DISSERTATIONES
MEDICINAE
UNIVERSITATIS
TARTUENSIS
344

SIRJE SAMMUL

Prevalence and risk factors of arterial hypertension and cardiovascular mortality: 13-year longitudinal study among 35- and 55-year-old adults in Estonia and Sweden

DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS
344

DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS
344

SIRJE SAMMUL

Prevalence and risk factors of arterial hypertension and cardiovascular mortality: 13-year longitudinal study among 35- and 55-year-old adults in Estonia and Sweden

UNIVERSITY OF TARTU
Press
1632

Institute of Family Medicine and Public Health, University of Tartu, Estonia

Dissertation accepted for the commencementof the degree of Doctor of Philosophy in Medicine on April 19th, 2023 by the Council of the Faculty of Medicine, University of Tartu, Estonia.

Supervisors: Tenured Full Professor Margus Viigimaa, MD, PhD
School of Information Technologies, Department of Health,
Tallinn University of Technology;
Research chief of the Centre of Cardiology,
North Estonia Medical Centre, Tallinn, Estonia

Associate Professor Kersti Pärna, MD, MPH, PhD
Department of Public Health
Institute of Family Medicine and Public Health
University of Tartu, Estonia

Reviewers: Associate Professor Marje Oona, MD, PhD
Department of Family Medicine
Institute of Family Medicine and Public Health
University of Tartu, Estonia

Research Fellow Tiia Ainla, MD, PhD
Department of Cardiology
Institute of Clinical Medicine
University of Tartu, Estonia;
Cardiologist
North Estonia Medical Centre, Tallinn, Estonia

Opponent: Associate Professor in epidemiology Axel C Carlsson, PhD
Department of Neurobiology, Care Sciences and Society
Division of Family Medicine and Primary Care
Karolinska Institute, Solna, Sweden;
Academic Primary Care Center
Region Stockholm, Stockholm, Sweden

Commencement: June 14th, 2023

Publication of this dissertation is granted by the University of Tartu.

ISSN 1024-395X (print)
ISBN 978-9916-27-202-2 (print)

ISSN 2806-240X (pdf)
ISBN 978-9916-27-203-9 (pdf)

University of Tartu Press
www.tyk.ee

I dedicate this doctoral thesis
to the memory of my Mother and Father

CONTENTS

LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following publications, which are referred to in the text by Roman numerals (I–III):

I Sammul, S., Jensen-Urstad, M., Johansson, J., Lenhoff, H., & Viigimaa, M. (2019). Psychosocial factors and personality traits and the prevalence of arterial hypertension among 35- and 55-year-old men and women in Sweden and Estonia: a SWESTONIA longitudinal study. *High Blood Pressure and Cardiovascular Prevention*, *26*, 475–82. https://doi.org/10.1007/s40292-019-00348-y

II Sammul, S., & Viigimaa, M. (2018). Rapid socio-economic changes, psychosocial factors and prevalence of hypertension among men and women aged 55 years at baseline in Estonia: a 13-year follow-up study. *Blood Pressure*, 27, 351–7. https://doi.org/10.1080/08037051.2018.1476054

III Jensen-Urstad, M., Viigimaa, M., Sammul, S., Lenhoff, H., Johansson, J. (2014). Impact of smoking: All-cause and cardiovascular mortality in a cohort of 55-year-old Swedes and Estonians. *Scandinavian Journal of Public Health*, *42*, 780–5. https://doi.org/10.1177/1403494814550177

Contribution of Sirje Sammul (SS) to the original publications:

Paper I: SS drafted the manuscript, performed data analysis, interpreted the results, coordinated cooperation with Swedish co-authors, revised the manuscript and was responsible for the manuscript throughout the peer review process.

Paper II: SS drafted the manuscript, performed data analysis, interpretated the results, revised the manuscript and was responsible for the manuscript throughout the peer review process.

Paper III: SS participated in the drafting and the writing of the manuscript and revised the manuscript.

Paper I, II and III: SS collected data in Estonia, entered data into the database, controlled the quality of data.

ABBREVIATIONS

ACC	American College of Cardiology
AHA	American Heart Association
AH	arterial hypertension
APA	American Psychological Association
BP	blood pressure
BMI	body mass index
CAD	coronary artery disease
CHD	coronary heart disease
CI	confidence interval
cm	centimetre
CRP	C-reactive protein
CVDs	cardiovascular diseases
DALYs	disability-adjusted life years
DBP	diastolic blood pressure
ESC	European Society of Cardiology
ESH	European Society of Hypertension
EST	Estonia
GNI	Gross National Income
HDI	Human Development Index
HDL	high-density lipoprotein
HR	hazard ratio
ICD-10	International Classification of Diseases-10
IHD	ischaemic heart disease
IL-6	interleukin-6
LDL	low-density lipoprotein
OR	odds ratio
RR	risk ratio
SBP	systolic blood pressure
SD	standard deviation
SDR	standardized death rate
SES	socioeconomic status
SHARE	Survey of Health, Ageing and Retirement
SLEs	stressful life events
SWE	Sweden
SWESTONIA	Sweden-Estonia cardiovascular diseases' risk study
TABP	type A behaviour pattern
WHO	World Health Organization

1. INTRODUCTION

Arterial hypertension (AH) is one of the most prevalent pathological conditions, being a crucial risk factor for mortality from cardiovascular diseases (CVDs), particularly from ischaemic heart disease (IHD) (Rapsomaniki et al., 2014). During the last three decades the prevalence of AH as well as mortality from CVDs has decreased in Europe, being higher in Eastern than in Western Europe (Forouzanfar et al., 2017; Roth et al., 2018). In Estonia, age-standardized prevalence of AH among adults aged 30–79 years has decreased from 46.3% in 1993 to 40.3% in 2018 (in Sweden from 38.9% to 30.8%, respectively) (WHO, 2022a). In terms of mortality, in Estonia, the standardized death rate (per 100 000) from diseases of the circulatory system in all ages has decreased from 712 in 1993 to 310 in 2016 (in Sweden from 320 to 151, respectively) (WHO, 2022b).

AH arises from many different, but interrelated etiologies (Oparil et al., 2018). Healthy lifestyle is the key factor for the management of AH, and it has been included in European guidelines of AH since 2003 (Zanchetti, 2003). Additionally, psychosocial factors and personality traits are related to the risk of CVDs (Infurna et al., 2018; Pedersen et al., 2017). From psychosocial factors, negative stressful life events (SLEs) and depressive mood have a positive link for the development of AH (Kivimäki & Steptoe, 2018; Von Känel, 2012). From personality traits, mastery and self-esteem are important key variables, increasing or reducing the harmful effects of psychosocial stress on health (Huang et al., 2017; Nicolaisen et al., 2018).

The association of psychosocial factors and personality traits with the diagnosis of AH has not previously been investigated in Estonia. This study attempts to fill this gap. Moreover, this study gives a unique opportunity to compare data in Estonia and Sweden, in countries with a different historical and political background and socioeconomic situation.

To provide a broader understanding of AH, cardiovascular mortality and its risk factors, a prospective longitudinal study among 35- and 55-year-old cohorts in Estonia and Sweden was designed, with a first wave in 1997 and with a second wave in 2010. From risk factors, the focus was on psychosocial factors, personality traits, lifestyle factors and health indicators.

2. REVIEW OF THE LITERATURE

2.1. Main characteristics of Estonia and Sweden

After a 51-year period of the annexation by the Soviet Union, Estonia became independent in 1991, while Sweden has been politically stable and not engaged in wars for 200 years.

The socioeconomic development of the countries is assessed using the Human Development Index (HDI), a parameter encompassing three dimensions: life expectancy at birth, a decent standard of living (Gross National Income, GNI) and mean years of schooling and the expected years of schooling (education index). The three HDI dimensions are combined into a composite index using geometric means. (UNDP, 2022a)

The life expectancy at birth was 70 years in Estonia and 80 years in Sweden in 1998; 76 and 82, respectively, in 2010; and 78 and 82, respectively in 2018. In Estonia, life expectancy among men increased from 64 in 1998 to 75 in 2018 (among women from 75 to 82, respectively) (Figure 1). In Sweden, life expectancy among men increased from 77 in 1998 to 81 in 2018 (among women from 82 to 84, respectively). (WHO, 2022c)

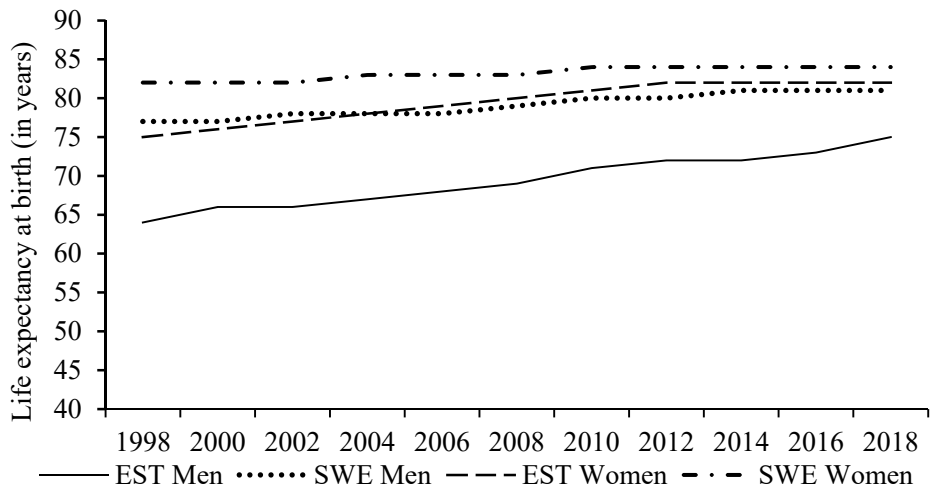


Figure 1. Life expectancy at birth (in years) by gender in Estonia and Sweden, 1998–2018 (WHO, 2022c)

In 1998–2018, GNI increased in Estonia and Sweden being lower in Estonia throughout the period. The difference of GNI between countries was the largest in 2000 (2.4 times) and the smallest in 2018 (1.6 times) (Figure 2). (UNDP, 2022b)

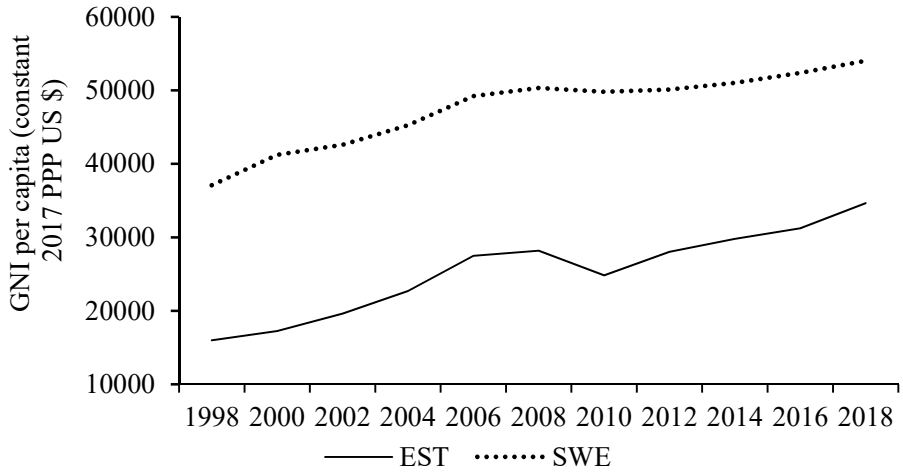


Figure 2. Gross national income (GNI) per capita (constant 2017 PPP in US $) in Estonia and Sweden, 1998–2018 (UNDP, 2022b)

Education index expressed as an index obtained by scaling with the corresponding maxima was 0.77 for Estonia and 0.87 for Sweden in 1998; 0.87 and 0.85, respectively, in 2010; and 0.88 and 0.91, respectively, in 2018. For comparison, education index was 0.74 in 1998 and 0.85 in 2018 in countries of very high human development. (UNDP, 2022c)

All the above indicators (life expectancy at birth, a decent standard of living, and education index) formulate HDI, whereby countries are divided into categories of very high human development (HDI ≥ 0.80), high human development (HDI 0.70–0.79), medium human development (HDI 0.55−0.69) and low human development (HDI≤0.54) (UNDP, 2020). In the World Health Organization (WHO) European Region, average HDI was 0.75 in 1998 and 0.84 in 2018 (WHO, 2022e).

In 1998–2018, HDI was lower in Estonia compared to Sweden: 0.76 and 0.89, respectively, in 1998; 0.85 and 0.90, respectively, in 2010; and 0.89 and 0.94, respectively, in 2018. Thus, in 1998 Estonia belonged to the countries of high human development and Sweden to the countries of very high human development, but since 2006 both belonged to the countries of very high human development. (UNDP, 2022a)

2.2. Arterial hypertension

AH is the strongest modifiable risk factor for development of CVDs. AH has an important role in overall disease burden (expressed as the disability-adjusted life years, DALYs), shortening healthy life expectancy (Forouzanfar et al., 2017; Rapsomaniki et al., 2014), and increasing the risk for cardiovascular mortality (Lozano et al., 2012).

According to pathophysiological processes, CVDs are divided into heart and vascular diseases. Heart diseases are subdivided into coronary heart diseases (CHD) (e.g. angina and myocardial infarction), arrhythmias, heart failure, valvular heart diseases, AH, general atherosclerosis and peripheral artery diseases. CHDs are called also ischaemic heart diseases (IHD) or coronay artery diseases (CAD). (Hammer & McPhee, 2014)

2.2.1. Definition of arterial hypertension

Essential (primary or systemic) AH (henceforth AH only) is known as elevated blood pressure (BP) that has no obvious secondary cause, accounting for 90-95% of all cases of hypertension (Fuster et al., 2017). Among hypertensive individuals, up to 5–10% have elevated BP due to secondary causes (e.g. renovascular disease, aldosteronism, pheochromocytoma, or gene mutations) (Fuster et al., 2017; Rimoldi et al., 2014). According to the International Classification of Diseases, version 2010 (ICD-10), AH is coded as I10, including all grades 1, 2 or 3 (ICD-10, 2010).

According to the guidelines for the management of AH by the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) in 2018, AH is defined as systolic blood pressure (SBP) of ≥140 mmHg and/or diastolic blood pressure (DBP) of ≥90 mmHg. The same classification is used for all ages beginning from the age of 16. BP category is defined according to seated clinic BP. Grade 1 hypertension signifies BP values 140-159 and/or 90-99 mmHg, grade 2 hypertension 160-179 and/or 100-109 mmHg, and grade 3 hypertension ≥180 and/or ≥110 mmHg, respectively (Williams et al., 2018).

Hypertension-mediated organ damage can be structural or functional changes in the arteries or end-organs (e.g. heart, blood vessels, kidney), expressing, e.g. left ventricular hypertrophy, arterial stiffness, atherosclerosis, microalbuminuria, heart failure. These conditions are defined as hypertensive heart disease due to hypertension (a code of diagnosis I11 by ICD-10), at grades 1, 2 or 3 (Piskorz, 2020). The other codes of diagnoses among hypertensive diseases by ICD-10 (excluding secondary hypertension, I15) are hypertensive renal disease (I12), and hypertensive heart and renal disease (I13) (ICD-10, 2010).

When BP levels are clearly above the reference levels recommended by guidelines for management of AH, non-pharmacological (lifestyle intervention) and pharmacological treatment (medications) are indicated, reducing complications due to high BP (Williams et al., 2018).

Comparing European (ESC/ESH) and American (American College of Cardiology, ACC; American Heart Association, AHA) guidelines for management of AH, there are differences of reference values for BP to define AH as measured in an office/clinic. The value of BP ≥140/90 mmHg by ESC/ESH guideline (Williams et al., 2018) and ≥138/80 mmHg by ACC/AHA guideline (Whelton et al., 2018) indicate AH. Comparing the age-specific BP treatment targets for older people (aged ≥65 years), the reference level of BP is from

<130/70 mmHg by ESC/ESH and <130/80 mmHg by ACC/AHA guidelines for management of AH (Bakris et al., 2019).

The current dissertation takes into account ESC/ESH guidelines for management of AH (Mancia et al., 2007; Mancia et al., 2013).

2.2.2. Aetiology of arterial hypertension

AH is a syndrome with a multifactorial aetiology (Oparil et al., 2018), a complex of pathophysiologic, behavioural, environmental, and genetic factors, that influence vascular and renal dysfunction, cardiovascular remodelling, and stimulation of the sympathetic nervous system (Touyz et al., 2020). Cardiovascular remodelling is a response to potentially harmful stimuli (e.g. haemodynamic, inflammatory), being initially an adaptive response. With the persistence of harmful stimuli, the process leads to structural pathogenic changes, e.g. atherosclerosis, vascular dysfunction and myocardial ischaemia (Harvey et al., 2015; Heusch et al., 2014).

The non-modifiable risk factors for the development of AH are gender (Gerdts et al., 2022; Yanes & Reckelhoff, 2011), older age (Hay et al., 2020), and family history of CVDs (genetic predisposition) (Warren et al., 2017). Modifiable risk factors for the development of AH are lifestyle factors (e.g. unhealthy lifestyle, excessive alcohol consumption, smoking) (Briasoulis et al., 2012; Oparil et al., 2018), overweight (pre-obesity) (Jayedi et al., 2018; Seven et al., 2014), obesity (Landsberg et al., 2013), chronic psychosocial stress (Cuffee et al., 2014; Sparrenberger et al., 2009), and air pollution (Rajagopalan et al., 2018; Tofield, 2017).

Resulting from an association of risk factors, the two common pathophysiological causes of AH are prolonged increase in cardiac output and increased peripheral vascular resistance. Cardiac output, expressed in litres/minute, is the amount of blood the heart pumps in one minute. Increased activity of the sympathic nervous system increases heart rate, causing elevated BP (Drummond et al., 2019). Elevated SBP contributes to the deterioration of kidney function through the renin-angiotensin-aldosterone system (RAAS), and increases the retention of sodium and water, causing the development of AH (Bakris et al., 2009). Increased peripheral vascular resistance is manifested through reduced vascular diameter (vasoconstriction) and increased vascular stiffness (Drummond et al., 2019; Mayet & Hughes, 2003).

Endothelial dysfunction is characterized by reduced vasodilation, increased vasoconstriction, increased risk of coagulation, and loss of integrity of the endothelial monolayer (the monolayer plays a role in the regulation of antithrombogenic and pro-inflammatory reactions in the blood vessel wall) (Xiao et al., 2014). Endothelial dysfunction leads to vascular damage, in which the oxidative stress process plays an important role (Briones & Touyz, 2010; Montezano et al., 2015; Touyz et al., 2020).

Oxidative stress is a key mechanistic mediator of AH and is defined as an imbalance between oxidants and antioxidants (Touyz et al., 2020). Excessive

bioavailability of reactive oxygen species (oxidants) causes the process of atherosclerosis; in conjunction with this, oxidative stress increases vascular injury and vascular stiffening, causing vascular remodelling (due to fibrosis and vascular calcification) (Briones & Touyz, 2010; Yang et al., 2017) and accelerating vascular aging (Harvey et al., 2015).

The development of AH is associated with increased level of inflammation that is caused in large part by oxidative stress (Guzik & Touyz, 2017; Yang et al., 2017). Production of inflammatory mediators (e.g. interleukins) and circulating levels of inflammatory biomarkers (e.g. C-reactive protein, CRP) are increased in the individuals with hypertension (Touyz et al., 2020).

From the neurohormonal system, the sympathetic nervous system is responsible for maintenance of cardiovascular homeostasis. The sympathetic nervous system is more activated in individuals with AH than in normotensive individuals (Mancia & Grassi, 2014).

2.2.3. Association of arterial hypertension with different diseases

The Global Burden of Disease Study showed that AH accounted for 10.7 million premature deaths and the loss of 211.8 million DALYs in 2015. From premature deaths, about 55% of cases of IHD, 58% of cases of haemorrhagic stroke, and 50% of cases of ischaemic stroke have been attributed to elevated SBP at the level ≥140 mmHg (Forouzanfar et al., 2017). The 5.2-year follow-up study with 1.25 million patients (including 83 098 cardiovascular events) showed that 30-year-old individuals with an elevated level of BP (especially SBP ≥140 mm Hg and/or use of blood pressure lowering medications) had a higher lifetime risk for development of CVDs compared to individuals with a normal level of BP (63.3%; 95% CI 62.9–63.8 *vs* 46.1%; 95% CI 45.5–46.8, respectively) (Rapsomaniki et al., 2014).

Prolonged AH causes ventricular hypertrophy, and leads to the development of systolic (decreased output) and diastolic (decreased blood filling) dysfunction, which can lead to heart failure (Bui 2011). At the same time, increased demand of myocardial oxygen can lead to either myocardial ischaemia (Rapsomaniki et al., 2014) or myocardial infarction (Rosengren et al., 2004).

Hypertension-induced arterial damage by oxidative stress accelerates the development of atherosclerosis, causing myocardial ischaemia (Rapsomaniki et al., 2014), ischaemic stroke (O'Donnell et al., 2010) and/or cognitive dysfunction (Hay et al., 2020; Shen et al., 2020). Hypertension-induced weakened vessel walls due to arterial damage cause structural alterations in cerebral vessels, leading to haemorrhagic stroke (Rapsomaniki et al., 2014). Hypertension-induced change in renal vessels can cause chronic kidney disease (Hsu et al., 2005; Kanno et al., 2012).

The presence of diabetes elicits different macrovascular and microvascular complications, causing CHD, heart failure, and cerebrovascular disease (Dal Canto et al., 2019). The association between AH, prolonged obesity, and meta-

bolic abnormalities contribute to the development of renal failure (Hall et al., 2015; Webster et al., 2017). In addition, common conditions such as dyslipidemia and AH (Briones & Touyz, 2010; Chrysohoou et al., 2007; Stocker & Keaney, 2004), and smoking (Barua & Ambrose, 2013; Niemann et al., 2017) are predisposing to atherosclerosis due to an increased production of reactive oxygen species (oxidants).

2.2.4. Trends in the prevalence of arterial hypertension in Estonia and Sweden

According to the database of the Global Health Observatory by the WHO, the age-standardized prevalence of hypertension among 30–79-year-old adults was higher among men and women in Estonia than in Sweden, and decreased in both countries in 1998–2018 (44.7% *vs* 38.7% in 1998; 42.0% *vs* 36.0% in 2010, and 40.3% *vs* 30.8% in 2018, respectively). (WHO, 2022h)

In Estonia, age-standardized prevalence of hypertension decreased among men from 51.0% in 1998 to 49.2% in 2010 and to 46.2% in 2018 (among women, from 38.8% to 35.0% and to 34.2%, respectively) (Figure 3). In Sweden, age-standardized prevalence of hypertension decreased among men from 43.1% in 1998 to 41.5% in 2010 and to 36.3% in 2018 (among women, from 34.1% to 30.3% and to 25.2%, respectively). (WHO, 2022h)

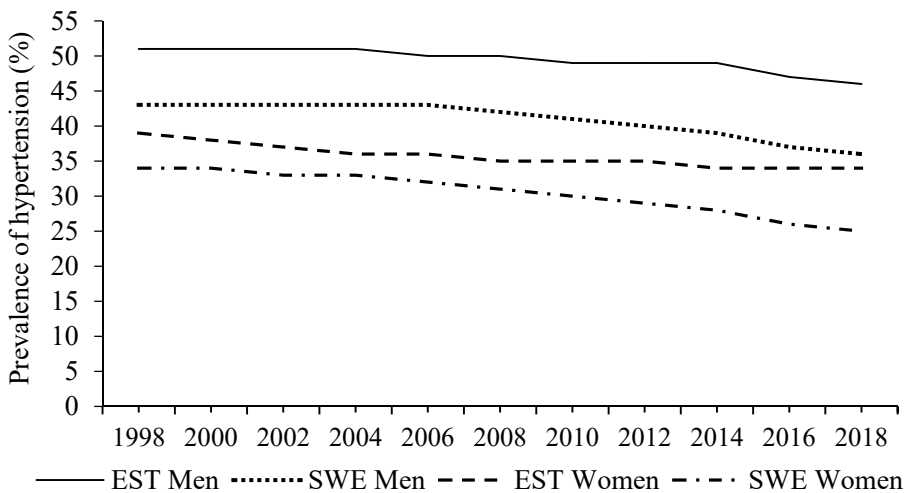


Figure 3. Age-standardized prevalence of hypertension among 30–79-year-old men and women in Estonia (EST) and Sweden (SWE), 1998–2018 (WHO, 2022h)

2.3. Risk factors of arterial hypertension and cardiovascular diseases

2.3.1. Background factors

From background factors, age, gender and family history of CVDs belong to the group of non-modifiable risk factors, but socioeconomic status belongs to the group of modifiable factors.

Age. Prevalence of AH increases with age due to deterioriated capacity of endothelial vasorelaxation, increased level of the process of inflammation and calcification in the endothelial, and arterial stiffness in aorta and arteries (Giannoni & Masi, 2018; Harvey et al., 2015; McEniery et al., 2007). Early vascular aging (premature development of vascular stiffness and remodelling) is an important risk factor of hypertension (Cunha et al., 2017; Nilsson et al., 2009). Long-term elevated BP level, impaired glucose metabolism (Nilsson, 2016), and chronic inflammation in the organism, and the process of oxidative stress cause early development of changes in the endothelia. Thus, ageing syndrome at a young age can be both the cause or the outcome of the AH (Nilsson, 2020).

Gender. At a younger age, high BP is more prevalent in men than women; after the age of 50 this reverses due to postmenopausal changes in the organism of women (Yanes & Reckelhoff, 2011). In addition, the deterioration in endothelian function occurs later in women than in men due to the impact of hormones (testosterone, follicle-stimulating hormone and luteinizing hormone) and the changes in the ratios of the steroid hormones (male-female differences) throughout the lifespan (Gerdts et al., 2022; Sandberg & Ji, 2012). During women's lives physiologic and pathophysiologic events (e.g. menstrual cycling; pregnancy; menopause, particularly early onset of menopause; oral contraceptive use and hormone replacement therapy) are associated with potential changes in the cardiovascular system that may cause the development of AH (Garovic & August, 2013; Wenger et al., 2016, 2018).

Family history of CVDs. An evidence-based relationship between SBP and genetic factors exists, indicating the central importance of the vasculature in BP regulation (Warren et al., 2017). The assessment of hypertension in the family history detects individual risk for AH through genetic and lifestyle factors (e.g. smoking, alcohol drinking, unhealthy eating) (Collins & Varmus, 2015). Early-onset (at the age of 55) of AH in grandparents will indicate elevated risk for hypertension in the third generation (Niiranen et al., 2017). The presence of CVDs in the family history before the age of 55 years in men and 60 years in women increases risk for CVDs (Horan et al., 2007).

Socioeconomic status (SES) is a complex variable that is conceptualized in different ways and is measured by a combination of different variables like education, income, and occupation (Baker, 2014). Increased risk of development of AH occurs in all three aforementioned indicators, indicating significant association with lower SES (Leng et al., 2015).

In health research it has been found that education level is an especially important indicator of SES, as it reflects better than the others indicators the knowledge and skills that are important for making health related behavioural choices (Brunello et al., 2016; Cutler & Lleras-Muney, 2010). Education has long-lasting effect on the health of both genders over the lifespan, being more expressed among women during the first half of life (Dilmaghani, 2020). Education is also an indicator for the ability to use knowledge more or less effectively to cope successfully with stressful life events (Ben-Zur & Michael, 2020; Frankham et al., 2020; Spruill, 2010; Thoits, 2010), and as a parameter for having more sense of control (e.g. mastery) in one's life (Dalgard et al., 2007; Mitchell et al., 2018).

2.3.2. Psychosocial factors

The term 'psychosocial' indicates the effect of social processes through a psychological understanding (Stansfeld & Rasul, 2006), which exert an effect on an individual's ability to cope in life (Taylor & Stanton, 2007). Psychosocial factors encompass different variables, divided into two broad categories: psychological (individual level), and social variables (surroundings, environment) (Macleod & Davey Smith, 2003; Schwardzer & Luszczynska, 2012; Singh-Manoux et al., 2003). Psychosocial factors can cause acute as well as chronic stress (Dimsdale, 2008; Kivimäki & Steptoe, 2018; Mittleman & Mostofsky, 2011). In biomedical sciences, a stress is described as a response of an organism to adverse stimulation, but in psychological sciences, as a process in which a person and an environment interact (Schwardzer & Luszczynska, 2012).

Based on a broadly known definition, a stressor means a problematic event, condition or experience that threatens the operating integrity of an organism and is a challenge to the adaptive capacities of an individual (Pearlin, 2010; Wheaton & Montazer, 2012). Stressors are associated with the social and economic status of the individual and are reflected in health status, e.g. mental health (Aneshensel & Avison, 2015; Pearlin, 2010). Acute stress (e.g. major sporting event, natural disaster) is usually short-term (minutes up to days) stress, which may lead to chronic stress (Dimsdale, 2008; Mittleman & Mostofsky, 2011). Chronic stress caused by external or internal stressors is long-term stress, which is characterized by both severity (low or moderate) and occurence (consistent or repetitive) (e.g. job strain, caring responsibilities, financial stress, marital problems) (Chida & Hamer, 2008; Kivimäki & Steptoe, 2018).

The clinical consequences of psychosocial stress are associated with increased cardiac electrical instability, plaque disruption from the endothelium (Kivimäki & Steptoe, 2018; Pedersen et al., 2017), as well as an elevated level of inflammatory and procoagulant markers that cause endothelial dysfunction (Dimsdale, 2008; Pedersen et al., 2017). Psychosocial stress causes poorer BP recovery (Chida & Hamer, 2008; Pedersen et al., 2017; Spruill, 2010).

Prolonged activation of the body by chronic psychosocial stress can cause changes in the hypothalamic-pituitary-adrenal axis (Chida & Hamer, 2008;

Herman, 2013; McEwen, 2007). The overactivity of sympathetic nervous system (particularly adrenergic activity) causes the elevation in BP (Mancia & Grassi, 2014), leading to AH (Albus et al., 2019; Cuffee et al., 2014; Esler, 2017; M. Y. Liu et al., 2017). Depressive mood can be a consequence of chronic psychosocial stress, leading to depression (Hänsel et al., 2010; Herman, 2013).

The following detailed description is focused on stressful life events, depressive mood, and quality of life, which best reflect the occurence of chronic psychosocial stress and an its effects on health.

Stressful life events (SLEs)

Although the type and division of stressors are different, e.g. physical environment, social/relationship, organizational, unhealthy lifestyle choices (Wheaton & Montazer, 2012), the best known type of stressors are life events, which are divided into usual life events (e.g. job transitions, marriage, retirement) and unusual life events (e.g. loss of someone, accident, serious illness) (Schwardzer & Luszczynska, 2012). SLEs are independent variables that lead to a number of negative outcomes and are characterized by intensity, duration, predictability, and controllability (Schwarzer & Schulz, 2002). Major negative SLEs predict depressive mood, and fear, due to the adverse stimulation caused by a stressful environment over time (Gotlib & Joormann, 2010; Hammen, 2016).

Depressive mood

It is important to distinguish depressive mood and depression. Depressive mood (also situational depression) is a short-term, stress-related type of depression that occurs as the result of changes in a person's life (e.g. ones own and/or a family member's illness). Depression is a negative affective state, interfering with daily life with various physical, cognitive and social changes, which in psychiatry is termed clinical depression (major depressive disorder) (APA, 2022). The diagnosis of clinical depression requires the presentation of at least two basic symptoms (e.g. decline in mood, loss of interest, loss of energy) and two additional symptoms (e.g. loss of concentration, change in appetite, sleep disturbances, suicidal thoughts), and that these symptoms occur over at least two weeks (Kleinberg et al., 2011).

