pressure (moderate-large effect sizes;d=0.35-0.46), after controlling for age, sex, and current blood pressure (Jorgensen et al., 1996). A prospective study in primarily normotensive participants showed that high defensiveness (measured by the BIDR) was associated with more than a sevenfold risk of developing hypertension 3-years later in individuals in the high defensiveness group compared to the less defensive counterparts (adjusted risk ratio: 7.5; 95% CI: 1.5-39.2). These results were the same even after adjusting for important covariates such as age, alcohol usage, hyperlipidemia, self-reported exercise levels, smoking, and year-1 ambulatory blood pressure (Rutledge & Linden, 2000). In addition, defensiveness and other related traits (e.g., Type D personality characterized by high social inhibition and distress) have been shown to predict poorer prognosis in patients with CAD, even after controlling for depressive symptoms, stress, and anger (Denollet et al., 2000 ; Denollet et al., 2006 ; Mols et al., 2010). Slightly more recently, Denollet and colleagues (2008) followed 731 CAD patients over five to ten years (mean follow-up= 6.60 years). They found that high scores on the MCSD predicted a two-fold increase in the risk of mortality, myocardial infarct, or other CAD events even after adjusting for psychosocial, behavioral and metabolic variables (e.g., blood pressure, exercise, type-D personality, depression, anxiety, anger) (Denollet, et al., 2008).

In sum, greater defensiveness has been associated with cardiovascular-related morbidity and mortality (Helmers et al., 1995; Jorgensen et al., 2001; Rutledge et al., 2000), hypertension (Glieberman, 2007), and elevations in blood pressure (Jorgensen et al., 1996; Nyklicek et al., 1998; Rutledge & Linden, 2003), lipids (Niaura et al., 1992), and glucose levels (Jamner et al., 1988; Lévesque et al., 2009). However, over the last decade, studies involving this construct as related to health outcomes have been scarce. Shortcomings of the current literature include a confusing array of defensiveness synonyms, and the use of measures with questionable construct validity.

1.2.5 Theoretical Models and Biological Mechanisms Relating Hostility and Defensiveness to CAD

The renewed interest in the centuries-old belief that personality traits contribute to the development of CAD reflects the realization that the etiology of this disease is complex. We aim here to better understand how defensiveness and hostility “gets under the skin” and may increase risk for disease. Certain theoretical models, not mutually exclusive, have been proposed to explain the association between hostility or defensiveness with disease, particularly cardiovascular disease. Hostility and defensiveness are thought to directly and indirectly lead to cardiovascular, autonomic, and neuroendocrine changes that facilitate the development and exacerbation of CAD.

Lazarus's transactional stress moderation model adapted to hostility (Smith & Pope, 1990) and the biospsychosocial synergistic model which includes defensiveness (Jorgensen et al., 1996) are of particular interest here. The prior proposes that hostile individuals experience more stressful interactions as they have a dynamic tendency to create conflict and simultaneously undermine support which heightens sympathetic reactivity. The latter proposes defensive individuals tend to be chronically hypersensitive to situations deemed as threatening to the ego and efforts to maintain a view of themselves as not emotionally reactive impacts stress reactivity, amongst other physiological mechanisms (Guerrero Rodriguez et al., 2018; Movius & Allen, 2005), and thus in turn may increase risk for CVD-related disease (Jorgensen, et al., 1996). For example, defensive individuals (identified at times as repressors) with chronic conditions such as back pain (Burns et al., 2000), asthma (Cooke et al., 2003), and CVD (Frasure-Smith et al., 2002) self-reported better adjustment, less stress, and fewer side effects than their less defensive counterparts, despite having poorer clinical outcomes (Myer et al., 2010).

A concept that expands upon stress reactivity and disease hypothesis is the allostatic load model. This model provides a more comprehensive framework to explain the long-term negative health consequences of stress, such as its relationship with cardiovascular disease. The concept of allostasis, which the allostatic load model is based on, means "achieving stability through change" (McEwen & Stellar, 1993). In other words, allostasis is a necessary process involving secretion of stress hormones (adrenaline, noradrenaline, cortisol) for our body to adapt quickly and flexibly to internal or external demands in order to restore homeostasis. For example, blood pressure and heart rate are increased during daily challenges such as waking up in the morning and engaging in physical activity.

When an event is perceived as stressful by an individual, there are physiological and behavioral changes that ensue in response to the challenge (McEwen & Seeman, 1999). Responses such as flight or fight or freeze, represent an immediate cascade of reactions triggered by the sympathetic nervous system when faced with a life-threatening stressor, to maximize chance of survival (Cannon, 1927; Cannon, 1929; Gallup, 1977). Thus allostasis is adaptive. However, a difficulty for our health arises when we are faced with recurrent stressors (subtle, long-standing life situations, failure to adapt to the same stressor) or major life events. While these stressors are not typically life-threatening, the stress responses mentioned above are still triggered to varying degrees (McEwen & Seeman, 1999). These represent variations along a continuum of multilevel adaptation/maladaption determined by biopsychosocial antecedents (e.g., type of attachment, social support, socioeconomic status, personality, genetics) (Juster et al., 2016).

Moreover, these stress responses may lead to changes in other mediators such as increases in unhealthy lifestyle choices (poor diet, smoking, sedentarism, alcoholism), immunological (e.g., pro- and anti-inflammatory cytokines), cardiovascular and autonomic disturbances (such as altered reactivity and recovery in blood pressure and heart rate variability) (Barger et al., 1997; Barger et al., 2000; McEwen & Seeman, 1999). It was later added by Picard, Juster, and McEwen (2014), that these primary mediators mentioned may alter cellular function and structure, generating oxidative stress and cellular damage (primary outcomes), including telomere shortening. It is suggested that these processes cumulatively worsen risk factors (secondary outcomes) reflected by abnormal metabolism (abdominal obesity, hyperlipidemia, hypertension; insuline resistance) and other risk factors for CVD such as waist-hip ratio (WHR), blood pressure, cholesterol/HDL ratio, HDL cholesterol, as well as TL and telomerase activity (Demissie et al., 2006; McEwen, 2015). Consequently, these processes may lead to disease, such as cardiovascular disease and diabetes mellitus, amongst other age-related diseases (tertiary outcomes) (Picard et al., 2014, see Figure 2 below).

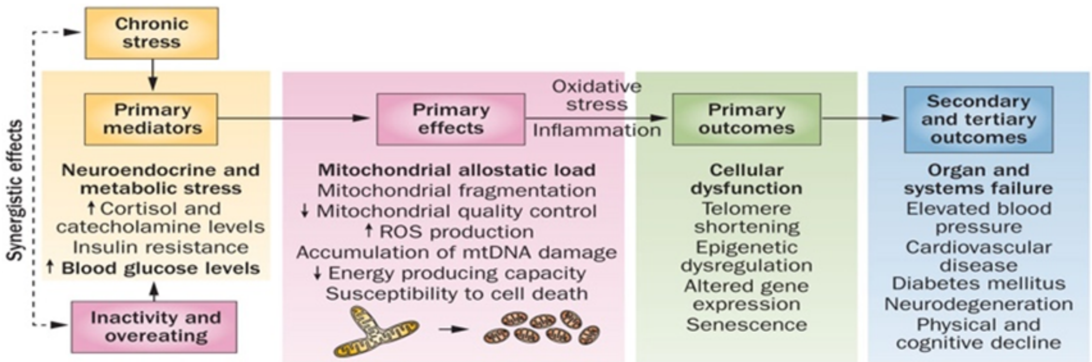


Figure 1.2 The stress–disease cascade and mitochondrial allostatic load (Picard et al., 2014).

Personality traits, such as hostility and defensiveness have been linked to increases in allostatic load (Juster et al., 2016;   Lévesque et al., 2009). For instance, we showed that higher defensiveness was associated with greater blood pressure and heart rate reactivity to acute stress (Lévesque et al., 2010). More recently, hostile and defensive individuals show slower blood pressure recovery in response to a standardized laboratory stressor compared to their low hostile and low defensive counterparts (Guerrero Rodiguez et al., 2018). Moreover, we showed that hostility was associated with greater increases in disturbances in allostatic responses (metabolic and inflammatory) over a three-year period among middle-age and older (range: 35-65) healthy individuals (D'Antono et al., 2013). In this same sample, decreases in anti-inflammatory activity post-stress were found in hostile women, which may put them at greater risk for CAD (Girard et al., 2016).

In conclusion, while these theoretical models propose that biological mechanisms are perturbed as a result of the altered stress responses of more hostile or defensive individuals, thereby increasing CAD risk and prognosis, the actual processes remain to be elucidated. General and pervasive effects of stress found in defensive and hostile individuals contribute to allostatic load, but also may have common cellular mechanisms (Tomiyama et al., 2012; Picard et al., 2014). Telomeres may be one of the common cellular mechanisms linking these personality traits to diseases of aging. One goal of this thesis is thus to examine the relationship between individual personality traits (hostility and defensiveness)—known for maladaptive coping patterns during stress, and telomere length (TL).

1.3 Telomere Biology

1.3.1 The Function of Telomere Length and Telomerase Activity

Telomere length (TL) is an emerging marker for biological age and is related to several age-related diseases (including CVD and cancer), as well as mortality, lifestyle, and psychological factors (Jylhävä et al., 2017; Deelen et al., 2014; Kimura et al., 2008; Haycock et al., 2014; D'Mello et al., 2015). A telomere is a region at each end of a chromosome made up of repetitive sequences of non-coding DNA that protect the DNA from loss during cell division (Blackburn, 1991). Every time a cell divides, a segment of the DNA sequence at the end of the chromosome made up of nucleotides that pair together (base pairs) is lost, leading to telomere shortening with each cell division. Telomeres eventually shorten to a critical length, a term coined the Hayflick Limit, as a normal process of aging. When reached, the cell undergoes cell cycle arrest and cellular senescence (Blackburn, 1991). Without cellular arrest, the cell would continue to replicate, despite potentially missing coding DNA (genetic information), which could lead to mutations or genomic instability (Houben et al., 2008). On the one hand, at least two mechanisms have been identified by which TL attrition occurs (Blasco et al., 2005). First, the DNA sequences located at the end of chromosomes are incapable of being entirely replicated by the DNA replication process. Second, it has been observed that the process of oxidative stress brought on by an increase of reactive oxygen species, can cause breaks at 5’-TTAGGG-3’ repeats, leading to the shortening of the TL (Baird, 2008).

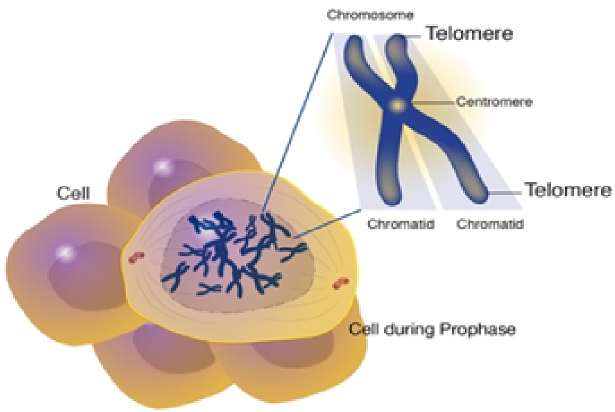


Figure 1.3 Telomere Length. Courtesy: National Human Genome Research Institute. Retrieved from: https://www.genome.gov/genetics-glossary/Telomere

Telomeres have been found to shorten with an increased rate of attrition in older individuals (Harris et al., 2016; Houben et al., 2011), while some individuals maintain and may even lengthen their average telomere over certain periods (Epel, 2012; Muezzinler et al., 2013). One mechanism by which these changes can occur is through changes in telomerase activity. Telomerase is an enzyme that serves to maintain and protect telomeres by adding basepairs (TTAGGG) at the ends of chromosomes with the help of its two main components: a gene encoding enzyme (hTERT) and a RNA component (TERC) that serves as a template for the synthesis of new telomeric DNA repeats (Bodnar et al., 1998). Telomerase is thus seen as a predictor of long-term cellular viability. Due to insufficient expression of telomerase to maintain telomeres, gradual telomere erosion occurs leading to cellular damage (Blasco, 2005) and increased risk for diseases including CAD (Haycock et al., 2014; D'Mello et al., 2015). The telomerase enzyme has several other duties that are independent of the TL, such as protection of mitochondrial functions and mediating DNA damage response for cell survival (amongst others) (Cong & Shay, 2008). These properties are essential for the anti-aging process. Investigations have demonstrated, for example, that alterations in telomerase levels might occur within minutes to a few hours following the exposure to specific chemical messengers, such as inflammatory markers (cytokines), stress hormones (e.g., adrenaline, cortisol), and growth factors (substances capable of stimulating cell multiplication) (de Punder et al., 2019). Although this enzyme has been said to be more detectable in other types of cells, it is now possible to quantify the low levels of telomerase in (human) white blood cells, which is what will be used in the second article of this dissertation.

In summary, with advancing age (and multiple replication cycles), cellular damage and increased risk for disease occurs in part due to insufficient telomerase activity and extensive telomere loss. While TL may not be a clear determinant of aging or aging-related diseases, it is a biological marker for underlying mechanisms that bring about premature (accelerated) aging (Vaiserman & Kranienkov, 2021).

1.3.2 Telomere Biology and Risk Factors for Cardiovascular Disease (CVD)

Telomere Length (TL) and CVD. As the first article of this thesis bears on individuals with and without CAD, we review here the evidence that telomeres and telomerase activity are associated with and play a role in the pathophysiology of CAD. Given that TL is associated with a variety of stressor exposures, TL may be conceptualized as a potential molecular-level measure of allostatic load. Indeed, shorter TL is associated with worse function across multiple regulatory systems, including greater inflammation, autonomic reactivity to stress, oxidative stress, insulin resistance, hypertension, hyperdislipidemia, metabolic syndrome, smoking, physical inactivity (Astuti et al., 2017; Aviv et al., 2009; Cheng et al., 2021; Epel et al., 2006; Starkweather et al., 2014; Tian et al., 2017); all of which are associated with greater risk for CAD.

To date, Haycock and colleagues' (2014) meta-analysis provided the most comprehensive examination to date of the association of TL with CVD, which included 8400 patients with CAD or cerebrovascular disease, from a total of 12 prospective and 12 retrospective studies. Results demonstrated that individuals in the lowest tertile versus the longest tertile for TL were 54% more likely to develop CAD. According to the prospective studies, the relative risk of developing CAD because of shorter TL was on average 42% greater (1.42, 95%, CI [1.17-1.73] $p<0.05$)

compared to those with longer TL, and was generally independent of age and typical behavioural, vascular, and inflammatory risk factors (Haycock et al., 2014). Shorter TL was also independantly associated with greater risk for all-cause mortality in stable CAD patients. For example, in a 9.2-year prospective study in 608 CAD patients, participants whose telomeres shortened the most (lowest tertile) in the first five years of follow-up had a 45 % rate of death, while the group of participants whose telomeres lengthened the most (highest tertile) had a death rate of only 11 % (Goglin et al., 2016). Interestingly, in one large study of 1917 participants (51% women, mean age 46.6 (18.4) years), there was a non-linear association of tertiles of TL with incident CAD events, with men in the middle tertile of TL having significantly increased risk of incident CAD compared with those in the shortest and longest tertiles. In contrast to men, elevated CAD risk was similar for both those in the middle and shortest tertiles of TL in women, although these findings did not reach statistical significance (Ye et al., 2013). It was proposed that male participants in the shortest tertile might have been affected by non-CAD outcomes which may have played a role in these unexpected findings. For example, previous studies have shown that individuals, specifically men, with the shortest TLs are at increased risk for incident cancers, CVD's, and infectious deaths (Cawthon et al., 2003 ; Fitzpatrick et al., 2011Goglin et al., 2016; Ye et al., 2013; Willeit et al., 2010 a,Willet et al, 2010 b), suggesting that the type of disease outcomes may vary by the severity of telomere shortening and sex. Such results suggest the need to consider the health status and sex of individuals when evaluating TL (Ye et al., 2013).

Telomerase activity and CVD. While the role of TL in the risk, onset, and progression of CAD has been extensively studied (D'Mello et al., 2015; Haycock et al., 2014), the direction of association between telomerase activity and CAD may be more complex and human studies investigating both telomerase and TL in the context of CAD risk have been scarcer. Low telomerase activity and short TL were shown to be associated with atherosclerotic plaque instability and higher risk for CAD or stroke (Tian et al., 2019; Zhan & Hägg, 2019). For example, in a cross-sectional investigation of mothers aged 20-50 without CAD but with controlled hypertension or hyperthyroidism, Epel and colleagues (2006) found that lower levels of telomerase were significantly associated with not only lower mood, but also major risk factors for CVD such as greater abdominal adiposity, and higher resting heart rate, systolic blood pressure, fasting glucose, LDL and total cholesterol, total/HDL cholesterol ratio, and a greater tendency toward lower resting heart rate variability (HRV) even after adjusting for age and BMI. Moreover, women with lower telomerase levels responded to stress differently (post standardized stressor, Trier Social Stress Test), with greater decreases in HRV compared to women with higher telomerase levels (Epel et al., 2006). Lower telomerase levels also appear to be present in those at risk for diabetes. For example, prolonged elevations of blood glucose levels (including those within the normal non-diabetic range), appeared to down regulate telomerase, and hence promote cellular aging, regardless of initial TL (Chan & Blackburn, 2003; Kim et al., 2003).

On the other hand, investigations on telomerase (and TL) in individuals with CAD or metabolic syndrome have led to contradictory results. Excessive loss of telomeres may increase telomerase activity to compensate telomeric loss. For example, among CAD patients, higher levels of telomerase are correlated with shorter telomeres (Matsubara et al., 2006). Higher telomerase was also found in individuals with diabetes type II compared with those with pre-diabetic and normoglycemic (controls) (Sharma et al., 2019).

In the CARDIA cross-sectional and prospective study of non-CAD men followed over 15 years (aged 40 at follow-up), higher levels of telomerase predicted higher prevalence of coronary artery calcium (a measure of calcified atherosclerosis), especially in individuals with shorter telomeres (Kroenke et al., 2012). Telomerase activity was significantly elevated in patients with metabolic syndrome when compared to healthy volunteers (Rentoukas et al., 2012). These findings corroborated a prior study in African-Americans at risk for CAD by virtue of obesity (Zhu et al., 2012). Taken together, increased telomerase may reflect a counterregulatory adaptation to physiological stressors that reduce TL, as shown in animal models and humans (Beery et al., 2012; Zalli et al., 2014). Hence, increased levels of telomerase could be a predictor of cardiovascular risk in high-risk population of metabolic syndrome.

In conclusion, inconsistencies in findings may be explained by possible sex differences, metabolic profile, and age in respect to TL and telomerase and raise the importance of taking into consideration these differences as they contribute to the heterogeneity in the literature to some extent.

1.3.3 Sex Differences in Telomere Biology

Women generally suffer from more stress, more illness, more years of disability, and when suffering from CAD, are more likely to die than men. Yet, paradoxically women live markedly longer than men in nearly every population, as reported in meta-analyses[2] (Barrett & Richardson, 2011; Gardner et al., 2014). This difference throughout the lifespan is mirrored in telomeres as well, although heterogeneity within studies does exist (Gardner et al., 2014). At birth, there are no sex differences in TL (Okuda et al., 2002), but thereafter, men's telomeres generally shorten faster than women's (Aviv et al., 2005; Stindl et al., 2004), including in adolescents (Zhu et al., 2011) in middle-age (Bekaert et al., 2007) and in older adults (⩾60 years) (e.g., Cawthon et al., 2003; Gardner et al., 2014). Moreover, shorter TL has been shown to be significantly associated with an unhealthy lifestyle (i.e., smoking and eating habits) and more risk-taking behavior in men, but not in women (Needham et al., 2014), suggesting different pathophysiological pathways for TL attrition in men versus women. In the longitudinal Heart and Soul Study, male sex was one of the independent predictors of TL shortening over 5 years (Farzaneh-Far et al., 2010). Consistent with this, in participants from the MacArthur Health Aging Study, the rate of TL shortening predicted a 2.3-fold-greater risk of 12-year cardiovascular mortality in men but not in women (only baseline TL in women was associated with CVD mortality) (Epel et al., 2009). This sex difference persists among individuals with stable CAD (Goglin et al., 2016). These findings suggest that risk factors may have different implications for telomere erosion as a function of whether one is man or woman (Bishcoff et al.,

[2] To note: through proportional analyses, Crimmins' (2002) study found that longer lives are accompanied by increases in the proportion of life spent in poor health and concludes that women suffer from worse health than men do, not in spite of living longer, but because they live longer.

2006; Mayer et al., 2006). In fact, these differences may be explained by a greater rate of attrition in TL. Male sex, high allostatic load, and comorbid illnesses have been associated with a higher attrition rate (Ghimire et al., 2019). These sex differences in TL become smaller at older ages (Cawthon et al., 2003; Needham et al., 2014). Interestingly, Needham and colleagues (2014) reported in a cross-sectional study of individuals without CVD, aged 45 to 85 years old, that neither behavioral nor biological factors (i.e., total testerone, estrogen, oxidative stress, body mass index) explained why the sex difference in TL was smaller at older ages.

1.3.4 Conclusion

In conclusion, TL shortens across the lifespan (Cawthon et al., 2003), increasing the risk for developing diseases of aging such as diabetes, arthritis, cancers, all-cause mortality and CAD morbidity and mortality independently of chronological age (Haycock et al., 2014; Vaiserman & Krasnienkov, 2021). The rate of telomeric attrition can be further accelerated by cell stressors (e.g., oxidative stress), or alternatively, arrested by increased telomerase levels (Kroenke et al., 2012). Importantly, non-physiological factors have also been shown to influence or be associated with TL. The next section will discuss the psychological correlates of telomere biology.

1.4 Psychological Factors and Telomere Biology

Significantly shorter telomeres have been reported in individuals with current depression (Deng et al., 2016; Lin et al., 2016; Ridout et al., 2016), lifetime major depression disorder (Wolkowitz et al., 2011), and anxiety disorders in comparison to their psychologically healthier counterparts (small to medium effect sizes) (Malouf &Schutte, 2017; Verhoeven et al., 2016). However, while recent research has examined the relationship between telomere biology and psychological states and disorders ((perceived) stress, depression, and anxiety) (Schutte & Malouf, 2016), fewer studies have looked at underlying personality traits and their association with TL. Indeed, given that some specific personality traits are known predictors of all-cause mortality (Graham et al., 2017; Vitori et al., 2021), physiological mechanisms underlying the associations between personality traits and health continue to be warranted.

1.4.1 Personality and Telomere Length

To date, only fifteen studies in fourteen different samples have looked at particular personality traits (e.g., Big Five traits, pessimism, optimism, hostility, Type D personality, and defensiveness) and their association with telomere biology (Brydon et al., 2012; Conklin et al., 2018; Edmonds et al., 2015; Huzen et al., 2010; Ikeda et al., 2014; Jordan et al., 2019; O'Donovan et al., 2009; Sadahiro et al., 2015; Savolainen et al., 2015; Schutte et al., 2016; Schoormans et al., 2018, Starnino et al., 2016; Van Ockenburg et al., 2014; Watkins et al, 2016). Five prospective investigations examined the relation between TL and components of the NEO-Five-Factor model (FFM) (Costa& McCrae, 1992) (extraversion, openness to experience, agreeableness and conscientiousness, neuroticism) with mixed results (Conklin et al., 2018; Edmonds et al., 2015; Sadahiro et al., 2015; Schoormans et al., 2018, Van Ockenburg et al., 2014). For example, in a cohort of older individuals (Mean age= 61.51 ± 2.90 years), none of the FFM personality dimensions were significantly associated with TL in the overall sample. However, when subgroup analyses were performed, it was found that men who scored higher on agreeableness ($ß = -0.09$, $p = 0.02$) and women who scored lower on agreeableness ($ß = 0.07$, $p = 0.02$) had shorter TL (Savolainen et al., 2015). In contrast to the former study, two other investigations did find the conscientiousness trait, defined as the propensity to be organised and adhere to social norms, to be associated with significantly longer TL in healthy women, but not men (Edmonds, et al., 2015; Sadahiro et al., 2015). In one case, however, the association was no longer significant after controlling for pertinent covariates (e.g. smoking and BMI)(Edmonds et al., 2015). In separate research on 36 healthy post-menopausal women (Mean age = 61±71), O'Donovan and colleagues found that higher pessimism (expecting negative outcomes for the future) was associated with shorter TL ($ß = -0.68$, $p<.001$), independently of its association with increased inflammatory interleukin-6 (IL-6) concentrations. Participants in the highest tertile of pessimism had a mean TL that was 705 base pairs shorter than those in the lowest tertile. This could represent the equivalent of 11-23 years difference in TL compared with non-pessimistic participants. These results between TL and pessimism were independent of age, optimism, neuroticism, perceived stress, caregiver status, BMI, sleep, and physical activity and represented a large effect size (O'Donovan et al., 2009). Similar results were found between pessimism and shorter TL over in a group of older men with and without cardiometabolic illness (e.g., hypertension, diabetes) (Ikeda et al., 2014). Discrepancies in findings among these studies relating personality to TL may be inherent to the study design, as affirmative studies mostly included older individuals (Ikeda et al., 2014; O'Donovan et al., 2009). Furthermore, these disparities may reflect whether or not researchers controlled for important lifestyle factors as in the study by Sadahiro and colleagues significant associations were found while adjusting for only age and sex (Sadahiro et al. 2015), whereas Savolainen and colleagues reported non-significant results while adjusting additionally for education, presence of chronic illnesses, depressive symptoms, and the lifestyle factors (e.g., BMI, alcohol use, smoking and physical activity) (Savolainen et al. 2015).

1.4.2 Hostility and Telomere Length

Very little is known regarding trait hostility's association with TL or telomerase activity. Only four studies to date involving different samples have investigated this issue (Brydon et al., 2012; Jordan et al., 2019; Starnino et al., 2016, Watkins et al., 2016), (see Appendix B for Summary Table). For example, in a healthy older sample (without CVD, diabetes, inflammatory disease or hypertension) involving 228 women and 206 men (Mean age: 63.31, range 54-76 years), Brydon and colleagues (2012) observed that hostility (assessed using the 10-item cynical subscale of the Cook-Medley Hostility Scale) was independently associated with shorter TL ($ß=-0.11$, $p=.02$) and greater telomerase activity ($ß=0.10$, $p=0.06$). When interactions terms were introduced (Sex and Hostility), this association was significant only in men, but not in women for both TL and TA. The authors also examined whether hostility predicted individuals who exhibited both shorter TL and higher telomerase levels compared to those with lower levels of either or both of these markers. Indeed, hostility increased the odds, adjusting for age, grade, BMI, and waist circumference, of having both short TL and high TA by 28% (95% CI: 1.07–1.53, $p <0.01$) per unit increase in hostility. In contrast to work on the Big 5 or pessimism, no significant associations were observed between hostility and TL or telomerase activity in women in Brydon's study. Although TL was similar in both men and women, and TA levels were greater in women than in men, the authors hypothesized that men may be more susceptible to the effects of stress on cellular aging, as well as the detrimental consequences of aging. Indeed, high telomerase levels might reflect a compensatory protective response to telomere shortening in men with greater hostility (Brydon et al., 2012). Zalli and colleagues (2014) re-examined Brydon's data and found that particpants with shorter TL and higher telomerase activity also exhibited blunted stress reactivity and recovery. Although this was a cross-sectional study, altered stress responses may be one mechanism linking hostility with telomere regulation. In this respect, this highlights the potential value in researching personality traits such as hostility and defensiveness, in whom maladaptive psychological ressources and coping skills may increase risk for premature aging.

In contrast to results obtained by Brydon and colleagues, greater hostility (and increases in hostility over a 3-year period) was associated with longer (not shorter) TL in a study conducted in our laboratory in 132 healthy men and women (Starnino et al., 2016). Results remained significant after controlling for age, exercise, alcohol consumption, systemic inflammation, and 24-hr mean arterial blood pressure (ß=. 256, p=.003). No sex differences were observed in this sample.

Moreover, only two studies have examined the relation between hostility and TL in individuals suffering from various chronic medical conditions (Jordan et al., 2019; Watkins et al., 2016). Watkins and colleagues performed a cross-sectional study using a predominantly male (92.5%) U.S military veterans and found that telomeres were shorter among older, more behaviorally hostile men (e.g., with difficulty managing their anger outbursts) compared to the less hostile counterparts, after adjusting for 17 covariates such as age, sex, sociodemographic, number of chronic conditions, lifestyle psychological outcomes. Indeed, TL decreased by 58% for each standard deviation (SD) increase on the hostility scale. However, TL was retrieved from saliva, which is known to be more sensitive to environmental confounds as compared to blood. Furthermore, the six items of the SCL-90-R used in Watkin's study (2016) encompassed only hostility's affective and behavioral symptoms (aggressive urges and impulses) over the last month, as opposed to its trait component as depicted in the Cook-Medley's Hostility Scale. No sex differences were reported in respect to hostility and TL, though this may not be surprising given the very small percentage of women in the study (7.5%).

Indeed, in a recent study in African-Americans (n=2516; women 61.29%), comprised of individuals with hypertension (57%), obesity (55%), and/or diabetes (23%), higher cynical hostility (Cynical CMho scale), higher anger-out, and higher expression of negative affect were associated with shorter TL among women (b's$\leqslant -0.13$, all p's$\leqslant 0.05$), but not men, after adjusting for age and level of education (Jordan et al., 2019). The association between hostility and TL became stronger (b=-0.18, *p*=0.059), though only marginally significant after controlling for additional health behaviours (smoking, alcohol intake, physical activity) and risk factors (BMI, C-reactive protein, smoking, diabetes, hypertension) (Jordan et al., 2019).

Taken together, reasons why opposite results were found between our sample and that of other researchers remain unclear. Differences in ways of obtaining DNA (blood vs saliva), TL measurement methods (PCR vs. Southern Blood), different measures of hostility (cynicism vs affective and behavioral vs trait hostility) may be at play here. Moreover, differential results may reflect the more heterogeneous nature of our previous sample compared to that of the Whitehall-II investigation, USA-veterans, and African Americans from Mississippi.

Thus, findings to date are mixed, and suggest the possibility that sex differences exist. Further research is required to shed light on the effects of hostility in men and women on aging. It is important to study the overall concept of hostility, rather than individual subcomponents (cognitive, affective, and behavioral) as has been done in three of the studies. Given the potential for sex differences, a sample with sufficient representation of men and women is needed. Which variables to control for remains contentious as many of these may actually be outcomes of hostility themselves. Their inclusion as covariates may remove part of the variance attributable to hostility. In this respect, it is important to include univariate associations of hostility with TL or telomerase. The addition of the various behavioural, medical, and physiological covariates can then speak to any additional variance explained by hostility. Although two previous studies (Brydon et al., 2012; Jordan et al., 2019) utilized categorical measures of hostility, literature consistently supports the superiority of continuous measures over artificially categorized measures in most circumstances (De Coster et al., 2009).

1.4.3 Defensiveness and Related Traits with Telomere Length

To date, only one investigation (Starnino et al., 2016) examined whether defensiveness was associated with TL. In that study involving 132 healthy men and women, individuals who reported greater defensiveness had shorter TL compared to those who were less defensive ($ß=-0.22$, $p=0.01$). This was independent of age, sex, depressive and anxious symptomatology, hostility, as well as sex, physical activity, C-Reactive Protein, and mean arterial pressure. Moreover, chronological age, but not sex, was found to moderate the relationship between defensiveness and TL, such that greater defensiveness was associated with significantly shorter TL among young and middle-aged individuals but not among older individuals, though the direction was the same.

In contrast, a cross-sectional study reported no significant association between Type-D (a concept similar to defensiveness) and TL in 890 patients (39% female) with chronic heart failure (Mean age= 73; Age range[64–79]) (Huzen et al. 2010). This said, a recent prospective study (Schoormans et al., 2018) in 2936 younger and middle-aged individuals (Mean Age= 41.8±13.1) with or without a current or remitted depressive or anxiety disorder, found that participants with Type D personality had significantly shorter TL at baseline and 6 years later, independently of other psychological variables. Moreover, those with Type D were also surprisingly less likely to show TL shortening over a period of 6 years compared to those without Type D (adjusting for physical health, anxiety and depressive disorder, lifestyle factors, and recent life stress) (Schoormans et al., 2018). These latter results are consistent with the hypothesis that shorter telomeres may be protected from further attrition via telomerase activation (not measured within Schoorman's study).

1.5 Limitations and Methodological Shortcomings of the Existing Literature on TL and Personality Risk Factors Associated with CAD

As seen above, inconsistencies were observed on the sparse literature published to date. Methodological differences relating to sample characteristics may partly be responsible. Although various characteristics may influence the association between personality traits and TL, sex and health status of participants will be the focus of this thesis.

1.5.1 Sex as a Moderator

Sex or gender differences may exist in the relation between the personality traits and TL. This has already been suggested by the results of two studies (Brydon et al., 2012; Jordan et al., 2019), and may be underscored by sex or gender differences in hostility, and in TL. For hostility specifically, men and women may endorse the same amount of experiential anger, yet men tend to score higher on the Cook-Medley Hostility Scale compared to women (Greenglass & Julkunen, 1989). Moreover, hostility has been more consistently shown to be an independant risk factor for CAD (Chida & Steptoe, 2009; Miller et al., 1996; Myrtek, 2001; Smaardjik et al., 2019; Wong et al., 2013) as well as long-term risk of hypertension, metabolic burden, behavioral risk actors, and all cause mortality in men than in women (Chida & Steptoe, 2009; Klabbers et al., 2013; Thomas et al., 2020). However, many of these studies were male-centric and rarely included representative samples of women. In studies that examined sex differences, different findings have emerged. For example, two prospective studies in post-menopausal women with and without CAD have shown an association between hostility (original Cook-Medley Hostility Scale) and CAD events, even after adjusting for socio-demographic and behavioral risk factors (Chaput et al., 2002; Olson et al., 2005). In the HERS (Heart and Estrogen/Progestin Replacement Study) investigation, trait hostility was found to be an independent risk factor for recurrent CAD events at the 4-year follow-up in older postmenopausal women (Mean Age=67 years) with CAD (after adjusting for CAD risk factors) (Chaput et al., 2002). In a cohort of slightly younger post-menopausal women (Mean age= 58 years old) with chest pains and suspected myocardial ischemia measured by angiograms, hostility was associated with a 3-to-6-year higher risk of CAD events (even after adjusting for age, level, education, cholesterol, history of diabetes, CAD, history of dyslipidemia (yes/no), race, waist circumference, smoking , current hormone therapy (Olson et al., 2005). While more recent studies have included both men and women and control for sex (Haukala et al., 2010), it is unclear whether hostility's impact on TL differs between men and women.

Both men and women appear susceptible to exhibit the defensiveness trait (or social desirability) in healthy and health-comprised samples (King et al., 1990; Lévesque et al., 2009; Nyklicek et al., 1998), but factors contributing, underlying it, or otherwise associated with it may differ. For example, denial of emotional distress tends to be more common among men than women and may also contribute to the fact that men show less help seeking, and clinicians are often less effective in recognizing distress in men (Ketterer et al. 2004). On the other hand, older women are more likely to inhibit undesirable behaviour than their male and younger counterparts (Diehl et al., 1996; John & Gross, 2004; Orgeta, 2009). This mirrors their worse metabolic profile in one study as compared to men and younger women (Lévesque et al., 2009). While menopausal status did tend to interact with defensiveness to predict metabolic syndrome (MS) burden and glucose, controlling for it did not alter the pattern of results (Lévesque et al., 2009). This is consistent with studies on blood pressure by King et al. (1990) and Niklycek et al. (1998) who found a positive relation between blood pressure and defensiveness in older women (Mean age = 48 and 47, respectively). As such, the interaction between age and defensiveness in women likely represents the cumulative effects of defensiveness on cardiovascular health over time rather than the impact of menopause.

These various sex- or gender-related differences in TL and personality could affect the relation that exists between TL and personality variables. This has partly been born out, though in contradictory directions (Brydon et al., 2012; Jordan et al., 2019; Starnino et al., 2016). Given the paucity of research on hostility or defensiveness and TL, and mixed results to date, continued research on sex differences is warranted.

1.5.2 Cardiac Health Status as a Moderator

As mentionned, it has been suggested that hostility and defensiveness are associated with CAD risk factors and CAD (Chida & Steptoe, 2009 ; Guerrero Rodriguez et al., 2018), however associations have not always been independent of medical conditions (Huzen et al., 2010; Savolainen et al., 2015). Given the poorer prognosis related to shorter TL in individuals with chronic illnesses such as CAD (Haycock et al., 2014), as well as the association between personality traits and the development of chronic illnesses and all-cause mortality (Appleton et al., 2016; Chen et al., 2019; Denollet et al., 2008; Klabbers et al., 2013), examination of the impact of cardiac health status on the relation between these particular traits and TL appears warranted. More hostile and defensive individuals who survive CAD may also be more biologically resilient to the effects of these traits. Conversely, among healthy individuals, we showed that hostility was associated with greater increases in metabolic and inflammatory disturbances over a three year period among older rather than younger individuals (D'Antono et al., 2013). We also previously showed that defensiveness in healthy individuals was associated with a worse metabolic profile among older women although not in men and younger women (Lévesque et al., 2009). Further investigations are needed to examine whether associations between personality traits and TL differ according to cardiac status.

For researchers and clinicians to understand the relation between these individual traits and biological aging processes, it appears necessary to determine how they are influenced by sex and health status (CAD status). Hence, greater awareness of the potentially differential role that personality plays as a function of these individual characteristics could lead to more personalized medical assessments, education, and interventions. This could include the possibility of promoting more adapted emotional styles of coping using psychosocial stress management programs, for examples, such as Mindfulness-Based Stress Reduction (MBSR). Emerging data suggests that such interventions could potentially alter telomere biology processes as well as improve clinical outcomes. This topic will be further explored below.

1.6 Pertinence of Psychosocial Stress Reduction Interventions for CAD Risk Factors

It has been suggested that hostility and defensiveness may impact telomere regulation in part, because of affective, behavioural, and physiological responses to stressful life situations observed in those with these traits (Chida & Hamer, 2008; Lévesque et al., 2010). This may in turn influence aging processes such as telomere biology in both men and women (Cheng et al., 2017; Révesz et al., 2014). It is possible that stress management may improve these psychological risk factors, as well as biomarkers of aging (TL and telomerase activity). Stress management approaches targeting both body and mind are of particular interest to this dissertation. The most frequently taught approaches include relaxation techniques, biofeedback, yoga, various forms of meditation and mindfulness.

These mind-body based stress management interventions, within a more holistic approach, are particularly pertinent because they a) cause very little to no physical side-effects, b) are fairly low in cost, c) may diminish or help to diminish hospitalizations, d) are very simple to learn and allow patients to actively participate in treatment, e) are accessible for the patient as many of the techniques can be done at home or elsewhere once learned, f) can be easily perfomed in larger groups, g) movements and exercises can be adjusted for older individuals, and h) can provide a sense of community and social benefits for older individuals (Britton et al., 2021; Herman et al., 2017; Parra et al., 2019; Younge et al., 2015).

1.6.1 Stress Reduction Programs for Hostility and Defensiveness

Psychosocial stress reduction programs have shown promises in reducing self-reported trait hostility, associated risk factors, and/or health consequences (Lavie & Milani, 2005; Suls, 2013). For instance, cognitive behavioral interventions and biofeedback interventions have shown to have consistent positive results in improving hostility levels (moderate to large effect sizes) in cardiac and non-cardiac patients, as well as in older healthy samples (Edelman et al., 2003; Fuller et al., 2010; Gidron et al., 1999; Lin et al., 2015; Russell et al., 2015; Sloan et al., 2010). Moreover, participants randomized to Cognitive Behavioral Stress Management programs have been shown to have fewer days of hospitalization and significantly lower hospitalization costs compared to usual care information-based control group (Davidson et al., 2007).

On the other hand, psychosocial interventions that have included defensiveness as an outcome (measured by the 13-item Marlowe-Crowne Social Desirability Scale) (Frasure-Smith et al., 2002) or defensive-related traits have for the most part obtained null results post-interventions (Shoval-Zuckerman et al., 2015). For example, in a large randomized control trial from the Montreal Heart Attack Readjustment Trial for post-myocardial infarction patients (n=1376; 66% male), participants were randomized to either usual medical care (n=684) or an intervention given by nurses treating non-specific psychological distress for 12 months (n=692) via monthly telephone monitoring psychological distress and five to six home nursing visits. After one year, there were no differences in either survival or psychological outcomes (including defensiveness) between the two groups (Frasure-Smith et al., 1997). Moreover, at five years' follow-up, the men and women in the treatment group that were more defensive at the baseline interview exhibited significantly reduced survival. Results suggested that the program may have increased distress in those with greater defensiveness, as they were more likely to be prescribed benzodiazepines and to have visited emergency rooms without being readmitted than those in the control group (Frasure-Smith et al., 2002). It is reasonable to believe that supportive interventions may not be sufficient in helping those with greater defensiveness. Indeed, increasing awareness of their disease status and distress could be an additional source of distress for patients who prefer a style of coping that is avoidant.

Over the last few years, interest has risen for mindfulness-based interventions' (MBIs) efficacy with respect to defensiveness or emotional inhibition, anger disturbances, and biological markers such as telomere length and telomerase activity. These topics will be reviewed in the upcoming sections, including MBI's impact on quality of life to ensure a holistic understanding of what we know so far in respect to these specific dimensions. Before turning to these topics, I briefly address the concept of mindfulness.

1.6.2 Origins of Mindfulness

> Mindfulness means paying attention in a particular way: on purpose, in the present moment, and non-judgementally. This kind of attention nurtures greater awareness, clarity, and acceptance of present-moment reality.
>
> -Jon Kabat-Zinn (1994, p.4)

The practice of mindfulness meditation has existed for thousands of years. Although various cultures have contributed to the evolution of mindfulness, much of this process has been attributed to the Buddhist tradition over the last 25 centuries. Buddhist meditation is thus a process whereby the mind learns to pause, become less reactionary, and respond to thoughts, emotions, and actions from a composed place of compassion (Kabat-Zinn,1990). This practice of meditation gives rise to mindfulness, which can be viewed as an orientation to our experience with awareness and acceptance. There are seven important pillars of mindfulness practice. First, the stance of non-judgement refers to taking the position of an impartial witness to one's individual experience. In this regard, the mindfulness practitioner comes to accept things as they are (good, bad, neutral), without trying to alter it; coming to peace with the notion that change is inevitable, and that the world is not black and white. The second pillar is that of patience, where understanding that the events of life will unfold in time, there is no need to rush to something better or different. Approaching situations with a beginner's mind is another central component of mindfulness that is about developing one's mind to perceive experiences as if it was the first time without the bias of our prior experiences influencing our perception. It is being open to new possibilities, and not allowing past experiences and knowledge to prevent us from viewing a situation clearly. The tenet of trust refers to having faith in one's intuition, trusting oneself and one's feelings. The principle of non-striving in mindfulness refers to accepting that meditation has no objective other than paying attention to oneself in the present and being true to oneself. Rather than constantly striving to meet goals, non-striving emphasizes focusing on seeing things as they are and accepting them from moment to moment, which in turn allows a natural progression towards achievement of goals. Acceptance does not imply resignation but rather signifies accepting what is occurring in the present moment and accepting oneself without abandoning principles and values. According to mindfulness principles, it is essential that one accepts who he or she is before inner change becomes possible. Finally, letting go refers to letting things be as they are, rather than allowing a stressor to gain a strong hold in our minds, occupying unnecessary attention and energy (Kabat-Zinn, 2003).

Various interpretations of mindfulness practice evolved in the Western world in the 20th century. Jon Kabat-Zinn, professor of medicine emeritus at the University of Massachusetts Medical School is among the prominent Western theorists who first translated Buddhist mindfulness to its current form used in the West. He developed a standardized program called the Mindfulness-Based Stress Reduction program (MBSR) in 1979, originally developed for the management of chronic pain. More specifically MBSR is an eight-week stress reduction program that embodies the fundamental pillars mentioned above. It is comprised of group sessions of 2–2.5 h duration each week for eight weeks. Participants are invited to engage in mindfulness practice (i.e., yoga, meditation) at home for at least 45 minutes per day for six days of every week. In addition, a half-day or day-long meditation session is usually held toward the end of the program (Kabat-Zinn, 1982). MBSR offers formal mindfulness meditation training which primarily include body scan, sitting meditation, and Hatha yoga. The body scan involves paying attention to individual parts of the body and bodily sensations in sequence from toes to head. In sitting meditation, the primary focus is to pay attention to the breath (the rising and falling abdomen) or the stream of thoughts and distractions that flow through the mind. Hatha yoga is based on paying attention to the moving of the body through a series of postures (seated or lying down) to develop greater strength, balance, flexibility, and body awareness. In all these exercises, when thoughts arise and attention wanders, the practice is to return the attention to the intended focus. An intensive silent retreat of one day is included towards the end of the program which includes a variety of these formal exercises practiced throughout the program to encourage a deeper exposure to the pillars of mindfulness.

1.6.3 Hostility and Mindfulness

Mindfulness may help to reduce the emotional reactivity typically elicited by anger provoking stimuli via a process of sustained, non-judgemental observation of anger-related sensations, without attempts to escape, act on, or avoid them (Baer, 2003). Practicing non-judgmental awareness of the self and others may help individuals to become more distant from their cynical attitudes and change the appraisal of the emotional experience without having to directly restructure thoughts (Wright et al., 2009). Moreoever, the practice and utilization of mindfulness, with repeated practice, is said to form an over-learned response such that experience in general is more likely to be regarded without harsh judgment (Harned et al. 2006).

To our knowledge, ten investigations have examined the impact of an MBI on hostility and related traits in various populations, with mixed findings (Brown Wright et al. 2011; Henderson et al., 2013; Jahangirpour et al., 2013; MacCoon et al., 2012; Olivo et al., 2009; Rosenkranz et al., 2013; Samuelson et al., 2007; Sibinga et al., 2011; Tamawaga et al., 2015; Young et al., 2009). Of these studies, the only three that measured trait hostility using a validated scale (Brown Wright et al., 2011; Olivo et al., 2009; Samuelson et al., 2007) found significant reductions in hostility post-intervention. For instance, in a non-randomized trial of 1350 prison inmates from six correctional institutions, trait hostility (Cook-Medley Hostility Scale) was significantly reduced by 9.2% in women and 7.0% in men following MBSR (Cohen'd= 0.23-0.28 (small effect sizes)), (Samuelson et al., 2007). While promising, to what extent these results are generalizable to individuals without antisocial behavioral issues is uncertain. Only two investigations of MBSR and hostility utilized a randomized controlled design and additionally included a follow-up assessment (Henderson et al., 2013; Brown Wright et al., 2011). Henderson and colleagues (2013) randomized 163 women with early- stage breast cancer and undergoing radiotherapy to MBSR (n=53), usual care group (n=58), or a nutritional education group (n=52) and found a significant reduction in hostility (measured by the Symptom-Checklist (SCL-90)) 4 months after beginning the MBSR program and the nutritional education group compared to the usual care group. Generalizability remains an issue given participants were currently in active treatment for a life-threatening condition. Of concern as well is the use of the SCL-90 in both Brown Wright (2011) and Henderson's studies as it only emcompasses the affective and behavioral symptoms (aggressive urges and impulses) over the last month, and thus may not be an appropriate reflection of the overall trait hostility concept. Hence, previous studies on the effects of MBIs on hostility have more often than not confounded the concepts of state anger and hostility, and/or not used a randomized-controlled design.

Thus, little is known on the impact of an MBI on the hostility of older individuals at higher risk for CAD but not currently battling a life-threatening condition. Only one randomized controlled trial examined the impact of mindfulness on trait hostility and 24-hour ambulatory blood pressure in 121 African American ninth graders (40.41% male) at increased risk for developing hypertension by virtue of higher systolic blood pressure (between the 50th and 95th percentiles) (Brown Wright et al., 2011). Adolescents were randomly assigned to breathing awareness meditation (BAM) (a component of MBSR), life skills and social training (LS), or health education (HE) and engaged in intervention sessions during health class for 3 months. Before, after, and 3 months following the intervention, self-reported hostility and 24-hour ambulatory blood pressure were measured. Results indicated that BAM participants displayed significant reductions in self-reported hostility ($p=0.04$) and ambulatory blood pressure ($p=0.02$) post-intervention, and hostility and blood pressure were moderately correlated at all time points (r's=0.34-0.46, $p<0.05$). In the LS group, a significant reduction in hostility was found only in the interval between post-intervention and follow- up, and changes in blood pressure and hostility were not as strongly correlated compared to the BAM group. No changes were found in either measure in the HE group (Brown Wright et al., 2011).

Hence, curiosity is raised on how hostility levels may be impacted by mindfulness in older individuals at risk of CAD by virtue of metabolic parameters. Indeed, little is known regarding the impact of MBI's on trait hostility and potential biological processes that may increase risk for CAD among older individuals. Given the lack of studies on the topic and the important methodological discrepancies in the current ones, there remains a need for further pilot testing in those with high risk for CAD disease.

1.6.4 Defensiveness and Mindfulness

Despite the negative impact of defensiveness discussed earlier, studies have only examined defensiveness or defensive-like traits as a moderating or control variable in MBI studies (Carlson et al., 2014; Keng et al., 2020; Robins et al., 2012; Tamawaga et al., 2015). For example, Tamawaga and colleagues found that defensive breast cancer survivors attended significantly fewer classes than their less defensive counterparts ($r=-0.41$, $p<0.50$) (Tamawaga et al., 2015). However, no studies have specifically examined the effects of MBIs on defensiveness. Nonetheless, MBIs, have been found to improve elements of defensiveness in non-experienced meditators (in small clinical and non-clinical samples), such as the capacity to tolerate negative emotions, improved self-compassion (Robins et al., 2012), and self-esteem (Randal et al., 2015). It remains to be investigated whether an MBI program can have an influence on levels of defensiveness, specifically in individuals at high risk for CAD. Taken together, trials examining the effect of MBSR on implicit maladaptive traits, such as hostility and defensiveness have been scarce.

1.6.5 Mindfulness-Based Interventions and Telomere Regulation

Psychosocial interventions targeting biological processes, such as TL and telomerase, have gained interest over the last decade. A small body of research has emerged addressing the relationship between meditation practice and telomere-related outcomes (telomere length and telomerase activity). Telomeres generally shorten slowly across the lifespan. There is, however, some degree of malleability. To the extent that TL and telomerase may be susceptible to psychosocial influences (Schutte & Malouf, 2016), including personality and associated stress, they may also be amenable to improvement using psychosocial interventions (see Figure 4 below for theoretical model).

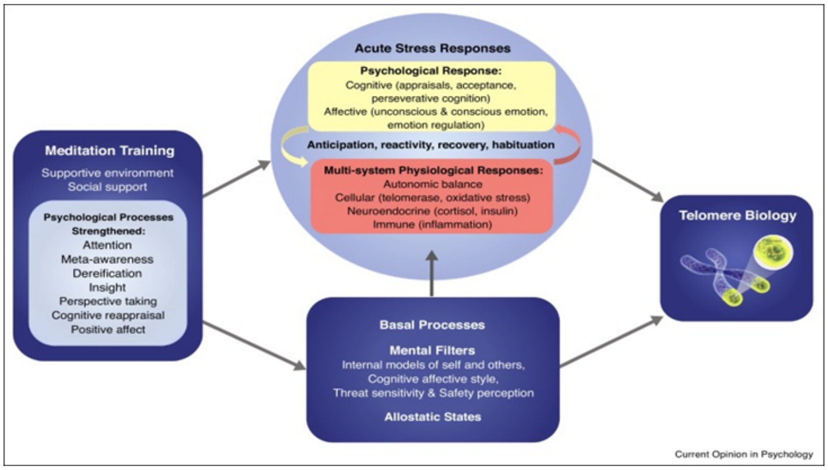


Figure 1.4. A theoretical model depicting how meditation training may impact telomere biology via stress processes (Conklin et al., 2019).

Indeed, a growing literature suggests that stress management may have beneficial effects for the telomere maintenance system in healthy (Schutte & Malouff, 2014), and clinical populations (Schutte et al., 2020) (please refer to Appendix C for summary table on RCT's for MBIs and Telomere Regulation). This will be further examined below.

A recent meta-analysis of mindfulness-based interventions (MBIs) in eleven samples (total n=861) found that telomeres were longer following a meditation-based program compared to control groups, though results were only significant in the four quasi-experimental, but not in the seven randomized controlled trials (RCTs) that found no change post-intervention (Schutte et al., 2020). Significant heterogeneity emerged across studies and may reflect greater amount of practice time performed and the healthier samples in the quasi–experimental trials compared to the randomized controlled trials, which were mostly comprised of participants with either physical or psychiatric illnesses (Schutte et al., 2020).

On the other hand, randomized controlled trials in clinical and nonclinical populations included in a meta-analysis have found that MBIs can increase telomerase activity (Schutte & Malouff, 2014). Of the six RCTs assessing change in TA (Daubenmier et al., 2012 ; Duan et al., 2016 ; Lavretsky et al., 2013; Lengacher et al., 2014 ; Ho et al., 2012) or telomerase gene expression (Duraimani et al., 2015) with MBIs, five (Duan et al., 2016 ; Duraimani et al., 2015; Ho et al., 2012 ; Lavretsky et al., 2013 ; Lengacher et al., 2014) found significant or marginally significant increases post-MBI relative to a waitlist/non-active (Daubenmier et al., 2012; Duan et al. 2016 ; Ho et al., 2012 ; Lengacher et al., 2014), health education stress management (Duraimani et al., 2015) or relaxation-based intervention control group (Lavretsky et al., 2013).

To date, only three investigations (Duraimani et al., 2015; Innes et al., 2018; Lengacher et al.,2014), two of which were RCTs (Innes et al., 2018; Lengacher et al.,2014), have looked at the impact of an MBI on both TL and telomerase within the same study. While increases in TA post-intervention were found in all three studies, TL did not change (Duraimani et al., 2015; Innes et al., 2018; Lengacher et al.,2014). For example, Lengacher and colleagues performed a RCT in which breast cancer patients underwent either a 6 week MBSR program or usual care (waitlist to receive MBSR). While no effect was found on TL, telomerase activity increased steadily over time (up to 17%) in the MBSR group while remaining relatively constant (3% increase) in the usual care group, after adjusting for baseline telomerase. It is plausible that the mindfulness training delivered in the context of MBSR is not sufficiently intensive to induce changes in TL other than telomere maintenance (Carlson et al., 2015), as most studies demonstrating positive effects on TL compared to the inactive control groups were non-randomized studies and performed in samples of physically healthy experienced meditators (Conklin et al., 2018; Hoge et al., 2013). Moreover, these two studies both employed more intensive modes of meditation practice, such as meditation retreats lasting three weeks or more (Conklin et al., 2018; Hoge et al., 2013).

While the results from these studies are encouraging, more randomized controlled trials exploring the impact of interventions on TL and telomerase are needed. Moreover, examining a sample without cancer would allow for a clearer understanding of results for telomerase, as this measure is typically increased in cancer cells. Importantly, there is a paucity of studies that examined whether telomere regulation can be improved through a standardized mindfulness training program in individuals at increased risk of CAD by virtue of metabolic abnormalities, in whom shorter TL poses additional prognostic risk (Bonfigli et al., 2016; Révesz et al., 2014.)

Of specific interest to this dissertation, only three investigations, examined whether an MBI can alter telomere regulation in individuals with metabolic risk factors. For instance, in a non-randomized trial involving forty-eight middle-aged and older individuals with hypertension who underwent either transcendental meditation stress reduction or an extensive health education stress management program, both groups demonstrated significant increases in telomerase activity (both p's<0.001), though no statistically significant between-group changes were observed (Duraimani et al., 2015). Additionally, a recent RCT randomized older participants (mean age=60.47± 1.17 years old) with clinically-relevant cognitive decline with or without CAD risk factors (i.e., hypertension, diabetes), to a 12-week Kirtan Kriya meditation (n=25)) or a music listening (ML; n=28) program. While no changes within or between groups were found for TL or telomerase post-intervention for either group, telomerase activity was found to be significantly increased in both groups among those with higher practice adherence and lower baseline TA. Beyond telomere regulation measures, both groups improved in cognitive and psychosocial status (p's< 0.05), with improvements in stress, mood, and mental-health quality of life greater in the Kirtan Kriya meditation group (Innes et al., 2018). As for the impact of MBSR specifically, Daubenmier and colleagues (2012), examined the effects of a pilot four-month RCT addressing the impact of MBSR versus waitlist-control on eating behaviors and telomerase activity in peripheral blood mononuclear cells in 47 younger and middle-aged overweight women. Findings showed a non-significant 39% increase in telomerase activity over the course of the MBSR program, compared to a 21% increase in telomerase in the waitlist control group.

Thus, while still in its infancy, emerging literature suggests that psychosocial interventions can impact TL regulation, including both TL and telomerase activity. Moreover, randomized controlled trials have been scarce, and only one study has looked at the impact of MBSR specifically in women, not men, at risk for CAD (Daubenmier et al., 2012). However, one non-randomized control study examined the potential effects of a stress-reducing, comprehensive lifestyle-modification program on TL in one group of 24 men diagnosed with low-risk prostate cancer and slightly elevated metabolic parameters (i.e., elevated waist circumference; systolic blood pressure, BMI). It was found that telomerase activity increased and psychological stress decreased following this 3-month program. The latter intervention comprised of dietary modification, moderate aerobic exercise and stress management 1.5 hr /day, 6 days per week. Stress management focused on gentle yoga-based stretching, breathing, meditation, imagery, and progressive relaxation techniques 60 min/day, 6 days/week, and a 1-hour group support session once per week. Improvements in risk factors for CAD (e.g. BMI, systolic and diastolic blood pressure, all $p<.001$) and in mental but not physical health-related quality of life ($p=0.003$) were also found (Ornish et al., 2008). The second study by Ornish et al (2013) investigated the long-term effects of this lifestyle intervention five years later, in 35 men identified as having low-risk prostate cancer undergoing active surveillance. TL was significantly increased in the 10 men who participated in the comprehensive lifestyle intervention and significantly decreased in the 25 control subjects. Importantly, the degree of adherence to lifestyle changes was significantly correlated with the extent of change in relative TL.

On a separate note, other than Ornish's initial study in men with prostate cancer and Innes's randomized controlled trial on Kirtan Kriya meditation in older adults with cognitive decline (Innes et al., 2018), other studies have failed to look at the holisitic impact of MBI's on telomere regulation, psychosocial measures, as well as quality of life, which will be included in this thesis.

1.6.6 Mindfulness-Based Stress Reduction Programs on Quality of Life

The World Health Organization (WHO, 2021) defines quality of life as: "a person's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns". No studies have addressed whether specifically MBSR can help improve individual's quality of life in respect to various life domains in relation to their own goals, and expectations. Most have focused on health-related quality of life (HRQoL), which emcompasses mental and physical health, and has been negatively associated with CAD prognosis (Ekici et al., 2014). MBSR programs have been shown to significantly improve (moderate to large effect size) health-related quality of life (HRQoL) in various physically healthy and clinical populations (De Vibe et al., 2017). For instance, in a randomized controlled trial with 60 younger and middle-aged CAD patients (20-49 years of age), MBSR was found to significantly increase HRQoL at post intervention and at the 3 month follow-up compared to the waitlist control group. Authors suggested that MBSR may influence HRQoL by modulating psychological processes (e.g., emotional regulation, self-efficacy) in those with CAD (Jalali et al., 2019). Outside of the health-related aspects of quality of life, only one investigation has included other domains of quality of life. Colle and colleagues (2010) performed a non-controlled study in 16 middle-aged participants with and without CVD where only one had elevated cholesterol and atrial fibrillation. They found statistically significant improvement in overall quality of life, mental well-being, physical well-being, emotional well-being, level of social activity, and spiritual well-being (all p's<0.05, medium effect sizes).

In summary, the need for randomized controlled studies measuring the impact of an MBI, such as MBSR on quality of life based in those at risk for CAD is warranted. Moreover, performing a randomized controlled trial where a measure of global quality of life based on personal life goals would be novel, and help create a more personalized approach to (behavioral) medicine by inviting participants to reflect on what values are important to them and notice how closely aligned they are with these life goals.

1.6.7 Limitations of the Existing Literature on Stress Reduction Interventions for Telomere Biology, Personality Traits, and Quality of Life

A summary of limitations and methodological shortcomings in MBI's hostility, defensiveness, telomere biology, and quality of life are summarized below.

Hostility and defensiveness. Methodological shortcomings of mindfulness-based stress management programs involve : a) lack of randomized controlled studies b) the use of short-term self-reported measures (e.g., over the last month), which may hinder our understanding of whether an MBI can improve personality traits; c) Randomized controlled trials and other trials have been done in either inmates, cancer patients or adolescents, which limits the generalizability to an older population at risk for CAD, d) absence of studies examining the impact of a MBI on defensiveness.

Telomere biology. Although most of the studies report promising results with regards to specifically altering telomerase activity through mindfulness-based interventions, there are methodological weaknesses and gaps in the literature. For instance a) only three studies (two randomized controlled trials) involving both telomerase and TL have been performed (Duraimani et al., 2015; Innes et al., 2018; Lengacher et al., 2014); b) Most stress reduction interventions on TL and TA have been performed in healthy or cancer patients and survivors (Carlson et al., 2015; Lengacher et al., 2014; Ornish et al., 2013; Schutte & Malouf, 2014) c) Blinding of the research staff and participants at baseline to avoid selection bias has been rare (Carlson et al., 2015; Daubenmier et al., 2012; Ho et al., 2012). Furthermore, blinding of research staff performing bioanalyses on TL or telomerase activity has not been reported; d) Examination of the potential impact of MBSR on TL regulation of older individuals at risk for CAD has never been performed. Only one study in younger and middle-aged women was a randomized controlled trial, the accepted gold standard for effectively testing an intervention effect (Daubenmier et al., 2012). However, it is difficult to interpret whether these increases found in telomerase (though non-significant) would be generalizable to older individuals ; e) Statistically controlling for baseline telomere measures to increase power to detect differences and help to control for initial group differences has not consistently been done (Jacobs et al., 2011; Ornish et al., 2008); f) Studies that have included a follow-up are rare. Only one randomized controlled trial included a follow-up (Lengacher et al., 2014). Adding a follow-up measure is desirable to establish whether an MBI has a meaningful effect on telomere maintenance over time; g) An important issue often overlooked is the potential for change in TL.

As mentioned earlier, on the results of several prospective studies suggests that detectable changes in TL in human beings may not be feasible within a 3-month period but may rather require at least a year to be observed (Ornish et al., 2008). Most studies performed to date have examined TL immediately following the intervention (e.g. 8 weeks after baseline) (Daubenmier et al., 2011; Lengacher et al., 2014). It appears more reasonable to measure telomerase instead of TL over shorter periods of time, as it may be more easily amenable to change over shorter time periods; h) Studies on this topic reporting a common effect size (ES), such as Cohen's d, to allow easy comparison between the studies have been scarce (Carlson et al., 2015; Schutte & Malouff, 2014; Schutte et al., 2020), which make it difficult to compare the effect of MBIs across studies of different sample sizes.

Quality of life. As mentioned earlier, studies have examined MBI's impact on health-related quality of life. However, little is known on whether MBSR can improve a global quality of life based on personal life goals and expectations. Performing a study and in which this measure can include physical health, as well as cognitive functioning (memory, concentration), social/family, couple, leisure, work, housekeeping, affectivity, and spirituality, would be indeed novel and more representative of the World's Health Organization's definition mentioned in a previous section.

1.6.8 Conclusion

Investigations examining the associations between CAD-related personality risk factors and TL or TA are scarce. Very little data currently exists on defensiveness, and the four studies on hostility have yielded mixed findings. The health status of individuals may impact on the results observed, as may other personal characteristics such as sex, but this has not been sufficiently examined. Moreover, there has not been enough research to establish whether a stress reduction intervention such as MBSR is feasible for an at risk-CAD sample, and whether it can improve personality traits, TL regulation, and global quality of life.

1.7 Objectives and Hypotheses

1.7.1 Objectives

The current thesis consists of two separate investigations presented in article format. The overarching goal of this research program is to improve understanding of the potential underlying mechanisms by which psychological traits might contribute to cardiovascular morbidity and mortality (Article 1) and to determine whether such mechanisms are amenable to change via psychosocial intervention (Article 2).

Study 1. A first observational study (Article 1) examined the concurrent associations of two personality traits (hostility and defensiveness) with TL in a sample of 1036 adults with and without cardiovascular disease. The moderating effect of sex and CAD status on these associations was an important focus. A secondary set of analyses was performed in as small sample of healthy individuals to examine if personality traits hostility and defensiveness and TL corroborated findings from an initial study in healthy participants conducted in our laboratory. Whether sex moderated the associations observed was again examined.

Study 2. The second study was of a small "proof of concept" randomized waiting-list controlled pilot study. Initially, it sought to obtain preliminary evidence on the feasibility and acceptability of MBSR for older adults with current or past metabolic syndrome and non-normative autonomic stress responses (Annex A), recruited from Study 1, in preparation for an eventual larger scale study. The objectives specific to this dissertation included investigating whether MBSR may improve self-reported hostility and defensiveness, as well as telomerase activity and TL, and quality of life based on life goals, post-intervention and if these changes were maintained at the two-month follow-up. Moreover, whether the practice of mindfulness at home associated with changes in variables of interest was examined. Direction of effects and effect sizes were of primary interest for the secondary objectives.

1.7.2 Hypotheses

Study 1. We hypothesized that hostility would be associated with TL, though the direction was unclear due to mixed results in the literature. We also hypothesized that defensiveness would be associated with shorter TL given our previous results in healthy individuals. Whether sex or health status would influence the direction of results remained exploratory given paucity of data on the issue. As for the healthy individuals without any disease, exploratory analyses aimed to corroborate our initial study, where lower hostility and greater defensiveness was associated with shorter TL.

Study 2. It was hypothesized that a 9-week MBSR would minimise telomeric loss, and improve telomerase activity, hostility, and quality of life based on life goals. The impact of a MBSR program on defensiveness was exploratory.

CHAPTER II: ARTICLE 1 AND ARTICLE 2

2.1 ARTICLE 1: THE ASSOCIATIONS OF HOSTILITY AND DEFENSIVENESS WITH TELOMERE ARE INFLUENCED BY SEX AND HEALTH STATUS

LES RELATIONS ENTRE L'HOSTILITÉ, L'ATTITUDE DÉFENSIVE ET LA LONGUEUR DES TÉLOMÈRES SONT MODÉRÉES PAR LE SEXE ET LE STATUT DE SANTÉ

ARTICLE PUBLISHED IN *BIOLOGY OF SEX DIFFERENCES*

STARNINO, L., DUPUIS, G., BUSQUE, L., BOURGOIN, V., DUBÉ, M. P., BUSSEUIL, D., & D'ANTONO, B. (2021). THE ASSOCIATIONS OF HOSTILITY AND DEFENSIVENESS WITH TELOMERE LENGTH ARE INFLUENCED BY SEX AND HEALTH STATUS. *BIOLOGY OF SEX DIFFERENCES*, *12*(1), 1-13.

The Associations of Hostility and Defensiveness with Telomere are Influenced by Sex and Health Status

Abbreviated title: Personality and Telomere Length by Sex and Health Status

Louisia Starnino [1,2], Gilles Dupuis [2], Lambert Busque [3], Vincent Bourgoin [3], Marie-Pierre Dubé[1], Bianca D'Antono [1, 2, 5]

1) Research Center, Montreal Heart Institute, Montreal, Canada

2) Department of Psychology, Université du Québec à Montréal, Montreal, Canada

3) Research Center, Hematology Division, Hôpital Maisonneuve-Rosemont, Université de Montréal, Montreal, Canada

4) Department of Medicine, Montreal Heart Institute and Université de Montréal, Montreal, Canada

5) Department of Psychology, Université de Montréal Pavillon Marie-Victorin, Montreal, Canada

Corresponding author: Bianca D'Antono bianca.d.antono@umontreal.ca

Montreal Heart Institute: 5000 Rue Bélanger, Montréal, QC H1T 1C8

Author Contributions: BDA designed the study in collaboration with LB and MPD. BDA, LS, and other personnel of BDA's Heart and Mind research unit in behavioural and complementary medicine executed the study. LS performed the data analyses and prepared the manuscript in collaboration with GD and BDA. LB and VB performed telomere length extraction from blood samples. All authors contributed to the revision of the manuscript.