Growing evidence has contributed to the understanding of the mechanisms by which SLEs cause depressive mood due to biological, psychological, and social issues (Avison & Turner, 1988; Pearlin et al., 1981; Pemberton & Fuller Tyszkiewicz, 2016; Weber et al., 2013). Depressive mood regarding negative SLEs reduces quality of life (Chaves et al., 2018; Marum et al., 2014; Schmitz & Brandt, 2019; Wicke et al., 2014). A higher score of depressive symptoms leads to a higher risk of AH (Nabi et al., 2011).

Quality of life

Based on the WHO definition, quality of life is the perception of individuals that their needs are being satisfied and they are not being denied opportunities to achieve happiness and fulfillment, regardless of physical health status, or

social and economic conditions (Nutbeam & Kickbusch, 1998). There are several domains in the comprehensive assesssment of quality of life, such as: physical, social and role functioning, emotional well-being, disease-specific symptoms, and general health perception (Mark, 2016).

The concept of health-related quality of life has evolved since the 1980s to encompass aspects that are related to physical or mental health at the level of individuals and community groups (McHorney, 1999). There are different understandings of quality of life, and health related quality of life (Karimi & Brazier, 2016). Quality of life accounts more for human needs, subjective well-being, expectations, and life satisfaction than health related quality of life (Power & Kuyken, 1998), which is compatible with the definition given by the WHO (The WHOQOL-Group, 1998). In recent years the quality of life has become a relevant parameter to measure the coping of individuals and/or progression of the therapy of cardiovascular patients, including AH (Bonaccio et al., 2018; Carris & Smith, 2015; Garin et al., 2009).

2.3.3. Personality traits

Personality traits are relatively stable, consistent, and enduring internal characteristics that are inferred from a pattern of behaviours, attitudes, feelings, and habits of individuals, which can be useful to explain a person's conduct (APA, 2022). Personality traits is a valuable contruct to understand differences in health between individuals (Aldwin et al., 2007).

Personality traits can have both mediating (as mediator) and moderating (as moderator) functions. A mediator is a possible explanation for a relationship between an independent variable (e.g. condition) and a dependent variable (e.g. effect), leading to a negative health outcome (e.g. AH). A moderator affects the magnitude of the effect (strength and direction) of an independent and dependent variable, increasing or reducing the harmful effects to health (MacKinnon & Luecken, 2008; Nicolaisen et al., 2018; Pudrovska et al., 2005).

The following detailed description focuses on three important personality traits, such as mastery and self-esteem (known as personal resources or self-concept) (McKean Skaff, 2007; Orth et al., 2015; Pearlin et al., 1981), and type A behaviour pattern (TABP, known as an action-emotion-based behavioural complex) (Chen et al., 2019; Karlberg et al., 1997).

Mastery

Originally, mastery was conceptualised as self-belief, a conviction that one is able to control the important events that are currently impinging on one's life (Pearlin & Schooler, 1978). Later definitions of mastery have referred to it as the individual's perception of ability to cope with psychosocial stress (Au, 2017; Pearlin et al., 1981), and as the generalized belief that most circumstances are under one's personal control (Thoits, 2010).

Higher level of mastery is associated with better cardiovascular reactivity to stress, with lower metabolic dysregulation and level of inflammation and blood

coagulation, and with lower risk for CVDs (Roepke & Grant, 2011), ensuring better functional health (e.g. activity of daily living) in later life (Infurna & Okun, 2015; Lee et al., 2016). Higher level of mastery is associated with lower occurence of depressive symptoms (Bjørkløf et al., 2013) and with better level of psychosocial functioning (Dalgard et al., 2007; Mitchell et al., 2018), ensuring better quality of life (Huang et al., 2017).

Negative SLEs (e.g. loss of income, illness of a relative or one's partner, death of one's partner or relative, relocation) have a greater impact for individuals with lower mastery (De Beurs et al., 2005), disturbing their ability to effectively cope with financial problems, physical health impairments, poorer health status (Crowe et al., 2016; Drewelies et al., 2018; Nicolaisen et al., 2018; Slagsvold & Sørensen, 2013). Prolonged occurence of stressors (e.g. financial hardship, caregiving stress), particularly early exposure to intractable hardship, affects effective coping among 65-year-old adults (Pearlin et al., 2007).

Generally, older adults have fewer mastering abilities, but it depends on gender and level of education (Nicolaisen et al., 2018). The level of mastery is relatively stable until the age of 55–60, and declines among over 60-year-olds, based on United States cohort (Mirowsky & Ross, 2007) or among ≥75-year-olds based on Norwegian cohort (Slagsvold & Sørensen, 2013). Lower mastery is associated with a lower level of education (Dalgard et al., 2007; Drewelies et al., 2018; Mitchell et al., 2018; Nicolaisen et al., 2018), and with living alone (Nicolaisen et al., 2018). A lower level of mastery occurs more often among women than men (Nicolaisen et al., 2018; Slagsvold & Sørensen, 2013).

Self-esteem

Originally, self-esteem was decribed as the positiveness of one's attitude toward oneself (Rosenberg, 1965). Later definitions of self-esteem have described it in different ways, e.g. as a measure of the competence an individual feels when approaching a stressful situation (Hughes, 2007), as a perception of himself/herself as a good, valued, and competent person (Thoits, 2010), and as the general evaluation of his or her worth as a person (Wagner et al., 2014).

Self-esteem increases from late adolescence to middle adulthood (until age 30), is stable until age 60 and declines at an older age (Orth et al., 2012, 2018; Orth & Luciano, 2015), being influenced by increasing and decreasing individual differences throughout adulthood (Wagner et al., 2014). Compared to women, men have a higher level of self-esteem during their lifespan (Bleidorn & Schwaba, 2018; Wagner et al., 2014), but in some studies, no significance differences have been found in the level of self-esteem by gender (Orth et al., 2015; Trzesniewski et al., 2003).

Higher self-esteem is associated with better mental well-being, effective social functioning (Mann et al., 2004; Taylor & Stanton, 2007), and with better coping with financial hardship (Frankham et al., 2020). The occurrence of negative SLEs decreases the level of self-esteem (Orth et al., 2015; Orth & Luciano, 2015), causing depressive symptoms (Orth et al., 2009). Higher level of education is associated with higher level of self-esteem (Wagner et al., 2014).

Type A behaviour pattern (TABP)

Originally, TABP has been defined as an action-emotion complex in which an individual's behaviour is characterized by expressed hostility, ambitiousness, competitiveness, impatience and an exaggerated sense of time urgency (Burns & Bluen, 1992). The mechanism for the relationship between TABP and CVDs may be associated with poorer cardiovascular reactivity (e.g. higher resting heart rate and BP) following stress situations, through the neuro-endocrine pathway and the hypothalamic-pituitary-adrenal axis (Chida & Hamer, 2008). Regarding CHD/IHD, the evidence is contradictory, as it has been found that TABP does not predict the risk of incidence of CHD (Ikeda et al., 2008) and this may exacerbate cardiovascular conditions in individuals with existing IHD (Chida & Steptoe, 2009; Du et al., 2016).

A positive link exists between TABP and cardiovascular reactivity, including elevated BP (Chida & Hamer, 2008). In the bibliometric analysis based on 1288 papers (1965–2018) a positive link between TABP and CHD through the hostility component was found. The positive link between AH and TABP occurs through work/occupation-related processes, being associated with burnout and work-related managerial roles (Chen et al., 2019).

2.3.4. Association between psychosocial factors, personality traits and health

The adapted Lifespan model of control and health (McKean Skaff, 2007) was used for the description of the association between psychosocial factors, personality traits and health. From two overriding sets of influences, socioeconomic influences affect an individual's beliefs regarding the self, the environment, and the association between the two; lifespan influences are associated with an individual's health through psychosocial factors and personality traits, being related to the historical context in which the person lives his/her life (Figure 4). All double-pointed arrows on this figure indicate a reciprocal relationship, forming a unitary whole.

Based on worldwide literature, the social context in which a person lives a personal life is influenced by both psychosocial factors (e.g. SLEs) and the presence of personal resources (e.g. mastery and self-esteem), infuencing health outcome (Aneshensel & Avison, 2015; McLeod, 2012; Pearlin et al., 1981). A higher level of SLEs increases the risk of suffering from depressive mood (McEwen, 2007; Pemberton & Fuller Tyszkiewicz, 2016; Weber et al., 2013). The presence of depressive mood is related to the occurrence of coexisting chronic diseases (Moussavi et al., 2007; Wicke et al., 2014). Among individuals with AH, depressive mood is common even without comorbidity conditions (Rantanen et al., 2018; Saboya et al., 2010). The occurrence of comorbidities (e.g. CVDs, obesity, mood disorders) reduces quality of life (Banegas et al., 2007; Zygmuntowicz et al., 2012). Quality of life is lower in the physical and mental subdomains among adults with AH (Trevisol et al., 2011).

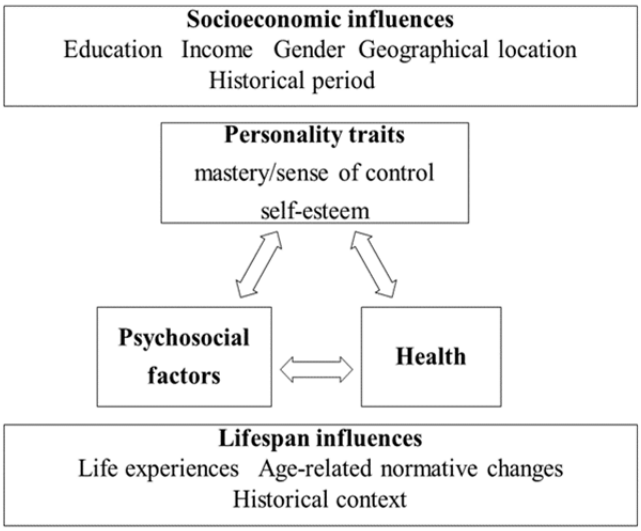


Figure 4. The association between psychosocial factors, personality traits and health. Adapted from a Lifespan model of control and health (McKean Skaff, 2007)

Although quality of life is influenced by age (lower in older age), lower level of education, and occupational position (Conde-Sala et al., 2017; Niedzwiedz et al., 2014), a better SES in society mirrors better subjective life satisfaction and higher quality of life (Abbott & Wallace, 2014; Niedzwiedz et al., 2014). From a historical and social context, the periods of SLEs and financial difficulties around the post-socialist transition period are associated with worse health above the age of 50 in Eastern European countries compared to Western European countries (Bíró & Branyiczki, 2019; Schmitz & Brandt, 2019).

Mastery and self-esteem, being personal resources (McKean Skaff, 2007; Pearlin et al., 1981), reduce the harmful effects of psychosocial stress on health (Frankham et al., 2020; Pearlin et al., 1981; Taylor & Stanton, 2007; Thoits, 2010). Higher level of mastery ensures better mental health (Crowe et al., 2016), lower rates of serious adverse health outcomes among patients of CVDs (DuBois et al., 2015), better coping with lifestyle changes (Drewelies et al., 2018; Infurna & Gerstorf, 2014), and more effective adaptation in the face of economic hardship (Marum et al., 2014; Mejía et al., 2016; Pudrovska et al., 2005). A higher level of self-esteem is associated with better mental health (Bookwala, 2014; Mann et al., 2004; Pearlin et al., 1981) and effective coping with life experiences, including negative SLEs (Bleidorn & Schwaba, 2018; Orth et al., 2012).

2.3.5. Lifestyle factors and health indicators

Lifestyle factors

A healthy lifestyle is a cornerstone for the prevention of CVDs, including AH, accounting for cardioprotective nutrition habits (including dietary sodium restriction), physical activity, normal body weight, non-smoking, and alcohol consumption at a low risk level. (Piepoli & Villani, 2017)

Nutrition

Saturated fatty acids and trans fats increase the total and LDL-cholesterol (Hooper et al., 2015, 2020), causing the progression of atherosclerotic plaques and narrowing the diameter of blood vessels, and lead to elevation of BP (Ference et al., 2018). An adequate amount of dietary fibre regulates and lowers total and LDL-cholesterol (Threapleton et al., 2013). Excess salt intake is associated with increased BP regarding water retention, vascular remodelling and endothelial dysfunction (Boegehold, 2013; Laffer et al., 2016).

Based on evidence-based research, recommendations for individuals with AH or high-normal BP are as follows: to increase consumption of vegetables, fresh fruits, nuts, fish and olive oil; to consume low-fat dairy products; to decrease consumption of red meat; and to avoid body mass index ≥30 kg/m² (Williams et al., 2018). In cardioprotective nutrition, saturated fatty acids should account for <10% and trans fats <1% of total energy intake per day; fish should be consumed at least twice a week, one of which should be oily fish; the intake per day of salt should be <5 g, fibres 30–45 grams, and fruits ≥200 grams and vegetables ≥200 grams (Visseren et al., 2021).

Physical activity

Adequate physical activity avoids energy imbalance, glycemic dysregulation and vascular dysfunction, and decreases the level of oxidative stress (Lavie et al., 2019). Regular physical activity of at least 30 minutes of moderate dynamic exercise on 5–7 days per week is recommended by guidelines for the management of AH (Williams et al., 2018). For individuals with a diagnosis of AH, it is advised to engage in at least 30 min of moderate-intensity aerobic training, such as walking, jogging, cycling, or swimming, on 5–7 days per week for at least 150 minutes a week (Borjesson et al., 2016; Pelliccia et al., 2021). Regular medium-to-high-intensity aerobic activity is associated with a mean reduction in SBP 11 mmHg and DBP of 5 mmHg (Borjesson et al., 2016).

Physical activity reduces the risk of CVDs progression among adults with a diagnosis of AH (Pescatello et al., 2019). The combination of hypocaloric eating habits with aerobic exercises two days per week (of 45 minutes) offers optimal non-pharmacological treatment to manage both high BP and body composition in overweight/obese and sedentary individuals with AH (Gorostegi-Anduaga et al., 2018).

Smoking

Current smoking is an established risk factor for the development of AH (Gao et al., 2017; Jatoi et al., 2007), as well as for CVDs, particularly CHD and myocardial infarction. Current and past history of smoking elevates cardiovascular risk in individuals with AH (Mähönen et al., 2004; Pirie et al., 2013; Yusuf et al., 2004). Current smoking accelerates the development of atherosclerosis (Virdis et al., 2010) due to oxidative stress (Barua et al., 2003; Barua & Ambrose, 2013), which can lead to cell and tissue damage (Niemann et al., 2017).

Cigarette-caused atherosclerosis causes prothrombotic effect due to platetet dysfunction, alteration of antithrombotic and prothrombotic factors, and fibrinolysis (Ambrose & Barua, 2004; Csordas & Bernhard, 2013). Several meta-analyses have demonstrated that cigarette smoking is an independent risk factor for development of atherosclerotic CVDs, including AH (Mons et al., 2015; Mucha et al., 2006; Pan et al., 2015).

Compared to never smokers, current smokers had significantly higher risk for smoking-related complications: relative risk (RR) 2.51 (95% CI 1.79–3.51) for CHD and 1.60 (95% CI 1.39–1.84) for total CVDs, particularly at age 40–64 years (Iso et al., 2005). Based on the INTERHEART case-control study, among current smokers the odds to have acute myocardial infarction (mainly caused by IHD) was significantly higher 2.95 (95% CI 2.72−3.20) (Yusuf et al., 2004). Thus, smoking cessation is recommended for the management of AH by guidelines for the management of AH (Williams et al., 2018).

Alcohol consumption

Based on guidelines for the management of AH, consumption of alcoholic beverages less than 14 units per week for men and less than 8 units per week for women is recommended (Williams et al., 2018). One unit of alcohol/one drink is equal to 10 grams of pure alcohol (Griswold et al., 2018). Based on a meta-analysis, excessive alcohol consumption (>21 grams per day) significantly increased the risk for hypertension in men and women. However, a low level of alcohol consumption (<10 g/day and 11–20 g/day) had no consistent effect on BP (Briasoulis et al., 2012). Although alcohol is a well-known vasodilator and, as such, ought to lower BP, then excessive alcohol consumption is related to elevated BP (Messerli et al., 2019).

Health indicators

For assessing cardiovascular health status, the important health indicators are body mass index and cardiovascular biomarkers.

Body mass index

According to the definition of the WHO, body mass index (BMI), formerly Quetelet index, is a measure to assess nutritional status in adults, and is defined as an individual's weight in kilograms divided by the square of the individual's height in metres (expressed kg/m^2). Based on this, nutritional status is divided into six groups: underweight (BMI<18.5), normal weight (18.5–24.9), pre-

obesity (overweight) (BMI 25.0–29.9), obesity class I (BMI 30.0–34.9), obesity class II (35.0–39.9), obesity class III BMI (>40). (WHO, 2022d)

BMI is a simple index to evaluate body weight in clinical practice, although individuals with similar BMI values have shown markedly different levels of health risks for CVDs due to subcutaneous or visceral body fat distribution (Neeland et al., 2018). Increased amount of fat abdominally (visceral/ ectopic fat), locating around the intra-abdominal organs and blood vessels (Haberka et al., 2018) accounts for 65–75% of cases of essential AH (Hall et al., 2015), increasing overall blood volume and causing renal tubular sodium reabsorption (Hall et al., 2015; Neeland et al., 2018).

Compared to individuals with a normal weight, pre-obese and obese individuals (with unknown fat deposition status) with higher BMI had a strong independent risk factor for the development of AH (Barrios et al., 2010; Bombelli et al., 2011; J. B. Cohen, 2017; Jayedi et al., 2018; Landsberg et al., 2013; Maatouk et al., 2016; Oda & Kawai, 2010; Seven et al., 2014).

Particularly, obesity is the strongest risk factor regarding subclinical organ damage (arterial stiffness, left ventricular hypertrophy, diastolic dysfunction, carotid artery tickening, microalbuminuria), dysbalance of neurohormal activity, insulin resistance, and metabolic syndrome (Barrios et al., 2010; J. B. Cohen, 2017; Guerra et al., 2011; Neeland et al., 2018; Varrenti et al., 2014).

Cardiovascular biomarkers

The routine test for evaluation of hypertensive individuals is the following: fasting blood glucose, blood lipids (total cholesterol, high-density lipoprotein, HDL-cholesterol; low-density lipoprotein, LDL-cholesterol), and blood triglycerides (Williams et al., 2018). Other biomarkers, like CRP and interleukin-6 (IL-6), are recommended for the assessment of the process of inflammation due to atherosclerosis, cardiovascular diseases (e.g. myocardial infarction) or comorbidity conditions (e.g. obesity, type 2 diabetes) (Abeywardena et al., 2009; Al Rifai et al., 2017). IL-6, as a multifunctional pro-inflammatory cytokine, is responsible for the stimulus of the synthesis and secretion of CRP (Abeywardena et al., 2009). Also, fibrinogen is one key player of coagulation regarding thrombosis (Davalos & Akassoglou, 2012).

Individuals with a higher level of total cholesterol and a lower level of HDL had a significantly higher risk of atherosclerotic CVDs (including hypertension) compared to those with a normal level of total cholesterol (Quispe et al., 2020). A low level of HDL in plasma was positively associated with the development of premature CHD/IHD in patients ≤55-years old (Shahid et al., 2016) and a higher level of HDL was inversely related to coronary atherosclerosis and CHD/IHD (Cooney et al., 2009).

Current smokers had higher markers of inflammation of the blood (especially CRP, IL-6) than non-smokers (Al Rifai et al., 2017; Jefferis et al., 2010; McEvoy et al., 2015). The level of LDL was significantly lower in current smokers than in non-smokers (Hozawa et al., 2006; Wannamethee et al., 2005).

2.4. Cardiovascular mortality

Cardiovascular mortality, embracing mortality from IHD, cerebrovascular disease (stroke), hypertensive heart disease, atrial fibrillation and flutter, cardiomyopathies, rheumatic heart disease, peripheral vascular diseases and aortic aneurysm, has been a leading cause of death globally since 1990 (Naghavi et al., 2015). From cardiovascular mortality, IHD is the leading cause of death (Forouzanfar et al., 2012; Levi et al., 2002; Roth et al., 2015), which is therefore often used to describe cardiovascular mortality. IHD is known as CHD, thus, mortality from IHD and from CHD are synonyms (Fuster et al., 2017).

2.4.1. Cardiovascular mortality in Estonia and Sweden

During the last 20 years IHD has been the leading cause of death among individuals of all ages and both genders in Estonia and Sweden (WHO, 2022g). In 1998–2016 the standardized death rate (SDR) from IHD per 100 000 inhabitants among 45–59-year-old adults was higher in Estonia than in Sweden (227 *vs* 37 in 1998; 91 *vs* 35 in 2010, and 53 *vs* 28 in 2016, respectively) (WHO, 2022f).

In Estonia, SDR from IHD (45−59-year-olds) decreased from 404 in 1998 to 161 in 2010 and to 99 in 2016 among men (from 81 to 30 and 12, respectively, among women). In Sweden, age-standardized death rate from IHD decreased from 59 in 1998 to 54 in 2010 and to 45 in 2016 among men (from 15 to 14 and to 11, respectively, among women). (WHO, 2022f) (Figure 5)

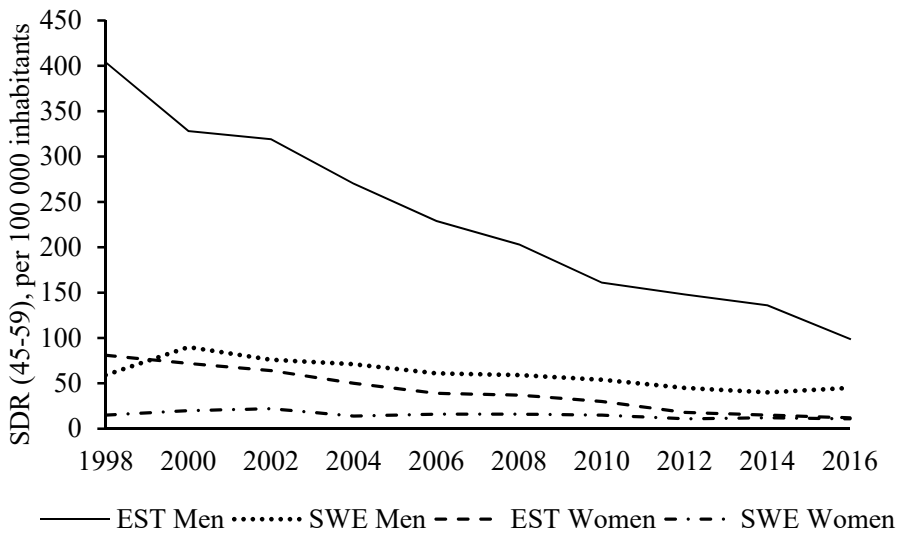


Figure 5. Age-standardized death rate (SDR) from IHD per 100 000 inhabitants among 45–59-year-old men and women in Estonia and Sweden, 1998–2016 (WHO, 2022f)

The SDR from all-causes of death per 100 000 inhabitants (WHO, 2022f) declined among all 45–59-year-old adults in Estonia and Sweden from 1998 to 2016, being higher in Estonia than in Sweden (1221 *vs* 363 in 1998; 672 *vs* 282 in 2010, and 569 *vs* 244 in 2016, respectively) (WHO, 2022f).

In Estonia, SDR from all-causes of death per 100 000 inhabitants decreased among 45–59-year-old men (from 1945 in 1998 to 1054 in 2010 and to 863 in 2016) and women (from 620 to 342 and to 302, respectively). In Sweden, age-standardized death rate per 100 000 inhabitants from all-causes of mortality decreased among men from 443 in 1998 to 346 in 2010 and to 291 in 2016 (among women from 282 to 217 to 196, respectively (WHO, 2022f).

In the countries of the former Soviet Union, the increase in CVD-related death was high in the early-mid-1990s. A decreasing trend in age-standardized CVD-related death rates among 30–69-year-old adults started since the mid-1990s, particularly among working-age men. A more detailed look reveals that the age-standardized CVD death rate per 100 000 inhabitants (based on WHO standard population) was 3.5 times higher among men compared to women in Estonia during 1980–2010, being related to political and social changes since the collapse of the former communist regime in the early 1990s (Ezzati et al., 2015). At the same time, compared to Mediterranean countries, the noticeable decline (approximately 52%) in IHD mortality in Western Europe occured in Nordic countries (including Sweden) in 1990–2009 (Vancheri et al., 2021).

2.4.2. Risk factors for cardiovascular mortality

In high-income countries (including Estonia and Sweden), according to GNI per capita (World Bank, 2022b), tobacco smoking, AH, and obesity made up almost half of the cardiovascular mortality attributable to risk factors (Dagenais et al., 2020; Wenger et al., 2018). Also, high level of total cholesterol, physical inactivity (Ford & Capewell, 2011; Moran et al., 2014; O'Flaherty et al., 2013), and excessive alcohol consumption (Ezzati et al., 2015; Neumann et al., 2021) play an important role in the mortality rate of IHD. The findings of the North-Karelia Project (1972–2012) in Finland have shown that changes in three risk factors: smoking cessation, reduction in the level of serum cholesterol, and decline in SBP, explained nearly all reduction in cardiovascular mortality (Jousilahti et al., 2016).

Smoking is a well-known risk factor for cardiovascular mortality (Doll et al., 2004; Iso et al., 2005; Mähönen et al., 2004; Mons et al., 2015; Nichols et al., 2013). Compared to never smokers, current smokers have an approximately 2-fold higher risk for all-cause mortality, for cardiovascular mortality as well as for non-cardiovascular mortality (Agudo et al., 2012; Carter et al., 2015; Gellert et al., 2012; Pirie et al., 2013). The harmful effects of smoking on mortality are dose dependent. Relative risk (RR) for IHD mortality is twice as high for those who smoke ≥25 cigarettes a day compared to those smoking <14 cigarettes a day (Banks et al., 2019).

Selected cardiovascular biomarkers in blood (e.g. CRP, fibrinogen, IL-6) have shown the association with cardiovascular, as well as with all-cause mortality (Barron et al., 2015; Baune et al., 2011; J. Liu et al., 2020; Patterson et al., 2015). Based on a meta-analysis, individuals with elevated level of IL-6 had a 69% higher cardiovascular and 49% higher all-cause mortality risk (Li et al., 2017). Elevated CRP (>3mg/l) was associated with 79% of the increase in cardiovascular mortality, but with 57% of the increase in all-cause mortality among men, but not among women (Doran et al., 2013).

Socioeconomic inequality in IHD mortality between Eastern and Western countries has been clearly reported (Avendano et al., 2006; Finegold et al., 2013; Ginter & Simko, 2012; Levi et al., 2002). The standardized mortality rate of IHD was significantly higher in Eastern European countries, where the decline in IHD mortality was much slower than in Western Europe (Németh et al., 2019).

2.5. Brief summary of literature review

AH is the leading cause of all major cardiovascular events (including IHD, stroke) that reduce life expectancy and increase DALYs. At the same time, cardiovascular mortality is the leading cause of death in European countries, including Estonia and Sweden. Some of the risk factors for AH and cardiovascular mortality are very well known and some less so.

This study focuses on AH, cardiovascular mortality, and associated risk factors in the 13-year follow-up period among a 35- and 55-year-old cohort in Estonia and Sweden. From risk factors, this study focuses on psychosocial factors, personality traits, lifestyle factors, and health indicators. To the best knowledge of the author of this thesis, the association of psychosocial factors and personality traits with AH has not been investigated previously in Estonia. This study attempts to fill this gap. Moreover, this study gives a unique opportunity to compare data in Estonia and Sweden, two countries with a different historical and political background and socioeconomic development.

3. AIMS OF THE STUDY

The general objective of the doctoral dissertation was to provide an evidence-based overview on the prevalence and risk factors of AH and cardiovascular mortality using a 13-year prospective longitudinal study among a 35- and 55-year-old cohort in Estonia and Sweden.

The specific objectives were:

1. to describe the prevalence of AH among a 55-year-old cohort after the 13-year follow-up, to explore psychosocial factors and personality traits among 35- and 55-years-old adults in both study waves, and to analyse the association of these factors with AH among a 55-year-old cohort in the second wave of the study in Estonia and Sweden (Paper I);
2. to describe the prevalence of AH in both study waves and to explore psychosocial factors, personality traits, lifestyle factors and health indicators associated with AH among a 55-year-old cohort in Estonia in the second wave of the study (Paper II);
3. to analyse cardiovascular mortality and its risk factors in the context of non-cardiovascular and all-cause mortality in a 55-year-old male cohort after a 13-year follow-up period in Estonia and Sweden (Paper III).

4. MATERIALS AND METHODS

4.1. Study sample

Primary data for this study was drawn from a study in Estonia and Sweden (Sweden-Estonia cardiovascular diseases' risk study, henceforth the SWESTONIA study) that was designed to explore CVDs and associated background and psychosocial factors, personality traits, lifestyle factors and health indicators. This prospective longitudinal study began with the first wave in 1997, had a 13-year follow-up period, and ended with the second wave in 2010 in Estonia and Sweden.

In the context of this thesis, the SWESTONIA study was divided into the main study and a substudy. The main study was carried out among 35- and 55-year-old men and women in two municipalities with a similar size in Estonia (Tartu municipality) and Sweden (Sollentuna municipality). The substudy was carried out among 55-year-old men and women in Estonia (Tartu) only.

Secondary data was used for this study in the second wave of the SWESTONIA study. Mortality data was drawn from Estonian and Swedish Causes of Death Register, and morbidity data from Estonian Health Insurance Fund and the Swedish National Patient Register.

4.1.1. Primary data sample

The first wave of the SWESTONIA study

Main study (Paper I, III)

In 1997, from the Estonian and Swedish Population Registers, 35- and 55-year-old men and women were randomly selected and invited to participate in the first wave of the study. Initial sample size (n=800) consisted of 100 men and 100 women in both age groups in Estonia and Sweden. In total, 549 subjects (277 Estonians and 272 Swedes) participated in the first wave (Table 1). The crude response rate among 35-year-olds was 70% and among 55-year-olds, 68.5% in Estonia, and 70% and 66%, respectively, in Sweden. In total, the crude response rate was 69.3% in Estonia and 68.0% in Sweden.

Estonian sub-study (Paper II)

In 1997, from the Estonian Population Register, 55-year-old men and women were randomly selected and invited to participate in the first wave of the Estonian sub-study. Initial sample size (n=500) consisted of 250 men and 250 women in Tartu (Table 1). Of them, 330 individuals participated in the first wave of the substudy. Crude response rate was 66.0%.

The second wave of the SWESTONIA study

Main study (Paper I, III)

In 2010, the 277 Estonians and 272 Swedish adults from the first wave of the SWESTONIA study formed the sample basis for the second wave of the prospective longitudinal SWESTONIA study being 48- and 68-year-olds at that time (henceforth, based on age in the first wave, 35- and 55-year-olds, are used). According to Estonian and Swedish Population Registries, from this sample, 31 participants in Estonia (four in the 35-year-old and 27 in the 55-year-old cohort) and five participants in Sweden (all in the 55-year-old cohort) had passed away before the second wave. In addition, the home addresses of ten Estonians (eight in the 35-year-old and two in the 55-year-old cohort) (Table 1) were not available in the Estonian Population Register.

Hence, the initial sample of the second wave consisted of 503 subjects (236 Estonians and 267 Swedes). In total, 371 subjects (158 Estonians and 213 Swedes) participated in the second wave. The crude response rate among 35-year-olds was 54.7% and among 55-year-olds 81.5% in Estonia, and 73.6% and 86.6%, respectively, in Sweden. In total, the crude response rate was 66.9% in Estonia and 79.8% in Sweden (Table 1).

Table 1. Initial sample size, number of respondents, crude response rate in Estonia and Sweden in the first wave and in the second wave of the SWESTONIA study (main study and Estonian substudy)

Initial sample size (n)					Respondents (n)					
Men		Women			Men		Women			
35-year-old	55-year-old	35-year-old	55-year-old	Total	35-year-old	55-year-old	35-year-old	55-year-old	Total	Crude response rate (%)
First wave in 1997										
Main study										
Estonia										
100	100	100	100	400	77	67	63	70	277	69.3
Sweden										
100	100	100	100	400	66	71	74	61	272	68.0
Estonian substudy										
-	250	-	250	500	-	163	-	167	330	66.0
Second wave in 2010										
Main study										
Estonia										
69	40	59	68	236	33	38	37	50	158	66.9
Sweden										
66	67	74	60	267	45	57	58	53	213	79.8
Estonian substudy										
-	135	-	151	286	-	102	-	117	219	76.6

Estonian substudy (Paper II)
In 2010, the 330 55-years-old participants from the first wave of the Estonian substudy formed the sample basis for the second wave of the substudy (Table 1). According to the Estonian Population Register, 44 participants had passed away before the second wave. The home addresses of all participants were obtained. Thus, the initial sample size of the follow-up substudy was 286. In total, 219 individuals participated in the second wave of the substudy. The crude response rate was 76.7%.

4.1.2. Secondary data

Morbidity data (Paper I, II)
In the second wave of the SWESTONIA study, morbidity data for the period 01.01.1999–31.03.2011 from the Estonian Health Insurance Fund and from the Swedish National Patient Register regarding diagnoses of CVDs (diseases of the circulatory system, I00-I99) on the basis of ICD-10 (ICD, 2010) of enrolled participants (n=236 and n=267, respectively) was used.

Mortality data (Paper III)
In the second wave of the SWESTONIA main study, all causes of death on the basis of ICD-10 (ICD, 2010) of 268 (excluding one Estonian man due to the absence of a home address) 55-year-old participants (n=27 and n=5, respectively) for the period 01.01.1999–31.03.2011 from Estonian and Swedish Cause of Death Registers were used. During the 13-year follow-up period, one woman from Estonia and one woman from Sweden deceased, while a total of 30 men died. Hence, the analysis of mortality was done for the male group only.

4.2. Data collection

First wave of the SWESTONIA main study and Estonian substudy
Invitation letters were sent to the home addresses of the potential respondents. The cover letter contained the following information: the purpose of the study; the content of the self-reported questionnaire; the statement about confidentiality; and the description of the physical measurement and the collecting of blood samples. If the subjects did not respond to the invitation within 10 days, a second invitation letter was sent. Finally, if there was no answer from the subjects, they were contacted by phone. Exclusion criteria of the study were the presence of serious acute or chronic diseases that did not allow participation in the study.

Participants were asked to visit the Tartu University Hospital in Estonia and the Karolinska Hospital (Stockholm) in Sweden, where the following procedures were performed:

1) Self-reported questionnaire concerning background, psychosocial factors and personality traits, lifestyle factors, medical anamnesis and use of medicines

(the last two were not used in the papers). Validated psychosocial, personality and lifestyle measures were used for data collection in the self-reported questionnaire (Avison & Turner, 1988; Eriksson et al., 1998; Karlberg et al., 1997; Pearlin et al., 1981; Tibblin et al., 1990). The questionaire was translated from Swedish to Estonian. The Swedish and Estonian versions were compared for consistency of the content and the meaning by two persons (Johansson et al., 2002).

2) Physical measurements (body height, body weight, SBP and DBP). BP was assessed twice from the left upper arm with the study participant sitting in an upright position.
3) Blood samples. Lipoprotein profile, such as total cholesterol, total triglycerides, HDL cholesterol, LDL cholesterol, CRV, IL-6, fibrinogen, plasma glucose. All blood samples were analysed at the Department of Clinical Chemistry, Karolinska Hospital, Sweden. Estonian samples were analyzed from frozen plasma and serum that had been transported by air to Sweden. Swedish samples were analysed from fresh serum and plasma.

Physical examination, blood sampling, and gathering of information by self-reported questionnaire followed a standardized procedure (Johansson et al., 2002). The study team from the two centres trained study procedures together, once before and once during the study, and the two centres were in regular communication.

Second wave of the SWESTONIA main study and Estonian substudy

1) The self-reported questionnaire was identical to the questionnaire used in the first wave. Additional questions concerning body height, body weight and BP were added into the questionnaire. The questionnaire together with a cover letter was sent to the home addresses of the potential respondents. The cover letter consisted of the following information: the purpose of the follow-up study; explanation that responding to the questionnaire is voluntary; that only pseudonymized (using numeric code instead of the name of the participant) collected data will be used; that only aggregated results will be published. Those who failed to return the questionnaire by mail within three weeks were contacted by phone. Researchers failed to contact 21 persons by phone because the phone number was unavailable. Thirteen of the 46 persons who were contacted by phone, refused to participate in the study. If the potential respondents refused to participate in the study, their decision was respected and accepted as non-responding.
2) Physical examination and collection of blood samples was not performed in the second wave of the SWESTONIA study.

4.3. Study variables

4.3.1. Primary data

Self-reported questionnaire (Appendix)

1) ***Background characteristics*** (age, gender, education, marital status) (Paper I, II, and III).
2) ***Psychosocial factors*** (Paper I, II)
   a) Negative SLEs (Avison & Turner, 1988) during past six month in two ways were evaluated: the occurrence (yes/no), and the influence on the individual (in centimetres, cm). Items (9) included: e.g. death of a close person, personal illness, financial problems. The single scores of the experienced events were summed to get a total score for the respondent. For each event that took place, the respondent was asked to mark a point on a line in the questionnaire to assess its influence. The influence of every event to the individual was measured with a ruler and the result was expressed in cm. One cm accounted for one tenth of the entire length of the scale.
   b) Depressive mood (based on the Depression Model) (Pearlin et al., 1981) in the past six month (yes/no). Items (9) covered: e.g. lack of enthusiasm for doing anything, crying easily or feeling like crying, feeling hopeless about the future. The number of 'yes' answers was summed, so that higher scores indicate a greater number of depressive symptoms.
   c) Quality of life (based on the Gothenburg Quality of Life Instrument) (Tibblin et al., 1990). Items (18) covered social well-being: e.g. home, work, financial status; physical well-being: e.g. health, fitness, appetite; and mental well-being: e.g. mood, energy, and believe in oneself; and feelings of being appreciate both within and outside of the home, which has seven-point Likert scale values from 'very bad' to 'excellent, could not be better'. Total score can range from 18 to 126 points.
3) ***Personality traits*** **(Paper I, II)**
   a) The Pearlin Mastery Scale (Pearlin et al., 1981) with seven items (e.g. 'There is really no way I can solve some of the problems I have'; 'I have little control over the things that happen to me') had values on a four-point Likert scale from 'not at all' to 'a lot'. Higher values showed a greater level of mastery. Total score can range from 7 to 28 points. On mastery scales the opposing statements were re-coded (Attitudinal Scales, 2021).
   b) The Rosenberg Self-esteem Scale (Pearlin et al., 1981) with ten items (e.g. 'I feel that I'm a person of worth, at least on an equal with others'; 'I feel that I have a number of good qualities'; 'in all, I am inclined to feel that I'm a failure') has values on a four-point Likert scale with values from 'not at all' to 'a lot'. A higher score indicates a higher level of self-esteem. Total score ranges from 7 to 40 points. Scoring of the

scale was based on the rule that some of the answers were coded in reverse order (Attitudinal Scales, 2021).

c) Type A behaviour pattern (Karlberg et al., 1997) with an 11-item (e.g. 'I easily get angry', 'I want everything done quickly', 'People often tell me to take it easy') scale with values from 'disagree' to 'fully agree'. Higher values show less TABP. The items describe hostile competitiveness and time urgency of respondents. Total score ranges from 11 to 33 points.

4) ***Lifestyle factors*** **(Paper I, II)**

The self-reported questionnaire accounted for nutrition, physical activity, alcohol consumption, and smoking status (Johansson et al., 2002).

a) Nutrition during the last four weeks was assessed on the basis of a scale-score questionnaire from 1–5. The questionnaire evaluates the consumption of saturated fatty acids compared to the consumption of mono- and polyunsaturated fatty acids. The individual nutrition quality scores (minimum score 21 points) for each answer were summed, and the highest score represented the highest content of unsaturated (mono- and polyunsaturated) fatty acids in food, which is a healthier diet than one that is high in saturated fatty acids (Eriksson et al., 1998)**.**

b) Physical activity over the last four weeks was evaluated by 'number of times 'and 'minutes 'for each of 15 types of sports (e.g. cycling, jogging, etc.) separately. Walking and cycling to work were included in physical activity if it lasted for at least 20 minutes. The level of physical activity was summed up across all types of sports.

c) Alcohol consumption (beer, wine and strong alcoholic beverages) over the last four weeks was assessed on a scale-score questionnaire from 1 (highest amount of alcohol used per day/per week to 5 (not drinking alcohol at all). The results were transferred into grams of pure ethanol per person per week from all types of alcohol.

d) Smoking status (current, past, never). A current smoking was defined as smoking tobacco one or more times per week during the last three months.

Health indicators

a) ***Physical measurements*** (Paper I, II) were carried out in the local clinics in the first wave and were self-reported in the second wave.

- Body weight, body height; calculation of BMI.
  BMI is a measure defined as an individual's weight in kilograms divided by the square of the individual's height in metres (expressed as kg/m^2), indicating nutritional status in adults. BMI was defined as follows: underweight (BMI≤18.5), normal weight (BMI 18.5–24.9), overweight (known as pre-obesity) (BMI 25.0–29.9), obesity (BMI ≥30.0) (WHO, 2022).
- SBP and DBP (Paper I, II, III)

AH was defined when SBP was ≥140 mmHg, DBP ≥90 mmHg or when the subject used antihypertensive medicines. (Mancia et al., 2013; Williams et al., 2018).

b) ***Blood samples*** – ***cardiovascular biomarkers*** **(Paper III).**
Fasting blood sample included the following markers:
- Fibrinogen (mg dL $^{-1}$)
- Plasma glucose (mmol L^{-1})
- CRP (mg L)
- IL-6 (ng L)
- Total cholesterol (mmol L^{-1})
- Total triglyceride (mmol L^{-1})
- HDL cholesterol (mmol L^{-1})
- LDL cholesterol (mmol L^{-1}).

4.3.2. Secondary data

Mortality data (Paper III)
Causes of death (ICD-10) were divided into the deaths caused by cardiovascular and non-cardiovascular diseases, which together constituted all-cause mortality.

Cardiovascular mortality was based on the diagnoses of deceased participants in 1999–2010:

1) ischaemic heart disease (IHD), including:
   - acute myocardial infarction (I21 by ICD-10))
   - chronic ischaemic heart disease (I25)
2) rheumatic heart disease (I05, I07)
3) peripheral arterial disease (I70.2)
4) acute vascular disorder of intestine (K55.0)
5) non-ischaemic cardiomyopathy (I42)

Non-cardiovascular mortality included all diagnoses not listed above.

Morbidity data (Paper I, II)
Diagnoses of CVDs regarding diseases of the circulatory system, based on ICD-10 (ICD, 2010), of study participants during the follow-up period were used.
The subjects were divided into two groups:

1) with diagnosis of AH
   - I10 – essential (primary) AH, including all grades (1, 2, 3)
   - I11 – hypertensive heart diseases, including all grades (1, 2, 3).

   In the second wave of the study, the subjects were classified into hypertension group according to morbidity data of the Estonian Health Insurance Fund and the Swedish National Patient Register. The confirmed diagnosis of AH (I10 or I11) and at least one prescription of antihypertensive drug must had been assigned to the study subject during the period 01.01.1999−31.03.2011.

   Individuals with the following diagnoses were excluded from the hypertension group, as these diagnoses are not causes of essential AH:

- I12 – hypertensive renal disease
- I13 – hypertensive heart and renal disease
- I15 – secondary hypertension

2) without diagnoses of AH.

4.4. Statistical analysis

The data in the first and second wave of this study was entered in Microsoft Excel 97 (v8.0) and Microsoft Excel 2010 (v14.0) in Estonia and Sweden, with Estonian (the author of current dissertation) and Swedish researchers using a data coding system based on similar principles, which was compatible with the database of the initial study (wave I). Thereafter, the data table was manually checked for inconsistencies. The database only lacked a few responses (maximum 5 per item).

Cronbach's alpha was used to evaluate the internal consistency of measures. A scale with a value of >0.7 was considered reliable (Dancey et al., 2014) (Table 2).

Table 2. Values of Cronbach' alpha for measures among 35- and 55-year-old participants compared to wave I and wave II in the SWESTONIA study (main study and substudy)

Characteristics	Age of study participants							
	35-year-olds				55-year-olds			
	EST	EST	SWE	SWE	EST	EST	SWE	SWE
	Wave I	Wave II	Wave I	Wave II	Wave I	Wave II	Wave I	Wave II
	Main study							
Depressive mood	0.75	0.80	0.80	0.82	0.78	0.76	0.75	0.75
Mastery	0.78	0.76	0.76	0.78	0.76	0.71	0.73	0.79
Self-esteem	0.80	0.84	0.71	0.86	0.70	0.80	0.81	0.80
Type A behavior	0.75	0.75	0.72	0.76	0.76	0.77	0.77	0.71
Stressful life events	0.72	0.79	0.71	0.79	0.72	0.81	0.78	0.80
Quality of life	0.83	0.94	0.86	0.90	0.88	0.92	0.84	0.86
	Substudy							
Depressive mood	-	-	-	-	0.76	0.72	-	-
Mastery	-	-	-	-	0.79	0.77	-	-
Self-esteem	-	-	-	-	0.73	0.80	-	-
Type A behavior	-	-	-	-	0.79	0.81	-	-
Stressful life events	-	-	-	-	0.73	0.82	-	-
Quality of life	-	-	-	-	0.88	0.99	-	-

AH, psychosocial factors and personality traits among the 35- and 55-years old cohort in Estonia and Sweden (Paper I). The Shapiro-Wilk W-test was used to test for normality. Values of psychosocial factors were presented as median and percentiles. Baseline differences both between men and women and between the Estonian and Swedish cohort were tested for significance ($p<0.05$) using t-test (parametric variables) or Wilcoxon test (nonparametric variables). Relations between variables were assessed by the Pearson (parametric variables) or Spearman (non-parametric variables) correlation coefficient. When comparing psychosocial factors among individuals with and without diagnosed AH, a nonparametric Mann-Whitney U test was used. The chi-square test statistics were used to test statistical independence for categorical data ($p<0.05$). Stepwise regression analysis was performed to determine whether the influence of negative SLEs and/or mastery was related to depressive mood.

Data was analysed using statistical software package SPSS Statistics 20 (2011). (SPSS Statistics, 2011)

AH and risk factors among the 55-year-old cohort in Estonia (Paper II). The Shapiro-Wilk W-test was used to test for normality. T-test (parametric variables) and Wilcoxon test (nonparametric variables) were used to compare groups for differences in continuous variables, and chi-square test, in categorical variables.

To evaluate differences between the hypertensive and non-hypertensive groups, the Mann-Whitney U test (nonparametric variables) and an independent t-test (parametric variables) were used. Correlation analysis was used to find the relationship between different variables ($p<0.05$). Stepwise linear regression analysis was performed to determine how BMI, SLEs or mastery were related to depressive mood.

Bivariate logistic regression analysis was used with AH (yes/no) as the dependent variable and age, gender, education, BMI, current smoking, alcohol consumption, physical activity, and depressive mood as independent variables. In multivariate logistic regression analysis, independent variables with $p\leq0.15$ in bivariate analysis were used (BMI, current smoking, alcohol consumption, depressive mood). Fully adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated. For multivariate logistic regression analysis, $p\leq0.05$ was considered statistically significant.

Data were analysed using statistical software package SPSS Statistics 20. (SPSS Statistics, 2011)

Risk factors for cardiovascular mortality among the 55-year-old Estonian and Swedish male cohort (Paper III). The Shapiro-Wilk W-test was used in testing for normality. Non-normally distributed variables, such as blood lipids, were logarithmically transformed before analysis**.** Variables were given as mean ± standard deviation (SD). Univariate analysis was performed by Student's t-test or the chi-square test. Cox-proportional hazard analysis was used for survival analysis between deceased and alive groups, based on collected data in

the first wave of this study. Comparisons between groups (alive and deceased) regarding mortality were made by log-rank analysis ($p<0.05$).

Data was analysed using statistical software package Statistica 6.0 (Statistica, 2001) and 10.0 (Statistica, 2010).

4.5. Ethics and consent

The study was approved by the local human research ethics committees in Estonia (Tallinn Medical Research Ethics committee, decision no. 95/759, 2007) and in Sweden (Ethics Committee at Karolinska Hospital, Stockholm, 2007). All participants gave informed consent in wave I and II in Estonia and in Sweden. The study was carried out in accordance with the principles of the declaration of Helsinki.

5. RESULTS

5.1. Arterial hypertension, psychosocial factors and personality traits (Paper I)

Prevalence of arterial hypertension after a 13-year follow-up period among 35- and 55-years old adults in Estonia and Sweden

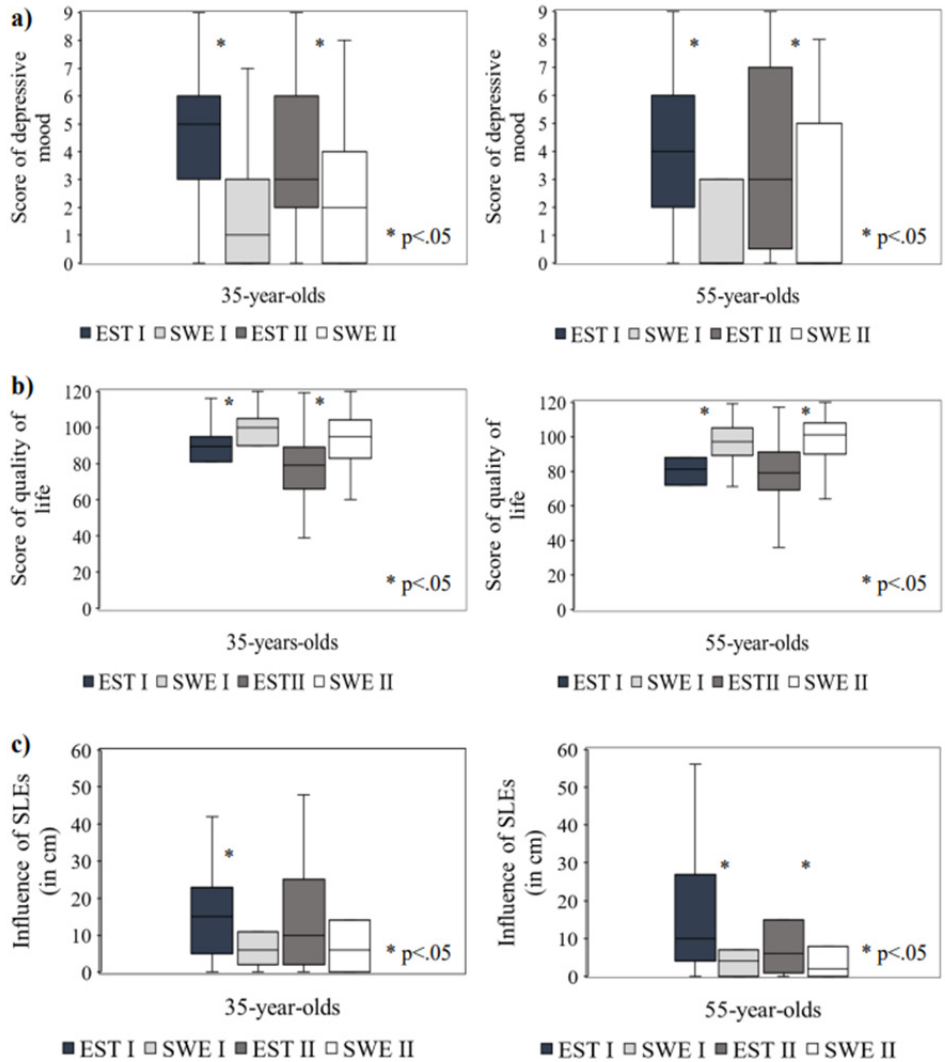
In the second wave of the SWESTONIA study, prevalence of AH among 35-year-olds was 21.4% in Estonia and 4.8% in Sweden ($p<0.001$), among 55-year-olds, 52.3% and 37.3%, respectively ($p<0.001$) (Table 3).

Table 3. The prevalence of AH (n, %, 95% CI) among 35- and 55-year-old cohort in the second wave of the SWESTONIA study

AH	EST			SWE			p-value
	n	%	95% CI	n	%	95% CI	
				35-year-olds			
Yes	15	21.4	12.5–32.9	5	4.8	1.6–11.0	<0.001
No	55	78.6	67.1–87.5	98	95.2	89.0–98.4	
Total	n	100		103	100		
				55-year-olds			
Yes	46	52.3	41.4–63.0	41	37.3	28.2–47.0	<0.001
No	42	47.7	35.0–58.7	69	62.7	53.0–71.8	
Total	88	100		110	100		

Psychosocial factors and personality traits over a 13-year follow-up period among 35- and 55-years old adults in Estonia and Sweden

From psychosocial factors, depressive mood was significantly higher ($p<0.001$) and the total score of quality of life significantly lower ($p<0.001$) among 35-year-old as well as 55-year-old adults in Estonia compared to Sweden in the first and second wave of this study. Both, the number of negative SLEs and their influence (in cm) of the entire length of the scale in the self-reported questionnaire were significantly higher ($p<0.001$) among the 35-year-old as well as the 55-year-old cohort in Estonia compared to Sweden, except among 35-year-olds in the second wave of the study (Figure 6; Table 2, Paper I).



* p-value was assessed between two country in the wave I and II

Figure 6. Comparison of (a) score of depressive mood, (b) score of quality of life and c) influence of SLEs, expressed in cm-s among 35-and 55-year-old cohort in Estonia (EST) and Sweden (SWE) in the wave I and wave II

From subdomains of quality of life among 55-year-old adults, social well-being increased significantly ($p<0.001$) in Sweden, but physical well-being decreased significanlty ($p<0.05$) in Estonia during the follow-up period (Figure 7; Figure 1, Paper I).

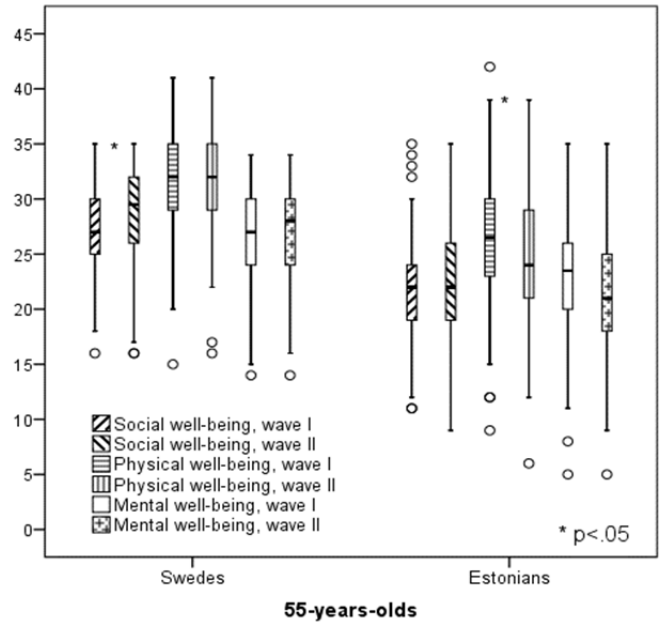


Figure 7. The score of subdomains (social, physical and mental well-being) for quality of life among 55-year-olds in Sweden and Estonia in the wave I and II

From **personality traits**, compared to 35-year-old adults in Sweden, mastery and self-esteem score was significantly lower ($p<0.001$ and $p<0.01$, respectively) in Estonia in both waves. Among 55-year-old adults, in Estonia, mastery score was significantly lower ($p<0.01$) in the first wave, self-esteem score lower in the second wave ($p<0.001$), and TABP score significantly lower in both waves ($p<0.05$ and $p<0.001$, respectively) (Table 2, Paper I).

Estonian 55-year-old adults with higher education had significantly higher mastery score ($p<0.001$) and higher self-esteem score ($p<0.001$). Swedish adults with higher education had higher self-esteem score ($p<0.05$).

Association of psychosocial factors and personality traits with arterial hypertension among the 55-year-old cohort in Estonia and Sweden over a 13-year follow-up period

Among the 55-year-old Estonian cohort with diagnosis of AH, the influence of negative SLEs was significantly higher ($p<0.05$) and mastery score significantly lower ($p<0.05$) compared to adults without a diagnosis of AH (Table 3, Paper I). From negative SLEs, financial problems, personal illness and concerns of sadness dominated among Estonians with AH, compared to those without AH, but not among Swedes in the second wave (Paper I).

In the 55-year-old cohort with a diagnosis of AH, the correlation analysis showed that negative SLEs were correlated with depressive mood ($p<0.01$), mastery score ($p<0.05$) and physical wellbeing ($p<0.05$) in Estonia, but with depressive mood ($p<0.05$) in Sweden (Table 4, Paper I).

Table 4. Correlation coefficients between the influence of negative SLEs and depressive mood, TABP, mastery, self-esteem, and both total score of quality of life and its subdomains among 55-year-olds Estonians and Swedes with a diagnosis of AH in the wave II

Characteristics	EST AH Yes (n=46)	p-value	SWE AH Yes (n=41)	p-value
Influence of negative stressful life events (in total, cm) *versus*				
Depressive mood	0.486	<0.01	0.440	<0.05
TABP	-0.110	0.47	-0.258	0.10
Mastery	-0.447	<0.01	-0.223	0.16
Self-esteem	-0.289	0.06	-0.050	0.76
Quality of life	-0.23	0.12	-0.318	0.07
Social well-being [1]	-0.213	0.16	-0.261	0.06
Physical well-being [1]	-0.348	<0.05	-0.151	0.34
Mental well-being [1]	-0.158	0.29	-0.229	0.09

[1] social, physical and mental well-being are subdomains of quality of life

Based on the linear regression analysis, after adjustment for gender, marital status and educational level, the influence of negative SLEs and low mastery score were related to depressive mood (R Square=0.311, $F^{2;43}$=22.69, p<0.001) among 55-year-old Estonians, but not among Swedes (p=0.07) in the second wave of this study (Paper I).

5.2. Arterial hypertension, psychosocial factors, personality traits, and lifestyle factors (Paper II)

Prevalence of arterial hypertension over the 13-year follow-up study among 55-year-old adults in Estonia

Prevalence of AH was 4.1% at baseline and 53.0% (p<0.001) in the second wave of the study (Table 5).

Table 5. Prevalence of AH (n, %, 95% CI) among 55-year-old adults in Estonia over a 13-year follow-up period

AH	55-year-olds						p-value
	Wave I			Wave II			
	n	%	95% CI	n	%	95% CI	
Yes	9	4.1	1.9–7.7	116	53.0	46.1–59.7	<0.001
No	210	95.9	92.3–98.1	103	47.0	40.3–53.9	
Total	219	100		219	100		

Psychosocial factors, personality traits, and lifestyle factors among the 55-year-old cohort in the first wave compared to the second wave

Compared to the first wave, in the second wave, from psychosocial factors, total score of quality of life and its related subdomains, such as social, physical and mental well-being, were significantly lower ($p<0.001$, $p<0.01$, $p<0.001$, $p<0.001$, respectively) among the 55-year-old Estonian cohort. Depressive mood and the number of negative SLEs were significantly lower ($p<0.001$, $p<0.01$, respectively) in the second wave compared to the first wave (Table 6).

From **personality traits,** both self-esteem and mastery were significantly higher among the 55-year-old Estonian cohort in the second wave compared to the first wave (Table 6).

Compared to the first wave, in the second wave, from **lifestyle factors,** food fat quality score and physical activity (times per month) were significantly higher ($p<0.001$ and $p<0.01$, respectively), but alcohol consumption (g ethanol per week) was significantly lower ($p<0.001$) (Table 6).

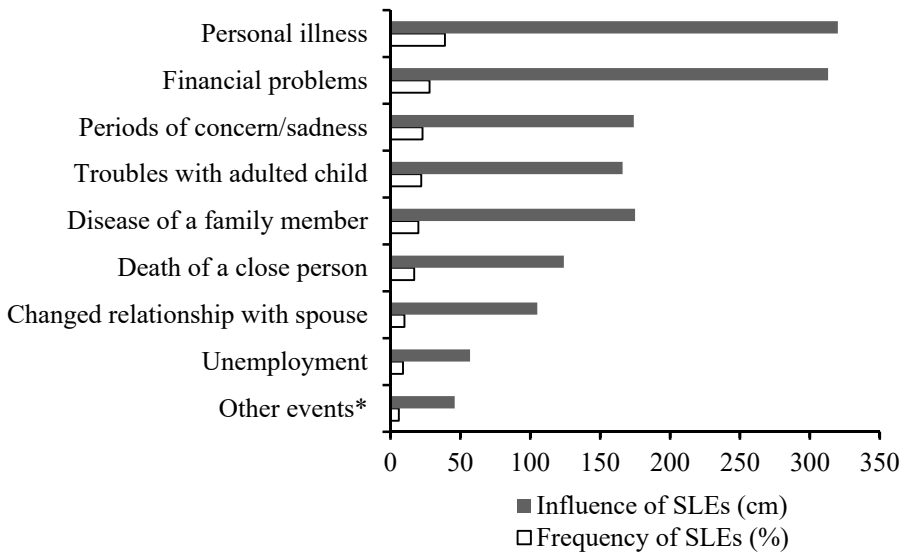
Table 6. Description of psychosocial factors, personality traits, lifestyle factors and health indicators among 55-year-old Estonians in wave I and II

Variables	55-year-olds Estonians				p-value
	Wave I		Wave II		
	Median	Percentiles (25^{th}, 75^{th})	Median	Percentiles (25^{th}, 75^{th})	
Psychosocial factors					
Quality of life	81	(71, 91)	73	(58, 86)	<0.001
Social well-being	22	(19, 25)	20	(16, 25)	<0.01
Physical well-being	27	(22, 31)	23	(18, 28)	<0.001
Mental well-being	23	(20, 27)	20	(16, 24)	<0.001
Depressive mood	4	(2, 6)	3	(2, 5)	<0.001
Number of SLEs	2	(1, 3)	1	(0, 2)	<0.01
Influence of SLE (in cm)	8	(2, 17)	7	(0, 15)	n.s.
Personality traits					
Mastery	16	(14, 20)	22	(20, 24)	<0.001
Self-esteem	24	(22, 27)	30	(28, 32)	<0.001
Lifestyle factors					
Food fat quality score	35	(32, 37)	37	(33, 40)	<0.001
Alcohol (g pure ethanol/week)	50	(0, 105)	35	(0, 85)	<0.01
Physical activity (times/month)	7	(3, 14)	10	(2, 31)	<0.001
Physical activity (min/month)	427	(116, 1260)	600	(60, 1800)	n.s.
Current smoking (%)	25.1	-	13.6	-	<0.001
Health indicators					
BMI (kg/m²)	26	(24, 29)	27	(24, 30)	<0.001
SBP (mmHg)	136	(123, 150)	135	(125, 148)	n.s.
DBP (mmHg)	85	(79, 92)	80	(78, 89)	<0.001

Psychosocial factors, personality traits, lifestyle factors, and health indicators among the 55-year-old Estonian cohort with and without diagnosed AH after a 13-year follow-up period

From psychosocial factors, the median score of total quality of life and physical well-being (subdomain of total quality of life) was significantly lower ($p<0.05$ and $p<0.01$, respectively), but the median of depressive mood and of influence of negative SLEs significantly higher ($p<0.05$ for both) among adults with a diagnosis of AH. No significant differences were found in psychosocial factors between men and women with diagnosis of AH (Table 1, Paper II).