All authors approved the final version of the manuscript before submission

Funding Information: This study was supported by grants awarded to Dr. D'Antono by the Canadian Institutes of Health Research (CIHR – MOP #111015) and the Montreal Heart Foundation. Louisia Starnino was supported by the Doctoral Training Award issued by the the Fonds de la recherche en santé du Québec (FRSQ). The funding sources had no involvement in this study.

Compliance with Ethical Standards: All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Informed Consent: Informed consent was obtained from all participants included in the study.

Conflict of Interest: Authors have no conflicts of interest to report.

Word count: 4541 (body); 7388 total including references and tables

Abstract

Background: Shorter telomere length (TL) may indicate premature cellular aging and increased risk for disease. While there is substantial evidence for shorter TL in individuals suffering from psychiatric disorders, data is scarce on maladaptive personality traits related to coronary artery disease (CAD). The purpose of this study was to evaluate the association of TL with hostility and defensiveness in individuals with CAD or other non-cardiovascular illnesses, and whether associations were moderated by CAD status and sex.

Methods: 1036 individuals (Mage=65.40 ± 6.73 yrs) with and without CAD completed the Marlowe-Crowne Social Desirability Scale and the Cook-Medley Hostility Scale. Relative TL was measured via quantitative polymerase chain reaction of total genomic DNA samples. Analyses involved hierarchical regressions on TL, performed separately for hostility and defensiveness, controlling for pertinent sociodemographic, behavioural, and medical risk factors. Separate analyses were performed on 25 healthy participants.

Results: A Hostility by Sex interaction emerged (β=-.08, p=.006) in the patient groups, where greater hostility was associated with shorter TL in women only (p<.01). A Defensiveness by CAD status interaction (β=-.06, p=.049) revealed longer TL in more defensive CAD patients only (p=.06). In healthy men, shorter TL were observed in those with greater defensiveness (ß=.52, p=.006) but lower hostility (ß=-.43, p=.049).

Conclusion: Hostility and defensiveness are differentially associated with TL as a function of sex and health status. The implication of these results for health remain to be determined, but propose an additional pathway through which the effect of maladaptive personality traits may contribute to CV and other disease.

Key Words: telomere length, hostility, defensiveness, cardiovascular disease, sex and age

List of Acronyms: TL= Telomere Length, CAD= Coronary Artery Disease, Non-CVD=participants with non cardiovascular illness; CMHo-T=39-item Cook-Medley Hostility Inventory; MCSD=14-item Marlowe-Crowne Social Desirability Scale; CI= confidence interval; BMI= Body Mass Index; qPCR= quantitative polymerase chain reaction

Introduction

Hostility is a stable personality trait accompanied by frequent feelings of anger, aggressive behaviour, and/or the tendency to devalue or to be cynical of others (Smith et al., 2004). It has been established as a robust risk factor for the development of coronary artery disease (CAD) and premature mortality (Bunde & Suls, 2006; Chida & Steptoe, 2009), as well as with all-cause mortality (Klabbers et al., 2013). Defensiveness, a personality trait characterized by the tendency to present oneself in a favorable manner (Crowne & Marlowe, 1960), has similarly been associated with an increased risk for CAD and mortality (Denollet et al., 2008; Mund & Mitte, 2012). In defensiveness, individuals deny, avoid, or repress personal information (e.g., physical symptoms, traits, behaviours, negative affect) perceived as non-desirable in order to protect one's vulnerable self-esteem and/or to maintain socials bonds (Garofalo et al., 2017; Van't Riet & Ruiter, 2013).

The biological mechanisms responsible for the ill effects of hostility and defensiveness remain to this day poorly understood. It is hypothesized, however, to at least partly reflect the sustained or cumulative impact of alterations in various intermediary risk factors for CAD (e.g., physiological reactivity to stress, inflammation, blood pressure, and other metabolic parameters) observed in more hostile or defensive individuals (D'Antono et al., 2013; Demarble et al., 2014; Guerrero Rodriguez et al., 2018; Lévesque et al., 2009, 2010; Murdock et al., 2017; Sahoo et al., 2018). Telomere regulation may also be impacted. Telomeres are specialized DNA-protein repetitive sequences that cap eukaryotic chromosome ends during cellular division in order to prevent end-to-end recombination, deterioration, or fusion with neighbouring chromosomes, and as such play an integral role in preventing the loss of genetic data (Lin et al., 2012). Telomere length (TL) shortens with every cell division, reflecting the cellular aging of organisms. Shortening depends on several factors, such as the rate of cellular division and levels of telomerase, a ribonucleoprotein reverse transcriptase enzyme that adds telomeric DNA (Srinivas et al., 2020).

CAD patients have significantly shorter leukocyte TL than their age-matched non-CVD counterparts (Brouillette et al., 2003). While conflicting data exist, shorter TL has been associated with increased incidence for CAD events, CAD progression and increased mortality from CAD (Bhattacharyya et al., 2017; Goglin et al., 2016; Haycock et al., 2014). Individuals at risk for CAD by virtue of metabolic dysregulations (Révész et al., 2018), hypertension (Tellechea & Pirolla, 2017), diabetes (Wang et al., 2016), and smoking (Astuti et al., 2017; Lin et al., 2012), have also been shown to possess shorter TL. As such, TL may be a potential biomarker for CVD risk and prognosis (Bhattacharyya et al., 2017).

While significantly shorter TL have been found in stressed ($r=-0.06$) (Mathur et al., 2016) or depressed ($r=-0.21$) (Lin et al., 2016) individuals in comparison with psychologically healthier individuals, research examining stable personality traits has been scarce (Brydon et al., 2012; Starnino et al., 2016; Watkins et al., 2016; Zalli et al., 2014), and has led to conflicting results. For example, in a moderate-sized cross-sectional study of older women and men without CVD, Brydon and colleagues (2012) found that men (but not women) with greater cynical hostility had shorter TL compared to those less hostile ($\beta=-0.25$, $p=0.001$), independently of age, grade of employment, body mass index (BMI), and waist circumference. In a sample of predominantly male U.S. military verterans suffering from various chronic medical conditions, those with shorter TL (based on relative TL <1), reported greater levels of hostility compared to those with longer TL (Watkins et al., 2016). In contrast, we recently reported that greater hostility (and increases in hostility over a 3-year period) was associated with longer (not shorter) TL in healthy men and women (Starnino et al., 2016). At this time, it remains unclear whether hostility is reliably associated with TL. Only one study examined whether TL differs as a function of defensiveness and found greater defensiveness was associated with shorter TL in healthy men and women (Starnino et al., 2016).

While data regarding potential sex differences in the relations between hostility, defensiveness and TL is scarce and mixed, men consistently show shorter TL (Dalgard et al., 2015; Gardner et al., 2014) and are more likely to harbor and express hostile attitudes and behaviour compared to women (Denson et al., 2018). They may also be at greater risk for cardiovascular events from hostility compared to women (Chida & Steptoe, 2009). On the other hand, differential biological mechanisms and socialization of women versus men may contribute to greater concern for interpersonal relationships (Barnett et al., 2014; Christov-Moore et al., 2014) and propensity to present a favorable impression in women versus men (Chung & Monroe, 2003) and hence to differential relations between defensiveness and TL in men versus women. In support of this, we have previously reported that in healthy individuals aged 20-64 years, higher levels of defensiveness were associated with greater cardiovascular stress reactivity (Lévesque et al., 2010) and a worse metabolic profile (Lévesque et al., 2009) in women but not men.

In addition, while differences in TL have been observed as a function of CAD status, it remains to be explored whether the relation between personality and TL also differs as a function of the health status of individuals.

The current study sought to confirm whether TL were associated with hostility and defensiveness in a large sample of older men and women with CAD, other non CVD illness, or a healthy profile, and whether these relations were influenced by sex and health status.

It was hypothesized that hostility and defensiveness would be associated with TL. However, given the limited and mixed findings for hostility and absence of studies among patient populations, no hypotheses were elaborated regarding the direction or magnitude of the relations nor any influence of sex or health status on the results.

Methods

Description of Cohort and Sample Selection

This study is part of an ongoing prospective research project (BEL-AGE) on psychological burden and premature aging. It was approved by the ethics committee of the Montreal Heart Institute. Recruitment for this study began September 2012 and finished May 2017.

At the time of preparing this manuscript, data were available for 1121 men (n=719) and women (n=402), 34-76 years of age (Mage=65.1±7.07). Participants were recruited from the André and France Desmarais Hospital Cohort of the Montreal Heart Institute. Any person working at or attending the hospital for any reason were eligible for the Montreal Heart Institute Cohort (Gentile et al., 2019).

Eligibility criteria for BEL-AGE were determined as follows: at entry in the MHI Cohort, (a) aged between 30 and 70 years (for reasons of feasibility of recruitment and follow-up), (b) living in the greater Montreal area, (c) speaks French or English, (d) no previous or current diagnosis of major cognitive impairment or serious psychological disorders (e.g. bipolar disorder, schizophrenia, delirium, or dementia as reported by patient and/or medical files) that would prevent understanding or participating in all aspects of the study, (e) no previous or current diagnosis of other major life-threatening diseases (e.g., Creutzfeldt-Jakob disease, amyotrophic lateral sclerosis, AIDS, cancer) (f) not currently pregnant or breast feeding (g) no family member (including spouse) already participating or scheduled to participate in the study. Skin cancer (n = 60) was not excluded given its high prevalence and benign course when diagnosed early. Presence of CAD was defined by the experience of a previous myocardial infarction, coronary artery bypass, coronary angioplasty, or stenosis more than 50% on an angiography. Non-CVD status was defined by the absence of CAD, angina, arrhythmia, congenital heart disease, heart failure, cardiomyopathy, and stroke. To ensure they met these criteria, individuals were interviewed by phone before being invited to participate and a medical chart review was performed to ascertain group (CAD vs. non-CVD) membership. The types of conditions experienced by the non-CVD illness group was diverse (e.g., arthritis, diabetes, hypertension, gastrointestinal diseases, hypercholesterolemia, asthma, etc.). While we had initally sought to recruit a larger sample of older individuals with no significant health issue, we were unable to secure a significant number of healthy participants within the population from which we recruited despite extended recruitment. Only 25 individuals suffered from no notable medical condition (very healthy group).

Data for the article were obtained during the BEL-AGE evaluation performed 4.88 (±0.76) years after participants' entry into the MHI cohort.

Procedure

Participants were scheduled for an interview between 8:00 and 10:00 in the morning on a weekday to control for circadian rhythm. They were asked to abstain from drinking (with the exception of water), smoking, and exercise for 12 hours before their scheduled appointment. They were also asked to refrain from the use of drugs or alcohol for the 24 hours preceding their appointment. Prescribed medication was permitted. Participants were sent home and their appointment rescheduled if they did not adhere to these instructions, or if they were presenting with symptoms of flu. Research assistants were trained to maintain a neutral tone and expression during testing. Once participants provided written consent, anthropomorphic data (weight, height, and waist circumference) and 35 mL of blood were obtained. Participants completed sociodemographic, health behavior, and psychological questionnaires.

Outcome Measures

Hostility. The short form of the Cook–Medley Hostility Inventory (CMHo-T) (Cook & Medley, 1954), consisting of 39 true-or false items was used to measure cynicism, hostile affect and aggressive responding (Barefoot et al., 1991) [41]. The short-form's internal consistency (α=0.85) (Boyle et al., 2004), and test-retest reliability (r=0.74) are both good (Han et al., 1995). In the current sample, the internal consistency was 0.81 while the 5-yr test-retest reliability was 0.84. (Refer to Appendix G)

Defensiveness. The short form of The Marlowe-Crowne Social Desirability scale (MCSD) (Crowne & Marlowe, 1960; Loo et al., 2000), consisting of 14 true or false items, was used to assess whether respondents are answering in a culturally sanctioned and desirable manner. The items present behaviors that are desirable but infrequent (e.g., ‘‘ I’m always willing to admit it when I make a mistake’’) and behaviors that are undesirable but frequent (e.g., ‘‘I like to gossip at times’’). The short- form MCSD has been found to have adequate psychometric properties, with internal consistency estimates of 0.62 - 0.77 (Loo et al., 2000) and a test-retest correlation of 0.74 (Li et al., 1985). In the current sample, the internal consistency was 0.68 and and the test-retest reliability was 0.78. The MCSD scale has been shown to be a valid measure of the defensiveness construct (Crowne & Marlow, 1964; Pauls & Stemmler, 2003) and has been frequently used to assess defensiveness in the area of cardiovascular health psychology. (Refer to Appendix G).

Telomere length. DNA was extracted from peripheral blood leukocytes using standard methods, and TL was measured by quantitative polymerase chain reaction (qPCR) using the modified method [48] of the protocol described by Cawthon (Cawthon, 2002). The DNA extraction was done automatically on the BioRobot M48 system (Qiagen). The buffy coat samples are thawed at room temperature. For each sample, 55 µL of cells are mixed with 95 µL of RPMI-1640 (Invitrogen, # 11875-093). Extraction on the BioRobot M48 is carried out using the MagAttract DNA Blood M48 kit (Qiagen, # 951356). DNA is diluted in 200 µL of RNase-free water. DNA is stored at -80°C and quantified by UV spectrophotometer (Tecan, Infinite M1000 Pro) by measuring the specific UV absorbance of nucleic acids at 260 nm. This modified method for TL (Cawthon et al., 2002; Epel et al., 2004) is based on determining the number of telomeric repeat sequence (T) on the number of copies of a single gene (RPLP0, 60S acidic ribosomal protein P0) (S). A T/S ratio was calculated for each sample of DNA tested. A relative ratio was obtained by comparing the ratio T/S of a sample to the ratio T/S of a reference DNA sample (obtained from a single individual and used to generate the standard curves) giving a value T/S of 1. Therefore, the relative ratio of a sample represents the number of copies of telomeres relative to the reference sample. For each DNA sample, T and S qPCR SYBR® green reactions are assembled with the epMotion 5075 TMX (Eppendorf) automated pipetting systems. Each 20 µL reaction contained : 7.5 ng of DNA, 10 µL of QuantiFast SYBR® Green PCR Master Mix (Qiagen, # 204057), 450 nM of primers Tel1b (CGGTTTGTTTGGGTTTGGGTTTGGGTTTGGGTTTGGGTT) and Tel2b (GGCTTGCCTTACCCTTACCCTTACCCTTACCCTTACCCT) for the T amplification or 300 nM of the primer 36B4u (CAGCAAGTGGGAAGGTGTAATCC) and 500 nM of the primer 36B4d (CCCATTCTATCATCAACGGGTACAA) for the S amplification. Serial dilutions of the reference DNA are made (25 to 1.562 ng/µL) for each 96-well plate and the values obtained were used to establish a standard curve in order to calculate the T and S values of the tested samples. All qPCR were performed on the ViiA™7 real-time PCR system (Applied Biosystems) and with the QuantStudio analysis software (Applied Biosystems). The thermal amplification profile of telomeres (T) is described as follows: 5 min at 95 °C, followed by 25 cycles of 95 °C for 10 sec and 56 °C for 1 min. The thermal amplification profile of the single copy gene (S) is described as follows: 5 min at 95 °C followed by 40 cycles of 95 °C for 10 sec and 60 °C for 40 sec. All samples were measured in triplicate, and their mean was used for analyses.

Sociodemographic and Health Confounders. Sociodemographic (sex, age, ethnicity, years of schooling, marital status, personal and family income), and personal and family medical history were collected via interview. Data on behavioral risk factors (tobacco, alcohol, caffeine consumption, diet, and physical activity), weight, height, waist circumference were also obtained.

Inflammatory and Metabolic Confounders. The blood samples were frozen (−80°C) and then assayed in batch. C-reactive protein (CRP) was measured from plasma using the Siemens CardioPhase hsCRP assay on the BN ProSpec Nephelometer (Siemens Healthcare Diagnostics Products GmbH, Marburd, Germany). The minimal detectable hsCRP concentration was 0.18 mg/L. Lipids and glucose were assayed using respective reagent Flex on the multianalyzer Dimension RxL Max (Dade Behring Diagnostics, Marburg, Germany) with heparinized plasma. To measure waist circumference (WC), the participant’s waistline was exposed and the bottom of a measuring tape was aligned with the top of the hip bone and stretched across the midsection over the navel (Rudolf et al., 2007). Blood pressure was obtained during a 5-minute continuous reading at rest using a Finometer (Finapres Finometer, Amsterdam, the Netherlands) and analyzed offline in LabChart (ADInstruments, Oxford, UK). The mean arterial pressure was used for statistical analyses.

Statistical Analyses

Analyses were performed on participants with complete sociodemographic, behavioural, telomere, biochemical, and psychological data (n=1 061).

Preliminary Analyses

No significant socio-demographic, psychological or physiological differences were observed in participants with (n=1061) or without (n=58) complete data.TL was positively skewed and a natural logarithm transformation was applied to ensure normal distribution.

Potential covariates were based on the TL literature (Benetos et al., 2004), as well as on the results of bivariate correlations with TL. Only covariates showing an association $p < 0.10$ with TL in our sample were retained. These included age, sex, employment status, waist circumference, number of cigarettes per day, hours of exercise/weekly, alcoholic beverages/weekly, mean arterial pressure, total cholesterol, glucose, as well as history of hypertension, diabetes, and/or dyslipidemia. To identify any differences between CAD and Non-CVD groups, independent samples T-Test (for continuous variables in unequal sample sizes) and Chi-squares (for categorical variables) were used on demographic measures. Welch's ANOVAs were performed to examine whether TL, CMHo-t, and MCSD differed as a function of CAD status and sex of participants. Effect sizes (Cohen's d) were calculated via a statistical tool by Lenhard & Lenhard (2016).

Multivariate associations of personality with TL and moderating influences of CAD status and/or sex among the patient groups

Relationships between psychological traits and TL in the patient groups were analyzed using hierarchical linear regression analyses, performed separately for hostility and defensiveness. Covariates and the potential moderators, sex and CAD status were forced into Block 1. The psychological trait was entered into Block 2, while its possible two- and three way interactions with CAD status and/or sex were entered stepwise in Block 3. Interactions were formed from centred variables.

Data were analyzed using the IBM SPSS Statistics 24.0 software (IBM Corporation, Somers, N.Y., USA) and moderation analyses were performed using the computational tool PROCESS version 3.4 (Hayes, 2017). A two-sided p-value < 0.05 was considered statistically significant for main effects. However, given reduced power to detect significant interactions, the latter were explored when they met a p-value < 0.10 to minimize type II error (Rosnow & Rosenthal, 1989; Winer, 1962). Simple slope analyses were performed on values $\pm$ 1 SD for hostility and defensiveness.

Analyses in healthy individuals

Given the much smaller sample size of the Healthy group and their vastly differing characteristics, analyses were performed separately for this group. The standardized residual of TL (controlling for age, BMI, employment status, and years of schooling) was used as the dependant variable. Sex, personality trait, and their interaction was included in each regression.

Results

Table 1 presents participant characteristics. Individuals with CAD had significantly more sociodemographic, behavioral, and medical risk factors for CVD than their non-CVD counterparts. Men showed a worse CV profile than women ($p<.001$), but did not differ on other demographic variables. In the Non-CVD illness group only, men were more likely to have a history of HTA, hypercholesterolemia, and diabetes compared to women (all p's$<.001$).

TL was negatively associated with age in all three groups (CAD: $r=-.22$, $p<.001$; Non-CVD illness: $r=-.29$, $p<.001$; Healthy: $r=-.43$, $p<.05$).

(INSERT TABLE 1 HERE)

Group differences in TL, hostility, and defensiveness

Individuals with CAD had shorter TL as compared with individuals with non-CV illness ($F(1,898.16)= 24.83$, $p<.001$, $d=.32$). A Sex main effect ($F(1, 685.40)=15.93$, $p<.001$, $d= .27$) indicated shorter TL in men compared to women. As for hostility, main effects of CAD Status emerged ($F(1, 944.96)= 9.02$, $p<.05$, $d=.19$), with greater hostility reported by individuals with CAD as compared with individuals with non-CVD illness. No group differences emerged for defensiveness. Among the healthy subsample ($n=25$), one–way ANOVAs revealed no statistically significant sex difference in TL, hostility and defensiveness (See Table 2 for Means).

Bivariate correlations between TL, hostility, and defensiveness

Table 2 provides the sex-specific and overall Pearson correlations between TL, hostility and defensiveness for CAD, non-CVD and healthy groups separately. Greater hostility was associated with shorter TL across all groups of women, though statistically significant only in the non-CVD group. The effect sizes of the correlations were within the small-to-medium range for all women, suggesting that lack of significance in the other two female groups was a function of their smaller sample size, as correlations were actually stronger than that of the non-CVD group. In healthy men, TL were longer among more hostile individuals whereas they were shorter among those who were more defensive.

Multivariate associations of personality with TL and moderating influences of CAD status and/or sex among the patient groups

Refer to Table 3 and Figure 1 for details.

Hostility. A significant Hostility by Sex interaction emerged among the patient groups when controlling for important demographic, medical, and metabolic covariates. Simple slope analyses indicated that greater hostility was associated with shorter TL in women (b=-.001, t=-2.82, p=.005), but not in men (b=.001, t=.78, p=.43).

Defensiveness. CAD Status moderated the relation between Defensiveness and TL. More specifically, greater defensiveness tended to be associated with longer TL among individuals with CAD (b=.001, t=1.93, p=.05), but not among patients with non-CV illnesses (b=-.001, t=-.93, p=.35).

(INSERT TABLE 3 and FIGURE 1 HERE)

Analyses in healthy individuals

Refer to Table 4 and Figure 1 for details.

Hostility. The Sex by Hostility interaction was significant. Greater hostility was associated with longer TL in healthy men (b=.09, t=2.37, p=.028).

Defensiveness. The Sex by Defensiveness interaction was significant. Greater defensiveness was associated with shorter TL in heatlhy men (b=-.30, t=-3.56, p=.002).

(INSERT TABLE 4 HERE)

Discussion

This cross-sectional study examined the relation between TL and two personality traits, and whether these associations differed as a function of CAD status and/or sex, controlling for sociodemographic, behavioural, and medical risk factors. Sex and health status were found to moderate the relationship between hostility, defensiveness and TL. More specifically, greater hostility was associated with significantly shorter TL in women (independent of health status) but with longer TL among healthy men, while greater defensiveness was associated with longer TL in individuals with CAD, but with shorter TL in healthy men.

The sex differential observed in the relation between hostility and TL was somewhat surprising. Indeed, we found robust evidence for shorter TL in more hostile as compared to less hostile women but this was not observed in the men. In contrast, two previous studies had observed such results in men more particularly. One sample included predominently male U.S. veterans with various medical conditions (including heart disease) (Watkins et al., 2016), while the other was comprised of a similar number of relatively healthy older British men and women (Brydon et al., 2012). Conversely and consistent with our current findings in the healthy men, we had previously reported a positive association between hostility (and increases in hostility over time) and TL in a sample of healthy adult men and women (Starnino et al., 2016). The reasons for these discrepant results across studies may relate in part to methodological differences. For example, our previous (Starnino et al., 2016) and current sample were more heterogeneous compared to that of the Whitehall-II investigation (Brydon et al., 2012). This reduced variability in the Whitehall-II investigation may explain why they showed no association between TL and chronological age as opposed to both our studies which showed the expected negative association. Although our current sample was similar in age to that of Whitehall-II investigation, it suffered from a wide range of health issues, including CAD. In Watkins' study, TL was isolated from saliva, which is more sensitive to environmental confounds as compared to blood (Watkins et al., 2016). Furthermore, the six items of the SCL-90-R used in Watkin's study encompassed only hostility's affective and behavioral symptoms (aggressive urges and impulses) over the last month, as opposed to its trait component as depicted in the Cook-Medley's Hostility Scale. At this time, conclusions regarding the associations of hostility with TL remain unclear, given mixed results from one sample to another. Though men are more commonly known to be at risk for adverse effects of trait hostility on health, there has been growing evidence of its impact on illness (CAD) severity in women (Pimple et al., 2019; Shah et al., 2014), and our robust findings contribute to the body of knowledge on the potential impact of trait hostility on women's health in particular.

Health status influenced not only the relation between TL and age, but also the relation between TL and defensiveness in the current study. Greater defensiveness was associated with longer TL amongst individuals with CAD but not among those with other non-CVD illnesses. Moreover, it was related to shorter TL in healthy men. We had previously reported shorter TL among men and women who were more defensive in a study involving healthy participants. Findings by Schoormans and colleagues (2018) may provide additional insight into the mixed results regarding TL and personality traits. They found that while those with Type D personality (a construct related to defensiveness) had shorter TL at study onset, they were also less likely to show TL shortening over a period of six years compared to those without Type D. Protection from TL loss over time may have occurred via activation of telomerase (Geserick & Blasco, 2006). Relatedly, initial TL has been shown to be the greatest predictor of TL change over time, with relatively long telomeres tending to shorten over time, while relatively short telomeres tending to lengthen over time, possibly due to these reparative mechanisms (Epel et al., 2009). Given the shorter TL of patients with CAD, a similar process of telomerase activation may have occurred, in essence altering the observed relations between TL and defensiveness in this study. Whether similar processes influenced the longer telomeres observed among the more hostile healthy men in this and our previous study (Starnino et al., 2016) remain unclear.

Different mechanisms have been suggested to underly the negative association of psychological risk factors with TL, including alterations in health behaviours, as well as metabolic and inflammatory processes. Importantly, we and others have previously shown that hostility and defensiveness are associated (particularly in women) with disruptions in metabolic and inflammatory activity, with increased oxidative DNA damage (D’Antono et al., 2013; Demarble et al., 2014; Elovainio et al., 2011; Guerrero Rodiguez, 2018; Irie et al., 2001; Lévesque et al., 2009, 2010), and poorer health habits such as physical inactivity and smoking (Révész et al., 2015). Although these physiological processes and health behaviours mentioned have been associated with shorter TL (Astuti et al., 2016; Révész et al., 2015), controlling for these potential mediating or confounding factors did not alter the pattern of results in the current investigation.

Strengths and Limitations

While the variance explained by all variables, except age, was low, the findings regarding the personality traits were robust and independent of a large number of behavioural sociodemographic, and medical variables. Moreover, controlling for symptoms of depression, anxiety, and stress did not alter the results (data not shown). The clinical significance of shorter TL in women with greater hostility compared to their low hostile counterparts in the current study remains to be evaluated. However, converting T/S ratio to base pairs (bp) indicates a 133 bp difference, suggestive of a 1-4 year biological difference (based on telomere attrition of 30-100 base pairs per year) (Aviv et al., 2006; Muezzinler et al., 2013; Harris et al., 2016).

Additional strengths of this study included a large sample size, use of validated questionnaires, and purposeful recruitment of as large a number of women as possible to examine sex differences. Findings differed significantly between men and women, which reinforces the importance of evaluating sex differences in this field of research. CAD status was also strictly defined and verified via medical files. Moreover, qPCR analyses were carefully controlled and assayed in batch in triplicate, reducing potential measurement errors.

Nonetheless, a few factors limit the conclusions that can be drawn from the current results. The cross-sectional design of our study limits any conclusions regarding causality.

Furthermore, given that hostility and defensiveness increase risk for premature mortality, those most susceptible to the effects of these personality traits may have already passed away, contributing to our unexpected results (e.g., greater defensiveness associated with longer TL in CAD participants). Moreover, the sample consisted of mostly Francophone Canadian Caucasians which may limit the generalizability of our findings to other populations. Indeed, there is evidence for differential patterns of association of TL with biological parameters (such as blood cell count) as a function of geographical location (De Meye et al., 2008; Mollica et al., 2009), that may reflect genetic differences (Kim et al., 2012), as well as differences in life exposures, access to healthcare, and/or coping resources (Gerominus et al., 2015). Furthermore, recent data suggests TL differs as a function of blood leukocyte composition, with longer TL observed in blood samples with higher proportions of CD8+ T cells and B cells (Kresovich et alk 2020). Notably, blood leukocyte composition changes from childhood to adulthood, and differs as a function of sex and health status (Aviv et al., 2006; Gomez-Sanchez et al., 2015; Kolbus et al., 2013; Lin et al., 2015), which may contribute to some of the unexpected findings observed here and in previous investigations. Future research examining TL should ideally control for potential leukocyte cell subtype differences. Finally, given the small sample size of the healthy group, it is possible that results concerning them may reflect Type 1 errors and are likely overfit. This, however, appears unlikely in light of the effect sizes observed in the correlations, the p values of the interactions, and the fact that results replicated those of a previous study in a healthy sample. Nonetheless, any results concerning them require replication in a larger sample.

Perspectives and Significance

Hostility and defensiveness were associated with altered TL among middle aged and older individuals though the direction of effect appears to depend on their sex and/or health status. Though the clinical relevance of these findings remains to be established, these traits reflect a relatively enduring pattern of intrapersonal and interpersonal conflict, which may not only be detrimental to one’s mental health and quality of life, but also to their cellular aging processes. Moreover, whether psychological interventions targeting hostility and/or defensiveness can protect from premature aging remains to be properly evaluated, though small-scale studies suggest that mindfulness, for example, may improve TL and the telomerase activity (Schutte & Malouf, 2014).

Acknowledgements

Thank you to the Canadian Institutes of Health Research (CIHR – MOP #111015) for their generous support and to colleagues of the Heart and Mind Research Unit in Behavioral and Complementary Medicine for their contributions to testing and data preparation. Finally, many thanks to the personnel and participants of the André and France Desmarais Hospital Cohort of the Montreal Heart Institute who made this research possible.

References

Astuti, Y., Wardhana, A., Watkins, J., & Wulaningsih, W. (2017). Cigarette smoking and telomere length: a systematic review of 84 studies and meta-analysis. *Environmental research*, *158*, 480-489. https://doi.org/10.1016/j.envres.2017.06.038

Aviv, A., Valdes, A. M., & Spector, T. D. (2006). Human telomere biology: pitfalls of moving from the laboratory to epidemiology. *International journal of epidemiology*, *35*(6), 1424-1429.https://doi.org/10.1093/ije/dyl169

Barefoot, J. C., Peterson, B. L., Dahlstrom, W. G., Siegler, I. C., Anderson, N. B., & Williams Jr, R. B. (1991). Hostility patterns and health implications: correlates of Cook-Medley Hostility Scale scores in a national survey. *Health Psychology*, *10*(1), 18. https://doi.org/10.1037/0278-6133.10.1.18

Barnett, R. C., & Baruch, G. K. (1987). Social roles, gender, and psychological distress.

Benetos, A., Gardner, J. P., Zureik, M., Labat, C., Xiaobin, L., Adamopoulos, C., & Aviv, A. (2004). Short telomeres are associated with increased carotid atherosclerosis in hypertensive subjects. *Hypertension*, *43*(2), 182-185.https://doi.org/10.1161/01.HYP.0000113081.42868.f4

Bhattacharyya, J., Mihara, K., Bhattacharjee, D., & Mukherjee, M. (2017). Telomere length as a potential biomarker of coronary artery disease. *The Indian journal of medical research*, *145*(6), 730.https://doi.org/10.4103/0971-5916.216974

Boyle, S. H., Williams, R. B., Mark, D. B., Brummett, B. H., Siegler, I. C., Helms, M. J., & Barefoot, J. C. (2004). Hostility as a predictor of survival in patients with coronary artery disease. *Psychosomatic medicine*, *66*(5), 629-632.https://doi.org/10.1097/01.psy.0000138122.93942.4a

Brouilette, S., Singh, R. K., Thompson, J. R., Goodall, A. H., & Samani, N. J. (2003). White cell telomere length and risk of premature myocardial infarction. *Arteriosclerosis, thrombosis, and vascular biology*, *23*(5), 842-846.https://doi.org/10.1161/01.ATV.0000067426.96344.32

Brydon, L., Lin, J., Butcher, L., Hamer, M., Erusalimsky, J. D., Blackburn, E. H., & Steptoe, A. (2012). Hostility and cellular aging in men from the Whitehall II cohort. *Biological psychiatry*, *71*(9), 767-773.https://doi.org/10.1016/j.biopsych.2011.08.020

Bunde, J., & Suls, J. (2006). A quantitative analysis of the relationship between the Cook-Medley Hostility Scale and traditional coronary artery disease risk factors. *Health Psychology*, *25*(4), 493. https://doi.org/10.1037/0278-6133.25.4.493

Cawthon, R. M. (2002). Telomere measurement by quantitative PCR. *Nucleic acids research*, *30*(10), e47-e47.https://doi.org/10.1093/nar/30.10.e47

Chida, Y., & Steptoe, A. (2009). The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. *Journal of the American college of cardiology*, *53*(11), 936-946. https://doi.org/10.1016/j.jacc.2008.11.044

Christov-Moore, L., Simpson, E. A., Coudé, G., Grigaityte, K., Iacoboni, M., & Ferrari, P. F. (2014). Empathy: Gender effects in brain and behavior. *Neuroscience & biobehavioral reviews*, *46*, 604-627.https://doi.org/10.1016/j.neubiorev.2014.09.001

Chung, J., & Monroe, G. S. (2003). Exploring social desirability bias. *Journal of Business Ethics*, *44*(4), 291-302.https://doi.org/10.1023/A:1023648703356

Cook, W. W., & Medley, D. M. (1954). Proposed hostility and pharisaic-virtue scales for the MMPI. *Journal of Applied psychology*, *38*(6), 414.https://doi.org/10.1037/h0060667

Crowne, D. P., & Marlowe, D. (1960). A new scale of social desirability independent of psychopathology. *Journal of consulting psychology*, *24*(4), 349.https://doi.org/10.1037/h0047358

Crowne, D. P., Crowne, D. P., & Marlowe, D. (1964). *The approval motive: Studies in evaluative dependence*. New York: Wiley.

D'Antono, B., Moskowitz, D. S., & Nigam, A. (2013). The metabolic costs of hostility in healthy adult men and women: cross-sectional and prospective analyses. *Journal of psychosomatic research*, *75*(3), 262-269. https://doi.org/10.1016/j.jpsychores.2013.05.010

Dalgård, C., Benetos, A., Verhulst, S., Labat, C., Kark, J. D., Christensen, K., & Aviv, A. (2015). Leukocyte telomere length dynamics in women and men: menopause vs age effects. *International journal of epidemiology*, *44*(5), 1688-1695.https://doi.org/10.1093/ije/dyv165

De Meyer, T., De Buyzere, M. L., Langlois, M., Rietzschel, E. R., Cassiman, P., De Bacquer, D., & Asklepios Investigators. (2008). Lower red blood cell counts in middle-aged subjects with shorter peripheral blood leukocyte telomere length. *Aging Cell*, *7*(5), 700-705.https://doi.org/10.1111/j.1474-9726.2008.00419.x

Demarble, J. B., Moskowitz, D. S., Tardif, J. C., & D'Antono, B. (2014). The relation between hostility and concurrent levels of inflammation is sex, age, and measure dependent. *Journal of psychosomatic research*, *76*(5), 384-393. https://doi.org/10.1016/j.jpsychores.2014.02.010

Denollet, J., Pedersen, S. S., Daemen, J., De Jaegere, P., Serruys, P. W., & Van Domburg, R. T. (2008). Reduced positive affect (anhedonia) predicts major clinical events following implantation of coronary-artery stents. *Journal of internal medicine*, *263*(2), 203-211. https://doi.org/10.1111/j.1365-2796.2007.01870.x

Denson, T. F., O'Dean, S. M., Blake, K. R., & Beames, J. R. (2018). Aggression in women: behavior, brain and hormones. *Frontiers in Behavioral Neuroscience*, 81.https://doi.org/10.3389/fnbeh.2018.00081

Elovainio, M., Merjonen, P., Pulkki-Råback, L., Kivimäki, M., Jokela, M., Mattson, N., & Keltikangas-Järvinen, L. (2011). Hostility, metabolic syndrome, inflammation and cardiac control in young adults: The Young Finns Study. *Biological psychology*, *87*(2), 234-240.https://doi.org/10.1016/j.biopsycho.2011.03.002

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. *Proceedings of the National Academy of Sciences*, *101*(49), 17312-17315.https://doi.org/10.1073/pnas.0407162101

Epel, E. S., Merkin, S. S., Cawthon, R., Blackburn, E. H., Adler, N. E., Pletcher, M. J., & Seeman, T. E. (2009). The rate of leukocyte telomere shortening predicts mortality from cardiovascular disease in elderly men. *Aging (Albany NY)*, *1*(1), 81.https://doi.org/10.18632/aging.100007

Gardner, M., Bann, D., Wiley, L., Cooper, R., Hardy, R., Nitsch, D., & Halcyon Study Team. (2014). Gender and telomere length: systematic review and meta-analysis. *Experimental gerontology*, *51*, 15-27.https://doi.org/10.1016/j.exger.2013.12.004

Garofalo, C., Velotti, P., Zavattini, G. C., & Kosson, D. S. (2017). Emotion dysregulation and interpersonal problems: the role of defensiveness. *Personality and Individual Differences*, *119*, 96-105. https://doi.org/10.1016/j.paid.2017.07.007

Gentile, C., Ditto, B., Deschamps, A., & D'Antono, B. (2019). Parasympathetic response patterns are associated with metabolic syndrome among older women but not men. *Annals of Behavioral Medicine*, *53*(6), 515-526.https://doi.org/10.1093/abm/kay063

Geronimus, A. T., Pearson, J. A., Linnenbringer, E., Schulz, A. J., Reyes, A. G., Epel, E. S., & Blackburn, E. H. (2015). Race-ethnicity, poverty, urban stressors, and telomere length in a Detroit community-based sample. *Journal of health and social behavior*, *56*(2), 199-224. https://doi.org/10.1177/0022146515582100

Geserick, C., & Blasco, M. A. (2006). Novel roles for telomerase in aging. *Mechanisms of ageing and development*, *127*(6), 579-583.https://doi.org/10.1016/j.mad.2006.01.017

Goglin, S. E., Farzaneh-Far, R., Epel, E. S., Lin, J., Blackburn, E. H., & Whooley, M. A. (2016). Change in leukocyte telomere length predicts mortality in patients with stable coronary heart disease from the heart and soul study. *PloS one*, *11*(10), e0160748.https://doi.org/10.1371/journal.pone.016074

Gomez-Sanchez, L., Garcia-Ortiz, L., Recio-Rodriguez, J. I., Patino-Alonso, M. C., Agudo-Conde, C., Rigo, F.(2015). Leukocyte subtype counts and its association with vascular structure and function in adults with intermediate cardiovascular risk. MARK study. *PLoS One*, *10*(4), e0119963. https://doi.org/10.1371/journal.pone.0119963

Guerrero Rodríguez, C., Palmero Cantero, F., & Gómez-Íñiguez, C. (2018). Blood pressure responses of defensive hostile women when facing a real stress task. *Psychology & Health*, *33*(8), 978-994.https://doi.org/10.1080/08870446.2018.1449952

Han, K., Weed, N. C., Calhoun, R. F., & Butcher, J. N. (1995). Psychometric characteristics of the MMPI-2 Cook-Medley Hostility scale. *Journal of Personality Assessment*, *65*(3), 567-585.https://doi.org/10.1207/s15327752jpa6503_15

Harris, S. E., Marioni, R. E., Martin-Ruiz, C., Pattie, A., Gow, A. J., Cox, S. R.,& Deary, I. J. (2016). Longitudinal telomere length shortening and cognitive and physical decline in later life: The Lothian Birth Cohorts 1936 and 1921. *Mechanisms of Ageing and Development*, *154*, 43-48.https://doi.org/10.1016/j.mad.2016.02.004

Haycock, P. C., Heydon, E. E., Kaptoge, S., Butterworth, A. S., Thompson, A., & Willeit, P. (2014). Leucocyte telomere length and risk of cardiovascular disease: systematic review and meta-analysis. *Bmj*, *349*.https://doi.org/10.1136/bmj.g4227

Hayes, A. F. (2017). *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. Guilford publications.

Ii, A. Z., & Sipps, G. J. (1985). Cross-validation of a short form of the Marlowe-Crowne Social Desirability Scale. *Journal of Clinical Psychology*, *41*(2), 236-238.https://doi.org/10.1002/1097-4679(198503)41

Irie, M., Asami, S., Nagata, S., Ikeda, M., Miyata, M., & Kasai, H. (2001). Psychosocial factors as a potential trigger of oxidative DNA damage in human leukocytes. *Japanese Journal of Cancer Research*, *92*(3), 367-376.https://doi.org/10.1111/j.1349-7006.2001.tb01104.x

Kim, S., Parks, C. G., Xu, Z., Carswell, G., DeRoo, L. A., Sandler, D. P., & Taylor, J. A. (2012). Association between genetic variants in DNA and histone methylation and telomere length. *PLoS One*, *7*(7), e40504. https://doi.org/10.1371/journal.pone.0040504

Klabbers, G., Bosma, H., van den Akker, M., Kempen, G. I. J. M., & van Eijk, J. T. M. (2013). Cognitive hostility predicts all-cause mortality irrespective of behavioural risk at late middle and older age. *The European Journal of Public Health*, *23*(4), 701-705.https://doi.org/10.1093/eurpub/cks060

Kolbus, D., Ljungcrantz, I., Andersson, L., Hedblad, B., Fredrikson, G. N., Björkbacka, H., & Nilsson, J. (2013). Association between CD 8+ T-cell subsets and cardiovascular disease. *Journal of internal medicine*, *274*(1), 41-51. https://doi.org/10.1111/joim.12038

Kresovich, J. K., Parks, C. G., Sandler, D. P., Weinberg, C. R., & Taylor, J. A. (2020). The role of blood cell composition in epidemiologic studies of telomeres. *Epidemiology (Cambridge, Mass.)*, *31*(4), e34.https://doi.org/10.1097/EDE.0000000000001187

Lenhard, W., & Lenhard, A. (2016). Calculation of effect sizes. Psychometrica.

Lévesque, K., Bureau, S., Moskowitz, D. S., Tardif, J. C., Lavoie, J., Dupuis, G., & D'Antono, B. (2009). Defensiveness and metabolic syndrome: Impact of sex and age. *Biological psychology*, *80*(3), 354-360.https://doi.org/10.1016/j.biopsycho.2008.12.003

Lévesque, K., Moskowitz, D. S., Tardif, J. C., Dupuis, G., & D'antono, B. (2010). Physiological stress responses in defensive individuals: Age and sex matter. *Psychophysiology*, *47*(2), 332-341.https://doi.org/10.1111/j.1469-8986.2009.00943.x

Lin, J., Epel, E., & Blackburn, E. (2012). Telomeres and lifestyle factors: roles in cellular aging. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, *730*(1-2), 85-89.https://doi.org/10.1016/j.mrfmmm.2011.08.003

Lin, P. Y., Huang, Y. C., & Hung, C. F. (2016). Shortened telomere length in patients with depression: a meta-analytic study. *Journal of Psychiatric Research*, *76*, 84-93.https://doi.org/10.1016/j.jpsychires.2016.01.015

Lin, Y., Damjanovic, A., Metter, E. J., Nguyen, H., Truong, T., Najarro, K., & Weng, N. P. (2015). Age-associated telomere attrition of lymphocytes in vivo is co-ordinated with changes in telomerase activity, composition of lymphocyte subsets and health conditions. *Clinical science*, *128*(6), 367-377.https://doi.org/10.1042/CS20140481

Loo, R., & Thorpe, K. (2000). Confirmatory factor analyses of the full and short versions of the Marlowe-Crowne Social Desirability Scale. *The Journal of social psychology*, *140*(5), 628-635.https://doi.org/10.1080/00224540009600503

Mathur, M. B., Epel, E., Kind, S., Desai, M., Parks, C. G., Sandler, D. P., & Khazeni, N. (2016). Perceived stress and telomere length: A systematic review, meta-analysis, and methodologic considerations for advancing the field. *Brain, behavior, and immunity*, *54*, 158-169.https://doi.org/10.1016/j.bbi.2016.02.002

Mollica, L., Fleury, I., Belisle, C., Provost, S., Roy, D. C., & Busque, L. (2009). No association between telomere length and blood cell counts in elderly individuals. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *64*(9), 965-967.https://doi.org/10.1093/gerona/glp065

Müezzinler, A., Zaineddin, A. K., & Brenner, H. (2013). A systematic review of leukocyte telomere length and age in adults. *Ageing research reviews*, *12*(2), 509-519.https://doi.org/10.1016/j.arr.2013.01.003

Mund, M., & Mitte, K. (2012). The costs of repression: a meta-analysis on the relation between repressive coping and somatic diseases. *Health psychology*, *31*(5), 640. https://doi.org/10.1037/a0026257

Murdock, K. W., LeRoy, A. S., & Fagundes, C. P. (2017). Trait hostility and cortisol sensitivity following a stressor: The moderating role of stress-induced heart rate variability. *Psychoneuroendocrinology*, *75*, 222-227.https://doi.org/10.1016/j.psyneuen.2016.10.014

Pauls, C. A., & Stemmler, G. (2003). Substance and bias in social desirability responding. *Personality and individual differences*, *35*(2), 263-275..https://doi.org/10.1016/S0191-8869(02)00187-3

Pimple, P., Lima, B. B., Hammadah, M., Wilmot, K., Ramadan, R., Levantsevych, O., & Vaccarino, V. (2019). Psychological distress and subsequent cardiovascular events in individuals with coronary artery disease. *Journal of the American Heart Association*, *8*(9), e011866.https://doi.org/10.1161/JAHA.118.011866

Révész, D., Milaneschi, Y., Verhoeven, J. E., Lin, J., & Penninx, B. W. (2015). Longitudinal associations between metabolic syndrome components and telomere shortening. *The Journal of Clinical Endocrinology & Metabolism*, *100*(8), 3050-3059.https://doi.org/10.1210/JC.2015-1995

Révész, D., Verhoeven, J. E., Picard, M., Lin, J., Sidney, S., Epel, E. S., & Puterman, E. (2018). Associations between cellular aging markers and metabolic syndrome: findings from the CARDIA study. *The Journal of Clinical Endocrinology & Metabolism*, *103*(1), 148-157.https://doi.org/10.1210/jc.2017-01625

Rosnow, R. L., & Rosenthal, R. (1992). Statistical procedures and the justification of knowledge in psychological science.https://doi.org/10.1037/0003-066X.44.10.1276

Rudolf, M. C., Walker, J., & Cole, T. J. (2007). What is the best way to measure waist circumference?. *International Journal of Pediatric Obesity*, *2*(1), 58-61.https://doi.org/10.1080/17477160601095177

Sahoo, S., Padhy, S. K., Padhee, B., Singla, N., & Sarkar, S. (2018). Role of personality in cardiovascular diseases: An issue that needs to be focused too!. *Indian heart journal*, *70*, S471-S477.https://doi.org/10.1016/j.ihj.2018.11.003

Schoormans, D., Verhoeven, J. E., Denollet, J., van de Poll-Franse, L., & Penninx, B. W. J. H. (2018). Leukocyte telomere length and personality: associations with the Big Five and Type D personality traits. *Psychological medicine*, *48*(6), 1008-1019.https://doi.org/10.1017/S0033291717002471

Schutte, N. S., & Malouff, J. M. (2014). A meta-analytic review of the effects of mindfulness meditation on telomerase activity. *Psychoneuroendocrinology*, *42*, 45-48.https://doi.org/10.1016/j.psyneuen.2013.12.017

Shah, A. J., Ghasemzadeh, N., Zaragoza-Macias, E., Patel, R., Eapen, D. J., Neeland, I. J., & Vaccarino, V. (2014). Sex and age differences in the association of depression with obstructive coronary artery disease and adverse cardiovascular events. *Journal of the American Heart Association*, *3*(3), e000741. https://doi.org/10.1161/JAHA.113.000741

Smith, T. W., Glazer, K., Ruiz, J. M., & Gallo, L. C. (2004). Hostility, anger, aggressiveness, and coronary heart disease: An interpersonal perspective on personality, emotion, and health. *Journal of personality*, *72*(6), 1217-1270. https://doi.org/10.1111/j.1467-6494.2004.00296.x

Srinivas, N., Rachakonda, S., & Kumar, R. (2020). Telomeres and telomere length: a general overview. *Cancers*, *12*(3), 558.https://doi.org/10.3390/cancers12030558

Starnino, L., Busque, L., Tardif, J. C., & D'Antono, B. (2016). Psychological profiles in the prediction of leukocyte telomere length in healthy individuals. *PloS one*, *11*(10), e0165482.https://doi.org/10.1371/journal.pone.0165482

Tellechea, M. L., & Pirola, C. J. (2017). The impact of hypertension on leukocyte telomere length: a systematic review and meta-analysis of human studies. *Journal of human hypertension*, *31*(2), 99-105.https://doi.org/10.1038/jhh.2016.45

Van 't Riet, J., & Ruiter, R. A. (2013). Defensive reactions to health-promoting information: An overview and implications for future research. *Health Psychology Review*, *7*(sup1), S104-S136. https://doi.org/10.1080/17437199.2011.606782

Wang, J., Dong, X., Cao, L., Sun, Y., Qiu, Y., Zhang, Y. & Zhong, L. (2016). Association between telomere length and diabetes mellitus: a meta-analysis. *Journal of International Medical Research*, *44*(6), 1156-1173. https://doi.org/10.1177/0300060516667132

Watkins, L. E., Harpaz-Rotem, I., Sippel, L. M., Krystal, J. H., Southwick, S. M., & Pietrzak, R. H. (2016). Hostility and telomere shortening among US military veterans: Results from the National Health and Resilience in Veterans Study. *Psychoneuroendocrinology*, *74*, 251-257.https://doi.org/10.1016/j.psyneuen.2016.09.006

Winer, B. J. (1962). Statistical principles in experimental design. https://doi.org/10.1037/11774-000

Wong, J. M., Na, B., Regan, M. C., & Whooley, M. A. (2013). Hostility, health behaviors, and risk of recurrent events in patients with stable coronary heart disease: findings from the heart and soul study. *Journal of the American Heart Association*, *2*(5), e000052.https://doi.org/10.1161/JAHA.113.000052

Zalli, A., Carvalho, L. A., Lin, J., Hamer, M., Erusalimsky, J. D., Blackburn, E. H., & Steptoe, A. (2014). Shorter telomeres with high telomerase activity are associated with raised allostatic load and impoverished psychosocial resources. *Proceedings of the National Academy of Sciences*, *111*(12), 4519-4524.https://doi.org/10.1073/pnas.1322145111

Table 1.

Participant Characteristics

	CAD *n*=598	Non-CVD *n*=438	CAD and Non-CVD Combined *n*=1036	Healthy *n*=25
***Demographic Variables, n (%)* or M (±SD); [Range]**				
Age (years)**	66.13 (±6.25); [40-76]	64.41 (±7.23); [35-76]	65.40 (±6.73); [35-76]	55.68 (±0.19); [34-70]
Sex, *n* (%) **				
Men	482 (80.60)	193 (44.10)	675 (65.20)	14 (56)
Caucasian, *n*(%)	593 (99.20)	428 (97.77)	1 021 (98.60)	24 (96)
Years of Schooling**	13.95 (3.76)	14.86 (3.58)	14.33 (3.71)	15.56 (3.66)
Currently Employed, *n*(%)**	135 (22.60)	141 (32.20)	276 (26.60)	14 (56)
Civil Status, *n* (%)				
Married/Living with Someone	427 (71.40)	326 (74.50)	753 (72.70)	21 (84)
Single	48 (8)	47 (10.70)	95 (9.20)	2 (8)
Divorced, Separated or Widowed	123 (20.60)	65 (14.88)	188 (18.20)	2 (8)
Annual Family Income, *n*(%)				
≤$29,999	86 (14.40)	27 (6.20)	113 (10.90)	2 (8)
$30,000-59,99	206 (34.40)	154 (35.20)	360 (34.70)	3 (12)
≥$60,000**	306 (51.17)	258 (58.90)	564 (54.33)	20 (80)
***Behavioral Variables, n (%)* or M (±SD)**				
Smoker, *n*(%)**	81 (13.50)	25 (5.70)	106 (10.20)	2 (8)
Hours of Exercise/Week,M (±SD)	2.85 (±3.29)	3.31 (±3.39)	3.04 (±3.34)	3.07 (±3.38)
Glasses of Alcohol/Week, M (±SD)	6.47 (±8.14)	5.70 (±6.57)	6.12 (±7.51)	4.96 (±5.01)
***Physiological Variables,* M (±SD)**				
Telomere length (T/S ratio)***	0.83 (±0.18); [0.44-1.5]	0.89 (±0.19); [0.48-1.68]	0.86 (±0.19); [0.44-1.68]	0.94 (±0.15); [0.72-1.26]
Body Mass Index (kg/m^2)**	29.80 (±5.11)	28.59 (±4.99)	29.28 (±5.10)	27.15 (±2.83)
Waist Circumference (cm)**	102.96 (±13.47)	96.42 (±13.78)	100.18 (±13.98)	90.64 (±10.91)

Mean Arterial Pressure (mmHG)**	89.88 (±13.85)	95.90 (±14.54)	92.36 (±14.41)	97.42(±14.38)
Glucose (mmol/L)**	6.46 (±1.53)	5.89 (±.97)	6.22 (±1.36)	5.64 (±1.03)
Triglycerides (mmol/L)**	1.69 (±0.80)	1.62 (±0.84)	1.67 (±0.82)	1.49 (±0.89)
C-Reactive Protein (mg/L)	2.65 (±6.83)	2.78 (±6.78)	2.71 (±6.78)	2.82 (±5.60)
***Psychological Variables,* M (±SD)**				
Hostility*	14.39 (±6.07)	13.27 (±6.05)	13.91 (±6.07)	11.72 (±6.84)
Defensivenesss	9.35 (±2.73)	9.33 (±2.77)	9.34 (±2.74)	9.08 (±2.64)
Medical History and Medication, n(%)				
Myocardial Infarction	387 (64.70)	-	-	-
Coronary Artery Bypass	211 (35.30)	-	-	-
Angioplasty	421 (70.40)	-	-	-
Arrythmia	146 (24.40)	-	-	
Diabetes**	147 (24.60)	45(10.30)	192 (18.50)	-
Hypercholesterolemia **	583 (97.50)	262 (59.80)	845 (81.60)	-
Hypertension**	414 (69.20)	183 (41.80)	597 (57.61)	-
Other Degenerative Diseases*	313 (52.34)	284 (64.55)	597 (57.51)	-
Family History of CVD**	421 (70.40)	256 (57.50)	677 (65.40)	14 (56)
Skin Cancer	23 (3.80)	20 (4.60)	43 (4.20)	-
Antidepressants**	61 (10.20)	32 (7.30)	94 (9.06)	2 (8)
Prescribed Cardiovascular Agents**	573 (95.82)	281 (65.20)	855 (82.37)	-

Note. CAD=coronary artery disease patients; Non-CVD=participants with non cardiovascular illness; Hostility=39-item Cook-Medley Hostility Inventory; Defensiveness=14-item Marlowe-Crowne Social Desirability Scale; Currently employed=includes part-time and full-time workers; Other chronic diseases=osteoarthritis, Autoimmume Disorders, Crohn's Disease, Irritable Bowel Syndrome; Prescribed Cardiovascular Agents=statins, beta-blockers, calcium channel blockers, and other agents.

*** $p < .001$, ** $p < .01$, * $p < .05$, ~p=.07 difference between CAD and Non-CVD illness group

Table 2.

Group Means and Pearson Correlations Between TL and Personality Traits as a Function of Health Status and Sex

	CAD		Non-CVD		Healthy	
Mean (±SD)	**Men (n=482)**	**Women (*n*=116)**	**Men (*n*=193)**	**Women (*n*=245)**	**Men (*n*=14)**	**Women (*n*=11)**
Telomere Length (T/S ratio)	0.83 (0.17)	0.86 (0.019)	0.87 (0.19)	0.90 (0.20)	0.96 (0.18)	0.91 (0.11)
Hostility	14.50 (5.18)	13.94 (5.56)	13.19 (6.26)	13.30 (5.85)	11.79 (5.79)	11.64 (8.29)
Defensiveness	9.36 (2.72)	9.32 (2.73)	9.59 (2.68)	9.13 (2.82)	9.29 (2.43)	8.82 (2.99)
Correlations with Telomere Length (*r*)						
Defensiveness	0.03	0.14	-0.07	-0.04	-0.65*	0.05
Hostility	-0.01	-0.17	0.04	-0.14*	0.36	-0.39

Note. No statistical differences between men and women emerged for all three groups.

*$p < .05$, ~p=.06; Effect size: r=.1 (small), r=.3 (medium), r=.5 (large)

Table 3.

Results of the Hierarchical Regression Analysis for Hostility and Defensiveness Predicting Telomere Length in the Patient Groups

	β	t	*p*	Semipartial r	95% CI
BLOCK 1					
Age	-0.24	-6.86	0.006*	-0.21	[-0.002, -0.001]
Sex	0.05	1.40	0.16	0.04	[-0.002, -0.011]
CAD Status	0.03	0.83	0.41	0.03	[-0.004, 0.009]
Employment Status	-0.01	-0.36	0.72	-0.01	[-0.008, 0.005]
#Cigarettes daily	-0.03	-1.13	0.26	-0.03	[-0.001, 0.000]
#Exercise Hrs/Wk	0.06	1.90	0.06	0.06	[0.000, -0.001]
#Alcohol beverages/Wk	-0.07	-2.10	0.04	-0.06	[-0.001, -0.002]
Waist circumference	-0.03	-0.99	0.32	-0.03	[0.000, -0.000]
Glucose	-0.01	-0.32	0.75	0.01	[-0.002, 0.002]
Mean Arterial Pressure	0.08	2.65	0.008*	0.08	[0.000, 0.000]
Cholesterol total	0.05	1.40	0.16	0.08	[-0.001, 0.005]
History of CVD Risk	-0.04	-1.02	0.31	-0.03	[-0.014, 0.004]
$F(12,1023)=11.08$, $p<0.001$ $R^2=0.115$ $R^2_{adj}=.105$					
Regression 1					
BLOCK 2					
Hostility	-0.03	-0.91	0.37	-0.03	[-0.001, 0.000]
$F(1, 1022)=0.82$, $p=0.37$ $R^2=0.116$ $R^2_{adj}=0.104$					
BLOCK 3					
Hostility*Sex	-0.08	-2.78	0.006*	-0.08	[-0.002, -0.0003]
$F(1,102)=7.72$, $p=0.007$ $R^2=0.122$ $R^2_{adj}=0.110$					
Regression 2					
BLOCK 2					
Defensiveness	0.03	0.84	0.40	0.03	[-0.001, 0.001]
$F(1, 1022)=0.71$, $p=0.40$ $R^2=0.116$ $R^2_{adj}=0.104$					
BLOCK3					
Defensiveness* CAD status	-0.06	-1.98	0.049*	-0.058	[-0.004, -0.000]
$F(1,1021)=3.90$, $p=0.007$ $R=0.119$ $R^2_{adj}=0.107$					

Note. CI= confidence interval; CAD status (dichotomized): with (1) or without CAD (2); Employment status (dichotomized)=retired or non-employed (1), full-time or part-time (2). History of CVD risk (dichotomized)=absence (0) or presence (1) of hypertension, (and/or) diabetes (and/or) hypercholesterolemia and CVD agents (e.g., dyslipidemic, antihypertensive agents, insulin, oral hyperglycemics); *$p<.05$

Table 4.

Results of the Hierarchical Regression Analysis for Hostility and Defensiveness Predicting Telomere Length in Healthy Individuals (n=25)

	β	t	p	Semipartial r	95% CI
<u>BLOCK 1</u>					
Sex	-0.27	-1.33	0.20	-0.27	[-1.23, 0.27]
F(1,24)=1.77, *p*=0.20 R^2=0.071					
<u>BLOCK 2</u>					
Hostility	0.20	0.97	0.34	0.20	[-0.03, 0.08]
F(2, 24) =1.35, *p*=0.28 R^2=0.110					
<u>BLOCK 3</u>					
Hostility*Sex	-0.43	-2.19	0.049*	-0.41	[-0.22, -0.01]
F(3, 24) =2.44, *p*=0.08 R^2=0.275					
<u>BLOCK 2</u>					
Defensiveness	-0.32	-1.65	0.11	-0.32	[-0.25, 0.03]
F(2,24) =2.31, *p*=0.12 R^2=0.174					
<u>BLOCK 3</u>					
Defensiveness* Sex	0.52	3.06	0.006**	0.51	[0.11, 0.59]
F(3,24) =5.25, *p*=0.007 R^2=0.428					

Note. Residualized telomere length controlling for age, body mass index, years of education and employment status; CI= confidence interval.

*$p < .05$

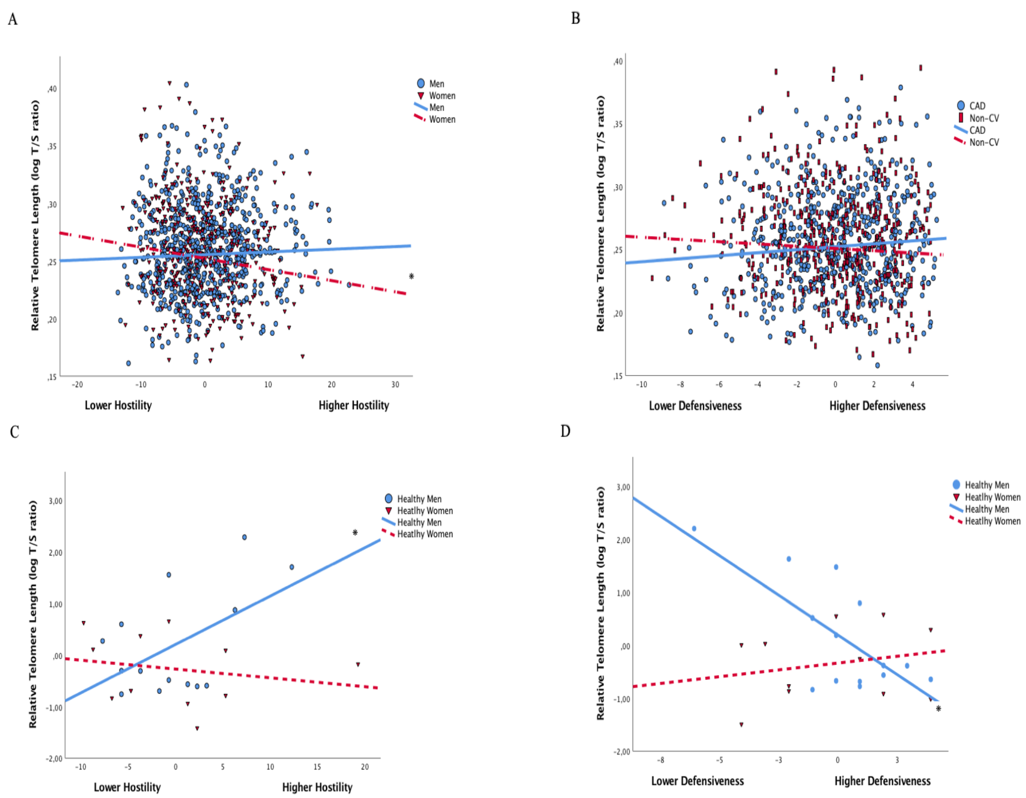


Figure 1. A) The relation between hostility and TL is moderated by sex in participants with CAD or non-CV illnesses (ß = -.08, t=-2.78, *p*=.006). Greater hostility was associated with shorter TL in women (b= -.001, t=-2.82, *p*=.005), but not in men (b= .001, t=0.78, *p*=.43). B) Among patients, the relationship between defensiveness and TL is moderated by CAD status (ß = -.06, t=-1.98, *p*=.049). Greater defensiveness was associated with longer TL among individuals with CAD (trend) (b=.001, t=1.93, *p*=.06), but not among patients with non-CV illnesses (b=-.001, t=-.93, *p*=.35). C) In healthy individuals, the sex by hostility interaction was significant. Greater hostility was associated with significantly longer TL among men (b=0.09, t=2.37, *p*=.028), not in women (b=-.02, t=-.54, *p*=.59). D) The relation between defensiveness and TL is moderated by sex in healthy participants. Greater defensiveness was associated with shorter TL in healthy men (b=-.30, t=-3.56, *p*=.002), but not in women (b=.05, t=.66, *p*=.52).
*$p < .05$

PREFACE: ARTICLE 2

Findings from Article 1 (Starnino et al., 2021) and a previous investigation (Starnino et al., 2016) suggest that hostility and defensiveness may contribute to premature aging, as reflected by altered telomere length (TL). Importantly, these psychological traits as well as shorter TL, have independently been associated with the development and progression of CAD (Wong et al., 2014; Denollet et al., 2008; Weischer et al., 2012; Willeit et al., 2010). If these factors are indeed involved in the development or progression of CAD, they could be amenable to change in order to improve prognosis. Such demonstrations would contribute additional evidence of their pathophysiological role. In line with this, as cardiovascular health psychologists, our role includes providing psychosocial interventions to reduce CAD risk factors and improve one's quality of life.

These considerations motivated the second study, performed specifically in older individuals at greater risk for CAD by virtue of metabolic syndrome and physiological vulnerability to stress. A pilot randomized controlled trial, for which I was a co-principle investigator, first examined the feasibility and acceptability of a Mindfulness-Based Stress Reduction (MBSR) program for older participants at risk for CAD recruited from Study 1, as well as potential changes in metabolic parameters and stress responses (refer to Annex 1 to read this article). This study was largely feasible and acceptable. MBSR led to a decrease of 15% in LDL cholesterol and 10% in total cholesterol versus 4.5% and 1%, respectively, in the waitlist. Within group analyses showed notable decreases in LDL, triglycerides, and waist circumference post-MBSR and 2 months later. Stress response measures of the autonomic nervous system (e.g., heart rate variability parameters) were normalized post-MBSR.

Article 2 of this dissertation reflect tertiary analyses of this pilot RCT and sought instead to obtain preliminary data on the potential effects of MBSR on hostility, defensiveness, and quality of life, as well as on telomere regulation, in particular telomere length and telomerase activity

2.2 ARTICLE 2

THE POTENTIAL IMPACT OF MINDFULNESS ON TELOMERE REGULATION, MALADAPTIVE TRAITS, AND QUALITY OF LIFE AMONG OLDER INDIVIDUALS: A PILOT RCT

L'IMPACT POTENTIEL DE LA PLEINE CONSCIENCE SUR LA RÉGULATION DES TÉLOMÈRES, LES TRAITS MALADAPTIFS ET LA QUALITÉ DE VIE CHEZ LES PERSONNES ÂGÉES: UNE ÉTUDE PILOTE RANDOMISÉE ET CONTRÔLÉE

ARTICLE SUBMITTED TO *CLINICAL GERONTOLOGIST*

The Potential Impact of Mindfulness on Telomere Regulation, Maladaptive Traits, and Quality of Life Among Older Individuals: a Pilot RCT

Louisia Starnino, BSc; Christina Gentile, PhD; Gilles Dupuis, PhD; Vincent Bourgoin, MSc; Lambert Busque, MD, PhD; Bianca D'Antono, PhD

Words: 5 311
Clinical registration trial number: AEARCTR-0006420

Abstract

Objectives: More hostile and defensive individuals are at increased risk for cardiovascular disease (CVD), altered telomere regulation, and impoverished quality of life (QoL). Mindfulness-based stress reduction (MBSR) may be helpful in mitigating their risk.

The objectives are to obtain preliminary data from a pilot randomized controlled trial (RCT) on the effects of MBSR on trait hostility, defensiveness, telomere length (TL), telomerase activity (TA), and QoL based on life goals in individuals at risk for CVD.

Methods: Nineteen older men and women (M_{age}=67.20 ± 7.70) with metabolic syndrome and non-normative stress responses in a prior study were randomized to a 9-week MBSR program versus a waitlist control group (WLC). Blood samples and self-report measures were obtained at baseline, post-intervention, and 2-months later. Between-group differences were examined via ANCOVAs controlling for baseline values. Within-group changes were analysed via Repeated Measures ANOVA. Associations between home mindfulness practice and changes in outcome measures were examined. Effect sizes (ES) are reported.

Results: MBSR led to decreases in TA compared to the WLC group (medium ES). Within-subject results revealed improvements in hostility and QoL, reductions in TA and maintained TL over follow-up (medium to large ES). Mindfulness practice at home was associated with changes in hostility and QoL (Spearman ρ's≥ -0.35) 2 months post-MBSR.

Conclusion: Promising effects of MBSR on hostility and QoL based on life goals were found. While TL was maintained at the two-month follow-up, TA decreased, warranting further research to better understand this unexpected finding.