From experienced negative SLEs over the last six months, the largest influence on the 55-year-old cohort with a diagnosis of AH was attributable to personal illnesses (38.8%, extent of influence 319.6 cm) and financial problems (27.8%, extent of influence 313.0 cm). The extent of these two events makes up nearly half of the total influence of all negative SLEs (Figure 8; Supplementary Table 2, Paper II).



* Other events: 'problems with neighbours', 'political events', 'problems at work', 'retirement', 'change of residence';

Figure 8. The influence of negative SLEs (in cm) and frequency of SLEs (%) over the last six month among the Estonian 55-year-old cohort with AH in the second wave.

From personality traits, median of mastery was significantly lower ($p<0.05$) among adults with AH. No signifcant differences were found in personality traits between men and women with a diagnosis of AH (Table 1, Paper II).

From lifestyle factors (nutrition quality score, alcohol intake, physical activity, current smoking), only median of current smoking was significantly lower among 55-year-old adults with AH compared to those without AH in Estonia ($p<0.05$). Compared to women, the median of nutrition quality score was significantly lower ($p<0.01$), but alcohol intake (grams ethanol per week) significantly higher ($p<0.01$) among men with a diagnosis of AH (Table 1, Paper II).

From health indicators, median of systolic ($p<0.01$) and diastolic ($p<0.05$) BP and median of BMI were significantly higher ($p<0.001$ for both) among adults with AH compared to those without AH. Prevalence of obesity was significantly higher among the 55-year-old cohort with AH compared to those without AH ($p<0.001$) (Table 1, Paper II). In the 55-year-old cohort with a diagnosis of AH, prevalence of obesity was 44%.

Association of psychosocial factors, lifestyle factors, and health indicators with AH among the 55-year-old Estonian cohort after a 13-year follow-up period

Based on multivariate logistic regression, after adjusting for all variables in the table, it was found that the obese (BMI $\leq$30.0 kg/m²) 55-year-old cohort had significantly higher odds (OR=4.03, 95% CI 1.63–10.01) to have a diagnosis of AH compared to those with normal weight (BMI $\geq$24.9 kg/m²) (Table 7; Table 2, Paper II).

Table 7. Multivariate logistic regression analysis for AH as dependent variable, and BMI, current smoking status, alcohol consumption, depressive mood as independent variables (OR and 95% CI)

Independent variables	OR	95% CI	p-value*
Depressive mood			
No	1		
Yes	0.84	0.72–1.01	0.27
Current smoking			
No	1		
Yes	1.17	0.57–2.38	0.68
Alcohol consumption			
No	1		
Yes	1.81	0.93–3.54	0.05
BMI category			
Normal weight (BMI≤24.9 kg/m²)	1		
Overweight (BMI 25.0–29.9 kg/m²)	1.45	0.77–2.75	0.25
Obesity (BMI≥30,0 kg/m²)	4.03	1.63–10.01	0.03

*For the multivariate logistic regression analysis $p<0.05$ was considered statistically significant.

5.3. Cardiovascular mortality and its risk factors in the context of non-cardiovascular and all-cause mortality (Paper III)

The total number of deceased men in Estonia and Sweden was 30 of 137 participants (21.9%) in the second wave of the study, 86.7% of them were from the Estonian cohort. From causes of death, 13 (43.3%) belonged to the group of cardiovascular mortality and 17 (56.7%) to the group of non-cardiovascular mortality. In the group of cardiovascular mortality, 76.9% died because of IHD.

Risk factors of cardiovascular, non-cardiovascular and all-cause mortality among the deceased and living 55-year-old male cohort in the second wave of the study in Estonia and Sweden

For cardiovascular mortality, among deceased Estonian and Swedish men the prevalence of current smoking in the baseline (in the first wave) was higher than among the currently living men ($p<0.001$). Also, deceased men had a higher level of IL-6, CRP and plasma glucose in their blood sample compared to living men ($p<0.001$, $p<0.02$, $p<0.02$, respectively) in the first wave of this study (Table 8; Table III, Paper III).

For non-cardiovascular mortality, among deceased men, the prevalence of current smoking was higher ($p<0.001$), and from blood samples, the level of IL-6, CRP and fibrinogen were higher ($p<0.001$, $p<0.01$, $p<0.05$, respectively) in the first wave of this study (Table 8; Table III, Paper III).

For all-cause mortality, among deceased men, the prevalence of current smoking was higher ($p<0.001$), and in blood samples, the level of IL-6, CRP, and fibrinogen was higher ($p<0.001$, $p<0.01$, $p<0.05$, respectively) in the first wave, but there was no statistically significant difference in the level of plasma glucose ($p=0.09$) between deceased and living men in the first wave of the study (Table 8; Table III, Paper III).

Based on Cox proportional hazards regression, for cardiovascular mortality, the hazard ratio (HR) for smoking was 6.4 (95% CI 1.7–23.1) ($p=0.005$) and, for IL-6, was 2.1 (95% CI 1.4–3.1) ($p<0.001$). (Figure 2, Paper III). For IHD mortality (the sub-group of cardiovascular mortality), the HR for smoking was 4.9 (95% CI 1.3–19.1) ($p=0.02$) and, for IL-6, was 2.2 (95% CI 1.4–3.4) ($p<0.001$) (Figure 2, Paper III). For non-cardiovascular mortality, the HR for current smoking was 4.6 (95% CI 1.6−13.2) ($p=0.005$) and, for IL-6, was 1.7 (95% CI 1.4−2.1) ($p<0.001$) (Figure 2, Paper III).

Table 8. Risk factors and cardiovascular, non-cardiovascular and all-cause mortality among the 55-year-old Estonian and Swedish male cohort in the first wave of the study

Characteristic	Cardiovascular mortality			Non-cardiovascular mortality			All-cause mortality		
	Deceased	Alive	p-value	Deceased	Alive	p-value	Deceased	Alive	p-value
No of subjects	13	107		17	107		30	107	
BMI (kg/m²)	26.6±5.9	26.1±3.4	0.66	24.8±3.3	26.1±3.4	0.14	25.5±4.5	26.1±3.4	0.47
SBP (mmHg)	147±21	137±19	0.11	141±19	137±19	0.41	143±19	137±19	0.13
DBP (mmHg)	93±16	90±11	0.51	89±12	90±11	0.71	90±14	90±11	0.92
Current smokers (%)	76.9	28.0	<0.001	70.6	28.0	<0.001	73.3	28.0	<0.001
Plasma glucose (mmol L^{-1})	6.4±2.4	5.4 ±1.1	0.02	5.5±1.1	5.4±1.1	0.70	5.9±2.4	5.4 ±1.1	0.09
Fibrinogen (mg dL^{-1})	3.2±0.8	2.8±0.6	0.08	3.2±1.2	2.8±0.6	0.04	3.2±.0	2.8 ±0.6	0.02
CRP (mg L)	4.1±5.0	2.2±2.3	0.02	4.9±7.2	2.2±2.3	0.003	4.6±6.3	2.2 ±2.3	0.002
IL-6 (ng L)	2.2±1.4	1.2±0.8	<0.001	3.4±3.0	1.2±0.8	<0.001	2.9±2.5	1.2 ±0.8	<0.001
Total cholesterol (mmol L^{-1})	5.5±1.2	5.9±1.1	0.22	5.9±1.1	5.9±1.1	0.91	5.7±1.1	5.9 ±1.1	0.50
Total triglyceride (mmol L^{-1})	1.5±1.1	1.5±0.7	0.78	1.5±1.2	1.5±0.7	0.78	1.5±1.1	1.5 ±0.7	0.72
HDL cholesterol (mmol L^{-1})	1.4±0.6	1.5±0.4	0.60	1.4±0.4	1.5±0.4	0.33	1.4±0.5	1.5±0.4	0.32
LDL cholesterol (mmol L^{-1})	3.4±1.1	3.8±1.0	0.18	3.9±1.3	3.8±1.0	0.64	3.7±1.1	3.8±1.0	0.67

6. DISCUSSION

This research was conducted to give an in-depth overview of the prevalence and risk factors of AH and cardiovascular mortality using a 13-year follow-up study from 1997 to 2010 among 35- and 55-year-old cohorts in Estonia and Sweden. From risk factors, psychosocial factors, personality traits, lifestyle factors and health indicators were analysed.

6.1. Prevalence of arterial hypertension (Paper I, II)

In the second wave of this study, the prevalence of AH was significantly higher among the 35-year-old as well as the 55-year-old cohort in Estonia than in Sweden. In the 35-year-old cohort, AH was diagnosed in one fifth of Estonians and in a few Swedes, but in the 55-year-old cohort, among more than half of Estonians and more than one third of Swedes. These results are in line with data of the WHO, whereby the prevalence of AH was higher in Estonia than Sweden (WHO, 2022h).

According to worldwide literature, the global burden of AH (SBP≥140 mmHg) has increased substantially between 1990 and 2015, even after controlling for changes in population ageing (Forouzanfar et al., 2017). While globally the age-standardized prevalence of AH increased in 2000−2010, then in high-income countries it decreased by 2.6% during these years (Mills et al., 2016).

Estonia belongs to higher income countries (based on GNI per capita) since 2006 (World Bank, 2022a). Despite prevalence of AH decreasing somewhat in high-income countries from 1990 to 2019 (Zhou et al., 2021), it has still higher among Estonians compared to Swedes during 1998−2018, especially among Estonian men (WHO, 2022h). Based on a systematic review, higher GNI per capita induces a better opportunity for higher living standard (Wirayuda & Chan, 2021). On the other hand, economic growth (belonging to high income countries) will not automatically lead to improved public health (Lange & Vollmer, 2017), due to the income inequality causes poverty between different population groups and reduces the chances of attaining a higher standard of living (Wirayuda & Chan, 2021).

The main causes of the difference in the prevalence of AH seem to be associated with different historical and socioeconomic development in Estonia and Sweden. In a systematic review based on 135 population-based studies from 90 countries (including Estonia and Sweden), that the prevalence of AH from 2000 to 2010 was affected by the socioeconomic status of countries at the time (Mills et al., 2016). At the same time, AH is currently the leading cause of morbitidy and mortality in adulthood in high income countries as well. Based on a systematic analysis of the Global Burden of Disease Study, IHD and stroke, as a complications of uncontrolled AH, were the most frequent causes of DALYs among individuals aged 50 and more from 1990 to 2019 (Abbafati et

al., 2020). AH is the syndrome with a multifactorial aetiology (Oparil et al., 2018), therefore the assessment of total cardiovascular risk is an important for the individuals with AH, (Williams et al., 2018).

Based on data from a sample of 55-year-old and older adults from twelve European countries reported that a large proportion of patients achieving treatment goals for risk factors of CVDs remained at high individual risk level due to differences in patients' clinical and socioeconomic characteristics, and in the sustainability of healthcare systems (Banegas et al., 2011). The management of risk factors for AH, preventing the development of CVDs, is crucial (Williams et al., 2018), using a combined strategies (e.g. screening, control, digital devices well-organised health care, public health policies) (Parati et al., 2023).

6.2. Risk factors of arterial hypertension (Paper I, II)

Psychosocial factors in Estonian and Swedish 35- and 55-year-old cohorts (Paper I, II)

From psychosocial factors, both the number of negative SLEs and the influence median score (expressed in cm) of SLEs were significantly higher among 35-year-old as well as 55-year-old cohorts in Estonia compared to Sweden in both waves, except among 35-year-old Estonians in the second wave of this study. The latter finding could be explained by the circumstance that at the age of 48 (35-year-old cohort in the second wave) a lower number of negative SLEs usually occur, due to more stable social roles (e.g. personal and work life, an absence of chronic diseases). Secondly, significantly lower response rate in the cohort of 35-year-old Estonians in the second wave of the study may affect the relevant comparison of the two countries.

Similarly, the score of depressive mood was significantly higher, but the score of quality of life significantly lower among 35-year-old, as well as 55-year-old adults in Estonia, compared to Sweden, in both waves of the study.

From the subdomains of quality of life (social, physical and mental well-being) among 55-year-old adults, compared to the first wave, in the second wave of the study the median score of social well-being was significantly higher in Sweden, but the median score of physical well-being was significantly lower in Estonia. Lower physical well-being among 55-year-old Estonians in the second wave of the study could be explained by the fact that significantly more study subjects had a diagnosis of AH in Estonia than in Sweden in the second wave, and adults with a diagnosis of AH could be less physically active and/or more obese, and more under stress. This finding is comparable with the meta-analysis, where a two times lower score in the physical and mental subdomains of quality of life was found among study subjects with AH compared to subjects without AH (Trevisol et al., 2011).

In this study, significantly higher the median score of depressive mood among 35-year-olds as well as 55-year-olds in Estonia than in Sweden throughout the follow-up period can be attributed to the different level of quality of life and its

subdomains (e.g. social well-being, mental well-being). During the follow-up period of the present study, a global economic crisis from 2007 may have caused a higher level of depressive mood in Estonia.

According to the results of the European Social Survey (including Estonia and Sweden), countries with a higher GDP per capita before the global economic crisis exhibit a lower level of depressive mood compared to other countries. For example, an average rate in the depressive scale was 6–7 points in Estonia, but 4.4–5 points in Sweden during 2006–2014 for all persons aged 15 and over (Reibling et al., 2017). Also, the Survey of Health, Ageing and Retirement (SHARE) survey showed that, in the age-group 60–85, the risk for depressive mood was lowest in Northern Europe (e.g. Sweden) and highest in Eastern Europe (e.g. Estonia) due to differences in their financial situations (Schmitz & Brandt, 2019).

Differences in all these psychosocial factors between Estonia and Sweden could be explained also by different living standards in these countries. In Estonia, rapid economic changes have taken place after re-independence from the Soviet Union in 1991. The rank of HDI, which is manifested in a long and healthy life, being knowledgeable and having a decent standard of living, confirmed the improvement of the situation in Estonia over the past twenty years. In more detail, the rank of HDI showed 13-fold difference between Estonia and Sweden in 1998, but a three-fold difference in 2010 (WHO, 2022c).

Moreover, worldwide literature confirmed that quality of life is higher in welfare state regimes (e.g. Sweden) than in the countries in Eastern Europe (e.g. Estonia), due to poorer socioeconomic conditions (Conde-Sala et al., 2017; Niedzwiedz et al., 2014) regarding the baseline level since the mid-1990s and later (e.g. in GNI per capita) (UNDP, 2022b). The internationally used quintile share ratio (a measure of the inequality of income distribution) showed the difference between Estonia and Sweden. In 2011, this indicator was 5.4 in Estonia, but 3.6 in Sweden (Statistics Estonia, 2013). Although the income of participants has not been asked in this study, the income quintile share ratio mirrors the difference in income between Estonia and Sweden.

Notwithstanding, the results from the European Quality of Life Survey among new European Union member states confirmed that the economic situation (’difficulty in making ends meet‘) and social control (’agree that life has become too complicated‘) has improved by half in Estonia in 2004–2007 (Abbott & Wallace, 2014). By contrast, the findings of this study showed that the median score of social well-being was at the same level among 55-year-old Estonians in both study waves, reflecting a stability in variables such as family, housing, working and free time.

Psychosocial factors in Estonian and Swedish 55-year-old cohort with and without a diagnosis of AH

From psychosocial factors, adults with a diagnosis of AH in Estonia, but not those in Sweden, demonstrated a significantly higher influence of negative SLEs compared to those without AH, though no difference was found in the total

number of single negative SLEs between hypertensive and non-hypertensive groups in Estonia and Sweden. Regarding the type of negative SLEs, financial problems, personal illness and periods of concern/sadness were prevalent among 55-year-old Estonians in the second wave of this study. In contrast to Estonians, no dominant SLEs were found among 55-year-old Swedes in the second wave. From nine negative SLEs, four (periods of concerns/sadness, changes in the relationship with spouse, disease of a close family member, and other events, e.g. political events, problems at work, problems with a neighbour), reached a relatively similar frequency distribution among Swedes. This finding may be associated with the lower median score of negative SLEs among Swedes with AH compared to Estonians with AH in the second wave.

The hypothalamic-pituitary-adrenocortical axis (the neuroendocrine system) is especially reactive to psychosocial stressors and plays an important role in linking long-term stressor exposure to disease throughout the life-course (Chida & Hamer, 2008; Cohen S. et al., 2019; Herman, 2013; McEwen, 2007). In this study, clinical tests to investigate the influence of psychosocial stress on the neuroendocrine system among study subjects have not been performed. However, compared to the cohort without AH, the cohort with AH experienced a significantly higher influence of negative SLEs. This finding may indicate that prolonged brain activation by psychosocial stress had caused changes in the hypothalamic-pituitary-adrenocortical axis, causing AH. According to previous studies, the influence of negative SLEs causes a considerable extra burden to somatic health (Albus et al., 2019), triggering a neurobiologically driven stress reaction and contributing directly and/or indirectly to AH (Mancia & Grassi, 2014; Von Känel, 2012).

In addition, the influence of negative SLEs among the Estonians with a diagnosis of AH compared to those without AH pointed to the likelihood of an initial problem, such as SES, which can be the one of crucial causes of psychosocial stress among Estonians, but not among Swedes. Based on the meta-analysis, a lower level of SES is associated with higher values of BP, although the association was the strongest for those with the lowest level of education (Leng et al., 2015).

In the comparison of the study subjects with and without AH in Sweden and in Estonia, no difference was found in the total score of quality of life and in the subdomains of quality of life, and in depressive mood. The main reason for this could be the quite small sample size in the comparison of adults with and without AH by countries. In contrast, in the Estonian substudy with the bigger sample size, a significant difference in quality of life and depressive mood between the hypertensive and non-hypertensive group was found.

In more detail, the medians of total score of quality of life and its subdomain, physical well-being, were significantly lower, but the median of depressive mood significantly higher among 55-year-old Estonians with a diagnosis of AH than among those without this diagnosis. These findings are in line with the results of a meta-analysis, whereby hypertensive individuals had nearly three times higher incidence of psychosocial stress compared to normotensive

individuals (Liu M. Y. et al., 2017). The impact of psychosocial stress (especially from negative SLEs) on the cardiovascular system has been affected by a response of the sympathetic nervous system, in which a release of catecholamines leads to increased BP, heart rate, and cardiac output (Pedersen et al., 2017). The neurohormonal system is responsible for maintenance of cardiovascular homeostasis (Mancia and Grassi, 2014).

In world-wide literature it has been found that coexistence of AH, chronic psychosocial stress and particularly non-adaptive response to stress (including depressive mood) are significant factors that probably cause sustained elevation of BP, leading to AH (Cuffee et al., 2014; Esler, 2017; Spruill, 2010). At the same time, AH, as a chronic disease, was associated with substantially reduced quality of life (Carris & Smith, 2015; Zygmuntowicz et al., 2012). This evidence-based knowledge is in line with the results of this study.

Personality traits in the Estonian and Swedish 35- and 55-year-old cohort (Paper I, II)

From personality traits, compared to 35- and 55-year-old adults in Sweden, the median score of mastery was significantly lower in Estonia in both waves of this study, except among 55-year-old adults in the second wave. Moreover, the findings of this study showed that 55-year-old Estonians, but not Swedes, with higher education had significantly higher mastery score. No difference was found in mastery by education among 35-year-old Estonians and Swedes. Based on evidence-based knowledge, a higher level of mastery has been found among individuals with a higher level of education (Dalgard et al., 2007; Drewelies et al., 2018; Mitchell et al., 2018).

Differently from mastery, the median score of self-esteem varied more within the two waves of this study. In detail, compared to Swedes the median score of self-esteem was significantly lower among 35-year-old Estonians in the first wave, and among 55-year-old Estonians in the second wave of this study. At the same time, compared to 35-year-old Swedes, the same age Estonians had significantly higher self-esteem in the second wave only.

According to published literature, mastery and self-esteem, known as personal resources, are two important dimensions of self-concept, referring to individual perception of ability to have control over events that importantly affect a person's lifes and the judgements regarding own self-worth, respectively (Au, 2017; Pearlin & Schooler, 1978). Based on worldwide literature (Au, 2017; McKean Skaff, 2007; Pearlin et al., 1981; Thoits, 2010), a generally lower level of mastery and self-esteem among Estonians compared to Swedes refers to a poorer perception of control in own life. A lower level of mastery reduces feelings of competency and self worth in everyday situations, causing further decline in the level of mastery and self-esteem (Pearlin & Schooler, 1978; Thoits, 2010). This diminishes the neural responses to threat and inhibits an individual from coping (Slagsvold & Sørensen, 2013; Taylor & Stanton, 2007).

In this study, the median of TABP was significantly lower among 55-year-old, but not among 35-year-old Estonians, compared to Swedes in the first and

second waves. It is important to reiterate that higher values illustrate less TABP, thus, compared to 55-year-old Swedes, Estonians had more TABP. In general, the individuals who possess TABP are at a higher risk of psychosocial stress (Chen et al., 2019) and of CVDs (Lohse et al., 2017). The prevalence of TABP is higher in the non-healthy population of middle-aged men than in the healthy one (Miller et al., 1991), and individuals with TABP show a difference in the control of the hypothalamic-pituitary-adrenal axis (Myrtek, 1995). In addition, the TABP construct is only important regarding health (e.g. injuries), as it pertains to the hostility component (Shi et al., 2013). In the present study, the instrument of TABP contained more time urgency and impatience than hostility component.

Personality traits in the Estonian and Swedish 55-year-old cohort with and without a diagnosis of AH

From personality traits, the median score of mastery was significantly lower among 55-year-old Estonian adults with a diagnosis of AH compared to those without this diagnosis. No difference was found in mastery among 55-year-old Swedish adults.

According to the substance of mastery (the self-belief, the ability to shape and exert influence over life circumstances) (Pearlin, 2010; Pearlin et al., 1981), good health status without chronic diseases can strengthen an individual's perceived mastery by letting the person believe that she/he has the inner power to be able to better cope in life, e.g. with chronic illness. Moreover, worldwide literature has described a positive link between higher level of mastery and lower risk for CVDs, including AH (DuBois et al., 2015; Infurna et al., 2018; Roepke & Grant, 2011). Based on 6-year longitudinal data from the US, with nearly two thousand participants, a study showed that higher level of mastery was associated with lower level of BP, fewer chronic conditions, better self-rated health and effective health behaviour (Drewelies et al., 2018).

In contrast to the aforementioned, an occurence of chronic health problems (e.g. hypertension, heart disases) on both an individual, and couple-level had a negative implication for level of mastery in a longitudinal study among middle-adulthood couples from three study waves (Polenick et al., 2022). In addition, based on published articles, perceived deterioration in personal health status regarding aging causes the feeling that chronic disease is permanent (Infurna & Gerstorf, 2014), leading to dynamic changes in mental and physicial health in the second part of the adult lifespan (Infurna et al., 2018; Infurna & Okun, 2015). This evidence is consistent with the finding of the current study among 55-year-old Estonians, whereby mastery was lower in the group with AH than in the group without AH.

Based on the clinical consensus statement from the European Association of Preventive Cardiology, the direct experience of mastery increases an individual's self-efficacy in coping with CVDs, including AH. Hence, it is important to enhance self-efficacy (including mastery) in CVD self-management programmes (Pedretti et al., 2023). Additionally, several studies have shown that mastery

can be either, a mediator leading to negative health outcomes, or a moderator increasing or reducing the harmful effects of negative SLEs (MacKinnon & Luecken, 2008; Nicolaisen et al., 2018).

The finding of this study showed that there was no difference in the median score of mastery among Swedes with AH compared to those without AH, and this can point to external factors as determining an individual's life circumtances, e.g. lifestyle habits, and better socio-economic status and/or general living standard. For example, in a research paper based on nine studies, it was found that a relationship between AH and socioeconomic status exists, manifested in a consistent and statistically significant increase in the odds (approximately two-fold) of AH regarding lower subjective SES (Tang et al., 2016). Though socioeconomic status had improved over the follow-up period in Estonia, the difference between Estonia and Sweden in key dimensions of human development by HDI still exists (UNDP, 2022b).

Differently from mastery, no difference was found in self-esteem of 55-year-old Estonians and Swedes with and without a diagnosis of AH in the second wave of the present study. In worldwide literature it is found that self-esteem increases up to middle adulthood, reaching a peak at the age of 60 years, and then declines (Orth et al., 2015). Although, the participants of the present study were 13 years older after the follow-up period, no such association was found between age and self-esteem. In addition, self-esteem can be influenced by different other factors. According to earlier studies, self-esteem is associated with a satisfaction with relationships, health, household income (Orth et al., 2015), social functioning ability (Taylor & Stanton, 2007), and self-regulative abilities throughout the life-course (Wagner et al., 2014).

Similarly to self-esteem, no difference was found in TABP among 55-year-old Estonians and Swedes with and without a diagnosis of AH in the second wave of this study. Since the 1970s, when the concept of TABP was introduced, TABP has been associated with a twice higher risk for the development of CHD/IHD, especially among 45–64-year-old men and women (Haynes, 1980). Also, later studies have demonstrated the same association (Chida & Steptoe, 2009; Du et al., 2016).

In worldwide literature, a link between TABP (regarding time-consuming subcomponent) and AH was found in a few studies only, whereby TABP was associated with increased reactivity of BP (Chida & Hamer, 2008; Munakata et al., 1999) and TABP occurs more among hypertensive individuals compared to normotensives individuals (Sanz et al., 2007). The last studies in the field of TABP have focused on the investigation of the hostility component, which has demonstrated a positive association with BP (Chen et al., 2019), but in this study, only the time-consuming subcomponent of TABP was explored.

Lifestyle factors in the Estonian 55-year-old cohort (Paper II)

In the cohort of 55-year-old Estonians, from lifestyle factors, both the median score of nutrition and frequency of physical activity (times per last four weeks) were significantly higher in the second wave than in the first wave of this study.

It is important to reiterate that a higher nutrition score indicated a higher intake of unsaturated fats in the second wave. At the same time, frequency of physical activity revealed that the study subjects were physically active only two times a week, on average. Although no difference was found in the duration of physical activity (minutes per last four week), the physical activity of participants in the second wave met the recommended minimum. Based on WHO guidelines, physical activity should, on average, be half an hour of moderate-intensity aerobic exercise on five to seven days a week (at least 150 minutes) for middle-aged and older adults (WHO, 2020).

In additon, the prevalence of current smoking and alcohol consumption was significantly lower among the 55-year-old cohort in the second wave than in the first wave. For instance, the prevalence of current smoking decreased by half among 55-year-old Estonians. It may be reasonable to assume that smoking cessation occurred due to a recommendation to live healthily. Both primary health care and occupational health specialists emphasize the need to quit smoking in order to reduce risk for CVDs. Based on the previous studies, different kinds of lifestyle factors (healthy nutrition, adequate physical activity, no or minimal alcohol consumption, non-smoking) are of crucial importance both in primary and secondary prevention of CVDs, including AH (Piepoli & Villani, 2017).

Population- and individual-based interventions for primary and secondary AH prevention in Estonia are needed. Based on the WHO report, from the risk factors of AH, the main focus of populaton intervention in Estonia has been on the consumption of tobacco and alcohol, but less attention has been paid to nutrition (including excess body weight) and physical activity. Management of all risk factors, an intersectoral cooperation and a political commitment to improving health are two of the greatest challenges faced by the health care system in Estonia (Lai et al., 2015).

Lifestyle factors in the Estonian 55-year-old cohort with and without a diagnosis of AH

From lifestyle factors, only prevalence of current smoking was two times lower among adults with AH compared to those without AH. Based on worldwide literature, tobacco smoking is an established risk factor for AH among men (Gao et al., 2017) and women (Bowman et al., 2007). Current smoking is an independent risk factor for AH, accelerating the development of atherosclerosis (Virdis et al., 2010), and leading to tissue damage and the alteration of antithrombotic and prothombotic factors (Ambrose & Barua, 2004; Csordas & Bernhard, 2013). Regarding current smoking, the European guidelines for the management of AH emphasize that smoking cessation is the single most effective measure for the prevention of AH and other CVDs (Williams et al., 2018).

No differences were found in physical activity between 55-year-olds with AH and without AH in the second wave of this study. However, the average level of monthly physical activity was below the recommended minimum level. Based on worldwide literature, individuals with a diagnosis of AH, are advised to engage in at least 30 min of moderate-intensity aerobic training (e.g. walking,

swimming) on 5–7 days per week (Borjesson et al., 2016; Pelliccia et al., 2021) in order to reduce the risk of CVDs progression (Pescatello et al., 2019).

In conclusion, regarding lifestyle factors, it is important to reiterate that healthy lifestyle is the cornerstone of the prevention and/or treatment (alongside farmacological treatment) of AH, comprising cardioprotective food (restricted amount of saturated fatty acid and trans fat, larger amount of fibre, fruit and vegetables per day), moderate physical activity, no smoking, low-risk alcohol consumption, and within the normal range of BMI (Piepoli & Villani, 2017; Threapleton et al., 2013). These activities require long-term, centrally co-ordinated, multidisciplinary lifestyle-based interventions at the individual and population levels across the lifespan. In Estonia, we have sufficient room for improvement in well-coordinated lifestyle interventions at the population and individual level.

Moreover, Estonia could proceed from the best practices of neighbouring countries. For instance, in Sweden, the Västerbotten Interventional Programme was integrated into routine health care with the individual counselling, allowing it to reach everyone in the target population (at the age of 40, 50 and 60). As a result of this programme, the prevalence of AH significantly dropped from 43.8% to 36.0% among men and 37.6% to 27.5% among women between 1990–2010 through increased awareness, treatment, and control of BP (Ng et al., 2012). Another best practice is from Finland (the North-Karelia Project), where both a population strategy and a personal (patient-based) high risk strategy to reduce risk factors of CVDs were used. This strategy has been very successful, showing a decline in IHD mortality in the middle-aged population by 84% from 1972 to 2014, of which two-thirds was explained by changes in risk factors (including decreased BP, healthier nutrition) (Vartiainen, 2018).

Health indicators in the Estonian 55-year-old cohort (Paper II)

In the cohort of 55-year-old Estonians, no significant differences were found in the values of BP between the two waves of this study. At the same time, BMI was significantly higher in the second wave than in the first wave of this study. The median score of BMI had increased by one unit (kg/m²). Based on the SHARE survey (aged 50 and more) it was found that the prevalence of BMI ≥30 kg/m² increased by 1.6 units among10 European countries (without Estonia) during 2005–2015, but the prevalence of obesity was significant in Germany only (Peralta et al., 2018).

Health indicators in the Estonian 55-year-old cohort with and without a diagnosis of AH.

In the second wave of the present study, the median values of BP were within the high normal (BP 130−139/85−89 mmHg) range among Estonians with AH, and within normal range (excluding SBP) among Estonians without AH by ESC/ESH Guidelines for the management of AH (Williams et al., 2018), but the median values of BP (both SBP and DBP) were significantly higher among adults with AH. An examination of the study subjects has not been performed

(e.g. measurement of BP) in the second wave of this study. In view of the latter fact, it is important to assess critically the values of self-measured BP, due to possible errors between different BP monitors used for measuring BP at home.

If a blood pressure monitor is sold by an accepted seller (e.g. a pharmacy), then, based on worldwide literature, there should be no significant differences in BP values measured at home or in the office (in the clinic), but, compared to office BP monitoring, self-monitoring BP at home detects the white-coat and masked hypertension phenomena (Parati et al., 2010; Stergiou & Bliziotis, 2011). Though, AH is defined as the values of BP at the physician are ≥140/90 mmHg and at home BP ≥135/85 mmHg (Williams et al., 2018). Moreover, compared to attended (by a doctor) BP measurement, during unattended (patient alone) BP measurement the cardiovascular and neural sympathetic response to the alerting reaction elicited by the measurement are nearly absent (Grassi et al., 2021).

The results of this study showed that in the cohort with a diagnosis of AH, prevalence of obesity (based on BMI) was 44%, which was twice as high as in the cohort without AH. Published literature has shown that obesity significantly worsens cardiovascular functioning (Barrios et al., 2010). In addition, co-existing obesity and AH cause both vascular and systemic inflammation, damage of endothelium, hyperinsulinaemia, dysbalance of neurohormonal activity and contribute to metabolic syndrome and microalbuminuria (Cohen J. B., 2017; Guerra et al., 2011; Neeland et al., 2018). Unfortunately, in the present study, fat distribution of the body was not assessed, although it is well known that increased abdominal fat (visceral adiposity) is associated with greater risk of AH due to increased overall blood volume and salt sensitivity (Haberka et al., 2018; Hall et al., 2015).

Association between psychosocial factors and personality traits in the Estonian and Swedish 55-year-old cohort with AH (Paper I)

In this study, after adjustment for gender, marital status and educational level, a linear regression model showed that the influence of negative SLEs and a low level of mastery were significantly related to depressive mood among 55-year-old Estonians. In more detail, any increase in the influence of negative SLEs increased depressive mood. Although, among Swedes with a diagnosis of AH, the influence of negative SLEs was correlated with depressive mood, then no significant association was found in linear regression analysis. The finding of the present study reflected the well-known bidirectional effect between psychosocial stress and its symptomatology (Di Pilla et al., 2016; Weber et al., 2013).

Based on evidence-based literature, the occurrence of negative SLEs leads to depressive reactions in the organism, expressed in depressive mood, and, in reverse, causing further SLEs, e.g. health problems (Hammen, 2016). In addition, depressive mood is common in middle-aged high-risk individuals (e.g. renal disease, type 2 diabetes or other established CVDs) with AH, even without comorbities, if the person is aware of his/her diagnosis of AH (Rantanen et al., 2018). Moreover, the findings from the present study are consistent with findings of other studies (Aneshensel & Avison, 2015; Au, 2017; Pearlin, 2010)

that the elevated level of negative SLEs has a direct effect (as a mediator), decreasing significantly the level of mastery and increasing the occurrence of depressive symptoms among Estonians, but not among Swedes. It is known from worldwide literature that higher level of mastery points to better management of psychosocial stress, reflecting a higher level of self-belief, which ensures control and coping in person's life (Pearlin, 2010; Pearlin & Schooler, 1978; Thoits, 2010).

According to the results of this study, among the 55-year-old Estonians with a diagnosis of AH, financial problems and personal illness were the most prevalent events. This finding indicates that rapid socioeconomic changes to achieve a higher standard of living could cause cumulative psychosocial stress for Estonians. Based on previous studies, a higher level of psychosocial stress is reflected in higher self-reported negative SLEs (Ben-Zur & Michael, 2020; Marum et al., 2014; Pearlin et al., 1981). A higher number of negative SLEs causes more depressive mood in adulthood (Musliner et al., 2015; Pearlin et al., 1981; Pemberton & Fuller Tyszkiewicz, 2016; Romanov et al., 2003). Moreover, individuals who experienced financial hardship at some point had a higher risk of onset of mental health problems than those never exposed to financial hardship (Crowe et al., 2016; Kiely et al., 2015).

Using the model that was adapted from McKean Skaff (McKean Skaff, 2007), two overriding influences, such as socioeconomic influences (e.g. education, income, historical period) and lifespan influences (e.g. life experiences) affect the remaining three interactive components (psychosocial factors, personality traits and health). As discussed previously, discrepancies in both socioeconomic and lifespan influences due to different historical development between Estonia and Sweden have affected the level of negative SLEs and depressive mood, reflected in person-based quality of life. In addition, mastery, as an important personality trait, mediates coping with psychosocial stressors. The higher and more prolonged the exposure to various psychosocial factors, the higher the probability to have poorer health outcome, e.g. diagnosis of AH.

Association of psychosocial factors, lifestyle factors, and health indicators with AH in the Estonian 55-year-old cohort (Paper II)

In the Estonian substudy, a multivariate logistic regression model including potential predictors of AH showed that obese (BMI≥30.0 kg/m2) study subjects had four times higher odds to have AH than those with normal weight. No association with AH was found for current smoking (smoking one or more times per week), alcohol consumption (grams of ethanol per week), and depressive mood among 55-year-old study subjects.

The findings from the present study were compatible with the results of a meta-analysis based on 57 prospective cohort studies, which found that obesity increases relative risk for AH by two times (Jayedi et al., 2018). Numerous studies have shown that obesity is an established risk factor for AH (Cohen J. B., 2017; Haberka et al., 2018; Oda & Kawai, 2010; Shihab et al., 2012), accounting for more than two thirds of cases of AH (Hall et al., 2015).

Results of a longitudinal study have demonstrated that an increase in BMI by one unit increases the risk for elevated BP by two and a half procent (Bombelli et al., 2011). Based on the findings of this study, among 55-year-old Estonians, the median of BMI increased by one unit over the 13-year follow-up period. According to published research, those with higher BMI have higher levels of BP and deterioriation of cardiac profile (e.g. left ventricular hypertrophy), leading to IHD (Barrios, 2010).

Although the study subjects were 13 years older in the second wave of the study, no statistically significant association was found between age and AH in this study. It is important to reiterate that the bivariate logistic regression analysis investigated all potential predictors of AH, including age. The finding of this study regarding age was different from other evidence-based literature, whereby the prevalence of AH increases with age (Harvey et al., 2015) due to endothelial dysfunction and increased vascular stiffness and inflammation (Giannoni & Masi, 2018; McEniery et al., 2007).

The findings of this study concerning the association of psychosocial factors, lifestyle factors, and health indicators with AH did not corroborate the findings reported in most studies, whereby current smoking (Jatoi et al., 2007; Pirie et al., 2013; Yusuf et al., 2004), alcohol consumption (Briasoulis et al., 2012; Messerli et al., 2019), depressive mood (Di Pilla et al., 2016; Rantanen et al., 2018; Saboya et al., 2010) increased the risk for the development of AH. Based on the results of a longitudinal study, the risk for development of AH increased with repeated experience of depressive episodes over a long time, which appeared to become more apparent at an age ≥55 years among men and women (Nabi et al., 2011).

In order to improve management of AH in Estonia some activities have been initiated. Since 2006 the Primary Health Care Quality System was implemented to more effectively monitor individuals with chronic conditions, including patients with AH at grades 1, 2 or 3 (Quality System, 2022). In 2015, in collaboration with the World Bank, the Estonian Health Insurance Fund and Estonian Association of Family Physicians created the evidence-based model 'Enhanced Care Management' in Estonia. The purpose of this pilot project was to assess needs and to plan the treatment of risk patients in a multidisciplinary team. In 2017, the initial results of the project showed that this model is applicable to Estonia. The pilot project has lasted until the current time, involving more and more general physicians (Enhanced Care Management, 2022). The latter project includes a lifestyle-based intervention. According to the result of the SWESTONIA study, psychosocial factors and personality traits, besides lifestyle factors, require more attention by health care workers in the treatment of patients with AH, using individual, group- and population-based approaches.

6.3. Cardiovascular mortality and its risk factors (Paper III)

Cardiovascular mortality in a 55-year-old Estonian and Swedish male cohort in the second wave of this study

The number of cardiovascular deaths over the 13-year follow-up period was significantly higher in Estonian than Swedish men. In more detail, almost every third man enrolled in the initial study in Estonia compared with every 17th man in Sweden deceased due to cardiovascular diseases over the 13-year follow-up period, showing a sixfold difference between the two countries. In total, in the observed Estonian and Swedish male cohorts almost half died due to cardiovascular diseases; of them, two thirds died because of IHD.

This finding is consistent with published literature that death rates from CVD, including IHD are higher in Eastern Europe than in Northern Europe in 1980−2010 (Løgstrup & O'Kelly, 2012). Across the European Union as a whole, the age-standardized mortality from IHD per 100 000 men has declined in Sweden by two thirds and in Estonia by nearly half in 1980−2009. Compared to other Baltic countries, in Estonia the decline in IHD mortality has been better, e.g. in Latvia (by one third), and in Lithuania (by one tenth) (Nichols et al., 2013).

Generally, based on worldwide literature, mortality from CVDs has been a leading cause of death globally and across Europe over the last three decades (Moran et al., 2014; Naghavi et al., 2015), accounting for nearly half of all causes of death in Europe (Løgstrup & O'Kelly, 2012). IHD by itself has been the leading cause of death among CVDs in Europe (Townsend et al., 2016). On average, one in five men died from IHD in Europe, based on statistics from the end of the 2000s (Løgstrup & O'Kelly, 2012). In this study, among a 55-year-old male cohort, IHD as the cause of death was higher than the European average, and it is important to reiterate that the vast majority of deceased men were from Estonia.

According to data of the WHO, higher mortality among Estonian men compared to Swedish ones has remained, although mortality from CVD has decreased, especially among Estonian men. For instance, SDR from IHD was nearly seven times higher among Estonian men compared to Swedish men in 1998, and three times higher in 2010, and about two times higher in 2016, respectively (WHO, 2022f). Over ten years (2012 *vs* 2002) the age-standardized mortality rate from CVDs has declined by one third among Estonian as well as among Swedish men.The age-standardized mortality rate from IHD has declined by nearly two-fifths in both countries (Townsend et al., 2016). This trend indicates an improvement in mortality rate from CVDs, especially among Estonians, but a worse initial position of Estonia in mortality from CVDs in the early 2000s, reflected in the result of this study, whereby the discrepancy of SDR between Estonian men and Swedish men is still apparent.

Based on worldwide literature, the difference in mortality between Estonia and Sweden could be explained as a consequence of political development (e.g. a stagnation period due to belonging to the Soviet Union in Estonia). The same opinion has been presented in other published articles, that higher mortality in

Eastern European countries compared to Western European countries could be explained by the transition to a market economy after re-independence in 1991 (Brainerd & Cutler, 2005; Ezzati et al., 2015), and by differences in the management of lifestyle factors and the quality of treatment of CVDs in 1990−2013 (Moran et al., 2014; Roth et al., 2015).

Risk factors for cardiovascular mortality in a 55-year-old male cohort in Estonia and Sweden in the second wave of the study

In the present study, smoking was identified as significant risk factor for cardiovascular, non-cardiovascular, as well as for all-cause mortality among Estonian and Swedish 55-year-old men over a 13-year follow-up period, as the prevalence of current smoking in the first wave was significantly higher among deceased men than living men. It is remarkable that nearly two fifths of male smokers died, compared to nearly one third of male non-smokers, over the follow-up period, and that half of smokers died from CVDs. The findings of the present study are consistent with other research that current smoking is a strong risk factor for both premature cardiovascular (Mons et al., 2015), as well as for all-cause mortality (Agudo et al., 2012; Gellert et al., 2012; Iso et al., 2005).

Although, the consequences of current smoking on the organism have not been investigated in this study, it is a well-documented fact that current smoking causes smoking-related atherosclerosis by enhancing oxidative stress (Barua & Ambrose, 2013; Virdis et al., 2010), resulting in atherosclerotic cardiovascular disease (Mucha et al., 2006; Pan et al., 2015). As discussed previously, these changes lead to premature death and to loss of daily adjusted life-years, especially in men (Reitsma et al., 2017).

Smoking must be prevented, and smoking cessation is the most effective action for patients with cardiovascular disease to reduce cardiovascular mortality, particulary among men. It is important to more vigorously emphasise the harmful effects of smoking on health. Among patients with high cardiovascular risk, an individual-based, sustainable, multidisciplinary intervention is fundamental. According to the best practice in Finland, smoking cessation was one component (alongside nutrition, serum cholesterol, blood pressure), contributing to the 84% decline in coronary heart mortality in the middle age population during 1972–2014 (Vartiainen, 2018).

Biomarkers for cardiovascular mortality in the 55-year-old male cohort in Estonia and Sweden in the second wave of the study. Blood tests collected in the first wave of this study showed that level of plasma glucose, CRP and IL-6 was significantly higher for cardiovascular mortality among those study subjects who died during the next 13 years compared to survivors in the second wave of the study. However, from biomarkers, only IL-6 was significant predictor for cardiovascular mortality in men in the Cox proportional model.

The results of the present study are almost in line with other observational studies, that CRP and IL-6 are predictors of earlier subclinical vascular damage (Al Rifai et al., 2017; McEvoy et al., 2015), predicting pronouncing lower sur-

vival of CVD among men (Liu J. et al., 2020), reflecting chronic level of inflammation in the body. For example, in the SWESTONIA study, the level of IL-6 in the blood of the subjects increased the risk for both cardiovascular and non-cardiovascular mortality by two times, which is in line with other studies (Li et al., 2017; Patterson et al., 2015). Moreover, based on worldwide literature, an elevated level of IL-6 in the blood of smokers compared to non-smokers was a risk factor for both cardiovascular mortality as well as for all-cause mortality (Baune et al., 2011; Li et al., 2017).

6.4. Strengths and limitations of the present study

Strengths of the present study were as follows:

1. Longitudinal design of this study enabled to observe the same participants over the 13-year follow-up period, to evaluate the prevalence and risk factors of AH, and to describe cardiovascular mortality in Estonia and Sweden.
2. The same methodology used in the first and second wave of this study in Estonia and Sweden allowed to compare two countries in two time points.
3. Collection of data on psychosocial factors, personality traits, lifestyle factors, health indicators, including cardiovascular biomarkers, allowed to provide a comprehensive and innovative overview of risk factors attributed to AH and cardiovascular mortality.
4. The use of morbidity data from Estonian and Swedish local registers enable to discover the proportion of AH among all CVD diagnosis and to assess risk factors of AH over the 13-year follow-up period. The use of mortality data from Estonian and Swedish Cause of Death Register allowed to give a precise overview of the causes of deaths among enrolled participants over the the 13-year follow-up period.

Limitations of the present study were as follows:

1. The sample sizes in Estonia and Sweden were quite small, hence, significant differences between study groups might have remained undetected.
2. The response rate in the follow-up study was lower than expected, particularly in Estonia, which did not allow to perform all the planned analyses in all subgroups and the study estimates were not as precise as one might wish.
3. Self-reported data can result in bias, as participants are less likely to be honest about information related to risk behaviours or indicators of unhealthy lifestyle.
4. Data on all risk factors was collected only in the first and last years of the study, therefore no information is available for the intervening years.

7. CONCLUSIONS

According to the results of the SWESTONIA study, the prevalence of AH was significantly higher in Estonian compared to Swedish cohorts after a 13-year follow-up period. Several psychosocial factors and personality traits were associated with AH in Estonia and Sweden. In the Estonian substudy, obesity was the main predictor of AH in the 55-year-old cohort in the second wave of the study. Based on the SWESTONIA study, CVD-related mortality was significantly higher among the 55-year-old cohort of men in Estonia than in Sweden in the second wave of this study.

The specific conclusions are as follows:

1. AH was diagnosed in more than half of Estonians, but in more than one-third of Swedes in the 55-year-old cohort after a 13-year follow-up period. Significantly higher depressive mood and influence of negative SLEs, but lower quality of life, prevailed in both cohorts of Estonians compared to Swedes in both study waves. Influence of negative SLEs was significantly higher, and mastery significantly lower among 55-year-old adults with a diagnosis of AH compared to those without this diagnosis in Estonia, but not in Sweden.
2. Prevalence of AH increased significantly in the Estonian 55-year-old cohort over the 13-year follow-up period. Several psychosocial and lifestyle factors, and health indicators showed independent association with AH, but in the final model, only obesity was significantly associated with AH in the second wave of this study.
3. One fifth of Estonian and Swedish men in the 55-year-old cohort died over the 13-year follow-up period. Nearly half of all causes of death were due to CVDs. The number of CVD-related deaths was six times higher in Estonia than in Sweden. Current smoking and plasma levels of IL-6 were significant predictors for cardiovascular mortality in the cohort of Estonian and Swedish men.

8. PRACTICAL IMPLICATIONS

The findings of the SWESTONIA study are beneficial for primary and secondary prevention. The sustainable management of risk factors is the cornerstone of measures to reduce the burden of morbidity of AH and the related mortality from CVDs in Estonia.

The specific practical recommendations are as follows:

1. Psychosocial factors and personality traits could be screened during primary and the secondary prevention of AH.
2. It is recommended to add the Pearlin Mastery Scale to the guidelines on the management of AH to measure individual self-belief to cope with psychosocial stress.
3. From lifestyle factors, special attention should be paid to the prevention of obesity and smoking, and to the cessation of smoking using individual, group- and population-based approaches.
4. People at lifetime risk of AH should be detected and treated early, using a comprehensive approach regarding all risk factors, and e-health strategies for the monitoring of treatment.
5. An effective, long-term, centrally coordinated intersectoral approach should be a central part of interventions in the prevention of AH, including focusing on vulnerable sub-groups of the population, and following best practices of neighbouring countries (e.g. Sweden, Finland).

REFERENCES

Abbafati, C., Abbas, K. M., Abbasi-Kangevari, M., Abd-Allah, F., Abdelalim, A., Abdollahi, M., Abdollahpour, I., Abegaz, K. H., Abolhassani, H., Aboyans, V., Abreu, L. G., Abrigo, M. R. M., Abualhasan, A., Abu-Raddad, L. J., Abushouk, … Murray, C. J. L. (2020). Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*, *396*, 1223−49. https://doi.org/10.1016/S0140-6736(20)30752-2

Abbott, P., & Wallace, C. (2014). Rising economic prosperity and social quality the case of new member states of the European Union. *Social Indicators Research*, *115*, 419−39. https://doi.org/10.1007/s11205-012-9992-0

Abeywardena, M., Leifert, W., Warnes, K., Varghese, J., & Head, R. (2009). Cardiovascular biology of interleukin-6. *Current Pharmaceutical Design*, *15*, 1809−21. https://doi.org/10.2174/138161209788186290

Agudo, A., Bonet, C., Travier, N., González, C. A., Vineis, P., Bueno-de-Mesquita, H. B., Trichopoulos, D., Boffetta, P., Clavel-Chapelon, F., Boutron-Ruault, M. C., Kaaks, R., Lukanova, A., Schuïze, M., Boeing, H., Tjonneland, A., … Riboli, E. (2012). Impact of cigarette smoking on cancer risk in the European prospective investigation into cancer and nutrition study. *Journal of Clinical Oncology*, *30*, 4550−57. https://doi.org/10.1200/JCO.2011.41.0183

Al Rifai, M., DeFillippis, A. P., McEvoy, J. W., Hall, M. E., Acien, A. N., Jones, M. R., Keith, R., Magid, H. S., Rodriguez, C. J., Barr, G. R., Benjamin, E. J., Robertson, R. M., Bhatnagar, A., & Blaha, M. J. (2017). The relationship between smoking intensity and subclinical cardiovascular injury: The Multi-Ethnic Study of Atherosclerosis (MESA). *Atherosclerosis*, *258,* 119−30. https://doi.org/10.1016/j.atherosclerosis.2017.01.021

Albus, C., Waller, C., Fritzsche, K., Gunold, H., Haass, M., Hamann, B., Kindermann, I., Köllner, V., Leithäuser, B., Marx, N., Meesmann, M., Michal, M., Ronel, J., Scherer, M., Schrader, V., Schwaab, B., Weber, C. S., & Herrmann-Lingen, C. (2019). Significance of psychosocial factors in cardiology: update 2018. *Clinical Research in Cardiology*, *108,* 1175−96. https://doi.org/10.1007/s00392-019-01488-w

Aldwin, C., Yancura, L. A., & Boeninger, D. K. (2007). Coping, health, and aging. In C. L. Aldwin, C. L. Park, & A. Spiro (Eds.), *Handbook of health psychology and aging* (III, pp. 210–226). The Guilford Press.

Ambrose, J. A., & Barua, R. S. (2004). The pathophysiology of cigarette smoking and cardiovascular disease: An update. *Journal of the American College of Cardiology, 43,* 1731−37. https://doi.org/10.1016/j.jacc.2003.12.047

Aneshensel, C. S., & Avison, W. R. (2015). The stress process: An appreciation of Leonard I. Pearlin. *Society and Mental Health*, *5*, 67−85. https://doi.org/10.1177/2156869315585388

APA. (2022). *APA Dictionary of psychology.* American Psyhological Association. http://Dictionary.Apa.Org (Assessed 15.02.22).

Attitudinal Scales. (2021). *Scales. National Longitudinal Surveys. Appendix 21.* Washington, DC 20212, United States. https://www.nlsinfo.org/ content/cohorts/ nlsy79/other-documentation/codebooksupplement/nlsy79-appendix-21-attitudinal-scales (Assessed 15.02.22).

Au, A. (2017). The sociological study of stress: An analysis and critique of the stress process model. *European Journal of Mental Health*, *12*, 53−72. https://doi.org/10.5708/EJMH.12.2017.1.4

Avendano, M., Kunst, A. E., Huisman, M., Lenthe, F. V., Bopp, M., Regidor, E., Glickman, M., Costa, G., Spadea, T., Deboosere, P., Borrell, C., Valkonen, T., Gisser, R., Borgan, J. K., Gadeyne, S., & Mackenbach, J. P. (2006). Socioeconomic status and ischaemic heart disease mortality in 10 western European populations during the 1990s. *Heart*, *92*, 225−32. https://doi.org/10.1136/hrt.2005.065532

Avison, W. R., & Turner, R. J. (1988). Stressful life events and depressive symptoms: disaggregating the effects of acute stressors and chronic strains. *Journal of Health and Social Behavior*, *29*, 253−64. https://doi.org/10.2307/2137036

Baker, E. H. (2014). Socioeconomic status, definition. In W. C. Cockerham, R. Dingwall, S. R. Quah (Eds.), *The Wiley Blackwell Encyclopedia of health, illness, behavior, and society,* (V, pp 2095−9). https://doi.org /10.1002/9781118410868.wbehibs395

Bakris, G., Ali, W., & Parati, G. (2019). ACC/AHA versus ESC/ESH on hypertension guidelines: JACC guideline comparison. *Journal of the American College of Cardiology, 73,* 3018−26. https://doi.org /10.1016 /j.jacc.2019.03.507

Bakris, G., Ritz, E., Guillemet, A., Couser, W., Beerkens, P., Reiser, T., Lantink, J., Abraham, G., Collins, A., Feehally, J., Kopple, J., Li, P., Riella, M., Rodriguez-Iturbe, B., & Wilson, A. (2009). The message for world kidney day 2009: Hypertension and kidney disease: A marriage that should be prevented. *Journal of Clinical Hypertension*, *11*, 144−47. https://doi.org/10.1111/j.1751-7176.2009.00092.x

Banegas, J. R., López-García, E., Dallongeville, J., Guallar, E., Halcox, J. P., Borghi, C., Massó-González, E. L., Jiménez, F. J., Perk, J., Steg, P. G., De Backer, G., & Rodríguez-Artalejo, F. (2011). Achievement of treatment goals for primary prevention of cardiovascular disease in clinical practice across Europe: The EURIKA study. *European Heart Journal*, *32*, 2143−52. https://doi.org/10.1093/eurheartj/ehr080

Banegas, J. R., López-García, E., Graciani, A., Guallar-Castillón, P., Gutierrez-Fisac, J. L., Alonso, J., & Rodríguez-Artalejo, F. (2007). Relationship between obesity, hypertension and diabetes, and health-related quality of life among the elderly. *European Journal of Preventive Cardiology*, *14*, 456−62. https://doi.org/10.1097/HJR.0b013e3280803f29

Banks, E., Joshy, G., Korda, R. J., Stavreski, B., Soga, K., Egger, S., Day, C., Clarke, N. E., Lewington, S., & Lopez, A. D. (2019). Tobacco smoking and risk of 36 cardiovascular disease subtypes: Fatal and non-fatal outcomes in a large prospective Australian study. *BMC Medicine*, *17*, 1−18. https://doi.org/10.1186/s12916-019-1351-4

Barrios, V., Escobar, C., & Calderón, A. (2010). Clinical profile and management of patients with hypertension and chronic ischemic heart disease according to BMI. *Obesity*, *18*, 2017−22. https://doi.org/10.1038/oby.2010.12

Barron, E., Lara, J., White, M., & Mathers, J. C. (2015). Blood-borne biomarkers of mortality risk: Systematic review of cohort studies. *PLoS ONE, 10,* 1−23. https://doi.org/10.1371/journal.pone.0127550

Barua, R. S., & Ambrose, J. A. (2013). Mechanisms of coronary thrombosis in cigarette smoke exposure. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *33*, 1460−7. https://doi.org/ 10.1161/ATVBAHA.112.300154

Barua, R. S., Ambrose, J. A., Srivastava, S., DeVoe, M. C., & Eales-Reynolds, L. J. (2003). Reactive oxygen species are involved in smoking-induced dysfunction of nitric oxide biosynthesis and upregulation of endothelial nitric oxide synthase: An in vitro demonstration in human coronary artery endothelial cells. *Circulation*, *107*, 2342−7. https://doi.org /10.1161/01.CIR.0000066691.52789.BE

Baune, B. T., Rothermundt, M., Ladwig, K. H., Meisinger, C., & Berger, K. (2011). Systemic inflammation (interleukin 6) predicts all-cause mortality in men: Results from a 9-year follow-up of the MEMO study. *Age*, *33*, 209−17. https://doi.org/10.1007/s11357-010-9165-5

Ben-Zur, H. (2016). Social and temporal comparisons as moderators of psychological resources associations with wellbeing. *Journal of Individual Differences*, *37*, 96−104. https://doi.org/10.1027/1614-0001/a000193

Ben-Zur, H., & Michael, K. (2020). Positivity and growth following stressful life events: Associations with psychosocial, health, and economic resources. *International Journal of Stress Management*, *27*, 1−9. https://doi.org/10.1037/str0000142

Bjørkløf, G. H., Engedal, K., Selbæk, G., Kouwenhoven, S. E., & Helvik, A. S. (2013). Coping and depression in old age: A literature review. *Dementia and Geriatric Cognitive Disorders*, 35, 121−54. https://doi.org/10.1159/000346633

Bleidorn, W., & Schwaba, T. (2018). Retirement is associated with change in self-esteem. *Psychology and Aging*, *33*, 586−4. https://doi.org/10.1037/pag0000253

Boegehold, M. A. (2013). The effect of high salt intake on endothelial function: Reduced vascular nitric oxide in the absence of hypertension. *Journal of Vascular Research, 50,* 458−67. https://doi.org/10.1159/000355270

Bombelli, M., Facchetti, R., Sega, R., Carugo, S., Fodri, D., Brambilla, G., Giannattasio, C., Grassi, G., & Mancia, G. (2011). Impact of body mass index and waist circumference on the long-term risk of diabetes mellitus, hypertension, and cardiac organ damage. *Hypertension*, *58*, 1029−35. https://doi.org/10.1161/HYPERTENSIONAHA.111.175125

Bonaccio, M., Di Castelnuovo, A., Costanzo, S., Persichillo, M., De Curtis, A., Cerletti, C., Donati, M. B., de Gaetano, G., & Iacoviello, L. (2018). Health-related quality of life and risk of composite coronary heart disease and cerebrovascular events in the Moli-sani study cohort. *European Journal of Preventive Cardiology*, *25,* 287−97. https://doi.org/10.1177/2047487317748452

Borjesson, M., Onerup, A., Lundqvist, S., & Dahlof, B. (2016). Physical activity and exercise lower blood pressure in individuals with hypertension: Narrative review of 27 RCTs. *British Journal of Sports Medicine, 50,* 356−61. https://doi.org/10.1136/bjsports-2015-095786

Bowman, T. S., Gaziano, J. M., Buring, J. E., & Sesso, H. D. (2007). A prospective study of cigarette smoking and risk of incident hypertension in women. *Journal of the American College of Cardiology*, *50*, 2085−92. https://doi.org/10.1016/j.jacc.2007.08.017

Briasoulis, A., Agarwal, V., & Messerli, F. H. (2012). Alcohol consumption and the risk of hypertension in men and women: A systematic review and meta-analysis. *Journal of Clinical Hypertension, 14,* 792–8. https://doi.org/10.1111/jch.12008

Briones, A. M., & Touyz, R. M. (2010). Oxidative stress and hypertension: Current concepts. *Current Hypertension Reports, 2,* 135−42. https://doi.org /10.1007/s11906-010-0100-z

Brunello, G., Fort, M., Schneeweis, N., & Winter-Ebmer, R. (2016). The causal effect of education on health: What is the role of health behaviors? *Health Economics (United Kingdom)*, *25*, 314−36. https://doi.org/10.1002/hec.3141

Burns, W., & Bluen, S. D. (1992). Assessing a multidimensional type A behaviour scale. *Personality and Individual Differences*, *13*, 977−86. https://doi.org/10.1016/0191-8869(92)90131-8

Carris, N. W., & Smith, S. M. (2015). Quality of life in treatment-resistant hypertension. *Current Hypertension Reports, 17,* 60−8. https://doi.org /10.1007/s11906-015-0578-5

Carter, B. D., Abnet, C. C., Feskanich, D., Freedman, N. D., Hartge, P., Lewis, C. E., Ockene, J. K., Prentice, R. L., Speizer, F. E., Thun, M. J., & Jacobs, E. J. (2015). Smoking and mortality − beyond established causes. *New England Journal of Medicine*, *372*, 631−40. https://doi.org/10.1056/nejmsa1407211

Chaves, C., Castellanos, T., Abrams, M., & Vazquez, C. (2018). The impact of economic recessions on depression and individual and social well-being: the case of Spain (2006–2013). *Social Psychiatry and Psychiatric Epidemiology*, *53*, 977−86. https://doi.org/10.1007/s00127-018-1558-2

Chen, H., Feng, Y., Li, S., Zhang, Y., & Yang, X. (2019). Bibliometric analysis of theme evolution and future research trends of the type a personality. *Personality and Individual Differences, 150,* 1−11. https://doi.org/10.1016 /j.paid.2019.109507

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*, 829−85. 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*, 936−46. https://doi.org/10.1016/j.jacc.2008.11.044

Chrysohoou, C., Panagiotakos, D. B., Pitsavos, C., Skoumas, J., Economou, M., Papadimitriou, L., & Stefanadis, C. (2007). The association between pre-hypertension status and oxidative stress markers related to atherosclerotic disease: The ATTICA study. *Atherosclerosis*, *192*, 169−76. https://doi.org/10.1016/j.atherosclerosis.2006.04.03 0

Cohen, J. B. (2017). Hypertension in obesity and the impact of weight loss. *Current Cardiology Reports, 19,* 1−14. https://doi.org/10.1007/s11886-017-0912-4

Cohen, S., Murphy, M. L. M., & Prather, A. A. (2019). Ten surprising facts about stressful life events and disease risk. *Annual Review of Psychology, 70,* 577−97. https://doi.org/10.1146/annurev-psych-010418-102857

Collins, F. S., & Varmus, H. (2015). A new initiative on precision medicine. *New England Journal of Medicine*, *372*, 793–95. https://doi.org /10.1056 /nejmp1500523

Conde-Sala, J. L., Portellano-Ortiz, C., Calvó-Perxas, L., & Garre-Olmo, J. (2017). Quality of life in people aged 65+ in Europe: associated factors and models of social welfare—analysis of data from the SHARE project (Wave 5). *Quality of Life Research*, *26*, 1059−70. https://doi.org/10.1007/s11136-016-1436-x

Cooney, M. T., Dudina, A., De Bacquer, D., Wilhelmsen, L., Sans, S., Menotti, A., De Backer, G., Jousilahti, P., Keil, U., Thomsen, T., Whincup, P., & Graham, I. M. (2009). HDL cholesterol protects against cardiovascular disease in both genders, at all ages and at all levels of risk. *Atherosclerosis*, *206*, 611−6. https://doi.org/10.1016/j.atherosclerosis.2009.02.041

Crowe, L., Butterworth, P., & Leach, L. (2016). Financial hardship, mastery and social support: Explaining poor mental health amongst the inadequately employed using data from the HILDA survey. *SSM Population Health*, *2,* 407−15. https://doi.org/10.1016/j.ssmph.2016.05.002

Csordas, A., & Bernhard, D. (2013). The biology behind the atherothrombotic effects of cigarette smoke. *Nature Reviews Cardiology*, *10*, 219–30. https://doi.org/10.1038/nrcardio.2013.8

Cuffee, Y., Ogedegbe, C., Williams, N. J., Ogedegbe, G., & Schoenthaler, A. (2014). Psychosocial risk factors for hypertension: an update of the literature. *Current Hypertension Reports, 16,* 483−94. https://doi.org/10.1007/s11906-014-0483-3

Cunha, P. G., Boutouyrie, P., Nilsson, P. M., & Laurent, S. (2017). Early Vascular Ageing (EVA): Definitions and clinical applicability. *Current Hypertension Reviews*, *13*, 8−15. https://doi.org/10.2174/1573402113666170413094319

Cutler, D. M., & Lleras-Muney, A. (2010). Understanding differences in health behaviors by education. *Journal of Health Economics*, *29*, 1−28. https://doi.org/10.1016/j.jhealeco.2009.10.003

Dagenais, G. R., Leong, D. P., Rangarajan, S., Lanas, F., Lopez-Jaramillo, P., Gupta, R., Diaz, R., Avezum, A., Oliveira, G. B. F., Wielgosz, A., Parambath, S. R., Mony, P., Alhabib, K. F., Temizhan, A., Ismail, N., Chifamba, J., Yeates, K., Khatib, R., Rahman, O., … Yusuf, S. (2020). Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. *The Lancet*, *395*, 785−94. https://doi.org/10.1016/S0140-6736(19)32007-0

Dal Canto, E., Ceriello, A., Rydén, L., Ferrini, M., Hansen, T. B., Schnell, O., Standl, E., & Beulens, J. W. J. (2019). Diabetes as a cardiovascular risk factor: An overview of global trends of macro and micro vascular complications. *European Journal of Preventive Cardiology*, *26*, Suppl 2, 25–32. https://doi.org/10.1177/ 2047487319878371

Dalgard, O. S., Mykletun, A., Rognerud, M., Johansen, R., & Zahl, P. H. (2007). Education, sense of mastery and mental health: Results from a nation wide health monitoring study in Norway. *BMC Psychiatry*, *7,* 20−9. https://doi.org/10.1186/1471-244X-7-20

Dancey, C. P., Reidy, J. G., & Rowe, R. (2014). *Statistics for the Health Sciences. A Non-Mathematical Introduction* (1st Ed.), 335−7. SAGE Publications Ltd.