Clinical Implications MBSR improved trait hostility and QoL and may lead to reduced loss of TL at follow-up in older individuals at risk of CAD.

Key words: MBSR, telomere, telomerase, hostility, defensiveness, metabolic syndrom

Introduction

Personality traits, such as hostility and defensiveness, have been shown to increase risk for cardiovascular morbidity (including metabolic syndrome) and mortality (Chida & Steptoe, 2009; D'Antono et al., 2013; Lévesque et al., 2010; Thomas et al., 2020), as well as reduce quality of life (QoL; Julkunen & Alhstrom, 2006; Truong et al., 2016). Hostility refers to the repeated experience of intense or prolonged anger, aggressive behaviour, and/or a cynical, mistrusting manner of seeing the world and others, that more frequently brings them into interpersonal conflict (Smith, 1994). Defensiveness, for its part, is defined by avoidance, denial or repression of personal information perceived as threatening by the individual. Defensive individuals adopt socially desirable behaviors in order to secure social bonds and/or protect their fragile self-esteem (Crowne & Marlowe, 1960; Paulhus,1984).

An emerging body of data suggests that these maladaptive traits may also be associated with altered telomere regulation (Brydon et al., 2012; Starnino et al., 2016; Starnino et al., 2021; Zalli et al., 2014), though the direction of association may differ as a function of sex and health status (Starnino et al., 2021). Telomeres are protective DNA caps at the ends of chromosomes that ensure genomic stability (Blackburn & Gall, 1978). Telomeres shorten over time as cells undergo divisions, though dynamic mechanisms are in play that help maintain telomere integrity. Telomerase (TA), an RNA enzyme for example, adds DNA repeat sequences to the ends of chromosomes by either elongating TL or slowing down their rate of attrition (Greider & Blackburn, 1985). Nonetheless, telomeres eventually reach a critical length leading to cellular senescence or apoptosis (Eisenberg, 2011). Short telomeres have been shown predict the development and prognosis of chronic illnesses such as coronary artery disease (CAD) and metabolic syndrome (Cheng et al., 2017; D'Mello, 2015, review; Khalangot et al., 2020; Révesz et al., 2014).

It has been hypothesized that hostility and defensiveness may impact TL regulation in part, as a result of affective and physiological responses to challenging life situations observed in those with these traits (Chida & Hamer, 2008; Lévesque et al., 2010; Tskikandilakis et al., 2020). In line with this, one study observed altered (blunted) physiological stress responses in middle-aged to older men with higher telomerase activity and shorter TL (Zalli et al., 2014). The latter were also associated with higher levels of hostility and lower levels of social support in that investigation.

There has been increasing interest in, and data demonstrating the efficacy of mindfulness-based interventions (MBIs), and in particular, mindfulness-based stress reduction (MBSR), in improving psychological and to a lesser extent, physiological outcomes in healthy (Sharma & Rush, 2014) and mixed chronic illness samples (De Vibe et al., 2017), including individuals with or at risk for CAD (Abbott et al., 2014). MBIs encourage participants to bring greater attention and awareness to their thoughts, emotions, body sensations, and breath, in a non-judgemental, curious, and self-compassionate manner such as to develop a clearer perspective of the situation in which calmer, wiser responses are possible. MBIs are believed to be appropriate interventions in individuals with anger disturbances (Wright et al., 2009), though results from ten investigations involving very diverse samples have been mixed regarding actual reductions in hostility following an MBI program (Brown Wright et al. 2011; Henderson et al., 2013; Jahangirpour et al., 2013; MacCoon et al., 2012; Momeni et al., 2016; Olivo et al., 2009; Rosenkranz et al., 2013; Samuelson et al., 2007; Sibinga et al., 2011; Young et al., 2009). Other than differences in sample characteristics, studies varied in the length and intensity of MBI programs, in the measure of hostility, and few included follow-up assessments (Brown Wright et al. 2011; Henderson et al., 2013).

No investigations have examined the effects of MBIs on defensiveness specifically, though they have been found to improve elements theoretically related to defensiveness in non-experienced meditators, such as self-esteem (Randal et al., 2015), emotional regulation skills (e.g. recognition and expression of negative emotions), and self-acceptance (Robins et al., 2012).

Furthermore, evidence suggesting that MBIs can prevent telomere loss and/or increase telomerase activity is emerging. For example, a meta-analysis by Schutte et al., (2020) based on eleven samples (total *n*=861, age range [33-77]) found that telomeres were longer following a meditation-based program compared to control groups, though results were only significant in the four quasi-experimental, but not in the seven RCT's. Significant heterogeneity across studies may reflect greater amount of practice time performed and the healthier samples in the quasi – experimental trials compared to the RCTs, which were mostly comprised of participants with either physical or psychiatric illnesses (Schutte et al., 2020). RCTs of MBSR in younger healthy adults (Keng et al., 2019) or breast cancer patients (Carlson et al., 2015; Lengacher et al., 2014) suggested instead that TL was maintained over the course of the intervention, such that no differences were found between the MBSR group and the waitlist or active control groups. Further research is required to determine whether the potential protective effects of MBSR are maintained over a longer follow-up and are associated with greater practice.

In contrast, RCTs in clinical and nonclinical populations have found that MBIs can increase telomerase activity (Schutte & Malouff, 2014). To date, only three trials have looked at both TL and telomerase within the same study (Duraimani et al., 2015; Innes et al., 2018; Lengacher et al., 2014). For example, Lengacher and colleagues performed an RCT in which breast cancer patients underwent either a 6 week MBSR program or usual care (UC ; waitlist to receive MBSR). While no effect was found on TL, telomerase activity increased steadily over time (up to 17%) in the MBSR group while remaining relatively constant (3% increase) in the UC group, after adjusting for baseline telomerase. Similar findings were obtained in a trial involving forty-eight individuals with hypertension who underwent either transcendental meditation stress reduction or an extensive health education stress management program (Duraimani et al.,2015) It remains to be examined whether telomere regulation can be improved through a standardized mindfulness training program in individuals at increased risk of CAD by virtue of metabolic abnormalities and vulnerability to stress, in whom shorter TL poses additional prognostic risk (Bonfigli et al., 2016; Révesz et al., 2014).

Secondary analyses of a previous pilot RCT with 2-month follow-up (Gentile et al., 2021) were undertaken to gather preliminary evidence on the potential effects of MBSR on hostility and defensiveness, as well as telomere regulation (TL/telomerase) and QoL outcomes in individuals at greater risk for CAD by virtue of metabolic burden and non-normative autonomic stress responses. To our knowledge, this is the first RCT looking at the impact of MBSR on these outcomes in this type of population. Previous trials have rarely included a follow-up evaluation, limiting our understanding of longer-term changes in TL regulation, maladaptive traits, and QoL post-MBSR intervention. It is hypothesized that hostility, defensiveness, and QoL will improve post-MBSR. While MBSR have been associated with improved health-related QoL outcomes in clinical and non-clinical samples (De Vibe et al., 2017), its impact on overall QoL based on life goals remains to be assessed. Based on the existing literature in other populations, and short follow-up period of the current investigation, it is expected that TL will be maintained post-MBSR, while telomerase activity will increase. Finally, we expect improvements to be maintained over the 2-month follow-up period.

Methods

The current study represents secondary analyses of the MBSR-MS pilot RCT (Clinical registration trial number: AEARCTR-0006420), for which main results on feasibility and acceptability were recently published (Gentile et al., 2021).

Participants

Nineteen participants (7 men; M_{age}= 67 years, *SD*=7.70) were recruited from an ongoing longitudinal study (BEL-AGE). One woman dropped out prior to starting the intervention due to scheduling conflicts, resulting in a total of 18 participants. Individuals met the following criteria: a) presence of metabolic syndrome (National Cholesterol Education Program, Alberti et al., 2009), and b) exaggerated or blunted cardiac autonomic (within the lower or higher tertile of sympathovagal) response to an anger recall task in a prior study within our laboratory (refer to

Gentile *et al.,* 2019 for protocol details), c) absence of a significant cognitive or psychological condition (e.g. delirium, psychosis, bipolar disorder, dementia) with the potential to limit understanding and/or participation in the research study and intervention program, d) absence of life-threatening conditions (e.g., cancer, HIV, CVD), e) were not currently participating in psychotherapy, f) and were not regular yoga or meditation practitioners. Refer to Gentile et al., (2021) (Annex A) for additional details on recruitment procedures, as well as for data on feasibility and acceptability of MBSR in this sample.

Randomization

Participants were randomly assigned to either the MBSR or wait-list control groups after their baseline evaluation. Randomization was stratified by sex and physiological stress response profile and was performed by an independent biostatistician using a random sequence generator. Allocation was hidden from the researcher performing the assessments using sequentially numbered sealed envelopes.

The two groups were recruited and tested concurrently to limit group differences resulting from a differential exposure to weather conditions, socioeconomic, political, or medical changes. Laboratory technicians conducting the blood draws were blind to group allocation and stress response style for the duration of the study. Those administering the stress protocol and entering the data were blind to group allocation until the end of the second evaluation, when feedback concerning their intervention experience was collected.

Procedure

Participants were scheduled for their first laboratory appointment between 8:00 a.m. and 9:00 a.m. on a weekday, to control for circadian rhythms. They were instructed not to smoke or engage in any strenuous activity and to abstain from eating and drinking (except water) for 12 hours prior to testing. The use of drugs/alcohol was not allowed 24 hours prior to their appointment. After written consent, anthropomorphic data, a blood sample, demographic and medical information were collected, and psychological questionnaires were completed.

The intervention group underwent three evaluation sessions: before the intervention (baseline), immediately following the intervention, and two months later. The control group participated in four evaluation sessions: one approximately two months before the start of the intervention (baseline for between group analyses), one immediately prior to the intervention, one immediately post-intervention, and one two months later (refer to Figure 1: Study Flow, in Gentile et al., (2021) for more information (p. 228 of this thesis). The Hospital Research and Ethics Board approved this study.

Mindfulness-Based Stress Reduction (MBSR) Intervention

The MBSR program was based on the program developed by Jon Kabat-Zinn and colleagues (Kabat-Zinn, 2003). Participants attended eight weekly two and a half hour sessions at a community center adjacent to the hospital. They also attended an additional five-hour silent retreat between weeks 7 and 8, which sought to further integrate and establish the various skills. Participants received these nine sessions over nine weeks in this study rather than eight, as the scheduled five-hour retreat would have otherwise fallen on a religious holiday for the group randomized to MBSR. Participants engaged in formal group exercises to cultivate mindfulness (sitting and walking meditation, body scan, loving kindness meditation and mild hatha yoga). The rest of the session was devoted to teacher instruction and group discussions on stress management. A senior psychologist, with more than four years of formal MBSR training, conducted the MBSR groups. Sessions were audiotaped and verified for standardization purposes (refer to Appendix H for weekly MBSR themes).

Participants were given audio recordings of mindfulness exercises to facilitate their daily practice at home and were requested to practice their meditation for 25 to 45 minutes a day.

They were invited to complete a daily log of their mindfulness practice for the duration of their participation in the study.

Measures

Sociodemographic variables. Data on sex, age in years, ethnicity, weight, height, marital status, income, years of education, and health behaviours were obtained.

Medical Variables. Body mass index, personal and family medical history, as well as a current list of any medications taken by the participant were obtained.

Hostility. The short-form of the Cook–Medley Hostility Inventory (CMHo) consisting of 39 true-false items measuring cynicism, hostile affect and aggressive responding was used (Barefoot et al., 1989). The internal consistency (original form α=0.82-0.86; short-form α=0.85) (Cook & Medley, 1954; Smith & Frohm, 1985; Boyle et al., 2004), and test-retest reliability (orginal form: r's>0.85; short form across a 10-year period r=0.74) of this instrument are both very good (Han et al.,1985). In this sample, internal consistency was $\alpha = 0.75$. (Refer to Appendix G).

Defensiveness. The short-form of the Marlowe-Crowne Social Desirability scale (MCSD) (Crowne & Marlowe, 1960; Reynolds, 1982) is composed of 14 true or false items assessing whether respondents are answering in a culturally sanctioned and desirable manner. The items present behaviors that are desirable but infrequent (e.g., ''I am always courteous, even to people who are disagreeable'') and behaviors that are undesirable but frequent (e.g., ''I like to gossip at times''). Scores on the short-form correlate very highly (r = 0.91 to 0.97) with the scores on the original 33- item scale (Loo & Thorpe, 2000). The internal consistency has been considered good for both the original and short-form questionnaires (α= 0.88 and 0.76, respectively) (Reynolds et al., 1982). In the current sample, internal consistency was $\alpha = 0.70$. (Refer to Appendix G).

Quality of life. Quality of Life Systemic Inventory **(**QoL) (Dupuis et al., 1989) consists of a global score and nine subscales: physical health, cognitive functioning (memory, concentration), social/family, couple, leisure, work, housekeeping, affectivity, and spirituality (work items were removed from the calculation, as 12 out of 19 participants were retired). Its score represents the gap between the respondent's present situation and their ideal situation for various aspects of life; the higher the score, the worse the quality of life. It is the only questionnaire to measure Quality of Life based on life goals, in keeping with one of the main elements of the WHO's definition of quality of life : "Quality of Life is individuals′ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (WHO, 2021). Global internal consistency is α= 0.87 (Dupuis et al., 2012), as per the current sample. (Refer to Appendix G)

Telomere length. Telomere length was measured by quantitative real-time PCR (qPCR (polymerase chain reaction)) using the modified method (Epel et al., 2004) of the protocol described by Cawthon (Cawthon, 2002). This method is based on determining the number of telomeric repeat sequence (T) on the number of copies of a single gene (*RPLP0*, 60S acidic ribosomal protein P0) (S). A T/S ratio was calculated for each sample of DNA tested. A relative ratio was obtained by comparing the ratio T/S of a sample to the ratio T/S of a reference DNA sample (obtained from a single individual and used to generate the standard curves) giving a value T/S of 1. Therefore, the relative ratio of a sample represents the number of copies of telomeres relative to the reference sample. For each DNA sample, T and S quantitative PCR SYBR green reactions are assembled with the epMotion 5075 TMX (Eppendorf) automated pipetting systems. Each 20 µl reaction contained : 7.5 ng DNA, 10 µl of QuantiFast SYBR Green PCR Master Mix (Qiagen, # 204057), 450 nM of primers Tel1b (CGGTTTGTTTGGGTTTGGGTTTGGGTTTGGGTTTGGGTT) and Tel2b (GGCTTGCCTTACCCTTACCCTTACCCTTACCCTTACCCT) for the T amplification or 300 nM of the primer 36B4u (CAGCAAGTGGGAAGGTGTAATCC) and 500 nM of the primer 36B4d (CCCATTCTATCATCAACGGGTACAA) for the S amplification. Serial dilutions of the reference DNA are made (25 to 1.562 ng/µl) for each 96-well plate and the values obtained were used to establish a standard curve in order to calculate the T and S values of the tested samples. All PCR were performed on the ViiA 7 real-time PCR system (Applied Biosystems) and with the QuantStudio analysis software (Applied Biosystems). The thermal amplification profile of telomeres (T) was: 5 min at 95 °C, followed by 25 cycles of 95 °C for 10 sec and 56 °C for 1 min. The thermal amplification profile of the single copy gene (S) was: 5 min at 95 °C followed by 40 cycles of 95 °C for 10 sec and 60 °C for 40 sec. All samples were measured in triplicate, and their mean was used for analyses.

Telomerase. For each participant, 10 ml of peripheral blood was collected in EDTA tubes. Each blood sample were centrifuged at 1500g for 10 min at room temperature. Immediately following centrifugation the upper plasma layer was removed, and the concentrated leukocyte layer was collected. Cells were washed in 1X PBS (Ca2+-, Mg2+-, EDTA- and RNAse-free), and centrifuged at 360g for 5 min at room temperature. Cell pellet was then resuspended in 1 ml of Recovery-cell culture freezing medium (Thermo Fisher Scientific, # 12648010). The cell suspensions were stored at -80°C until further processing. Telomerase was tested according to the instructions provided by the TeloTAGGG Telomerase PCR ELISA PLUS kit (Roche, # 12013789001). In brief, -80°C stored cells were thawed in RPMI (Thermo Fisher Scientific, # 11875093)/15% FBSi (Hyclone, # SV30014.03)/0.04% Sodium Bicarbonate (Thermo Fisher Scientific, # 25080094)/25 mM HEPES (Thermo Fisher Scientific, # 15630130), centrifuged at 260g for 10 min at room temperature, cells were resuspended in 1X PBS and automatically counted with the Coulter AC•T diff2 hematology analyzer (Beckman Coulter). Cells were then centrifuged, the leukocyte pellets were lysed in lysis reagent at a concentration of 10 000 cells/µl, and 10 µl of the obtained protein extract (equivalent to 100 000 cells) was used for the subsequent telomerase-catalyzed biotin-labeled primer elongation and PCR reaction. The thermal protocol was one cycle at 25°C for 30 min for primer elongation followed by one cycle at 94°C for 5 min for telomerase inactivation. The subsequent amplification protocol (TRAP) was 30 cycles of 94°C for 30 sec for denaturation, 50°C for 30 sec for annealing and 72°C for 90 sec for polymerisation. One final cycle at 72°C for 10 min for terminal elongation was performed. Then 2.5 µl of the PCR product was denatured, hybridized to digoxigenin-labeled probes, and immobilized to streptavidin-coated wells. Finally, the digoxigenin-labeled products were visualized by a horseradish peroxidase conjugated anti-digoxigenin antibody and tetramethyl benzidine acting as a peroxidase substrate. The level of telomerase is in proportion to the colorimetric measures taken at 450 nm using Infinite M1000 (Tecan). Relative telomerase of each sample was determined by normalization with the HEK 293 cells value (positive control) after extrapolation based upon TS8 (control template provided by the ELISA kit), heat-treated sample (negative control) and the separate reaction where an internal standard (IS, provided by the ELISA kit) were added to the sample. Analyses were done in duplicate.

Statistical Analyses

Data analysis was performed using IBM SPSS, Version 26. This pilot study was not powered to detect statically significant differences/changes in outcomes. Instead, effect sizes, direction of effects, and clinical significance were of interest, though *p* values were calculated. Confidence intervals were given when possible (Odgaard & Fowler, 2010).

Baseline differences in demographic and clinical measures between intervention group and control group were assessed using Fisher's exact tests (categorical variables), independent samples t-tests (for continuous variables) or Mann–Whitney U test (non-normally distributed continuous variables).

Absolute values of TL, TA, hostility, and quality of life were log-transformed to reach a normal or near normal distribution (defensiveness). Change scores were normally distributed and required no transformation.

To evaluate differences between the MBSR and waitlist control group, ANCOVAs controlling for baseline values were conducted on change scores (Evaluation 2 – Baseline). Separate analyses were performed for each dependent variable.

To examine within-group changes as a result of MBSR, repeated measures ANOVAs were performed on each variable comparing the evaluation period prior to MBSR to that post-MBSR and at two-month post intervention. These analyses were performed separately for each dependent variable on all 18 participants (WLCs also underwent the intervention following their second evaluation), as per an intent to treat approach. The Last-Observation-Carry-Forward (LOCF) method was used for one participant who completed the intervention but did not attend the follow-up evaluation. The other five individuals who did not complete the program still attended the follow-up evaluation. The within-subjects analysis was then repeated for individuals (n=13) who completed the MBSR program (i.e. attended at least 6 of the intervention sessions).

Finally, bivariate associations between change scores on each dependant variable (Post minus Pre; Follow-Up minus Pre) and the duration (minutes of practice per week) of formal mindfulness practice at home for those whose who completed the intervention were examined using Spearman correlations (ρ).

Results

Table 1 describes the participants included in the study. No statistically significant differences were observed between the MBSR and WLC groups. No significant baseline differences were observed between those who completed the intervention (N =13) and those who dropped out (N =5) (statistics not shown) except for socioeconomic status which was higher in the MBSR group.

Group (MBSR vs. Waitlist) differences in TL, TA, and psychological change scores

No statistically significant group differences were found for TL, TA, hostility, defensiveness, and QLSI (see table 2). A medium effect size for TA reflected decreased TA in MBSR participants versus an increase in the WLC group. Effect sizes for the other variables were small, or negligible.

Within-Subjects Effects of MBSR as per an Intention-to-Treat Approach (n=18)

There was a statistically significant main effect of Time for TA and QLSI (*p*'s<0.01; both large ES), as indicated in Table 3.

No significant differences were observed in TL (T/S ratio) (*p*'s=ns, small ES). A trend was observed for hostility to decrease over the follow-up period (14.71%, *p*=0.06, medium to large ES). While no change occurred from pre to post MBSR, a 7.35% increase in defensiveness was found over the follow-up period (medium ES).

Within-Subjects Effects of MBSR for Completers (n=13)

Results obtained in those who completed the program were similar to those found in intention-to-treat analyses (refer to Table 3).

Association between at Home Practice Time and Change Scores

Formal MBSR skills were practiced on average 283.80 ±114.60 minutes per week. The amount of weekly home practice was correlated with greater improvements in hostility and TL post-MBSR (small ES's), and continued improvements for hostility (moderate ES) and QoL (small ES) at the 2-month follow-up (refer to Table 4).

Discussion

This pilot RCT examined the possible effects of MBSR on hostility, defensiveness, QoL based on life goals, and telomere regulation in older individuals at risk for CAD by virtue of metabolic risk factors and non-normative autonomic responses to stress. Emphasis was put on direction of effect and effect size in preparation for a larger RCT. In sum, MBSR was associated with improvements in hostility and QoL, stable TL and defensiveness, but surprisingly, with decreases in telomerase. The amount of mindfulness practiced at home was associated with moderate changes in hostility and small changes in QoL, which appears promising for future studies.

Personality traits and MBSR

Hostility scores remained nearly unchanged in the intervention group post-MBSR while it increased by 10.80% in the WLC group. In a previous prospective study in older CAD patients, a difference of 10.80% on the 39-item CMHo was associated with an 18% greater risk (per SD increase) of mortality 3.70 years later (Wong et al., 2014). In analyses combining both groups, two-months following MBSR, there was a near significant, medium-sized decrease of 14.71% (*p*=0.06) in trait hostility, with the greatest change occurring between the end of the intervention and follow-up, suggesting cumulative effects of mindfulness training on hostility over time. These results are consistent with those of Samuelson et al. (2007) who observed a 7.50% reduction in trait hostility (CMHo) post-MBSR in male and female inmates. Findings were corroborated by our participants' feedback that MBSR helped them reduce hostility by promoting better recognition and acceptance of unpleasant affect such as anger: (*"I am less aggravated by my colleagues"; "I feel less angry when I drive"; "I am less reactive and feel that I have better control over my anger"),* providing encouraging preliminary evidence that MBSR may decrease hostility to a clinically significant degree in older individuals at risk for CAD.

No group differences in defensiveness emerged in between-group analyses, though defensiveness did appear to increase over time (by +7.4% at the 2-month follow-up). This is somewhat consistent with a prior cross-sectional study that observed a positive correlation between higher levels of mindfulness and defensiveness (Al Ibrahim, 2013). The meaning of this increase is unclear, though may represent greater interest in wise (noble) choice than an increase in (self- or other-) deception per se, as they reported greater awareness and expression of negative affect and social connectedness, as exemplified by such self-reports as *"When I was angry after the retreat, I told myself -at least I am aware of my anger"* and *"Meeting others and seeing each of their journeys. We were happy to see each other. I want to continue to practice mindfulness every day"*.

Quality of life based on life goals and MBSR

Consistent with previous literature on health-related QoL (De Vibe et al., 2017), QoL improved significantly over the follow-up period post-MBSR in the current study. Indeed, it showed the most notable (34.6%) change amongst our psychological measures, reflecting a large effect size. In contrast to prior investigations that mostly addressed health-related QoL (HRQoL), the current investigation examined a more global, holistic QoL measure based on the extent to which individuals are able to attain their goals in different life domains. This approach may be more appropriate for assessing the impact of holistic interventions such as MBSR whose impacts are broader than solely physical and mental health (Leplège & Hunt, 1997). Our participants' greater ability to attain their life goals, or at least greater appreciation for the life goals achieved, was supported by self-reported improvements in physical health (e.g., *"The MBSR program motivated me to start my physical training again"; "The program helped with my physical illness, to be calmer, and to distract myself from my illness"*), cognitive functioning (*"I am less forgetful of my keys, I look less for my things, and have changed my bridge strategy because I am more self-aware"*), social/family/couple ("*I am a better listener, and more conscious of other's needs, of their joy and of their pain;)*, leisure ("*I also got my best bowling scores ever after doing informal mindfulness practice")*, work ("*I think I have reached my goal to be less stressed at work"*), affectivity ("*I feel happier after I've meditated*") and spirituality (*"I developed self-awareness, and understood what it means to be in the present moment*"). Given that metabolic syndrome has been associated with poorer HRQoL (Ford & Li, 2008), these findings are particularly encouraging.

Telomere and Telomerase Activity

No statistically significant differences in TL were observed post-intervention in the MBSR versus WLC group. In analyses involving both groups post-MBSR, TL decreased slightly post-intervention (small to medium ES) and then stabilized by the 2-month follow-up. Similar decreases in TL were reported post-MBI in middle-aged or older hypertensive (Duraimani et al., 2015) and healthy participants (Le Nguyen et al., 2019), as were stabilization of TL (Schutte et al., 2020). These changes in TL immediately post-MBSR may reflect inter-assay variations, though samples from different time points were assayed in batch to minimize such effects. Alternatively, it may reflect short-term dynamic change prior to stabilization at follow-up, though this remains to be explored. In contrast to our results and those previously mentioned, three larger studies in healthy individuals, experienced meditators, individuals who had undergone more intensive meditation training, and/or who had a much longer follow-up period did find statistically significant increases in TL following an MBI (Conklin et al., 2018; Hoge et al., 2013; Ornish et al., 2013;). Thus, the evidence for increases in TL as a result of an MBI is currently underwhelming, requiring more rigorous investigation using RCT's in larger samples, with longer follow-ups to appreciate the potential cumulative or delayed effects in comparison to non-treated individuals. Results pertaining to telomerase were surprising, with a 44.7% reduction in telomerase activity occurring from pre-MBSR to follow-up. In contrast, most other MBI studies, including some RCTs, had reported increases ranging from 15% to 57.3% in samples drawn from different populations (Schutte & Malouf, 2014; Lengacher et al., 2014), though telomerase increases were also found to a lesser extent in the control group as well (Daubenmier et al. ,2012; Lengacher et al., 2014). It is unclear at this time whether these changes in telomerase have clinical implications, and what could explain differences in findings between this and existing literature. It is possible that the metabolic burden of our participants and subsequent improvements post-MBSR (see Gentile et al., 2021, Annex A) may be implicated. Indeed, higher telomerase levels have been reported among middle-aged men and women with metabolic syndrome (Rentoukas et al., 2012) compared to healthy counterparts, possibly in response to a persisting chronic inflammatory state (Narducci et al., 2007). In that respect, improvements in metabolic burden could be expected to lead to reductions in telomerase.

Influence of Home Practice Time on Outcomes

The benefits of formal home practice in our trial appeared to be maintained and even improve over time for hostility and QoL. To our knowledge, only one previous study investigated the link between home practice and anger in 60 cardiac patients, and reductions in anger were not associated with the home practice measure (Momeni et al., 2016). As for QoL, our findings were slightly greater (small to moderate ES) than two previous studies reported in a meta-analysis that found little to no association between home practice and QoL (very small ES) (Parsons et al. 2017). Defensiveness did not correlate with number or duration of home practice which is not surprising given the limited change that occurred in this measure. A small effect size between home practice and longer TL, but not telomerase, was found; although difficult to interpret at this stage, this was the first study to report effects of home practice on these measures.

Strengths, Limitations, and Future Directions

A major strength of this pilot RCT with waitlist control lies in the rigorous mixed-methods methodology employed, and inclusion of a 2-month follow-up assessment. Moreover, randomization was stratified by sex and stress-response profile, and data on home practice was collected. In addition, the trial conducted in a cardiology institution as a complimentary secondary preventive approach for those at risk for CAD. We measured biological, psychological, and goals-based QoL for a more holistic portrait of change. TL was measured in triplicate and its mean was used for analyses, while telomerase activity was measured in duplicate. To limit bias, the staff performing the psychological measurements or assays were blind to group allocation, while the psychologist facilitating the programme was blind to the participant's stress profile. We also required that participants not have formal experience with mindfulness/meditation training, as experienced practitioners may differ in many respects from novices (e.g, Conklin et al. 2018; Epel et al, 2016).

Nonetheless, the sample size of the current study is an important limitation, and lacked power to detect significant findings. The effect sizes observed however, suggest a promising avenue to conduct larger studies. Given the sample size, we were unable to control for important confounders, other than baseline values, or to examine potential moderator effects of sex or stress response style. Furthermore, this RCT was not conceptualised from the onset to evaluate the effects of MBSR on hostility or defensiveness, but rather to improve metabolic parameters and stress responses. Finally, when fresh blood samples are possible, it would be important to measure the distribution of B- and T- cells separately as their individual rates of TL attrition and telomerase level may differ and affect results (Lin et al., 2010; Lin et al., 2016).

In conclusion, larger RCT's are warranted as engaging in MBSR as an older adult at risk for CAD is not only feasible and well-accepted (Gentile et al., 2021), but our preliminary data suggests that it might also contribute to changes in metabolic burden (Gentile et al., 2021), telomerase, hostility, and QoL. The participants' self-reports and QoL speaks to the added benefit of such interventions in this population of older individuals at risk for CAD. Given the ageing of our population worldwide, and heavy load of chronic disease (WHO, 2018), continued efforts are needed to research efficacy in complementary MBIs.

Clinical implications:

- MBSR decreased trait hostility and improved QoL in older individuals at risk of CAD
- MBSR may lead to TL maintenance at follow-up, though longer programs and follow-up periods are needed to confirm these results.
- Benefits of home practice may be cumulative over time for hostility and QoL, but its impact on telomere regulation needs to be further examined.

Acknowledgements. We would like to thank Anne Lynch, psychologist, for her warm approach to MBSR teaching. Additional thanks to the BEL-AGE participants for their dedication to this project. Thank you to Sea of Tranquility for providing equipment at reduced cost. Finally, thank you to the Canadian Institutes of Health Research, the Montreal Heart Foundation, and the *Ordre Fraternal des Aigles 3176 Inc* (St-Jérome), whose funding made this research possible.

Funding. This study was supported by grants awarded to Dr. D'Antono by the Canadian Institutes of Health Research (CIHR – MOP #111015) and the Montreal Heart Foundation. A dedicated donation was offered to Bianca D'Antono by *Ordre Fraternal des Aigles 3176 Inc* (St-Jérome). Louisia Starnino and Christina Gentile were supported by the Doctoral Training Award issued by the the Fonds de la recherche en santé du Québec (FRSQ). The funding sources had no involvement in this study. No additional funding was received.

Author Information

Affiliations

Research Center, Montreal Heart Institute, 5000 Bélanger street, Montreal, Quebec, Canada, H1T 1C8
Christina Gentile, Louisia Starnino & Bianca D'Antono

Department of Psychology, Université de Montréal, Montreal, Canada
Christina Gentile & Bianca D'Antono
Department of Psychology, Université du Québec à Montréal, Montreal, Canada
Louisia Starnino & Gilles Dupuis
Research Center, Hematology Division, Hôpital Maisonneuve-Rosemont
Lambert Busque & Vincent Bourgoin

Author Contributions. LS, principle investigator, assisted in the design and execution the study, conducted the literature review, performed statistical analyses, and wrote the manuscript. CG, co-principle investigator, designed and executed the study, assisted in the preparation of the manuscript. GD collaborated in the preparation of the manuscript. VB and LB conducted the telomere length and telomerase measurements in laboratory. BDA, co-principle investigator, co-designed and secured funding for the study, collaborated in the writing and editing of the manuscript. All authors approved the final version of the manuscript before submission.

Corresponding author. Correspondence to Bianca D'Antono bianca.d.antono@umontreal.ca

Conflict of Interest. The authors declare that they have no conflict of interest.

Complicance with Ethical Declarations. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

References

Abbott, R. A., Whear, R., Rodgers, L. R., Bethel, A., Coon, J. T., Kuyken, W., & Dickens, C. (2014). Effectiveness of mindfulness-based stress reduction and mindfulness based cognitive therapy in vascular disease: A systematic review and meta-analysis of randomised controlled trials. Journal of psychosomatic research, 76(5), 341-351.https://doi.org/10.1016/j.jpsychores.2014.02.012

Alberti, K. G. M. M., Eckel, R. H., Grundy, S. M., Zimmet, P. Z., Cleeman, J. I., Donato, K. A., & Smith Jr, S. C. (2009). Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation, 120(16), 1640-1645.https://doi.org/10.1161/CIRCULATIONAHA.109.192644

Al Ibrahim, J. (2013). Relationship between dispositional mindfulness and repressive coping style: an exploratory dissertation.

Barefoot, J. C., Dodge, K. A., Peterson, B. L., Dahlstrom, W. G., & Williams, R. B. (1989). The Cook-Medley hostility scale: item content and ability to predict survival. Psychosomatic medicinehttps://doi.org/10.1097/00006842-198901000-00005

Black, D. S., & Slavich, G. M. (2016). Mindfulness meditation and the immune system: a systematic review of randomized controlled trials. Annals of the New York Academy of Sciences, 1373(1), 13.https://doi.org/10.1111/nyas.12998

Blackburn, E. H., Epel, E. S., & Lin, J. (2015). Human telomere biology: a contributory and interactive factor in aging, disease risks, and protection. Science, 350(6265), 1193-1198.https://doi.org/10.1126/science.aab3389

Blackburn, E. H., & Gall, J. G. (1978). A tandemly repeated sequence at the termini of the extrachromosomal ribosomal RNA genes in Tetrahymena. Journal of molecular biology, 120(1), 33-53.https://doi.org/10.1016/0022-2836(78)90294-2

Boyle, S. H., Williams, R. B., Mark, D. B., Brummett, B. H., Siegler, I. C., Helms, M. J., & Barefoot, J. C. (2004). Hostility as a predictor of survival in patients with coronary artery disease. Psychosomatic medicine, 66(5), 629-632.https://doi.org/10.1097/01.psy.0000138122.93942.4a

Brown Wright, L., Gregoski, M. J., Tingen, M. S., Barnes, V. A., & Treiber, F. A. (2011). Impact of stress reduction interventions on hostility and ambulatory systolic blood pressure in African American adolescents. Journal of Black Psychology, 37(2), 210233.https://doi.org/10.1177/0095798410380203

Brydon, L., Lin, J., Butcher, L., Hamer, M., Erusalimsky, J. D., Blackburn, E. H., & Steptoe, A. (2012). Hostility and cellular aging in men from the Whitehall II cohort. Biological psychiatry, 71(9), 767-773.https://doi.org/10.1016/j.biopsych.2011.08.020

Bonfigli, A. R., Spazzafumo, L., Prattichizzo, F., Bonafè, M., Mensà, E., Micolucci, L., Giuliani, A., Fabbietti, P., Testa, R., Boemi, M., Lattanzio, F., & Olivieri, F. (2016). Leukocyte telomere length and mortality risk in patients with type 2 diabetes. Oncotarget, 7(32), 50835-50844.https://doi.org/10.18632/oncotarget.10615

Carlson, L. E., Beattie, T. L., Giese‐Davis, J., Faris, P., Tamagawa, R., Fick, L. J., & Speca, M. (2015). Mindfulness‐based cancer recovery and supportive‐expressive therapy maintain telomere length relative to controls in distressed breast cancer survivors. Cancer, 121(3), 476-484.https://doi.org/10.1002/cncr.29063

Cawthon, R. M. (2002). Telomere measurement by quantitative PCR. Nucleic acids research, 30(10), e47-e47.https://doi.org/10.1093/nar/30.10.e47

Cheng, Y. Y., Kao, T. W., Chang, Y. W., Wu, C. J., Peng, T. C., Wu, L. W., & Chen, W. L. (2017). Examining the gender difference in the association between metabolic syndrome and the mean leukocyte telomere length. PLoS One, 12(7), e0180687.https://doi.org/10.1371/journal.pone.0180687

Chida, Y., & Hamer, M. (2008). Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: a quantitative review of 30 years of investigations. Psychological bulletin, 134(6), 829.https://doi.org/10.1037/a0013342

Chida, Y., & Steptoe, A. (2009). The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. Journal of the American college of cardiology, 53(11), 936-946.https://doi.org/10.1016/j.jacc.2008.11.044

Conklin, Q. A., King, B. G., Zanesco, A. P., Lin, J., Hamidi, A. B., Pokorny, J. J., & Saron, C. D. (2018). Insight meditation and telomere biology: The effects of intensive retreat and the moderating role of personality. Brain, behavior, and immunity, 70, 233-245.https://doi.org/10.1016/j.bbi.2018.03.00

Cook, W. W., & Medley, D. M. (1954). Proposed hostility and pharisaic-virtue scales for the MMPI. Journal of Applied psychology, 38(6), 414.https://doi.org/10.1037/h0060667

Crowne, D. P., & Marlowe, D. (1960). A new scale of social desirability independent of psychopathology. Journal of consulting psychology, 24(4), 349.https://doi.org/10.1037/h0047358

D'Antono, B., Moskowitz, D. S., & Nigam, A. (2013). The metabolic costs of hostility in healthy adult men and women: cross-sectional and prospective analyses. Journal of psychosomatic research, 75(3), 262-269.https://doi.org/10.1016/j.jpsychores.2013.05.010

Daubenmier, J., Lin, J., Blackburn, E., Hecht, F. M., Kristeller, J., Maninger, N.,& Epel, E. (2012). Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study. Psychoneuroendocrinology, 37(7), 917-928.https://doi.org/10.1016/j.psyneuen.2011.10.008

De Vibe, M., Bjørndal, A., Fattah, S., Dyrdal, G. M., Halland, E., & Tanner‐Smith, E. E. (2017). Mindfulness‐based stress reduction (MBSR) for improving health, quality of life and social functioning in adults: a systematic review and meta‐analysis. Campbell systematic reviews, 13(1), 1-264.https://doi.org/10.4073/csr.2017.11

D'Mello, M. J., Ross, S. A., Briel, M., Anand, S. S., Gerstein, H., & Paré, G. (2015). Association between shortened leukocyte telomere length and cardiometabolic outcomes: systematic review and meta-analysis. Circulation: cardiovascular genetics, 8(1), 82-90.https://doi.org/10.1161/CIRCGENETICS.113.000485

Dupuis, G., Marois, D., & Etienne, A. M. (2012). La mesure de la qualité de vie: le modèle des systèmes de contrôle, une approche théorique pratique pour parler du bonheur. Revue Francophone de Clinique Comportementale et Cognitive, 17(1), 4-14.

Dupuis, G., Perrault, J., Lambany, M. C., Kennedy, E., & David, P. (1989). A new tool to assess quality of life: The quality of life systemic inventory. Quality of life and cardiovascular care, 5(1), 36-45.

Duraimani, S., Schneider, R. H., Randall, O. S., Nidich, S. I., Xu, S., Ketete, M., Rainforth, M. A., Gaylord-King, C., Salerno, J. W., & Fagan, J. (2015). Effects of Lifestyle Modification on Telomerase Gene Expression in Hypertensive Patients: A Pilot Trial of Stress Reduction and Health Education Programs in African Americans. PloS one, 10(11), e0142689. https://doi.org/10.1371/journal.pone.0142689

Eisenberg, D. T. (2011). An evolutionary review of human telomere biology: the thrifty telomere hypothesis and notes on potential adaptive paternal effects. American Journal of Human Biology, 23(2), 149-167.https://doi.org/10.1002/ajhb.21127

Epel, E. S., Puterman, E., Lin, J., Blackburn, E. H., Lum, P. Y., Beckmann, N. D., & Schadt, E. E. (2016). Meditation and vacation effects have an impact on disease-associated molecular phenotypes. Translational psychiatry, 6(8), e880-e880.https://doi.org/10.1038/tp.2016.164

Ford, E. S., & Li, C. (2008). Metabolic syndrome and health-related quality of life among US adults. Annals of epidemiology, 18(3), 165-171. https://doi.org/10.1016/j.annepidem.2007.10.009

Gentile, C., Ditto, B., Deschamps, A., & D'Antono, B. (2019). Parasympathetic response patterns are associated with metabolic syndrome among older women but not men. Annals of Behavioral Medicine, 53(6), 515-526.https://doi.org/10.1093/abm/kay063

Gentile, C., Starnino, L., Dupuis, G., & D'Antono, B. (2021). Mindfulness-Based Stress Reduction in Older Adults at Risk for Coronary Artery Disease: A Pilot Randomized Trial. Clinical Gerontologist, 1-15.https://doi.org/10.1257/rct.6420-1.0

Greider, C. W., & Blackburn, E. H. (1985). Identification of a specific telomere terminal transferase activity in Tetrahymena extracts. cell, 43(2), 405-413.https://doi.org/10.1016/0092-8674(85)90170-9

Henderson, V. P., Massion, A. O., Clemow, L., Hurley, T. G., Druker, S., & Hébert, J. R. (2013). A randomized controlled trial of mindfulness-based stress reduction for women with early-stage breast cancer receiving radiotherapy. Integrative cancer therapies, 12(5), 404-413.https://doi.org/10.1177/1534735412473640

Hoge, E. A., Chen, M. M., Orr, E., Metcalf, C. A., Fischer, L. E., Pollack, M. H., & Simon, N. M. (2013). Loving-Kindness Meditation practice associated with longer telomeres in women. Brain, behavior, and immunity, 32, 159-163.https://doi.org/10.1016/j.bbi.2013.04.005

Innes, K. E., Selfe, T. K., Brundage, K., Montgomery, C., Wen, S., Kandati, S., & Huysmans, Z. (2018). Effects of meditation and music-listening on blood biomarkers of cellular aging and Alzheimer's disease in adults with subjective cognitive decline: An exploratory randomized clinical trial. Journal of Alzheimer's Disease, 66(3), 947-970.https://doi.org/10.3233/JAD-180164

Jahangirpour, M., Musavi, S. V., Khosrojavid, M., Salari, A., & Rezaei, S. (2013). The effectiveness of group mindfulness training on depression, hostility and anxiety in individuals with coronary heart disease. Studies in Medical Sciences, 24(9), 730-739.

Jorgensen, R. S., Frankowski, J. J., Lantinga, L. J., Phadke, K., Sprafkin, R. P., & Abdul-Karim, K. W. (2001). Defensive hostility and coronary heart disease: a preliminary investigation of male veterans. Psychosomatic medicine, 63(3), 463-469.https://doi.org/10.1097/00006842-200105000-00016

Julkunen, J., & Ahlström, R. (2006). Hostility, anger, and sense of coherence as predictors of health-related quality of life. Results of an ASCOT substudy. Journal of Psychosomatic Research, 61(1), 33-39.https://doi.org/10.1016/j.jpsychores.2005.12.005

Kabat-Zinn, J. (2003). Mindfulness-based stress reduction (MBSR). Constructivism in the Human Sciences, 8(2), 73.

Keng, S. L., Yim, O. S., San Lai, P., Chew, S. H., & Ebstein, R. P. (2019). Association among dispositional mindfulness, self-compassion, and leukocyte telomere length in Chinese adults. BMC psychology, 7(1), 1-10.https://doi.org/10.1186/s40359-019-0323-y

Khalangot, M., Krasnienkov, D., & Vaiserman, A. (2020). Telomere length in different metabolic categories: Clinical associations and modification potential. Experimental Biology and Medicine, 245(13), 1115-1121.https://doi.org/10.1177/1535370220931509

Lengacher, C. A., Reich, R. R., Kip, K. E., Barta, M., Ramesar, S., Paterson, C. L., & Park, J. Y. (2014). Influence of mindfulness-based stress reduction (MBSR) on telomerase activity in women with breast cancer (BC). Biological research for nursing, 16(4), 438-447.https://doi.org/10.1177/1099800413519495

Le Nguyen, K. D., Lin, J., Algoe, S. B., Brantley, M. M., Kim, S. L., Brantley, J., & Fredrickson, B. L. (2019). Loving-kindness meditation slows biological aging in novices: Evidence from a 12-week randomized controlled trial. Psychoneuroendocrinology, 108, 20-27.https://doi.org/10.1016/j.psyneuen.2019.05.020

Leplège A, Hunt S. The Problem of Quality of Life in Medicine. JAMA. 1997;278(1):47-50.https://doi.org/10.1001/jama.278.1.47

Lévesque, K., Moskowitz, D. S., Tardif, J. C., Dupuis, G., & D'antono, B. (2010). Physiological stress responses in defensive individuals: Age and sex matter. Psychophysiology, 47(2), 332-341.https://doi.org/10.1111/j.1469-8986.2009.00943.x

Lin, J., Cheon, J., Brown, R., Coccia, M., Puterman, E., Aschbacher, K., & Blackburn, E. H. (2016). Systematic and cell type-specific telomere length changes in subsets of lymphocytes. Journal of immunology research, 2016.https://doi.org/10.1155/2016/5371050

Lin, J., Epel, E., Cheon, J., Kroenke, C., Sinclair, E., Bigos, M., & Blackburn, E. (2010). Analyses and comparisons of telomerase activity and telomere length in human T and B cells: insights for epidemiology of telomere maintenance. Journal of immunological methods, 352(1-2), 71-80.https://doi.org/10.1016/j.jim.2009.09.012

Lin, I. M., Weng, C. Y., Lin, T. K., & Lin, C. L. (2015). The Relationship between Expressive/Suppressive Hostility Behavior and Cardiac Autonomic Activations in Patients with Coronary Artery Disease. Acta Cardiologica Sinica, 31(4), 308-316. https://doi.org/10.1007/s12671-017-0813-z

Lloyd, A., White, R., Eames, C., & Crane, R. (2018). The utility of home-practice in mindfulness-based group interventions: a systematic review. Mindfulness, 9(3), 673-692.https://doi.org/10.1007/s12671-017-0813-z

Loo, R., & Thorpe, K. (2000). Confirmatory factor analyses of the full and short versions of the Marlowe-Crowne Social Desirability Scale. The Journal of social psychology, 140(5), 628-635.https://doi.org/10.1080/00224540009600503

MacCoon, D. G., Imel, Z. E., Rosenkranz, M. A., Sheftel, J. G., Weng, H. Y., Sullivan, J. C., & Lutz, A. (2012). The validation of an active control intervention for Mindfulness Based Stress Reduction (MBSR). Behaviour research and therapy, 50(1), 3-12.https://doi.org/10.1016/j.brat.2011.10.011

Momeni, J., Omidi, A., Raygan, F., & Akbari, H. (2016). The effects of mindfulness-based stress reduction on cardiac patients' blood pressure, perceived stress, and anger: a single-blind randomized controlled trial. Journal of the American Society of Hypertension, 10(10), 763-771.https://doi.org/10.1016/j.jash.2016.07.007

Narducci, M. L., Grasselli, A., Biasucci, L. M., Farsetti, A., Mulè, A., Liuzzo, G., & Crea, F. (2007). High telomerase activity in neutrophils from unstable coronary plaques. Journal of the American College of Cardiology, 50(25), 2369-2374.https://doi.org/10.1016/j.jacc.2007.08.048

Niaura, R., Todaro, J. F., Stroud, L., Spiro III, A., Ward, K. D., & Weiss, S. (2002). Hostility, the metabolic syndrome, and incident coronary heart disease. Health Psychology, 21(6), 588.https://doi.org/10.1037/0278-6133.21.6.588

Norman, H., Marzano, L., Coulson, M., & Oskis, A. (2019). Effects of mindfulness-based interventions on alexithymia: a systematic review. Evidence-based mental health, 22(1), 36-43.https://doi.org/10.1136/ebmental-2018-300029

Robins, C. J., Keng, S. L., Ekblad, A. G., & Brantley, J. G. (2012). Effects of mindfulness - based stress reduction on emotional experience and expression: A randomized controlled trial. Journal of clinical psychology, 68(1), 117-131.https://doi.org/10.1002/jclp.20857

Odgaard, E. C., & Fowler, R. L. (2010). Confidence intervals for effect sizes: Compliance and clinical significance in the Journal of Consulting and Clinical Psychology.. Journal of Consulting and Clinical Psychology, 78(3), 287.https://doi.org/10.1037/a0019294

Olivo, E. L., Dodson-Lavelle, B., Wren, A., Fang, Y., & Oz, M. C. (2009). Feasibility and effectiveness of a brief meditation-based stress management intervention for patients diagnosed with or at risk for coronary heart disease: a pilot study. Psychology, health & medicine, 14(5), 513-523.https://doi.org/10.1080/13548500902890087

Ornish, D., Lin, J., Chan, J. M., Epel, E., Kemp, C., Weidner, G., & Blackburn, E. H. (2013). Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study. The lancet oncology, 14(11), 1112-1120.https://doi.org/10.1016/S1470-2045(13)70366-8

Parsons, C. E., Crane, C., Parsons, L. J., Fjorback, L. O., & Kuyken, W. (2017). Home practice in mindfulness-based cognitive therapy and mindfulness-based stress reduction: a systematic review and meta-analysis of participants' mindfulness practice and its association with outcomes. Behaviour research and therapy, 95, 29-41.https://doi.org/10.1016/j.brat.2017.05.004

Paulhus, D. L. (1984). Two-component models of socially desirable responding. Journal of personality and social psychology, 46(3), 598.https://doi.org/10.1037/0022-3514.46.3.598

Randal, C., Pratt, D., & Bucci, S. (2015). Mindfulness and self-esteem: a systematic review. Mindfulness, 6(6), 1366-1378.https://doi.org/10.1007/s12671-015-0407-6

Rentoukas, E., Tsarouhas, K., Kaplanis, I., Korou, E., Nikolaou, M., Marathonitis, G., & Tsitsimpikou, C. (2012). Connection between telomerase activity in PBMC and markers of inflammation and endothelial dysfunction in patients with metabolic syndrome. PloS one, 7(4), e35739.https://doi.org/10.1371/journal.pone.0035739

Reynolds, W. M. (1982). Development of reliable and valid short forms of the Marlowe‐Crowne Social Desirability Scale. Journal of clinical psychology, 38(1), 119-125.https://doi.org/10.1002/1097-4679(198201)38:1<119::AID-JCLP2270380118>3.0.CO;2-I

Révész, D., Milaneschi, Y., Verhoeven, J. E., & Penninx, B. W. (2014). Telomere length as a marker of cellular aging is associated with prevalence and progression of metabolic syndrome. The Journal of Clinical Endocrinology & Metabolism, 99(12), 4607-4615.https://doi.org/10.1210/jc.2014-1851

Rosenkranz, M. A., Davidson, R. J., MacCoon, D. G., Sheridan, J. F., Kalin, N. H., & Lutz, A. (2013). A comparison of mindfulness-based stress reduction and an active control in modulation of neurogenic inflammation. Brain, behavior, and immunity, 27, 174-184.https://doi.org/10.1016/j.bbi.2012.10.013

Samuelson, M., Carmody, J., Kabat-Zinn, J., & Bratt, M. A. (2007). Mindfulness-based stress reduction in Massachusetts correctional facilities. The Prison Journal, 87(2), 254-268.https://doi.org/10.1177/0032885507303753

Schutte, N. S., & Malouff, J. M. (2014). A meta-analytic review of the effects of mindfulness meditation on telomerase activity. Psychoneuroendocrinology, 42, 45-48.https://doi.org/10.1016/j.psyneuen.2013.12.017

Schutte, N. S., Malouff, J. M., & Keng, S. L. (2020). Meditation and telomere length: a meta-analysis. Psychology & health, 35(8), 901-915.https://doi.org/10.1080/08870446.2019.1707827

Sharma, M., & Rush, S. E. (2014). Mindfulness-based stress reduction as a stress management intervention for healthy individuals: a systematic review. Journal of evidence-based complementary & alternative medicine, 19(4), 271-286.https://doi.org/10.1177/2156587214543143

Sibinga, E. M., Kerrigan, D., Stewart, M., Johnson, K., Magyari, T., & Ellen, J. M. (2011). Mindfulness-based stress reduction for urban youth. The Journal of Alternative and Complementary Medicine, 17(3), 213-218.https://doi.org/10.1089/acm.2009.0605

Smith, T. W. (1994). Concepts and methods in the study of anger, hostility, and health. Anger, hostility, and the heart, 23-42.

Smith, T. W., & Frohm, K. D. (1985). What's so unhealthy about hostility? Construct validity and psychosocial correlates of the Cook and Medley Ho scale. Health Psychology, 4(6), 503.https://doi.org/10.1037/0278-6133.4.6.503

Starnino, L., Busque, L., Tardif, J. C., & D'Antono, B. (2016). Psychological profiles in the prediction of leukocyte telomere length in healthy individuals. PloS one, 11(10), e0165482.https://doi.org/10.1371/journal.pone.0165482

Starnino, L., Dupuis, G., Busque, L., Bourgoin, V., Dubé, M. P., Busseuil, D., & D'Antono, B. (2021). The associations of hostility and defensiveness with telomere length are influenced by sex and health status. Biology of Sex Differences, 12(1), 1-13.https://doi.org/10.1186/s13293-020-00349-w

Thomas, M. C., Kamarck, T. W., Wright, A. G., Matthews, K. A., Muldoon, M. F., & Manuck, S. B. (2020). Hostility Dimensions and Metabolic Syndrome in a Healthy, Midlife Sample. International journal of behavioral medicine, 1-6.https://doi.org/10.1007/s12529-020-09855-y

Truong, E. A., Olson, K. L., & Emery, C. F. (2016). Repressive coping, stigmatization, psychological distress, and quality of life among behavioral weight management participants. Eating behaviors, 22, 206-210.https://doi.org/10.1016/j.eatbeh.2016.06.007

Tsikandilakis, M., Bali, P., Derrfuss, J., & Chapman, P. (2020). Anger and hostility: are they different? An analytical exploration of facial-expressive differences, and physiological and facial-emotional responses. Cognition and Emotion, 34(3), 581-595.https://doi.org/10.1080/02699931.2019.1664415

Wang, Q., Zhan, Y., Pedersen, N. L., Fang, F., & Hägg, S. (2018). Telomere length and all-cause mortality: a meta-analysis. Ageing research reviews, 48, 11-20.https://doi.org/10.1016/j.arr.2018.09.002

Wong, J. M., Sin, N. L., & Whooley, M. A. (2014). A comparison of cook-medley hostility subscales and mortality in patients with coronary heart disease: data from the heart and soul study. Psychosomatic Medicine, 76(4), 311-317.https://doi.org/10.1097/PSY.0000000000000059

World Health Organization. (2018). Aging and Health. Retrieved from https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

World Health Organization. (2021). Measuring Quality of Life. Retrieved from https://www.who.int/tools/whoqol

Wright, S., Day, A., & Howells, K. (2009). Mindfulness and the treatment of anger problems. Aggression and Violent Behavior, 14(5), 396-401.https://doi.org/10.1016/j.avb.2009.06.008

Young, L. A., Cappola, A. R., & Baime, M. J. (2009). Mindfulness based stress reduction: effect on emotional distress in diabetes. Practical Diabetes International, 26(6), 222-224.https://doi.org/10.1002/pdi.1380

Zalli, A., Carvalho, L. A., Lin, J., Hamer, M., Erusalimsky, J. D., Blackburn, E. H., & Steptoe, A. (2014). Shorter telomeres with high telomerase activity are associated with raised allostatic load and impoverished psychosocial resources. Proceedings of the National Academy of Sciences, 111(12), 4519-4524.https://doi.org/10.1073/pnas.1322145111

Zhang, J., Niaura, R., Todaro, J. F., McCaffery, J. M., Shen, B. J., Spiro, A., & Ward, K. D. (2005). Suppressed hostility predicted hypertension incidence among middle-aged men:

The normative aging study. Journal of behavioral medicine, 28(5), 443-454. https://doi.org/10.1007/s10865-005-9016-5

Table 1.

Participant characteristics (Mean ± SD or %) at Baseline

	MBSR (n=9)	**Waitlist (n=10)**	**Baseline Group Differences**		
Parameters	*M (SD)* or *n* *(%)*	*M (SD)* or *n* *(%)*	*p*	Cohen's *d*	*Cramer's V*
Sex, male[a]	4 (44.4)	3 (33.3)	0.63	-	.11
Age (years)[b]	69.56 (5.0)	64.78 (9.8)	0.21	.61	-
BMI (kg/m^2) [b]	29.46 (4.6)	31.86 (4.4)	0.27	.53	-
Years of schooling[b]	14.56 (3.4)	14.11 (2.3)	0.75	.16	-
Marital Status[a]					
Single	2 (22.2)	2 (20)	1.00	-	.00
Civil union/married	6 (66.7)	4 (40)	0.34	-	.15
Separated/divorced	1 (11.1)	3 (30)	0.58	-	.27
Employment Status[a]					
*Full-time**	1 (11.1)	3 (30)	0.58	-	.27
Part-time	1 (11.1)	2 (20)	0.53	-	.15
*Retired**	7 (77.8)	4 (40)	0.15	-	.34
Annual family income[a]					
≤ $29 999	0 (0)	4 (40)	0.023	-	.54
*$30 000 - $59 999**	5 (55.6)	1 (10)	0.046	-	.47
$60 000 - $99 999	2 (22.2)	2 (20)	1.00	-	.00
≥ $100 000	2 (22.2)	2 (20)	1.00	-	.00
Hours of exercise/week[b]	5.10 (4.28)	2.89 (3.29)	0.24	.58	
Medications[a]					
Blood pressure agents	7 (78)	3 (30)	0.06	-	.45
Blood glucose regulators	1 (11)	3 (30)	0.26	-	.27
Dyslipidemic agents	6 (66)	4 (40)	0.34	-	.22
Antidepressants	0 (0)	1 (10)	0.30	-	.24
MetS criteria[a]					
≥ 3 criteria	3 (33%)	6 (60)	0.69	-	.33
2 criteria	3 (33%)	2 (20)	0.81	-	.12

1 criteria	3 (33%)	1 (10)	0.59	-	.27
Psychological Parameters[b]					
Hostility (CMHo)	12.78 (4.98)	14.33 (4.80)	0.51	.02	-
Defensiveness (MCSD)	9.00 (2.12)	9.67 (2.05)	0.48	.33	-
Quality of life (QoL)	4.81 (4.69)	3.47 (2.06)	0.42	.37	-
Telomere Regulation					
Telomere length (T/S ratio)	0.91 (0.17)	0.96 (0.23)	0.61	.25	-
Telomerase (RTA ratio)	1.92 (1.98)	1.40 (1.10)	0.49	.32	-

Note. [a]*n,* (%); [b]mean (±SD); Independent samples t-test were used for continuous variables and Fisher's Exact Test or Chi^2 were used for categorical variables. Effect sizes (ES)=Cohen's d: .2 (small ES), .5 (medium ES), .8 (large ES) for continuous variables; Cramer's V:.1 (small ES), .3 (medium ES), .5 (large ES) for categorical variables. MetS=metabolic syndrome; T/S=telomere to single-copy gene ratio units; RTA=Relative Telomerase activity is expressed as equivalent of the number of human leukocyte 293T cell control per 10 000 peripheral blood mononuclear cells; CMHo=Cook-Medley Hostility Scale ; MCSD=Marlowe-Crowne Social Desirability Scale; QoL=Quality of life Systemic Inventory based on life goals.

Table 2.

Impact of MBSR compared to Waitlist Control Group for Intention to Treat (n=18)

Parameters	MBSR group (n =9)	Waitlist control group (n=9)	Between-group Change Score Comparison
	Mean (SD)	Mean (SD)	ANCOVA[c] Effect Size, 95% CI
Hostility			
Pre-intervention	12.78 (4.92)	13.33 (3.93)	
Post-intervention	13.00 (6.42)	14.78 (3.70)	F(1,17)=0.54 *p*=.47
Change Score	0.22 (4.35)	1.44 (2.92)	$\eta^2{}_p$= .04 [0.00-0.27]
Percent Change	+1.72%	+10.80%	
Defensiveness			
Pre-intervention	9.00 (2.12)	9.67 (2.18)	
Post-intervention	9.33 (3.87)	9.22 (2.95)	F(1,17)=0.52 *p*=.48
Change Score	0.33 (2.60)	-0.44 (2.29)	$\eta^2{}_p$= .03 [0.00-0.26]
Percent Change	+3.67%	-4.55%	
Quality of Life			
Pre-intervention	4.81 (4.69)	3.61 (2.15)	
Post-intervention	3.91 (6.57)	3.10 (1.88)	F(1,17)=0.30 *p*=0.59
Change Score	-0.91 (2.58)	-0.54 (1.92)	$\eta^2{}_p$= 0.02, [0.00-0.25]
Percent Change	-18.92%	-14.96%	
Telomere Length[a]			
Pre-intervention	0.91 (0.17)	0.98 (0.23)	
Post-intervention	0.93 (0.25)	0.99 (0.23)	F(1,17)=0.001 *p*=.98
Change Score	0.02 (0.13)	0.01 (0.13)	$\eta^2{}_p$ =<.01 [0.00-0.002]
Percent Change	+2.20%	+1.02%	
Telomerase Activity[b]			
Pre-intervention	1.92 (1.98)	1.24 (1.02)	
Post-intervention	1.19 (0.74)	1.89 (1.54)	F(1,17)=1.16 *p*=.30
Change Score	-0.74 (2.04)	0.64 (2.15)	$\eta^2{}_p$= .07 [0.00-0.38]
Percent Change	-38.54%	+51.61%	

Note. Means represent raw data. Effect size (partial n^2): 0.01 (small), 0.06 (medium) and 0.14 (large). [a]Telomere Length is expressed by relative telomere to single-copy gene ratio units

[b]Telomerase activity is expressed by a ratio *relative* to *telomerase* activity of the positive control (HEK)

[c]ANCOVA: controlled for baseline values

Table 3.

Changes in Telomere Regulation, Psychological Traits, and Quality of Life Using an Intent-to Treat Approach (n = 18) and in Completers (n=13)

Parameters	**Intention-to-reat** (n=18); **Completers** (n=13)	**Pre - MBSR**	**Post-MBSR**	**Follow-up**	**% Change** Post-Pre	**% Change** Follow-Up - Pre	**% Change** Follow-up-Post	**Repeated Measures Anova**	
		M (SD)	*M (SD)*	*M (SD)*				*F*	*partial* n^2
Hostility	18	14.00 (4.91)	13.33 (5.73)	11.94 (4.63)	-4.79	-14.71	-10.43	2.38	.12
	13	15.31 (4.80)	14.85 (5.32)	13.23 (4.00)	-3.00	-13.59	-10.91	1.24	.09
Defensiveness	18	9.11 (2.49)	9.11 (3.31)	9.78 (3.14)	0.00	7.35	7.35	1.46	.08
	13	8.85 (2.23)	8.69 (3.40)	9.54 (3.20)	-1.81	7.80	9.78	1.08	.08
Quality of Life	18	3.96 (3.58)	3.26 (4.65)	2.51 (2.97)	-17.68	-36.62	-23.01	5.92**	.26
	13	4.37 (4.02)	3.76 (5.42)	2.87(3.44)	-13.96	-34.32	-23.67	4.44*	.27
Telomere Length	18	0.95 (0.20)	0.93 (0.24)	0.92 (0.15)	-2.10	-3.16	-1.08	0.79	.04
	13	0.93 (0.18)	0.88 (0.19)	0.88 (0.13)	-5.91	-5.16	-0.79	1.64	.12
Telomerase Activity	18	1.90 (1.72)	1.63 (2.15)	1.05 (1.36)	-14.21	-44.74	-35.59	6.21**	.27
	13	1.53 (1.68)	1.54 (2.47)	1.15 (1.39)	0.65	-24.84	-25.32	2.03	.15

Note. Means (SD) and % change performed on raw data; analyses were performed on transformed data. Effect size partial η^2: .01 (small), .06 (medium), .14 (large)

*$p < .05$. **$p < .01$

Table 4.

Bivariate Associations Between at Home Mindfulness Practice and Outcome Measures

Change Scores (Post-Pre MBSR)	**Minutes of Practice /Week** Spearman's ρ	*p*
Hostility	-.30	.32
Defensiveness	.06	.84
Quality of life	-.20	.52
Telomere Length	.29	.33
Telomerase Activity	-.17	.58
Change Scores (FU-Pre MBSR)		
Hostility	-.44	.19
Defensiveness	.07	.82
Quality of life[a]	-.35	.24
Telomere Length	.11	.72
Telomerase Activity	-.15	.63

Note. Spearman coefficient effect size: .00-.19 (very small); .20-.39 (small); .40-.59 (moderate); .60-.79 (strong); .80-1.0 (very strong).

a. Greater values on QoL measure represent worse Qol, as it represents a greater gap between one's current situation and desired outcome on a variety of dimensions.

CHAPTER III: GENERAL DISCUSSION

The following chapter will synthesize the main findings from this dissertation, the clinical and methodological implications, highlight its strengths and limitations, as well as provide recommendations and ideas for knowledge transfer.

3.1 Summary

A body of cross-sectional and prospective evidence suggests that individuals whose personality traits include greater hostility and/or defensiveness are at increased risk for disease development and mortality, including coronary artery disease (CAD) (Chida & Steptoe, 2009; Denollet et al., 2008). It has been suggested that this increase in risk may be a consequence of the pathophysiological dysregulations, in response to (di)stress, of the cardiovascular, autonomic, and endocrine systems observed in individuals bearing these personality traits (D'Antono et al, 2013; Jorgensen et al., 1996; King et al., 1990; Shimbo et al., 2009). The ensuing allostatic load may in turn have deleterious effects on cellular processes and contribute to premature biological aging (Ahrens et al., 2016; McEwen et al. 1998; Picard et al., 2014), as reflected by the length of telomeres. Consistent with this, recent evidence suggests an association between the length of telomeres in cells, hostility and defensiveness (Brydon et al., 2012; Jordan et al., 2019; Starnino et al., 2016). However, investigations pertaining to these and other related traits (e.g. pessimism, neuroticism, lower agreeablenesss, Type-D personality) have been limited. Moreover, results found for hostility and TL have been mixed. While some have reported hostility to be negatively associated with TL, we previously found the opposite (Brydon et al., 2012; Jordan et al., 2019; Starnino al., 2016; Watkins et al., 2016). Some researchers have suggested sex or age differences in some instances (Brydon et al., 2012; Jordan et al., 2019; Savolainen et al., 2015; Starnino et al., 2016), and associations have not always been independent of medical conditions or cardiometabolic risk factors (Huzen et al., 2010; Savolainen et al., 2015). Given the poorer prognosis related to shorter TL in individuals with chronic illnesses such as CAD (Haycock et al., 2014), as well as the association between personality traits and the development of chronic illnesses and all-cause mortality (Appleton et al., 2016; Chen et al., 2019; Denollet et al., 2008; Klabbers et al., 2013), examination of the impact of health status on the relation between these particular traits and TL appeared warranted.

Developmental changes among older individuals, and their greater likelihood of suffering from a variety of ailments could theoretically alter the relation between personality and TL, but this had yet to be examined before this thesis. For example, meta-analyses suggest that hostility contributes to a higher risk of CAD events in healthy men compared to women (Chida & Steptoe, 2009) and in older (60 years and over) individuals compared to their younger counterparts (Chen et al., 2019). Nonetheless, greater hostility particularly in older healthy women, increases risk for all-cause mortality compared to their less hostile female counterparts (Tindle et al., 2009).

Moreover, accessible group psychosocial interventions such as mindfulness-based stress reduction programs (e.g., MBSR) targeting these traits, as well as telomere regulation, in older individuals at risk for CAD have similarly been scarce. Investigations with follow-up evaluations and/or adopting a more holistic examination of the potential impact of MBI's on telomere regulation, psychosocial measures, as well as quality of life based on life goals are scant.

This thesis was composed of two independent investigations, a larger cross-sectional study and a small pilot randomized controlled trial. The prior aimed to explore the relationship between maladaptive personality traits, such as hostility and defensiveness, and their relationship with TL, in individuals with or without CAD (study 1) while examining the moderating effect of sex and health status. Secondary analyses were performed in a small group of healthy individuals, in order to attempt to support findings from a prior study performed in our laboratory (Starnino et al., 2016). The randomized controlled pilot trial, for its part, sought to assess the feasibility and acceptability of MBSR versus a waitlist control group in an older sample of individuals at increased risk for CAD (Annex A). It also sought to assess its potential impact on trait hostility, defensiveness, quality of life based on life goals, and telomere regulation (TL and telomerase enzyme), following treatment and 2-months later.