Davalos, D., & Akassoglou, K. (2012). Fibrinogen as a key regulator of inflammation in disease. *Seminars in Immunopathology, 34,* 46−62. https://doi.org /10.1007/s00281-011-0290-8

De Beurs, E., Comijs, H., Twisk, J. W. R., Sonnenberg, C., Beekman, A. T. F., & Deeg, D. (2005). Stability and change of emotional functioning in late life: Modelling of vulnerability profiles. *Journal of Affective Disorders*, *84*, 53−62. https://doi.org/10.1016/j.jad.2004.09.006

Di Pilla, M., Bruno, R. M., Taddei, S., & Virdis, A. (2016). Gender differences in the relationships between psychosocial factors and hypertension. *Maturitas, 93,* 58−64. https://doi.org /10.1016/j.maturitas.2016.06.003

Dilmaghani, M. (2020). The causal effects of education on health over the life course: evidence from Canada. *Public Health*, *186,* 170−7. https://doi.org/10.1016/j.puhe.2020.05.060

Dimsdale, J. E. (2008). Psychological stress and cardiovascular disease. *Journal of America College of Cardiology*, *51*, 1237–1246.

Doll, R., Peto, R., Boreham, J., & Sutherland, I. (2004). Mortality in relation to smoking: 50 years' observations on male British doctors. *British Medical Journal*, *328*, 1519−28. https://doi.org/.1136/bmj.38142.554479.ae

Doran, B., Zhu, W., & Muennig, P. (2013). Gender differences in cardiovascular mortality by C-reactive protein level in the United States: Evidence from the National Health and Nutrition Examination Survey III. *American Heart Journal*, *166*, 45−51. https://doi.org/10.1016/j.ahj.2013.03.017

Drewelies, J., Chopik, W. J., Hoppmann, C. A., Smith, J., & Gerstorf, D. (2018). Linked lives: Dyadic associations of mastery beliefs with health (behavior) and health (behavior) change among older partners. *Journals of Gerontology – Series B Psychological Sciences and Social Sciences*, *73*, 787−98. https://doi.org/10.1093/geronb/gbw058

Drummond, G. R., Vinh, A., Guzik, T. J., & Sobey, C. G. (2019). Immune mechanisms of hypertension. *Nature Reviews Immunology*, 19, 517−32. https://doi.org/10.1038/s41577-019-0160-5

Du, J., Zhang, D., Yin, Y., Zhang, X., Li, J., Liu, D., Pan, F., & Chen, W. (2016). The personality and psychological stress predict major adverse cardiovascular events in patients with coronary heart disease after percutaneous coronary intervention for five years. *Medicine (United States)*, *95*, 1−6. https://doi.org/10.1097/MD.0000000000003364

DuBois, C. M., Lopez, O. V., Beale, E. E., Healy, B. C., Boehm, J. K., & Huffman, J. C. (2015). Relationships between positive psychological constructs and health outcomes in patients with cardiovascular disease: A systematic review. *International Journal of Cardiology*, *195*, 265–80. https://doi.org /10.1016/j.ijcard.2015.05.121

Enhanced Care Management. (2022). *Estonian Health Insurance Fund.* http://www.haigekassa.ee/partnerile/raviasutsuele/perearstile/ravi-juhtimise-pilootprojekt (Assessed 18.11.22).

Eriksson, M., Hådell, K., Holme, I., Walldius, G., & Kjellström, T. (1998). Compliance with and efficacy of treatment with pravastatin and cholestyramine: A randomized study on lipid-lowering in primary care. *Journal of Internal Medicine*, *243*, 373−80. https://doi.org/10.1046/j.1365-2796.1998.00294.x

Esler, M. (2017). Mental stress and human cardiovascular disease. *Neuroscience and Biobehavioral Reviews*, *74,* 269−76. https://doi.org/10.1016/j.neubiorev.2016.10.011

Ezzati, M., Obermeyer, Z., Tzoulaki, I., Mayosi, B. M., Elliott, P., & Leon, D. A. (2015). Contributions of risk factors and medical care to cardiovascular mortality trends. *Nature Reviews Cardiology, 12,* 508−30. https://doi.org /10.1038/nrcardio.2015.82

Ference, B. A., Graham, I., Tokgozoglu, L., & Catapano, A. L. (2018). Impact of lipids on cardiovascular health: JACC health promotion series. *Journal of the American College of Cardiology, 72,* 1141−56. https://doi.org /10.1016 /j.jacc.2018.06.046

Finegold, J. A., Asaria, P., & Francis, D. P. (2013). Mortality from ischaemic heart disease by country, region, and age: Statistics from World Health Organisation and United Nations. *International Journal of Cardiology*, *168*, 934−45. https://doi.org/10.1016/j.ijcard.2012.10.046

Ford, E. S., & Capewell, S. (2011). Proportion of the decline in cardiovascular mortality disease due to prevention versus treatment: Public health versus clinical care. *Annual Review of Public Health*, *32,* 5−22. https://doi.org/10.1146/annurev-publhealth-031210-101211

Forouzanfar, M. H., Liu, P., Roth, G. A., Ng, M., Biryukov, S., Marczak, L., Alexander, L., Estep, K., Abate, K. H., Akinyemiju, T. F., Ali, R., Alvis-Guzman, N., Azzopardi, P., Banerjee, A., Bärnighausen, T., Basu, A., … Murray, C. J. L. (2017). Global burden of hypertension and systolic blood pressure of at least 110 to 115mmHg, 1990-2015. *JAMA - Journal of the American Medical Association*, *317*, 165–82. https://doi.org/10.1001/jama.2016.19043

Forouzanfar, M. H., Moran, A. E., Flaxman, A. D., Roth, G., Mensah, G. A., Ezzati, M., Naghavi, M., & Murray, C. J. L. (2012). Assessing the global burden of ischemic heart disease: Part 2: Analytic methods and estimates of the global epidemiology of ischemic heart disease in 2010. *Global Heart*, *7*, 331−42. https://doi.org/10.1016/j.gheart.2012.10.003

Frankham, C., Richardson, T., & Maguire, N. (2020). Psychological factors associated with financial hardship and mental health: A systematic review. *Clinical Psychology Review, 77,* 1−24. https://doi.org/10.1016/j.cpr.2020.101832

Fuster, V., Harrington, R. A., Narula, J., & Eapan Zubin J. (2017). *Hurst's The Heart* (14th Ed.). McGraw-Hill Education.

Gao, K., Shi, X., & Wang, W. (2017). The life-course impact of smoking on hypertension, myocardial infarction and respiratory diseases. *Scientific Reports*, *7*, 1−7. https://doi.org/10.1038/s41598-017-04552-5

Garin, O., Ferrer, M., Pont, À., Rué, M., Kotzeva, A., Wiklund, I., Van Ganse, E., & Alonso, J. (2009). Disease-specific health-related quality of life questionnaires for heart failure: A systematic review with meta-analyses. *Quality of Life Research, 18,* 71−85. https://doi.org/10.1007/s11136-008-9416-4

Garovic, V. D., & August, P. (2013). Preeclampsia and the future risk of hypertension: The pregnant evidence. *Current Hypertension Reports*, *15,* 114–121. https://doi.org/10.1007/s11906-013-0329-4

Gellert, C., Schöttker, B., & Brenner, H. (2012). Smoking and all-cause mortality in older people: Systematic review and meta-analysis. *Archives of Internal Medicine, 172,* 837−44. https://doi.org/10.1001/archinternmed.2012.1397

Gerdts, E., Sudano, I., Brouwers, S., Borghi, C., Bruno, R. M., Ceconi, C., & Cornelissen, V. A. (2022). Sex differences in arterial hypertension. *European Heart Journal*, *43*, 4777–88. https://doi.org/http://doi.org/10.1093/eurheart/ehac470

Giannoni, A., & Masi, S. (2018). Arterial hypertension and the turbulent ageing of the aortic valve. *European Heart Journal*, *39,* 3604–707. https:// doi.org /10.1093 /eurheartj/ehy518

Ginter, E., & Simko, V. (2012). Dramatic decline of ischaemic heart disease mortality in post communist Central Europe: Recovery from totality. *Central European Journal of Public Health*, *20*, 101−3. https://doi.org/10.21101/cejph.a3658

Gorostegi-Anduaga, I., Corres, P., MartinezAguirre-Betolaza, A., Pérez-Asenjo, J., Aispuru, G. R., Fryer, S. M., & Maldonado-Martín, S. (2018). Effects of different aerobic exercise programmes with nutritional intervention in sedentary adults with overweight/obesity and hypertension: EXERDIET-HTA study. *European Journal of Preventive Cardiology*, *25*, 343−53. https://doi.org/10.1177/2047487317749956

Gotlib, I. H., & Joormann, J. (2010). Cognition and depression: Current status and future directions. *Annual Review of Clinical Psychology*, *6*, 285–312. https://doi.org/10.1146/annurev.clinpsy.121208.131305

Grassi, G., Quarti-Trevano, F., Seravalle, G., Dell'oro, R., Vanoli, J., Perseghin, G., & Mancia, G. (2021). Sympathetic neural mechanisms underlying attended and unattended blood pressure measurement. *Hypertension*, *78*, 1126–33.

Griswold, M. G., Fullman, N., Hawley, C., Arian, N., Zimsen, S. R. M., Tymeson, H. D., Venkateswaran, V., Tapp, A. D., Forouzanfar, M. H., Salama, J. S., Abate, K. H., Abate, D., Abay, S. M., Abbafati, C., Abdulkader, R. S., … Gakidou, E. (2018). Alcohol use and burden for 195 countries and territories, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, *392,* 1015−35. https://doi.org/10.1016/S0140-6736(18)31310-2

Guerra, F., Mancinelli, L., Buglioni, A., Pierini, V., Rappelli, A., Dess-Fulgheri, P., & Sarzani, R. (2011). Microalbuminuria and left ventricular mass in overweight and obese hypertensive patients: Role of the metabolic syndrome. *High Blood Pressure and Cardiovascular Prevention*, *18*, 195−201. https://doi.org/10.2165/11593650-000000000-00000

Guzik, T. J., & Touyz, R. M. (2017). Oxidative stress, inflammation, and vascular aging in hypertension. *Hypertension*, *70*, 660−67. https://doi.org/10.1161/HYPERTENSIONAHA.117.07802

Haberka, M., Stolarz-Skrzypek, K., Biedroń, M., Szóstak-Janiak, K., Partyka, M., Olszanecka-Glinianowicz, M., & Gasior, Z. (2018). Obesity, visceral fat, and hypertension-related complications. *Metabolic Syndrome and Related Disorders*, *16*, 521–9. https://doi.org/10.1089/met.2018.0062

Hall, J. E., Do Carmo, J. M., Da Silva, A. A., Wang, Z., & Hall, M. E. (2015). Obesity-induced hypertension: Interaction of neurohumoral and renal mechanisms. *Circulation Research*, *116*, 991–1006. https://doi.org/10.1161/ CIRCRESAHA.116.305697

Hammen, C. (2016). Depression and stressful environments: identifying gaps in conceptualization and measurement. *Anxiety, Stress and Coping*, *29*, 335−51. https://doi.org/10.1080/10615806.2015.1134788

Hammer, G. D., & McPhee, S. J. (2014). *Pathophysiology of disease. An introduction to clinical medicine* (VII, pp 310–14). McGraw-Hill Education.

Hänsel, A., Hong, S., Cámara, R. J. A., & von Känel, R. (2010). Inflammation as a psychophysiological biomarker in chronic psychosocial stress. In *Neuroscience and Biobehavioral Reviews, 35,* 115−21. https://doi.org /10.1016/j.neubiorev.2009.12.012

Harvey, A., Montezano, A. C., & Touyz, R. M. (2015). Vascular biology of ageing-implications in hypertension. *Journal of Molecular and Cellular Cardiology*, *83*, 112–21. https://doi.org/10.1016/j.yjmcc.2015.04.011

Hay, M., Barnes, C., Huentelman, M., Brinton, R., & Ryan, L. (2020). Hypertension and age-related cognitive impairment: Common risk factors and a role for precision aging. *Current Hypertension Reports*, *22,* 79−94. https://doi.org /10.1007/s11906-020-01090-w

Herman, J. P. (2013). Neural control of chronic stress adaptation. *Frontiers in Behavioral Neuroscience*, *7,* 1−12. https://doi. org/10.3389/fnbeh.2013.00061

Heusch, G., Libby, P., Gersh, B., Yellon, D., Böhm, M., Lopaschuk, G., & Opie, L. (2014). Cardiovascular remodelling in coronary artery disease and heart failure. *The Lancet*, 383, 1933−43. https://doi.org/10.1016/S0140-6736(14)60107-0

Hooper, L., Martin, N., Abdelhamid, A., & Davey Smith, G. (2015). Reduction in saturated fat intake for cardiovascular disease. *Cochrane Database of Systematic Reviews, 2015,* 1–151. https://doi.org/10.1002/14651858.CD011737

Hooper, L., Martin, N., Jimoh, O. F., Kirk, C., Foster, E., & Abdelhamid, A. S. (2020). Reduction in saturated fat intake for cardiovascular disease. *Cochrane Database of Systematic Reviews, 2020,* 1−187. https://doi.org /10.1002/14651858.CD011737.pub3

Horan, P. G., Kamaruddin, M. S., Moore, M. J., McCarty, D., Spence, M. S., McGlinchey, P. G., Murphy, G., Jardine, T. C. L., Patterson, C. C., & McKeown, P. P. (2007). Cardiovascular disease risk profiles among 'healthy' siblings of patients with early-onset cardiovascular disease: application of the new SCORE system. *European Journal of Cardiovascular Prevention & Rehabilitation*, *14*, 521–525. https://doi.org/10.1097/HJR.0b013e328011c493

Hozawa, A., Folsom, A. R., Sharrett, A. R., Payne, T. J., & Chambless, L. E. (2006). Does the impact of smoking on coronary heart disease differ by low-density lipoprotein cholesterol level? The Atherosclerosis Risk in Communities (ARIC) Study. *Circulation Journal*, *70*, 1105−10. https://doi.org/10.1253/circj.70.1105

Hsu, C. Y., McCulloch, C. E., Darbinian, J., Go, A. S., & Iribarren, C. (2005). Elevated blood pressure and risk of end-stage renal disease in subjects without baseline kidney disease. *Archives of Internal Medicine*, *165*, 923−8. https://doi.org/10.1001/archinte.165.8.923

Huang, I. C., Lee, J. L., Ketheeswaran, P., Jones, C. M., Revicki, D. A., & Wu, A. W. (2017). Does personality affect health-related quality of life? A systematic review. *PLoS ONE*, *12*, 1−31. https://doi.org/10.1371/journal.pone.0173806

Hughes, B. M. (2007). Self-esteem, performance feedback, and cardiovascular stress reactivity. *Anxiety, Stress and Coping*, *20*, 239−52. https://doi.org/10.1080/10615800701330218

ICD-10. (2010). International Classification of Diseases 10th Revision. World Health Organization. http://Icd.Who.Int/Browse10/2010/En#/I10-I15 (Assessed 15.03.22).

Ikeda, A., Iso, H., Kawachi, I., Inoue, M., & Tsugane, S. (2008). Type A behaviour and risk of coronary heart disease: The JPHC study. *International Journal of Epidemiology*, *37*, 1395−405. https://doi.org/10.1093/ije/dyn124

Infurna, F. J., & Gerstorf, D. (2014). Perceived control relates to better functional health and lower cardio-metabolic risk: The mediating role of physical activity. *Health Psychology*, *33*, 85−94. https://doi.org/10.1037/a0030208

Infurna, F. J., Mayer, A., & Anstey, K. J. (2018). The effect of perceived control on self-reported cardiovascular disease incidence across adulthood and old age. *Psychology and Health*, *33*, 340−60. https://doi.org/10.1080 /08870446.2017.1341513

Infurna, F. J., & Okun, M. A. (2015). Antecedents and outcomes of level and rates of change in perceived control: The moderating role of age. *Developmental Psychology*, *51*, 1420−37. https://doi.org/10.1037/a0039530

Iso, H., Date, C., Yamamoto, A., Toyoshima, H., Watanabe, Y., Kikuchi, S., Koizumi, A., Wada, Y., Kondo, T., Inaba, Y., & Tamakoshi, A. (2005). Smoking cessation and mortality from cardiovascular disease among Japanese men and women: The JACC study. *American Journal of Epidemiology*, *161,* 170−9. https://doi.org/10.1093/aje/kwi027

Jatoi, N. A., Jerrard-Dunne, P., Feely, J., & Mahmud, A. (2007). Impact of smoking and smoking cessation on arterial stiffness and aortic wave reflection in hypertension. *Hypertension*, *49*, 981−5. https://doi.org/10.1161/HYPERTENSIONAHA.107.087338

Jayedi, A., Rashidy-Pour, A., Khorshidi, M., & Shab-Bidar, S. (2018). Body mass index, abdominal adiposity, weight gain and risk of developing hypertension: a systematic review and dose–response meta-analysis of more than 2.3 million participants. *Obesity Reviews, 19,* 654−67. https://doi.org/10.1111/obr.12656

Jefferis, B. J., Lowe, G. D. O., Welsh, P., Rumley, A., Lawlor, D. A., Ebrahim, S., Carson, C., Doig, M., Feyerabend, C., McMeekin, L., Wannamethee, S. G., Cook, D. G., & Whincup, P. H. (2010). Secondhand smoke (SHS) exposure is associated with circulating markers of inflammation and endothelial function in adult men and women. *Atherosclerosis*, *208*, 550−6. https://doi.org/10.1016/j.atherosclerosis.2009.07.044

Johansson, J., Viigimaa, M., Jensen-Urstad, M., Krakaui, I., & Hansson, L. O. (2002). Risk factors for coronary heart disease in 55- and 35-year-old men and women in Sweden and Estonia. *Journal of Internal Medicine*, *252*, 551−60. https://doi.org/10.1046/j.1365-2796.2002.01068.x

Jousilahti, P., Laatikainen, T., Salomaa, V., Pietilä, A., Vartiainen, E., & Puska, P. (2016). 40-Year CHD Mortality trends and the role of risk factors in mortality decline: The North Karelia project experience. *Global Heart, 11,* 207−12. https://doi.org/10.1016/j.gheart.2016.04.004

Kanno, A., Kikuya, M., Ohkubo, T., Hashimoto, T., Satoh, M., Hirose, T., Obara, T., Metoki, H., Inoue, R., Asayama, K., Shishido, Y., Hoshi, H., Nakayama, M., Totsune, K., Satoh, H., Sato, H., & Imai, Y. (2012). Pre-hypertension as a significant predictor of chronic kidney disease in a general population: The Ohasama Study. *Nephrology Dialysis Transplantation*, *27*, 3218−23. https://doi.org/10.1093/ndt/gfs054

Karimi, M., & Brazier, J. (2016). Health, health-related quality of life, and quality of life: What is the difference? *PharmacoEconomics*, *34*, 645−9. https://doi.org/10.1007/s40273-016-0389-9

Karlberg, L., Krakau, I., Sjödén, P. O., & Undén, A. L. (1997). Psychometric properties of a brief self-report type A questionnaire for use in primary health care. *Scandinavian Journal of Primary Health Care*, *15*, 52−6. https://doi.org/10.3109/02813439709043431

Kiely, K. M., Leach, L. S., Olesen, S. C., & Butterworth, P. (2015). How financial hardship is associated with the onset of mental health problems over time. *Social Psychiatry and Psychiatric Epidemiology*, *50*, 909−19. https://doi.org/10.1007/s00127-015-1027-0

Kivimäki, M., & Steptoe, A. (2018). Effects of stress on the development and progression of cardiovascular disease. *Nature Reviews Cardiology*, *15,* 909−18. https://doi.org/10.1038/nrcardio.2017.189

Kleinberg, A., Jaanson, P., Lehtmets, A., Aluoja, A., Vasar, V., Suija, K., & Ööpik, P. (2011). Depressiooni ravijuhend perearstidele. *Eesti Arst*, *90*, 431–46 (in Estonian).

Laffer, C. L., Scott, R. C., Titze, J. M., Luft, F. C., & Elijovich, F. (2016). Hemodynamics and salt-and-water balance link sodium storage and vascular dysfunction in salt-sensitive subjects. *Hypertension*, *68*, 195−203. https://doi.org/10.1161/HYPERTENSIONAHA.116.07289

Lai, T., Johanson, A. S., Breda Joao, Reinap, M., Dorner Thomas, Maningh, F., Jewell, J., & Jakab, M. (2015). *Better noncommunicable disease outcomes: challenges and oppurtunites for health systems: Estonia. Country assessment*. WHO. https://apps.who.int/iris/bitstream/handle/10665/350491/WHO-EURO-2015-4520-44283 62552 -eng.pdf?sequence=1&isAllowed=y (Assessed 03.09.22)

Landsberg, L., Aronne, L. J., Beilin, L. J., Burke, V., Igel, L. I., Lloyd-Jones, D., & Sowers, J. (2013). Obesity-related hypertension: Pathogenesis, cardiovascular risk, and treatment-a position paper of the the obesity society and the American society of hypertension. *Obesity, 21,* 8−24. https://doi.org/10.1002/oby.20181

Lange, S., & Vollmer, S. (2017). The effect of economic development on population health: A review of the empirical evidence. *British Medical Bulletin, 121,* 47−60. https://doi.org/10.1093/bmb/ldw052

Lavie, C. J., Ozemek, C., & Kachur, S. (2019). Promoting physical activity in primary and secondary prevention. *European Heart Journal*, *40,* 3556−8. https://doi.org/10.1093/eurheartj/ehz697

Lee, W. J., Chen, L. K., Peng, L. N., Chiou, S. T., & Chou, P. (2016). Personal mastery attenuates the adverse effect of frailty on declines in physical function of older people A 6-year population-based cohort study. *Medicine (United States)*, *95,* 1−7. https://doi.org /10.1097/MD.0000000000004661

Leng, B., Jin, Y., Li, G., Chen, L., & Jin, N. (2015). Socioeconomic status and hypertension: A meta-analysis. *Journal of Hypertension*, *33,* 221−9. https://doi.org/10.1097/HJH.0000000000000428

Levi, F., Lucchini, F., Negri, E., & La Vecchia, C. (2002). Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. *Heart*, *88*, 119−24. https://doi.org /10.1136/heart.88.2.119

Li, H., Liu, W., & Xie, J. (2017). Circulating interleukin-6 levels and cardiovascular and all-cause mortality in the elderly population: A meta-analysis. *Archives of Gerontology and Geriatrics*, *73,* 257−62. https://doi.org /10.1016/j.archger.2017.08.007

Liu, J., Zhang, Y., Lavie, C. J., Tabung, F. K., Xu, J., Hu, Q., He, L., & Zhang, Y. (2020). Associations of C-reactive protein and fibrinogen with mortality from all-causes, cardiovascular disease and cancer among U.S. adults. *Preventive Medicine*, *139*, 1−9. https://doi.org/10.1016/j.ypmed.2020.106044

Liu, M. Y., Li, N., Li, W. A., & Khan, H. (2017). Association between psychosocial stress and hypertension: a systematic review and meta-analysis. *Neurological Research*, *39*, 573−80. https://doi.org/10.1080/01616412.2017.1317904

Løgstrup, S., & O'Kelly, S. (2012). *European Cardiovascular Disease Statistics. 2012 edition. European Heart Network, European Society of Cardiology*. https://www.escardio.org/static-file/Escardio/Press-media/press-releases /2013/ EU-cardiovascular-disease-statistics-2012.pdf (Assessed 02-09-22)

Lohse, T., Rohrmann, S., Richard, A., Bopp, M., & Faeh, D. (2017). Type A personality and mortality: Competitiveness but not speed is associated with increased risk. *Atherosclerosis*, *262,* 19−24. https://doi.org/10.1016/j.atherosclerosis.2017.04.016

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., Abraham, J., Adair, T., Aggarwal, R., Ahn, S. Y., … Murray, C. J. L. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*, *380*, 2095−128. https://doi.org/10.1016/S0140-6736(12)61728-0

Maatouk, I., Herzog, W., Böhlen, F., Quinzler, R., Löwe, B., Saum, K. U., Brenner, H., & Wild, B. (2016). Association of hypertension with depression and generalized anxiety symptoms in a large population-based sample of older adults. *Journal of Hypertension*, *34*, 1711−20. https://doi.org /10.1097/HJH.0000000000001006

MacKinnon, D. P., & Luecken, L. J. (2008). How and for whom? Mediation and moderation in health psychology. *Health Psychology*, *27,* Suppl 2. https://doi.org/10.1037/0278-6133.27.2(Suppl.).S99

Macleod, J., & Davey Smith, G. (2003). Psychosocial factors and public health: A suitable case for treatment? *Journal of Epidemiology and Community Health, 57,* 172−86. https://doi.org/10.1136/jech.57.8.565

Mähönen, M. S., McElduff, P., Dobson, A. J., Kuulasmaa, K. A., & Evans, A. E. (2004). Current smoking and the risk of non-fatal myocardial infarction in the WHO MONICA Project populations. *Tobacco Control*, *13,* 244−50. https://doi.org/10.1136/tc.2003.003269

Mancia, G., De Backer, G., Dominiczak, A., Cifkova, R., Fagard, R., Germano, G., Grassi, G., Heagerty, A. M., Kjeldsen, S. E., Laurent, S., Narkiewicz, K., Ruilope,

L., Rynkiewicz, A., Schmieder, R. E., Struijker Boudier, H. A. J., & Zanchetti, A. (2007). 2007 Guidelines for the management of arterial hypertension. *European Heart Journal, 28*. https://doi.org/10.1093/eurheartj/ehm236

Mancia, G., Fagard, R., Narkiewicz, K., Redon, J., Zanchetti, A., Böhm, M., Christiaens, T., Cifkova, R., De Backer, G., Dominiczak, A., Galderisi, M., Grobbee, D. E., Jaarsma, T., Kirchhof, P., Kjeldsen, S. E., … Wood, D. A. (2013). 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *European Heart Journal*, *34*, 2159−219 . https://doi.org/10.1093/eurheartj/eht151

Mancia, G., & Grassi, G. (2014). The autonomic nervous system and hypertension. *Circulation Research*, *114*, 1804−14. https://doi.org/10.1161/CIRCRESAHA.114.302524

Mann, M., Hosman, C. M. H., Schaalma, H. P., & De Vries, N. K. (2004). Self-esteem in a broad-spectrum approach for mental health promotion. *Health Education Research, 19,* 357−72. https://doi.org/10.1093/her/cyg041

Mark, D. B. (2016). Assessing quality-of-life outcomes in cardiovascular clinical research. *Nature Reviews Cardiology, 13,* 289−308. https://doi.org /10.1038/nrcardio.2016.10

Marum, G., Clench-Aas, J., Nes, R. B., & Raanaas, R. K. (2014). The relationship between negative life events, psychological distress and life satisfaction: A population-based study. *Quality of Life Research*, *23*, 601−11. https://doi.org/10.1007/s11136-013-0512-8

Mayet, J., & Hughes, A. (2003). Cardiac and vascular pathophysiology in hypertension. *Heart, 89,* 1104−09. https://doi.org /10.1136/heart.89.9.1104

McEniery, C. M., Wilkinson, I. B., & Avolio, A. P. (2007). Age, hypertension and arterial function. *Clinical and Experimental Pharmacology and Physiology, 34,* 665–671. https://doi.org/10.1111/j.1440-1681.2007.04657.x

McEvoy, J. W., Nasir, K., Defilippis, A. P., Lima, J. A. C., Bluemke, D. A., Hundley, W. G., Barr, R. G., Budoff, M. J., Szklo, M., Navas-Acien, A., Polak, J. F., Blumenthal, R. S., Post, W. S., & Blaha, M. J. (2015). Relationship of cigarette smoking with inflammation and subclinical vascular disease: The multi-ethnic study of atherosclerosis. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *35*, 1002−10. https://doi.org/10.1161/ATVBAHA.114.304960

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiological Reviews, 87,* 873−04. https://doi.org/10.1152/physrev.00041.2006

McHorney, C. A. (1999). Health status assessment methods for adults: Past accomplishments and future challenges. *Annual Review of Public Health*, *20,* 309−35. https://doi.org /10.1146/annurev.publhealth.20.1.309

McKean Skaff, M. (2007). Sense of control and health. In C. Aldwin, C. L. Park, & A. Spiro (Eds.), *Handbook of Health Psychology* (III, pp. 186–209). Guilford Publication.