3.2 Results in Context for Article 1

This cross-sectional study found that sex and health status moderate the relationship between hostility, defensiveness, and TL. More specifically, greater hostility was associated with significantly shorter TL in women (independent of CAD health status) but with longer TL among healthy men, while greater defensiveness was associated with longer TL in individuals with CAD, but with shorter TL in healthy men.

The most robust finding from Article 1 of this thesis was that TL were shorter among women who were more hostile versus less hostile, independently of a number of sociodemographic, behavioural, and medical covariates, including symptoms of depression, anxiety, and perceived stress. In healthy men, on the other hand, hostility was associated with longer, not shorter telomeres. Results in regard to hostility in women was consistent with some of the literature suggesting shorter TL in those with higher levels of hostility (Brydon et al., 2012; Watkins et al., 2016). The results found for Caucasian women in our sample corroborated those of Jordan and colleagues (2019) who also reported an inverse relation between hostility and TL in a sample of African-American women, but not men, regardless of their current physical health status (with or without chronic disease). This independence of the results from health status in that and in the current investigation, suggests that shorter TL are not necessarily a result of pathophysiological changes associated with these present illnesses. It might rather reflect, at least, in part, processes that may have contributed to disease development. What these processes are require further research.

The longer TL among our more hostile healthy men contradicts the findings of two previous studies (Brydon et al., 2012; Watkins et al., 2016), but is partially consistent with those of our previous investigation (Starnino et al., 2016), in which a positive association between TL and hostility was observed. The prognostic significance of longer TL with greater hostility among healthy men remains to be determined. However, results may reflect that these more hostile men who remained healthy despite their older age are more resilient to the effects of their hostility – genetically, physically, or psychologically, and/or conversely, those that were specifically vulnerable to the effects of hostility may have died prematurely and thus not been able to participate in BEL-AGE. Unpublished data from a thesis tends to support the idea of an age effect on the relation between hostility and TL (Carroll, 2010). In that study, that included 160 untreated hypertensive Caucasian and African-American men, an inverse association between hostility with TL was found among younger participants (40's), in contrast to a positive association among older individuals (60's) after controlling for important sociodemographic, behavioural, and medical covariates. Nonetheless, in an earlier study (Starnino et al., 2016), we observed no moderating effect of age on the positive association between TL and hostility among individuals 18-65 years of age. A noteworthy fact in our earlier study was our attention to ensuring similar distributions of people across the age span. Discrepant findings such as these may also represent a file-drawer problem (Rosenthal, 1979), where null or unexpected findings (such as longer TL with hostility) are less likely to be published, hence skewing our understanding of the implications of hostility on telomeres.

Alternatively, while longer TL is typically considered to be healthier, there is data to suggest that longer TL may in some cases be more pathogenic. For example, longer TL has been reported in individuals with left ventricular hypertrophy compared with control subjects (Kunetsova et al., 2010; Vasan et al., 2009). Longer TL in peripheral blood leukocytes has also been associated with a significantly increased risk of various forms of cancers such as pancreatic, breast, prostate, and lung cancer amongst others (Lan et al., 2013; Luu et al., 2019; Sun et al., 2015), though conflicting results are apparent for colorectal cancer (Wang et al., 2017). In the case of cancer, it has been proposed that the additional rounds of cell division occurring because of the long telomeres provide the cell (and its daughter cells) the opportunity to accumulate genetic mutations that block the pathways to cellular aging (senescence) and cellular death (apoptosis), thereby promoting cancer (Shay & Wright, 2011). Among cells in which the pathways to cellular senescence and apoptosis are blocked, those with shorter telomeres can also be prone to end-to-end chromosome fusions and consequent chromosomal instability, a contributor to the development of cancer (Shay & Wright, 2011). Thus, it has been suggested that a balance between elongation by telomerase and telomere shortening is important to produce a stabilized 'optimal' length that is critical for cell proliferation, senescence, and control (Ducray et al., 1999). Moreover, longer TL has also been prospectively related to diseases not related to cancer, such as dementia in patients with Parkinson's disease or Progressive Supranuclear Palsy (Degerman et al., 2014). These emerging data remind us that our understanding of telomere biology and its sequelae is still preliminary, and that interpretation of shorter TL as "bad or worse" is clearly too facile.

3.2.1 Hostility in Women and Men

Reasons underlying the sex difference observed in the relation between hostility and TL in the current study are for the most part speculative, but may partly reflect gender-based differences in hostility. Gender stereotypes commonly reflect a distinction between two dimensions; agency (self-assertion, competency, efficiency), and communion (connection with others) (Eagly, 2009; Jost & Kay, 2005). While many gender-related biases have been on the decline in western society (Tabassum & Nayak, 2021), men are still generally thought to be more agentic—that is, competent, assertive, independent, and achievement oriented, as well as more hostile. Women, for their part, are generally thought to be more communal—that is, friendly, nurturing, unselfish, relationship oriented, as well as emotionally expressive (Eagly & Mladinic, 1989). Learning experiences as a result of social conditioning may partly explain that women tend to express more vulnerability, shame, anxiety, depression than men, yet express less anger and hostile/quarrelsome behaviour than men (Brody & Hall, 2010), while being just as assertive as men (Park et al., 2016). Indeed, girls learn from a young age from their environment (e.g., parents, school) that overt expressions of hostility are proscribed. As such, they may learn to internalize their hostility or express it in more passive ways that may not permit healthy resolution and may impact their mental health (Chaplin et al., 2005; Chaplin et al., 2015). Moreover, not only do women typically report their emotions more than men, they experience them at a greater intensity (Chaplin, 2015; Kring & Gordon, 1998), and are more likely to ruminate about negative emotions (including anger) specifically (Nolen-Hoeksema & Corte, 2004, p.413), especially when generated in interpersonal contexts (Mezulis et al., 2002) and/ or triggered by attachment-related concerns (Moreira & Maia, 2021). The physiological and behavioural arousal resulting from these recurrent emotional experiences could impart a significant cost on women's health. Of course, there is also a vast literature showing that hostility is associated with negative psychological and physical sequaelae in men as well (Chida & Steptoe, 2009; Lemogne et al., 2013; Timkova et al., 2020). In fact, decreased social support and quality of life, increased conflictual relations, greater susceptibility and responses to stress are all associated with higher hostility, in men and women (Brydon et al., 2012; Chida & Hamer, 2008; Holt-Lunstad et al., 2008; Wells et al., 2021). In addition, differences in hormone levels (e.g., estrogen and testosterone) between men and women and among the same sex, is thought to play a role given the proposed role of estrogen on TL (Aviv et al., 2002). However, our results are unlikely estrogen related given that the vast majority of women in the study were postmenopausal, and hence less protected by estrogen.

3.2.2 Defensiveness and Telomere Length

Sex moderated the relationship between defensiveness and TL in the small sample of very healthy individuals. More specifically, higher defensiveness was associated with shorter TL in very healthy men, but not women. We had previously observed a negative association between defensiveness and TL among a larger sample of healthy men and women in the only study performed to date on the issue (Starnino et al., 2016).

Given that the Marlowe-Crowne Social Desirability Scale scores appear to increase with age (Erskine et al., 2016), defensive tendencies may have an accumulated impact on biological aging processes. As Sigmund Freud (1856-1939) once said: “unexpressed emotions will never die. They are buried alive and will come forth later in an uglier way”. Prospective research is thus warranted to better understand the outcome of shorter TL in healthy individuals scoring higher on defensiveness.

In contrast to healthy men, participants with CAD showed a trend towards longer TL as a function of greater defensiveness. This could reflect an “adaptive” response in CAD patients to secure greater social connection with others. Increases on these scores may also reflect developmental changes in the meaning of social desirability rather than an increase in maladjustment. However, prospective studies in this area of research are encouraged, as are qualitative studies to better understanding the meaning of defensiveness as a function of age and health status.

3.3 Theoretical Implications for Article 1

The results of this thesis may contribute to our understanding of the transactional model of stress and the biospsychosocial synergistic model, mentioned earlier in the introduction (Chapter I, p. 17*).* The prior proposes that hostile individuals experience more stressful interactions as they have a dynamic tendency to create conflict and simultaneously undermine support which heightens sympathetic reactivity to stress. Our results on hostility suggests that the stress on the body associated with hostility may elicit a change at the cellular level as part of or in addition to the proposed pathway leading to illness. The biospsychosocial synergistic model, for its part, proposes defensive individuals tend to be chronically hypersensitive to situations deemed as threatening to the ego and efforts to maintain a view of themselves as not emotionally reactive actually increases stress reactivity. It has been suggested that they are less able to modulate parasympathetic activity in response to stressful stimuli (Movius et al., 2005). In turn, these reactions to stress increase risk for CAD and other age-related diseases (Jorgensen, et al., 1996). In defensive individuals who are physically healthy, shortening of TL may indeed be an additional process by which defensiveness impacts premature aging. In sum, to the extent that telomere attrition may predict increased risk of illness development, the transactional model of stress and the biospsychosocial synergistic model appear to be supported. Our data, and those of others, do suggest, however, that individual factors, such as sex, age, or health status (for example, presence of CAD or other chronic illnesses) may need to be considered further in future elaborations of these theories.

The transdisciplinary model and mitochondrial model of allostatic load are also of interest and potentially supported by these and other data (Juster et al., 2016; Picard et al., 2014). The transdisplinary model suggests that chronic stress is brought on by antecedents including maladaptive personality traits, which lead to increases in allostatic load and worse health outcomes such as CVD and mortality (Juster et al., 2016). The mitochondrial allostatic load model adds specificity by explaining a possible pathway by which chronic stress disrupts adaptive glucocorticoid signalling and glucose levels (primary mediators) that in turn alter mitochondrial structure and function (primary effects), generating oxidative stress, inflammation, and cellular damage, such as telomere shortening (primary outcomes). This process cumulatively worsens risk factors (secondary outcomes) reflected by abnormal metabolism (abdominal obesity, hyperlipidemia, hypertension; insuline resistance) and other risk factors for CVD such as waist-hip ratio (WHR), blood pressure, cholesterol/HDL ratio, HDL cholesterol. This in turn, consequently leads to disease, such as CAD (tertiary outcomes) (Picard et al., 2014) (for more details, please refer back to Chapter I, p. 19).

Within that context, greater hostility in women and defensiveness in healthy men may have led to shorter TL as a result of an allostatic overload and consequent impact on the mitochondria. There is a body of evidence, for example, suggesting higher levels of inflammatory activity at rest and post stress in more hostile individuals, particularly women (Boisclair-Demarble et al., 2014; Girard et al., 2016; Suarez et al., 2004). Indeed, we previously reported significantly greater pro-inflammatory activity (e.g., tumor-necrosis factor-alpha; interleukin-6) in more hostile healthy women but not in men (Boisclair-Demarbles et al., 2014). Hostile women also showed a dampened anti-inflammatory response (interleukin-10) to stress compared to men in that same study (Girard et al., 2016). Moreover, we and other have previously reported that hostility and defensiveness have been associated with a worse metabolic profile in cross-sectional and prospective studies (D'Antono et al., 2013: Niaura et al., 2002; Rutledge & Linden, 2000). Sex has also been found to moderate these relationships. For example, higher (cynical) hostility scores have been associated with elevated metabolic syndrome parameters in young adult women but not men (Elovainio et al., 2011). Similarly, metabolic syndrome parameters such as greater waist circumference, have been associated with higher levels of hostility in mid-life women, not men (Thomas et al., 2020). However, other studies consisting of individuals either with CVD, metabolic syndrome or elevations in metabolic risk factors, did not find that sex moderated this association (D'Antono et al., 2013 ; Gremigni et al., 2006 ; Lemche et al., 2014). Moreover, defensiveness has also been associated with metabolic parameters, such as hypertension in studies which included younger men and women (Mean Age: 27.3 years old) (Rutledge & Linden, 2000). However, in a cohort including older individuals, greater defensiveness has been found to be associated with worse overall metabolic profile and glucose levels, particularly in post-menopausal women (Lévesque et al., 2009).

Patients with CAD and other chronic diseases, such as in the current study, may be more likely to exhibit an overabundance of energetic substrates (i.e. elevations in glucose and lipids) relative to actual cellular energy demand, in addition to other disturbances, such as in inflammatory activity and a worse metabolic profile. The subsequent metabolic stress and other changes, could then, according to this model, contribute to cellular dysfunction, and thus shorter TL.

While these different models are particularly interesting, they nonetheless lack empirical evidence from experimental, or at least from mediational analyses performed on prospective data. Such investigations, though expensive and demanding, are required to fully test whether the proposed pathways are viable.

3.4 Results in Context for Article 2

The second study of this thesis, a pilot RCT with waitlist control group (WLC), sought to explore whether a 9 –week MBSR program can reduce hostility and defensiveness, as well as improve telomere regulation (i.e., telomerase activity and TL) and quality of life based on life goals among older individuals at risk for CAD by virtue of metabolic syndrome and non-normative stress responses. Primary analyses from this pilot RCT had already indicated it was largely feasible and MBSR acceptable (Gentile et al., 2021). Moreover, MBSR led to a decrease of 15% in LDL and 10% in cholesterol versus 4.5% and 1%, respectively in the waitlist. Within group analyses showed notable decreases in LDL, triglycerides, and waist circumference post-MBSR and 2 months later (Annex A).

Our secondary analyses indicated no statistical differences post-intervention between the MBSR group and WLC groups on any of these secondary measures, though changes in telomerase activity and quality of life from pre- to post-MBSR were significant. This said, the investigation was not powered for such analyses. Examination of effect sizes, on the other hand, was more informative on noteworthy changes in both between- and within group analyses, particularly as concerns, telomerase activity, hostility, and quality of life.

While trait hostility scores remained nearly unchanged in the intervention group post-MBSR, it actually increased by 10.80% in the WLC group. Moreover, in within group analyses, trait hostility decreased by 14.71% over the four-month period (p=0.06) suggestive of a medium to large ES. This would appear to be clinically significant. Indeed, Wong and colleagues (2014) found that a 10.80% difference in hostility scores on the CMHo among CAD patients was associated with a greater risk in mortality over a four-year follow-up. Given that personality traits are by nature stable, our result is rather encouraging. That greater decreases in hostility over the two-month follow-up period were associated with spending more time on mindfulness practice at home further adds support to the potential benefits of this intervention on hostility. Our results concur with similar decreases in hostility following an MBI stress management program observed among younger individuals at risk for hypertension (Brown Wright et al., 2011; Nidich et al., 2009), in individuals who are physically healthy (Conklin et al., 2018), as well in prison inmates (Samuelson et al., 2007). In contrast, the use of other MBI's (transcendental meditation) in two studies with individuals with existing CAD or metabolic disturbances (e.g., hypertension) did not observe a notable change in hostility (Duraimani et al., 2015; Schneider et al., 2012). Whether intrasubject change in hostility over our follow-up period was specific to the MBSR approach used in our study, which also included a loving kindness component, and was performed in a smaller group format (e.g., 8-10 participants) is open for speculation. As compared to other studies with groups larger than 20 individuals (for e.g., Duraimani et al., 2015), this ensured that every participant was seen and heard. This may have had an impact on hostility, a trait which is often heightened by unmet attachment needs (Martin et al., 2019).

Findings for defensiveness were underwhelming. It did appear to slightly increase over time (by +7.4% at the 2-month follow-up), which is somewhat consistent with a prior cross-sectional study that observed a positive correlation between higher levels of mindfulness and defensiveness (Al Ibrahim, 2013). However, it is unlikely that an increase in scores from 9.11 to 9.78 over the four months has any clinical significance. Nontheless, given that the motivation underlying defensiveness is to avoid social disapproval and protect a vulnerable sense of self, maintaining greater social desirability may actually be adaptative in a group context with other older individuals at risk for CAD. This finding may go hand in hand with the idea that defensiveness may play an "adaptive" role in those with CAD.

As for quality of life, according to a systematic review and meta-analysis, MBSR is a moderately well-documented method for helping adults improve their health and cope better with the challenges and stress that life brings (De Vibe et al., 2017). However, prior to our research, there was limited evidence for MBSR's impact on global quality of life in adults whose health is compromised (Zhang et al., 2019). The results of our study suggest that a short-term MBSR program can lead to improvements in the QoL of adults even beyond the 9-week intervention. Indeed, it showed the most notable (34.6%) change amongst our psychological measures, reflecting a large effect size. Moreover, the more mindfulness was practiced, the greater the decreases in QLSI scores (i.e., increases in QoL as the the gap between the person's goals versus actual experiences diminishes). The QLSI measure moves beyond one's health-related QoL by addressing individuals' personal hierarchical goals in different life domains, as well as the perceived gap that exists between these goals and what they are actually living. This approach differs from what is typically captured by a measurement of QoL and may indeed better be able capture the holistic impact of interventions such as MBSR who's benefits may be broader than solely physical and mental health, as is frequently measured by typical HRQoL questionnaires (Bélisle et al. 2021; Leplège & Hunt, 1997). These important changes in QoL were further supported by participants own self-reports in the qualitative interview (Annex A, Table 6). For example: *"The program helped with my physical illness, to be calmer, and to distract myself from my illness". "Since starting the program, my partner and I have gotten closer because I am less stressed"; "I am less forgetful of my keys, I look less for my things, and have changed my bridge strategy because I am more self-aware"; "We observed positive changes in blood results since doing meditation". "When I meditate, I sleep better afterwards".* The QLSI scores post-MBSR from Article 2 suggest comparable scores obtained in healthy individuals (Marois & Dupuis, 2006). Moreover, the QLSI continued to improve at follow-up beyond or equivalent to what has been found in healthier samples of individuals (Marois & Dupuis, 2006).

As for telomere regulation, a recent meta-analysis showed that in eleven RCT's, little change in TL between the MBI and the comparison groups (active or WLC) (small mean weighted effect size, g=0.12, p=ns) was found (Schutte et al., 2020). Data from studies in which treatments and follow-ups were more intensive and/or over longer periods of time, did show greater decreases in TL (moderate effect sizes) and happen to be in physically healthy samples (Conklin et al., 2018; Toluhanase et al., 2018). Within the current investigation, both between- and within –group analyses showed little change or difference. In analyses involving both groups post-MBSR, TL decreased slightly post-intervention (small to medium effect size) and then stabilized by the 2-month follow-up, which is what we had predicted would occur. These changes in TL immediately post-MBSR may reflect inter-assay variations, though samples from different time points were assayed in batch to minimize such effects. Similar decreases in TL were reported post-MBI in middle-aged or older hypertensive (Duraimani et al., 2015) and healthy participants (Le Nguyen et al., 2019), as were stabilization of TL (Schutte et al., 2020). Lack of notable changes in TL in this and other studies following MBSR may actually suggest that this intervention is protecting participants from further TL attrition, though obviously this remains to be tested in larger RCTs with longer follow-up periods.

In contrast to TL, telomerase activity increased in the WLC group (51.61%), but decreased (38.54%) in the MBSR group (medium effect size). Within analyses showed a 44.7% reduction in telomerase activity from pre-MBSR to follow-up. This result was surprising as most other MBI studies, including some RCTs, had reported increases ranging from 15% to 57.3% in samples drawn from different populations (Schutte & Malouf, 2014; Lengacher et al., 2014), though telomerase increases were also found to a lesser extent in the control group as well (Daubenmier et al. ,2012; Lengacher et al., 2014).-What these decreases in telomerase reflect in study 2 is unclear. It is possible that the initial metabolic burden of our participants and subsequent improvements post-MBSR (see Annex A; Gentile et al., 2021) may be implicated. Indeed, higher telomerase levels have been reported among middle-aged men and women with metabolic syndrome (Rentoukas et al., 2012) compared to healthy counterparts, possibly in response to a persisting chronic inflammatory state (Narducci et al., 2007). Hence, a reduction in both metabolic burden and inflammatory activity as a result of MBSR could potentially have led to decreased telomerase in the current study, in contrast to the initial increase observed in the control group, prior to getting the MBSR intervention.

In conclusion, our understanding of these changes remain rather speculative, and must be interpreted with caution given the small sample size.

3.5 Theoretical Implications for Article 2

Conklin and colleagues (2019) presented a theoretical model depicting how meditation training may counter the effects of stress responses (cognitive, affective, and physiological) on telomere regulation (for more details please refer to Figure 4 of Chapter I, p. 45). For instance, training attention to one's present-moment experience has shown to reduce elaborative processing of stimuli, promoting more accurate and less catastrophic appraisals of one's present experience, as well as more adaptive behavioral responses to stressful events. Mindfulness meditation training could, in theory, alter TL through changes in psychological processes which have been associated with TL, such as reappraising negative thoughts and decreasing experiential avoidance. This may be a particularly beneficial training format for individuals prone to maladaptive acute stress responses, such as those found in hostile and defensive individuals, or with more ingrained telomere vulnerability factors, including experiences of early adversity and insecure attachments (Ein-Dor et al., 2011; Ridout et al., 2018). For defensiveness, it may not feel safe to express negative affect and thus denial of psychological distress during social interactions may occur (Garssen, 2007). As for hostility, observing and distancing oneself from distrustful or cynical thinking without judgement can be helpful (Harned et al., 2006). Moreover, meditation training often occurs in the context of a highly supportive environment, which can provide a physically and interpersonally safe environment capable of facilitating self-expression of genuine emotions. Additionally, relationships with trusted teachers and a community of similarly motivated practitioners may promote feelings of safety and activate schemas of secure attachment and interconnectedness. These elements may play an important role in altering stress processes over and above the mental training aspects of meditation (Conklin et al., 2019).

These changes may in turn impact the activity of multiple physiological systems involved in the stress response, including autonomic and HPA reactivity, metabolic measures, and telomerase activity, the sum of which may serve to stabilise or lengthen TL (Conklin et al., 2019). However, to our our knowledge, no intervention study has simultaneously assessed changes in stress appraisals and telomere biology to test this mediational pathway. While our prior analyses did show improvements in autonomic stress responses and metabolic activity (Annex A, Gentile et al., 2021), these changes were not accompanied by longer TL, though length was somewhat stabilized. Understanding *if* and *how* these practices affect telomere biology in a meaningful way will require a more systematic investigation.

3.6 Implications

3.6.1 Methodological Implications

Trait hostility is proposed to contribute to premature aging through *years* of accumulated wear and tear on a number of physiological systems. Although there is evidence that trait measures of hostility are highly correlated over short periods of time (i.e. a few years; Barefoot, 1983; Bishop & Quah, 1998; Jacobs et al., 1988; Shekelle et al., 1983; Spielberger, 1988), the test-retest reliability of these dimensions over decades is less impressive (coefficient of $r = 0.39$ when measurement spans 22-years; Siegler et al., 1992). This reflects the dynamic changes observed in individuals over a lifetime. For example, there is data suggesting developmental changes in hostility, with higher Cook-Medley hostility scores among young adults, slightly lower levels in middle age, and a trend toward increasing levels in the elderly (Barefoot, 1991). These developmental changes could reduce the test-retest correlations depending on the periods in which the measures are obtained. Such changes also suggest that while stable over time, the hostility trait is not rigidly immutable to change. This is rather encouraging for those wanting to help more hostile individuals reduce their psychological and medical risk. Improvements in hostility observed in study 2 of the current thesis, in addition to those seen in other studies on MBSR further contribute to the recognition that interventions targeting hostility in individuals without rage disorders are amenable and effective. This said, and as pertains to our own study, it is noteworthy that that one participant who dropped out prior to the beginning of the intervention actually had a hostility score that was two standard deviations greater compared to the mean, which may signify that greater efforts may need to be implemented to retain individuals that are remarkably more hostile. For example, perhaps an individual session with the MBSR instructor before the start of the group intervention can be offered to allow them to build an alliance. Involvement of medical doctors within a more global program could be helpful to encourage patients to becoming actively engaged in the management of their psychological and physiological risk factors.

Defensiveness, for its part, is a complex concept. While questionnaires, such as the MCSD, can measure the trait on a continuum, the extent to which this is useful in clinical practice is questionable. Moreover, there is no clinical cut-off score that can be used to identify defensive individuals who may be at greater risk for premature aging. This is particularly troublesome given the positive image portrayed by those with higher defensiveness, who may be « faking good » to their health-practionners by underreporting physical symptoms or distress, or by overstating positive attributes which could complicate treatment (Williams et al., 2019). For example, defensiveneness can lead patients to deny symptoms and psychological problems to appear psychologically adjusted. Individuals may behave in this way out of fear of experiencing emotions and fear of disapproval or for example, if they are inpatients wanting to be discharged sooner. To our knowledge, other questionnaires perform no better in addressing this issue in relation to health risks. While a systematic review examining 35 studies found that the Marlowe-Crowne Social Desirability scale remains the most used scale to measure this trait as a one-dimensional variable, there are results from a three studies that used the Balanced Inventory of Desirable Responding (BIDR; Paulhus, 1988) and operationalized this trait as a multifactorial construct by disentangling impression management from self-deception. These authors propose that examining this trait as two separate dimensions is useful because these two components could lead to different conclusions (Perinelli & Gremigni, 2016). For instance, impression management but not self-deception was significantly related to self-reports of undesirable behaviors such as conjugal violence (Freeman et al., 2015), alcohol use (Davis et al., 2010) whereas only self-deception has been shown to be protective factor against depression, hopelessness, and suicide risk (Pompili et al., 2011; Surbey, 2011).

3.6.2 Clinical Implications

It is interesting that while men had slightly higher levels of hostility than women did, we found that higher hostility in women (but not men) was associated with shorter TL. Indeed, on the basis of base-pair comparisons (Wang et al., 2018), women reporting greater hostility were biologically older by more than 4 years compared to their less hostile female counterparts, after controlling for chronological age, health behaviours, sociodemographic, and medical factors. These results are in agreement with previous data suggesting that hostility is a significant risk factor for premature aging in women. It is encouraging that mind-body interventions, such as MBSR, might lead to clinically significant reductions in hostility, as shown in individuals at risk for CAD in Study 2. Qualitative data further supported these quantitative findings from our study. For example: "*The program helped me to be calmer. I am less angry when I drive. I am also less reactive, and have better control over my anger. MBSR should be offered to anyone else who experiences a lot of stress*." (Please refer to Annex A, table 6 Participants' Verbal Feedback). These results contribute to the growing literature suggesting efficacy of psychosocial stress management programs to reduce hostility (Brown Wright et al., 2011; Gidron et al., 1999). Indeed, some other programs, such as cognitive-behavioral interventions in CAD patients have also been shown to decrease hospitalisation stays and offset medical costs (598$ saved per patient) in the six months' post-intervention (Davidson et al., 2007). Moreover, emerging data suggests that patients following a stress management training, while not routinely included as a component of cardiac rehabilitation programs, have had an almost 50% lower risk for cardiac events (including all-cause mortality, fatal and nonfatal myocardial infarction, coronary or peripheral artery revascularization, stroke or transient ischaemic attack, or unstable angina requiring hospitalization) compared to standard cardiac rehabilitation (Blumenthal et al., 2016).

Nonetheless, stress management programs can come with some additional risks to consider. For example, one participant reported that increased awareness of her anger as a result of greater mindfulness led her to be more assertive in her relationship with her spouse, which sparked more conflict with him. Learning to become more mindful of one's present emotions and experiences - emotions that had been previously hidden or avoided can be uncomfortable and confronting (Shapiro et al., 2006). While this is a common occurrence, it is rarely discussed in MBSR intervention studies. It is increasingly recognized and needs to be discussed openly with participants during the recruitment process as well as during the groups sessions. It also needs to be discussed within the published articles.

It is important to keep in mind that our studies may not be representative of extremely hostile individuals, who by nature, would probably not participate in clinical studies due to their cynicism and mistrust of others such as research assistants and medical staff. This being said, slight changes in CMHo scores can be clinically relevant in the general population, not just in those with severe hostile traits (e.g., antisocial personality). For example, Wong and colleagues reported that patients with stable CAD were twice more likely to pass away (age-adjusted HR = 2.09, 95% CI = 1.24-3.55, p = .006), 3.7 (SD=1.2) years later if their CMHo scores were (slightly) higher. The specific mean scores of the 39-item CMHo of those who had passed away was of 15.3 (SD=7.2) vs 13.8 (SD=7.1) for those who had survived (Wong et al., 2014). In study 1 of this thesis, the mean scores on the 39-item CMHo was 14.39 (SD=6.07) in the CAD and 13.29 (SD=6.05) in the non-CVD groups combined and lower in those who were very healthy (M=11.72, SD=6.84). Importantly, in our pilot study, hostility levels in those at risk for CAD started at 14.00 (SD=4.91), lowered to 13.33 (SD=5.73) by end of MBSR, then decreased further to 11.94 (SD=4.63) by the end of follow-up. Thus, the MBSR intervention led to a decrease in hostility to levels similar to older individuals who remained physically healthy (without any chronic illness) despite their age. It is thus possible that this seemingly small change in hostility may have survival benefit for our participants, though this would require testing. Much longer follow-up evaluations in a representative sample would be required to evaluate the long-term benefits of such decreases.

On a separate note, when individuals that are more hostile seek out psychotherapy, it is not always necessarily to work on this trait, but rather they may seek to work on their symptoms of stress, depression, interpersonal issues, bipolar and personality disorders, and/or substance use disorders, for example (Brydon et al., 2010; Constantino et al., 2008; Floyd et al., 2006; Lahera et al., 2015). As psychologists, it may be useful to consider hostility as a potential target of intervention if the client is amenable to it. Sources of hostility include lack of safety, overwhelming anxiety, vulnerability to attack, prejudice and fear of exclusion, loss of control and narcissistic injury (Gans et al., 2010). Stress management interventions, including MBSR may help reduce not only the hostility trait, but also the negative effects of hostility on affect, social relatedness, and stress responses. Biofeedback (of the cardiovascular or autonomic systems) could also enable people who show non-normative stress responses become more aware of their body's messages and learn to modulate their own reactions to reduce the physiological cost to their mind and body. Results on premature aging from our Article 1 can be used as psycho-education to help motivate them to continue working on themselves, particularly for women. For example, this trait could have been adaptive as a means for survival from a developmental standpoint to keep them safe from a dysfunctional upbringing. However, these traits carry costs into their adult lives (Luecken & Roubinov, 2012). We may be able to motivate them to stay in therapy post symptom management, by creating a sense of safety through stability within the therapeutic relationship and helping to continue to learn new strategies to regulate negative affect and let go of maladaptive or no longer adaptive ways of appraising threat in others (Ball Cooper et al., 2021). A particular challenge comes from the fact that more hostile individuals may elicit hostile reactions and feelings of indaquency in the therapist working with them (Von der Lippe et al., 2008). In this respect, it is essential that the therapists also be attuned to their own responses to secure a safe working alliance.

It is difficult to understand the clinical implications of defensiveness in relation to TL in CAD patients at this time. In contrast, for healthy individuals, we replicated the finding of shorter telomeres with greater defensiveness, particularly in men. Defensiveness is not a pathological trait, and it remains difficult to clinically interpret the scores of the MCSD scale: 9.35 (SD=2.74) in the CAD and non-CV groups and 9.08 (SD=2.64) in the healthy group (similar scores in our pilot study were found). For the 14-item MCSD used in this study, we are aware that these scores found are higher than in other studies, mean of 5.76 (SD=2.68) in healthy younger individuals (Reynolds et al., 1982), yet resemble those of middle-aged and older adults suffering from other non-CV illness such as ashtma (9.0, range [7-10]) (Beyhan et al., 2020). Our study supports that defensiveness may increase with age and disease processes (Erskine et al., 2016).

In healthcare, it would be important to keep an eye out for these more defensive patients, who may report high adherence to medical recommendations or shows uncharacteristically little evidence of distress or physical symptoms. These particular characteristics, while potentially pleasing to health professional as it "facilates" their care and self-esteem, may actually hide a person who is suffering psychologically or physically, and/or may not be actually following the treatment regimen. Such patients may simply not be identified early because of the overly socially acceptable facade they present. Unfortunately, the current pilot study on MBSR did not provide preliminary evidence that it might improve defensiveness. Of course, a larger study would be needed to confirm these results. As individuals with greater defensiveness appear to be more preoccupied with the fear of disapproval (Bonanno & Signer, 1990), as mentioned they tend to deny psychological distress in order to maintain social bonds and protect their self-esteem. Furthermore, a growing literature suggests that more defensive individuals are less likely to seek out psychotherapy and they are less likey to know people in their entourage who have received psychological help, compared to their highly anxious and non-defensive counterparts. Individuals with higher defensiveness, however, still reported believing that clients of psychotherapy can have frequent positive reactions as well as less frequent negative reactions about psychotherapy, compared to their counterparts mentioned above (Furnham & Lay, 2016).

These authors suggest that defensive individuals could be suppressing their negative beliefs about their understanding of psychotherapy when answering questions regarding psychotherapy, showing attentional strategies that are hypersensitive towards negative or threatening feedback compared to their less defensive or more anxious counterparts. Moreover, Westmaas & Jamner (2006), showed that defensive individuals, compared to less defensive individuals, did not benefit from social support as it appeared to be more threatening to their self-esteem. However, their study included only women and would need to be replicated in men and individuals with or at risk for age-related illnesses where the need for support may differ.

In addition, Shaw and colleagues (1985) demonstrated that those with greater defensiveness were less knowledgeable about risk factors for CAD and rehabilitation exercises post heart attack. Techniques such as motivational interviewing in bevhavioral medicine (Miller & Rollnick, 1991) may be an interesting more active client-centered option to help more defensive individuals to get a better handle on their health by eliciting reasons for change from the patient (e.g., “What worries you about your blood pressure” ; “What would be different in your life if you stopped smoking"), rather than advising them of the reasons why they would benefit from changing or learning new behaviours (e.g., “Take your medication everyday to reduce your blood pressure”; “Smoking will kill, you should stop!”). In motivational interviewing, the strategy is to ask open-ended questions and use a collaborative style to empower the patient to change unhealthy behaviors. Therefore, it may be more effective in bypassing defensiveness than other types of approaches which may be more confrontational. In theory, motivational interviewing intervention can be integrated in the health care routine by a nurse or doctor; however in practice it has been more difficult for practionners to adhere to these skills (Bacon et al., 2018; Emmons & Rollnick, 2001). Additionally, ressources for effective communication and self-assertiveness techniques may be recommended beyond MBSR. However, working towards helping patients challenge their negative beliefs, identify and validate their own emotions (including negative affect) must be potentially targeted first in order to improve self-esteem.

An additional contribution of clinical value pertains to the manner in which quality of life was measured in study 2. Quality of life is more than one's physical or even mental health as measured by most health-related QoL questionnaires. From a systemic point of view, it emphasizes an individual's life goals in domains that encompass, cognitive functioning (memory, concentration), social/family, couple, leisure, work, housekeeping, affectivity, and spirituality, in addition to physical health; all of which are at the heart of one's overall health (Dupuis t al., 1989; Dupuis et al., 2012). As described by the World Health Organization (WHO) since 1948, health is defined as "the state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (World Health Organization, 1948).

Of course, having a serious illness or being at high risk for one may be associated with decreases in well-being. Yet, being physically healthy does not guarantee a sense of well-being either. In 1998, the WHO added the following to their definition of QoL "an individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards, and concerns". Therefore, having a measure that moves beyond one's health-related QoL, by addressing individuals' personal hierarchical goals in different life domains, as well as the perceived gap that exists between these goals and what they are actually living is crucial in better grasping their overall QoL, as described by the WHO. The systemic QoL model developed by Dupuis and colleagues, suggests that a larger gap between their current situation and their hierarchically organized life goals (with reference to an imagined ideal) may actually generate feelings of anxiety, frustration, and anger which may eventually lead to resignation, low self-worth and depression if objectives are not reached (Bélisle et al., 2021; Dupuis et al., 2012). From this model, the Quality of Life Systemic Inventory (QLSI) was developed. When working with the QLSI as a clinical tool, a clinician may be better able to identify which life domains are important to the client, and which within these are currently experienced as suboptimal. Discussions around this evaluation with clients/patients can help them better understand the effects of such gaps in desired versus actual conditions on their lives and health. Working on these goals can become a target in itself within therapy for example. In some cases, it might be important to recognize that certain life goals may no longer be feasible given changing physical conditions, however we can adapt by either reducing goals or changing the importance given to them in order to maintain a satisfying QoL. For example, an older man working in construction has recently undergone cardiac surgery. His most cherished life domain had been work. In order to maintain a satisfying quality of life, he may need to adapt to his physical illness by reducing the intensity of his work and work objectives or lower the importance he has given to this life domain given his new physical condition. Otherwise, he may feel hopeless, more irritable and depressed, which implies that he is not psychologically adjusting to his current life situation (Bélisle et al., 2021).

3.7 Strengths

Article 1. This thesis comprises several noteworthy strengths. First, this is the first to our knowledge to examine the relation between TL and coronary-prone personality traits (trait hostility and defensiveness) in older individuals with CAD and other chronic diseases. This is important because it allows us to gain greater awareness of the potentially differential role that personality plays as a function of these individual characteristics which could lead to more personalized medical assessments, education, and interventions. Second, the sample size was relatively large, and sufficiently powered to control for relevant covariates strongly correlated with TL. Third, the purposeful recruitment of as large a number of women as possible to examine sex differences led to the discovery of notable differences between men and women in the relation between the personality traits and TL. Fourth, it included standardized questionnaires of hostility and defensiveness permitting comparisons with other research within behavioral medicine as they were those most commonly utilized within the field. Fifth, CAD status was also strictly defined and verified via medical files. Sixth, examining the moderating effect of CAD status was also novel, although results were difficult to interpret at this stage.

Seventh, the use of quantitative polymerase chain reaction (qPCR) to measure TL can also be viewed as a strength. This technique was developed to assess the length of telomeres in high quantities throughout laboratories, is rapid, and requires less DNA than Southern blot. While Southern Blot is said to be a more accurate method, it remains less applicable to many studies due to its need for a large amount of DNA. To this day, qPCR remains the dominant method in epidemiological studies and has proven useful in the investigation of the biology of telomeres and the roles they play in the molecular pathophysiology of multiple diseases of aging. Additionally, in our studies, qPCR analyses for TL were carefully controlled and assayed in batch in triplicate, reducing potential measurement errors. The use of leukocyte TL is clinically relevant as it reflects potential organ dysfunction elsewhere in the body. A prime example is how significantly reduced TL was found in leukocytes as well as in myocardial and arterial wall tissue in CVD patients (Chang et al., 2005; Oh et al., 2003).

Article 2. The following reflects important strengths of article 2. For instance, the randomized controlled pilot study was built using CONSORT guidelines (Thabane et al., 2016). Moreover, we recruited individuals known to be physiologically vulnerable to stress, and hence who might better benefit from such an intervention to manage stress. In addition, this study confirmed that an MBSR trial was feasible and the intervention acceptable in an older population at risk for CAD. Importantly, the sample was stratified by sex and initial stress response style and successful randomization was confirmed by the fact that the randomization groups did not differ statistically at baseline (refer to Annex A). Other strengths include that the MBSR program was animated by an experienced psychologist and participants had access to a large comfortable setting and high-quality materials conducive to mindfulness meditation. This pilot work also provides an example of how observational data from two articles on hostility, defensiveness, and TL (Starnino et al. 2016; Starnino et al., 2021) may be applied and tested within a clinical setting to potentially improve outcomes for older individuals at risk for CAD. Moreover, our pilot study was the first article to bring forward both telomere markers of aging, personality traits, and quality of life, as well as metabolic parameters and stress responses, within a secondary preventative stress management program. This provides preliminary evidence for MBSR's potential holistic impact on health.

3.8 Limitations

Article 1. Several limitations in the current project limit in some ways, the conclusions that can be drawn from our results and suggest that further research is required. The current study focuses primarily on TL among a sample of patients with CAD or other non-CVD diseases. The overwhelming influence of disease-related biological factors on TL in our sample of individuals with CAD or other non-CVD illnesses may have obscured the subtler influences of psychosocial factors, such as hostility and defensiveness that may occur in healthy people. Indeed, these personality traits only explained 0.1% of the variance. It should be noted, however, that the large number of covariates included into the first block of the hierarchical regressions, cumulatively only explained 12% ($R^2_{adjusted}$=0.105) of the variance of TL. This highlights how little we know of the factors contributing to TL, and hence our limited understanding of this biological marker given the wide variation in phenotype dependant on the genetic and environmental interplay (Dugdale & Richardson, 2018; Martens et al., 2021).

Given that the analyses were cross-sectional, it is impossible to determine the directionality of the results. Furthermore, given that hostility and defensiveness increase risk for premature mortality, those most susceptible to the effects of these personality traits may have already passed away representing a survivor bias, and may have contributed to our unexpected results (e.g., greater defensiveness associated with longer TL in CAD participants). Moreover, the sample consisted of mostly Francophone Caucasians, which may limit the generalizability of our findings to other populations. Unfortunately, despite a desire to recruit across different ethnicities, the majority of those who participated were Caucasian, limiting the extent to which the results can be generalized. Indeed, there is evidence for differential patterns of association of TL with biological parameters (such as blood cell count) as a function of geographical location (e.g., De Meyer et al., 2008; Mollica et al., 2009), that may reflect genetic differences (Kim et al., 2012), as well as differences in life exposures, access to healthcare, and/or coping resources (Geronimus et al., 2015). Finally, the sample size for healthy individuals being very small, any results concerning them must be seen as hypothesis generating at this time, though results were in partial agreement with our prior investigation in healthy individuals.

Article 2. Secondary analyses from pilot RCT have some important limitations. It was not conceptualised from the onset to evaluate the effects of MBSR on hostility or defensiveness, but rather to test feasibility, acceptability, and impact on metabolic parameters and stress responses. This is an important limitation as we are unable to truly determine if this study can clinically help those with greater levels of hostility and defensiveness. However, as mentioned earlier the levels of hostility of the samples were within ranges that increased risk for mortality (Wong et al., 2014) but are not necessarily in the more severe end of the spectrum. In addition to this concern, small differences found in questionnaires scores can be due to measurement error or habituation effect.

Given the older age group, it would have been important to evaluate their cognitive functioning prior to their participation in the program. However, no cognitive impairment issues were raised.

Finally, when fresh blood samples are possible, it would be important to measure the distribution of B- and T- cells separately as their individual rates of TL attrition and telomerase level may differ and affect results (Lin et al., 2015; Lin et al., 2016).

3.9 Future Directions

The following section discusses future directions for research examining hostility, defensiveness and possible mediation factors. We will also discuss the methodological recommendations for future trials measuring the impact of stress management in older adults at risk for CAD. Addtionally, recommendations for biobehavioural research including telomere biology measures will be provided.

It would be important to examine the relation between hostility and TL longitudinally, as well as determine the clinical significance over time of the sex differences observed in this relation. As BEL-AGE is a prospective investigation, this will be possible in the coming years. Mediation analyses could be performed to better understand which factors may be contributing to sex differences and increased risk. One such mediator may be social support. Lower social support and loneliness have recently been associated with shorter TL particularly amongst middle-aged and older adults (Carroll et al., 2013; Wilson et al., 2019). Hostile individuals may be more sensitive to the type of social support received (Vella et al., 2008). Literature suggests that, like defensive individuals, individuals that are more hostile may derive less benefit from social support, even when they do receive it. However, they are less likely to receive social support because of their interpersonal style. Future research may want to include the potential mediating effect of different types of social support (i.e., intimate vs. intrumental social support) and/or loneliness between hostility, defensiveness and TL. In older individuals, increases in defensive coping might serve a psychologically protective function as one approaches a later stage of life. According to Erickson's personality theory, this stage of life is where one starts to reflect inwards on their life with a sense of satisfaction or failure (Erickson & Erickson, 1998). This may pose a threat to the self-concept, which would be particularly taxing in those with greater levels of defensiveness. However, this hypothesis would need to be tested using a mixed-method research approach. For example, it would be helpful to include qualitative data to support statistical findings, especially since scores on standardized questionnaires used for both hostility and defensiveness may be difficult to interpret and compare due to absence of clinical cut-off scores.

Our pilot RCT requires replication on a larger scale. To reach more individuals at risk for CAD, collaborations will likely be required with other health care professionals (e.g., general practitioners, cardiologists, nurses) to facilitate recruitment. Indeed, motivation to engage in stress management might be improved if individuals were first introduced to the topic by their trusted physician and perceived it as part of their medical care. For our study, recruitment was limited to the sample of individuals from study 1 who met our criteria, and to the use of letters to recruit as per the limitations imposed by the ethics committee of the Montreal Heart Institute (refer to Appendix F). Other recruitment methods in future trials could include presentations to groups of patients in hospital or community settings or public postings may also be of interest depending on the type of sample desired. It would be interesting to determine in a larger scale study whether benefits of MBSR or other intervention differ based on physiological stress response style. It would be recommended that the MBSR program be offered at more than one time period (e.g. day and evening) in order to accommodate both working and retired participants. For older adults, offering the program during the daytime is recommended; an evening class was not feasible for our participants, who expressed concerns regarding driving at night and in the winter. In line with this, an additional suggestion is that future studies recruit individuals that are homogeneous in age and working status, at least within groups, which may facilitate participant retention. For example, in our study, the youngest participant (41 years old) expressed that she could not relate to the group and dropped out of the program. Moreover, retirees were more likely to complete MBSR compared to active workers, possibly due to more available time to devote to the program. One way to facilitate adherence to program would be to deliver it via Web. A systematic review (Moulton-Perkins et al., 2020) revealed that this approach is feasible and acceptable and do not appear to be less effective than in-person program.

In order to enhance future research on the efficacy of home-practice in the MBSR program, we propose the use of the the Mindfulness Home Practice Monitoring Form (MHMF) (refer to Lloyd et al., 2018), a measurement tool that is proposed to monitor formal and informal home-practice in MBI trials. The MHMF is more specific in its way of monitoring different types of practice in MBSR (e.g., minutes per sitting meditation or yoga), resources used (e.g., meditation audio, practice booklet), and identifying barriers to practice. This would allow researchers to better assess how greater types of certain types of mindfulness practice may be associated with improved intervention outcomes.

If funding permits, it would be interesting to include the use of a preference-based non-randomized effectiveness design alongside a fully randomized efficacy trial of two interventions and include randomized waitlists in each case (Carlson et al., 2017). This unique design offers certain advantages. These include: 1) patients who have a strong preference for one type of intervention will get the desired one, maximizing recruitment and allowing exploration of the effects of preference on outcomes by comparing outcomes between those who choose an intervention and those randomized to the same treatment without a preference for it. However, a limitation of allowing preference-based assignment is that groups may also differ by demographic and disease risk factors, and the design could introduce other biases caused by preference for certain days/times classes are offered, etc. 2) A full standard comparative efficacy RCT with two active interventions (for example, MBSR *versus* Health Education) and a waitlist control is embedded in the design, which allows testing the efficacy of both interventions compared with each other and compared with the control. 3) Randomized control groups will allow us to see the natural course of changes over time, which will be especially valuable if there are no differences between the active intervention groups on any of the outcomes. Moreover, with respect to telomere regulation within an intervention trial, additional evaluation time points are required. For example, it would be helpful if TL were measured at 6 months to a year later post intervention to add clarity on whether these interventions have a sustained impact on TL regulation processes.

As for telomere biology, in the context of biobehavioral research, it is important for future studies to include the following to fully grasp important factors for premature aging (a) sociodemographic factors: age, sex, body mass index, ethnicity, exercise patterns, diet, smoking, or acute and chronic psychological (di)stress, and past trauma and (b) biological specimen to be evaluated (i.e., peripheral blood versus specific tissues) (Starweather et al., 2014). For example, regarding the latter point, the type of biological specimen to be evaluated (i.e., peripheral blood versus specific tissues), telomere shortening is dependent on the rate at which the cell replicates. Thus, one may anticipate that cells having a higher replication rate might show more rapid shortening of TL. Moreover, peripheral blood leukocytes, used in this thesis, and one of the most frequent biological specimens evaluated in telomere research, will reflect the lengths of the different kinds of white blood cells, all of which divide at different rates. Specifically, granulocytes (including, neutrophils, eosinophils, and basophils) have a lifespan of hours to days, while agranulocytes (including, lymphocytes and monocytes) can have a lifespan of days to years. Therefore, it may be helpful to evaluate the differential proportions of the blood cell constituents, as these might impact the findings of the study (Lin et al., 2015). As telomeres are a measure of biological aging, and research in this field has exploded within the last decade, it would be eventually helpful to understand whether TL can be used clinically as a prognostic marker to better identify if one's TL is at a greater risk for illness. As mentioned, emerging data suggests that longer TL may also be problematic, and thus relationships may not be linear. More research is needed to better understand under what circumstances, beyond the "longer versus shorter" descriptors for TL, are a risk factor. Indeed, it may not be a specific cut-off point that is relevant but rather a range above and below which there is greater risk of certain pathologies. Moreover, it may be helpful to associate TL with levels of telomerase activity for each participant (creating a ratio) which can also provide us with more information the risk for illness (Zalli et al., 2014).

As methods of measuring telomere biology become more reliable and available, the next generation of studies will be able to determine more definitively if MBI's impact telomere biology in a meaningful way. Understanding how these practices affect telomere biology will require a more systematic investigation of the various dimensions that make up mindfulness stress management programs, as well as better methods for capturing the psychosocialand psychophysiological changes that might occur.

3.10 Transfer of Knowledge Strategy

Some of these findings have already been disseminated to the scientific community by means of international research conferences or peer-reviewed publications. For instance, Article 1 entitled "The Associations of Hostility and Defensiveness with Telomere Length are Influenced by Sex and Health Status" was published in 2021 in the journal of Biology of Sex Differences, with a notable impact factor of 3.3. Results were also presented at the Society of Behavioral Medicine Conference in San Diego, California and Canadian Symposium On Genome Integrity and Telomeres conference in Québec, Canada. The RCT's feasibility, acceptability, and metabolic data was published in 2021 in the Clinical Gerontologist journal and the Article 2 has been submitted to the same journal. These results were also presented at the Society of Behavioral Medecine in New Orleans, Louisiana. Abstracts from presentations at the Society of Behavioral Medecine were all published in the Annals of Behavioral Medecine journal.

As for the transfer of knowledge outside of the academic field of behavioral medecine, our results on personality traits and TL can be shared with corporate groups. For instance, the Montreal Business Women's Club, a non-profit organisation of women who are interested in the creation, management and development of their business, may be interested in gaining better knowledge on the potential impact that hostility on women's aging. Moreover, the results from this thesis can be further disseminated to Le Centre AvantÂge at the Institut Universitaire de Gériatrie de Montréal, where online and in-person conferences on lifestyle, mental and physical health are open to the public. For example, older individuals can gain awareness on new ways to improve their quality of life, such as through MBSR.

Finally, it is my conviction that patients would benefit from having frank discussions with health professionals about the behavioural and psychological factors that may put them at risk for illnesses such as CAD, hypertension, and others illness. Presenting these results during lunch presentations at the MHI to doctors can help in the transfer of knowledge. In addition, it may be important for stress management to be emphasized in the same way that exercise and maintaining a healthy diet is often discussed. We have recently been invited by l'Université de Montréal to perform an interview and to present published results from article 1, which we are looking into doing. This would allow for these results to be disseminated to academic disciplines outside of psychology. Moreover, the use of health and wellness podcasts to disseminate these results can be of interest in order to reach different non-academic populations.

I was recently hired by the Alan Edwards Pain Management Unit at the Montreal General Hospital, where I will be holding group and individual's psychotherapy sessions for individuals suffering from chronic pain, as well as training other healthcare professionals in performing psychological assessments. This will give me the opportunity to emphasize the importance of stress management using mindfulness skills in another population of individuals. Moreover, it will be essential as a clinician to assess individuals for defensiveness and hostile tendencies, as this will impact my work within this population as well (Burns, 2000; Fishbain et al., 2010). I forsee presenting these results during clinical rounds to the multidisciplinary team in efforts to better understand barriers to pain management, and the risk of worse health outcome if not taking these traits into consideration.

CONCLUSION

“The body is not a thing, it is a situation: it is our grasp on the world and the outline for our projects.”

-Simone de Beauvoir (1949)

Cardiovascular disease (CVD) remains the first cause of death worldwide for men and women (WHO, 2021). In the current health care scenario, the “perfect storm” brews: an aging population with an increasing number of CVD risk factors and multiple comorbidities. Within the context of a global pandemic, these factors have converged to create a healthcare crisis because emphasis on disease prevention has been ignored. Fragmented, episodic, acute care remains a major focus of the healthcare system. Primary disease prevention that can be fostered by access to a family doctor for prescription management, as well as psychosocial interventions, to improve health (physically, mentally, socially, and spiritually) receives far less attention. However, whether in primary to tertiary prevention, individuals’ personality traits (i.e. hostility or defensiveness) may pose a barrier for healthcare professionals. This thesis aimed to investigate the relations between these traits and TL, as well as provide preliminary findings on a feasible and acceptable psychosocial intervention, more specifically stress management.

At the end of this thesis, I dare to dream of a healthcare system or better yet, a view of the world which holds a holisitic vision for heatlhcare. One where healing, by using preventative measures, is prioritized, especially given the nuanced needs of our aging population.

ANNEX A: ARTICLE 3

MINDFULNESS-BASED STRESS REDUCTION IN OLDER ADULTS AT RISK FOR CORONARY ARTERY DISEASE: A PILOT RANDOMIZED TRIAL

LA GESTION DU STRESS PAR LA PLEINE CONSCIENCE CHEZ LES PERSONNES ÂGÉES À RISQUE POUR LA MALADIE CORONARIENNE : UNE ÉTUDE PILOTE RANDOMISÉE ET CONTRÔLÉE

ARTICLE PUBLISHED IN *CLINICAL GERONTOLOGIST*

GENTILE, C., STARNINO, L., DUPUIS, G., & D'ANTONO, B. (2021). MINDFULNESS-BASED STRESS REDUCTION IN OLDER ADULTS AT RISK FOR CORONARY ARTERY DISEASE: A PILOT RANDOMIZED TRIAL. *CLINICAL GERONTOLOGIST*, 1-15.

Mindfulness-Based Stress Reduction in Older Adults at Risk for Coronary Artery Disease: A Pilot Randomized Trial

Christina Gentile, PhD, Louisia Starnino, BSc, Gilles Dupuis, PhD & Bianca D'Antono, PhD

Word Count : 5 642

Abstract

Objectives: Stress influences metabolic activity and increases risk for cardiovascular disease (CVD). We sought to a) examine feasibility and acceptability of mindfulness-based stress reduction (MBSR) in older adults at risk for CVD, and b) obtain preliminary data on its metabolic impact.

Methods: A pilot RCT was conducted using a pre-post, 2-month follow-up design. Eighty-one individuals with metabolic syndrome and non-normative responses to stress in a previous investigation were invited. Participants were randomized (by sex and stress response) to a 9-week MBSR or a wait-list control group. Feasibility and acceptability were assessed and blood assayed. Between-subjects (MBSR vs waitlist control) ANOVAs on metabolic parameter change scores, and one-way repeated measures ANOVAs (pre-, post-, follow-up) were performed.

Results: Thirty-three individuals (41%) responded to invitations, 26 were interested, of whom 19 were randomized (M_{age}= 67 years, *SD*=7.70). Completion rate of MBSR was 72% and overall attendance was 96 %. Reported benefits included increased relaxation, greater interpersonal connection, and increased body awareness. MBSR led to a decrease of 15% in LDL and 10% in cholesterol versus 4.5% and 1%, respectively in the waitlist. Within group analyses showed notable decreases in LDL, triglycerides, and waist circumference post-MBSR and 2 months later.

Conclusions: The RCT was largely feasible and MBSR acceptable to participants. MBSR may lead to sustained decreases in cholesterol levels, warranting development of large-scale research on this topic.

Clinical Implications: Given the role of stress in CVD, addition of stress management interventions may serve as a useful complement to risk management among older individuals.

Key Words: Aging, mindfulness, clinical trial, stress, cholesterol, MBSR, acceptability, feasibility, metabolic syndrome, autonomic stress responses

Introduction

Metabolic syndrome affects 40 percent of adults over age 60 and doubles risk for cardiovascular disease (CVD), the leading cause of death in men and women worldwide (Alberti et al., 2009; Riediger & Clara, 2011). Metabolic syndrome typically refers to the presence of at least three of the following interconnected factors: central adiposity, high blood pressure (BP), elevated triglycerides, increased fasting blood glucose, and low levels of high-density lipoprotein (HDL) cholesterol (Alberti et al., 2009). Psychological stress may contribute to metabolic syndrome and its individual parameters (Kuo et al., 2019), in part through activation of heightened or prolonged physiological stress responses (Chandola, et al., 2006).

Consistent with the stress reactivity hypothesis of cardiovascular disease (CVD) (Obrist, 1981), exaggerated increases in cardiovascular activity in response to stress have been associated with increased risk of CVD (Carroll et al., 2011) and high blood pressure (for a meta-analysis, see Chida & Steptoe, 2010). We have also shown that non-normative responses (both hyper- and hyporeactivity) to stress within the autonomic nervous system (ANS), and especially of the parasympathetic nervous system, are related to significantly greater risk of metabolic dysfunction (Gentile et al., 2014; Gentile, et al 2019). Other emerging data suggests that blunted physiological response to stress may also be associated with adverse outcomes, including central adiposity (Carroll et al., 2008; Phillips et al., 2012; Singh & Shen, 2013). Since moderate reactions to stress may reflect more adaptive, flexible responses to frequently changing environmental or internal demands (Lovallo, 2011), non-normative stress responses may constitute powerful targets in secondary prevention efforts aimed at reducing metabolic syndrome.

Mindfulness-based stress reduction (MBSR), a standardized, 8-week secular program, involving the practice of mediation, yoga, and non-judgmental awareness and acceptance of present moment experience (Kabat-Zinn, 1990), has already shown promise for health issues exacerbated by stress (e.g. irritable bowel syndrome, chronic pain) (Khoo et al., 2019, Lakhan & Schofield, 2013). Limited data suggests the feasibility and effectiveness of MBSR in older adults with lower back pain or insomnia but further investigations on the feasibility and impact of MBSR in older adult samples with other chronic medical conditions are required (Hazlett & Stevens, 2019), including metabolic syndrome and other CVD risk factors (for a review by the AHA, see Levine et al., 2017).Therefore, whether MBSR is feasible and acceptable as an adjunct to usual treatment for those at risk for CVD (i.e. older adults with high metabolic burden and showing non-normative stress responses), in whom preventive efforts are typically pharmacological, remains to be evaluated.

To our knowledge, no studies have investigated the influence of MBSR across all metabolic syndrome parameters within one study, though several have examined individual components. While conflicting results have emerged (Campbell et al., 2012; Hartmann et al., 2012), investigations report average mean reductions of 11/6 mm Hg in SBP/DBP in individuals participating in MBSR as compared with individuals allocated to waitlist or active control conditions whose BP remained stable or increased slightly (Nyklicek et al., 2013; Parswani et al., 2013). The effects appear slightly more pronounced in those with baseline hypertension (Solano Lopez, 2018). Research on the effects of MBSR on remaining parameters of metabolic syndrome is scant and mixed, and is comprised principally of studies on weight loss, in which glucose and BMI were sometimes included (Daubenmier et al., 2012; Ellis et al., 2018; Parswani et al., 2013; Rosenzweig et al., 2010; Youngwanichsetha et al., 2014). No studies to our knowledge have examined the impact of MBSR on lipids.

We propose that MBSR may influence metabolic outcomes, in part, through its impact on physiological reactivity to or recovery from stress. Only one study examined the influence of MBSR on cardiovascular and autonomic stress reactivity (Nyklíček et al., 2013). The latter found MBSR to be associated with greater reductions in BP reactivity to stress when compared to waitlist controls, though no effects were observed in HRV and cortisol responses. Habituation to the testing environment was unlikely to explain results as controls displayed little change in BP reactivity over a similar time period despite repeated testing.

The primary objective of this pilot RCT was to collect feasibility and acceptability data pertaining to MBSR in older individuals who met criteria for metabolic syndrome and showed non-normative ANS responses to stress in previous testing. This objective was prioritized in order to further corroborate an eventual large-scale RCT and to illustrate interest in an adjunct, non-medical intervention in individuals with CVD risk factors. As secondary objectives, we investigated whether MBSR a) improves metabolic syndrome components and b) assessed whether changes in metabolic parameters correlated with changes in physiological reactivity post-intervention and with daily practice of mindfulness.

Methods

This pilot study is a randomized-controlled trial with a waitlist control group that utilized a repeated measures (pre-test/post-test) design (AEARCTR-0006420). Metabolic parameters were also re-assessed two months post-MBSR. Testing was conducted at the Montreal Heart Institute (MHI) between 11/2015 and 09/2016.

Participants

Individuals were recruited from BEL-AGE, an ongoing large-scale prospective investigation on pathological aging. For full inclusion/exclusion criteria of BEL-AGE, please refer to Gentile et al. (2019).

Participants were invited to participate in the current study if, at the time of their participation in BEL-AGE, a) they met criteria for metabolic syndrome as specified by the National Cholesterol Education Program (Alberti et al., 2009), b) if they exhibited exaggerated or blunted sympathovagal response as measured by membership in the lower or higher tertile of LF/HF – HRV reactivity to an acute stressor (anger recall task) in previous BEL-AGE testing (refer to Gentile et al., 2019 for details), and 3) if they had no history of cardiovascular disease (including angina symptoms). Those with an exaggerated sympathovagal response are referred to as "hyper-reactors" in this paper while those with a blunted response are referred to as "blunted responders". This resulted in a recruitment pool of 81 potential participants. Interested individuals were excluded if they a) had a significant cognitive or psychological condition limiting the extent to which they could participate in the research study and intervention program (e.g. delirium, psychosis, bipolar disorder, dementia); b) suffered from cardiovascular disease, including CAD, angina symptoms, arrhythmia, congenital heart disease, heart failure, cardiomyopathy and stroke; c) had cancer, HIV, or any other illness with potential to impact longevity and capacity to participate in follow-up; d) were concurrently participating in psychotherapy; e) were regular yoga or meditation practitioners.

Procedure

Recruitment letters were sent to the 81 individuals recruited from BEL-AGE who met inclusion criteria for this study. A reminder was mailed six weeks later. Interested individuals were instructed to contact the laboratory and were screened for exclusion criteria.

Once deemed eligible, availabilities for the MBSR intervention were collected and a final schedule determined to accommodate the greatest number of participants. Testing was performed between 8:00 a.m and 9:00 am on a weekday to control for circadian rhythms and to limit the fasting period. Participants abstained from eating, drinking (besides water), smoking, or doing strenuous exercise for 12 hours prior to testing. They also abstained from using drugs or alcohol 24 hours prior.

Once participants provided written consent, weight, height, and waist circumference were obtained. Participants then underwent a blood draw, followed by a structured interview assessing demographic and medical information. The electrodes for electrocardiographic (ECG) monitoring were attached in a bipolar configuration to the lower side of the rib cage, and a ground electrode under the right clavicle. The ECG was obtained using PowerLab (ADInstruments, Oxford, UK). A Finopres Finometer (Amsterdam, The Netherlands) was placed on the middle finger of the non-dominant hand to measure BP. Participants then completed brief questionnaires, while they acclimated to testing equipment before the stress protocol.

The stress protocol involved a 10 minute baseline period and two 5 minute psychological stressors: the Paced Auditory Serial Addition Test (PASAT) and a debate task. Each stressor was followed by a 5 min recovery period. Participants completed measures of affect, arousal, and stress perceptions before and after each task. ECG, BP, and respiration were recorded continuously throughout the baseline, stress, and recovery periods. This study was approved by the Research and Ethics Board of the MHI.

Laboratory Stress Tasks. Participants were informed that they would be video recorded during the PASAT and debate, and that their performances would be evaluated and compared to participants of their sex and age group.

Paced Auditory Serial Addition Test (PASAT) (5 min): The PASAT is a standardized short-term memory and arithmetic task in which a series of single digit numbers are presented from a standardized audio-recording and participants are instructed to add the number they just heard with the number presented immediately prior to it. This task has been shown to elicit significant increases in both physiological and affective reactivity (Carroll, Phillips, Der, Hunt, & Benzeval, 2011; Steffen & Larson, 2015).

Debate Task (5 min): Participants engaged in a non-scripted debate with a research assistant on socially salient topics such as abortion (session 1), the right to die (session 2), and same-sex marriage (session 3). Once participants chose the side they wished to argue, they were provided sample arguments to consult for two minutes. The participant and research assistant then alternated between speaking and listening for one minute each, for a total of three minutes of active debate for the participant and two minutes of listening. This task has been associated with significant elevations in physiological and affective arousal, (for example, see Gentile et al., 2014).

Randomization. Participants were randomly assigned to either the MBSR or wait-list control groups after their baseline evaluation. Randomization was stratified by sex and physiological stress response profile and was performed by an independent biostatistician using a random sequence generator. Allocation was hidden from the researcher performing the assessments using sequentially numbered sealed envelopes.

All participants were recruited and tested within a similar time period to limit group differences resulting from passage of time and differential exposure to weather, socioeconomic, political, or other variables. Laboratory technicians conducting the blood draws and the psychologist facilitating the MBSR intervention were blind to the participants' grouping and stress response style. Those administering the stress protocol and entering the data were blind until the end of the second evaluation, when participant feedback was collected. Participants in the intervention group underwent three evaluations, while those in the control group participated in four. For more information on study flow, please see Figure 1.

Follow-up Visits. Evaluations 1-4 were performed at approximately two month intervals. The procedures for Evaluations 2, 3, and 4 were nearly identical to that of Evaluation 1, with the exception that the topics of debate were changed, and full socio-demographic, medical and health behavior questionnaires were not re-administered unless changes had occurred.

The Intervention. The MBSR program constituted eight weekly 2.5 hour sessions at a community center adjacent to the MHI. They also attended an additional five hour "retreat" between weeks 7 and 8 which sought to further integrate acquired skills. The nine sessions were delivered over nine rather than eight weeks to avoid holding a session on a religious holiday. Sessions were facilitated by a psychologist/MBSR teacher with over 25 years of psychotherapy experience. They were audio-recorded and reviewed by the senior investigator (BDA), a psychologist with over 23 years of experience in stress management and mindfulness-based stress interventions, in order to verify adherence to the standardized program.

Participants were assigned weekly homework activities and instructed to practice formal mindfulness skills for 25 to 45 minutes a day and record their minutes of daily practice. Audio recordings of mindfulness exercises were provided to the participants in order to facilitate daily practice at home.

Measures

Feasibility. Feasibility was examined via response rate, recruitment rate, and refusal rates. Response rate refers to the number of participants that responded to the initial recruitment letter, divided by the total number of participants approached. Recruitment rate was defined as the number of participants that agreed to participate, divided by the total number that responded. Refusal rate refers to the number of participants who refused to participate divided by the total number that responded.

Acceptability. Acceptability was measured via the program completion rate and attendance. An adapted version of the Treatment Acceptability and Preferences Questionnaire (Sidani et al., 2009) was also administered; it consisted of 11 questions measuring the extent to which participants perceived the intervention as efficacious, appropriate and acceptable by means of Likert scales ranging from 0 *(not at all)* to 4 *(extremely).* Participants indicated how beneficial they perceived each MBSR component to be (teacher instruction, meditation, yoga, group discussions, etc.), using the same Likert scale. They were also queried with open-ended questions regarding the intervention (e.g. "why did you participate in this project on stress management"; "what aspect(s) of the MBSR program did you particularly enjoy"; "what aspect(s) of the MBSR program did you particularly dislike") and their responses were recorded.

Sociodemographic variables. Data on sex, age in years, ethnicity, weight, height, marital status, income, and years of schooling were obtained, as were behavioral risk factors (tobacco, alcohol, physical activity).

Affect and arousal. These were assessed during the baseline, stress, and recovery phases of the protocol using the Self-Assessment Manikin (SAM) (Hodes, 1985).

Biological outcome variables

Plasma blood sample. Blood samples were analyzed for cholesterol, triglycerides and glucose at the MHI. These determinations were made using respective reagent Flex on the multianalyzer Dimension RxL Max (Dade Behring Diagnostics, Marburg, Germany) with heparinized plasma. The samples were analyzed upon reception.

Blood pressure/ECG. Participants were given approximately 10 minutes to adapt to the physiological equipment before baseline measures were recorded. Baseline BP obtained during the stress protocol was utilized as resting BP. ***Heart rate variability (***HRV) parameters were obtained from the electrocardiogram (ECG) and were analyzed offline in LabChart (ADInstruments, Dunedin, New Zealand). HRV parameters of interest included high frequency (HF; 0.15–0.40 Hz) and low frequency components (LF; 0.04– 0.15 Hz) as recommended by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). For more information, please refer to Gentile et al. (2019).