Mcleod, J. D. (2012). The meanings of stress: Expanding the stress process model. *Society and Mental Health*, *2*, 172−86. https://doi.org/10.1177/2156869312452877

Messerli, F. H., Neagoe, A., & Messerli, A. W. (2019). The alcohol blood pressure paradox. *European Heart Journal, 40,* 711−12. https://doi.org/10.1093/eurheartj/ehz038

Miller, T. Q., Turner, C. W., Scott Tindale, R., Posavac, E. J., & Dugoni, B. L. (1991). Reasons for the trend toward null findings in research on type a behavior. *Psychological Bulletin*, *110*, 469−85. https://doi.org/10.1037/0033-2909.110.3.469

Mills, K. T., Bundy, J. D., Kelly, T. N., Reed, J. E., Kearney, P. M., Reynolds, K., Chen, J., & He, J. (2016). Global disparities of hypertension prevalence and control. *Circulation*, *134,* 441−50. https://doi.org/10.1161/CIRCULATIONAHA.115.018912

Mirowsky, J., & Ross, C. E. (2007). Life course trajectories of perceived control and their relationship to education. *American Journal of Sociology*, *112*, 1339−82. https://doi.org/10.1086/511800

Mitchell, U. A., Ailshire, J. A., Brown, L. L., Levine, M. E., & Crimmins, E. M. (2018). Education and psychosocial functioning among older adults: 4-year change in sense of control and hopelessness. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *73*, 849−59. https://doi.org/10.1093/geronb/gbw031

Mittleman, M. A., & Mostofsky, E. (2011). Physical, psychological and chemical triggers of acute cardiovascular events: Preventive strategies. *Circulation*, *124*, 346−54. https://doi.org /10.1161/CIRCULATIONAHA.110.968776

Mons, U., Müezzinler, A., Gellert, C., Schöttker, B., Abnet, C. C., Bobak, M., De Groot, L., Freedman, N. D., Jansen, E., Kee, F., Kromhout, D., Kuulasmaa, K., … Wennberg, P. (2015). Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: Meta-analysis of Individual participant data from prospective cohort studies of the CHANCES consortium. *The British Medical Journal*, *350*, 1551−60. https://doi.org/10.1136/bmj.h1551

Montezano, A. C., Dulak-Lis, M., Tsiropoulou, S., Harvey, A., Briones, A. M., & Touyz, R. M. (2015). Oxidative stress and human hypertension: Vascular mechanisms, biomarkers, and novel therapies. *Canadian Journal of Cardiology*, *31,* 631–641. https://doi.org /10.1016/j.cjca.2015.02.008

Moran, A. E., Forouzanfar, M. H., Roth, G. A., Mensah, G. A., Ezzati, M., Murray, C. J. L., & Naghavi, M. (2014). Temporal trends in ischemic heart disease mortality in 21 world regions, 1980 to 2010: The global burden of disease 2010 study. *Circulation*, *129,* 1483−93. https://doi.org/10.1161 /CIRCULATIONAHA.113.004042

Moussavi, S., Chatterji, S., Verdes, E., Tandon, A., Patel, V., & Ustun, B. (2007). Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *The Lancet*, *370*, 851−8. https://doi.org/10.1016/S0140-6736(07)61415-9

Mucha, L., Stephenson, J., Morandi, N., & Dirani, R. (2006). Meta-analysis of disease risk associated with smoking, by gender and intensity of smoking. *Gender Medicine*, *3*, 279−91. https://doi.org/10.1016/S1550-8579(06)80216-0

Munakata, M., Hiraizumi, T., Nunokawa, T., Ito, N., Taguchi, F., Yamauchi, Y., & Yoshinaga, K. (1999). Type A behavior is associated with an increased risk of left ventricular hypertrophy in male patients with essential hypertension. *Journal of Hypertension*, *17*, 553−69. https://doi.org/10.1097/00004872-199917010-00017

Musliner, K. L., Seifuddin, F., Judy, J. A., Pirooznia, M., Goes, F. S., & Zandi, P. P. (2015). Polygenic risk, stressful life events and depressive symptoms in older adults: A polygenic score analysis. *Psychological Medicine*, *45*, 1709−20. https://doi.org/10.1017/S0033291714002839

Myrtek, M. (1995). Type A behavior pattern, personality factors, disease, and physiological reactivity: A meta-analytic update. *Personality and Individual Differences*, *18*, 245−51. https://doi.org/10.1016/0191-8869(94)00197-Z

Nabi, H., Chastang, J. F., Lefèvre, T., Dugravot, A., Melchior, M., Marmot, M. G., Shipley, M. J., Kivimäki, M., & Singh-Manoux, A. (2011). Trajectories of depressive episodes and hypertension over 24 years: The whitehall ii prospective cohort study. *Hypertension*, *57*, 710−16. https://doi.org/10.1161 /HYPERTENSIONAHA.110.164061

Naghavi, M., Wang, H., Lozano, R., Davis, A., Liang, X., Zhou, M., Vollset, S. E., Abbasoglu Ozgoren, A., Abdalla, S., Abd-Allah, F., Abdel Aziz, M. I., Abera, S. F., Aboyans, V., Abraham, B., Abraham, J. P., … Temesgen, A. M. (2015). Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*, *385,* 117−72. https://doi.org/10.1016/S0140-6736(14)61682-2

Neeland, I. J., Poirier, P., & Després, J. P. (2018). Cardiovascular and metabolic heterogeneity of obesity: Clinical challenges and implications for management. *Circulation*, *137*, 1391–406. https://doi.org/10.1161/CIRCULATIONAHA.117.029617

Németh, N., Elmer, D., Horváth, L., Csákvári, T., Pónusz, R., Boncz, I., & Endrei, D. (2019). PCV61. Comparing ischaemic heart disease mortality between Eastern and Western European countries. *Value in Health*, *22,* 130−6. https://doi.org/10. 1016/j.jval.2019.04.497

Neumann, J. T., Freak-Poli, R., Orchard, S. G., Wolfe, R., Reid, C. M., Tonkin, A. M., Beilin, L. J., McNeil, J. J., Ryan, J., & Woods, R. L. (2021). Alcohol consumption and risks of cardiovascular disease and all-cause mortality in healthy older adults. *European Journal of Preventive Cardiology, 29,* 230−9. https://doi.org /10.1093/eurjpc/zwab177

Ng, N., Carlberg, B., Weinehall, L., & Norberg, M. (2012). Trends of blood pressure levels and management in Västerbotten County, Sweden, during 1990−2010. *Global Health Action*, *5,* 18195. https://doi.org/10.3402/gha.v5i0.18195

Nichols, M., Townsend, N., Scarborough, P., & Rayner, M. (2013). Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980−2009. *European Heart Journal*, *34*, 3017−27. https://doi.org /10.1093/eurheartj/eht159

Nicolaisen, M., Moum, T., & Thorsen, K. (2018). Mastery and depressive symptoms: How does mastery influence the impact of stressors from midlife to old age? *Journal of Aging and Health*, *30*, 1084−07. https://doi.org/10.1177/0898264317705782

Niedzwiedz, C. L., Katikireddi, S. V., Pell, J. P., & Mitchell, R. (2014). Socioeconomic inequalities in the quality of life of older Europeans in different welfare regimes. *European Journal of Public Health*, *24*, 364−70. https://doi.org/10.1093/eurpub/cku017

Niemann, B., Rohrbach, S., Miller, M. R., Newby, D. E., Fuster, V., & Kovacic, J. C. (2017). Oxidative stress and cardiovascular risk: Obesity, diabetes, smoking, and pollution: Part 3 of a 3-part Series. *Journal of the American College of Cardiology, 70,* 230−51. https://doi.org/10.1016/j.jacc.2017.05.043

Niiranen, T. J., McCabe, E. L., Larson, M. G., Henglin, M., Lakdawala, N. K., Vasan, R. S., & Cheng, S. (2017). Risk for hypertension crosses generations in the community: Amulti-generational cohort study. *European Heart Journal*, *38*, 2300–2308. https://doi.org /10.1093/eurheartj/ehx134

Nilsson, P. M. (2016). Early vascular ageing as a new model to understand hypertension and arterial disease. *Cardiovascular Endocrinology*, *5,*133−36. https://doi.org/10.1097/XCE.0000000000000099

Nilsson, P. M. (2020). Early vascular aging in hypertension. *Frontiers in Cardiovascular Medicine*, *7,* 106−12. https://doi.org/ 10.3389/fcvm.2020.00006

Nilsson, P. M., Boutouyrie, P., & Laurent, S. (2009). Vascular aging: A tale of eva and ADAM in cardiovascular risk assessment and prevention. *Hypertension, 54,* 3−10. https://doi.org /10.1161/HYPERTENSIONAHA.109.129114

Nutbeam, D., & Kickbusch, I. (1998). Health promotion glossary. *Health Promotion International, 13,* 349−64. https://doi.org /10.1093/heapro/13.4.349

O'Donnell, M. J., Denis, X., Liu, L., Zhang, H., Chin, S. L., Rao-Melacini, P., Rangarajan, S., Islam, S., Pais, P., McQueen, M. J., Mondo, C., Damasceno, A., Lopez-Jaramillo, P., Hankey, G. J., Dans, A. L., … Yusuf, S. (2010). Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): A case-control study. *The Lancet*, *376*, 112–23. https://doi.org/10.1016/S0140-6736(10)60834-3

O'Flaherty, M., Buchan, I., & Capewell, S. (2013). Contributions of treatment and lifestyle to declining CVD mortality: Why have CVD mortality rates declined so much since the 1960s? *Heart*, 99, 159−62. https://doi.org/10.1136/heartjnl-2012-302300

Oda, E., & Kawai, R. (2010). Body mass index is more strongly associated with hypertension than waist circumference in apparently healthy Japanese men and women. *Acta Diabetologica*, *47*, 309−13. https://doi.org/10.1007/s00592-010-0203-7

Oparil, S., Acelajado, M. C., Bakris, G. L., Berlowitz, D. R., Cífková, R., Dominiczak, A. F., Grassi, G., Jordan, J., Poulter, N. R., Rodgers, A., & Whelton, P. K. (2018). Hypertension. *Nature Reviews Disease Primers*, *4,* 18014. https://doi.org/10.1038/nrdp.2018.14

Orth, U., Erol, R. Y., & Luciano, E. C. (2018). Development of self-esteem from age 4 to 94 Years: A meta-analysis of longitudinal studies. *Psychological Bulletin*, *144*, 1045−80. https://doi.org /10.1037/bul0000161

Orth, U., & Luciano, E. C. (2015). Self-esteem, narcissism, and stressful life events: Testing for selection and socialization. *Journal of Personality and Social Psychology*, *109*, 707−21. https://doi.org /10.1037/pspp0000049

Orth, U., Maes, J., & Schmitt, M. (2015). Self-esteem development across the life span: A longitudinal study with a large sample from Germany. *Developmental Psychology*, *51*, 248−59. https://doi.org /10.1037/a0038481

Orth, U., Robins, R. W., Trzesniewski, K. H., Maes, J., & Schmitt, M. (2009). Low self-esteem is a risk factor for depressive symptoms from young adulthood to old age. *Journal of Abnormal Psychology*, *118*, 472−8. https://doi.org/10.1037/a0015922

Orth, U., Robins, R. W., & Widaman, K. F. (2012). Life-span development of self-esteem and its effects on important life outcomes. *Journal of Personality and Social Psychology*, *102,* 1271−88. https://doi.org/10.1037/a0025558

Pan, A., Wang, Y., Talaei, M., & Hu, F. B. (2015). Relation of smoking with total mortality and cardiovascular events among patients with diabetes mellitus: A meta-analysis and systematic review. *Circulation*, *132*, 1795−804. https://doi.org/10.1161/CIRCULATIONAHA.115.017926

Parati, G., Goncalves, A., Soergel, D., Bruno, R. M., Caiani, E. G., Gerdts, E., Mahfoud, F., Mantovani, L. G., McManus, R., Santalucia, P., & Kahan, T. (2023). New perspectives for hypertension management: progress in methodological and technological developments. *European Journal of Preventive Cardiology*, *30*, 48–60. https://doi.org/http://doi.org/10.1093/eurjpc/zwac203

Parati, G., Stergiou, G. S., Asmar, R., Bilo, G., De Leeuw, P., Imai, Y., Kario, K., Lurbe, E., Manolis, A., Mengden, T., O'Brien, E., Ohkubo, T., Padfield, P., Palatini, P., Pickering, T. G., … Mancia, G. (2010). European Society of Hypertension Practice Guidelines for home blood pressure monitoring. *Journal of Human Hypertension, 24,* 779−85. https://doi.org/10.1038/jhh.2010.54

Patterson, C. C., Blankenberg, S., Ben-Shlomo, Y., Heslop, L., Bayer, A., Lowe, G., Zeller, T., Gallacher, J., Young, I., & Yarnell, J. (2015). Which biomarkers are predictive specifically for cardiovascular or for non-cardiovascular mortality in men? Evidence from the Caerphilly Prospective Study (CaPS). *International Journal of Cardiology*, *201,* 113−8. https://doi.org/10.1016/j.ijcard.2015.07.106

Pearlin, L. I. (2010). The life course and the stress process: Some conceptual comparisons. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *65B,* 207−15. https://doi.org/10.1093/geronb/gbp106

Pearlin, L. I., Menaghan, E. G., Lieberman, M. A., & Mullan, J. T. (1981). The Stress Process. *Journal of Health and Social Behavior*, *22*, 337−56. https://doi.org/10.2307/2136676

Pearlin, L. I., Nguyen, K. B., Schieman, S., & Milkie, M. A. (2007). The life-course origins of mastery among older people. *Journal of Health and Social Behavior*, *48*, 164−79. https://doi.org /10.1177/002214650704800205

Pearlin, L. I., & Schooler, C. (1978). The structure of coping. *Journal of Health and Social Behavior*, *19*, 2−21. http://www.jstor.org/stable/2136319 (Assessed 08.02.23)

Pedersen, S. S., von Känel, R., Tully, P. J., & Denollet, J. (2017). Psychosocial perspectives in cardiovascular disease. *European Journal of Preventive Cardiology*, *24*, 108–15. https://doi.org /10.1177/2047487317703827

Pedretti, R. F. E., Hansen, D., Ambrosetti, M., Back, M., Berger, T., Ferreira, M. C., Cornelissen, V., Davos, C. H., Doehner, W., de Pablo Y Zarzosa, C., Frederix, I., Greco, A., Kurpas, D., Michal, M., Osto, E., Pedersen, S. S., Salvador, R. E., Simonenko, M., Steca, P., … Abreu, A. (2023). How to optimize the adherence to a guideline-directed medical therapy in the secondary prevention of cardiovascular diseases: a clinical consensus statement from the European Association of Preventive Cardiology. *European Journal of Preventive Cardiology*, *30*, 149−66. https://doi.org/10.1093/eurjpc/zwac204

Pelliccia, A., Sharma, S., Gati, S., Bäck, M., Börjesson, M., Caselli, S., Collet, J. P., Corrado, D., Drezner, J. A., Halle, M., Hansen, D., Heidbuchel, H., Myers, J., Niebauer, J., Papadakis, M., Piepoli, M. F., Prescott, E., Roos-Hesselink, J. W., Graham Stuart, A., … Wijns, W. (2021). 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *European Heart Journal, 42*, 30−5. https://doi.org/10.1093/eurheartj/ehaa605

Pemberton, R., & Fuller Tyszkiewicz, M. D. (2016). Factors contributing to depressive mood states in everyday life: A systematic review. *Journal of Affective Disorders*, *200,* 103−10. https://doi.org /10.1016/j.jad.2016.04.023

Peralta, M., Ramos, M., Lipert, A., Martins, J., & Marques, A. (2018). Prevalence and trends of overweight and obesity in older adults from 10 European countries from 2005 to 2013. *Scandinavian Journal of Public Health*, *46*, 522−9. https://doi.org/10.1177/1403494818764810

Pescatello, L. S., Buchner, D. M., Jakicic, J. M., Powell, K. E., Kraus, W. E., Bloodgood, B., Campbell, W. W., Dietz, S., Dipietro, L., George, S. M., Macko, R. F., McTiernan, A., Pate, R. R., & Piercy, K. L. (2019). Physical activity to prevent

and treat hypertension: A systematic review. *Medicine and Science in Sports and Exercise, 51,* 1314−23. https://doi.org/10.1249/MSS.0000000000001943

Piepoli, M. F., & Villani, G. Q. (2017). Lifestyle modification in secondary prevention. *European Journal of Preventive Cardiology*, *24*, 101−7. https://doi.org/10.1177/2047487317703828

Pirie, K., Peto, R., Reeves, G. K., Green, J., & Beral, V. (2013). The 21st century hazards of smoking and benefits of stopping: A prospective study of one million women in the UK. *The Lancet*, *381*, 134−43. https://doi.org/10.1016/S0140-6736(12)61720-6

Piskorz, D. (2020). Hypertensive mediated organ damage and hypertension management. How to assess beneficial effects of antihypertensive treatments? *High Blood Pressure and Cardiovascular Prevention, 27,* 9−17. https://doi.org/10.1007/s40292-020-00361-6

Polenick, C. A., Birditt, K. S., Turkelson, A., Shattuck, S. M., & Kales, H. C. (2022). Longitudinal associations between chronic condition discordance and perceived control among older couples. *Psychology and Aging, 27,* 371−87. https://doi.org/10.1037/pag0000679

Power, M., & Kuyken, W. (1998). World Health Organization Quality of of Life Assessment (WHOQOL): Development and general psychometric properties. *Social Science and Medicine, 46, 1569−85.* https://doi.org/10.1016/S0277-9536(98)00009-4

Pudrovska, T., Schieman, S., Pearlin, L. I., & Nguyen, K. (2005). The sense of mastery as a mediator and moderator in the association between economic hardship and health in late life. *Journal of Aging and Health*, *17*, 634−60. https://doi.org/10.1177/0898264305279874

Quality System. (2022). *Primary Health Care Quality System. Estonian Health Insurance Fund.* http://www.haigekassa.ee/en/partner/primary-health-care-quality-system (Assessed 18.11.22).

Quispe, R., Elshazly, M. B., Zhao, D., Toth, P. P., Puri, R., Virani, S. S., Blumenthal, R. S., Martin, S. S., Jones, S. R., & Michos, E. D. (2020). Total cholesterol/HDL-cholesterol ratio discordance with LDL-cholesterol and non-HDL-cholesterol and incidence of atherosclerotic cardiovascular disease in primary prevention: The ARIC study. *European Journal of Preventive Cardiology*, *27*, 1597−605. https://doi.org/10.1177/2047487319862401

Rajagopalan, S., Al-Kindi, S. G., & Brook, R. D. (2018). Air pollution and cardiovascular disease: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*, *72,* 2054–70. https://doi.org/10.1016/j.jacc.2018.07.099

Rantanen, A. T., Korkeila, J. J. A., Löyttyniemi, E. S., Saxén, U. K. M., & Korhonen, P. E. (2018). Awareness of hypertension and depressive symptoms: a cross-sectional study in a primary care population. *Scandinavian Journal of Primary Health Care*, *36*, 323−8. https://doi.org/10.1080/02813432.2018.1499588

Rapsomaniki, E., Timmis, A., George, J., Pujades-Rodriguez, M., Shah, A. D., Denaxas, S., White, I. R., Caulfield, M. J., Deanfield, J. E., Smeeth, L., Williams, B., Hingorani, A., & Hemingway, H. (2014). Blood pressure and incidence of twelve cardiovascular diseases: Lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. *The Lancet*, *383,*1899–911. https://doi.org /10.1016/S0140-6736(14)60685-1

Reibling, N., Beckfield, J., Huijts, T., Schmidt-Catran, A., Thomson, K. H., & Wendt, C. (2017). Depressed during the depression: Has the economic crisis affected mental health inequalities in Europe? Findings from the European Social Survey (2014)

special module on the determinants of health. *European Journal of Public Health*, 27, 47−54. https://doi.org/10.1093/eurpub/ckw225

Reitsma, M. B., Fullman, N., Ng, M., Salama, J. S., Abajobir, A., Abate, K. H., Abbafati, C., Abera, S. F., Abraham, B., Abyu, G. Y., Adebiyi, A. O., Al-Aly, Z., Aleman, A. V., Ali, R., Alkerwi, A.,… Gakidou, E. (2017). Smoking prevalence and attributable disease burden in 195 countries and territories, 1990-2015: A systematic analysis from the global burden of disease study 2015. *The Lancet*, *389*, 1885−906. https://doi.org/10.1016/S0140-6736(17)30819-X

Rimoldi, S. F., Scherrer, U., & Messerli, F. H. (2014). Secondary arterial hypertension: When, who, and how to screen? *European Heart Journal*, *35,* 1245−54. https://doi.org/10.1093/eurheartj/eht534

Roepke, S. K., & Grant, I. (2011). Toward a more complete understanding of the effects of personal mastery on cardiometabolic health. *Health Psychology*, *30*, 615−32. https://doi.org/10.1037/a0023480

Romanov, K., Varjonen, J., Kaprio, J., & Koskenvuo, M. (2003). Life events and depressiveness - The effect of adjustment for psychosocial factors, somatic health and genetic liability. *Acta Psychiatrica Scandinavica*, *107*, 25−33. https://doi.org/10.1034/j.1600-0447.2003.01419.x

Rosenberg, M. (1965). Rosenberg: society and the adolescent self-image. In *Social Forces*. Princeton, NJ: Princeton University Press.

Rosengren, A., Hawken, S., Ôunpuu, S., Sliwa, P. K., Zubaid, M., Almahmeed, W. A., Ngu Blackett, K., Sitthi-Amorn, C., Sato, H., & Yusuf, P. S. (2004). Association of psychosocial risk factors with risk of acute myocardial infarction in 11 119 cases and 13 648 controls from 52 countries (the INTERHEART study): Case-control study. *The Lancet*, *364*, 953–62. https://doi.org/10.1016/S0140-6736(04)17019-0

Roth, G. A., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdela, J., Abdelalim, A., Abdollahpour, I., Abdulkader, R. S., Abebe, H. T., Abebe, M., Abebe, Z., … Murray, C. J. L. (2018). Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, *392*, 1736−88. https://doi.org/10.1016/S0140-6736(18)32203-7

Roth, G. A., Forouzanfar, M. H., Moran, A. E., Barber, R., Nguyen, G., Feigin, V. L., Naghavi, M., Mensah, G. A., & Murray, C. J. L. (2015). Demographic and epidemiologic drivers of global cardiovascular mortality. *New England Journal of Medicine*, *372*, 1333−41. https://doi.org/10.1056/nejmoa1406656

Saboya, P. M. H. P., Zimmermann, P. R., & Bodanese, L. C. (2010). Association between anxiety or depressive symptoms and arterial hypertension, and their impact on the quality of life. *International Journal of Psychiatry in Medicine*, *40*, 307−20. https://doi.org/10.2190/PM.40.3.f

Sandberg, K., & Ji, H. (2012). Sex differences in primary hypertension. *Biology of Sex Differences*, *3*, 7−28. https://doi.org/10.1186/2042-6410-3-7

Sanz, J., García-Vera, M. P., Magán, I., Espinosa, R., & Fortún, M. (2007). Differences in personality between sustained hypertension, isolated clinic hypertension and normotension. *European Journal of Personality*, *21*, 209−24. https://doi.org/10.1002/per.605

Schmitz, A., & Brandt, M. (2019). Gendered patterns of depression and its determinants in older Europeans. *Archives of Gerontology and Geriatrics*, *82*, 207−16. https://doi.org/10.1016/j.archger.2019.02.015

Schwardzer, R., & Luszczynska, A. (2012). Stressful Life Events. In I. B. Weiner, A. M. Nezu, C. M. Nezu, & P. A. Geller (Eds.), *Handbool of Psychology* (2nd Ed., pp. 29–56). John Wiley & Sons, Incorporated.

Schwarzer, R., & Schulz, U. (2002). The role of stressful life events. In *Comprehensive Handbook of Psychology Assessment.*(IX, pp. 522−33), John Wiley&Sons, Inc.

Seven, E., Husemoen, L. L. N., Wachtell, K., Ibsen, H., Linneberg, A., & Jeppesen, J. L. (2014). Overweight, adipocytokines and hypertension: A prospective population-based study. *Journal of Hypertension*, *32,* 1488−94. https://doi.org/10.1097/HJH.0000000000000207

Shahid, M., Sun, R. L., Liu, Y., Bao, J. L., Huang, C. X., Liao, Y., Zhou, S. X., Wang, J. F., & Zhang, Y. L. (2016). Is high high-density lipoprotein cholesterol beneficial for premature coronary heart disease? A meta-analysis. *European Journal of Preventive Cardiology, 23,* 704−13. https://doi.org /10.1177/2047487315610662

Shen, J., Tozer, D. J., Markus, H. S., & Tay, J. (2020). Network efficiency mediates the relationship between vascular burden and cognitive impairment: A diffusion tensor imaging study in UK Biobank. *Stroke, 51,* 1682−9. https://doi.org/10.1161/STROKEAHA.119.028587

Shi, H., Yang, X., Wang, J., Xi, H., Huang, C., He, J., Chu, M., & Zhuang, G. (2013). Type A personality, hostility, time urgency and unintentional injuries among Chinese undergraduates: A matched case-control study. *BMC Public Health*, *13*, 1066−75. https://doi.org/10.1186/1471-2458-13-1066

Shihab, H. M., Meoni, L. A., Chu, A. Y., Wang, N. Y., Ford, D. E., Liang, K. Y., Gallo, J. J., & Klag, M. J. (2012). Body mass index and risk of incident hypertension over the life course: The johns hopkins precursors study. *Circulation*, *126*, 2983−9. https://doi.org/10.1161/CIRCULATIONAHA.112.117333

Singh-Manoux, A., Macleod, J., & Davey Smith, G. (2003). Psychosocial factors and public health. *Journal of Epidemiology and Community Health*, *57*, 553−6. https://doi.org/10.1136/jech.57.8.553

Slagsvold, B., & Sørensen, A. (2013). Changes in sense of control in the second half of life: Results from a 5-year panel study. *International Journal of Aging and Human Development*, *77*, 289−308. https://doi.org/10.2190/AG.77.4.b

Sparrenberger, F., Cichelero, F. T., Ascoli, A. M., Fonseca, F. P., Weiss, G., Berwanger, O., Fuchs, S. C., Moreira, L. B., & Fuchs, F. D. (2009). Does psychosocial stress cause hypertension? A systematic review of observational studies. *Journal of Human Hypertension, 23,* 12−9. https://doi.org /10.1038/jhh.2008.74

Spruill, T. M. (2010). Chronic psychosocial stress and hypertension. *Current Hypertension Reports*, *12*, 10−6. https://doi.org/10.1007/s11906-009-0084-8

SPSS Statistics. (2011). *IBM Corporate,* New York, 10504-1722, United States.

Stansfeld, S., & Rasul, F. (2006). Psychosocial factors, depression and illness. In A. Steptoe (ed.). *Depression and Physical Illness* (II, pp. 19−50). Cambridge University Press. https://doi.org/10.1017/CBO9780511544293.003

Statistica. (2001). *TIBCO Software Inc.,* Palo Alto, CA 94304, United States.

Statistica. (2010). *TIBCO Software Inc.,* Palo Alto, CA 94304, Unites States.

Statistics Estonia. (2013). *Sotsiaaltrendid. Social Trends. Statistics Estonia.* http://www.stat.ee/sites/default/files/2020-07/Sotsiaaltrendid_6.pdf (Assessed 11.03.22).

Stergiou, G. S., & Bliziotis, I. A. (2011). Home blood pressure monitoring in the diagnosis and treatment of hypertension: A systematic review. *American Journal of Hypertension*, *24,* 123−34. http://doi.org/10.1038/ajh.2010.194

Stocker, R., & Keaney, J. F. (2004). Role of oxidative modifications in atherosclerosis. *Physiological Reviews, 84,* 1381−478. https://doi.org /10.1152/physrev.00047.2003

Tang, K. L., Rashid, R., Godley, J., & Ghali, W. A. (2016). Association between subjective social status and cardiovascular disease and cardiovascular risk factors: A systematic review and meta-analysis. *British Medical Journal Open*, *6,* e010137. https://doi.org/ 10.1136/bmjopen-2015-010137

Taylor, S. E., & Stanton, A. L. (2007). Coping resources, coping processes, and mental health. *Annual Review of Clinical Psychology*, 3, 377−401 https://doi.org/10.1146/annurev.clinpsy.3.022806.091520

The WHOQOL-Group. (1998). The development of the World Health Organization quality of life assessment: International perspectives. *Psychological Medicine*, *28,* 551−8. http://doi.org /10.1017/s0033291798006667.

Thoits, P. A. (2010). Stress and health: Major findings and policy implications. *Journal of Health and Social Behavior*, *51*, Suppl 1, S41–S53. https://doi.org/10.1177/0022146510383499

Threapleton, D. E., Greenwood, D. C., Evans, C. E. L., Cleghorn, C. L., Nykjaer, C., Woodhead, C., Cade, J. E., Gale, C. P., & Burley, V. J. (2013). Dietary fibre intake and risk of cardiovascular disease: Systematic review and meta-analysis. *British Medical Journal (Online)*, 347. https://doi.org/10.1136/bmj.f6879

Tibblin, G., Tibblin, B., Peciva, S., Kullman, S., & Svärdsudd, K. (1990). 'The Göteborg quality of life instrument'- an assessment of well-being and symptoms among men born 1913 and 1923. Methods and validity. *Scandinavian Journal of Primary Health Care,* Suppl, 1, S33−8.