Data reduction. SBP, DBP, HR, HF-HRV, HF_{nu}, and LF/HF readings were averaged over each baseline, stress, and post-stress period. The two stress periods (PASAT, debate) and recovery periods were then averaged to create a composite stress and recovery scores for each parameter. Such composite scores are more reliable and representative of trait-like responses than responses to individual tasks (Kamarck & Lovallo, 2003). Stress reactivity (stress-baseline) and recovery (recovery-baseline) change scores were computed for each parameter.

Statistical Analyses

This pilot study was not powered to detect significant differences in metabolic parameters pre and post MBSR. Means, standard deviations, and percentages were obtained in order to address primary objectives. For secondary objectives, effect sizes, direction of effects, and clinical significance were of interest, though *p* values are provided. Since effect sizes estimates from small pilot studies may be unreliable (Leon, David & Kraemer, 2011), confidence intervals were provided where possible.

In preliminary analyses, independent samples t-tests were conducted to assess whether the intervention group and control group differed on variables of interest at study onset.

In order to evaluate between-group differences in metabolic parameters, ANOVAs were conducted using change scores (Evaluation 2 – Baseline), with Grouping (MBSR or waitlist control) as a between-subjects factor.

To examine within-group changes as a result of the intervention, one-way repeated measures ANOVAs were performed on each variable comparing the evaluation period immediately prior to MBSR to that immediately post-MBSR and at two-month post intervention. T-tests were used to make post-hoc comparisons between the three time points.

Analyses were performed separately for each metabolic factor. First, analyses were conducted on the whole sample (n=18) as per an intent to treat approach. The within-subjects analysis was then repeated for individuals (n=13) who completed the MBSR program (i.e. attended at least 6 sessions of the intervention). The Last-Observation-Carry-Forward (LOCF) method was used for one participant who completed the intervention, but did not attend Evaluation 3 (2 months post-intervention).

Percent change was calculated as (Post Value - Pre Value)/Pre-Value)*100) and used to explore spearman correlations (r_s) between changes in metabolic parameters, practice time, and changes in physiological responses to stress.

Data were analyzed using the IBM SPSS Statistics 24.0 software (IBM Corporation, Somers, N.Y., USA)

Results

Feasibility of MBSR

Response rate, refusal rate, and recruitment rate. Of the 81 participants invited to participate, 51 % (*n*=41) were women and 52 % (*n*=42) were hyper-reactors to stress. Women comprised 45% (*n*=19) of the hyper-reactivity group and 56% (*n*=22) of the blunted reactivity group. A total of 33 individuals contacted the laboratory after receiving the letter, a response rate of nearly 41%. Of these individuals, 79% consented to participate, while seven (21%) refused. Given scheduling conflicts and one participant who withdrew prior to randomization, a final n of 18 was obtained. For more information regarding participant recruitment and study flow, please refer to Figure 2.

Participant Characteristics

For a full summary of participant characteristics, please refer to Table 1. Participants were mostly retired, older adults (M_{age} = 67, *SD*= 7.7) with an average BMI within the obesity range. Although many participants were on medication capable of reducing metabolic syndrome or its constituents, a total of 47 percent still met metabolic syndrome criteria at first evaluation, while 74 percent met criteria for at least two components. The intervention and control groups did not differ significantly in age, weight, BMI, nor on any baseline metabolic and HRV parameters

Acceptability of MBSR

Completion rate. Completion rate of the MBSR program was 72 percent, with 7 out of 9 completing the MBSR program in the intervention group versus 6 out of 9 in those initially waitlisted. Reasons for non-completion included difficulty with commute (n=1), work scheduling conflicts (n=1), too busy (n=2), and belief that MBSR would not be beneficial (n=2). Sixty percent of non-completers were working at least part-time. All non-completers returned for laboratory assessment.

Practice performed. On average, participants reported practicing formal MBSR skills 40.6 ± 16.4 minutes a day.

Attendance of MBSR. Overall attendance by completers of the MBSR program was 96 percent (112 out of 117 sessions attended). Missed sessions were due to prior engagements or illness.

Attendance of evaluations. All participants attended the first and second evaluation sessions, with the exception of one individual who withdrew from the study after Evaluation 1 and who was removed from analyses. A total of 89 percent of participants (n =16) attended the third evaluation. Loss to follow-up included desire to avoid another blood draw (n=1), and failure to arrive in a fasting state to Evaluation 3 and refusal to reschedule (n=1). All other waitlist control participants were present for the fourth evaluation.

Acceptability questionnaire post-intervention. For full results of the acceptability questionnaire, please refer to Table 2. In sum, the majority of participants rated the program as moderately, very, or extremely efficacious, appropriate, and acceptable in the reduction of stress (94%, 88% and 96%, respectively). The most appreciated components of the MBSR program were the teacher instruction and sitting meditation, while the least appreciated components were the walking meditation and the 5-hour retreat. A total of 64% of participants indicated that they would be very or extremely likely to participate in the program again, while 76% were moderately, very or extremely likely to continue their mindfulness practice. Traffic and commute to the hospital were stated as primary reasons for unwillingness to hypothetically participate a second time in MBSR.

Participant verbal feedback is summarized in the supplementary online only Table 6**.** In general, participants reported that MBSR engendered relaxation, facilitated connection with their loved ones, and increased awareness of their body, which fostered participation in physical activity. MBSR also helped participants become more in tune with their emotions which was pleasant for most participants but distressing for one individual who did not complete MBSR. Others expressed that MBSR should be widely available for older adults or those working in high-stress environments.

Secondary Objectives

Changes in Metabolic Outcomes in Response to MBSR

Between-Subjects Effects (n=18) as per an Intention-to-Treat Approach. Those participating in MBSR exhibited greater decreases in total cholesterol and especially LDL, compared to controls, with moderate to large effect sizes. Although triglycerides in the MBSR group were nearly unchanged post-intervention, control participants exhibited a notable increase in triglycerides over the two-month period. For full results, please refer to Table 3.

Within-Subjects Effects (n=18) as per an Intention-to-Treat Approach. There was a significant main effect of time period. With the exception of glucose, all metabolic parameters decreased post-MBSR. The greatest decreases were observed in LDL, total cholesterol, and waist circumference with large effect sizes. Reductions in LDL and total cholesterol were largely maintained two months following completion of the program. Waist circumference continued to decrease two months after the end of MBSR, as did triglycerides and HDL. For a full summary of follow-up data, please refer to Table 4.

Within-Subjects Effects (n=13) for MBSR Completers. Analyses performed in those who completed the MBSR program showed *greater* decreases in LDL and total cholesterol. SBP was maintained within the normal range (less than 130 mm Hg) at two month follow-up in MBSR completers, whereas in non-completers, SBP exceeded 130 mm Hg two months later. For a full summary of results for MBSR completers, please refer to Table 5.

Changes in Autonomic Stress Responses after MBSR

MBSR led to systematic changes in physiological responses to stress. Those in the blunted LF/HF response groups became *more* reactive in measures of parasympathetic activity (HR, HF, and $HF_{nu)}$ upon completion of MBSR, while those who were initially more reactive became *less* reactive on these same measures. Decreases in LF/HF reactivity post-MBSR were observed in both groups. While there was little change in SBP and DBP reactivity post-intervention in heightened LF/HF responders, SBP and DBP reactivity decreased in blunted LF/HF responders. Please refer to supplemental online Tables 7a and 7b for details.

Changes in Stress Response vs. Change in Cholesterol (by Stress Reactivity Grouping)

In those with blunted LF/HF-HRV stress responses, change in HF reactivity was positively correlated with change in triglycerides (r_s=0.71, p=0.07), with greater parasympathetic withdrawal to stress post-MBSR associated with greater decreases in triglyceride levels. In LF/HF-HRV hyper-reactors, less $HF\text{-}HRV_{log}$ reactivity to stress post-MBSR was correlated with larger drops in total cholesterol *(r_s=-0.367,* p=0.332) and LDL cholesterol (r_s=*-0.383,* p=0.308).

Influence of Practice Time on Metabolic Parameters. More minutes practiced per week correlated with decreases in total cholesterol (r =-0.52) (see supplemental online Table 8).

Discussion

The primary goal of the pilot study was to assess the feasibility and acceptability of MBSR for older adults at risk for CVD by virtue of metabolic risk factors and non-normative autonomic responses to stress. Secondary objectives included examining whether MBSR improves metabolic syndrome components. Tertiary goals addressed associations between metabolic changes post- MBSR with changes in physiological stress responses and daily practice of mindfulness.

Recruitment for this study was moderately feasible and the methods and intervention largely acceptable to participants. Forty-one percent of individuals invited to participate responded to the recruitment letter. Response rates may have been higher if potentially eligible participants were contacted directly by phone rather than by mail (Cohen et al., 2008), though constraints imposed by our institutional ethics board prohibited recruitment through phone contact. It is difficult to compare our response rate with those of other MBSR intervention studies utilizing clinical samples, as eligible participants in those investigations tended to be referred directly from healthcare providers after in-person visits (Campbell et al., 2012; Lengacher et al., 2012). Nevertheless, our response rate is high compared to studies utilizing invitation letters for other health interventions (7-32 percent) (Halbert, et al., 1999; McClure et al., 2006; Stopponi et al., 2009). This suggests that our older adults at risk of CVD were very motivated to learn stress management strategies. However, as letters were sent to individuals who had previously engaged in (health psychology) research, they may represent a group particularly motivated by this research, irrespective of their age or CVD risk factors. Replication in a large community sample similar in age and health profile is required to corroborate older adults' motivation to engage in stress management for their metabolic health.

Of those invited to participate in the study, 32 percent (79 percent of those who contacted the team) consented. This is comparable to the recruitment rates reported by other authors utilizing samples of older and middle-aged adults with metabolic syndrome (29 and 38 percent, respectively) (Cohen et al., 2008; Kim et al., 2014). The primary reason for refusal was the time commitment and commute to hospital. Scheduling conflicts were also a barrier to feasibility; several interested participants were unable to attend MBSR at the scheduled time and were excluded.

Acceptability of MBSR was high as evidenced by a completion rate of 72 percent, similar to that observed in other MBSR studies (Campbell et al., 2012; Kim et al., 2014). Older age and retiree status facilitated completion; specifically, the participants' shared older age appeared to favor group cohesion, likely increasing participant motivation to attend all sessions. The youngest participant (41 years old) expressed that she could not relate to the group and dropped out of the program. This suggests that recruiting individuals that are homogeneous in age may facilitate participant retention in future studies. Additionally, retirees were more likely to complete MBSR compared to active workers, possibly due to more available time to devote to the program. This was evidenced by the participants' home practice of mindfulness for 41 minutes a day, which was near the upper limit of recommended practice time, and higher than what is typically reported (18-33 minutes a day) in other studies (Lengacher et al., 2009; Parsons et al., 2017). Most participants who were working happened to be randomized to the control group, which could explain the greater drop-out rate in this group. It is also possible that waiting for two months for MBSR may have decreased interest to participate. While it is frequently difficult to recruit men into studies testing psychological interventions, including mindfulness based interventions (e.g., Müller-Engelmann et al., 2017), in the current study, not only was 40%

of our sample male, but the latter also showed a slightly better completion rate than the women (72% vs. 64%, respectively), suggesting that as presented and administered, the program was well targeted to both men and women.

The majority of participants rated the MBSR program as highly efficacious, appropriate, and acceptable in the reduction of stress. Most were also likely to participate in the program again and to continue their mindfulness practice. They reported increased self-awareness and lowered distress post-MBSR, which contributed, according to them, to improving different life domains, including intra/interpersonal well-being. These findings suggest efficacy of MBSR in older individuals, favoring its inclusion in hospital settings including cardiac rehabilitation centers and preventive healthcare programs. Nonetheless, MBSR was distressing for one individual who dropped out of the program. She reported feeling like a failure due to her difficulty being mindful. This is consistent with some emerging literature examining the potential adverse effects of mindfulness, including possible increases in depressive and anxious states in some individuals (Britton, 2019). However, qualitative interviews from the current study suggest that MBSR may have increased awareness of pre-existing psychological distress, rather than induce it directly. Greater attention to and normalization of these reactions are recommended, including the reminder that recognizing that one has not been mindful in a particular situation is both an indicator of increased mindfulness, and an opportunity for practice.

MBSR & Metabolic Outcomes

The most notable impact of MBSR was observed for LDL and total cholesterol, which decreased by 15 and 10 percent respectively in the MBSR group. Effect sizes associated with these changes were large and reductions were mostly maintained at two-month follow-up. A meta-analysis reported that a reduction of 10 percent in total cholesterol results in a 10 to 11 percent decrease in the risk of all-cause mortality and a 13 to 15 percent decrease in CVD-related mortality, indicating substantial clinical significance of these findings (Gould et al., 1998). Moreover, these reductions were additional to benefits already achieved by medication (58 percent of the sample was taking dyslipidemic agents). The influence of MBSR on the remaining metabolic components was also mostly positive. Given that BP tends to increase acutely in medical and laboratory settings, especially in older adults, it is possible that habituation of baseline BP occurred across consecutive evaluations, accounting for the decreases in SBP in both groups (Franklin et al., 2013). It remains unclear why participants in both groups exhibited small increases in glucose post-MBSR, though this pattern was previously reported in another study (Daubenmier et al., 2012). It will be important to verify whether this finding replicates in a large-scale RCT.

As per other literature (e.g., Carlson et al., 2001; Lengacher et al., 2009), the more individuals practiced MBSR during and across weeks, the greater the improvements were observed. This suggests that mindfulness training is most effective when practiced on a regular basis. Which aspects are most important to practice remain to be determined.

MBSR and Physiological Stress Responses

This study provides preliminary evidence that participating in a stress reduction intervention may "normalize" physiological stress responses in those with either heightened or blunted sympathovagal response styles. Indeed, those participants that had shown blunted sympathovagal responses to stress in BEL-AGE showed greater parasympathetic withdrawal to stress upon completion of MBSR, while those who were initially more reactive became *less* reactive on these same measures. Decreases in LF/HF reactivity post-MBSR were observed in both groups, while SBP and DBP reactivity decreased mainly in blunted LF/HF responders. Given that decreases were observed in *both* groups for LF/HF and BP indices, it is unlikely that findings can be explained by regression towards the mean. Only one previous study examined the impact of MBSR on cardiovascular and autonomic reactivity specifically. In their randomized-controlled trial of 88 healthy individuals, Nyklicek and colleagues (2013) reported that participation in MBSR resulted in significant decreases in SBP and DBP reactivity compared to waitlist controls, but no change in HRV post-intervention. However, these authors did not stratify their sample according to initial stress response; if reactivity groupings had been combined in our analyses, changes observed for HRV parameters would have been masked. Research from our group (Gentile et al. 2014; Gentile et al., 2019) highlight the importance of individuals' autonomic responses to stress in metabolism. Not only do exaggerated and blunted parasympathetic stress responses appear to increase risk for metabolic burden, but this study suggests that effects may be reversed through stress management, such as MBSR. Improved emotional awareness, regulation, and health behaviors may also be involved.

Limitations, Strengths, and Future Research

Although the primary objectives of this study were to assess feasibility and acceptability, the number of participants randomized was small. This limits the conclusions that can be drawn regarding the impact of MBSR as well as the generalizability of results (Simmons, Nelson & Simonsohn, 2011). While statistical differences did not exist between MBSR and waitlist control groups, perusal of participant characteristics suggested a worse sociodemographic and metabolic profile in the control group versus MBSR group. Unfortunately, given the sample size, it was not possible to control for these potential confounders. An average of approximately two years elapsed between participation in BEL-AGE and the first evaluation for the current study, allowing time for changes in initial stress response style. However, we previously reported that autonomic stress responses are stable over three years (Dragomir, Gentile, Nolan, & D'Antono, 2014). It is also possible that habituation or practice effects across repeated administrations of the stress protocol may have occurred, although participants reported significant stress across all three evaluation sessions**.**

Strengths include a randomized controlled trial that employed rigorous methodology. The sample was clustered by initial stress response grouping and sex and the randomization groups did not differ significantly from each other at baseline. The MBSR program was facilitated by an experienced psychologist. Different debate topics were also chosen for each evaluation of the stress protocol, which limited participants' ability to practice between sessions.

In sum, this pilot investigation suggests that implementing MBSR in an older population at risk for cardiovascular disease is highly acceptable and feasible, though additional recruitment strategies would be required to secure a larger pool of participants. Collaborating with healthcare providers could facilitate access to potential participants and increase motivation to engage in stress management as part of a more holistic approach to health care. For research purposes, the MBSR program should ideally be offered at more than one time period in order to accommodate both working and retired participants. Importantly, preliminary data indicate that MBSR may be particularly useful in decreasing LDL and total cholesterol among older individuals, suggesting the potential for a non-invasive intervention with few to no side effects to lower cardiovascular risk, including in individuals receiving pharmacotherapy for metabolic syndrome components.

Clinical implications

* The current results suggest that a large-scale investigation on MBSR for older adults at risk for CVD would be largely acceptable and feasible.

* Programs targeting stress and its physiological correlates (HRV) may serve as useful adjuncts in the management of CVD risk among older individuals, though large-scale studies are needed.

Acknowledgements

We would like to thank Anne Lynch for her thoughtful and gentle approach to MBSR teaching. Additional thanks to the BEL-AGE participants for their dedication to this project. Thank you to Sea of Tranquility for providing equipment at reduced cost. Finally, thank you to the Canadian Institutes of Health Research, Montreal Heart Foundation, and l'*Ordre Fraternal des Aigles 3176 Inc* (St-Jérome) whose funding made this research possible.

Funding

This study was supported by grants awarded to Dr. D'Antono by the Canadian Institutes of Health Research (CIHR – MOP #111015) and the Montreal Heart Foundation. A dedicated donation was offered to Bianca D'Antono by *Ordre Fraternal des Aigles 3176 Inc* (St-Jérome). Christina Gentile and Louisia Starnino were supported by the Doctoral Training Award issued by the Fonds de la recherche en santé du Québec (FRSQ). The funding sources had no involvement in this study. No additional funding was received.

Author Information

Affiliations

Research Center, Montreal Heart Institute, 5000 Bélanger street, Montreal, Quebec, Canada, H1T 1C8

Christina Gentile, Louisia Starnino & Bianca D'Antono

Department of Psychology, Université de Montréal, Montreal, Canada

Christina Gentile & Bianca D'Antono

Department of Psychology, Université du Québec à Montréal, Montreal, Canada

Louisia Starnino & Gilles Dupuis

Author Contributions. CG, principle investigator, designed and executed the study, conducted the literature review, performed statistical analyses, and wrote the manuscript. LS, co-principle investigator, assisted in the design and execution of the study, performed statistical analyses, and assisted in the preparation of the manuscript. GD collaborated in the editing of the final manuscript. BDA, co-principle investigator, designed and secured funding for the study, collaborated in the writing and editing of the manuscript. All authors approved the final version of the manuscript before submission.

Corresponding author. Correspondence to Bianca D'Antono bianca.d.antono@umontreal.ca

Conflict of Interest. The authors declare that they have no conflict of interest.

Compliance with Ethical Declarations. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

References

Alberti, K. G., Eckel, R. H., Grundy, S. M., Zimmet, P. Z., Cleeman, J. I., Donato, K. A., Fruchart, J.C, James, W.P., Loria, C.M., & Smith, S.C. Jr. International Association for the Study of, Obesity. (2009). Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation, 120(16).https://doi.org/10.1161/CIRCULATIONAHA.109.192644

Bacon, S. L., Ring, C., Lip, G. Y., & Carroll, D. (2004). Increases in lipids and immune cells in response to exercise and mental stress in patients with suspected coronary artery disease: effects of adjustment for shifts in plasma volume. Biological psychology, 65(3), 237-250.https://doi.org/10.1016/S0301-0511(03)00113-3

Britton, W. B. (2019). Can mindfulness be too much of a good thing? The value of a middle way. Current opinion in psychology, 28, 159-165.https://doi.org/10.1016/j.copsyc.2018.12.011

Campbell, T. S., Labelle, L. E., Bacon, S. L., Faris, P., & Carlson, L. E. (2012). Impact of mindfulness-based stress reduction (MBSR) on attention, rumination and resting blood pressure in women with cancer: a waitlist-controlled study. Journal of Behavioral Medicine, 35(3), 262-271.https://doi.org/10.1007/s10865-011-9357-1

Carlson, L. E., Ursuliak, Z., Goodey, E., Angen, M., & Speca, M. (2001). The effects of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients: 6-month follow-up. Supportive care in Cancer, 9(2), 112-123.https://doi.org/10.1007/s005200000206

Carroll, D., Phillips, A. C., & Der, G. (2008). Body mass index, abdominal adiposity, obesity, and cardiovascular reactions to psychological stress in a large community sample. Psychosomatic Medicine, 70(6), 653-660.https://doi.org/10.1097/PSY.0b013e31817b9382

Carroll, D., Phillips, A. C., Der, G., Hunt, K., & Benzeval, M. (2011). Blood pressure reactions to acute mental stress and future blood pressure status: data from the 12-year follow-up of the West of Scotland Study. Psychosomatic Medicine, 73(9), 737-742.https://doi.org/10.1097/PSY.0b013e3182359808

Chandola, T., Brunner, E., & Marmot, M. (2006). Chronic stress at work and the metabolic syndrome: prospective study. Bmj, 332(7540), 521-525.https://doi.org/10.1136/bmj.38693.435301.80

Chida, Y., Hamer, M., (2008). Chronic psychosocial factors and acute physiological response to laboratory-induced stress in healthy populations: A quantitative review of 30 years of investigations. Psychol. Bull. 134, 829-855.https://doi.org/10.1037/a0013342

Chida, Y., & Steptoe, A. (2010). Greater cardiovascular responses to laboratory mental stress are associated with poor subsequent cardiovascular risk status: a meta-analysis of prospective evidence. Hypertension, 55(4), 1026-1032.https://doi.org/10.1161/HYPERTENSIONAHA.109.146621

Cohen, B. E., Chang, A. A., Grady, D., & Kanaya, A. M. (2008). Restorative yoga in adults with metabolic syndrome: a randomized, controlled pilot trial.Metabolic syndrome and related disorders, 6(3), 223-229.https://doi.org/10.1089/met.2008.0016

Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale, NJ: Lawrence Earlbaum Associates.

Crane, C., Crane, R. S., Eames, C., Fennell, M. J. V., Silverton, S., Williams, J. M. G., & Barnhofer, T. (2014). The effects of amount of home meditation practice in Mindfulness Based Cognitive Therapy on hazard of relapse to depression in the Staying Well after Depression Trial. Behaviour Research and Therapy, 63, 17-24.https://doi.org/10.1016/j.brat.2014.08.015

Daubenmier, J., Epel, E. S., Moran, P. J., Thompson, J., Mason, A. E., Acree, M., Goldman, V., Kristeller J., Hecht F.M., & Mendes, W. B. (2019). A Randomized Controlled Trial of a Mindfulness-Based Weight Loss Intervention on Cardiovascular Reactivity to Social-Evaluative Threat Among Adults with Obesity. Mindfulness, 10(12), 2583-2595.https://doi.org/10.1007/s12671-019-01232-5

Daubenmier, J., Lin, J., Blackburn, E., Hecht, F. M., Kristeller, J., Maninger, N., & Epel, E. (2012). Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study. Psychoneuroendocrinology, 37(7), 917-928.https://doi.org/10.1016/j.psyneuen.2011.10.008

Dragomir, A. I., Gentile, C., Nolan, R. P., & D'Antono, B. (2014). Three ‐ year stability of cardiovascular and autonomic nervous system responses to psychological stress. Psychophysiology, 51(9), 921-931.https://doi.org/10.1111/psyp.12231

Ellis, D. A., Carcone, A., Slatcher, R., & Sibinga, E. (2018). Feasibility of Mindfulness-Based Stress Reduction for older adolescents and young adults with poorly controlled type 1 diabetes. Health psychology and behavioral medicine, 6(1), 1-14.https://doi.org/10.1080/21642850.2017.1415810

Epel, E., Lapidus, R., McEwen, B., & Brownell, K. (2001). Stress may add bite to appetite in women: a laboratory study of stress-induced cortisol and eating behavior. Psychoneuroendocrinology, 26(1), 37-49.https://doi.org/10.1016/S0306-4530(00)00035-4

Franklin, S. S., Thijs, L., Hansen, T. W., O'Brien, E., & Staessen, J. A. (2013). White-coat hypertension. Hypertension, 62(6), 982-987.https://doi.org/10.1161/HYPERTENSIONAHA.113.01275

Gentile, C., Dragomir, A. I., Solomon, C., Nigam, A., & D'Antono, B. (2014). Sex differences in the prediction of metabolic burden from physiological responses to stress. Annals of Behavioral Medicine, 49(1), 112-127.https://doi.org/10.1007/s12160-014-9639-2

Gentile, C., Ditto, B., Deschamps, A., & D'Antono, B. (2019). Parasympathetic Response Patterns are Associated with Metabolic Syndrome Among Older Women but Not Men. Annals of Behavioral Medicine, 53(6), 515-526.https://doi.org/10.1093/abm/kay063

Gould, A. L., Rossouw, J. E., Santanello, N. C., Heyse, J. F., & Furberg, C. D. (1998). Cholesterol reduction yields clinical benefit. Circulation, 97(10), 946-952.https://doi.org/10.1161/01.CIR.97.10.946

Halbert, J. A., Silagy, C. A., Finucane, P., Withers, R. T., & Hamdorf, P. A. (1999). Recruitment of older adults for a randomized, controlled trial of exercise advice in a general practice setting. Journal of the American Geriatrics Society, 47(4), 477-481.https://doi.org/10.1111/j.1532-5415.1999.tb07242.x

Hazlett-Stevens, H., Singer, J., & Chong, A. (2019). Mindfulness-based stress reduction and mindfulness-based cognitive therapy with older adults: a qualitative review of randomized controlled outcome research. Clinical gerontologist, 42(4), 347-358.https://doi.org/10.1080/07317115.2018.1518282

Hartmann, M., Kopf, S., Kircher, C., Faude-Lang, V., Djuric, Z., Augstein, F., Friedrich, H.C., Kieser, M., Bierhause, A., Humpert, P.M., Herzog, W., & Nawroth, P. P. (2012). Sustained effects of a mindfulness-based stress-reduction intervention in type 2 diabetic patients design and first results of a randomized controlled trial (the Heidelberger diabetes and stress-study). Diabetes Care, 35(5), 945-947.https://doi.org/10.2337/dc11-1343

Hodes, R. L., Cook, E. W., & Lang, P. J. (1985). Individual differences in autonomic response: conditioned association or conditioned fear? Psychophysiology, 22(5), 545-560.https://doi.org/10.1111/j.1469-8986.1985.tb01649.x

Kabat-Zinn, J. (1990). Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness. New York, N.Y: Delacorte Press

Kamarck, T. W., & Lovallo, W. R. (2003). Cardiovascular reactivity to psychological challenge: conceptual and measurement considerations. Psychosomatic medicine, 65(1), 9-21.https://doi.org/10.1097/01.PSY.0000030390.34416.3E

Khoo, E. L., Small, R., Cheng, W., Hatchard, T., Glynn, B., Rice, D. B., Skidmore, E., Kenny, S.,Hutton, B., & Poulin, P. A. (2019). Comparative evaluation of group-based mindfulness-based stress reduction and cognitive behavioural therapy for the treatment and management of chronic pain: A systematic review and network meta-analysis. Evidence-based mental health, 22(1), 26-35.https://doi.org/10.1136/ebmental-2018-300062

Kim, C. J., Park, J. W., & Park, H. R. (2014). Effects of a community-based intervention on cardio-metabolic risk and self-care behaviour in older adults with metabolic syndrome. International journal of nursing practice, 20(2), 212-220.https://doi.org/10.1111/ijn.12139

Kuo, W. C., Bratzke, L. C., Oakley, L. D., Kuo, F., Wang, H., & Brown, R. L. (2019). The association between psychological stress and metabolic syndrome: A systematic review and meta - analysis. Obesity Reviews, 20(11), 1651-1664.https://doi.org/10.1111/obr.12915

Lakhan, S. E., & Schofield, K. L. (2013). Mindfulness-based therapies in the treatment of somatization disorders: a systematic review and meta-analysis. PloS one, 8(8), e71834.https://doi.org/10.1371/journal.pone.0071834

Lakka, H. M., Laaksonen, D. E., Lakka, T. A., Niskanen, L. K., Kumpusalo, E., Tuomilehto, J., & Salonen, J. T. (2002). The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. Jama, 288(21), 2709-2716.https://doi.org/10.1001/jama.288.21.2709

Lengacher, C. A., Johnson - Mallard, V., Post - White, J., Moscoso, M. S., Jacobsen, P. B., Klein, T. W., Widen R.H., Fitzgerald S.G., Shelton M.M, Barta, M., & Goodman, M. (2009). Randomized controlled trial of mindfulness - based stress reduction (MBSR) for survivors of breast cancer. Psycho - Oncology, 18(12), 1261-1272.https://doi.org/10.1002/pon.1529

Lengacher, C. A., Kip, K. E., Barta, M., Post-White, J., Jacobsen, P. B., Groer, M., Lehman, B., Moscoso, M.S., Kadel, R., & Loftus, L. (2012). A pilot study evaluating the effect of mindfulness-based stress reduction on psychological status, physical status, salivary cortisol, and interleukin-6 among advanced-stage cancer patients and their caregivers. Journal of Holistic Nursing, 30(3), 170-185.https://doi.org/10.1177/089801011143594

Leon, A. C., Davis, L. L., & Kraemer, H. C. (2011). The role and interpretation of pilot studies in clinical research. Journal of psychiatric research, 45(5), 626-629.https://doi.org/10.1016/j.jpsychires.2010.10.008

Levine, G. N., Lange, R. A., Bairey - Merz, C. N., Davidson, R. J., Jamerson, K., Mehta, P. K., & Shah, T. (2017). Meditation and cardiovascular risk reduction: a scientific statement from the American Heart Association. Journal of the American Heart Association, 6(10), e002218.https://doi.org/10.1161/JAHA.117.002218

Lovallo, W. R. (2011). Do low levels of stress reactivity signal poor states of health? Biological psychology, 86(2), 121-128.https://doi.org/10.1016/j.biopsycho.2010.01.006

McClure, J. B., Greene, S. M., Wiese, C., Johnson, K. E., Alexander, G., & Strecher, V. (2006). Interest in an online smoking cessation program and effective recruitment strategies: results from Project Quit. Journal of Medical Internet Research, 8(3).https://doi.org/10.2196/jmir.8.3.e14

Miller, J. J., Fletcher, K., & Kabat-Zinn, J. (1995). Three-year follow-up and clinical implications of a mindfulness meditation-based stress reduction intervention in the treatment of anxiety disorders. General hospital psychiatry,17(3), 192-200.https://doi.org/10.1016/0163-8343(95)00025-M

Müller-Engelmann, M., Wünsch, S., Volk, M., & Steil, R. (2017). Mindfulness-based stress reduction (MBSR) as a standalone intervention for posttraumatic stress disorder after mixed traumatic events: a mixed-methods feasibility study. Frontiers in psychology, 8, 1407.https://doi.org/10.3389/fpsyg.2017.01407

Nyklíček, I., Mommersteeg, P., Van Beugen, S., Ramakers, C., & Van Boxtel, G. J. (2013). Mindfulness-based stress reduction and physiological activity during acute stress: A randomized controlled trial. Health Psychology, 32(10), 1110.https://doi.org/10.1037/a0032200

Obrist, P.A. (1981) Cardiovascular Psychophysiology: a Perspective. Plenum. New York.https://doi.org/10.1007/978-1-4684-8491-5

Parsons, C. E., Crane, C., Parsons, L. J., Fjorback, L. O., & Kuyken, W. (2017). Home practice in Mindfulness-Based Cognitive Therapy and Mindfulness-Based Stress Reduction: A systematic review and meta-analysis of participants' mindfulness practice and its association with outcomes. Behaviour Research and Therapy, 95, 29-41.https://doi.org/10.1016/j.brat.2017.05.004

Parswani, M. J., Sharma, M. P., & Iyengar, S. S. (2013). Mindfulness-based stress reduction program in coronary heart disease: A randomized control trial. International journal of yoga, 6(2), 111.https://doi.org/10.4103/0973-6131.113405

Phillips, A. C., Roseboom, T. J., Carroll, D., & de Rooij, S. R. (2012). Cardiovascular and cortisol reactions to acute psychological stress and adiposity: cross-sectional and prospective associations in the Dutch Famine Birth Cohort Study. Psychosomatic Medicine, 74(7), 699-710.https://doi.org/10.1097/PSY.0b013e31825e3b9

Riediger, N. D., & Clara, I. (2011). Prevalence of metabolic syndrome in the Canadian adult population. Cmaj, 183(15), E1127-E1134.https://doi.org/10.1503/cmaj.110070

Rosenzweig, S., Greeson, J. M., Reibel, D. K., Green, J. S., Jasser, S. A., & Beasley, D. (2010). Mindfulness-based stress reduction for chronic pain conditions: variation in treatment outcomes and role of home meditation practice. Journal of psychosomatic research, 68(1), 29-36.https://doi.org/10.1016/j.jpsychores.2009.03.010

Sidani, S., Epstein, D. R., Bootzin, R. R., Moritz, P., & Miranda, J. (2009). Assessment of preferences for treatment: validation of a measure. Research in nursing & health, 32(4), 419-431.https://doi.org/10.1002/nur.20329

Simmons, J. P., Nelson, L. D., & Simonsohn, U. (2011). False-positive psychology: Undisclosed flexibility in data collection and analysis allows presenting anything as significant. Psychological science, 22(11), 1359-1366.https://doi.org/10.1177/0956797611417632

Singh, K., & Shen, B. J. (2013). Abdominal obesity and chronic stress interact to predict blunted cardiovascular reactivity. International Journal of Psychophysiology, 90(1), 73-79.https://doi.org/10.1016/j.ijpsycho.2013.03.010

Solano Lopez, A. L. (2018). Effectiveness of the Mindfulness - Based Stress Reduction Program on Blood Pressure: A Systematic Review of Literature. Worldviews on Evidence - Based Nursing, 15(5), 344-352.Steffen, P. R., & Larson, M. J. (2015). A Brief Mindfulness Exercise Reduces Cardiovascular Reactivity During a Laboratory Stressor Paradigm. Mindfulness, 6(4), 803-811.https://doi.org/10.1111/wvn.12319

Stopponi, M. A., Alexander, G. L., McClure, J. B., Carroll, N. M., Divine, G. W., Calvi, J. H., Rolnick, S. J., Strecher, V.J., Johnson, C.J., & Ritzwoller, D. P. (2009). Recruitment to a randomized web-based nutritional intervention trial: characteristics of participants compared to non-participants. Journal of Medical Internet Research, 11(3), e38.https://doi.org/10.2196/jmir.1086

Youngwanichsetha, S., Phumdoung, S., & Ingkathawornwong, T. (2014). The effects of mindfulness eating and yoga exercise on blood sugar levels of pregnant women with gestational diabetes mellitus. Applied Nursing Research, 27(4), 227-230https://doi.org/10.1016/j.apnr.2014.02.002

Table 1
Participant characteristics at Evaluation 1 (Baseline)

Baseline Characteristics	MBSR (n=9)		Waitlist (n=9)	
	M or n	*SD or %*	*M or n*	*SD or %*
Sex (male)[a]	4	44.4	3	33.3
Age (years)[b]	69.6	5.0	64.8	9.8
Weight (kg)[b]	79.07	17.1	87.03	9.1
Body Mass Index (kg/m^2)[b]	29.5	4.6	31.9	4.4
Years of schooling[b]	14.6	3.4	14.1	2.3
Marital Status [a]				
Single	2	22.2	2	22.2
Civil union/married	6	66.7	4	44.4
Separated/divorced	1	11.1	3	33.3
Employment Status[a]				
Full-time	1	11.1	3	33.3
Part-time	1	11.1	2	22.2
Retired	7	77.8	4	44.4
Annual family income[a]				
≤ $29 999	0	0	4	44.4
$30 000 - $59 999	5	55.6	1	11.1
$60 000 - $99 999	2	22.2	2	22.2
≥ $100 000	2	22.2	2	22.2
Hours of exercise/week[b]	5.1	4.3	2.9	3.3
Medications[a]				
BP agents	7	78	3	33
Blood glucose regulators	1	11	3	33
Dyslipidemic agents	6	66	4	44
Anxiolytics	2	22	2	22
Baseline Metabolic[a] Parameters[b]				
SBP (mm Hg)	133.1	13.9	134.2	13.5
DBP (mm Hg)	63.5	5.3	65.8	12.2
Waist circumference (cm)	100.8	13.6	103.9	7.01
Glucose (mmol/L)	5.8	1.3	5.9	1.02
Triglycerides (mmol/L)	1.7	0.41	1.8	0.81
HDL (mmol/L)	1.4	0.32	1.4	0.32
LDL (mmol/L)	2.7	1.0	2.6	1.1
Total cholesterol (mmol/L)	4.7	1.2	4.9	1.2
MetSyn criteria[a]				
≥ 3 criteria	3	33	6	67
2 criteria	3	33	2	22
1 criteria	3	33	1	11
Baseline ANS Measures[a]				
HR (bpm)	68.6	9.8	74.1	9.4
HF-HRV (ms^2)	349.02	595.8	1500.1	3550.6

LF/HF	1.44	1.5	2.7	2.4
HF_{nu}	0.54	0.31	0.40	0.3
Blunted stress response at baseline[a]	4	44.4	4	44.4

Note. SBP = systolic blood pressure, DBP = diastolic blood pressure, HDL = high-density lipoprotein cholesterol, LDL = low-density lipoprotein cholesterol, HR = heart rate, HF-HRV = high frequency heart rate variability, HF_{nu} = high frequency heart rate variability in normalized units MetSyn = metabolic syndrome. All participants were non-smokers.

[a] *n* (%)

[b] M (±SD)

Table 2

Acceptability of MBSR Program

Acceptability *To what extent did you find MBSR:*	*n*	Not at all (%)	Slightly (%)	Moderately (%)	Very (%)	Extremely (%)
1. Efficacious	17	0	6	29	53	12
2. Appropriate	17	0	12	12	64	12
3. Acceptable	17	0	6	18	70	6
*4. To what extent did you find these MBSR components **beneficial?***						
a) Teacher instruction	17	0	0	6	82	12
b) Meditation: *lying down*	17	18	0	29	47	6
c) Meditation: *sitting*	16	12.5	12.5	6	50	19
d) Meditation: *walking*	15	6	20	47	27	0
e) Meditation: *loving-kindness*	13	15	8	23	31	23
f) Retreat	13	8	15	31	38	8
g) Yoga postures	16	6	19	19	56	0
h) Group discussion	16	6	6	31	50	6
i) Home exercises	17	6	12	35	29	18
5. To what extent would you participate in the MBSR program again?	16	12	12	12	29	35
6. How likely are you to continue your mindfulness practice?	16	0	13	25	56	6

Note. The Likert Scale ranged from 0 (not al all) to 4 (extremely); data for Likert scale represents the percentage of the sample. As of question 3c, the number of respondents per question varies, as those who dropped out of MBSR did not respond to questions regarding aspects they did not participate in.

Table 3

MBSR vs. Waitlist Control Group Differences in Metabolic Parameter Change Scores from Evaluation 1 (Baseline) to Evaluation 2 Using an Intention-to-Treat Approach

	MBSR Group (n=9)			Waitlist Group (*n*=9)				
	M Change	*SD*	% change	M Change	*SD*	% change	F(2,32)	Cohen's d (95% CI)
WC (cm)	-1.0	1.8	-1.0	0.08	2.9	-0.07	0.91	0.45 (-0.49-1.4)
SBP (mm Hg)	-5.9	15.6	-4.4	-6.2	15.1	-4.6	0.00	0.02 (-0.92-0.96)
DBP (mm Hg)	-3.5	7.9	-5.5	-0.90	6.2	-1.4	0.60	0.37 (-0.57-1.3)
Glucose (mmol/L)	0.23	0.67	+4.04	0.32	0.53	+5.5	0.10	0.15 (-0.79-1.1)
Triglycerides (mmol/L)	0.01	0.21	+0.55	0.21	0.35	+11.5	2.3	0.71 (-0.23-1.7)
HDL (mmol/L)	-0.08	0.13	-5.5	0.04	0.25	+2.8	0.39	0.29 (-0.65-1.2)
LDL (mmol/L)	-0.40	0.54	-15.0	-0.12	0.34	-4.5	1.8	0.64 (-0.30-1.6)
Total cholesterol (mmol/L)	-0.49	0.68	-10.4	-0.05	0.56	-0.94	2.2	0.72 (-0.22-1.7)

Note. WC= waist circumference, SBP = systolic blood pressure, DBP =diastolic blood pressure, HDL = high density lipoprotein cholesterol, LDL = low density lipoprotein cholesterol.

All *p*'s<0.15.

Cohen's d (Effect size): 0.2 (small)l, 0.5 (medium), 0.8 (large)

Table 4

Differences in Metabolic Parameters (Pre-MBSR, Post-MBSR and at the two-month follow-up) Using an Intention-to-Treat Approach (n = 18)

Metabolic Parameters (*n*=18)	Pre-MBSR		Post-MBSR		Follow-Up		% Change Post-Pre	% Change Follow-Up-Pre	*F* (2,34)	η^2
	M	*SD*	*M*	*SD*	*M*	*SD*				
WC (cm)	102.4	10.8	100.8	10.9	100.1	10.8	-1.5	-2.3	6.5**	0.28
SBP (mm Hg)	128.5	14.9	127.7	19.8	130.4	13.7	-0.61	+1.5	0.29	0.02
DBP (mm Hg)	62.3	6.6	60.0	0.08	63.3	8.8	-3.7	+0.88	1.5	0.09
Glucose (mmol/L)	6.0	1.2	6.2	1.6	6.04	1.5	+2.8	+1.0	0.72	0.04
Triglycerides (mmol/L)	1.6	0.6	1.6	0.71	1.4	0.6	-0.64	-11.5	2.3	0.12
HDL (mmol/L)	1.4	0.3	1.4	0.3	1.5	0.29	-0.70	+4.2	2.0	0.11
LDL (mmol/L)	2.7	1.0	2.4	1.0	2.4	0.9	-9.5	-9.0	3.5†	0.18
Total cholesterol (mmol/L)	4.8	1.1	4.5	1.0	4.5	1.0	-5.7	-5.0	3.2†	0.16

Note. WC= waist circumference, SBP = systolic blood pressure, DBP =diastolic blood pressure, HDL = high density lipoprotein cholesterol, LDL = low density lipoprotein cholesterol. BP, glucose, triglycerides, and cholesterol are missing for one participant at Evaluation 3 and another participant at Evaluation 3 and 4. LOCF was performed for this missing data. Effect size η^2: 0.01 (small), 0.06 (medium), 0.14 (large)

† $p < .10$. *$p < .05$. **$p < .01$.

Table 5

Differences in Metabolic Parameters (Pre-, Post-and at 2 months following MBSR) for Completers of MBSR Only (n = 13)

Metabolic Parameters (n=13)	Pre-MBSR		Post-MBSR		Follow-Up		% Change Post-Pre	% Change Follow-Up-Pre	F (2, 24)	η^2
	M	SD	M	SD	M	SD				
WC (cm)	104.2	11.1	102.5	10.8	101.1	11.4	-1.6	-3.0	7.81**	0.39
SBP (mm Hg)	129.1	14.8	129.5	19.6	128.8	12.8	+0.27	-0.27	0.02	0.001
DBP (mm Hg)	61.3	5.6	59.4	7.8	60.9	6.3	-3.1	-0.59	0.47	0.04
Glucose (mmol/L)	6.2	1.3	6.3	1.7	6.3	1.6	+2.0	+0.64	0.26	0.02
Triglycerides (mmol/L)	1.6	0.71	1.6	0.81	1.5	0.72	0.00	-6.3	0.81	0.04
HDL (mmol/L)	1.4	0.31	1.4	0.22	1.5	0.31	-3.6	+2.8	2.1	0.15
LDL (mmol/L)	2.6	1.0	2.3	0.91	2.3	0.91	-12.2	-12.2	4.0*	0.25
Total cholesterol (mmol/L)	4.8	1.2	4.4	1.01	4.5	1.02	-7.6	-6.3	3.5*	0.23

Note. WC= Waist circumference, SBP = systolic blood pressure, DBP =diastolic blood pressure, HDL = high density lipoprotein cholesterol, LDL = low density lipoprotein cholesterol

Effect size η^2: 0.01 (small), 0.06 (medium), 0.14 (large)

*$p < .05$. **$p < .01$.

Figure 1.

Study Flow

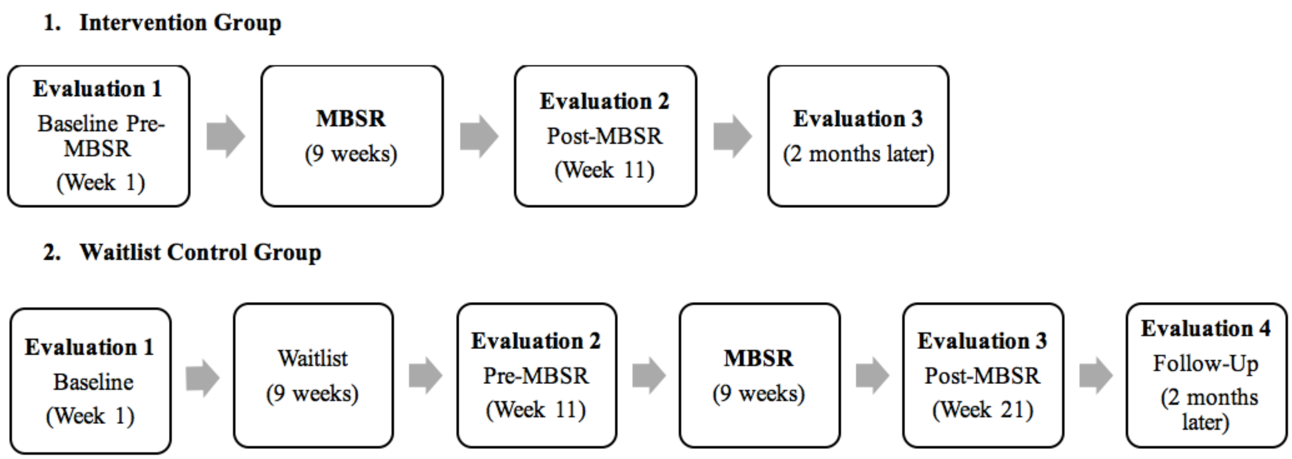
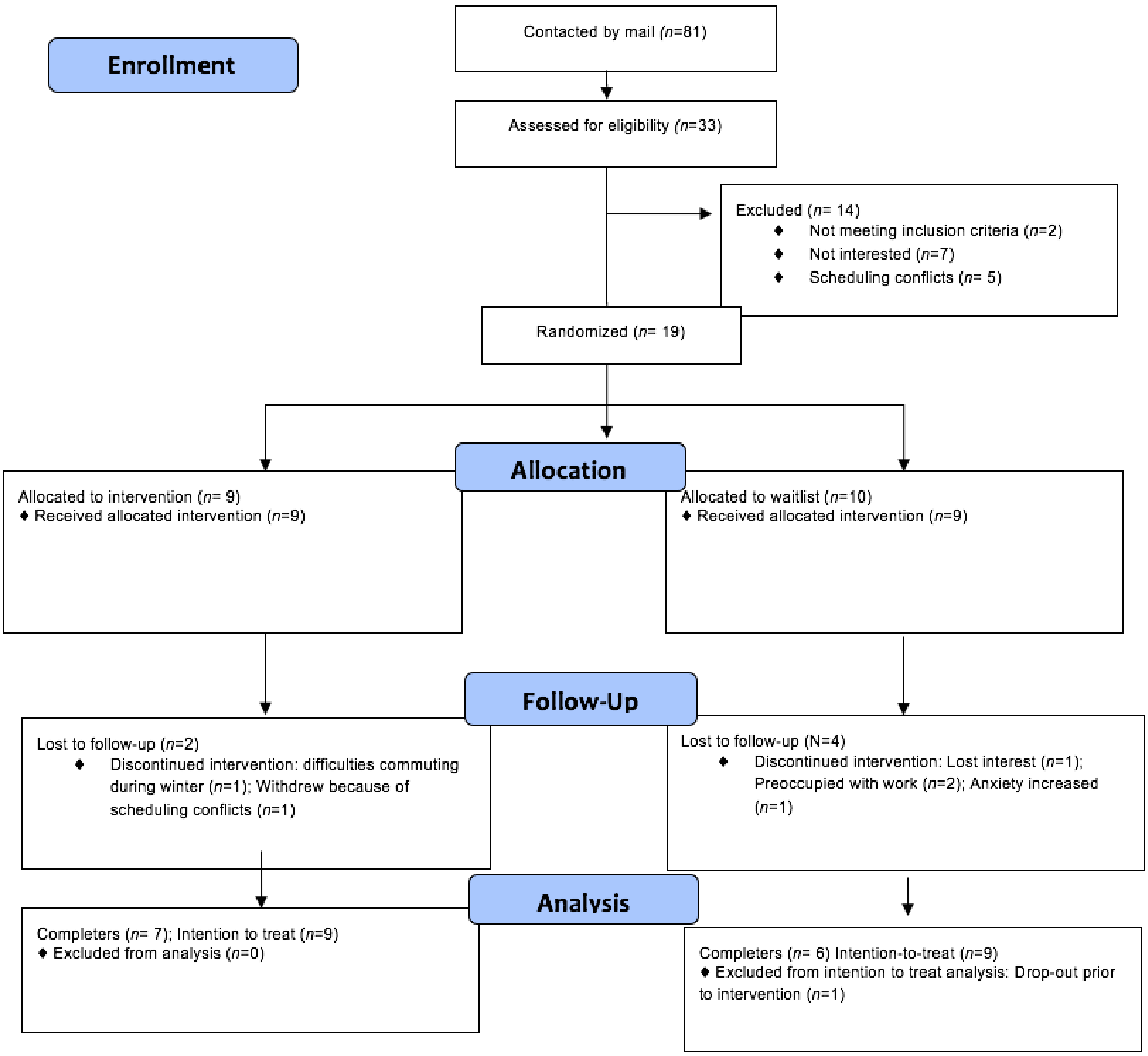


Figure 2.

CONSORT Flowchart of Participants



Mindfulness-Based Stress Reduction in Older Adults at Risk for Coronary Artery Disease:

A Pilot Randomized Trial

Supplementary Online Materials

Christina Gentile, Louisia Starnino, Gilles Dupuis, and Bianca D'Antono

Supplementary Online Only Table 6.

Participant Verbal Feedback

What aspects of MBSR did you appreciate?	What didn't you appreciate about MBSR?	What did you learn from MBSR?
"The presentation was simple; the time spent doing yoga and meditation was well balanced. The sessions would pass by fast, I did not feel obliged to talk. I felt lighter after every session.	"I found there to be a lot of homework. The emotions in the log sheets were very similar and I had difficulty distinguishing between them."	"I learned to think about myself, and to put less pressure on myself. I let go of problems I had with close ones."
"Nice group, no judgement. I enjoyed the audio material provided and tools from the workbook to help me continue to practice."	"The meditation would make me think of uncomfortable things. Instead of the one-day retreat, I would have preferred an individual session with the therapist. "	"I am more assertive with my husband, which has increased conflict between us. Since developing my self-awareness, I noticed having more anger than before."
"I enjoyed the social aspect, the discussions, it was good group. The therapist and assistant were good. The time of the session suited me."	"I had difficulty with the yoga, as I am not flexible and it was difficult to stay lying down."	"The program helped me to be calmer. I am less angry when I drive. I am also less reactive, and have better control over my anger. MBSR should be offered to anyone else who experiences a lot of stress."
"The therapist was very good and had a soft voice. I am continuing to do my exercises without any obligation. I did not believe in meditation prior to MBSR, but now I do. "	"It was difficult to commit on a weekly basis; the dyadic discussions were sometimes too long".	"I snack less before dinner; I try to more conscious of what I eat. I decreased my alcohol consumption and lost a lot of weight.".
"The therapist and the group were really good. I enjoyed the body scan and the mindfulness concept. I could not lie down, I felt nauseous",	"Doing things slowly, increases my stress level. I did not like the group discussions, I could not hear properly because the room was too big".	"I do the breathing exercises in the morning and before going to bed, and I used these breathing exercises when my partner was hospitalized.".

"I really enjoyed the body scan, and the group, it made me realize that I am not alone".	"It was long. The third meditation set of the audiotape-I was incapable, I would avoid doing it".	"I would do a lot of exercise before, without noticing my breathing. Now, my breathing is better while jogging. The MBSR program motivated me to start my physical training again, even if I do it alone".
"I really enjoyed the way the therapist would present the material. She had a soothing voice. I was eager to attend the sessions, it was enjoyable".	"Walking and sitting meditation, did not speak to me, the sitting meditation was physically uncomfortable".	"I am a better listener, and more conscious of other's needs, of their joy and of their pain".
"Meeting others and seeing each of their journeys. We were happy to see each other. I want to continue to practice mindfulness every day. I was involved in the group, and enjoyed improvising".	"I found the therapist had a monotone voice on the audiotape, I lost focus. I did not like the 5 -hour long retreat, I came home angry. I felt stuck, as if I were obliged to do certain things.".	"I developed self-awareness, and understood what it means to be in the present moment. For example, when I was angry after the retreat, I told myself - at least I am aware of my anger. Mindfulness meditation is like vitamins- if you don't do practice, you will notice the difference".
"I enjoyed the group. The program helped gain self-awareness about certain behaviors that I could change".	"I did not feel comfortable with the program. Mindfulness became an obsession; I would over-think my behaviors and judge myself. Maybe I am too harsh with myself, but this is how I got ahead in life.".	"The program made me realize that I am rather more anxious than stressed. The program made me hear other people's perception, where I realised that I am not alone and not as bad as I thought".
"I enjoyed taking the time to be the present moment, and realized the extent at which I was on autopilot".	"Nothing in particular".	"I am less forgetful of my keys, I look less for my things, and have changed my bridge strategy because I am

		more self-aware. My partner does meditation with me; it has become a routine for us. We observed positive changes in blood results since doing meditation."
"I enjoyed the therapist's teaching. We had a nice group spirit".	"I did not enjoy the therapist's monotone voice on the audiotape. I would have preferred to be in the winter group".	"The program helped with my physical illness, to be calmer, and to distract myself from my illness. Since starting the program, my partner and I have gotten closer because I am less stressed. When I meditate, I sleep better afterwards.".
"Meditation, I have always wanted to do it more regularly. It was a good group. I was very at ease with the therapist and assistant. Even if the program was difficult at times, it was a beautiful experience".	"Filling out the logbook every day was a burden. I had difficulty performing some of the yoga postures".	"I learned in mindfulness that often we do things on autopilot, without thinking. Now, I am ready to pay more attention to what I am doing.".
"I enjoyed the meditation, the focus on the breath, I do it every day when something is bothering me, it gives me such an immense relief. I come back to my breath, even when I have negative thoughts, and it helps me. It also made me aware that people experience stress differently."	"I did not understand the point of the five hours of silence in the retreat. There were a lot of exercises, I would have appreciated thirty minutes more to deepen the discussion on certain topics".	"I am more calm at work, more open. I am less aggravated by my colleagues. I see the program as a medication; we have to give to those who need it, who are stressed or ill. Individuals over 50 years of age should all follow this program.".

"I enjoyed the program, the location was ideal, and parking was easy and the room was good. There was a lot of respect between the therapists and participants".	"Nothing in particular".	"I breathe more since I have started the program and am more aware of my movements. I did not know anything about mindfulness before starting and I do not regret participating in the program".

The psychological stressfulness of the protocol. The protocol elicited significant increases in subjective stress arousal at the first, second, and third evaluations (all p's < .01). It also elicited significant decreases in positive affect across all three evaluations, (all p's < .01). Given that half the participants were specifically recruited because of their blunted autonomic responses to stress, changes in physiological parameters across the overall sample were not utilized as an indicator of task stressfulness in this study

Supplementary Online Only Table 7.

	WC	SBP	DBP	Glucose	Total Cholesterol	HDL	LDL	Triglycerides
Minutes of practice per week	0.16	0.20	0.22	-0.23	-0.52	-0.57*	-0.18	-0.29

Correlations between MBSR Home Practice and Percent Change in Metabolic Parameters

*p<0.05, **p<0.01, bolded values represent trends, p < 0.10; r=0.1: small effect, r=0.3: moderate effect, r>0.5= large effect

Supplementary Online Only Tables 8a

Within-Subjects Analysis using Reactivity Change Scores in Heightened LF/HF Responders (n=10)

Change Scores	Pre-MBSR	Post-MBSR	*% Change*	*p*	η^2
	M *(SD)*	M *(SD)*			
SBP (mm Hg)	21.1 (10.6)	22.8 (11.3)	+8.2	0.59	0.03
DBP (mm Hg)	8.3 (8.7)	8.9 (6.2)	+6.5	0.80	0.01
HR (bpm)	4.7 (1.7)	4.2 (2.2)	-10.1	0.44	0.07
HF-HRV (m/s^2)	-0.16 (0.4)	-0.15 (0.2)	+7.5	0.92	0.00
LF/HF (m/s^2)	0.36 (0.27)	0.24 (0.29)	-32.0	0.34	0.10
HFnu	-0.16 (0.16)	-0.10 (0.14)	+6.0	0.28	0.13

Note. SBP = systolic blood pressure, DBP =diastolic blood pressure, HR= Heart rate variability, HF-HRV= high-frequency heart rate variability, LF/HF= low frequency/high frequency heart rate variability, HFnu= index of modulation of the parasympathetic branch of the autonomic nervous system (ANS) as it influences the sinoatrial node of the heart, HF and LF/HF were log transformed in order to increase the normality of their distributions. Change scores = stress score minus baseline score for every parameter. Parasympathetic activation (HF) is expected to decrease during stress; in hyper-responders, we expected *less* parasympathetic withdrawal following participation in MBSR. In contrast, in hypo-responders, we expected *greater* parasympathetic withdrawal. Stress response data is missing for one participant due to error during testing.

Effect size η^2: 0.01 (small), 0.06 (medium), 0.14 (large)

Supplementary Online Only Table 8b

Within-Subjects Analysis using Reactivity Change Scores in Blunted LF/HF Responders (n=7)

Change Scores	*Pre-MBSR*	*Post-MBSR*	*% change*	*p*	η^2
	M (SD)	*M (SD)*			
SBP (mm Hg)	26.60 (12.5)	17.68 (12.2)	-33.5	0.03	0.58
DBP (mm Hg)	12.14 (5.1)	7.33 (4.4)	-39.6	0.03	0.58
HR (bpm)	4.41 (4.8)	5.41 (6.2)	+22.7	0.32	0.20
HF-HRV (m/s^2)	0.10 (0.14)	-0.08 (0.42)	-17.7	0.23	0.27
LF/HF (m/s^2)	0.06 (0.21)	0.04 (0.48)	-37.5	0.84	0.01
HFnu	-0.04 (0.09)	-0.06 (0.18)	-40.0	0.70	0.03

Note. SBP = systolic blood pressure, DBP =diastolic blood pressure, HR= Heart rate variability, HF-HRV= high-frequency heart rate variability, LF/HF= low frequency/high frequency heart rate variability, HFnu= index of modulation of the parasympathetic branch of the autonomic nervous system (ANS) as it influences the sinoatrial node of the heart, HF and LF/HF were log transformed in order to increase the normality of their distributions. Change scores = stress score minus baseline score for every parameter. Parasympathetic activation (HF) is expected to decrease during stress; in hyper-responders, we expected *less* parasympathetic withdrawal following participation in MBSR. In contrast, in hypo-responders, we expected *greater* parasympathetic withdrawal. Stress response data is missing for one participant due to error during testing. Effect size η^2: 0.01 (small), 0.06 (medium), 0.14 (large)

APPENDIX A

[METABOLIC SYNDROME DEFINITION AND CUTOFF VALUES]

Metabolic Syndrome Definition and Cutoff Values

Individual must possess three or more of the following five factors:		
Fasting blood glucose	≥ 5.6 mmol/L	
Blood pressure	≥ 130/85 mm Hg	
Triglycerides	≥ 1.7 mmol/L	
HDL cholesterol	*Men*: < 1.04 mmol/L	*Women*: < 1.29 mmol/L
Waist circumference	*Men*: > 102 cm	*Women*: > 88 cm

Table adapted from: American Diabetes Association., Standards of medical care in diabetes. Diabetes Care, 2004. 27: p. S15-S35 and Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, 2002 Circulation 106, 3143–3421

APPENDIX B

[SUMMARY TABLE FOR HOSTILITY AND TELOMERE LENGTH]

Table Appendix B

Summary Table Of Studies Examining The Association Between Hostility And Telomere Length

Author	Population	Age	Sex	Hostility (+ Other Psychological outcomes)	TL Measurement	TL value	Covariates Included in Analyses	Results	Limitations
Brydon et al., 2012 (cross-sectional) Whitehall II Cohort	*n* =434 healthy; White Collar; Caucasian (British)	Mean = 63 ± 5.6; Range 54–76 years	48% male	10-item Cynical Hostility (CMHo)	DNA (blood); PCR method ; TA (TRAPeze)	TL : 0.99 (0.07) T/S ratio; Range: (0.79-1.24); log TA 2.14 (0.67); Range: (1.23-39.98)	Model 1: Age, employment grade; BMI, waist circumference; sex; Model 2: salivary cortisol; Model 3: SBP, DBP, Model 4: lipids Model 5: inflammatory markers (IL-6; CRP), Model 6: smoking, alcohol intake, physical activity	**Main Effects:** ↑Cynical hostility associated with ↓ TL (for full sample). No association between TL and age ; and no association between TL and TA. **Interaction:** Sex by Hostility significant; ↑Cynical hostility with ↓ TL in men only (same for TA). **Other results:** 23.6% of men with highest cynical hostility scores were in the short TL/high TA group, compared with 7.8% of those in the lowest hostility tertile.	1) Tertiles of hostility were used 2) Narrow age range 3) Health status limited to detect differences 4) Only used cynicism subscale of CMHo
Starnino et al., 2016 (cross-sectional & Prospective)	*n* =132 mostly healthy (12% metabolic syndrome); Caucasian from Greater Montreal Area, Canada	Mean = 45 ± 11.6; Range 22–66 years	41% male	50-item CMHo; BAI; MCSD; BDI-II	DNA (blood);PCR	1.72 (0.33) T/S ratio	Model 1: Age, sex, physical activity, C-reactive protein; mean arterial pressure; alcohol intake	**Main Effects:** ↑Hostility and anxiety were associated with ↑ TL; ↑ Defensiveness with ↓ TL. **Interactions:** TL and hostility or anxiety not moderated by age or sex. Defensiveness by age: ↑ Defensiveness with ↓ TL young and mid-aged individuals but not dignificant among older individuals **Post-hoc other results**: No correlation with TL and LF/F-HRV. SBP, salivary cortisol, age and TL all significantly negatively correlated. ↑Hostility were similarly associated with ↑TL at 3 year follow-up	1) Healthy status may be limited to detect differences
Watkins et al. 2016 (cross-sectional)	*n* =468 USA-veteran; 79.3% Caucasian; Mixed Chronic conditions (including CAD without specification)	Mean=63.7 (12.8) Range=22-89	92% male	SCL-90 hostility subscale (6 items); PTSD checklist; Lifetime Trauma; Alcohol Abuse Assessment; Patient Health Questionnaire; Pittsburgh Sleep	DNA (saliva); PCR	T/S: Ratios <1 were coded as shorter telomere length and ratios ≥1 were coded as normal length	All entered in binary logistic regression: Age, sex, ethnicity, education, married, combat veteran status; lifetime of trauma; lifetime PTSD and depression; alcohol and drug abuse disorders; chronic medical conditions; BMI; sleep quality; psychological distress; perceived stress	**Main Effects:** ↓TL associated with↑ hostility scores (OR = 1.58) (not any other psychological variable). Each SD increase in hostility scores was associated with 58% greater likelihood of having shorter TL **Post-hoc** : difficulties controlling anger subscale were significant, but scores on the aggressive urges or impulses subscale not significantly associated with TL; **Post-Hoc:** Hostility and TL not mediated by smoking	1) Use of saliva (TL longer)2) short self-reports 2) Covariates did not include cardiovascular variables 4) Split TL longer vs shorter 5) SCL for hostility
Jordan et al., 2019 (cross-sectional) Jackson Heart Study	*n* =2516 African Americans from Mississippi; non CAD; Hypertension (57%); Diabetes (23%); Obesity (55%)	Mean Age=55.3 (12.4)	39% % male	10-item Cynical CMHo; Anger Expression (16-Spielberger trait anger-in anger-out); CES-D for depression; WSI stressful life events; MLE inventory of life events; Global Perceived Stress Scale	DNA (blood); Southern Blot	Mean LTL: 7.2 (0.7) (men) and 7.1 (0.7) women	Model 1: age and education Model 2: smoking, physical activity, alcohol intake, BMI, hypertension, diabetes; CRP	**Main Effects:** Men ↓TL than women; Men ↑cynical than women; **Interactions**: ↑(vs. low) cynical distrust with ↓LTL among women ; attenuated association in model 2 ($b = -0.18$, $p = 0.059$). In models 1 and 2, ↑(vs. low) anger out with ↓ TL among women. ↑ (vs. low) expressed negative affect summary score was also significantly associated with ↓TL among women in both models. **Other Results**: No other psychological variable were associated with TL.	1) Not be generalizable to African Americans in other areas within the United States, due to cultural and regional differences. 2) Analyses were not corrected for multiple testing 3) Tertiales of hostility were used 4) Only used cynicsim subscale

Note. BAI: Beck Anxiety Inventory; BDI-II: Beck Depression Inventory-II; CMHo: Cook-Medley Hostility InventoryCRP: C-reactive protein;LF/HF HRV: low frequency/high frequency heart rate variability; MAP: mean arterial pressure; MCSD: Marlowe-Crowne Social Desirability Scale; PCR:Polymerase Chain Reaction ; PTSD: Post-Traumatic Stress Disorder; SCL-90: Symptom Checklist Revised-90; TL: telomere Length; TA: Telomerase activity
↓ : lower ; ↑: higher

APPENDIX C

[SUMMARY TABLE OF RANDOMIZED CONTROLLED TRIALS]

Table Appendix C

Summary Table of Randomized Controlled Trials Examining the Relation between Meditation-Based Interventions and Telomere-Related Measures

RCT	Participants	Stratification and Blinding	Control Treatment	Intervention	Intervention Length & Intensity	Sample Collection	Telomere-Related Measures	Telomere-Related Findings	Effect Size (d) Between Intervention and Control groups
Jacobs et al., 2011	32 healthy experienced meditators (93% women; Mean Age: 47.5)	Yes by age, sex, BMI, and prior meditation experience; no blinding mentioned	WLC (n=17)	Samatha Meditation Retreat (n=25)	12 weeks: silent residential retreat including meditation 6 hrs/day + vegetarian diet	Post Retreat (week 12)	TA	1) Greater TA in retreat participants than controls post-retreat; 2) TA was mediated by ↑ in perceived control and decreases in neuroticism in retreat participants	(only 1 group)
Daubenmier et al., 2012	47 Overweight/ Obese (no history of CAD); 100% women; pre-menopausal	Yes, by BMI, age (+/- 40), antidepressant medication ; yes blinding of research assistants for group assignment	WLC (n=18)	MBSR for stress eating (n=19)	16 weeks; 9 3.5hr group sessions + day silent retreat	Baseline, post	TA	1) ↑ TA in both groups post MBSR 2) Changes in TA were negatively correlated with chronic stresss, anxiety, dietary retraints, fat intake, cortisol, and glucose	NA
Ho et al., 2012	64 chronic fatigue syndrome (100% women; Mean Age: 42.3)	No stratification; yes for blinding of research assistants for group assignment	WLC (n=31)	Qiqong (n=33)	2hrs of training for 5 weeks+ 30 minutes at home training for 4 months	Baseline, post 4 months	TA	1) TA ↑ in the intervention group 2) TA was higher in the intervention group compared to the WLC after 4 months	Medium
Lavrestky et al., 2013	39 NA female dementia caregivers with mild depressive symptoms (Mean Age: 60.5%)	No stratification; no blinding	Listening to relaxation music (n=16)	Kirtan Kriya (KK) (n=23)	8 weeks; meditation with CD 12 min/day	Baseline, post	TA	1) ↑ in TA for KK meditation group, but not for relaxation controls 2) ↑ in TA was associated with increase in quality of life in meditation group only	NA
Lengacher et al., 2014	142 NA breast cancer patients (stage I-III) (Mean Age: 55.3)	Stratification by1) by type of surgery (lumpectomy vs. mastectomy), 2) adjuvant BC treatment (chemotherapy with or without radiation vs. radiation alone), 3) and stage of BC (Stage 0/I vs. II/III). No blinding mentioned	WLC-treatment as usual for cancer (n=64)	MBSR modified for cancer patients (n=70)	6 weeks: meditation & hatha yoga group sessions 2 hrs/wk + 15–45 min/d au formal meditation + 15–45 min/day informal practice	Baseline, week 6, week 12	TA & TL	1) ↑ in TA in MBSR participants (lower at baseline) compared to controls 2) No change for TL	Small
Carlson et al., 2015	88 NA breast cancer survivors (Mean Age: 54.8)	No stratification; Yes blinding for research assitants for group assignment	12-week supportive-expressive therapy (SET; n=36) or 1-day stress management (n=18)	Mindfulness-based cancer recovery (MBCR; n=34)	8 weeks: group meetings 1.5 hrs/wk + 1 day silent retreat	MBSR: Baseline, week 8. SET: Baseline, week 12; Control: Baseline, week 10	TL	1) TL was *maintained* in both intervention groups, but declined in controls	Small to medium

Table Appendix C continued.

RCT	Participants	Stratification and Blinding	Control Treatment	Intervention	Intervention Length & Intensity	Sample Collection	Telomere-Related Measures	Telomere-Related Findings	Effect Size (d) Between Intervention and Control groups
Duraimani et al., 2015	48 AA hypertensive patients (46% men; Mean Age: 58)	Stratification : 1)no medication, 2) diuretic only, 3) or non-diuretic antihypertensive medication; yes blinding of research assistants	Extensive health education program (n=24)	TM meditation + health education course (n=24)	16 weeks: 1.5-2 hr meetings for first 6 days + 1 h meetings follow- up twice/month length + two 20 min meditation	Baseline, week 16	TL & TA (hTR and hTERT mRNA expression)	1) ↑ in TA (hTR and hTERT mRNA expression) in both groups 2) TL *maintained* in both groups	Small
Wang et al., 2017	501 NA Patients with depression, anxiety or stress & adjustment disorders (Mean age: 44) and presumed healthier	adjusted for age and stratified by sex; no blinding	Treatment as usual (mostly CBT; n=320)	Mindfulness-based group therapy (n=181)	8 weeks: mindfulness-based group therapy 2 hrs/wk +	Baseline, Week 8	TL	1) Individuals with psychiatric condition had shorter TL at baseline compared to health participants 2) TL maintained in both groups post-intervention	Very small
Innes et al., 2018	53 older mostly C sample with subjective cognitive decline, or cognitive impairment and dementia ; Mean Age: 60.47 (range 50-84 years); Women: 86.79%	Stratification in post-hoc analyses only; No blinding mentioned	Music Listening (ML) (n=28)	Kirtan Kriya (KK) meditation (n=25)	12 weeks; One 45 min individual session about meditation; 12 min /day for 12	Baseline and 3 Months	TL, TA	1) ↑ TA in both groups, although increases were significant only among those with higher practice adherence and lower baseline TA 2) Changes in both TL and TA varied by their baseline values, with greater increases among	Small for TL and TA (both groups
Le Nguyen et al., 2019	142 healthy midlife participants (77% C)(Mean age: 48. 45 (range 36-65 years old); Women: 69.72%	No stratification; no blinding mentioned	WLC (n=51)	Mindfulness Meditation (MM) (n= 63)or Love and Kindness Meditation	6 weeks + 20 min of daily practice	2 weeks pre-intervention and 3 weeks post-intervention	TL	1) TL ↓in all 3 groups, but only significantly for the MM group and the control group (controlled for demographic covariates and baseline TL) 2) control group showed the most shortening 3) LKM showed *no*	Small
Keng et al., 2020	Healthy younger Ch sample(Mean Age: 27.24 (5.24)(Women: 63.30%)	No stratification; no blinding mentioned	Music therapy-based stress reduction (MTSR) (n=79)(20-25 participants per group ; groups analysed together)	MBSR (n=79)(20-25 participants per group ; groups analysed together)	8 weeks; 2.5-hour weekly sessions of meditation + half day retreat, + home practice	within 2 weeks pre and post intervention	TL	1) TL *maintained* in both groups. 2) Duration of home mindfulness practice predicted ↑ in TL (a trend effect) among MBSR participants.	Medium

Note. Ch: Chinese; C: Caucasian; AA: African-American; NA= not announced in the article

RCT'S all used peripheral blood mononuclear cells and qPCR for TL and TA assay method

↑: increases ↓: decreases

APPENDIX D

[CONSENT FORM FOR STUDY 1 (BEL-AGE)]

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

AFFILIÉ À Université de Montréal

APPROUVÉ / APPROVED
Comité d'éthique ICM
MHI – Research Ethics Board
Date : 18 juin 2015

FORMULAIRE DE CONSENTEMENT

PROJET DE RECHERCHE : ICM #11-1313

Fardeau psychologique et le vieillissement pathologique chez les individus avec ou sans maladie cardiovasculaire.

BEL-AGE

Investigateur principal et collaborateurs

Bianca D'Antono, PhD., Lambert Busque, MD., Marie-Pierre Dubé, PhD., Sylvie Perreault, PhD., Jean-Claude Tardif, MD.

Commanditaires : Instituts de Recherche en Santé du Canada (IRSC) octroyé au Dre Bianca D'Antono, PhD.

INFORMATION

DESCRIPTION GÉNÉRALE

Nous vous invitons à participer à un projet de recherche portant sur le vieillissement pathologique ou précoce chez des personnes avec ou sans maladie coronarienne. Vous avez été sélectionné à partir de la banque de données de la Cohorte hospitalière de l'Institut de Cardiologie de Montréal par ce que 1) vous avez généreusement complété l'ensemble des questionnaires d'ordre psychologique lors de votre première participation dans la Cohorte hospitalière de l'ICM, 2) vous aviez accepté d'être contacté pour des sous-projets lors de cette même participation, et 3) lors de votre appel de suivi avec la Cohorte hospitalière de l'ICM, vous avez accepté qu'un membre de l'équipe de recherche de BEL-AGE vous contacte pour de plus amples informations sur cette étude.

Ce projet est financé par les Instituts de Recherche en Santé du Canada (IRSC : investigatrice principale : Dre Bianca D'Antono, PhD) qui accorde des fonds à l'ICM et à ses chercheurs pour gérer cette étude.

Ce formulaire de consentement décrit les procédures que vous devrez suivre si vous acceptez de participer à cette étude.

Avant de signer ce formulaire de consentement, veuillez prendre tout le temps nécessaire pour lire (ou vous faire lire) et comprendre l'information présentée ci-dessous. Vous pouvez consulter vos proches avant de prendre votre décision. Veuillez poser à votre médecin ou à l'équipe de recherche toutes les questions que vous avez sur la présente étude et sur vos droits. Ils devraient être en mesure de répondre à toutes vos questions.

La participation simultanée à plusieurs études peut être dangereuse pour vous. Si vous participez déjà à une étude clinique, veuillez en aviser votre médecin.

Initiales du patient: _______________

But de l'étude:

Ceci est un projet de recherche exploratoire destiné à avancer nos connaissances quant à l'impact de facteurs psychologiques (dont le stress, la dépression, l'anxiété, l'hostilité) sur la santé physique et cognitive de personnes de différents âges, et par le fait même notre compréhension du développement de maladies cardiovasculaires ou troubles connexes.

L'objectif de cette étude est de documenter la relation entre des facteurs psychologiques et le vieillissement pathologique ou précoce des individus avec ou sans maladie coronarienne. Plus particulièrement, nous voulons savoir si le fardeau psychologique (actuel et passé) prédit le vieillissement pathologique et surtout par quels mécanismes cet impact a lieu.

Nous anticipons que les résultats de cette recherche nous aideront à plus long terme à dépister de façon précoce les personnes à risque de troubles cardiovasculaires lorsqu'elles sont encore en santé, ainsi que de développer des traitements préventifs susceptibles de les aider à demeurer en santé.

Un total de 1518 individus âgés entre 30 et 70 ans, avec ou sans maladie coronarienne, et ayant complété leur premier suivi auprès de la Cohorte hospitalière de l'ICM, participeront à ce projet à l'Institut de Cardiologie de Montréal. Vous serez invité à venir en laboratoire à deux (ou trois) reprises selon notre financement, et ce, sur une période d'environ 6 ans : la première rencontre aura lieu peu de temps après votre premier suivi auprès de la Cohorte Hospitalière de l'ICM, tandis que les autres auront lieu au 2-3 ans par la suite, toujours après un suivi avec la Cohorte hospitalière.

DÉROULEMENT DE L'ÉTUDE

Si vous acceptez de participer à cette étude, un membre de notre équipe vous rencontrera au Centre de recherche de l'Institut de Cardiologie, et vous emmènera au laboratoire de psychophysiologie de la Dre D'Antono, PhD.

Lors de votre participation à l'étude, vous compléterez deux à trois sessions d'évaluation. Si vous acceptez de participer à l'étude suite à la lecture de ce consentement, la première évaluation aura lieu aujourd'hui. Les autres évaluations coïncideront dans le temps avec vos suivis auprès de la Cohorte hospitalière.

Lors de ces évaluations :

1. Nous obtiendrons un prélèvement de sang à jeun, pour un maximum de 35 ml (soit environ deux cuillères à table), afin que l'on puisse en extraire l'ADN, l'ARN, et le plasma. L'ADN et l'ARN renferment les instructions nécessaires à la création de tous les organismes vivants. Les télomères et la télomérase permettent de protéger l'intégrité de ces instructions lors de la réplication des cellules. Lorsque les télomères raccourcissent et que les niveaux de télomérase diminuent, les cellules peuvent mal se répliquer, contribuant ainsi au vieillissement précoce de l'organisme. À partir de l'ADN et l'ARN fournis, nous pourrons mesurer la longueur des télomères ainsi que les niveaux de télomérase. À partir du plasma, nous pourrons également obtenir de l'information quant à certains de vos facteurs de risque cardiovasculaire, dont ceux portant sur les niveaux de cholestérol, de sucre, et d'insuline présente dans votre sang, ainsi que des marqueurs révélateurs d'inflammation et de stress. C'est pour cette raison que nous vous rencontrons le matin après vous avoir demandé de ne pas fumer, manger ou faire de l'exercice depuis 12 heures, et de ne pas boire d'alcool depuis 24 heures.
2. Nous obtiendrons un échantillon de cheveux (1-3 mèches si possible) permettant de mesurer les élévations de cortisol dans votre corps (indicateur d'exposition chronique au stress).

Initiales du patient: ________________

3. Vous remplirez des questionnaires psychologiques n'ayant pas été remplis lors du suivi à la Cohorte hospitalière. Ces questionnaires portent notamment sur votre état psychologique actuel et passé ainsi que sur votre soutien social.
4. Vous compléterez une brève évaluation (5 minutes) de vos fonctions cognitives.
5. À moins qu'exceptionnellement le laboratoire psychophysiologique ne soit pas disponible, vous compléterez une évaluation physiologique de 15 minutes dans laquelle nous mesurerons votre fréquence cardiaque, rythme respiratoire et pression artérielle. Afin de faire ceci, l'assistant de recherche appliquera trois électrodes sur votre peau (au niveau du thorax), une ceinture sera placée autour de votre diaphragme et un capteur sera placé sur l'index de votre main gauche. Durant cette évaluation nous vous demanderons de faire une tâche qui peut être de légèrement à modérément stressante ainsi qu'une autre tâche plutôt neutre ou relaxante. La tâche stressante implique de parler d'une situation particulière pendant quelques minutes. Cette situation vous sera décrite le moment venu. Cette tâche a été utilisée dans de nombreuses études, tant chez des personnes en santé que des personnes atteintes de maladies cardiovasculaires.

Cette visite sera d'une durée approximative de 1 heure.

Mise à jour des données

En acceptant de prendre part à cette étude, vous acceptez qu'un suivi de votre état de santé soit fait par l'entremise de votre dossier médical, des bases de données de l'ICM, et celles du gouvernement.

Les données sur les services médicaux, les hospitalisations et les décès nous parviendront des fichiers de la Régie de l'assurance maladie du Québec (RAMQ) et du fichier des hospitalisations du Québec (MED-ECHO); ces données seront consultées sur une période de cinq ans précédant votre participation à BEL-AGE. Les données sur les médicaments que vous achetez à la pharmacie nous parviendront des fichiers de la RAMQ si vous êtes assuré par la RAMQ pour vos médicaments. Pour l'accès au fichier des services pharmaceutiques de la RAMQ, la période de consultation de ces informations est de 2 ans avant la date de votre participation à cette étude observationnelle.

Dans le cadre de ce projet de recherche, ces bases de données pourront être consultées au maximum une fois par année pendant une période allant jusqu'à 10 ans suivant votre dernière participation à BEL-AGE et les informations recueillies fourniront des données générales sur votre santé. Les données recueillies à partir de ces bases de données seront jumelées avec les données provenant des entrevues sur la base de votre numéro d'assurance maladie.

Advenant que vous deveniez inapte au cours de ce projet, nous ne vous contacterions plus, mais nous poursuivrons la mise à jour de vos données à partir des bases informatisées nommées plus haut, à moins que votre tuteur, mandataire ou le curateur nous signale qu'il soit préférable de vous retirer du projet. Nous vous invitons donc à parler de votre participation à ce projet à un membre de votre famille.

RISQUES ET INCONVÉNIENTS

Les prélèvements sanguins peuvent provoquer des ecchymoses (bleu) et une douleur au site de ponction. L'inconvénient principal de votre participation à ce projet réside dans le temps que vous devrez consacrer à l'étude ainsi qu'au déplacement pour venir aux diverses sessions.

Les risques normalement connus comme étant associés à la participation aux recherches faites à partir d'une biobanque sont principalement liés à la découverte d'une condition médicale nouvelle pour le participant ou à la divulgation de celle-ci à une autre personne. Les recherches pourraient identifier des risques médicaux non prévisibles qui vous concernent. Ce projet n'a pas pour objectif de vous communiquer des renseignements personnels et l'équipe a mis tout en place pour maintenir la confidentialité des données. Bien que de l'ADN soit prélevée, l'équipe du Dre D'Antono n'en fera pas l'analyse pour découvrir des maladies. L'étude vise seulement à mesurer la longueur des télomères. L'ADN sera remis à la cohorte pour des études plus poussées. Les analyses d'ADN seront donc fait sous l'autorité de la Cohorte hospitalière et selon les règles habituelles (et selon le formulaire de consentement que vous avez signé avec la cohorte). Donc l'équipe du Dre d'Antono n'en apprendront pas plus sur les maladies génétiques, limitant ainsi les risques.

De plus, afin de minimiser le risque d'indentification des participants de la Cohorte hospitalière, l'équipe de la cohorte a mis en place des mesures extraordinaires pour que l'équipe de recherche du Dre Bianca D'Antono ne puisse pas (et ne tente pas) connaître les codes permettant d'identification des participants dans celle-ci.

La participation à ce projet ne fait courir aucun risque connu sur le plan psychologique. Par ailleurs, si vous ressentez des difficultés de tout ordre suite à des questions soulevées par les entrevues, questionnaires ou la tâche stressante en laboratoire, nous pourrons en discuter et vous suggérer à une personne ressource au besoin.

GROSSESSE ET ALLAITEMENT

Vous ne pouvez pas participer à cette étude si vous êtes enceinte ou si vous allaitez votre bébé. La grossesse et l'allaitement sont associés à des changements physiologiques, biochimiques, et émotionnels qui peuvent biaiser les résultats de l'étude.

AVANTAGES

Vous ne retirerez aucun bénéfice direct en participant à cette étude. Toutefois votre participation à ce projet de recherche contribuera à l'avancement des connaissances dans le domaine de la cardiologie. De plus, si vous le désirez, les résultats de prise de sang (cholestérol, glycémie, inflammation seulement) pourront être communiqués à votre médecin de famille.

PARTICIPATION VOLONTAIRE

Vous êtes libre de participer à cette étude ou de vous en retirer en tout temps sur simple avis verbal sans avoir à préciser les motifs de votre décision. Si vous décidez de ne pas y participer ou de vous en retirer, vous recevrez les soins médicaux usuels pour le traitement de votre condition. Quelle que soit votre décision, celle-ci n'influencera en rien la qualité des soins que vous êtes en droit de recevoir.

Si vous décidez de retirer votre consentement à l'étude, l'équipe de recherche cessera de recueillir des données à votre sujet et les échantillons sanguins et d'ADN qui n'auront pas encore été analysés seront détruits. Les données déjà analysées continueront cependant d'être utilisées avec les données des autres participants.

Vous serez informé de toute nouvelle découverte importante faite au cours de l'étude et susceptible d'influencer votre décision de maintenir ou non votre participation à l'étude.

CONFIDENTIALITÉ

Durant votre participation à ce projet, le chercheur responsable ainsi que son personnel recueilleront et consigneront dans un dossier de recherche les renseignements vous concernant. Seuls les renseignements nécessaires pour répondre aux objectifs scientifiques de ce projet seront recueillis.

Initiales du patient: ________________

Ces renseignements peuvent comprendre les informations contenues dans vos dossiers médicaux concernant votre état de santé passé et présent, vos habitudes de vie ainsi que les résultats de tous les tests, examens et procédures que vous aurez à subir durant ce projet.

Tous les renseignements obtenus seront strictement confidentiels (à moins d'une autorisation de votre part à les communiquer à d'autres personnes ou d'une exception de la loi nous autorisant à les communiquer).

L'équipe de recherche utilisera vos données et les analysera avec les données des autres participants pour réaliser ce projet de recherche. Pour protéger votre identité, vos données personnelles ne seront identifiées que par un code qui vous sera assigné en remplacement de votre nom. Les données révélant votre identité sont conservées à l'ICM sous la responsabilité de Dr. Bianca D'Antono, PhD, chercheuse-psychologue. Tous les dossiers de recherche seront conservés sous clé et dans des fichiers sécurisés pendant 25 ans.

Pour les fins de ce projet, les échantillons de sang seront acheminés à trois endroits : pour y être analysés puis détruits, à l'exception de la cohorte hospitalière ou les échantillons seront conservés selon les politiques de la cohorte pour usages futurs :

1) Si vous acceptez ce volet, 10 ml (2 cuillères à thé) de sang seront envoyés au Centre de Pharmacogénomique de l'Institut de Cardiologie de Montréal pour y être conservés avec vos échantillons originaux obtenus lors de votre première évaluation avec la Cohorte. Cet échantillon maximisera la réserve de la Cohorte et pourrait éviter un potentiel prélèvement ultérieur en cas d'épuisement de votre réserve d'échantillons. Ils seront conservés selon les politiques de la cohorte pour usages futurs.

2) 5 ml (1 cuillère à thé) de sang seront envoyés au laboratoire de Biochimie à l'Institut de Cardiologie de Montréal sous la supervision du Dr Joël Lavoie, pour analyses des facteurs de risque cardiovasculaire (lipides, glucose, insuline, inflammation). Suite à leur analyse les échantillons seront détruits.

3) 20 ml (4 cuillères à thé) de sang seront envoyés au laboratoire du Dr Busque à l'Hôpital Maisonneuve-Rosemont pour analyses des télomères et de la télomérase. Ils seront également analysés puis détruits.

Les échantillons de cheveux seront conservés dans le laboratoire de Dre Bianca D'Antono jusqu'au moment de l'analyse en Allemagne par le Dr Kirschbaum, l'expert mondial en mesure du cortisol. Les échantillons qui lui seront envoyés ne contiendront aucune information pouvant vous identifier.

Puisque plusieurs données de recherches vous concernant proviennent de la Biobanque (Cohorte hospitalière de l'ICM) et afin de maximiser la protection de vos données, l'équipe fera appel à un tiers de confiance (Centre de coordination des essais cliniques de l'ICM) pour gérer les clés de codes provenant des diverses sources de données : RAMQ, Biobanque, projet BEL-AGE. Ainsi, le tiers de confiance assignera à toutes ces données vous concernant un code unique (code d'étude) qui sera par la suite transmis à l'équipe de recherche. Ce sera le seul code avec lequel nous pourrons vous identifier. La clé entre ce code de l'étude BEL-AGE et votre nom sera conservée par l'équipe de recherche sous la responsabilité de la chercheuse principale, Dr Bianca D'Antono.

Aux fins de s'assurer du bon déroulement du projet, il est possible qu'un délégué du comité d'éthique de la recherche ou des organismes réglementaires tels que Santé Canada consultent les données de recherche et votre dossier médical. Ces personnes adhèrent à une politique de confidentialité.

Initiales du patient: ________________

Les résultats de cette étude seront publiés et diffusés mais aucune information permettant de vous identifier ne sera alors dévoilée.

À des fins de protection, notamment afin de pouvoir communiquer avec vous rapidement, vos noms et prénoms, vos coordonnées et la date de début et de fin de votre participation au projet seront conservés pendant un an après la fin du projet dans un répertoire à part maintenu par l'établissement.

COMPENSATION

Dans l'éventualité où vous seriez victime d'un préjudice causé par toute procédure ou technologie requis par le protocole de recherche, l'Institut de Cardiologie de Montréal veillera à ce que vous receviez tous les soins que nécessite votre état de santé.

Si votre participation engendrait d'autres coûts qui ne sont pas présentement assurés par les régimes d'assurance-hospitalisation et d'assurance-maladie du Québec, ceux-ci ne sont pas couverts. Vous devrez donc en débourser les frais. De plus, aucune compensation pour perte de revenus, invalidité ou inconfort n'est prévue.

Toutefois, en signant ce formulaire de consentement, vous ne renoncez à aucun de vos droits. Notamment, vous ne libérez pas l'investigateur de ses responsabilités légales et professionnelles advenant une situation qui vous causerait préjudice.

Si vous encourez des dépenses pour participer à ce projet de recherche (ex. stationnement, repas, etc.), veuillez discuter avec l'assistant de recherche de la possibilité d'en obtenir le remboursement et de la procédure à suivre.

IDENTIFICATION DES PERSONNES-RESSOURCES

Si vous avez des questions concernant le projet de recherche ou si vous éprouvez un problème que vous croyez relié à votre participation au projet de recherche, vous pouvez communiquer avec le chercheur responsable du projet de recherche aux numéros suivants :

Vous pouvez communiquer en tout temps avec :

Institut de Cardiologie de Montréal

Docteure Bianca D'Antono, PhD., Chercheure-psychologue :	Tél. :	(514) 376-3330, poste 4047
L'équipe de recherche :	Tél. :	(514) 376-3330, poste 2011 ou poste 2411

Pour toute question concernant vos droits en tant que sujet participant à ce projet de recherche ou si vous avez des plaintes ou des commentaires à formuler, vous pouvez communiquer avec le commissaire local aux plaintes et à la qualité des services de l'Institut de Cardiologie de Montréal au numéro suivant : (514) 376-3330 poste 3398.

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

AFFILIÉ À Université de Montréal

APPROUVÉ / APPROVED
Comité d'éthique ICM
MHI – Research Ethics Board
Date : 18 juin 2015

FORMULAIRE DE CONSENTEMENT

PROJET DE RECHERCHE : ICM #11-1313

Fardeau psychologique et le vieillissement pathologique chez les individus avec ou sans maladie cardiovasculaire.

BEL-AGE

Investigateur principal et collaborateurs
Bianca D'Antono, PhD., Lambert Busque, MD., Marie-Pierre Dubé, PhD., Sylvie Perreault, PhD., Jean-Claude Tardif, MD.

Commanditaires : Instituts de Recherche en Santé du Canada (IRSC) octroyé au Dre Bianca D'Antono, PhD.

J'ai eu l'occasion de poser toutes les questions voulues au sujet de ce projet et on y a répondu à ma satisfaction.

Je comprends que je demeure libre de me retirer de ce projet en tout temps sans que cela n'affecte en aucune façon les soins dont je pourrais bénéficier à l'avenir.

J'ai lu ou l'on m'a lu ce formulaire de consentement et j'en comprends le contenu.

Je consens à participer à ce projet de recherche aux conditions qui y sont énoncées. Une copie signée et datée du présent formulaire d'information et de consentement m'a été remise.

Utilisation de mon échantillon d'ADN au fins de la Cohorte hospitalière de l'ICM. Une fois rendu anonyme, cet échantillon pourra servir à d'autres recherches sur des maladies cardiovasculaires ou facteurs de risque (obésité, hypertension, diabète, etc.) seulement après avoir reçu l'approbation du comité d'éthique de la recherche de l'ICM. Je réalise qu'il ne me sera pas possible de me retirer de ces autres recherches une fois que les données me concernant seront anonymisées.	J'accepte ❐ Je refuse ❐ Initiales du patient : ________
Contact pour complément d'information. L'équipe de recherche peut me contacter au cours de l'étude même après complétude des entrevues planifiées pour compléter des informations manquantes	J'accepte ❐ Je refuse ❐ Initiales du patient : ________
Contact pour participation à des études ultérieures. L'équipe de recherche peut me contacter au cours de l'étude et même après sa complétion pour m'inviter à de nouvelles études découlant ou non de BEL-AGE.	J'accepte ❐ Je refuse ❐ Initiales du patient : ________

J'accepte que mon médecin de famille soit informé de ma participation à ce projet : ☐**oui** ☐**non**

Signature du patient	*Nom du patient en lettres moulées*	*Date (a/m/j)*	*Heure*
Signature de l'un des chercheurs	*Nom du chercheur en lettres moulées*	*Date (a/m/j)*	*Heure*

Je certifie que j'ai expliqué les buts du projet à ______________________et il(elle) a signé le consentement en ma présence.

Signature du chercheur ou de son délégué	*Nom du chercheur ou de son délégué en lettres moulées*	*Date (a/m/j)*	*Heure*

Le Comité d'éthique de la recherche et du développement des nouvelles technologies de l'Institut de Cardiologie de Montréal autorise le début du recrutement en date du 10 janvier 2012. La version courante no. 4 du consentement en français datée du 18 juin 2015 est approuvée.

N.B. : L'original de ce formulaire doit être inséré au dossier de recherche du participant et une copie remise au participant. Aucune copie ne doit figurer au dossier médical.

APPENDIX E

[CONSENT FORM FOR STUDY 2 (ARTICLE 2 & ANNEX A)]

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

AFFILIÉ À Université de Montréal

* I C M 3 1 4 *

APPROUVÉ / APPROVED
Comité d'éthique ICM
MHI – Research Ethics Board
Date : 17 sept. 2015

FORMULAIRE D'INFORMATION ET DE CONSENTEMENT

PROJET DE RECHERCHE : ICM # 2015-1819

La gestion du stress et le syndrome métabolique : une étude pilote

MBSR-MS

Investigateur principal et collaborateurs
Bianca D'Antono, PhD, Christina Gentile, B.A.,
Louisia Starnino, B.Sc., Gilles Dupuis, PhD

Commanditaires ou organismes subventionnaires
Fondation de l'Institut de Cardiologie de Montréal
et les Instituts de recherche en Santé du Canada

PRÉAMBULE

Nous vous invitons à participer à ce projet de recherche puisque lors de votre participation à l'étude BEL-AGE (ICM #2011-202, 1313) vous avez présenté un ou plusieurs facteurs de risque pour les maladies cardiovasculaires (soit une pression artérielle élevée ; un taux de glucose sanguin élevé ; un excès de poids abdominal ; un faible taux de « bon » cholestérol ; et/ou un taux élevé de *triglycérides*) ainsi que des réponses au stress pouvant augmenter ces paramètres métaboliques.

Avant d'accepter de participer à ce projet et de signer ce formulaire d'information et de consentement, veuillez prendre le temps de lire, de comprendre et de considérer attentivement les renseignements qui suivent.

Ce formulaire peut contenir des mots que vous ne comprenez pas. Nous vous invitons à poser toutes les questions que vous jugerez utiles au chercheur responsable du projet ou aux autres membres du personnel affecté au projet de recherche et à leur demander de vous expliquer tout mot ou renseignement qui n'est pas clair.

NATURE ET OBJECTIFS DU PROJET DE RECHERCHE

Ce projet pilote vise à obtenir des données préliminaires sur l'efficacité d'un programme de Réduction du Stress par la Pleine Conscience (MBSR) à améliorer l'état de santé psychologique et physique des personnes à risque de développer une maladie cardiovasculaire. Le stress contribue au développement des maladies cardiovasculaires ainsi qu'au développement de certains de ses facteurs de risque.

Initiales du participant: ____________________

Par exemple, selon les recherches menées dans notre laboratoire et ailleurs, les réactions corporelles notables ou prolongées au stress psychologique peuvent contribuer au développement ou à la progression d'anomalies métaboliques et inflammatoires, et augmentent de façon importante le risque pour les maladies cardiovasculaires.

La pleine conscience se définit tout simplement comme une attention particulière et sans jugement que l'on porte sur le moment présent. Le MBSR a été conçu pour favoriser la gestion du stress, notamment, en présence de maladies.

L'objectif de notre étude est d'évaluer l'impact de cette intervention thérapeutique sur vos réponses physiologiques et émotionnelles face au stress, ainsi que sur votre profil de risque cardiovasculaire, vos symptômes psychologiques (anxiété, dépression, colère) et sur votre qualité de vie en général.

La MBSR a contribué à l'amélioration de la qualité de vie de nombreux patients souffrant de diverses maladies. En effet, de nombreuses études ont démontré l'efficacité du programme MBSR dans la réduction de la douleur, de la pression artérielle, des troubles digestifs, et de symptômes psychologiques divers. À ce jour, plus de 17 000 personnes ont suivi ce programme et plus de 5000 médecins et professionnels de la santé, à travers le monde s'y réfère dans leur travail quotidien.

Ainsi nous considérons, sur la base de ces données, que cette intervention pourrait vous aider à diminuer certains de vos facteurs de risque cardiovasculaires. Toutefois, aucune étude n'a à ce jour démontré l'efficacité du MBSR à diminuer les facteurs de risques métaboliques. Cette étude clinique est donc destinée à soutenir le développement de modes d'intervention complémentaires ayant le potentiel de réduire ces risques et à améliorer les résultats des traitements usuels que vous recevez présentement.

Approximativement 40 personnes participant déjà au projet Bel-Age à l'Institut de Cardiologie de Montréal participeront également à cette nouvelle étude. La durée de l'étude sera d'environ quatre à six mois selon le groupe auquel vous serez randomisé.

FINANCEMENT DU PROJET DE RECHERCHE

Ce projet de recherche est financé par la Fondation de l'Institut de Cardiologie de Montréal (FICM : investigatrice principale : Dre Bianca D'Antono, PhD) qui accorde des fonds à l'ICM et à ses chercheurs pour gérer cette étude et par les Instituts de recherche en santé du Canada.

DÉROULEMENT DU PROJET DE RECHERCHE

L'étude se déroulera à l'Institut de Cardiologie de Montréal dans le laboratoire Cœurs et âmes : unité de recherche en médecine comportementale et complémentaire du Dr. D'Antono, Ph.D., chercheur-psychologue ainsi qu'au Centre Épic (ou autre lieu à proximité selon la disponibilité des salles) où aura lieu le programme de MBSR.

Si vous consentez à participer à ce projet de recherche, vous prendrez part à un programme de MBSR qui inclura 9 sessions sur une période de 8 semaines, données par un professionnel de la santé mental et certifié en MBSR. Les sessions durent 2.5 heures par semaine, en plus des exercices à pratiquer quotidiennement à domicile.

Initiales du participant: ____________________

Votre participation et votre présence à chacune des sessions sont demandées afin de pouvoir retirer tous les bénéfices du programme et d'en faire l'analyse adéquate.

Ce projet est un essai clinique randomisé où la répartition entre le groupe recevant l'intervention et le groupe «liste d'attente » est faite de manière aléatoire. Si vous êtes assigné(e) dans le premier groupe, vous commencerez le programme dans les quelques semaines suivant la première évaluation. Si vous êtes assigné(e) dans le deuxième groupe, le programme d'intervention commencera deux mois après la première évaluation.

Des informations seront prises dans votre dossier médical par les responsables du projet à des fins de comparaison et d'analyse. Parmi les informations recueillies, nous récolterons vos diagnostics médicaux, votre médication et vos traitements ainsi que de l'information sur vos hospitalisations durant l'étude.

Trois à quatre séances d'évaluation seront prévues au cours des quatre à six mois de votre participation à l'étude. Pour l'ensemble des participants, la première évaluation aura lieu dès l'entrée dans l'étude. Suite à la première évaluation, les participants seront informés de leur groupe d'appartenance dans l'étude : « intervention » ou « attente ». Le groupe « intervention » commencera l'intervention MSBR dans un délai d'une à trois semaines, suivant la première évaluation. Le groupe «liste d'attente » devra attendre huit semaines avant de commencer l'intervention. Pour le groupe « intervention », les suivis auront lieu à la fin du programme MBSR et deux mois plus tard. Pour les participants du groupe « attente », les suivis auront lieu suite à deux mois d'attente et à la fin du programme MBSR et puis deux mois plus tard.

Lors des sessions d'évaluation :

1. Nous obtiendrons un prélèvement de sang (soit environ 2 cuillères à table), afin que l'on puisse extraire le plasma ainsi que l'ADN et l'ARN. À partir du plasma, nous pourrons obtenir de l'information quant à certains de vos facteurs de risque cardiovasculaires en lien avec le syndrome métabolique, dont ceux portant sur les niveaux de cholestérol, et de glucose (sucre) présents dans votre sang. C'est pour cette raison que nous vous demandons de venir au laboratoire à jeun : ne pas manger ou boire (sauf de l'eau) ni fumer, ou faire de l'exercice 12 heures au préalable, et de ne pas consommer de l'alcool ou autre drogue dans les 24 heures précédent votre visite. L'ADN et l'ARN renferment les instructions nécessaires à la création de tous les organismes vivants, et serviront dans cette étude à mesurer la longueur des télomères ainsi que la télomérase. Les télomères et la télomérase permettent de protéger l'intégrité des gènes lors de la réplication des cellules. Lorsque les télomères raccourcissent et que les niveaux de télomérase diminuent les cellules peuvent mal se répliquer contribuant ainsi au vieillissement précoce de l'organisme.

2. Vous allez par la suite remplir plusieurs questionnaires portant sur vos comportements de santé, votre état psychologique et votre qualité de vie durant une période d'environ 1 heure.

Vous compléterez également une évaluation physiologique de 40 minutes dans laquelle nous mesurerons votre fréquence cardiaque, rythme respiratoire et pression artérielle. Pour l'obtention de ces mesures, l'assistant de recherche appliquera trois électrodes sur votre peau (au niveau du thorax).

Une ceinture de respiration sera placée autour de votre diaphragme et un capteur sera placé sur l'index de votre main gauche. Durant cette évaluation, nous vous demanderons d'effectuer trois tâches pouvant être de légèrement à modérément stressantes. Ces tâches vous seront décrites le moment venu. Ces tâches ont été utilisées dans plusieurs études, chez des personnes avec ou sans maladie cardiovasculaire.

La première évaluation durera environ **2.5 heures.** Les évaluations subséquentes seront d'une durée d'environ 1.75 heure.

En ce qui concerne le programme MBSR, huit rencontres hebdomadaires auront lieu au Centre Épic (ou dans un établissement proche de l'hôpital), et seront d'une durée d'environ 2 h 30. Il y aura une rencontre additionnelle d'environ 6 heures entre les séances 6 et 7

Ce programme consiste en un **entraînement à la méditation de pleine conscience**.
Un nouveau thème sera abordé chaque semaine et visera à approfondir votre compréhension et la maitrise de ***votre*** stress à travers la pleine conscience, ainsi qu'à approfondir votre pratique de celle-ci. Chaque séance sera consacrée à l'apprentissage et à la pratique reliée au thème de la semaine et aux discussions de groupe ou en dyade. Vous ne serez pas obligé de parler lors du groupe, mais votre participation aux différentes composantes de l'intervention assurera de meilleures chances de succès. Vous explorerez diverses manières d'être pleinement conscient et attentif au moment présent, de façon délibérée et sans jugement par des pratiques de méditation diverses : telles le scan corporel en position allongée, les méditations assises, des pratiques de méditation en mouvement (yoga, marche méditative), et la communication interpersonnelle efficace. À travers ces pratiques, vous pourrez reconnaitre et défaire les façons automatiques de penser et d'agir que vous avez développées au fil des années et qui nuisent aujourd'hui à votre pleine participation, acceptation, et jouissance de la vie.

Après chaque atelier, il vous sera demandé de pratiquer ces nouvelles compétences sur une base quotidienne pendant au moins 20-45 minutes/jour. Vous serez également invité à remplir un journal quotidien sur les pratiques accomplies. Des enregistrements audio vous seront fournis pour faciliter la pratique quotidienne à la maison.Vous serez en mesure de conserver tous les documents qui vous seront remis à la fin du programme pour pouvoir continuer cette pratique à la maison.

Le tableau suivant résume votre participation au projet de recherche :

GROUPE D'INTERVENTION					
	Évaluation 1	MBSR	Évaluation 2	Évaluation 3	Durée (min.)
Semaines	Semaine #0	Semaine #1-8	Semaine #9	Semaine #17	-
Lieu	ICM	Centre ÉPIC	ICM	ICM	-
		Mesures			
1. Formulaire de consentement	✓				10-15
2. Prise de sang	✓		✓	✓	10
3. Mesures corporelles	✓		✓	✓	10
4. Questionnaires	✓		✓	✓	60-75
5. Protocole de stress	✓		✓	✓	40

GROUPE LISTE D'ATTENTE						
	Évaluation 1	Évaluation 2 (2 mois plus tard)	MBSR	Evaluation 3	Evaluation 4	Durée (min.)
Semaines	Semaine #0	Semaine #8	Semaine #9-17	Semaine #18	Semaine #26	-
Lieu	ICM	ICM	Centre EPIC	ICM		-
			Mesures			
1. Formulaire de consentement	✓					10-15
2. Prise de sang	✓	✓		✓	✓	10
3. Mesures corporelles						10
4. Questionnaires	✓	✓		✓	✓	60-75
5. Protocole de stress	✓	✓		✓	✓	40

RISQUES ET INCONVÉNIENTS ASSOCIÉS AU PROJET DE RECHERCHE

Les prélèvements sanguins peuvent provoquer des ecchymoses (bleus) et une douleur au site de ponction. L'inconvénient principal de votre participation réside dans le temps que vous consacrerez à l'étude ainsi qu'au déplacement pour venir aux diverses sessions.

La participation au projet MBSR-MS n'engendre aucun risque connu sur le plan psychologique. Par ailleurs, si vous ressentez des difficultés de tout ordre suite à des questions soulevées lors des évaluations ou lors du programme d'intervention MBSR, nous pourrons en discuter et vous référer à une personne ressource au besoin.

AVANTAGES

En vous engageant dans ce programme MBSR, vous pourriez retirer plusieurs bénéfices sur le plan physique et psychologique. Cependant, puisque le but est d'obtenir des données préliminaires sur l'impact du MBSR sur certains de ces paramètres, ceci ne peut vous être garanti.

Par ailleurs, les résultats obtenus contribueront à l'avancement des connaissances scientifiques dans ce domaine et seront d'une utilité certaine pour le développement d'approches complémentaires dans la prévention des maladies cardiovasculaires

COLLABORATION DU PARTICIPANT

Il est important d'être à jeun (sauf pour boire de l'eau) et de ne pas faire de l'exercice vigoureux ni fumer 12 heures avant chaque évaluation. Similairement, veuillez ne pas consommer d'alcool pendant les 24 heures précédant les évaluations.

Afin de bénéficier pleinement du programme, votre présence, engagement, et votre participation sont nécessaires pendant toute la durée du programme.

PARTICIPATION VOLONTAIRE ET POSSIBILITÉ DE RETRAIT

Votre participation à ce projet de recherche est volontaire. Vous êtes donc libre de refuser d'y participer. Vous pouvez également vous retirer de ce projet à n'importe quel moment, sans avoir à donner de raisons, en faisant connaître votre décision au chercheur responsable du projet ou à l'un des membres du personnel affecté au projet.

Si vous vous retirez du projet ou si on a mis fin à votre participation, l'information déjà obtenue dans le cadre de ce projet sera conservée jusqu'à la fin du projet et détruite par la suite. Toutefois, les données non-analysées seront détruites sans délai.

CONFIDENTIALITÉ

Durant votre participation à ce projet, le chercheur responsable ainsi que son équipe recueilleront et consigneront dans un dossier de recherche les renseignements vous concernant. Seuls les renseignements nécessaires pour répondre aux objectifs scientifiques de ce projet seront recueillis.

Ces renseignements peuvent comprendre les informations contenues dans vos dossiers médicaux concernant votre état de santé passé et présent, vos habitudes de vie ainsi que les résultats de tous les tests, examens et procédures que vous aurez à subir

Initiales du participant: ____________________

durant ce projet. Votre dossier peut aussi comprendre d'autres renseignements tels que votre nom, votre sexe, votre date de naissance et votre origine ethnique.

Tous les renseignements recueillis demeureront strictement confidentiels dans les limites prévues par la loi. Afin de préserver votre identité et la confidentialité des renseignements, vous ne serez identifié que par un numéro de code. La clé du code reliant votre nom à votre dossier de recherche sera conservée par le chercheur responsable. Il est à noter que puisque les ateliers du MBSR se font en groupe, la confidentialité de la participation à la recherche est limitée. Toutefois, nous aurons obtenu l'engagement signé de tous les participants, qui stipule (page 10) que toutes les informations partagées par les participants durant les séances devront demeurer strictement confidentielles.

Le chercheur responsable du projet utilisera les données à des fins de recherche dans le but de répondre aux objectifs scientifiques du projet décrits dans le présent formulaire d'information et de consentement. Ces données seront conservées pendant 10 ans par le chercheur responsable.

Aux fins de ce projet, les échantillons de sang seront acheminés à deux endroits et conservés et détruits après leur analyse :

1) 5 ml (1 cuillère à thé) de sang sera envoyé au laboratoire de biochimie de l'Institut de Cardiologie de Montréal sous la supervision de Dr. Joel Lavoie pour l'analyse des facteurs métaboliques dans le plasma (lipides (cholestérol), glucose). Suite à leurs analyses, les échantillons seront détruits.

2) 20 ml (4 cuillères à thé) de sang sera envoyé au laboratoire du Dr Lambert Busque à l'hôpital Maisonneuve-Rosemont pour analyses des télomères et télomérase. Le sang prélevé sera également détruit suite à ces analyses.
Bien que de l'ADN soit prélevé, l'équipe du Dre D'Antono n'en fera pas une analyse génétique pour découvrir des maladies. L'étude vise seulement à mesurer la longueur des télomères et l'enzyme télomérase. Les échantillons seront détruits suite à leur analyse.

Les données de la recherche pourront être publiées dans des revues spécialisées ou faire l'objet de discussions scientifiques, mais il ne sera pas possible de vous identifier.

À des fins de protection, notamment afin de pouvoir communiquer avec vous rapidement, vos noms et prénoms, vos coordonnées et la date de début et de fin de votre participation au projet seront conservés pendant un an après la fin du projet dans un répertoire à part maintenu par le chercheur responsable ou par l'établissement.

INDEMNISATION EN CAS DE PRÉJUDICE ET DROITS DU PARTICIPANT À LA RECHERCHE

Dans l'éventualité où vous seriez victime d'un préjudice causé par toute procédure ou technologie requise par le protocole de recherche, le laboratoire du Dre Bianca D'Antono veillera à ce que vous receviez tous les soins requis par votre état de santé.

Initiales du participant: ____________________

Si votre participation engendrait d'autres coûts qui ne sont pas présentement assurés par les régimes d'assurance-hospitalisation et d'assurance-maladie du Québec, ceux-ci ne sont pas couverts. Vous devrez donc en assumer les frais. De plus, aucune compensation pour perte de revenus, invalidité ou inconfort n'est prévue.

En signant ce formulaire de consentement, vous ne renoncez à aucun de vos droits. Notamment, vous ne libérez pas l'investigateur de ses responsabilités légales et professionnelles advenant une situation qui vous causerait préjudice.

REMBOURSEMENT DES DÉPENSES

Vous ne retirerez aucune compensation monétaire pour votre participation à l'étude. Si vous encourez des dépenses pour participer à ce projet de recherche (ex. déplacements, repas, etc.), veuillez en discuter avec l'assistant de recherche de la possibilité d'en obtenir le remboursement et de la procédure à suivre.

IDENTIFICATION DES PERSONNES-RESSOURCES

Si vous avez des questions concernant le projet de recherche ou si vous éprouvez un problème que vous croyez relié à votre participation au projet de recherche, vous pouvez communiquer avec le chercheur responsable du projet de recherche aux numéros suivants :

Vous pouvez communiquer en tout temps avec :

Institut de Cardiologie de Montréal

Dr. Bianca D'Antono, Ph.D, Chercheure principale Tél. : (514) 376-3330 (poste 4047)

Christina Gentile et Louisia Starnino,

Candidates au doctorat en psychologie Tél. : (514) 376-330 (poste 2011)

Pour toute question concernant vos droits en tant que participant à ce projet de recherche ou si vous avez des plaintes ou des commentaires à formuler vous pouvez communiquer avec le commissaire local aux plaintes et à la qualité des services de l'Institut de Cardiologie de Montréal au numéro suivant : (514) 376-3330 poste 3398.

Advenant votre décès, vos héritiers et représentants légaux peuvent aussi adresser toute plainte ou commentaire au commissaire local aux plaintes et à la qualité des services de l'ICM et ce, en composant le même numéro

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

AFFILIÉE À Université de Montréal

* I C M 3 1 4 *

APPROUVÉ / APPROVED
Comité d'éthique ICM
MHI – Research Ethics Board
Date : 17 sept. 2015

FORMULAIRE DE CONSENTEMENT

PROJET DE RECHERCHE : ICM # 2015-1819

La gestion du stress et le syndrome métabolique : une étude pilote

MBSR-MS

Investigateur principal et collaborateurs
Bianca D'Antono, PhD, Christina Gentile, B.A., Louisia Starnino, B.Sc., Gilles Dupuis, PhD

Commanditaire ou organisme subventionnaire
Fondation de l'Institut de Cardiologie de Montréal et les Instituts de recherche en Santé du Canada

J'ai eu l'occasion de poser toutes les questions voulues au sujet de ce projet de recherche et on y a répondu à ma satisfaction.

Je comprends que je demeure libre de me retirer de ce projet en tout temps sans que cela n'affecte d'aucune façon les soins dont je pourrais bénéficier à l'avenir.

J'ai lu ou l'on m'a lu ce formulaire d'information et de consentement et j'en comprends le contenu.

Après réflexion, j'accepte de participer à ce projet de recherche aux conditions qui y sont énoncées.

J'autorise le chercheur à informer mon médecin traitant de ma participation à ce projet. Nom et adresse du médecin traitant : ____________________________ ____________________________	☐ J'accepte	☐ Je refuse
Dans l'éventualité où les résultats obtenus dans cette recherche donnaient lieu à l'élaboration d'un autre projet recherche (sous-étude ou nouvelle recherche découlant directement de ce projet), j'accepte d'être recontacté pour que l'on me demande si je suis intéressé à participer à cette sous-étude ou ce nouveau projet.	☐ J'accepte	☐ Je refuse
Puisque les formations MBSR se font en rencontres de groupe, la confidentialité à propos de ce qui est dit par les divers membres est essentielle afin de	☐ J'accepte	☐ Je refuse

5000, rue Bélanger, Montréal (Québec) H1T 1C8 | Tél. : 514-376-3330 | Téléc. : 514-376-1355

favoriser les discussions ouvertes. J'accepte, en signant ce formulaire, de respecter la confidentialité des membres du groupe auquel je participerai. Je ne discuterai pas de ce que les autres membres disent ou font pendant les sessions avec des personnes extérieures au groupe.		

Signature du participant	*Nom du participant en lettres moulées*	*Date (jj-mm-aaaa)*
Signature de l'un des chercheurs	*Nom du chercheur en lettres moulées*	*Date (jj-mm-aaaa)*

J'ai expliqué au participant à la recherche les termes du présent formulaire d'information et de consentement et j'ai répondu aux questions qu'il m'a posées.

Signature du chercheur ou de son délégué	*Nom du chercheur ou de son délégué en lettres moulées*	*Date (jj-mm-aaaa)*

Le Comité d'éthique de la recherche et du développement des nouvelles technologies de l'Institut de Cardiologie de Montréal autorise le début du recrutement en date du 17 septembre 2015. La version courante no. 1 du consentement en français datée du 17 septembre 2015 est approuvée.

N.B. : Une copie signée et datée du présent formulaire d'information et de consentement sera déposée au dossier du participant, une copie gardée par l'investigateur et une copie remise au participant.

APPENDIX F

[LETTER OF RECRUITMENT FOR THE MBSR STUDY (ARTICLE 2 AND ANNEX A)]

« Le paradis n'est pas un endroit, mais un état de conscience » – Sri Chinmoy

Cher _________,

Nos dossiers indiquent que vous faites partie de la Biobanque de l'Institut de Cardiologie de Montréal. Lors de votre première participation, vous avez consenti à être recontacté pour de futurs projets de recherche. C'est ainsi que vous avez été invité à participer à notre projet **BEL-AGE** : le fardeau psychologique et le vieillissement pathologique chez les individus avec ou sans maladie cardiovasculaire.

Nous tenons à vous remercier de votre participation lors de votre première visite pour le projet BEL-AGE le _____. En nous basant sur les résultats obtenus lors de celle-ci, nous croyons que vous pourriez retirer certains bénéfices en participant à une étude pilote qui se déroulera dans notre laboratoire à partir de l'automne 2015. Celle-ci comporte, entre autre, un **programme de huit semaines sur la gestion du stress.**

L'expérience du stress est associée à de nombreuses conséquences de santé néfastes, incluant le développement des maladies cardiovasculaires. La réduction du stress peut ainsi servir comme facteur protecteur contre certains comportements qui aggravent le risque d'être atteint d'une maladie chronique.

De nombreuses études ont montré l'efficacité de ce programme, non seulement pour la réduction du stress, mais aussi de la douleur, de la pression artérielle, de troubles digestifs et de symptômes psychologiques divers. À ce jour, plus de 17 000 personnes ont suivi ce programme et plus de 5000 médecins et professionnels de la santé à travers le monde s'y réfèrent quotidiennement dans le cadre de leur travail.

Nous vous offrons ce programme gratuitement en retour de votre participation à cette nouvelle étude.

La participation à cette étude pilote pourrait vous aider à réaliser des objectifs importants, soit l'amélioration de votre santé physique, et mentale et plus globalement, de votre qualité de vie. Si vous êtes intéressé à obtenir de plus amples informations concernant ce projet et désirez y participer, veuillez contacter Christina Gentile ou Louisia Starnino au 514-376-3330 poste 2011.

Cordialement,

Dr. Bianca D'Antono, Ph.D, chercheure principale
Christina Gentile & Louisia Starnino, candidates au doctorat en psychologie clinique
Coeurs et âmes: unité de recherche en médecine comportementale et complémentaire

APPENDIX G

[QUESTIONNAIRES]

[COOK-MEDLEY HOSTILITY SCALE (39-ITEMS)]

INSTITUT DE
CARDIOLOGIE
DE MONTRÉAL

ID sujet :		Date : AAAA MM JJ
Visite : 1 2 3 4		Administré par : ___

ÉTUDE MBSR-MS
COOK-MEDLEY SCALE

Pensez à la façon dont chaque énoncé suivant s'applique à vos croyances et/ou comportements. Indiquez si l'énoncé est plutôt vrai ou faux selon vous, en encerclant la réponse. S.V.P., répondre à **tous** les énoncés.

1.	Lorsque quelqu'un me fait du tort, je sens que je devrais me venger, si possible, uniquement par principe.	Vrai	Faux
2.	J'ai souvent dû obéir à des gens qui n'en savaient pas autant que moi.	Vrai	Faux
3.	Je crois que nombre de gens exagèrent leurs malheurs pour s'attirer la sympathie et l'aide des autres.	Vrai	Faux
4.	Il faut apporter beaucoup d'arguments pour convaincre la plupart des gens de la vérité.	Vrai	Faux
5.	Je crois que la plupart des gens mentiraient pour réussir.	Vrai	Faux
6.	Quelqu'un m'en veut.	Vrai	Faux
7.	La plupart des gens sont honnêtes surtout parce qu'ils ont peur de se faire prendre.	Vrai	Faux
8.	La plupart des gens vont employer des moyens quelques peu malhonnêtes pour obtenir un gain ou un avantage plutôt que de le perdre.	Vrai	Faux
9.	Lorsqu'une personne est gentille avec moi, je me demande souvent quels sont ses véritables motifs.	Vrai	Faux

CMHo_MBSR-MS
- 1/3 -

10.	Quand je travaille sur quelque chose d'important, cela m'impatiente que les gens me demandent conseil ou m'interrompent.	Vrai	Faux
11.	Je crois avoir été souvent puni(e) sans raison.	Vrai	Faux
12.	Certains membres de ma famille ont des habitudes qui m'agacent et m'ennuient profondément.	Vrai	Faux
13.	La plupart des membres de ma famille sympathisent avec moi.	Vrai	Faux
14.	Ma façon de faire est souvent mal comprise par les autres.	Vrai	Faux
15.	Je ne blâme personne d'essayer de s'approprier tout ce qu'on peut en ce bas monde.	Vrai	Faux
16.	Les gens se soucient peu de ce qui vous arrive.	Vrai	Faux
17.	Je peux être ami(e) avec des gens qui commettent des actions que je considère mauvaises.	Vrai	Faux
18.	Il est plus sûr de ne se fier à personne.	Vrai	Faux
19.	Je ne blâme pas quelqu'un qui profite d'un autre qui se laisse faire.	Vrai	Faux
20.	J'ai souvent senti que des inconnus me regardaient de façon critique.	Vrai	Faux
21.	La plupart des gens se font des amis parce que ces amis leur seront probablement utiles.	Vrai	Faux
22.	Je suis sûr(e) qu'on parle de moi.	Vrai	Faux

23.	Dans leur for intérieur, la plupart des gens détestent se déranger pour aider les autres.	Vrai	Faux
24.	J'ai tendance à être sur mes gardes avec les gens qui sont plus sympathiques que ce à quoi je m'attendais.	Vrai	Faux
25.	Les gens me déçoivent souvent.	Vrai	Faux
26.	Je ne me fâche pas facilement.	Vrai	Faux
27.	J'ai souvent rencontré de supposés experts qui n'étaient pas meilleurs que moi.	Vrai	Faux
28.	J'éprouverais certainement du plaisir à battre un escroc à son propre jeu.	Vrai	Faux
29.	J'ai dû parfois être brutal(e) avec des gens grossiers ou importuns.	Vrai	Faux
30.	En général, les gens exigent plus de respect de leur propres droits qu'ils ne sont prêts à en accorder à ceux des autres.	Vrai	Faux
31.	Je déteste certaines personnes au point de me sentir heureux(se) intérieurement lorsqu'elles sont punies pour ce qu'elles ont fait.	Vrai	Faux
32.	Je suis souvent porté(e) à fournir des efforts pour faire triompher mon point de vue contre mes adversaires.	Vrai	Faux
33.	L'homme qui s'est surtout occupé de moi durant mon enfance (père, beau-père) était très strict.	Vrai	Faux
34.	Souvent les gens sont jaloux de mes bonnes idées parce qu'ils n'y ont pas pensé en premier.	Vrai	Faux
35.	Je ne tente pas de cacher à une personne la piètre opinion que j'ai d'elle ou la pitié qu'elle m'inspire.	Vrai	Faux
36.	J'ai souvent travaillé pour des gens qui s'appropriaient le crédit du bon travail et attribuaient les erreurs à leurs subordonnés.	Vrai	Faux
37.	Règle générale, je défends énergiquement mes opinions.	Vrai	Faux
38.	Parfois, je suis sûr(e) que les gens peuvent deviner ce que je pense.	Vrai	Faux
39.	Un grand nombre de gens sont coupables de mauvaise conduite sexuelle.	Vrai	Faux

[MARLOWE-CROWNE SOCIAL DESIRABILITY SCALE (14-ITEMS)]

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID sujet :	Date : AAAA MM JJ
Visite : 1 2 3 4	Administré par :

ÉTUDE MBSR-MS

Voici une liste d'affirmations concernant les traits et attitudes personnels. Indiquez si ces affirmations sont vraies ou fausses en ce qui vous concerne.

1. Je trouve parfois difficile de faire mon travail si je ne suis pas encouragé(e).	Vrai	Faux
2. Je suis parfois irrité(e) si je n'arrive pas à mes fins.	Vrai	Faux
3. J'aime faire des commérages quelques fois.	Vrai	Faux
4. Quelquefois, j'ai eu envie de me rebeller contre des gens qui exercent l'autorité même si je savais qu'ils avaient raison.	Vrai	Faux
5. Peu importe avec qui je converse, je sais toujours bien écouter.	Vrai	Faux
6. Il m'est déjà arrivé de profiter de quelqu'un.	Vrai	Faux
7. Lorsque je fais une erreur, je suis toujours prêt(e) à l'admettre.	Vrai	Faux
8. Je suis toujours courtois (se) même envers les gens qui sont désagréables.	Vrai	Faux
9. Il m'est arrivé d'avoir le goût de casser quelque chose.	Vrai	Faux
10. Je ne suis jamais contrarié(e) lorsqu'on me demande de remettre une faveur à quelqu'un.	Vrai	Faux
11. Je n'ai jamais été contrarié(e) lorsque des gens ont exprimé des idées très différentes des miennes.	Vrai	Faux
12. Il m'est arrivé d'être jaloux(se) du bonheur des autres.	Vrai	Faux
13. Je n'ai jamais eu l'impression d'être puni(e) sans raison.	Vrai	Faux
14. Je n'ai jamais dit quelque chose pour blesser quelqu'un de façon délibérée.	Vrai	Faux

1/1

[QUALITY OF LIFE SYSTEMIC INVENTORY]

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

ÉTUDE MBSR-MS : ISQV

***Ce questionnaire peut être rempli en ligne ***

Le principal objectif de ce questionnaire est d'évaluer dans quelle mesure vous parvenez à atteindre les buts que vous vous fixez dans divers domaines de votre vie. Ces buts sont parfois clairement identifiés, alors que dans d'autres cas, nous les poursuivons sans les définir précisément

Ce questionnaire touche 28 domaines de votre vie (ex : alimentation, sommeil, loisirs). Pour chacun de ces domaines, vous aurez à évaluer votre **SITUATION ACTUELLE**, la **SITUATION** que vous considérez **SATISFAISANTE** et la vitesse à laquelle vous vous approchez ou éloignez de la **SITUATION IDÉALE.** Voici quelques définitions qui devraient faciliter votre compréhension.

SITUATION IDÉALE : Une situation idéale vous est suggérée pour chacun des domaines couverts par ce questionnaire. Vous les trouverez juste au-dessus des encadrés accompagnant chaque question. La situation idéale constitue ce à quoi toute personne aspire sans que ce ne soit nécessairement atteignable. Dans une relation conjugale, par exemple, la situation idéale s'atteint lorsque vous êtes **parfaitement heureux** avec votre partenaire et qu'**absolument rien** ne pourrait être amélioré. Cet état est illustré par un petit cercle blanc sur le cadran de l'encadré de gauche (voir l'exemple au bas de la page).

SITUATION ACTUELLE : La situation actuelle est votre évaluation de la qualité de votre relation de couple, par exemple, au cours des 3 dernières semaines. Plus cette situation est bonne, plus elle est **près** de la situation idéale. Plus elle est mauvaise, plus elle en est **éloignée.**

SITUATION SATISFAISANTE : Étant donné que la situation idéale est difficilement atteignable, la situation satisfaisante représente une situation que vous jugeriez acceptable ou satisfaisante s'il vous était possible de l'atteindre.

IMPACT : L'impact représente la situation où, à votre avis, vous vous trouveriez sans la condition étudiée (ex : traitement ou maladie).

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

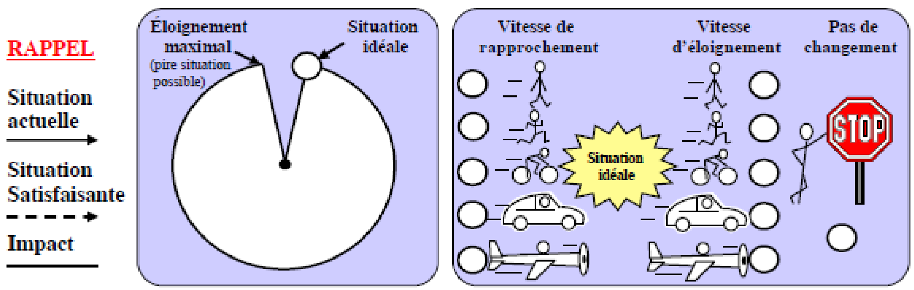
ID ____________________

Date ____________________
AAAA – MM – JJ

Les exemples suivants devraient vous aider à répondre au questionnaire.

Relation de couple (marque d'affection, entente, communication)

<u>**Situation idéale**</u> : être parfaitement heureux(se) dans ce domaine



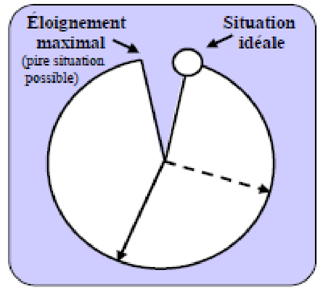
Vous devez indiquer vos réponses en utilisant ces deux encadrés. Premièrement, sur l'encadré de gauche, vous devez indiquer à l'aide d'une flèche pleine votre situation actuelle en vous référant à la situation idéale suggérée dans la question. Deuxièmement, sur le même encadré, vous devez indiquer la position de votre situation satisfaisante à l'aide d'une flèche pointillée. À la page suivante, les 4 types de situations possibles vous sont présentés (en utilisant toujours l'exemple de la relation de couple) avec la position des flèches correspondant à chacune de ces situations.

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ______________________

Date ______________________
AAAA – MM – JJ

Exemple 1 : « C'est moins bien que ce que je souhaite »

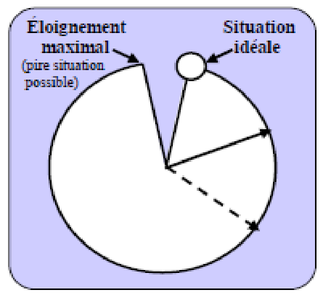


Situation actuelle : Cette personne considère que sa relation de couple pourrait s'améliorer. Elle place donc la flèche pleine de sa situation actuelle à une certaine distance du cercle blanc représentant la situation idéale.

Situation satisfaisante : Sachant que la situation idéale est difficilement atteignable, cette personne indique, à l'aide d'une flèche pointillée, à quelle distance de l'idéal se trouve sa situation satisfaisante.

Autrement dit, elle perçoit sa situation actuelle moins bonne que sa situation satisfaisante.

Exemple 2 : « Ça va au-delà de mes espérances »



Situation actuelle : Cette personne considère que sa relation couple n'est pas à l'idéal. Elle place donc la flèche pleine représentant sa situation actuelle à une certaine distance du cercle blanc de la situation idéale.

Situation satisfaisante : Malgré cela, elle considère sa situation actuelle au-delà de ses espérances. Elle place donc la flèche pointillée représentant sa situation satisfaisante plus loin de la situation idéale que ne l'est la flèche pleine représentant sa situation actuelle.

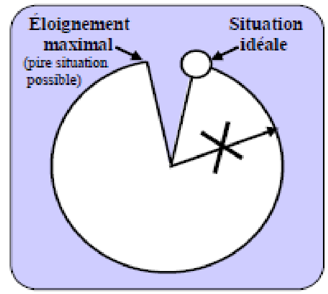
Autrement dit, elle perçoit sa situation actuelle meilleure que sa situation satisfaisante.

3/17

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ______________________

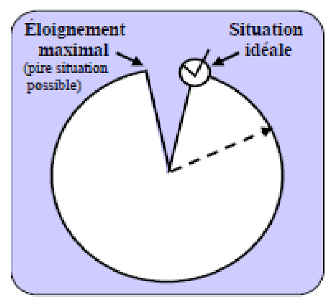
Date ____________________
AAAA – MM – JJ



Exemple 3 : « C'est bien comme ça »

Situation actuelle et satisfaisante : Sans être idéale, cette personne considère que sa situation actuelle est identique à sa situation satisfaisante. Elle place donc sa flèche pleine à une certaine distance de l'idéal. Pour éviter toute confusion, elle fait un **X** sur la flèche pleine signifiant que les deux flèches sont superposées.

Autrement dit, elle perçoit sa situation actuelle au niveau de sa situation satisfaisante.



Exemple 4 : « Ça ne peut pas aller mieux »

Situation actuelle : Bien que cette situation soit difficilement atteignable, cette personne considère que sa relation de couple est idéale, qu'il n'y a pas de place pour de l'amélioration. Elle fait donc un crochet dans le cercle blanc représentant la situatin idéale.

Situation satisfaisante : Si cette personne se contentait de moins que la situation idéale, elle placerait la flèche pointillée représentant sa situation satisfaisante à une certaine distance du cercle blanc représentant la situation idéale.

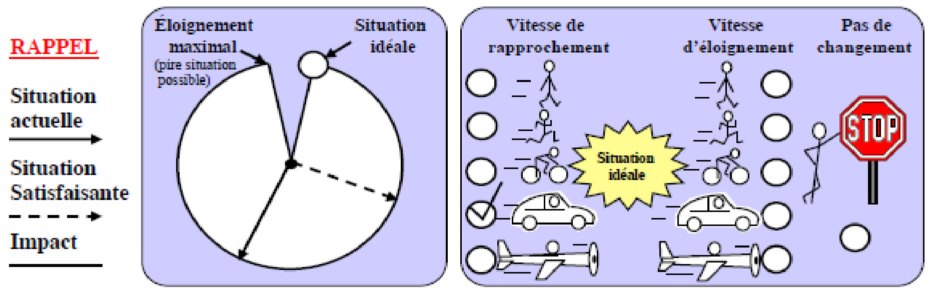
INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

L'encadré de droite permet d'indiquer si votre situation actuelle s'approche, s'éloigne ou demeure inchangée par rapport à la situation idéale. Si vous considérez qu'actuellement votre situation s'améliore, cochez, sous **"Vitesse de rapprochement"**, le cercle près du dessin représentant le mieux la vitesse d'amélioration. S'il y a détérioration de votre situation, choisissez plutôt un dessin sous **"Vitesse d'éloignement"**. Si vous pensez qu'il n'y a pas de changement, cochez le cercle sous le dessin au-dessus duquel est indiqué **"Pas de changement"**.

Pour illustrer ce qui précède, reprenons l'exemple 1 de la page précédente. Sur l'encadré de gauche, cette personne indique que sa relation de couple doit s'améliorer pour atteindre un niveau qu'elle considère satisfaisant. Sur l'encadré de droite, cette personne indique que, malgré tout, sa situation s'améliore et que les changements sont assez rapides.



<u>*IMPORTANT :</u>

Si une question **ne vous concerne pas directement** (par exemple "Interaction avec vos enfants" alors que vous n'avez pas d'enfants) et que cette situation (le fait de ne pas avoir d'enfants) **influence votre vie**, indiquez, toujours à l'aide des flèches, à quelle distance vous êtes de la situation idéale qui est d'être **parfaitement heureux(se)**. Par contre, si ce domaine ne vous préoccupe pas, ne répondez pas à la question et indiquez-le en faisant un **<u>X</u>** sur les cadrans.

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

1. Sommeil (capacité de bien dormir)

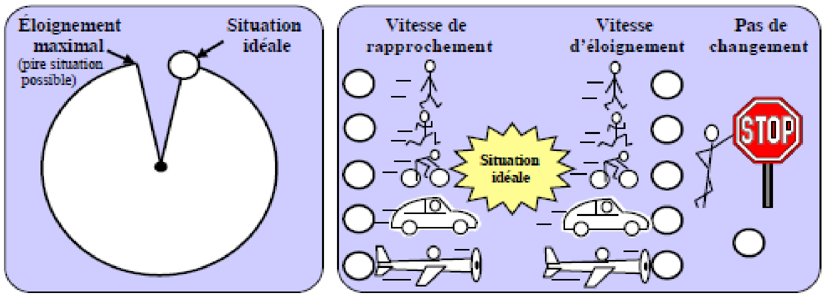
Situation idéale : être parfaitement heureux(se) de la qualité de mon sommeil

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact ——



2. Capacité physique : capacité d'accomplir les activités journalières (marcher, monter des escaliers, se laver, etc,)

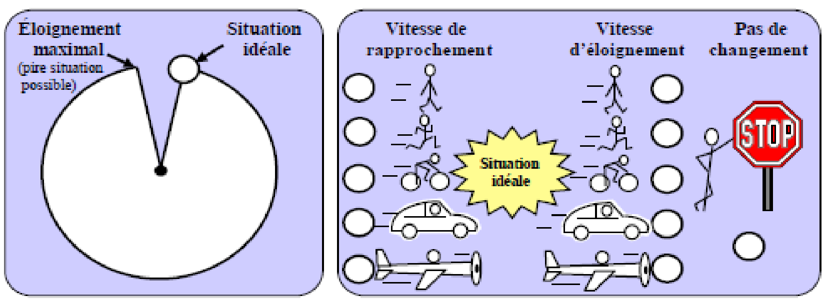
Situation idéale : être parfaitement heureux(se) de mon efficacité dans ces activités

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact ——



3. Alimentation (type d'aliments, de diète, etc,)

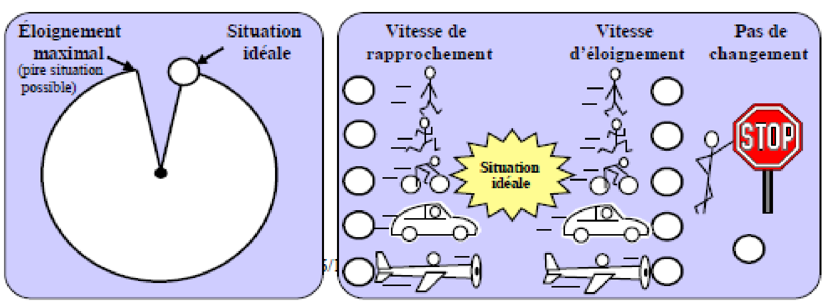
Situation idéale : être parfaitement heureux(se) de ce que je mange (quantité et qualité)

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact ——



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

4. Douleur physique

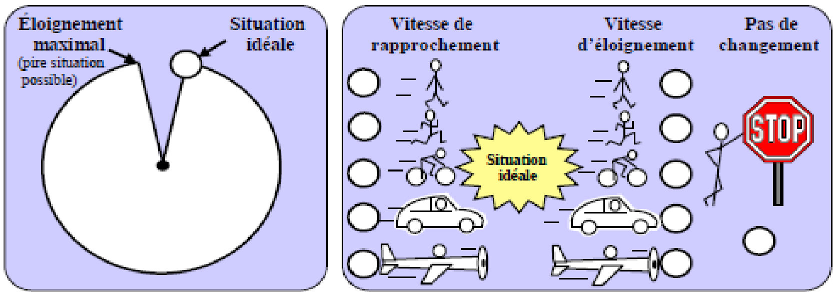
Situation idéale : n'avoir aucune douleur physique

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



5. Santé physique globale

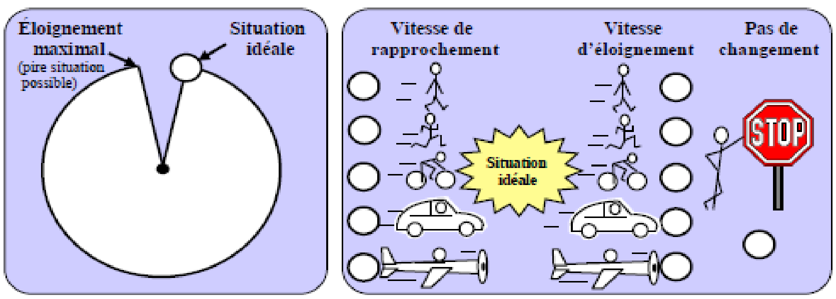
Situation idéale : être parfaitement heureux(se) de ma santé physique

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



6. Loisirs de détente (lecture, télévision, musique, etc.) permettant de relaxer, d'oublier ses soucis et ses préoccupations

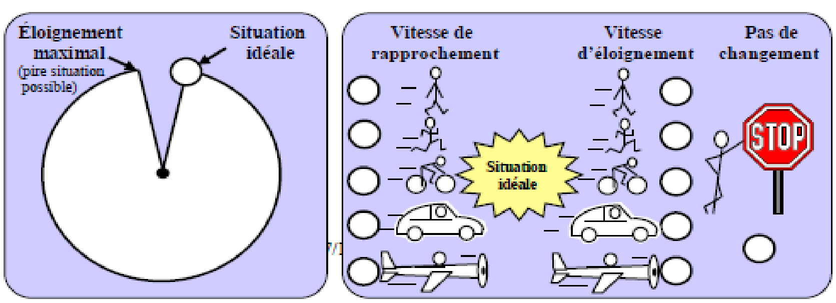
Situation idéale : être parfaitement heureux(se) de la fréquence et de la qualité de mes moments de détente

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ______________________

Date ______________________

AAAA – MM – JJ

7. Loisirs actifs exigeant une dépense d'énergie (sport, bricolage, jardinage, etc.)

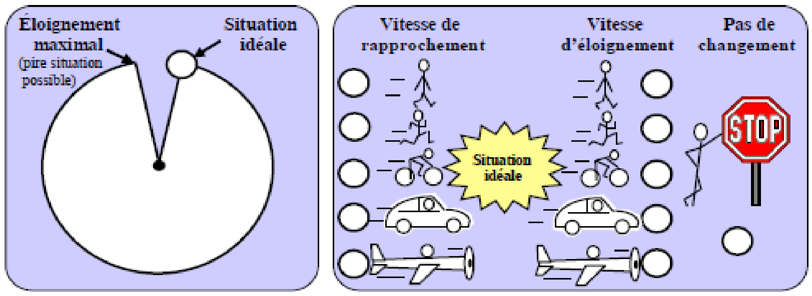
Situation idéale : être parfaitement heureux(se) de ce que je fais

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact ——



8. Sorties (cinéma, restaurant, visiter des amis, etc.)

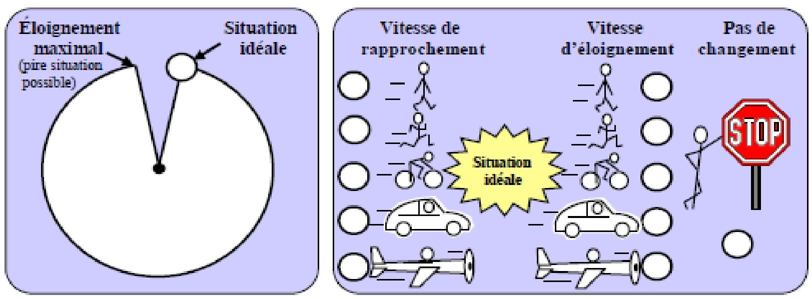
Situation idéale : être parfaitement heureux(se) de ce que je fais

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact ——



9. Interactions avec mes enfants

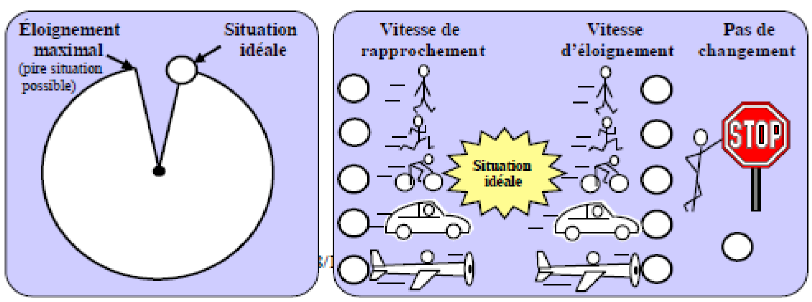
Situation idéale :être parfaitement heureux(se) dans ce domaine

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact ——



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

10. Interactions avec la famille (frères, sœurs, belle-famille, etc.)

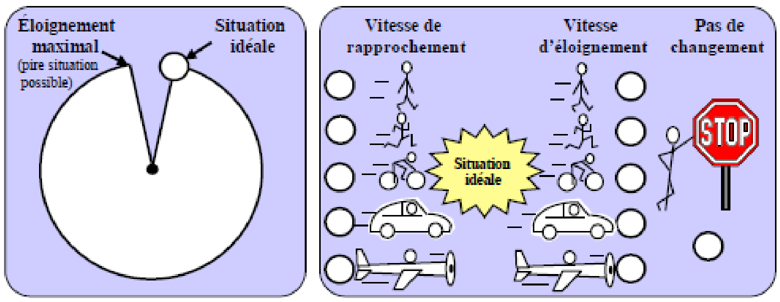
Situation idéale : être parfaitement heureux(se) dans ce domaine

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



11. Interactions avec mes amis(es)

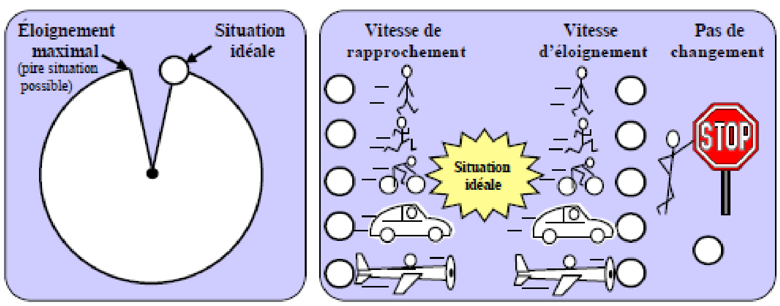
Situation idéale : être parfaitement heureux(se) dans ce domaine

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



12. Type de travail

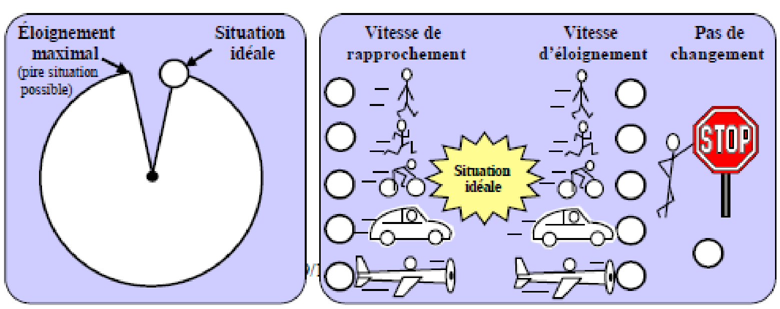
Situation idéale : être parfaitement heureux(se) de ce que je fais

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

13. Efficacité au travail

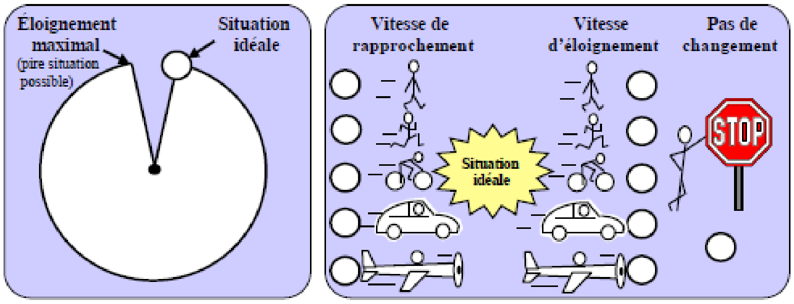
Situation idéale : être parfaitement heureux(se) de mon efficacité au travail (quantité et qualité)

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact



14. Interactions avec les collègues durant les heures de travail

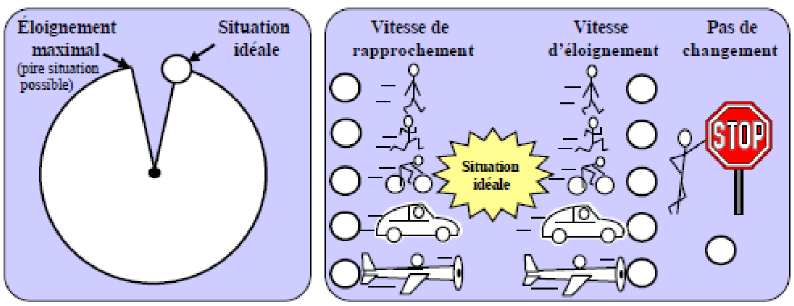
Situation idéale : être parfaitement heureux(se) de mes interactions avec eux (elles)

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact



15. Interactions avec les employeurs(es) ou supérieurs(es) immédiats durant le travail

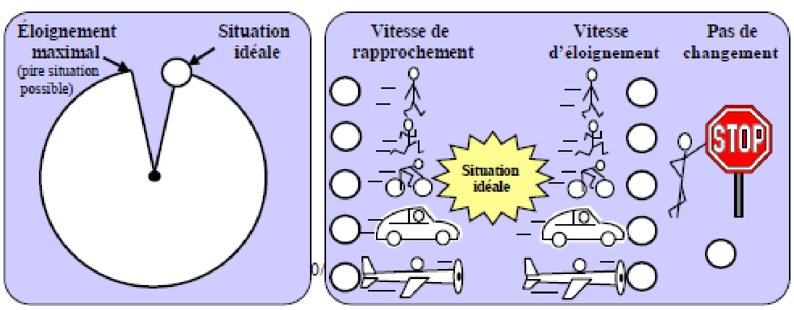
Situation idéale : être parfaitement heureux(se) de mes interactions avec eux elles

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

16. Finances (revenu, budget, etc.)

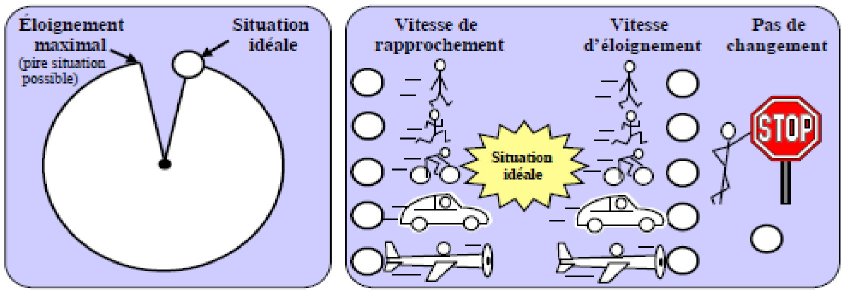
Situation idéale : être parfaitement heureux(se) de mon niveau de vie

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



17. Activités non-rémunérées (bénévolat, etc.)

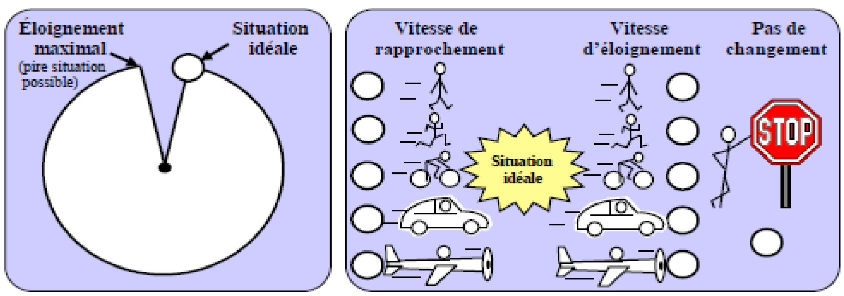
Situation idéale : être parfaitement heureux(se) dans ce domaine

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



18. Travail domestique (travaux légers : vaisselle, époussetage, préparation des repas, etc,)

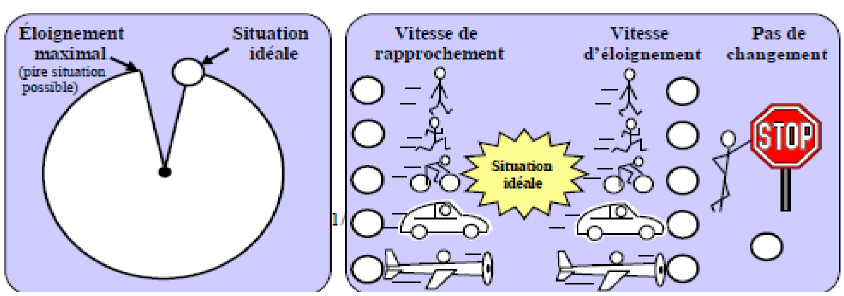
Situation idéale : **être parfaitement heureux(se) de mon efficacité dans ce que je fais**

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ______________________

Date ______________________ AAAA – MM – JJ

19. Entretien de la maison (appartement) et de la cour (s'il y a lieu) (travaux lourds : peinture, réparation, laver les planchers, les fenêtres, entretien de la pelouse, etc.)

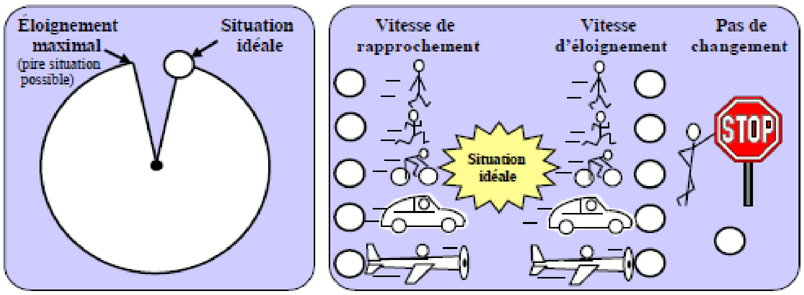
Situation idéale : être parfaitement heureux(se) de mon efficacité dans ce que je fais

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



20. Mémoire (capacité de se rappeler des choses à faire, des noms, des mots, des événements, etc.)

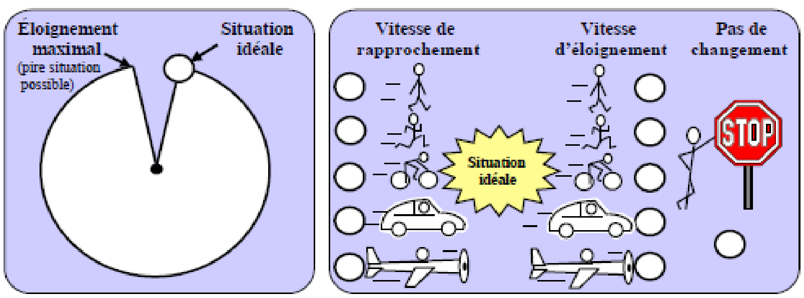
Situation idéale : être parfaitement heureux(se) de mon efficacité dans ce domaine

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



21. Concentration et attention (pouvoir me concentrer sur une tâche comme lire, être attentif(ve) à une discussion, à une émission de télévision, etc.)

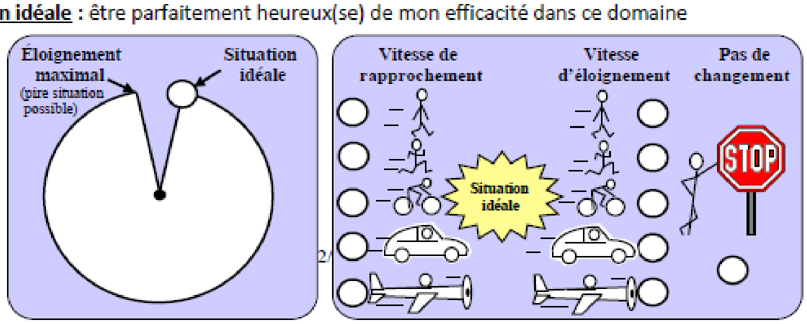
Situation idéale : être parfaitement heureux(se) de mon efficacité dans ce domaine

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



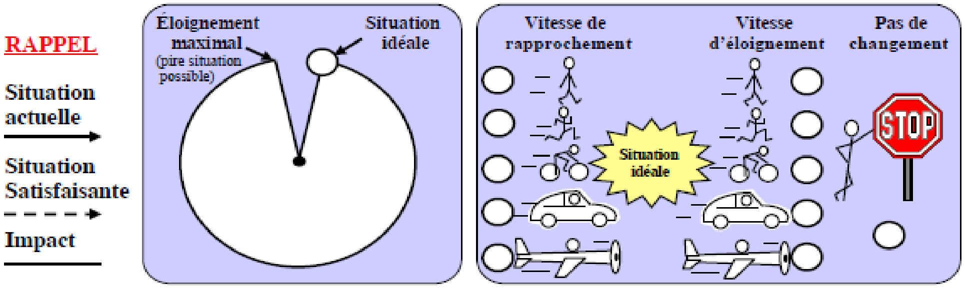
INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ______________________

Date ______________________
AAAA – MM – JJ

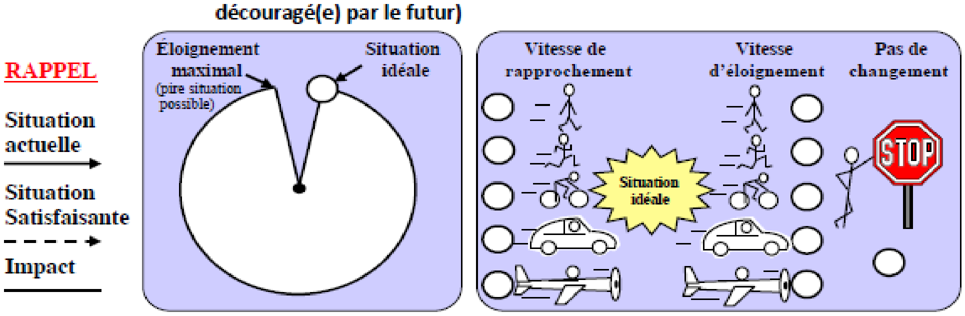
22. Estime de soi (opinion globale de soi)

Situation idéale : avoir une excellente estime de soi (avoir parfaitement confiance en soi, en ses capacités)



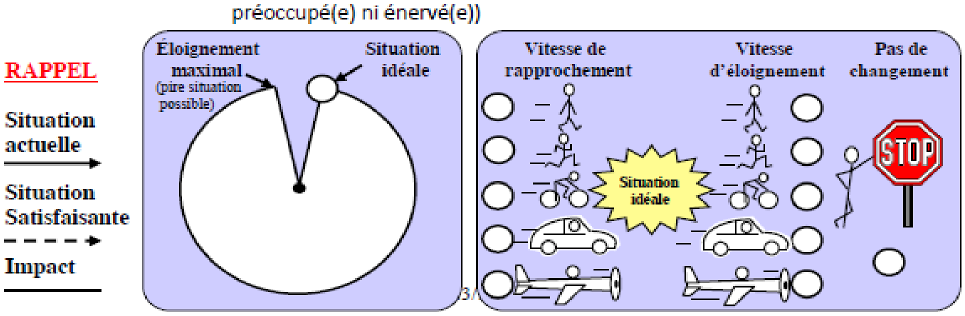
23. Moral

Situation idéale : **avoir un excellent moral, (être très heureux(se), pas déprimé(e) ni découragé(e) par le futur)**



24. Tranquillité d'esprit

Situation idéale : être parfaitement calme et serein(e) (ne pas être inquiet(te), anxieux(se) ni préoccupé(e) ni énervé(e))



3/

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ______________________

Date ______________________
AAAA – MM – JJ

25. Relation de couple (marque d'affection, entente, communication)

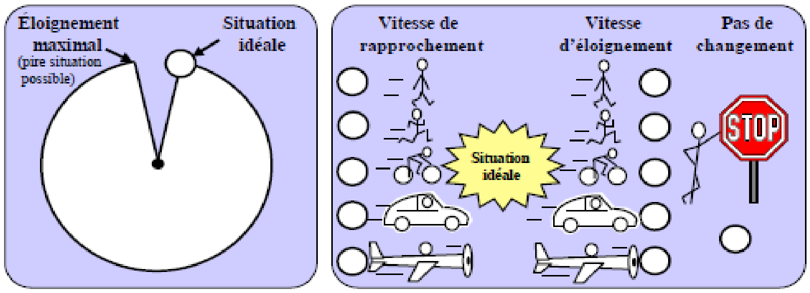
Situation idéale : être parfaitement heureux(se) dans ce domaine

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



26. Relations sexuelles

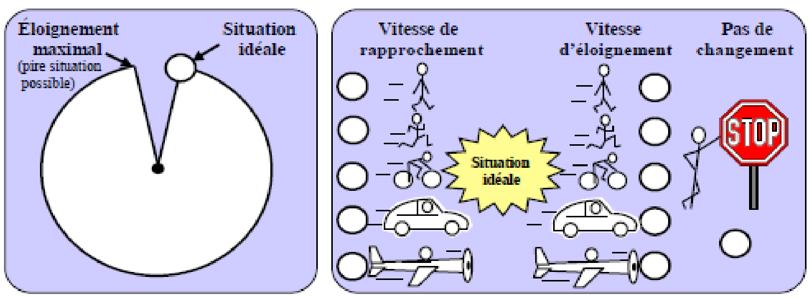
Situation idéale : être parfaitement heureux(se) dans ce domaine

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



27. Vie spirituelle ou religieuse

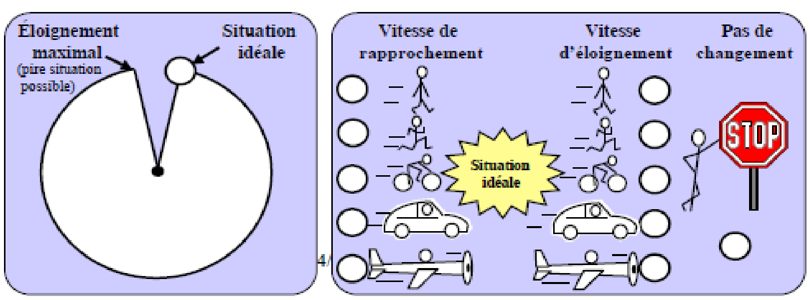
Situation idéale : être parfaitement heureux(se) de ce que m'apporte ma vie spirituelle ou religieuse

RAPPEL

Situation actuelle

Situation Satisfaisante

Impact



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

28. Activités spirituelles ou religieuses (devoirs et obligations demandés par ma religion ou mes croyances)

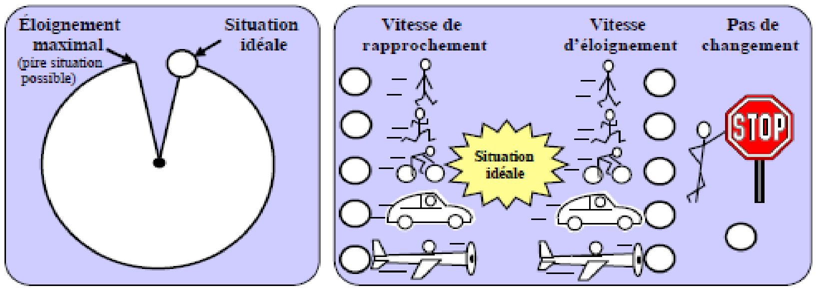
Situation idéale : être parfaitement heureux(se) de ma capacité à faire ces activités

RAPPEL

Situation actuelle →

Situation Satisfaisante - - - →

Impact ——



INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ____________________

Date ____________________
AAAA – MM – JJ

Maintenant que vous avez terminé de répondre à la première section, voici, à nouveau, l'ensemble des domaines de vie couverts par ce questionnaire. Pour chaque domaine, indiquez sur l'échelle de « ESSENTIEL » à « INUTILE », l'importance que vous lui accordez en cochant le cercle approprié.

	1 ESSENTIEL	2 *TRÈS* IMPORTANT	3 IMPORTANT	4 MOYENNEMENT IMPORTANT	5 PEU IMPORTANT	6 SANS IMPORTANCE	7 INUTILE
1. Sommeil	◯	◯	◯	◯	◯	◯	◯
2. Capacités physiques	◯	◯	◯	◯	◯	◯	◯
3. Alimentation	◯	◯	◯	◯	◯	◯	◯
4. Douleur physique	◯	◯	◯	◯	◯	◯	◯
5. Santé physique	◯	◯	◯	◯	◯	◯	◯
6. Loisirs de détente	◯	◯	◯	◯	◯	◯	◯
7. Loisirs actifs	◯	◯	◯	◯	◯	◯	◯
8. Sorties	◯	◯	◯	◯	◯	◯	◯
9. Interactions avec mes enfants	◯	◯	◯	◯	◯	◯	◯
10. Interactions avec ma famille	◯	◯	◯	◯	◯	◯	◯
11. Interactions avec mes amis(es)	◯	◯	◯	◯	◯	◯	◯
12. Type de travail	◯	◯	◯	◯	◯	◯	◯
13. Efficacité au travail	◯	◯	◯	◯	◯	◯	◯
14. Interactions avec les collègues de travail	◯	◯	◯	◯	◯	◯	◯
15. Interactions avec les employeurs(es)	◯	◯	◯	◯	◯	◯	◯
16. Finances	◯	◯	◯	◯	◯	◯	◯
17. Activités non-rémunérées	◯	◯	◯	◯	◯	◯	◯
18. Travail domestique	◯	◯	◯	◯	◯	◯	◯
19. Entretien de la maison	◯	◯	◯	◯	◯	◯	◯
20. Mémoire	◯	◯	◯	◯	◯	◯	◯
21. Concentration et attention	◯	◯	◯	◯	◯	◯	◯

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

ID ______________________

Date ______________________
AAAA – MM – JJ

22. Estime de soi	◯	◯	◯	◯	◯	◯	◯
23. Moral	◯	◯	◯	◯	◯	◯	◯
24. Tranquillité d'esprit	◯	◯	◯	◯	◯	◯	◯
25. Relation de couple	◯	◯	◯	◯	◯	◯	◯
26. Relations sexuelles	◯	◯	◯	◯	◯	◯	◯
27. Vie spirituelle et religieuse	◯	◯	◯	◯	◯	◯	◯
28. Activités spirituelles ou religieuses	◯	◯	◯	◯	◯	◯	◯

APPENDIX H

[WEEKLY MBSR THEMES]

Mindfulness-Based Stress Reduction Program – Weekly Breakdown

Week	**Theme**
1	Introduction to the program and mindfulness; theory and evidence of mind-body medicine and how to applies in daily life; discussion of personal resources and strengths; body-scan meditation practice
2	Examination of participant assumptions and perceptions of themselves, others, and their environment; mindful hatha yoga practice, body scan; mindful eating; sitting meditation
3	Mindfulness versus mindlessness; discovering the pleasure and power of being present; mindful hatha yoga practice; walking meditation
4	Learn to pay attention with curiosity and openness to a full range of experiences; learn the psychological and physiological bases of stress reactivity; practice mindful strategies of responding to stress in positive and proactive ways
5	Identify repetitive unhealthy patterns for stress management that may be reduced or eliminated via mindful awareness; short sitting meditation
6	Effective interpersonal communication; preparation for silent meditation retreat
7	Silent meditation retreat (5 hours) (sitting meditation, yoga, body scan; love and kind poem; walking meditation)
8	Learn how to integrate mindfulness more fully into daily life; maintaining discipline and flexibility of daily practice as life circumstances change; brief love and kindness meditation

9	Review and keeping up the practice; discussion of available resources; celebration

Weekly guide from MBSR manual (Kabat-Zinn, 2009)

REFERENCES

Ahrens, K. A., Rossen, L. M., & Simon, A. E. (2016). Relationship Between Mean Leucocyte Telomere Length and Measures of Allostatic Load in US Reproductive‐Aged Women, NHANES 1999-2002. Paediatric and perinatal epidemiology, 30(4), 325-335.https://doi.org/10.1111/ppe.12277

Al Ibrahim, J. (2013). Relationship between dispositional mindfulness and repressive coping style: an exploratory dissertation.

Albanese, E., Matthews, K. A., Zhang, J., Jacobs, D. R., Whitmer, R. A., Wadley, V. G., & Launer, L. J. (2016). Hostile attitudes and effortful coping in young adulthood predict cognition 25 years later. Neurology, 86(13), 1227-1234.https://doi.org/10.1212/WNL.0000000000002517

Appleton, K. M., Woodside, J. V., Arveiler, D., Haas, B., Amouyel, P., Montaye, M., Ferrieres, J., Ruidavets, J. B., Yarnell, J. W. G., Kee, F., Evans, A., Bingham, A., Ducimetiere, P., Patterson, C. C., & SpringerLink (Online service). (2016). A role for behavior in the relationships between depression and hostility and cardiovascular disease incidence, mortality, and all-cause mortality: the prime study, Day:15https://doi.org/10.1007/s12160-016-9784-x

Aurelius, M. (2013). *Marcus Aurelius: Meditations, Books 1-6*. Oxford University Press.

Astuti, Y., Wardhana, A., Watkins, J., & Wulaningsih, W. (2017). Cigarette smoking and telomere length: a systematic review of 84 studies and meta-analysis. Environmental Research, 158, 480-489. https://doi.org/10.1016/j.envres.2017.06.038

Aviv, A. (2002). Telomeres, sex, reactive oxygen species, and human cardiovascular aging. *Journal of Molecular Medicine*, *80*(11), 689-695.https://doi.org/10.1007/s00109-002-0377-8

Aviv, A. (2009). Leukocyte telomere length, hypertension, and atherosclerosis: are there potential mechanistic explanations? Hypertension, 53(4), 590-591. https://doi: 10.1161/HYPERTENSIONAHA.109.128926

Aviv, A., Shay, J., Christensen, K., & Wright, W. (2005). The longevity gender gap: are telomeres the explanation. Sci Aging Knowledge Environ, 23(1), 16.https://doi.org/10.1126/sageke.2005.23.pe16

Bacon, S. L., Dragomir, A. I., Julien, C. A., Boucher, V. G., Lavoie, K. L., Campbell, T. S., & Vallis, M. T. (2018). Training physicians in behavioural change counseling: A systematic review. Patient Education and Counseling. https://doi.org/10.1016/j.pec.2018.08.025

Baer, R. A. (2003). Mindfulness training as a clinical intervention: a conceptual and empirical review. Clinical psychology: Science and practice, 10(2), 125.https://doi.org/10.1093/clipsy.bpg015

Baird, D. M. (2008). Telomere dynamics in human cells. Biochimie, 90(1), 116-121.https://doi.org/10.1016/j.biochi.2007.08.003

Ball Cooper, E., Anderson, J. L., Sharp, C., Langley, H. A., & Venta, A. (2021). Attachment, Mentalization, and Criterion B of the Alternative DSM-5 Model for Personality Disorders (AMPD). Borderline Personality Disorder and Emotion Dysregulation, 8(1), 1-14.https://doi.org/10.1186/s40479-021-00163-9

Barefoot, J. C., Dahlstrom, W. G., & Williams, R. B. (1983). Hostility, CHD incidence, and total mortality: A 25-yr follow-up study of 255 physicians. Psychosomatic medicine.https://doi.org/10.1097/00006842-198303000-00008

Barefoot, J. C., Dahlstrom, W. G., & Williams, R. B., Jr. (1983). Hostility, CHD incidence, and total mortality: a 25-year follow-up study of 255 physicians. Psychosom Med, 45(1), 59-63. https://doi.org/10.1097/00006842-198303000-00008

Barefoot, J. C., Dodge, K. A., Peterson, B. L., Dahlstrom, W. G., & Williams, R. B., Jr. (1989). The Cook-Medley hostility scale: item content and ability to predict survival. Psychosom Med, 51(1), 46-57.https://doi.org/10.1097/00006842-198901000-00005

Barefoot, J. C., Larsen, S., von der Lieth, L., & Schroll, M. (1995). Hostility, incidence of acute myocardial infarction, and mortality in a sample of older Danish men and women. Am J Epidemiol, 142(5), 477-484. https://doi.org/10.1093/oxfordjournals.aje.a117663

Barefoot, J. C., Peterson, B. L., Dahlstrom, W. G., Siegler, I. C., Anderson, N. B., & Williams Jr, R. B. (1991). Hostility patterns and health implications: correlates of Cook-Medley Hostility Scale scores in a national survey. Health Psychology, 10(1), 18.https://doi.org/10.1037/0278-6133.10.1.18

Barger, S. D., Bachen, E. A., Marsland, A. L., & Manuck, S. B. (2000). Repressive coping and blood measures of disease risk: lipids and endocrine and immunological responses to a laboratory stressor1. Journal of Applied Social Psychology, 30(8), 1619-1638.https://doi.org/10.1111/j.1559-1816.2000.tb02458.x

Barger, S. D., Kircher, J. C., & Croyle, R. T. (1997). The effects of social context and defensiveness on the physiological responses of repressive copers. J Pers Soc Psychol, 73(5), 1118-1128. https://doi.org/10.1037/0022-3514.73.5.1118

Barrett, E. L., & Richardson, D. S. (2011). Sex differences in telomeres and lifespan. Aging cell, 10(6), 913-921.Barth, J., Schumacher, M., & Herrmann-Lingen, C. (2004). Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. Psychosomatic medicine, 66(6), 802-813.https://doi.org/10.1111/j.1474-9726.2011.00741.x

Beauvoir, S. d., & Parshley, H. M. 1. (1952). The second sex. New York: Knopf.

Beery, A. K., Lin, J., Biddle, J. S., Francis, D. D., Blackburn, E. H., & Epel, E. S. (2012). Chronic stress elevates telomerase activity in rats. Biology letters, 8(6), 1063-1066. https://doi.org/10.1098/rsbl.2012.0747

Bekaert, S., De Meyer, T., Rietzschel, E. R., De Buyzere, M. L., De Bacquer, D., Langlois, M., Van Oostveldt, P. (2007). Telomere length and cardiovascular risk factors in a middle-aged population free of overt cardiovascular disease. Aging Cell, 6(5), 639-647.https://doi: 10.1111/j.1474-9726.2007.00321.x

Bélisle, M. P., Lanctôt, D., Anestin, A., Badaroudine, F., & Dupuis, G. (2021). L'inventaire systémique de la qualité de vie: rôle des objectifs de vie et leur atteinte dans l'ajustement psychologique des femmes ayant un diagnostic de cancer du sein. science et comportement, 31(1), 75-87.

Beyhan Sagmen, S., Yildizeli, S. O., Baykan, H., Ozdemir, M., & Ceyhan, B. (2020). The effects of anxiety and depression on asthma control and their association with strategies for coping with stress and social acceptance. Revue Française d'Allergologie, 60(5), 401-406. https://doi.org/10.1016/j.reval.2020.05.006

Bulwer-Lytton, Edward G. Quotes. (n.d.). BrainyQuote.com. Retrieved December 21, 2021, from BrainyQuote.com Web site. https://www.brainyquote.com/quotes/edward_g_bulwerlytton_150264

Bird, T., Tarsia, M., & Schwannauer, M. (2018). Interpersonal styles in major and chronic depression: a systematic review and meta-analysis. Journal of affective disorders, 239, 93-101. https://doi.org/10.1016/j.jad.2018.05.057

Bishop, G. D., & Quah, S. H. (1998). Reliability and validity of measures of anger/hostility in Singapore: Cook & Medley Ho Scale, STAXI and Buss-Durkee hostility inventory.

Personality and Individual Differences, 24(6), 867-878.https://doi.org/10.1016/S0191-8869(98)00024-5

Bishop, G. D., & Quah, S.-H. (1998). Reliability and validity of measures of anger/hostility in Singapore: Cook & Medley Ho Scale, STAXI and Buss-Durkee Hostility Inventory. Personality and Individual Differences, 24(6), 867-878.https://doi.org/10.1016/S0191-8869(98)00024-5

Blackburn, E. H. (1991). Structure and function of telomeres. Nature, 350(6319), 569-573.https://doi.org/10.1038/350569a0

Blasco, M. A. (2005). Telomeres and human disease: ageing, cancer and beyond. Nat Rev Genet, 6(8), 611-622. https://doi.org/10.1038/nrg1656

Blumenthal, J. A., Sherwood, A., Smith, P. J., Watkins, L., Mabe, S., Kraus, W. E.& Hinderliter, A. (2016). Enhancing cardiac rehabilitation with stress management training: a randomized, clinical efficacy trial. Circulation, 133(14), 1341-1350. https://doi.org/10.1161/CIRCULATIONAHA.115.018926

Boden, J. M., Hyland, M. E., & Dale, K. L. (2005). Defensiveness and symptom reporting. Current Psychology, 24(3), 153-170. https://doi.org/10.1007/s12144-005-1019-4

Bodnar, A. G., Ouellette, M., Frolkis, M., Holt, S. E., Chiu, C. P., Morin, G. B., & Wright, W. E. (1998). Extension of life-span by introduction of telomerase into normal human cells. science, 279(5349), 349-352. https://doi.org/10.1126/science.279.5349.349

Boisclair Demarble, J., Moskowitz, D. S., Tardif, J. C., & D'Antono, B. (2014). The relation between hostility and concurrent levels of inflammation is sex, age, and measure dependent. J Psychosom Res, 76(5), 384-393.https://doi.org/10.1016/j.jpsychores.2014.02.010

Bonanno, G. A., & Singer, J. L. (1990). Repressive personality style: Theoretical and methodological implications for health and pathology.

Bonanno, G. A., Davis, P. J., Singer, J. L., & Schwartz, G. E. (1991). The repressor personality and avoidant information processing: A dichotic listening study. Journal of Research in Personality, 25(4), 386-401.https://doi.org/10.1016/0092-6566(91)90029-P

Bonfigli, A. R., Spazzafumo, L., Prattichizzo, F., Bonafè, M., Mensà, E., Micolucci, L., & Olivieri, F. (2016). Leukocyte telomere length and mortality risk in patients with type 2 diabetes. Oncotarget, 7(32), 50835.https://doi.org/10.18632/oncotarget.10615

Boyle, S. H., Williams, R. B., Mark, D. B., Brummett, B. H., Siegler, I. C., Helms, M. J., & Barefoot, J. C. (2004). Hostility as a predictor of survival in patients with coronary artery disease. Psychosomatic medicine, 66(5), 629.https://doi.org/10.1097/01.psy.0000138122.93942.4a

Boyle, S. H., Williams, R. B., Mark, D. B., Brummett, B. H., Siegler, I. C., & Barefoot, J. C. (2005). Hostility, age, and mortality in a sample of cardiac patients. The American journal of cardiology, 96(1), 64-66.https://doi.org/10.1016/j.amjcard.2005.02.04

Britton, W. B., Lindahl, J. R., Cooper, D. J., Canby, N. K., & Palitsky, R. (2021). Defining and measuring meditation-related adverse effects in mindfulness-based programs. Clinical Psychological Science, 2167702621996340.https://doi.org/10.1177/2167702621996340

Brody L.R., Hall J.A. (2010) Gender, Emotion, and Socialization. In: Chrisler J., McCreary D. (eds) Handbook of Gender Research in Psychology. Springer, New York, NY. pp 429-454. https://doi.org/10.1007/978-1-4419-1465-1_21

Brown Wright, L., Gregoski, M. J., Tingen, M. S., Barnes, V. A., & Treiber, F. A. (2011). Impact of stress reduction interventions on hostility and ambulatory systolic blood pressure in African American adolescents. Journal of Black Psychology, 37(2), 210-233.https://doi.org/10.1177/0095798410380203

Brydon, L., Lin, J., Butcher, L., Hamer, M., Erusalimsky, J. D., Blackburn, E. H., & Steptoe, A. (2012). Hostility and cellular aging in men from the Whitehall II cohort. Biol Psychiatry, 71(9), 767-773. https://doi.org/10.1016/j.biopsych.2011.08.020

Brydon, L., Strike, P. C., Bhattacharyya, M. R., Whitehead, D. L., McEwan, J., Zachary, I., & Steptoe, A. (2010). Hostility and physiological responses to laboratory stress in acute coronary syndrome patients. Journal of psychosomatic research, 68(2), 109-116.https://doi.org/10.1016/j.jpsychores.2009.06.007

Bunde, J., & Suls, J. (2006). A quantitative analysis of the relationship between the Cook-Medley Hostility Scale and traditional coronary artery disease risk factors. Health Psychol, 25(4), 493-500. doi: 10.1037/0278-6133.25.4.493.https://doi.org/10.1037/0278-6133.25.4.493

Burns, J. W. (2000). Repression in chronic pain: An idea worth recovering. Applied and Preventive Psychology, 9(3), 173-190.https://doi.org/10.1016/S0962-1849(05)80003-4

Burns, J. W. (2000). Repression predicts outcome following multidisciplinary treatmentof chronic pain. Health Psychology, 19(1), 75.https://doi.org/10.1037/0278-6133.19.1.75

Buss, A. H. (1961). The psychology of aggression. Wiley.https://doi.org/10.1037/11160-000

Buss, A. H., & Durkee, A. (1957). An inventory for assessing different kinds of hostility. Journal of consulting psychology, 21(4), 343.https://doi.org/10.1037/h0046900

Cannon, W. B. (1927). The James-Lange theory of emotions: A critical examination and an alternative theory. American Journal of Psychology, 39, 106-124.https://doi.org/10.2307/1415404

Cannon, W. B. (1929). Bodily changes in pain, hunger, fear and rage (2nd ed.). New York: Appleton, Century, Crofts.https://doi.org/10.1097/00007611-192909000-00037

Carlson, L. E., Beattie, T. L., Giese-Davis, J., Faris, P., Tamagawa, R., Fick, L. J., & Speca, M. (2015). Mindfulness-based cancer recovery and supportive-expressive therapy maintain telomere length relative to controls in distressed breast cancer survivors. Cancer, 121(3), 476-484. https://doi.org/10.1002/cncr.29063

Carlson, L. E., Tamagawa, R., Stephen, J., Doll, R., Faris, P., Dirkse, D., & Speca, M. (2014). Tailoring mind-body therapies to individual needs: patients' program preference and psychological traits as moderators of the effects of mindfulness-based cancer recovery and supportive-expressive therapy in distressed breast cancer survivors. Journal of the National Cancer Institute Monographs, 2014(50), 308-314.https://doi.org/10.1093/jncimonographs/lgu034

Carlson, L. E., Zelinski, E. L., Speca, M., Balneaves, L. G., Jones, J. M., Santa Mina, D., & Vohra, S. (2017). Protocol for the MATCH study (Mindfulness and Tai Chi for cancer health): A preference-based multi-site randomized comparative effectiveness trial (CET) of Mindfulness-Based Cancer Recovery (MBCR) vs. Tai Chi/Qigong (TCQ) for cancer survivors. Contemporary clinical trials, 59, 64-76.https://doi.org/10.1016/j.cct.2017.05.015

Carroll, J. E. (2010). The association of affective, behavioral, and cognitive components of hostility with telomere length, a marker of biological aging (Doctoral dissertation, University of Pittsburgh).

Carroll, J. E., Roux, A. V. D., Fitzpatrick, A. L., & Seeman, T. (2013). Low social support is associated with shorter leukocyte telomere length in late life: Multi-ethnic study of atherosclerosis (MESA). Psychosomatic medicine, 75(2).https://doi.org/10.1097/PSY.0b013e31828233bf

Carroll, Judith E (2010) The association of affective, behavioral, and cognitive components of hostility with telomere length, a marker of biological aging. Doctoral Dissertation, University of Pittsburgh. (Unpublished) retrieved from: http://d-scholarship.pitt.edu/id/eprint/8106

Carver, C. S. (1996). Emergent integration in contemporary personality psychology. Journal of Research in Personality, 30(3), 319-334.https://doi.org/10.1006/jrpe.1996.0022

Cawthon, R. M., Smith, K. R., O'Brien, E., Sivatchenko, A., & Kerber, R. A. (2003). Association between telomere length in blood and mortality in people aged 60 years or older. Lancet, 361(9355), 393-395. https://doi.org/10.1016/S0140-6736(03)12384-7

Celano, C. M., Millstein, R. A., Bedoya, C. A., Healy, B. C., Roest, A. M., & Huffman, J. C. (2015). Association between anxiety and mortality in patients with coronary artery disease: A meta-analysis. American heart journal, 170(6), 1105-1115.https://doi.org/10.1016/j.ahj.2015.09.013

Chang E, Harley CB. Telomere length and replicative aging in human vascular tissues. ProcNatlAcad Sci U S A. 1995; 92:11190-11194.https://doi.org/10.1073/pnas.92.24.11190

Chaplin T. M. (2015). Gender and Emotion Expression: A Developmental Contextual Perspective. Emotion review : journal of the International Society for Research on Emotion, 7(1), 14-21.https://doi.org/10.1177/1754073914544408

Chaplin, T. M., Hong, K., Bergquist, K., & Sinha, R. (2008). Gender differences in response to emotional stress: an assessment across subjective, behavioral, and physiological domains and relations to alcohol craving. Alcoholism: Clinical and Experimental Research, 32(7), 1242-1250.https://doi.org/10.1111/j.1530-0277.2008.00679.x

Chaput, L. A., Adams, S. H., Simon, J. A., Blumenthal, R. S., Vittinghoff, E., Lin, F., Matthews, K. A. (2002). Hostility predicts recurrent events among postmenopausal women with coronary heart disease. Am J Epidemiol, 156(12), 1092-1099.https://doi.org/10.1093/aje/kwf158

Chen, H., Zhang, B., Xue, W., Li, J., Li, Y., Fu, K., & Teng, W. (2019). Anger, hostility and risk of stroke: a meta-analysis of cohort studies. Journal of neurology, 266(4), 1016-1026.https://doi.org/10.1007/s00415-019-09231-1

Cheng, F., Luk, A. O., Wu, H., Lim, C. K., Carroll, L., Tam, C. H., & Ma, R. C. (2021). Shortened relative leukocyte telomere length is associated with all-cause mortality in type

2 diabetes-analysis from the Hong Kong Diabetes Register. Diabetes Research and Clinical Practice, 173, 108649.https://doi.org/10.1016/j.diabres.2021.108649

Cheng, Y. Y., Kao, T. W., Chang, Y. W., Wu, C. J., Peng, T. C., Wu, L. W., & Chen, W. L. (2017). Examining the gender difference in the association between metabolic syndrome and the mean leukocyte telomere length. PLoS One, 12(7), e0180687.https://doi.org/10.1371/journal.pone.0180687

Chida, Y., & Hamer, M. (2008). Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: a quantitative review of 30 years of investigations. Psychological bulletin, 134(6), 829.https://doi.org/10.1037/a0013342

Chida, Y., & Hamer, M. (2008). Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: a quantitative review of 30 years of investigations. Psychological bulletin, 134(6), 829.https://doi.org/10.1037/a0013342

Chida, Y., & Steptoe, A. (2009). The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. J Am Coll Cardiol, 53(11), 936-946.https://doi.org/10.1016/j.jacc.2008.11.044

Chida, Y., & Steptoe, A. (2009). The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. Journal of the American college of cardiology, 53(11), 936-946.https://doi.org/10.1016/j.jacc.2008.11.044

Colle, K. F. F., Vincent, A., Cha, S. S., Loehrer, L. L., Bauer, B. A., & Wahner-Roedler, D. L. (2010). Measurement of quality of life and participant experience with the mindfulness-based stress reduction program. Complementary Therapies in Clinical Practice, 16(1), 36-40.https://doi.org/10.1016/j.ctcp.2009.06.008

Cong, Y., & Shay, J. W. (2008). Actions of human telomerase beyond telomeres. Cell research, 18(7), 725-732.https://doi.org/10.1038/cr.2008.74

Conklin, Q. A., Crosswell, A. D., Saron, C. D., & Epel, E. S. (2019). Meditation, stress processes, and telomere biology. Current opinion in psychology, 28, 92-101.https://doi.org/10.1016/j.copsyc.2018.11.009

Conklin, Q. A., King, B. G., Zanesco, A. P., Lin, J., Hamidi, A. B., Pokorny, J. J., & Saron, C. D. (2018). Insight meditation and telomere biology: The effects of intensive retreat and the moderating role of personality. Brain, behavior, and immunity, 70, 233-245.https://doi.org/10.1016/j.bbi.2018.03.003

Constantino, M. J., Manber, R., DeGeorge, J., McBride, C., Ravitz, P., Zuroff, D. C., & Arnow, B. A. (2008). Interpersonal styles of chronically depressed outpatients: Profiles and therapeutic change. Psychotherapy: Theory, Research, Practice, Training, 45(4), 491.https://doi.org/10.1037/a0014335

Contrada, R. J., Czarnecki, E. M., & Li-Chern Pan, R. (1997). Health-damaging personality traits and verbal-autonomic dissociation: the role of self-control and environmental control. Health Psychol, 16(5), 451-457.https://doi.org/10.1037/0278-6133.16.5.451

Cook W.W., Medley D.M. (1954).Proposed hostility and pharisaic-virtue for the MMPI. J Appl Psychol,38:414-8.https://doi.org/10.1037/h0060667

Cooke, L., Myers, L. B., & Derakshan, N. (2003). Lung function, adherence and denial in asthma patients who exhibit a repressive coping style. Psychology, health & medicine, 8(1), 35-44.https://doi.org/10.1080/1354850021000059241

Costa, P. T., & McCrae, R. R. (1992). Normal personality assessment in clinical practice: The NEO Personality Inventory. Psychological assessment, 4(1), 5.https://doi.org/10.1037/1040-3590.4.1.5

Crimmins, E. M., Kim, J. K., & Hagedorn, A. (2002). Life with and without disease: women experience more of both. Journal of women & aging, 14(1-2), 47-59 .https://doi.org/10.1300/J074v14n01_04

Crowne, D.P., Marlowe, D., 1964. The approval motive: Studies in evaluative dependence. New York: Wiley.

D'Antono, B., Moskowitz, D. S., & Nigam, A. (2013). The metabolic costs of hostility in healthy adult men and women: cross-sectional and prospective analyses. J Psychosom Res, 75(3), 262-269.https://doi.org/10.1016/j.jpsychores.2013.05.010

D'Mello, M. J., Ross, S. A., Briel, M., Anand, S. S., Gerstein, H., & Paré, G. (2015). Association between shortened leukocyte telomere length and cardiometabolic outcomes: systematic review and meta-analysis. Circulation: cardiovascular genetics, 8(1), 82-90.https://doi.org/10.1161/CIRCGENETICS.113.000485

Daubenmier, J., Lin, J., Blackburn, E., Hecht, F. M., Kristeller, J., Maninger, N., Epel, E. (2012). Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study. Psychoneuroendocrinology, 37(7), 917-92.https://doi.org/10.1016/j.psyneuen.2011.10.008

Davidson, K. W., Gidron, Y., Mostofsky, E., & Trudeau, K. J. (2007). Hospitalization cost offset of a hostility intervention for coronary heart disease patients. Journal of consulting and clinical psychology, 75(4), 657.https://doi.org/10.1037/0022-006X.75.4.657

Davis, C. G., Thake, J., & Vilhena, N. (2010). Social desirability biases in self-reported alcohol consumption and harms. Addictive behaviors, 35(4), 302-311.https://doi.org/10.1016/j.addbeh.2009.11.001

De Meyer T, De Buyzere ML, Langlois M, Rietzschel ER, Cassiman P, De Bacquer D, et al. Lower red blood cell counts in middle-aged subjects with shorter peripheral blood leukocyte telomere length. Aging Cell. 2008;5:700-5.https://doi.org/10.1111/j.1474-9726.2008.00419.x

de Punder, K., Heim, C., Wadhwa, P. D., & Entringer, S. (2019). Stress and immunosenescence: The role of telomerase. Psychoneuroendocrinology, 101, 87-100.https://doi.org/10.1016/j.psyneuen.2018.10.019

de Vibe, M., Bjørndal, A., Fattah, S., Dyrdal, G. M., Halland, E., & Tanner-Smith, E. E. (2017). Mindfulness-based stress reduction (MBSR) for improving health, quality of life and social functioning in adults: a systematic review and meta-analysis. Campbell systematic reviews, 13(1), 1-264.https://doi.org/10.4073/csr.2017.11

Deelen, J., Beekman, M., Codd, V., Trompet, S., Broer, L., Hägg, S., & Eline Slagboom, P. (2014). Leukocyte telomere length associates with prospective mortality independent of immune-related parameters and known genetic markers. International journal of epidemiology, 43(3), 878-886.https://doi.org/10.1093/ije/dyt267

Degerman, S., Domellöf, M., Landfors, M., Linder, J., Lundin, M., Haraldsson, S., & Forsgren, L. (2014). Long leukocyte telomere length at diagnosis is a risk factor for dementia progression in idiopathic parkinsonism. PloS one, 9(12), e113387.https://doi.org/10.1371/journal.pone.0113387

Deng, W., Cheung, S. T., Tsao, S. W., Wang, X. M., & Tiwari, A. F. Y. (2016). Telomerase activity and its association with psychological stress, mental disorders, lifestyle factors and interventions: A systematic review. Psychoneuroendocrinology, 64, 150-163.https://doi.org/10.1016/j.psyneuen.2015.11.017

Denollet, J. (1991). Negative affectivity and repressive coping: pervasive influence on self-reported mood, health, and coronary-prone behavior. Psychosom Med, 53(5), 538-556.https://doi.org/10.1097/00006842-199109000-00005

Denollet, J., Martens, E. J., Nyklicek, I., Conraads, V. M., & de Gelder, B. (2008). Clinical events in coronary patients who report low distress: adverse effect of repressive coping. Health Psychol, 27(3), 302-308. doi: 10.1037/0278-6133.27.3.302.https://doi.org/10.1037/0278-6133.27.3.302

Denollet, J., Pedersen, S. S., Vrints, C. J., & Conraads, V. M. (2006). Usefulness of type D personality in predicting five-year cardiac events above and beyond concurrent symptoms of stress in patients with coronary heart disease. The American journal of cardiology, 97(7), 970-973.https://doi.org/10.1016/j.amjcard.2005.10.035

Denollet, J., Sys, S. U., Stroobant, N., Rombouts, H., Gillebert, T. C., & Brutsaert, D. L. (1996). Personality as independent predictor of long-term mortality in patients with coronary heart disease. Lancet, 347(8999), 417-421.https://doi.org/10.1016/S0140-6736(96)90007-0

Diehl, M., Coyle, N., & Labouvie-Vief, G. (1996). Age and sex differences in strategies of coping and defense across the life span. Psychology and Aging, 11, 127-139.https://doi.org/10.1037/0882-7974.11.1.127

Duan, G. X., Wang, K., Su, Y. H., Tang, S. Y., Jia, H. L., Chen, X. M., & Xie, H. H. (2016). Effects of Tai Chi on telomerase activity and gerotranscendence in middle aged and elderly adults in Chinese society. International Journal of Nursing Sciences, 3(3), 235-241.https://doi.org/10.1016/j.ijnss.2016.07.005

Ducray, C., Pommier, J. P., Martins, L., Boussin, F. D., & Sabatier, L. (1999). Telomere dynamics, end-to-end fusions and telomerase activation during the human fibroblast immortalization process. Oncogene, 18(29), 4211-4223.https://doi.org/10.1038/sj.onc.1202797

Dugdale, H. L., & Richardson, D. S. (2018). Heritability of telomere variation: it is all about the environment!. Philosophical transactions of the Royal Society of London. Series B, Biological sciences, 373(1741), 20160450.https://doi.org/10.1098/rstb.2016.0450

Dupuis, G., Marois, D., & Etienne, A. M. (2012). La mesure de la qualité de vie: le modèle des systèmes de contrôle, une approche théorique pratique pour parler du bonheur. Revue Francophone de Clinique Comportementale et Cognitive, 17(1), 4-14.https://doi.org/10.1098/rstb.2016.0450

Dupuis, G., Perrault, J., Lambany, M.-C., Kennedy, E. et David, P. (1989). A new tool to assess quality of life: The quality of life systemic inventory. Quality of Life and Cardiovascular, 5, 36-45.

Duraimani, S., Schneider, R. H., Randall, O. S., Nidich, S. I., Xu, S., Ketete, M., Fagan, J. (2015). Effects of Lifestyle Modification on Telomerase Gene Expression in Hypertensive Patients: A Pilot Trial of Stress Reduction and Health Education Programs in African Americans. PLoS One, 10(11), e0142689.https://doi.org/10.1371/journal.pone.0142689

Eagly, A. H. (2009). The his and hers of prosocial behavior: an examination of the social psychology of gender. American psychologist, 64(8), 644.https://doi.org/10.1037/0003-066X.64.8.644

Eagly, A. H., & Mladinic, A. (1989). Gender stereotypes and attitudes toward women and men. Personality and social psychology bulletin, 15(4), 543-558.https://doi.org/10.1177/0146167289154008

Edelman, S., Lemon, J., & Kidman, A. (2003). The perceived benefits of a group CBT intervention for patients with coronary heart disease. Journal of Cognitive Psychotherapy, 17(1), 59-65.https://doi.org/10.1891/jcop.17.1.59.58268

Edmonds, G. W., Cote, H. C., & Hampson, S. E. (2015). Childhood Conscientiousness and Leukocyte Telomere Length 40 Years Later in Adult Women--Preliminary Findings of a Prospective Association. PLoS One, 10(7), e0134077.https://doi.org/10.1371/journal.pone.0134077

Edwards, A. L. (1957). The social desirability variable in personality assessment and research.

Ein-Dor T, Mikulincer M, Shaver PR: Attachment insecurities and the processing of threat-related information: studying the schemas involved in insecure people's coping strategies. J Pers Soc Psychol 2011, 101:78-93.https://doi.org/10.1037/a0022503

Ekici, B., Ercan, E. A., Cehreli, S., & Töre, H. F. (2014). The effect of emotional status and health-related quality of life on the severity of coronary artery disease. Kardiologia Polska (Polish Heart Journal), 72(7), 617-623.https://doi.org/10.5603/KP.a2014.0023

Elovainio, M., Ferrie, J. E., Singh-Manoux, A., Shipley, M., Batty, G. D., Head, J., & Kivimäki, M. (2011). Socioeconomic differences in cardiometabolic factors: social causation or health-related selection? Evidence from the Whitehall II Cohort Study, 1991-2004. American journal of epidemiology, 174(7), 779-789.https://doi.org/10.1093/aje/kwr149

Emmons, K. M., & Rollnick, S. (2001). Motivational interviewing in health care settings: opportunities and limitations. American journal of preventive medicine, 20(1), 68-74.https://doi.org/10.1016/S0749-3797(00)00254-3

Epel, E. (2012). How "reversible" is telomeric aging? Cancer Prev Res (Phila), 5(10), 1163-1168. doi: 10.1158/1940-6207.CAPR-12-0370.https://doi.org/10.1158/1940-6207.CAPR-12-0370

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. Proceedings of the National Academy of Sciences, 101(49), 17312-17315.https://doi.org/10.1073/pnas.0407162101

Epel, E. S., Lin, J., Wilhelm, F. H., Wolkowitz, O. M., Cawthon, R., Adler, N. E., & Blackburn, E. H. (2006). Cell aging in relation to stress arousal and cardiovascular disease risk factors. Psychoneuroendocrinology, 31(3), 277-287.https://doi.org/10.1016/j.psyneuen.2005.08.011

Epel, E. S., Merkin, S. S., Cawthon, R., Blackburn, E. H., Adler, N. E., Pletcher, M. J., & Seeman, T. E. (2009). The rate of leukocyte telomere shortening predicts mortality from cardiovascular disease in elderly men. Aging (Albany NY), 1(1), 81.https://doi.org/10.18632/aging.100007

Epel, E., Daubenmier, J., Moskowitz, J. T., Folkman, S., & Blackburn, E. (2009). Can meditation slow rate of cellular aging? Cognitive stress, mindfulness, and telomeres. Ann N Y Acad Sci, 1172, 34-53. https://doi.org/10.1111/j.1749-6632.2009.04414.x

Erikson, E. H., & Erikson, J. M. (1998). The life cycle completed (extended version). WW Norton & Company. p.61

Erskine, J. A., Kvavilashvili, L., Conway, M. A., & Myers, L. (2007). The effects of age on psychopathology, well-being and repressive coping. Aging and Mental Health, 11(4), 394-404.https://doi.org/10.1080/13607860600963737

Erskine, J., Kvavilashvili, L., Myers, L., Leggett, S., Davies, S., Hiskey, S., & Georgiou, G. (2016). A longitudinal investigation of repressive coping and ageing. Aging & mental health, 20(10), 1010-1020.https://doi.org/10.1080/13607863.2015.1060941

Erskine, J., Kvavilashvili, L., Myers, L., Leggett, S., Davies, S., Hiskey, S., & Georgiou, G. (2016). A longitudinal investigation of repressive coping and ageing. Aging & mental health, 20(10), 1010-1020.https://doi.org/10.1080/13607863.2015.1060941

Everson-Rose, S. A., Roetker, N. S., Lutsey, P. L., Kershaw, K. N., Longstreth, W. T. J., Sacco, R. L., Diez, R. A. V., & Alonso, A. (2014). Chronic stress, depressive symptoms, anger, hostility, and risk of stroke and transient ischemic attack in the multi-ethnic study of atherosclerosis. Stroke, 45(8), 2318-23.https://doi.org/10.1161/STROKEAHA.114.004815

Farzaneh-Far, R., Lin, J., Epel, E., Lapham, K., Blackburn, E., & Whooley, M. A. (2010). Telomere length trajectory and its determinants in persons with coronary artery disease: longitudinal findings from the heart and soul study. PloS one, 5(1), e8612.https://doi.org/10.1371/journal.pone.0008612

Feldman, J. M., Lehrer, P. M., Hochron, S. M., & Schwartz, G. E. (2002). Defensiveness and individual response stereotypy in asthma. Psychosomatic Medicine, 64(2), 294.https://doi.org/10.1097/00006842-200203000-00013

Fishbain, D. A., Lewis, J. E., Bruns, D., Disorbio, J. M., Gao, J., & Meyer, L. J. (2011).Exploration of anger constructs in acute and chronic pain patients vs. community patients. Pain Practice, 11(3), 240-251.https://doi.org/10.1111/j.1533-2500.2010.00410.x

Fitzpatrick AL, Kronmal RA, Kimura M, Gardner JP, Psaty BM, Jenny NS, Tracy RP, Hardikar S, Aviv A. Leukocyte telomere length and mortality in the Cardiovascular Health Study. J Gerontol A Biol Sci Med Sci. 2011; 66:421-429. https://doi.org/10.1093/gerona/glq224

Floyd, F. J., Cranford, J. A., Daugherty, M. K., Fitzgerald, H. E., & Zucker, R. A. (2006). Marital interaction in alcoholic and nonalcoholic couples: Alcoholic subtype variations and wives' alcoholism status. Journal of Abnormal Psychology, 115(1), 121-130.https://doi.org/10.1037/0021-843X.115.1.121

Flynn, K. E., & Smith, M. A. (2007). Personality and health care decision-making style. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 62(5), P261-P267.https://doi.org/10.1093/geronb/62.5.P261

Frasure-Smith, N., Lespérance, F., Gravel, G., Masson, A., Juneau, M., & Bourassa, M. G. (2002). Long-term survival differences among low-anxious, high-anxious and repressive copers enrolled in the Montreal heart attack readjustment trial. Psychosomatic Medicine, 64(4), 571-579. https://doi.org/10.1097/01.PSY.0000021950.04969.F8

Freeman, A. J., Schumacher, J. A., & Coffey, S. F. (2015). Social desirability and partner agreement of men's reporting of intimate partner violence in substance abuse treatment settings. Journal of interpersonal violence, 30(4), 565-579.https://doi.org/10.1177/0886260514535263

Freud, A. (1946). The ego and the mechanisms of defense. New York: International Universities Press.

Friedman, H. S., Kern, M. L., & Reynolds, C. A. (2010). Personality and health, subjective well-being, and longevity. J Pers, 78(1), 179-216. https://doi.org/10.1111/j.1467-6494.2009.00613.x

Furnham, A., & Lay, A. (2016). Repressive coping and theories about psychotherapy. J Psychol Psychother, 6(283), 2161-0487.https://doi.org/10.4172/2161-0487.1000283

Gallup, G. G. (1977). Tonic immobility: The role of fear and predation. Psychological Record, 27, 41-61.https://doi.org/10.1007/BF03394432

Gans, J. S. (Ed.). (2010). Hostility. In J. S. Gans (Ed.), Difficult topics in group psychotherapy: My journey from shame to courage (pp. 41-61). Karnac Books.https://doi.org/10.4324/9780429473722-2

Gardner, M., Bann, D., Wiley, L., Cooper, R., Hardy, R., Nitsch, D., & Halcyon Study Team. (2014). Gender and telomere length: systematic review and meta-analysis. Experimental gerontology, 51, 15-27.https://doi.org/10.1016/j.exger.2013.12.004

Garssen, B. (2007). Repression: finding our way in the maze of concepts. J Behav Med, 30(6), 471-481. https://doi.org/10.1007/s10865-007-9122-7

Garssen, B., Remie, M., & van der Lee, M. (2010). Repression questionnaires compared. Psychology of Denial, 103-130.

Geronimus AT, Pearson JA, Linnenbringer E, Schulz AJ, Reyes AG, Epel ES, et al. Race-ethnicity, poverty, urban stressors, and telomere length in a Detroit community-based sample. J Health Soc Behav. 2015;56(2):199-224.https://doi.org/10.1177/0022146515582100

Ghimire, S., Hill, C. V., Sy, F. S., & Rodriguez, R. (2019). Decline in telomere length by age and effect modification by gender, allostatic load and comorbidities in National Health and Nutrition Examination Survey (1999-2002). PloS one, 14(8), e0221690.https://doi.org/10.1371/journal.pone.0221690

Gidron, Y., Davidson, K., & Bata, I. (1999). The short-term effects of a hostility-reduction intervention on male coronary heart disease patients. Health Psychology, 18(4), 416.https://doi.org/10.1037/0278-6133.18.4.416

Gidron, Y., Davidson, K., & Bata, I. (1999). The short-term effects of a hostility-reduction intervention on male coronary heart disease patients. Health Psychology, 18(4), 416.https://doi.org/10.1037/0278-6133.18.4.416

Ginzburg, K., Solomon, Z., & Bleich, A. (2002). Repressive coping style, acute stress disorder, and posttraumatic stress disorder after myocardial infarction. Psychosomatic medicine, 64(5), 748-757.https://doi.org/10.1097/01.PSY.0000021949.04969.2E

Girard, D., Tardif, J. C., Boisclair Demarble, J., & D'Antono, B. (2016). Trait hostility and acute inflammatory responses to stress in the laboratory. PloS one, 11(6), e0156329.https://doi.org/10.1371/journal.pone.0156329

Goglin, S. E., Farzaneh-Far, R., Epel, E. S., Lin, J., Blackburn, E. H., & Whooley, M. A. (2016). Change in leukocyte telomere length predicts mortality in patients with stable coronary heart disease from the heart and soul study. PloS one, 11(10), e0160748.https://doi.org/10.1371/journal.pone.0160748

Greenglass, E. R., & Julkunen, J. (1989). Construct validity and sex differences in Cook-Medley hostility. Personality and Individual differences, 10(2), 209-218.https://doi.org/10.1016/0191-8869(89)90206-7

Gremigni, P. (2006). Cynical hostility and the metabolic syndrome: A case-control study. Monaldi Archives for Chest Disease, 66(3).https://doi.org/10.4081/monaldi.2006.524

Guerrero Rodríguez, C., Palmero Cantero, F., & Gómez-Íñiguez, C. (2018). Blood pressure responses of defensive hostile women when facing a real stress task. Psychology & health, 33(8), 978-994.https://doi.org/10.1080/08870446.2018.1449952

Hackett, R. A., Lazzarino, A. I., Carvalho, L. A., Hamer, M., & Steptoe, A. (2015). Hostility and physiological responses to acute stress in people with type 2 diabetes. Psychosomatic medicine, 77(4), 458.https://doi.org/10.1097/PSY.0000000000000172

Hampson, S. E., Andrews, J. A., Barckley, M., Lichtenstein, E., & Lee, M. E. (2006). Personality traits, perceived risk, and risk-reduction behaviors: a further study of smoking and radon. Health Psychology, 25(4), 530.https://doi.org/10.1037/0278-6133.25.4.530

Harned, M. S., Banawan, S. F., & Lynch, T. R. (2006). Dialectical behavior therapy: An emotion-focused treatment for borderline personality disorder. Journal of Contemporary Psychotherapy, 36(2), 67-75.https://doi.org/10.1007/s10879-006-9009-x

Harris, S. E., Marioni, R. E., Martin-Ruiz, C., Pattie, A., Gow, A. J., Cox, S. R., & Deary, I. J. (2016). Longitudinal telomere length shortening and cognitive and physical decline in later life: The Lothian Birth Cohorts 1936 and 1921. Mechanisms of Ageing and Development, 154, 43-48.https://doi.org/10.1016/j.mad.2016.02.004

Hathaway, S. R., & McKinley, J. C. (1951). Minnesota Multiphasic Personality Inventory; Manual, revised.

Haukkala, A., Konttinen, H., Laatikainen, T., Kawachi, I., & Uutela, A. (2010). Hostility, anger control, and anger expression as predictors of cardiovascular disease. Psychosom Med, 72(6), 556-562. https://doi.org/10.1097/PSY.0b013e3181dbab87

Haycock, P. C., Heydon, E. E., Kaptoge, S., Butterworth, A. S., Thompson, A., & Willeit, P. (2014). Leucocyte telomere length and risk of cardiovascular disease: systematic review and meta-analysis. BMJ, 349, g4227. https://doi.org/10.1136/bmj.g4227

Helmers, K. F., Krantz, D. S., Merz, C. N., Klein, J., Kop, W. J., Gottdiener, J. S., & Rozanski, A. (1995). Defensive hostility: relationship to multiple markers of cardiac ischemia in patients with coronary disease. Health Psychol, 14(3), 202-209.https://doi.org/10.1037/0278-6133.14.3.202

Henderson, V. P., Massion, A. O., Clemow, L., Hurley, T. G., Druker, S., & Hebert, J. R. (2013). A randomized controlled trial of mindfulness-based stress reduction for women with early-stage breast cancer receiving radiotherapy. Integr Cancer Ther, 12(5), 404-413. https://doi.org/10.1177/1534735412473640

Herman, P. M., Anderson, M. L., Sherman, K. J., Balderson, B. H., Turner, J. A., & Cherkin, D. C. (2017). Cost-effectiveness of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care among adults with chronic low-back pain. Spine, 42(20), 1511.https://doi.org/10.1097/BRS.0000000000002344

Ho, R. T., Chan, J. S., Wang, C. W., Lau, B. W., So, K. F., Yuen, L. P., Chan, C. L. (2012). A randomized controlled trial of qigong exercise on fatigue symptoms, functioning, and telomerase activity in persons with chronic fatigue or chronic fatigue syndrome. Ann Behav Med, 44(2), 160-170. doi: 10.1007/s12160-012-9381-6.https://doi.org/10.1007/s12160-012-9381-6

Hoge, E. A., Chen, M. M., Orr, E., Metcalf, C. A., Fischer, L. E., Pollack, M. H., Simon, N. M. (2013). Loving-Kindness Meditation practice associated with longer telomeres in women. Brain Behav Immun, 32, 159-163. https://doi.org/10.1016/j.bbi.2013.04.005

Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspectives on psychological science, 10(2), 227-237.https://doi.org/10.1177/1745691614568352

Holt-Lunstad, J., Smith, T. W., & Uchino, B. N. (2008). Can hostility interfere with the health benefits of giving and receiving social support? The impact of cynical hostility on cardiovascular reactivity during social support interactions among friends. Annals of Behavioral Medicine, 35(3), 319-330.https://doi.org/10.1007/s12160-008-9041-z

Houben, J. M., Giltay, E. J., Rius-Ottenheim, N., Hageman, G. J., & Kromhout, D. (2011). Telomere length and mortality in elderly men: the Zutphen Elderly Study. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 66(1), 38-44.https://doi.org/10.1093/gerona/glq164

Houben, J. M., Moonen, H. J., van Schooten, F. J., & Hageman, G. J. (2008). Telomere length assessment: biomarker of chronic oxidative stress? Free Radic Biol Med, 44(3), 235-246.https://doi: 10.1016/j.freeradbiomed.2007.10.001

Huzen, J., van der Harst, P., de Boer, R. A., Lesman-Leegte, I., Voors, A. A., van Gilst, W. H., & van Veldhuisen, D. J. (2010). Telomere length and psychological well-being in patients with chronic heart failure. Age and ageing, 39(2), 223-227.https://doi.org/10.1093/ageing/afp256

Ikeda, A., Schwartz, J., Peters, J. L., Baccarelli, A. A., Hoxha, M., Dioni, L., Spiro, A., Sparrow, D., Vokonas, P., & Kubzansky, L. D. (2014). Pessimistic orientation in relation to telomere length in older men: the va normative aging study. Psychoneuroendocrinology, 42, 68-76.https://doi.org/10.1016/j.psyneuen.2014.01.001

Izawa, S., Kodama, M., & Nomura, S. (2005). Study on self and other ratings of hostility. Shinrigaku kenkyu: The Japanese journal of psychology, 75(6), 530-535.https://doi.org/10.4992/jjpsy.75.530

Jacobs, G. A., Latham, L. E., & Brown, M. S. (1988). Test-retest reliability of the State-Trait Personality Inventory and the Anger Expression Scale. Anxiety Research, 1(3), 263-265.https://doi.org/10.1080/08917778808248724

Jacobs, T. L., Epel, E. S., Lin, J., Blackburn, E. H., Wolkowitz, O. M., Bridwell, D. A., . . . Saron, C. D. (2011). Intensive meditation training, immune cell telomerase activity, and psychological mediators. Psychoneuroendocrinology, 36(5), 664-681. doi: 10.1016/j.psyneuen.2010.09.010https://doi.org/10.1016/j.psyneuen.2010.09.010

Jahangirpour, M., Musavi, S. V., Khosrojavid, M., Salari, A., & Rezaei, S. (2013). The effectiveness of group mindfulness training on depression, hostility and anxiety in individuals with coronary heart disease. Studies in Medical Sciences, 24(9), 730-739.https://doi.org/10.1016/j.ijcha.2019.100356

Jalali, D., Abdolazimi, M., Alaei, Z., & Solati, K. (2019). Effectiveness of mindfulness-based stress reduction program on quality of life in cardiovascular disease patients. IJC Heart & Vasculature, 23, 100356.https://doi.org/10.1016/j.ijcha.2019.100356

Jamner, L. D., Shapiro, D., Goldstein, I. B., & Hug, R. (1991). Ambulatory blood pressure and heart rate in paramedics: effects of cynical hostility and defensiveness. Psychosom Med, 53(4), 393-406.https://doi.org/10.1097/00006842-199107000-00005

Jensen, M. R. (1987). Psychobiological factors predicting the course of breast cancer. Journal of personality, 55(2), 317-342.https://doi.org/10.1111/j.1467-6494.1987.tb00439.x

John, O.P., & Gross, J.J. (2004). Healthy and unhealthy emotion regulation: Personality processes, individual differences, and life span development. Journal of Personality, 72, 1301-1333.https://doi.org/10.1111/j.1467-6494.2004.00298.x

Jordan, C. D., Glover, L. M., Gao, Y., Musani, S. K., Mwasongwe, S., Wilson, J. G., & Sims, M. (2019). Association of psychosocial factors with leukocyte telomere length among African Americans in the Jackson Heart Study. Stress and Health, 35(2), 138-145.https://doi.org/10.1002/smi.2848

Jørgensen, M. M., & Zachariae, R. (2006). Repressive coping style and autonomic reactions to two experimental stressors in healthy men and women. Scandinavian Journal of Psychology, 47(2), 137-148.https://doi.org/10.1111/j.1467-9450.2006.00501.x

Jorgensen, R. S., & Thibodeau, R. (2007). Defensive avoidance of disapproval: the relationship of a defensive style to physical and mental health. Harvard review of psychiatry, 15(1), 9-17.https://doi.org/10.1080/10673220601183923

Jorgensen, R. S., Frankowski, J. J., Lantinga, L. J., Phadke, K., Sprafkin, R. P., & Abdul-Karim, K. W. (2001). Defensive hostility and coronary heart disease: a preliminary investigation of male veterans. Psychosom Med, 63(3), 463-469https://doi.org/10.1097/00006842-200105000-00016

Jorgensen, R. S., Johnson, B. T., Kolodziej, M. E., & Schreer, G. E. (1996). Elevated blood pressure and personality: a meta-analytic review. Psychol Bull, 120(2), 293-320.https://doi.org/10.1037/0033-2909.120.2.293

Jost, J. T., & Kay, A. C. (2005). Exposure to benevolent sexism and complementary gender stereotypes: consequences for specific and diffuse forms of system justification. Journal of personality and social psychology, 88(3), 498.https://doi.org/10.1037/0022-3514.88.3.498

Juster, R.-P., Russell, J. J., Almeida, D., & Picard, M. (2016). Allostatic load and comorbidities: a mitochondrial, epigenetic, and evolutionary perspective. Development and Psychopathology, 28(4pt1), 1117-1146. https://doi.org/10.1017/S0954579416000730https://doi.org/10.1017/S0954579416000730

Jylhävä, J., Pedersen, N. L., & Hägg, S. (2017). Biological age predictors. EBioMedicine, 21, 29-36.https://doi.org/10.1016/j.ebiom.2017.03.046

Kabat-Zinn J. Wherever you go there you are: Mindfulness meditation in everyday life. New York, NY: Hyperion; 1994.p. 4

Kabat-Zinn, J. (1982). An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: Theoretical considerations and preliminary results. General hospital psychiatry, 4(1), 33-47.https://doi.org/10.1016/0163-8343(82)90026-3

Kabat-Zinn, J. (1990).Full catastrophe living: Using the wisdom of your body and mind to face stress, pain, and illness.New York: Dell Pub-ishing

Kabat-Zinn, J. (2003). Mindfulness-based stress reduction (MBSR). Constructivism in the Human Sciences, 8(2), 73.

Keith, F., Krantz, D. S., Chen, R., Harris, K. M., Ware, C. M., Lee, A. K., & Gottlieb, S. S. (2017). Anger, hostility, and hospitalizations in patients with heart failure. Health Psychology, 36(9), 829.https://doi.org/10.1037/hea0000519

Keng, S. L., Looi, P. S., Tan, E. L. Y., Yim, O. S., San Lai, P., Chew, S. H., & Ebstein, R. P. (2020). Effects of mindfulness-based stress reduction on psychological symptoms and telomere length: a randomized active-controlled trial. Behavior Therapy, 51(6), 984-996.https://doi.org/10.1016/j.beth.2020.01.005

Ketterer, M. W., Denollet, J., Chapp, J., Keteyian, S., Farha, A. J., Clark, V., Hudson, M., Hakim, A., Greenbaum, A., Schairer, J., & Cao, J. J. (2004). Familial transmissability of early age at initial diagnosis in coronary heart disease (chd): males only, and mediated by psychosocial/emotional distress? Journal of Behavioral Medicine, 27(1), 1-10. https://doi.org/10.1023/B:JOBM.0000013640.69802.fa

Kim S, Parks CG, Xu Z, Carswell G, DeRoo LA, Sandler DP, Taylor JA. Association between genetic variants in DNA and histone methylation and telomere length. PLoS One. 2012;7(7):e40504.https://doi.org/10.1371/journal.pone.0040504

Kim, M., Xu, L., & Blackburn, E. H. (2003). Catalytically active human telomerase mutants with allele-specific biological properties. Exp Cell Res, 288(2), 277-287.https://doi.org/10.1016/S0014-4827(03)00217-9

Kimura, M., Hjelmborg, J. V. B., Gardner, J. P., Bathum, L., Brimacombe, M., Lu, X., & Christensen, K. (2008). Telomere length and mortality: a study of leukocytes in elderly Danish twins. American journal of epidemiology, 167(7), 799-806.https://doi.org/10.1093/aje/kwm380

King, A. C., Taylor, C. B., Albright, C. A., & Haskell, W. L. (1990). The relationship between repressive and defensive coping styles and blood pressure responses in healthy, middle-aged men and women. J Psychosom Res, 34(4), 461-471.

https://doi.org/10.1016/0022-3999(90)90070-K

Klabbers, G., Bosma, H., van den Akker, M., Kempen, G. I. J. M., & van Eijk, J. T. M. (2013). Cognitive hostility predicts all-cause mortality irrespective of behavioural risk at late middle and older age. The European Journal of Public Health, 23(4), 701-705.https://doi.org/10.1093/eurpub/cks060

Kriegbaum, M., Lund, R., Schmidt, L., Rod, N. H., & Christensen, U. (2019). The joint effect of unemployment and cynical hostility on all-cause mortality: results from a prospective cohort study. BMC public health, 19(1), 1-8.https://doi.org/10.1186/s12889-019-6622-7

Kring, A. M., & Gordon, A. H. (1998). Sex differences in emotion: expression, experience, and physiology. Journal of personality and social psychology, 74(3), 686.https://doi.org/10.1037/0022-3514.74.3.686

Kroenke, C. H., Pletcher, M. J., Lin, J., Blackburn, E., Adler, N., Matthews, K., & Epel, E. (2012). Telomerase, telomere length, and coronary artery calcium in black and white men in the CARDIA study. Atherosclerosis, 220(2), 506-512. doi: 10.1016/j.atherosclerosis.2011.10.041.https://doi.org/10.1016/j.atherosclerosis.2011.10.041

Kuznetsova, T., Codd, V., Brouilette, S., Thijs, L., González, A., Jin, Y., & Samani, N. J. (2010). Association between left ventricular mass and telomere length in a population study. American journal of epidemiology, 172(4), 440-450.https://doi.org/10.1093/aje/kwq142

Lahera, G., Herrera, S., Reinares, M., Benito, A., Rullas, M., González-Cases, J., & Vieta, E. (2015). Hostile attributions in bipolar disorder and schizophrenia contribute to poor social functioning. Acta Psychiatrica Scandinavica, 131(6), 472-482.https://doi.org/10.1111/acps.12399

Lan, Q., Cawthon, R., Gao, Y., Hu, W., Hosgood III, H. D., Barone-Adesi, F., & Rothman, N. (2013). Longer telomere length in peripheral white blood cells is associated with risk of lung cancer and the rs2736100 (CLPTM1L-TERT) polymorphism in a prospective cohort study among women in China. PloS one, 8(3), e59230.https://doi.org/10.1371/journal.pone.0059230

Lange, A., Pahlich, A., Sarucco, M., Smits, G., Dehghani, B., & Hanewald, G. (1995). Psychometric characteristics and validity of the Dutch adaptation of the Buss-Durkee Hostility Inventory (the BDHI-D). Behaviour research and therapy, 33(2), 223-227.https://doi.org/10.1016/0005-7967(94)00043-J

Lavie, C. J., & Milani, R. V. (2005). Prevalence of hostility in young coronary artery disease patients and effects of cardiac rehabilitation and exercise training. Mayo Clin Proc, 80(3), 335-342. https://doi.org/10.4065/80.3.335

Lavretsky, H., Epel, E. S., Siddarth, P., Nazarian, N., Cyr, N. S., Khalsa, D. S., & Irwin, M. R. (2013). A pilot study of yogic meditation for family dementia caregivers with depressive symptoms: effects on mental health, cognition, and telomerase activity. International journal of geriatric psychiatry, 28(1), 57-65.https://doi.org/10.1002/gps.3790

Lazarus, R. S., & Folkman, S. (1984). Stress, appraisal, and coping. Springer publishing company.

Lemche, A. V., Chaban, O. S., & Lemche, E. (2014). Aggressivity and hostility traits affect different cardiovascular risk profiles in the metabolic syndrome. International journal of cardiology, 171(3), e76-e77.https://doi.org/10.1016/j.ijcard.2013.11.101

Lemogne, C., Consoli, S. M., Geoffroy-Perez, B., Coeuret-Pellicer, M., Nabi, H., Melchior, M., Limosin, F., Zins, M., Ducimetière, P., Goldberg, M., & Cordier, S. (2013). Personality and the risk of cancer: a 16-year follow-up study of the GAZEL cohort. Psychosomatic medicine, 75(3), 262-271. https://doi.org/10.1097/PSY.0b013e31828b5366

Lemogne, C., Consoli, S. M., Geoffroy-Perez, B., Coeuret-Pellicer, M., Nabi, H., Melchior, M., Limosin, F., Zins, M., Ducimetière, P., Goldberg, M., & Cordier, S. (2013). Personality and the risk of cancer: a 16-year follow-up study of the GAZEL cohort. Psychosomatic medicine, 75(3), 262-271. https://doi.org/10.1097/PSY.0b013e31828b5366

Lengacher, C. A., Reich, R. R., Kip, K. E., Barta, M., Ramesar, S., Paterson, C. L., . . . Park, J. Y. (2014). Influence of mindfulness-based stress reduction (MBSR) on telomerase activity in women with breast cancer (BC). Biol Res Nurs, 16(4), 438-447. https://doi.org/10.1177/1099800413519495

Leplege, A., & Hunt, S. (1997). The problem of quality of life in medicine. Jama, 278(1), 47-50.https://doi.org/10.1001/jama.278.1.47

Levesque, K., Bureau, S., Moskowitz, D. S., Tardif, J. C., Lavoie, J., Dupuis, G., & D'Antono, B. (2009). Defensiveness and metabolic syndrome: impact of sex and age. Biol Psychol, 80(3), 354-360. https://doi.org/10.1016/j.biopsycho.2008.12.003

Levesque, K., Moskowitz, D. S., Tardif, J. C., Dupuis, G., & D'Antono, B. (2010). Physiological stress responses in defensive individuals: age and sex matter. Psychophysiology, 47(2), 332-341. https://doi.org/10.1111/j.1469-8986.2009.00943.x

Levine, G. N., Cohen, B. E., Commodore-Mensah, Y., Fleury, J., Huffman, J. C., Khalid, U., & American Heart Association Council on Clinical Cardiology; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; and Council on Lifestyle and Cardiometabolic Health. (2021). Psychological health, well-being, and the mind-heart-body connection: a scientific statement from the American Heart Association. Circulation, 143(10), e763-e783.https://doi.org/10.1161/CIR.0000000000000947

Liguori, I., Russo, G., Curcio, F., Bulli, G., Aran, L., Della-Morte, D., & Abete, P. (2018). Oxidative stress, aging, and diseases. Clinical interventions in aging, 13, 757.https://doi.org/10.2147/CIA.S158513

Lin, I. M., Weng, C. Y., Lin, T. K., & Lin, C. L. (2015). The relationship between expressive/suppressive hostility behavior and cardiac autonomic activations in patients with coronary artery disease. Acta Cardiologica Sinica, 31(4), 308. https://doi.org/10.1016/j.brat.2015.05.001

Lin, I.M, Fan, S.Y., Lu, H.C, Lin, T.H., Chu, C.S., Kuo, H.F, Lu, Y.H.(2015). Randomized controlled trial of heart rate variability biofeedback in cardiac autonomic and hostility among patients with coronary artery disease. Behav Res Ther,70:38-46.https://doi.org/10.1016/j.brat.2015.05.001

Lin, J., Cheon, J., Brown, R., Coccia, M., Puterman, E., Aschbacher, K., & Blackburn, E. H. (2016). Systematic and cell type-specific telomere length changes in subsets of lymphocytes. Journal of immunology research, 2016.https://doi.org/10.1155/2016/5371050

Lin, P. Y., Huang, Y. C., & Hung, C. F. (2016). Shortened telomere length in patients with depression: a meta-analytic study. Journal of psychiatric research, 76, 84-93.https://doi.org/10.1016/j.jpsychires.2016.01.015

Lin, Y., Damjanovic, A., Metter, E. J., Nguyen, H., Truong, T., Najarro, K., & Weng, N. P. (2015). Age-associated telomere attrition of lymphocytes in vivo is co-ordinated with changes in telomerase activity, composition of lymphocyte subsets and health conditions. Clinical science, 128(6), 367-377.https://doi.org/10.1042/CS20140481

Lloyd, A., White, R., Eames, C., & Crane, R. (2018). The utility of home-practice in mindfulness-based group interventions: a systematic review. Mindfulness, 9(3), 673-692.https://doi.org/10.1007/s12671-017-0813-z

Luecken, L. J., & Roubinov, D. S. (2012). Hostile behavior links negative childhood family relationships to heart rate reactivity and recovery in young adulthood. International journal of psychophysiology, 84(2), 172-179.https://doi.org/10.1016/j.ijpsycho.2012.02.003

MacCoon, D. G., Imel, Z. E., Rosenkranz, M. A., Sheftel, J. G., Weng, H. Y., Sullivan, J. C., & Lutz, A. (2012). The validation of an active control intervention for Mindfulness Based Stress Reduction (MBSR). Behaviour research and therapy, 50(1), 3-12.https://doi.org/10.1016/j.brat.2011.10.011

Mann, S. J., & James, G. D. (1998). Defensiveness and essential hypertension. Journal of psychosomatic research, 45(2), 139-148.https://doi.org/10.1016/S0022-3999(97)00293-6

Markovitz, J. H., Matthews, K. A., Kiss, J., & Smitherman, T. C. (1996). Effects of hostility on platelet reactivity to psychological stress in coronary heart disease patients and in healthy controls. Psychosomatic Medicine, 58(2), 143-149.https://doi.org/10.1097/00006842-199603000-00008

Marois, D., & Dupuis, G. (2006). Comparaison de la qualité de vie globale entre plusieurs groupes de sujets affectés par différents troubles de santé ainsi qu'avec des sujets en santé. Retrieved May, 2006, from Université du Québec à Montréalhttp://www.psycho.uqam.ca/NUND/d_fichiers_etud/Theses_honneurs/Marois_2006.pdf

Martens, D. S., Van Der Stukken, C., Derom, C., Thiery, E., Bijnens, E. M., & Nawrot, T. S. (2021). Newborn telomere length predicts later life telomere length: Tracking telomere length from birth to child-and adulthood. EBioMedicine, 63, 103164.https://doi.org/10.1016/j.ebiom.2020.103164

Martin, M. J., Sturge-Apple, M. L., Davies, P. T., & Gutierrez, G. (2019). Attachment behavior and hostility as explanatory factors linking parent-adolescent conflict and adolescent adjustment. Journal of Family Psychology, 33(5), 586.https://doi.org/10.1037/fam0000529

Mathes, B. M., Quick, A. D., Albanese, B. J., Morabito, D. M., Bedford, C. E., & Schmidt, N. B. (2020). Hostility and Suicide Risk Among Veterans: The Mediating Role of Perceived Burdensomeness. Cognitive Therapy & Research, 44(3).https://doi.org/10.1007/s10608-020-10082-8

Matsubara, Y., Murata, M., Watanabe, K., Saito, I., Miyaki, K., Omae, K., Ishikawa, M., Matsushita, K., Iwanaga, S., Ogawa, S., & Ikeda, Y. (2006). Coronary artery disease and a functional polymorphism of htert. Biochemical and Biophysical Research Communications, 348(2), 669-672.https://doi.org/10.1016/j.bbrc.2006.07.103https://doi.org/10.1016/j.bbrc.2006.07.103

Mayer, S., Brüderlein, S., Perner, S., Waibel, I., Holdenried, A., Ciloglu, N., & Möller, P. (2006). Sex-specific telomere length profiles and age-dependent erosion dynamics of individual chromosome arms in humans. Cytogenetic and genome research, 112(3-4), 194-201.https://doi.org/10.1159/000089870

McCrae, R. R., & Costa, P. T. (2003). Personality in adulthood: A five-factor theory perspective. Guilford Press. p. 20. https://doi.org/10.4324/9780203428412

McEwen, B. S. (1998). Stress, adaptation, and disease: Allostasis and allostatic load. Annals of the New York academy of sciences, 840(1), 33-44.https://doi.org/10.1111/j.1749-6632.1998.tb09546.x

McEwen, B. S., & Stellar, E. (1993). Stress and the individual: Mechanisms leading to disease. Archives of internal medicine, 153(18), 2093-2101.https://doi.org/10.1001/archinte.153.18.2093

McEwen, B. S., & Seeman, T. (1999). Protective and damaging effects of mediators of stress. elaborating and testing the concepts of allostasis and allostatic load. Annals of the New York Academy of Sciences, 896, 30-47.https://doi.org/10.1111/j.1749-6632.1999.tb08103.x

Mezulis, A. H., Abramson, L. Y., & Hyde, J. S. (2002). Domain specificity of gender differences in rumination. Journal of Cognitive Psychotherapy, 16(4), 421-434.https://doi.org/10.1891/jcop.16.4.421.52524

Miller, T. Q., Jenkins, C. D., Kaplan, G. A., & Salonen, J. T. (1995). Are All Hostility Scales Alike? Factor Structure and Covariation Among Measures of Hostility 1. Journal of Applied Social Psychology, 25(13), 1142-1168.https://doi.org/10.1111/j.1559-1816.1995.tb02611.x

Miller, T. Q., Smith, T. W., Turner, C. W., Guijarro, M. L., & Hallet, A. J. (1996). A meta-analytic review of research on hostility and physical health. Psychol Bull, 119(2), 322-348.https://doi.org/10.1037/0033-2909.119.2.322

Mollica L, Fleury I, Belisle C, Provost S, Roy DC, Busque L. No association between telomere length and blood cell counts in elderly individuals. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences. 2009;64(9):965-7.https://doi.org/10.1093/gerona/glp065

Mols, F., Martens, E. J., & Denollet, J. (2010). Type D personality and depressive symptoms are independent predictors of impaired health status following acute myocardial infarction. Heart, 96(1), 30-35.https://doi.org/10.1136/hrt.2009.170357

Moreira, H., & Maia, B. R. (2021). Self-critical rumination as a mediator between attachment orientations and perceived stress: Evidence from a cross-cultural validation of the self-critical rumination scale. Current Psychology, 40(3), 1071-1082.https://doi.org/10.1007/s12144-018-0025-2

Moulton-Perkins, A., Moulton, D., Cavanagh, K., Jozavi, A., & Strauss, C. (2020). Systematic review of mindfulness-based cognitive therapy and mindfulness-based stress reduction via group videoconferencing: Feasibility, acceptability, safety, and efficacy. Journal of Psychotherapy Integration.https://doi.org/10.1037/int0000216

Movius, H. L., & Allen, J. J. B. (2005). Cardiac vagal tone, defensiveness, and motivational style. Biological Psychology, 68(2), 147-162. https://doi.org/10.1016/j.biopsycho.2004.03.019

Muezzinler, A., Zaineddin, A. K., & Brenner, H. (2013). A systematic review of leukocyte telomere length and age in adults. Ageing Res Rev, 12(2), 509-519. https://doi.org/10.1016/j.arr.2013.01.003

Mund, M., & Mitte, K. (2012). The costs of repression: A meta-analysis on the relation between repressive coping and somatic diseases. Health psychology, 31(5), 640.https://doi.org/10.1037/a0026257

Myers, L. B. (2010). The importance of the repressive coping style: findings from 30 years of research. Anxiety, Stress & Coping, 23(1), 3-17.https://doi.org/10.1080/10615800903366945

Myers, L. B., & Reynolds, D. (2000). How optimistic are repressors? The relationship between repressive coping, controllability, self-esteem and comparative optimism for health-related events. Psychology and Health, 15(5), 677-687. https://doi.org/10.1080/08870440008405479

Myers, L. B., Burns, J. W., Derakshan, N., Elfant, E., Eysenck, M. W., & Phipps, S. (2008). Current issues in repressive coping and health. In Emotion regulation (pp. 69-86). Springer, Boston, MA.10.1016/j.nrl.2015.07.014. https://doi.org/10.1007/978-0-387-29986-0_5

Myrtek, M. (2001). Meta-analyses of prospective studies on coronary heart disease, type A personality, and hostility. Int J Cardiol, 79(2-3), 245-251.https://doi.org/10.1016/S0167-5273(01)00441-7

Narducci, M. L., Grasselli, A., Biasucci, L. M., Farsetti, A., Mulè, A., Liuzzo, G., & Crea, F. (2007). High telomerase activity in neutrophils from unstable coronary plaques. Journal of the American College of Cardiology, 50(25), 2369-2374.https://doi.org/10.1016/j.jacc.2007.08.048

Needham, B. L., Diez, R. A. V., Bird, C. E., Bradley, R., Fitzpatrick, A. L., Jacobs, D. R., Ouyang, P., Seeman, T. E., Thurston, R. C., Vaidya, D., & Wang, S. (2014). A test of biological and behavioral explanations for gender differences in telomere length: the multi-ethnic study of atherosclerosis. Biodemography and Social Biology, 60(2), 156-73.https://doi.org/10.1080/19485565.2014.947471

Niaura, R., Herbert, P. N., McMahon, N., & Sommerville, L. (1992). Repressive coping and blood lipids in men and women. Psychosomatic Medicine.https://doi.org/10.1097/00006842-199211000-00010

Niaura, R., Todaro, J. F., Stroud, L., Spiro, A. I. I. I., Ward, K. D., & Weiss, S. (2002). Hostility, the metabolic syndrome, and incident coronary heart disease. Health Psychology, 21(6), 588-593. https://doi.org/10.1037/0278-6133.21.6.588

Nidich, S. I., Rainforth, M. V., Haaga, D. A., Hagelin, J., Salerno, J. W., Travis, F., & Schneider, R. H. (2009). A randomized controlled trial on effects of the Transcendental Meditation program on blood pressure, psychological distress, and coping in young adults. American journal of hypertension, 22(12), 1326-1331.https://doi.org/10.1038/ajh.2009.184

Nolen-Hoeksema, S., & Corte, C. (2004). Gender and self-regulation. Handbook of self-regulation, 411-421.

Nyklicek, I., Vingerhoets, A. J., Van Heck, G. L., & Van Limpt, M. C. (1998). Defensive coping in relation to casual blood pressure and self-reported daily hassles and life events. J Behav Med, 21(2), 145-161.https://doi.org/10.1023/A:1018775807593

O'Donovan, A., Lin, J., Tillie, J., Dhabhar, F. S., Wolkowitz, O. M., Blackburn, E. H., & Epel, E. S. (2009). Pessimism correlates with leukocyte telomere shortness and elevated interleukin-6 in post-menopausal women. Brain Behav Immun, 23(4), 446-449. https://doi.org/10.1016/j.bbi.2008.11.006

Oh H, Wang SC, Prahash A, Sano M, Moravec CS, Taffet GE, et al. Telomere attrition and Chk2activation in human heart failure. Proc Natl Acad Sci U S A. 2003; 100:5378-5383.https://doi.org/10.1073/pnas.0836098100

Okuda, K., Bardeguez, A., Gardner, J. P., Rodriguez, P., Ganesh, V., Kimura, M., & Aviv, A. (2002). Telomere length in the newborn. Pediatric research, 52(3), 377-381.https://doi.org/10.1203/00006450-200209000-00012

Olivo, E. L., Dodson-Lavelle, B., Wren, A., Fang, Y., & Oz, M. C. (2009). Feasibility and effectiveness of a brief meditation-based stress management intervention for patients diagnosed with or at risk for coronary heart disease: a pilot study. Psychology, health & medicine, 14(5), 513-523.https://doi.org/10.1080/13548500902890087

Olson, M. B., Krantz, D. S., Kelsey, S. F., Pepine, C. J., Sopko, G., Handberg, E., & WISE Study Group. (2005). Hostility scores are associated with increased risk of cardiovascular events in women undergoing coronary angiography: a report from the NHLBI-Sponsored WISE Study. Psychosomatic Medicine, 67(4), 546-552.https://doi.org/10.1097/01.psy.0000170830.99263.4e

Orgeta, V. (2009). Specificity of age differences in emotion regulation. Aging and Mental Health, 13(6), 818-826.https://doi.org/10.1080/13607860902989661

Ornish, D., Lin, J., Chan, J. M., Epel, E., Kemp, C., Weidner, G., . . . Blackburn, E. H. (2013). Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study. Lancet Oncol, 14(11), 1112-1120. https://doi.org/10.1016/S1470-2045(13)70366-8

Ornish, D., Lin, J., Daubenmier, J., Weidner, G., Epel, E., Kemp, C., . . . Blackburn, E. H. (2008). Increased telomerase activity and comprehensive lifestyle changes: a pilot study. Lancet Oncol, 9(11), 1048-1057. https://doi.org/10.1016/S1470-2045(08)70234-1

Park, G., Yaden, D. B., Schwartz, H. A., Kern, M. L., Eichstaedt, J. C., Kosinski, M., & Seligman, M. E. (2016). Women are warmer but no less assertive than men: Gender and language on Facebook. PloS one, 11(5), e0155885.https://doi.org/10.1371/journal.pone.0155885

Paulhus, D. L. (1984). Two-component models of socially desirable responding. Journal of personality and social psychology, 46(3), 598.https://doi.org/10.1037/0022-3514.46.3.598

Paulhus, D. L. (1988). Assessing self-deception and impression management in self-reports: The Balanced Inventory of Desirable Responding. Unpublished manuscript, University of British Columbia.

Perinelli, E., & Gremigni, P. (2016). Use of social desirability scales in clinical psychology: A systematic review. Journal of clinical psychology, 72(6), 534-551.https://doi.org/10.1002/jclp.22284

Peters, B. J., Reis, H. T., & Jamieson, J. P. (2018). Cardiovascular indexes of threat impair responsiveness in situations of conflicting interests. International Journal of Psychophysiology, 123, 1-7.https://doi.org/10.1016/j.ijpsycho.2017.12.005

Picard, M., Juster, R. P., & McEwen, B. S. (2014). Mitochondrial allostatic load puts the'gluc'back in glucocorticoids. Nature Reviews Endocrinology, 10(5), 303-310.https://doi.org/10.1038/nrendo.2014.22

Pomatto, L. C., & Davies, K. J. (2017). The role of declining adaptive homeostasis in ageing. The Journal of physiology, 595(24), 7275-7309.https://doi.org/10.1113/JP275072

Pompili, M., Iliceto, P., Luciano, D., Innamorati, M., Serafini, G., Del Casale, A., & Lester, D. (2011). Higher hopelessness and suicide risk predict lower self-deception among psychiatric patients and non-clinical individuals. Rivista di psichiatria, 46(1), 24-30.

Pragodpol, P., & Ryan, C. (2013). Critical review of factors predicting health-related quality of life in newly diagnosed coronary artery disease patients. J Cardiovasc Nurs, 28(3), 277-284. https://doi.org/10.1097/JCN.0b013e31824af56e

Rafanelli, C., Gostoli, S., Tully, P. J., & Roncuzzi, R. (2016). Hostility and the clinical course of outpatients with congestive heart failure. Psychol Health, 1-11. https://doi.org/10.1080/08870446.2015.1095299

Randal, C., Pratt, D., & Bucci, S. (2015). Mindfulness and self-esteem: a systematic review. Mindfulness, 6(6), 1366-1378.https://doi.org/10.1007/s12671-015-0407-6

Ranjit N, Diez-Roux A V, Shea S, Cushman M, Seeman T, Jackson SA, et al. Psychosocial factors and inflammation in the multi-ethnic study of atherosclerosis. Arch Intern Med. 2007;167: 174-181. https://doi.org/10.1001/archinte.167.2.174

Rentoukas, E., Tsarouhas, K., Kaplanis, I., Korou, E., Nikolaou, M., Marathonitis, G., Kokkinou, S., Haliassos, A., Mamalaki, A., Kouretas, D., & Tsitsimpikou, C. (2012). Connection between telomerase activity in pbmc and markers of inflammation and endothelial dysfunction in patients with metabolic syndrome. Plos One, 7(4), 35739.https://doi.org/10.1371/journal.pone.0035739

Révész, D., Verhoeven, J. E., Milaneschi, Y., de Geus, E. J., Wolkowitz, O. M., & Penninx, B. W. (2014). Dysregulated physiological stress systems and accelerated cellular aging. Neurobiology of aging, 35(6), 1422-1430.https://doi.org/10.1016/j.neurobiolaging.2013.12.027

Reynolds, W. M. (1982). Development of reliable and valid short forms of the Marlowe-Crowne Social Desirability Scale. Journal of clinical psychology, 38(1), 119-125.https://doi.org/10.1002/1097-4679(198201)38:1<119::AID-JCLP2270380118>3.0.CO;2-

Ridout, K. K., Levandowski, M., Ridout, S. J., Gantz, L., Goonan, K., Palermo, D., & Tyrka, A. R. (2018). Early life adversity and telomere length: a meta-analysis. Molecular psychiatry, 23(4), 858-871.https://doi.org/10.1038/mp.2017.26

Ridout, K. K., Ridout, S. J., Price, L. H., Sen, S., & Tyrka, A. R. (2016). Depression and telomere length: A meta-analysis. Journal of affective disorders, 191, 237-247.https://doi.org/10.1016/j.jad.2015.11.052

Roberts, B. W., & Mroczek, D. (2008). Personality trait change in adulthood. *Current directions in psychological science*, *17*(1), 31-35.https://doi.org/10.1111/j.1467-8721.2008.00543.x

Roberts, B. W., Walton, K. E., & Viechtbauer, W. (2006). Patterns of mean-level change in personality traits across the life course: a meta-analysis of longitudinal studies. Psychological bulletin, 132(1), 1.https://doi.org/10.1037/0033-2909.132.1.1

Robins, C. J., Keng, S. L., Ekblad, A. G., & Brantley, J. G. (2012). Effects of mindfulness-based stress reduction on emotional experience and expression: a randomized controlled trial. J Clin Psychol, 68(1), 117-131.https://doi.org/10.1002/jclp.20857

Rosenkranz, M. A., Davidson, R. J., MacCoon, D. G., Sheridan, J. F., Kalin, N. H., & Lutz, A. (2013). A comparison of mindfulness-based stress reduction and an active control in modulation of neurogenic inflammation. Brain, behavior, and immunity, 27, 174-184.https://doi.org/10.1016/j.bbi.2012.10.013

Rosenthal, R. (1979). The file drawer problem and tolerance for null results. Psychological bulletin, 86(3), 638.https://doi.org/10.1037/0033-2909.86.3.638

Rutledge, T., & Linden, W. (2000). Defensiveness status predicts 3-year incidence of hypertension. J Hypertens, 18(2), 153-159.https://doi.org/10.1097/00004872-200018020-00004

Sadahiro, R., Suzuki, A., Enokido, M., Matsumoto, Y., Shibuya, N., Kamata, M., . . . Otani, K. (2015). Relationship between leukocyte telomere length and personality traits in healthy subjects. Eur Psychiatry, 30(2), 291-295.https://doi.org/10.1016/j.eurpsy.2014.03.003

Sahoo, S., Padhy, S. K., Padhee, B., Singla, N., & Sarkar, S. (2018). Role of personality in cardiovascular diseases: An issue that needs to be focused too!. Indian heart journal, 70, S471-S477. https://doi.org/10.1016/j.ihj.2018.11.003

Samuelson, M., Carmody, J., Kabat-Zinn, J., & Bratt, M. A. (2007). Mindfulness-based stress reduction in Massachusetts correctional facilities. The Prison Journal, 87(2), 254-268.https://doi.org/10.1177/0032885507303753

Savolainen K., Eriksson J.G., Kajantie E., Pesonen A.K., Räikkönen K.(2015). Associations between the five-factor model of personality and leukocyte telomere length in elderly men and women: The Helsinki Birth Cohort Study (HBCS). J Psychosom Res.79(3):233-8.https://doi.org/10.1016/j.jpsychores.2015.04.011

Schmitt, D. P., Long, A. E., McPhearson, A., O'Brien, K., Remmert, B., & Shah, S. H. (2017). Personality and gender differences in global perspective. International Journal of Psychology, 52, 45-56.https://doi.org/10.1002/ijop.12265

Schneider, R. H., Grim, C. E., Rainforth, M. V., Kotchen, T., Nidich, S. I., Gaylord-King, C., & Alexander, C. N. (2012). Stress reduction in the secondary prevention of cardiovascular disease: randomized, controlled trial of transcendental meditation and health education in Blacks. Circulation: Cardiovascular Quality and Outcomes, 5(6), 750-758.https://doi.org/10.1161/CIRCOUTCOMES.112.967406

Schoormans, D., Verhoeven, J. E., Denollet, J., van de Poll-Franse, L., & Penninx, B. W. J. H. (2018). Leukocyte telomere length and personality: associations with the Big Five and Type D personality traits. Psychological medicine, 48(6), 1008-1019.https://doi.org/10.1017/S0033291717002471

Schutte, N. S., & Malouff, J. M. (2014). A meta-analytic review of the effects of mindfulness meditation on telomerase activity. Psychoneuroendocrinology, 42, 45-48. https://doi.org/10.1016/j.psyneuen.2013.12.017

Schutte, N. S., & Malouff, J. M. (2016). The relationship between perceived stress and telomere length: A meta-analysis. Stress and health, 32(4), 313-319.https://doi.org/10.1002/smi.2607

Schutte, N. S., Malouff, J. M., & Keng, S. L. (2020). Meditation and telomere length: a meta-analysis. Psychology & health, 35(8), 901-915.https://doi.org/10.1080/08870446.2019.1707827

Schutte, N. S., Palanisamy, S. K., & McFarlane, J. R. (2016). The relationship between positive psychological characteristics and longer telomeres. Psychology & Health, 31(12), 1466-1480.https://doi.org/10.1080/08870446.2016.1226308

Shapiro, D., Goldstein, I. B., & Jamner, L. D. (1995). Effects of anger/hostility, defensiveness, gender, and family history of hypertension on cardiovascular reactivity. Psychophysiology, 32(5), 425-435.https://doi.org/10.1111/j.1469-8986.1995.tb02093.x

Shapiro, S. L., Carlson, L. E., Astin, J. A., & Freedman, B. (2006). Mechanisms of mindfulness. Journal of clinical psychology, 62(3), 373-386.https://doi.org/10.1002/jclp.20237

Shaw, R. E., Cohen, F., Doyle, B., & Palesky, J. (1985). The impact of denial and repressive style on information gain and rehabilitation outcomes in myocardial infarction patients. Psychosomatic medicine.https://doi.org/10.1097/00006842-198505000-00004

Shay, J. W., & Wright, W. E. (2011). Role of telomeres and telomerase in cancer. In Seminars in cancer biology (Vol. 21, No. 6, pp. 349-353). Academic Press.https://doi.org/10.1016/j.semcancer.2011.10.001

Shekelle, R. B., Gale, M., Ostfeld, A. M., & Paul, O. (1983). Hostility, risk of coronary heart disease, and mortality. Psychosom Med, 45(2), 109-114.https://doi.org/10.1097/00006842-198305000-00003

Shekelle, R. B., Gale, M., Ostfeld, A. M., & Paul, O. (1983). Hostility, risk of coronary heart disease, and mortality. Psychosomatic Medicine, 45(2), 109-114.https://doi.org/10.1097/00006842-198305000-00003

Shimbo, D., Chaplin, W., Wasson, L. T., & Burg, M. M. (2009). Hostility and platelet reactivity in individuals without a history of cardiovascular disease events. Psychosomatic medicine, 71(7), 741.https://doi.org/10.1097/PSY.0b013e3181ad18b6

Shimbo, D., Chaplin, W., Wasson, L. T., & Burg, M. M. (2009). Hostility and platelet reactivity in individuals without a history of cardiovascular disease events. Psychosomatic medicine, 71(7), 741.https://doi.org/10.1097/PSY.0b013e3181ad18b6

Shoval-Zuckerman, Y. (2015). The effectiveness of early group intervention for military reserves soldiers: the role of the repressive coping style. Israel Journal of Psychiatry, 52(3), 49

Sibinga, E. M., Kerrigan, D., Stewart, M., Johnson, K., Magyari, T., & Ellen, J. M. (2011). Mindfulness-based stress reduction for urban youth. The Journal of Alternative and Complementary Medicine, 17(3), 213-218.https://doi.org/10.1089/acm.2009.0605

Siegler, I. C., Peterson, B. L., Barfoot, J. C., & Williams, R. B. (1992). Hostility during late adolescence predicts coronary risk factors at mid-life. American journal of epidemiology, 136(2), 146-154.https://doi.org/10.1093/oxfordjournals.aje.a116481

Simon, N. M., Smoller, J. W., McNamara, K. L., Maser, R. S., Zalta, A. K., Pollack, M. H., Wong, K. K. (2006). Telomere shortening and mood disorders: preliminary support for a chronic stress model of accelerated aging. Biol Psychiatry, 60(5), 432-435. https://doi.org/10.1016/j.biopsych.2006.02.004

Sloan, R. P., Shapiro, P. A., Gorenstein, E. E., Tager, F. A., Monk, C. E., McKinley, P. S., & Bigger Jr, J. T. (2010). Cardiac autonomic control and treatment of hostility: a randomized controlled trial. Psychosomatic medicine, 72(1), 1.https://doi.org/10.1097/PSY.0b013e3181c8a529

Smaardijk, V. R., Lodder, P., Kop, W. J., van Gennep, B., Maas, A. H., & Mommersteeg, P. M. (2019). Sex-and Gender-Stratified Risks of Psychological Factors for Incident Ischemic Heart Disease: Systematic Review and Meta-Analysis. Journal of the American Heart Association, 8(9), e010859.https://doi.org/10.1161/JAHA.118.010859

Smith, B. W. (1994). Chaotic family dynamics. Arch Fam Med, 3(3), 231-238.https://doi.org/10.1001/archfami.3.3.231

Smith, T. W., & Pope, M. K. (1990). Cynical hostility as a health risk: Current status and future directions. *Journal of Social Behavior and Personality*, *5*(1), 77.

Soubelet, A., & Salthouse, T. A. (2011). Influence of social desirability on age differences in self-reports of mood and personality. Journal of personality, 79(4), 741-762.https://doi.org/10.1111/j.1467-6494.2011.00700.x

Spielberger, C. D., Jacobs, G., Russell, S., & Crane, R. S. (1983). Assessment of anger: The state-trait anger scale. Advances in personality assessment, 2, 159-187.

Spielberger, C. D., Krasner, S. S., & Solomon, E. P. (1988). The experience, expression, and control of anger. In Individual differences, stress, and health psychology (pp. 89-108). Springer, New York, NY.https://doi.org/10.1007/978-1-4612-3824-9_5

Starkweather, A. R., Alhaeeri, A. A., Montpetit, A., Brumelle, J., Filler, K., Montpetit, M., Mohanraj, L., Lyon, D. E., & Jackson-Cook, C. K. (2014). An integrative review of factors associated with telomere length and implications for biobehavioral research. Nursing research, 63(1), 36-50. https://doi.org/10.1097/NNR.0000000000000009

Starkweather, A. R., Alhaeeri, A. A., Montpetit, A., Brumelle, J., Filler, K., Montpetit, M., & Jackson-Cook, C. K. (2014). An integrative review of factors associated with telomere length and implications for biobehavioral research. Nursing research, 63(1), 36.https://doi.org/10.1097/NNR.0000000000000009

Starnino, L., Busque, L., Tardif, J. C., & D'Antono, B. (2016). Psychological profiles in the prediction of leukocyte telomere length in healthy individuals. PloS one, 11(10), e0165482.https://doi.org/10.1371/journal.pone.0165482

Starnino, L., Dupuis, G., Busque, L., Bourgoin, V., Dubé, M. P., Busseuil, D., & D'Antono, B. (2021). The associations of hostility and defensiveness with telomere length are influenced by sex and health status. Biology of Sex Differences, 12(1), 1-13.https://doi.org/10.1186/s13293-020-00349-w

Statistics Canada (2019). Population projections : Canada, provinces and territories, 2018 to 2068. Retrieved from https://www150.statcan.gc.ca/n1/daily-quotidien/190917/dq190917b-eng.htm

Stindl, R. (2004). Tying it all together: telomeres, sexual size dimorphism and the gender gap in life expectancy. Medical hypotheses, 62(1), 151-154.https://doi.org/10.1016/S0306-9877(03)00316-5

Strong, D. R., Kahler, C. W., Greene, R. L., & Schinka, J. (2005). Isolating a primary dimension within the Cook-Medley hostility scale: A Rasch analysis. Personality and Individual Differences, 39(1), 21-33.https://doi.org/10.1016/j.paid.2004.08.011

Suarez, E. C., Lewis, J. G., Krishnan, R. R., & Young, K. H. (2004). Enhanced expression of cytokines and chemokines by blood monocytes to in vitro lipopolysaccharide stimulation are associated with hostility and severity of depressive symptoms in healthy women. Psychoneuroendocrinology, 29(9), 1119-1128.https://doi.org/10.1016/j.psyneuen.2004.01.002

Suls, J. (2013). Anger and the heart: perspectives on cardiac risk, mechanisms and interventions. Prog Cardiovasc Dis, 55(6), 538-547.https://doi.org/10.1016/j.pcad.2013.03.002

Sun, B., Wang, Y., Kota, K., Shi, Y., Motlak, S., Makambi, K., & Zheng, Y. L. (2015). Telomere length variation: A potential new telomere biomarker for lung cancer risk. Lung cancer, 88(3), 297-303.https://doi.org/10.1016/j.lungcan.2015.03.011

Surbey, M. K. (2011). Adaptive significance of low levels of self-deception and cooperation in depression. Evolution and Human Behavior, 32(1), 29-40.https://doi.org/10.1016/j.evolhumbehav.2010.08.009

Tabassum, N., & Nayak, B. S. (2021). Gender stereotypes and their impact on women's career progressions from a managerial perspective. IIM Kozhikode Society & Management Review, 2277975220975513.https://doi.org/10.1177/2277975220975513

Tamagawa, R., Speca, M., Stephen, J., Pickering, B., Lawlor-Savage, L., & Carlson, L. E. (2015). Predictors and effects of class attendance and home practice of yoga and meditation among breast cancer survivors in a mindfulness-based cancer recovery (mbcr) program. Mindfulness, 6(5), 1201-121.https://doi.org/10.1007/s12671-014-0381-4

Thabane, L., Hopewell, S., Lancaster, G. A., Bond, C. M., Coleman, C. L., Campbell, M. J., & Eldridge, S. M. (2016). Methods and processes for development of a CONSORT extension for reporting pilot randomized controlled trials. Pilot and feasibility studies, 2(1), 25.https://doi.org/10.1186/s40814-016-0065-z

Thomas, M. C., Kamarck, T. W., Wright, A. G., Matthews, K. A., Muldoon, M. F., & Manuck, S. B. (2020). Hostility Dimensions and Metabolic Syndrome in a Healthy, Midlife Sample. International journal of behavioral medicine, 27(4), 475-480.https://doi.org/10.1007/s12529-020-09855-y

Tian, R., Zhang, L. N., Zhang, T. T., Pang, H. Y., Chen, L. F., Shen, Z. J., & Zhang, S. Y. (2017). Association between oxidative stress and peripheral leukocyte telomere length in patients with premature coronary artery disease. Medical science monitor: international medical journal of experimental and clinical research, 23, 4382.https://doi.org/10.12659/MSM.902106

Tian, Y., Wang, S., Jiao, F., Kong, Q., Liu, C., & Wu, Y. (2019). Telomere length: a potential biomarker for the risk and prognosis of stroke. Frontiers in neurology, 10, 624.https://doi.org/10.3389/fneur.2019.00624

Timkova, V., Nagyova, I., Reijneveld, S. A., Tkacova, R., van Dijk, J. P., & Bültmann, U. (2020). Psychological distress in patients with obstructive sleep apnoea: the role of hostility and coping self-efficacy. Journal of health psychology, 25(13-14), 2244-2259.https://doi.org/10.1177/1359105318792080

Tindle, H. A., Chang, Y.-F., Kuller, L. H., Manson, J. E., Robinson, J. G., Rosal, M. C., Siegle, G. J., & Matthews, K. A. (2009). Optimism, cynical hostility, and incident coronary heart disease and mortality in the women's health initiative. Circulation, 120(8), 656.https://doi.org/10.1161/CIRCULATIONAHA.108.827642

Todaro, J. F., Con, A., Niaura, R., Spiro, A. 3rd, Ward, K. D., & Roytberg, A. (2005). Combined effect of the metabolic syndrome and hostility on the incidence of myocardial infarction (the normative aging study). The American Journal of Cardiology, 96(2), 221-6.https://doi.org/10.1016/j.amjcard.2005.03.049

Tomiyama, A. J., O'Donovan, A., Lin, J., Puterman, E., Lazaro, A., Chan, J.,and Epel, E. (2012). Does cellular aging relate to patterns of allostasis?: An examination of basal and stress reactive HPA axis activity and telomere length. Physiology & behavior, 106(1), 40-45.https://doi.org/10.1016/j.physbeh.2011.11.016

Turiano, Nicholas A., Benjamin P. Chapman, Tara L. Gruenewald, & Daniel K. Mroczek. "Personality and the leading behavioral contributors of mortality." Health Psychology 34, no. 1 (2015): 51.https://doi.org/10.1037/hea0000038

Uziel, L. (2010). Rethinking social desirability scales: From impression management to interpersonally oriented self-control. Perspectives on Psychological Science, 5(3), 243-262.https://doi.org/10.1177/1745691610369465

Vahedian-Azimi, A., & Moayed, M. S. (2019). Updating the meta-analysis of perceived stress and its association with the incidence of coronary heart disease. International Journal of Medical Reviews, 6(4), 146-153.

Vaiserman, A., & Krasnienkov, D. (2021). Telomere length as a marker of biological age: state-of-the-art, open issues, and future perspectives. Frontiers in Genetics, 11, 1816.https://doi.org/10.3389/fgene.2020.630186

Vakonaki, E., Tsiminikaki, K., Plaitis, S., Fragkiadaki, P., Tsoukalas, D., Katsikantami, I., & Tsatsakis, A. M. (2018). Common mental disorders and association with telomere length. Biomedical reports, 8(2), 111-116.https://doi.org/10.3892/br.2018.1040

Van der Kolk, B. A. 1996. *The Body Keeps the Score*. La Vergne: Memories of Ages Press.

Van Lieshout, J. J., Wieling, W., Wesseling, K. H., Endert, E., & Karemaker, J. M. (1990). Orthostatic hypotension caused by sympathectomies performed for hyperhidrosis. The Netherlands journal of medicine, 36(1-2), 53-57.

Van Ockenburg, S. L., De Jonge, P., Van der Harst, P., Ormel, J., & Rosmalen, J. G. M. (2014). Does neuroticism make you old? Prospective associations between neuroticism and leukocyte telomere length. Psychological medicine, 44(4), 723-729.https://doi.org/10.1017/S0033291713001657

Van Teffelen, M. W., Lobbestael, J., Voncken, M. J., & Peeters, F. (2020). Uncovering the hierarchical structure of self-reported hostility. PloS one, 15(9), e0239631.https://doi.org/10.1371/journal.pone.0239631

Vasan, R. S., Demissie, S., Kimura, M., Cupples, L. A., White, C., Gardner, J. P., & Aviv, A. (2009). Association of leukocyte telomere length with echocardiographic left ventricular mass: the Framingham heart study. Circulation, 120(13), 1195-1202.https://doi.org/10.1161/CIRCULATIONAHA.109.853895

Vassar, M., & Hale, W. (2009). Reliability reporting across studies using the Buss Durkee Hostility Inventory. Journal of Interpersonal Violence, 24(1), 20-37.https://doi.org/10.1177/0886260508314931

Vella, E. J., Kamarck, T. W., & Shiffman, S. (2008). Hostility moderates the effects of social support and intimacy on blood pressure in daily social interactions. Health Psychology, 27(2S), S155.https://doi.org/10.1037/0278-6133.27.2(Suppl.).S155

Verhoeven, J. E., van Oppen, P., Révész, D., Wolkowitz, O. M., & Penninx, B. W. (2016). Depressive and anxiety disorders showing robust, but non-dynamic, 6-year longitudinal association with short leukocyte telomere length. American Journal of Psychiatry, 173(6), 617-624.https://doi.org/10.1176/appi.ajp.2015.15070887

Vitori, T. K., Frazier, S. K., Biddle, M. J., Mudd-Martin, G., Pelter, M. M., Dracup, K., & Moser, D. K. (2021). Hostility predicts mortality but not recurrent acute coronary syndrome. European Journal of Cardiovascular Nursing : Journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology, 20(2), 132-137.https://doi.org/10.1177/1474515120950913

Von Der Lippe, A. L., Monsen, J. T., R⊘ nnestad, M. H., & Eilertsen, D. E. (2008). Treatment failure in psychotherapy: The pull of hostility. Psychotherapy Research, 18(4), 420-432.https://doi.org/10.1080/10503300701810793

von Zglinicki, T., Pilger, R., & Sitte, N. (2000). Accumulation of single-strand breaks is the major cause of telomere shortening in human fibroblasts. Free Radic Biol Med, 28(1), 64-74.https://doi.org/10.1016/S0891-5849(99)00207-5

Walton, A. S., & Krum, H. (2005). The Heartpod implantable heart failure therapy system. Heart Lung Circ, 14 Suppl 2, S31-33. doi: 10.1016/j.hlc.2005.09.00.https://doi.org/10.1016/j.hlc.2005.09.003

Wang, R. (2021). Can Hostile Attitudes and Hostile Affections Lead to Depressive Symptoms Under Stress? A Study Based on Racial/Ethnic and Gender Differences. Journal of Racial and Ethnic Health Disparities, 8(2), 394-401.https://doi.org/10.1007/s40615-020-00793-9

Wang, X., Sundquist, K., Hedelius, A., Palmér, K., Memon, A. A., & Sundquist, J. (2017). Leukocyte telomere length and depression, anxiety and stress and adjustment disorders in primary health care patients. *BMC psychiatry*, *17*(1), 1-10.https://doi.org/10.1186/s12888-017-1308-0

Wang, W., Zheng, L., Zhou, N., Li, N., Bulibu, G., Xu, C., & Tang, Y. (2017). Meta-analysis of associations between telomere length and colorectal cancer survival from observational studies. Oncotarget, 8(37), 62500.https://doi.org/10.18632/oncotarget.20055

Wang, Y., Savage, S. A., Alsaggaf, R., Aubert, G., Dagnall, C. L., Spellman, S. R., & Gadalla, S. M. (2018). Telomere length calibration from qPCR measurement: limitations of current method. Cells, 7(11), 183.https://doi.org/10.3390/cells7110183

Wasserman, D., Geijer, T., Sokolowski, M., Rozanov, V., & Wasserman, J. (2007). Genetic variation in the hypothalamic-pituitary-adrenocortical axis regulatory factor, T-box 19, and the angry/hostility personality trait. Genes, brain and behavior, 6(4), 321-328.https://doi.org/10.1111/j.1601-183X.2006.00259.x

Watkins, L. E., Harpaz-Rotem, I., Sippel, L. M., Krystal, J. H., Southwick, S. M., & Pietrzak, R. H. (2016). Hostility and telomere shortening among US military veterans: Results from the National Health and Resilience in Veterans Study. Psychoneuroendocrinology, 74, 251-257.https://doi.org/10.1016/j.psyneuen.2016.09.006

Weinberger, D. A. (1990). The construct validity of the repressive coping style. In J. L. Singer (Ed.), Repression and dissociation: Implications for personality, theory, psychopathology, and health (pp. 337-386). Chicago: University of Chicago Press.

Weischer, M., Bojesen, S. E., Cawthon, R. M., Freiberg, J. J., Tybjaerg-Hansen, A., & Nordestgaard, B. G. (2012). Short telomere length, myocardial infarction, ischemic heart disease, and early death. Arterioscler Thromb Vasc Biol, 32(3), 822-829. https://doi.org/10.1161/ATVBAHA.111.237271

Wells, S. Y., Brennan, C. L., Van Voorhees, E. E., Beckham, J. C., Calhoun, P. S., Clancy, C. P., & Dillon, K. H. (2021). The Impact of Hostility on Quality of Life, Functioning, and Suicidal Ideation Among Male Veterans with Posttraumatic Stress Disorder. Journal of traumatic stress.https://doi.org/10.1002/jts.22691

Westmaas, J. L., & Jamner, L. D. (2006). Paradoxical effects of social support on blood pressure reactivity among defensive individuals. Annals of Behavioral Medicine, 31(3), 238-247.https://doi.org/10.1207/s15324796abm3103_5

Whoqol Group. (1998). Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychological medicine, 28(3), 551-558.https://doi.org/10.1017/S0033291798006667

Willeit P, Willeit J, Mayr A, Weger S, Oberhollenzer F, Brandstatter A, Kronenberg F, Kiechl S. Telomere length and risk of incident cancer and cancer mortality. JAMA. 2010; 304:69-75. https://doi.org/10.1001/jama.2010.897

Willeit, P., Willeit, J., Brandstatter, A., Ehrlenbach, S., Mayr, A., Gasperi, A., . . . Kiechl, S. (2010). Cellular aging reflected by leukocyte telomere length predicts advanced atherosclerosis and cardiovascular disease risk. Arterioscler Thromb Vasc Biol, 30(8), 1649-1656.https://doi.org/10.1161/ATVBAHA.110.205492

Williams, M. M., Rogers, R., Sharf, A. J., & Ross, C. A. (2019). Faking good: An investigation of social desirability and defensiveness in an inpatient sample with personality disorder traits. Journal of personality assessment, 101(3), 253-263.https://doi.org/10.1080/00223891.2018.1455691

Wilson, S. J., Woody, A., Padin, A. C., Lin, J., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2019). Loneliness and telomere length: immune and parasympathetic function in associations with accelerated aging. Annals of Behavioral Medicine, 53(6), 541-550.https://doi.org/10.1093/abm/kay064

Wolkowitz, O. M., Mellon, S. H., Epel, E. S., Lin, J., Dhabhar, F. S., Su, Y., Blackburn, E. H. (2011). Leukocyte telomere length in major depression: correlations with chronicity, inflammation and oxidative stress--preliminary findings. PLoS One, 6(3), e17837. https://doi.org/10.1371/journal.pone.0017837

Wong, J. M., Sin, N. L., & Whooley, M. A. (2014). A comparison of cook-medley hostility subscales and mortality in patients with coronary heart disease: data from the heart and soul study. Psychosomatic Medicine, 76(4), 311-317.https://doi.org/10.1097/PSY.0000000000000059

Wong, J. M., Wong, J. M., Na, B., Regan, M. C., & Whooley, M. A. (2013). Hostility, health behaviors, and risk of recurrent events in patients with stable coronary heart disease: findings from the heart and soul study. Journal of the American Heart Association, Vol 2, Iss 5, E000052-e000052. https://doi.org/10.1161/JAHA.113.000052

World Health Organisation. (2021). Cardiovascular Diseases (CVDs).retrieved from : https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

World Health Organization (1948). The Definition of Health. Retrieved from https://www.who.int/about/governance/constitution

World Health Organization. (2018). Aging and Health. Retrieved from https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

World Health Organization. (2021). Measuring Quality of Life. Retrieved from https://www.who.int/tools/whoqol

Wu, X., Amos, C. I., Zhu, Y., Zhao, H., Grossman, B. H., Shay, J. W., Spitz, M. R. (2003). Telomere dysfunction: a potential cancer predisposition factor. J Natl Cancer Inst, 95(16), 1211-1218.https://doi.org/10.1093/jnci/djg011

Ye, S., Shaffer, J. A., Kang, M. S., Harlapur, M., Muntner, P., Epel, E., & Shimbo, D. (2013). Relation between leukocyte telomere length and incident coronary heart disease events (from the 1995 Canadian Nova Scotia Health Survey). The American journal of cardiology, 111(7), 962-967.https://doi.org/10.1016/j.amjcard.2012.12.017

Young, L. A., Cappola, A. R., & Baime, M. J. (2009). Mindfulness based stress reduction: effect on emotional distress in diabetes. Practical Diabetes International, 26(6), 222-224.https://doi.org/10.1002/pdi.1380

Younge, J. O., Gotink, R. A., Baena, C. P., Roos-Hesselink, J. W., & Hunink, M. M. (2015). Mind-body practices for patients with cardiac disease: a systematic review and meta-analysis. European journal of preventive cardiology, 22(11), 1385-1398.https://doi.org/10.1177/2047487314549927

Zalli, A., Carvalho, L. A., Lin, J., Hamer, M., Erusalimsky, J. D., Blackburn, E. H., & Steptoe, A. (2014). Shorter telomeres with high telomerase activity are associated with raised allostatic load and impoverished psychosocial resources. Proc Natl Acad Sci U S A, 111(12), 4519-4524. https://doi.org/10.1073/pnas.1322145111

Zhan, Y., & Hägg, S. (2019). Telomere length and cardiovascular disease risk. Current opinion in cardiology, 34(3), 270-274.https://doi.org/10.1097/HCO.0000000000000613

Zhang, Q., Zhao, H., & Zheng, Y. (2019). Effectiveness of mindfulness-based stress reduction (MBSR) on symptom variables and health-related quality of life in breast cancer patients-a systematic review and meta-analysis. Supportive Care in Cancer, 27(3), 771-781.https://doi.org/10.1007/s00520-018-4570-x

Zhu, H., Guo, D., Li, K., Pedersen-White, J., Stallmann-Jorgensen, I. S., Huang, Y., & Dong, Y. (2012). Increased telomerase activity and vitamin D supplementation in overweight African Americans. International journal of obesity, 36(6), 805-809.https://doi.org/10.1038/ijo.2011.197