Tofield, A. (2017). Air pollution and traffic noise effect on blood pressure. *European Heart Journal*, *38*, 71−2. https://doi.org /10.1093/eurheartj/ehw607

Touyz, R. M., Rios, F. J., Alves-Lopes, R., Neves, K. B., Camargo, L. L., & Montezano, A. C. (2020). Oxidative stress: A unifying paradigm in hypertension. *Canadian Journal of Cardiology*, *36,* 659−70. https://doi.org/10.1016/j.cjca.2020.02.081

Townsend, N., Wilson, L., Bhatnagar, P., Wickramasinghe, K., Rayner, M., & Nichols, M. (2016). Cardiovascular disease in Europe: Epidemiological update 2016. *European Heart Journal, 37,* 3232−45. https://doi.org /10.1093/eurheartj/ehw334

Trevisol, D. J., Moreira, L. B., Kerkhoff, A., Fuchs, S. C., & Fuchs, F. D. (2011). Health-related quality of life and hypertension: A systematic review and meta-analysis of observational studies. *Journal of Hypertension*, *29,* 179−88. https://doi.org/10.1097/HJH.0b013e328340d76f

Trzesniewski, K. H., Donnellan, M. B., & Robins, R. W. (2003). Stability of Self-Esteem Across the Life Span. *Journal of Personality and Social Psychology*, *84*, 205−20. https://doi.org/10.1037/0022-3514.84.1.205

Undén, A. L., Elofsson, S., Viigimaa, M., Johansson, J., & Knox, S. (2001). A psychosocial comparison of 35- and 55-year-old men and women in Sweden and Estonia: The Swestonia cardiovascular risk factor study. *International Journal of Behavioral Medicine*, *8*, 149−62. https://doi.org/10.1207/s15327558ijbm0802_05

UNDP. (2020). *The 2020 Human Development Report: The next frontier.* Human development and the Anthropocene. In UNDP: New York, NY, USA.

UNDP. (2022a). *Dimensions and Indicators of Human Development Index (HDI).* United Nations Development Programme. http://hdr.undp.org/data-center/human-development-index#/indicies/HDI (Assessed 15.02.22).

UNDP. (2022b). *Explore HDI. Human Development Programme.* UNDP. http://hdr.undp.org/data-center/human-development-index#/indicies /HDI (Assessed 11.04.22)
UNDP. (2022c). *Human Development Report. Education Index (1990-2019).*UNDP. http://hdr.undp.org/en/indicators/103706 (Assessed 11.02.22)
Vancheri, F., Tate, A. R., Henein, M., Backlund, L., Donfrancesco, C., Palmieri, L., & Strender, L.-E. (2021). Time trends in ischaemic heart disease incidence and mortality over three decades (1990–2019) in 20 Western European countries: systematic analysis of the Global Burden of Disease Study 2019. *European Journal of Preventive Cardiology*, 396−403. https://doi.org/10.1093/eurjpc/zwab134
Varrenti, M., Cesana, F., Greco, A., Frigerio, L., Mascolo, M., Mauri, S., Giupponi, L., Meani, P., Stucchi, M., D'Addario, M., Magrin, M. E., Miglioretti, M., Steca, P., & Giannattasio, C. (2014). Associations between cardiovascular risk factors, subclinical organ damage and psychological characteristics in a cohort of hypertensive patients. *High Blood Pressure and Cardiovascular Prevention*, *21*, 358–9. http://www.embase.com/search/results?subaction=viewrecor&from=export&id=L71990815 (Assessed 01.03.23)
Vartiainen, E. (2018). The North Karelia project: Cardiovascular disease prevention in Finland. *Global Cardiology Science and Practice*, *2018*, 504−18. https://doi.org/10.21542/gcsp.2018.13
Virdis, A., Giannarelli, C., Fritsch Neves, M., Taddei, S., & Ghiadoni, L. (2010). Cigarette smoking and hypertension. *Current Pharmaceutical Design*, *16*, 2518–25. https://doi.org/10.2174/138161210792062920
Visseren, F. L. J., MacH, F., Smulders, Y. M., Carballo, D., Koskinas, K. C., Bäck, M., Benetos, A., Biffi, A., Boavida, J. M., Capodanno, D., Cosyns, B., Crawford, C., Davos, C. H., Desormais, I., DI Angelantonio, E., Franco, O. H., Halvorsen, S., Hobbs, F. D. R., Hollander, M., … Williams, B. (2021). 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *European Heart Journal, 42*, 3269–72. https://doi.org/10.1093/eurheartj/ehab484
Von Känel, R. (2012). Psychosocial stress and cardiovascular risk – current opinion. In *Swiss Medical Weekly, 12,* 142−53. https://doi.org/10.4414/smw.2012.13502
Wagner, J., Lang, F. R., Neyer, F. J., & Wagner, G. G. (2014). Self-esteem across adulthood: The role of resources. *European Journal of Ageing*, *11*, 109−19. https://doi.org/10.1007/s10433-013-0299-z
Wannamethee, S. G., Lowe, G. D. O., Shaper, A. G., Rumley, A., Lennon, L., & Whincup, P. H. (2005). Associations between cigarette smoking, pipe/cigar smoking, and smoking cessation, and haemostatic and inflammatory markers for cardiovascular disease. *European Heart Journal*, *26*, 1765−73. https://doi.org/10.1093/eurheartj/ehi183
Warren, H. R., Evangelou, E., Cabrera, C. P., Gao, H., Ren, M., Mifsud, B., Ntalla, I., Surendran, P., Liu, C., Cook, J. P., Kraja, A. T., Drenos, F., Loh, M., Verweij, N., Marten, J., … Morris, A. P. (2017). Genome-wide association analysis identifies novel blood pressure loci and offers biological insights into cardiovascular risk. *Nature Genetics*, *49*, 403–15. https://doi.org/10.1038/ng.3768
Weber, K., Giannakopoulos, P., Herrmann, F. R., Bartolomei, J., Digiorgio, S., Ortiz Chicherio, N., Delaloye, C., Ghisletta, P., Lecerf, T., De Ribaupierre, A., & Canuto, A. (2013). Stressful life events and neuroticism as predictors of late-life versus early-life depression. *Psychogeriatrics*, *13*, 221−8. https://doi.org/10.1111/psyg.12024

Webster, A. C., Nagler, E. V., Morton, R. L., & Masson, P. (2017). Chronic kidney disease. *The Lancet*, 389, 1238–52. https://doi.org/10.1016/S0140-6736(16)32064-5

Wenger, N. K., Arnold, A., Bairey Merz, C. N., Cooper-DeHoff, R. M., Ferdinand, K. C., Fleg, J. L., Gulati, M., Isiadinso, I., Itchhaporia, D., Light-McGroary, K. A., Lindley, K. J., Mieres, J. H., Rosser, M. L., Saade, G. R., Walsh, M. N., & Pepine, C. J. (2018). Hypertension across a woman's life cycle. *Journal of the American College of Cardiology*, *71,* 1797–813. https://doi.org/10.1016/j.jacc.2018.02.033

Wenger, N. K., Ferdinand, K. C., Bairey Merz, C. N., Walsh, M. N., Gulati, M., & Pepine, C. J. (2016). Women, hypertension, and the systolic blood pressure intervention trial. *American Journal of Medicine*, *129,* 1030–6. https://doi.org/10.1016/j.amjmed.2016.06.022

Wheaton, B., & Montazer, S. (2012). Stressors, stress, and distress. In T.L. Scheid, T.N.Brown (Eds), *A handbook for the study of mental health*. (II, pp. 171-99). Cambridge University Press. https://doi.org/10.1017/cbo9780511984945.013

Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Collins, K. J., Dennison Himmelfarb, C., DePalma, S. M., Gidding, S., Jamerson, K. A., Jones, D. W., MacLaughlin, E. J., Muntner, P., Ovbiagele, B., … Wright, J. T. (2018). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS /APhA/ASH/ASPC/NMA /PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Pr. *Journal of the American College of Cardiology*, *71*, 127−248. https://doi.org/10.1016/j.jacc.2017.11.006

WHO. (2020). *The WHO guidelines on physical activity and sedentary behaviour*. Geneva: World Health Organization.

WHO. (2022a). *Age-standardized prevalence of hypertension among adults aged 30−79.* The Global Health Observatory. World Health Organization. http://who.int/data/gho/data/indicator-details/GHO/prevalence-of-hypertension-among adults -aged-30-79. (Assessed 17.02.23).

WHO. (2022b). *All ages SDR per 100 000 from diseases of circulatory system.* European Health Information Gateway. World Health Organization. http://www.gateway.euro.who.int/en/indicators/hfa_101-1320-sdr-diseases-of-circulatory-system-all-ages (Assessed 18.01.23).

WHO. (2022c). *At birth (years) life expectancy.* European Health Information Gateway. World Health Organization. http://who.int/data/gho/data/indicators/indicator-details/GHO/life-expectancy-at-birth-(years) (Assessed 18.02.22)

WHO. (2022d). *Body mass index.* World Health Organization. www.euro.who (Assessed 11.02.22).

WHO. (2022e). *Human Development index (HDI).* European Health Information Gateway. World Health Organization. http://gateway.euro.int/en/indicators/hfa_43-0500-undp-human-development-index-hdi/visualizations/#id =18849 (Assessed 18.02.22).

WHO. (2022f). *Ischaemic heart disease, age-standardized death rate.* European Health Information Gateway. World Health Organization. http://www.gateway.euro.who.int/en/datasets/european-mortality-database/#circulatory-and-respiratory-systems (Assessed 03.01.23).

WHO. (2022g). *Leading causes of death.* The Global Health Observatory. World Health Organization. http://www.euro.int/data/gho/data/themes/mortality-and-global-health-estimate /gho-leading-causes-of-death (Assessed 01.03.22).

WHO. (2022h). Prevalence of hypertension among aged 30-79 years, age-standardized. The Global Health Observatory indicators. World Health Organization. http://www.who.int/data/gho/data/indicators-details/GHO/prevalence-of-hypertension-among-adults-aged-30-70-years (Assessed 27.02.22).

Wicke, F. S., Güthlin, C., Mergenthal, K., Gensichen, J., Löffler, C., Bickel, H., Maier, W., Riedel-Heller, S. G., Weyerer, S., Wiese, B., König, H. H., Schön, G., Hansen, H., Van Den Bussche, H., Scherer, M., & Dahlhaus, A. (2014). Depressive mood mediates the influence of social support on health-related quality of life in elderly, multimorbid patients. *BMC Family Practice*, *15*, 61−4. https://doi.org/10.1186/1471-2296-15-62

Williams, B., Mancia, G., Spiering, W., Rosei, E. A., Azizi, M., Burnier, M., Clement, D. L., Coca, A., De Simone, G., Dominiczak, A., Kahan, T., Mahfoud, F., Redon, J., Ruilope, L., Zanchetti, A., … Zamorano, J. L. (2018). 2018 ESC/ESH Guidelines for themanagement of arterial hypertension. *European Heart Journal*, *39,* 3021−104. https://doi.org/10.1093/eurheartj/ehy339

Wirayuda, A. A. B., & Chan, M. F. (2021). A systematic review of sociodemographic, macroeconomic, and health resources factors on life expectancy. *Asia-Pacific Journal of Public Health*, 33, 335−56. https://doi.org/10.1177/1010539520983671

World Bank. (2022a). *The World by income.* The World Bank. http://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html (Assessed 11.04.2022).

World Bank. (2022b). *World development indicators. DataBank.* http://databank.worldbank.org/data/reports.aspx?source=Health%20Nutrition%20and%20Population%20Statistics#. (Assessed 21.01.22).

Xiao, L., Liu, Y., & Wang, N. (2014). New paradigms in inflammatory signaling in vascular endothelial cells. In *American Journal of Physiology – Heart and Circulatory Physiology*, 306, 317−23. https://doi.org/ 10.1152/ajpheart.00182.2013

Yanes, L. L., & Reckelhoff, J. F. (2011). Postmenopausal hypertension. *American Journal of Hypertension*, *24*, 740–9. https://doi.org /10.1038/ajh.2011.71

Yang, X., Li, Y., Li, Y., Ren, X., Zhang, X., Hu, D., Gao, Y., Xing, Y., & Shang, H. (2017). Oxidative stress-mediated atherosclerosis: Mechanisms and therapies. *Frontiers in Physiology, 8,* (online). https://doi.org/10.3389/fphys.2017.00600

Yusuf, P. S., Hawken, S., Õunpuu, S., Dans, T., Avezum, A., Lanas, F., McQueen, M., Budaj, A., Pais, P., Varigos, J., & Lisheng, L. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *The Lancet*, *364*, 937−52. https://doi.org/10.1016/S0140-6736(04)17018-9

Zanchetti, A. (2003). 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *Journal of Hypertension, 21,* 1011−53. https://doi.org/10.1097/00004872-200306000-00001

Zhou, B., Carrillo-Larco, R. M., Danaei, G., Riley, L. M., Paciorek, C. J., Stevens, G. A., Gregg, E. W., Bennett, J. E., Solomon, B., Singleton, R. K., Sophiea, M. K., Iurilli, M. L., Lhoste, V. P., Cowan, M. J., … Ezzati, M. (2021). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet*, *398*, 957−80. https://doi.org/10.1016/S0140-6736(21)01330-1

Zygmuntowicz, M., Owczarek, A., Elibol, A., & Chudek, J. (2012). Comorbidities and the quality of life in hypertensive patients. *Polskie Archiwum Medycyny Wewnetrznej*, *122*, 333−40. https://doi.org/10.20452/pamw.1345

SUMMARY IN ESTONIAN

Arteriaalse hüpertensiooni levimus, kardiovaskulaarne suremus ja nendega seotud riskitegurid: 13-aastane longituuduuring 35- ja 55-aastaste täiskasvanute hulgas Eestis ja Rootsis

Arteriaalne hüpertensioon (AH) on levinud haigus, mis tõstab oluliselt riski kardiovaskulaarseks (KV) haigestumuseks (Abbafati et al., 2020) ja suremuseks (Lozano et al., 2012). AH, mida defineeritakse kui süstoolne vererõhk ≥140 mmHg ja/või diastoolne vererõhk ≥90 mmHg (Williams et al., 2018), tüsistub ennekõike isheemilise südamehaigusena (ISH) (Rapsomaniki et al., 2014).

AH mittemodifitseeritavateks riskiteguriteks on vanus (Hay et al., 2020), sugu (Gerdts et al., 2022) ja pärilikkus (Horan et al., 2007). AH modifitseeritavateks riskiteguriteks on elustiili tegurid (ebatervislik toitumine, kehaline inaktiivsus, liigne alkoholi tarvitamine, suitsetamine) (Williams et al., 2018) ning normist kõrgem kehamassiindeks (KMI) (Hall et al., 2015; Landsberg et al., 2013).

Lisaks on AH kujunemine seotud kroonilise psühhosotsiaalse stressi (Infurna et al., 2018; Kivimäki & Steptoe, 2018; Pedersen et al., 2017) ja isiksuseomadustega (Infurna & Okun, 2015; Roepke & Grant, 2011). Isiksuseomadustest võivad madal meisterlikkuse ja enesehinnangu tase olla kas mediaatoriteks või moderaatoriteks, mille kaudu psühhosotsiaalsed tegurid avaldavad negatiivset mõju indiviidi tervisele (Ben-Zur, 2016; Bleidorn & Schwaba, 2018).

Eesti ja Rootsi poliitiline ja sotsiaalmajanduslik areng on olnud erinev. Kui Eesti vabanes Nõukogude Liidu koosseisust ja taastas riigi iseseisvuse 1991. aastal, siis Rootsi areng on olnud stabiilne viimased 200 aastat. Viimase 30 aasta jooksul on inimarengu indeks olnud Eestis madalam kui Rootsis. Näiteks 2018. aastal oli see Eestis 0,89 ja Rootsis 0,94 (UNDP, 2022a).

Möödunud 30 aasta jooksul on vanusele standarditud AH levimus 30−79-aastaste täiskasvanute hulgas Eestis vähenenud 46,3%-lt 1993. aastal 40,3%-le 2018. aastal (Rootsis vastavalt 38,9%-lt 30,8%-le) (WHO, 2022a). Vanusele standarditud suremus (100 000 inimese kohta) vereringeelundite haigustesse on vähenenud 712-lt 1993. aastal 310-le 2016. aastal (Rootsis vastavalt 320-lt 151-le) (WHO, 2022b).

AH levimuse ja KV suremuse ning nendega seotud riskitegurite laiemaks mõistmiseks kavandati Eestis ja Rootsis 35- ja 55-aastaste kohortide prospektiivne longituuduuring I lainega 1997. aastal (Johansson et al., 2002; Undén et al., 2001) ja II lainega 2010. aastal. Riskiteguritest keskenduti psühhosotsiaalsetele teguritele, isiksuseomadustele, elustiili teguritele ja tervisenäitajatele. Uuringu uudsus seisnes selles, et Eestis uuriti psühhosotsiaalsete tegurite ja isiksuseomaduste seost AH-ga esimest korda. Lisaks andsid uuringu tulemused ainulaadse võimaluse võrrelda Eestit ja Rootsit kui erineva poliitilise ja sotsiaalmajandusliku arenguga riiki.

Eesmärgid

Doktoriväitekirja üldeesmärgiks oli saada tõenduspõhine ülevaade AH levimusest, KV suremusest ning nendega seotud riskiteguritest Eesti ja Rootsi 35- ja 55-aastaste kohortides 13-aastase prospektiivse longituuduuringuga.

Uurimuse alaeesmärgid olid järgmised:

1. Kirjeldada AH levimust 13-aastase jälgimisperioodi möödudes, uurida psühhosotsiaalseid tegureid ja isiksuseomadusi Eesti ja Rootsi 35- ja 55-aastaste kohordis mõlemas uuringulaines ning analüüsida nende tegurite seost AH-ga Eesti ja Rootsi 55-aastaste kohordis uuringu II laines (I artikkel).
2. Kirjeldada AH levimust mõlemas uuringulaines ning uurida psühhosotsiaalsete tegurite, isiksuseomaduste, elustiili tegurite ja tervisenäitajate seost AH diagnoosiga 55-aastaste kohordis uuringu II laines Eestis (II artikkel).
3. Analüüsida KV suremust ja sellega seotud riskitegureid mitte-KV ja üldsuremuse kontekstis Eesti ja Rootsi 55-aastaste meeste kohordis pärast 13-aastast jälgimisperioodi (III artikkel).

Metoodika

Uuring põhines prospektiivsel longituuduuringul, mis viidi samaaegselt läbi Eestis ja Rootsis (SWESTONIA uuring) I lainena 1997. aastal ja II lainena 2010. aastal. SWESTONIA uuring jaotati põhi- ja alamuuringuks. Põhiuuring viidi läbi Tartus (Eesti) ja Sollentunas (Rootsi) 35- ja 55-aastaste meeste ja naiste hulgas Alamuuring viidi läbi 55-aastaste meeste ja naiste hulgas ainult Tartus. Põhi- ja alamuuringuga saadud andmed jagunesid primaarseteks ja sekundaarseteks.

Uuringu valim

Primaarsed andmed SWESTONIA uuringu I laines

Põhiuuring (I ja III artikkel). Vastavalt Eesti ja Rootsi Rahvastikuregistritest saadud andmetele 35- ja 55-aastaste isikute kohta kutsuti juhuvaliku alusel uuringusse kummaski riigis 100 meest ja 100 naist mõlemast vanuskohordist (n=800). Uuringu I laines osales kokku 549 uuritavat (277 Eestis ja 272 Rootsis). Täpsustamata vastamismäär Eesti 35-aastaste kohordis oli 70,0% ja 55-aastaste kohordis 68,5% ning Rootsis vastavalt 70,0% ja 66,0%.

Alamuuring (II artikkel). Vastavalt Eesti Rahvastikuregistrist saadud andmetele 55-aastaste isikute kohta kutsuti juhuvaliku teel uuringusse Tartus 250 meest ja 250 naist (n=500), kellest osales uuringus 330. Täpsustamata vastamismäär oli 66,0%.

Primaarsed andmed SWESTONIA uuringu II laines

Põhiuuring (I ja III artikkel). Aastal 2010 moodustasid II laine algse valimi 277 uuringu I laines osalenut Eestist ja 272 Rootsist. Vastavalt mõlema riigi Rahvastikuregistritest saadud andmetele oli uuringu II laine alguseks surnud 36 I laines osalenut, neist Eestist neli isikut 35-aastaste ja 27 isikut 55-aastaste

kohordist ning Rootsist viis isikut, kõik 55-aastaste kohordist. Lisaks puudusid Eesti Rahvastikuregistris kodused aadressid 10 uuritava kohta, kes osalesid I uuringulaines. Seega kaasati põhiuuringu II lainesse kokku 503 uuritavat (236 Eestist ja 267 Rootsist), kellest osales 371 (158 Eestist ja 213 Rootsist). Täpsustamata vastamismäär oli Eestis 35-aastaste kohordis (kes olid saanud 48-aastaseks) 54,7% ja 55-aastaste kohordis (kes olid saanud 68-aastaseks) 81,5% ning Rootsis vastavalt 73,6% ja 86,6%.

Alamuuring (II artikkel). Aastal 2010 moodustas II laine algse valimi Eestis 55-aastaste kohordist 330 I laines osalenut. Eesti Rahvastikuregistrist saadud andmete järgi oli II laine alguseks surnud 44 isikut. Seega kaasati alamuuringu II lainesse 55-aastaste kohordist (kes olid saanud 68-aastaseks) 286 meest ja naist, kellest osales 219. Täpsustamata vastamismäär oli 76,7%. Edaspidi kasutatakse vanuskohortide kirjeldamisel uuritavate vanust I laine järgi.

Sekundaarsed andmed SWESTONIA uuringu II laines

Haigestumuse andmed *(I ja II artikkel)*

II uuringulaine alguses saadi Eesti Haigekassast ja Rootsi Rahvuslikust Patsientide Registrist kõigi I laines osalejate kohta haigestumuse andmed diagnoosikoodide I00–I99 (vereringeelundite haigused) kohta perioodil 01.01.1999−31.03.2011 Rahvusvahelise Haiguste Klassifikatsiooni versioon 10 (RHK-10) järgi (ICD, 2010).

Suremuse andmed *(III artikkel)*

I uuringulaines kuulus Eesti ja Rootsi 55-aastaste kohorti kokku 268 isikut. Vastavalt Eesti ja Rootsi Rahvastikuregistritest saadud andmetele oli uuringu II laine alguseks neist surnud 32 isikut (27 Eestist ja viis Rootsist), kellest 30 olid mehed. Eesti ja Rootsi Surmapõhjuste Registritest saadi surmapõhjused 32 surnud isiku kohta perioodil 01.01.1999−31.03.2011 RHK-10 järgi (ICD, 2010).

Andmete kogumine

Primaarsed andmed SWESTONIA põhi- ja alamuuringu I laines

Kutse (kaaskiri, küsimustik ja ettemakstud vastusümbrik) uuringus osalemiseks saadeti potentsiaalsetele uuritavatele posti teel. Meeldetuletuskiri saadeti 10 päeva pärast neile, kes ei olnud vastanud esimesele kutsele. Kui uuritav ei olnud saatnud vastust teisele uuringukutsele, kontakteeruti temaga telefoni teel.

Uuringukutse kaaskirjas paluti uuritaval tulla visiidile Tartu Ülikooli Kliinikumi Eestis ja Karolinska Ülikooli haiglasse Rootsis. Visiidi käigus viidi läbi kehaline hindamine, võeti vereanalüüs ja paluti uuritaval täita küsimustik. Eesti ja Rootsi uuritavate vereproovid analüüsiti Karolinska Ülikooli haigla laboris Rootsis.

Primaarsed andmed SWESTONIA põhi- ja alamuuringu II laines

II laines ei teostatud uuritavate kehalist hindamist ega võetud vereanalüüse, kuid kasutati I lainega identset küsimustikku, millesse lisati küsimused keha-

kaalu, -pikkuse ja süstoolse, diastoolse vererõhu kohta. Küsimustik koos kutsega (kaaskiri ja ettemakstud vastus-ümbrik) saadeti potentsiaalsetele uuritavatele postiga. Kui uuritav ei vastanud kolme nädala jooksul, kontakteeruti temaga telefonitsi. Uuringu läbiviijad ei saanud kontakti 21 isikuga (telefoninumber polnud kättesaadav) ja 13 isikut keeldusid uuringus osalemisest.

Uuringus kasutatud tunnused

Primaarsed tunnused

Küsimustik (vt Lisa)

1) **Taustategurid** (I, II, III artikkel). Kasutati vanus, sugu, haridustase, perekonnaseis.
2) **Psühhosotsiaalsed tegurid** (I, II artikkel). Kasutati valideeritud mõõdikuid: negatiivsed stressitekitavad elusündmused (NSES) (*Life stress)* (Avison & Turner, 1988), depressiivne meeleolu (*Depression Model*) (Pearlin et al., 1981), Göteborgi elukvaliteedi instrument (*Gothenburg Quality of Life Instrument*) (Tibblin et al., 1990).
3) **Isiksuseomadused** (I, II artikkel). Kasutati valideeritud mõõdikuid: Pearlin'i meisterlikkuse skaala (*Pearlin Mastery Scale*) (Pearlin et al., 1981), Rosenberg'i enesehinnangu skaala (*Rosenberg Self-esteem Scale*) (Pearlin et al., 1981) ja A-tüüpi käitumismuster (*Type A behaviour pattern*) (Karlberg et al., 1997).
4) **Elustiili tegurid** (I, II artikkel). Uuriti toitumist, kehalist aktiivsust, alkoholi tarvitamist ja suitsetamist (Johansson et al., 2002).
5) **Tervisenäitajad** (I, II artikkel). I laines mõõdeti uuritava kehalisel hindamisel kehakaal, -pikkus ja arvutati KMI; mõõdeti süstoolne ja diastoolne vererõhk ning määrati KV biomarkerid: üldkolesterool ja selle fraktsioonid, triglütseriidid, C-reaktiivne valk, interleukiin-6, fibrinogeen ja vereglükoos. II laines saadi uuritava kehakaal, -pikkus, süstoolne ja diastoolne vererõhk küsimustikust.

Sekundaarsed tunnused

Haigestumuse andmed (I ja II artikkel) hõlmasid diagnoose I00–I99 (vereringeelundite haigused) RHK-10 järgi (ICD, 2010). Uuringu II laines osalejad jaotati AH-ga ja AH-ta kohortidesse. AH-ga kohorti kuulusid uuritavad, kellel esines perioodil 01.01.1999−31.03.2011 raviteenuste arvetel diagnoosikood I10 (raskusaste I–III) või I11 (raskusaste I–III) ja oli väljastatud vähemalt üks retsept antihüpertensiivsele ravimile.

Suremuse andmed (III artikkel). Surmapõhjused jagati KV-ks (I21, I25, I05, I07, I70.2, K55.0, I42) ja mitte-KV-ks RHK-10 tuginedes (ICD, 2010).

Statistiline andmeanalüüs

Andmeanalüüsiks kasutati statistika tarkvarapakette *Statistica ja SPSS*. Psühhomeetriliste mõõdikute sisereliaablust hinnati *Cronbach a*-kordajaga, mis jäi vahemikku 0,70−0,99. Andmete normaaljaotust hinnati *Wilk W*-testiga; rühmadevahelist erinevust *t*-testiga (parameetrilised tunnused) ja *Wilcoxon* testiga (mitte-

parameetrilised tunnused); kategoorilisi tunnuseid võrreldi hii-ruut testiga ning kahte mittesõltuvat kohorti (AH-ga ja AH-ta uuritavad) *Mann-Whitney U*-testiga. Tunnuste vahelist seost hinnati lineaarse ja logistilise regressioonanalüüsi ning elulemust *Cox*'i regressioonmudeli abil.

Tulemused

Arteriaalse hüpertensiooni levimus, psühhosotsiaalsed tegurid ja isiksuseomadused SWESTONIA põhiuuringus (I artikkel)

Pärast 13-aastast jälgimisperioodi oli AH levimus 35-aastaste kohordis Eestis 21,4% ja Rootsis 4,8% ($p<0,001$) ning 55-aastaste kohordis vastavalt 52,3% ja 37.3% ($p<0,001$).

Psühhosotsiaalsetest teguritest oli depressiivse meeleolu mediaanskoor oluliselt kõrgem ($p<0,001$) ja üldine elukvaliteedi mediaanskoor oluliselt madalam ($p<0.001$) Eestis võrreldes Rootsiga nii 35- kui 55-aastaste kohordis I ja II laines. NSES arv ja NSES mõju indiviidile (cm-s) kogumõjust mediaanskoorid olid oluliselt kõrgemad ($p<0,001$) Eesti mõlemas vanuskohordis võrreldes Rootsiga I ja II laines, v.a Eesti 35-aastastel II laines.

Isiksuseomadustest olid meisterlikkuse ja enesehinnangu mediaanskoorid oluliselt madalamad (vastavalt $p<0,001$ ja $p<0,01$) 35-aastastel Eestis võrreldes Rootsiga I ja II laines. 55-aastastel Eestis võrreldes Rootsiga oli meisterlikkuse mediaanskoor oluliselt madalam ($p<0,01$) I laines, enesehinnangu mediaanskoor oluliselt madalam ($p<0,001$) II laines ning A-tüüpi käitumismustri mediaanskoor oluliselt madalam I ja II laines (vastavalt $p<0,05$ ja $p<0,001$).

Võrreldes Eesti 55-aastaste AH-ta kohordiga oli AH-ga kohordis NSES-st mõju mediaanskoor oluliselt kõrgem ($p<0,05$) ja meisterlikkuse mediaanskoor oluliselt madalam ($p<0,05$). Lineaarne regressioonanalüüs (pärast soole, perekonnaseisule ja haridustasemele kohandamist) näitas, et AH-ga 55-aastastel eestlastel oli NSES-st mõju ja meisterlikkus seotud depressiivse meeleoluga (R Square=0,311, $F^{2,43}=22,69$, $p<0,001$). Rootslastel taolist seost ei leitud ($p=0,07$).

Arteriaalne hüpertensioon, psühhosotsiaalsed tegurid, isiksuseomadused, elustiili tegurid ja tervisenäitajad Eesti 55-aastaste alamuuringus (II artikkel)

13-aastase jälgimisperioodi järel oli 55-aastaste eestlaste hulgas AH levimus suurenenud 4,1%-lt 53,0%-ni.

Võrreldes uuringu I lainega olid II laines:

- psühhosotsiaalsetest teguritest üldise elukvaliteedi ja sellega seotud alamdomeenide (sotsiaalne, füüsiline ja vaimne heaolu) mediaanskoorid oluliselt madalamad (vastavalt $p<0,001$, $p<0,01$, $p<0,001$, $p<0,001$) ning depressiivse meeleolu ja NSES arvu mediaanskoorid oluliselt madalamad (vastavalt $p<0,001$, $p<0,01$).
- isiksuseomadustest nii enesehinnangu kui meisterlikkuse mediaanskoorid oluliselt kõrgemad ($p<0.001$).

– elustiili teguritest toidurasva kvaliteedi (kõrgem skoor näitas rohkem polü- ja monoküllastumata rasvhappeid toidusedelis) mediaanskoor ja kehaline aktiivsus (korda kuus) oluliselt kõrgemad (vastavalt $p<0,001$ ja $p<0,01$) ning alkoholi tarvitamise mediaanskoor (grammi puhast etanooli nädalas) ja suitsetamise levimus oluliselt madalamad (vastavalt $p<0,001$ ja $p<0,001$).

Võrreldes AH-ta uuritavatega olid AH-ga uuritavatel II laines:

– psühhosotsiaalsetest teguritest nii üldine elukvaliteedi kui selle alamdomeeni füüsilise heaolu mediaanskoor oluliselt madalamad (vastavalt $p<0,05$ ja $p<0,01$), kuid depressiivse meeleolu mediaanskoor ja NSES mõju indiviidile mediaanskoor oluliselt kõrgemad (vastavalt $p<0,05$ ja $p<0,05$). NSES hulgas oli suurim mõju isiklikul haigusel (38,8%, mõju ulatus 319,6 cm kogumõjust) ja finantsprobleemidel (27,8%, mõju ulatus 313,0 cm kogumõjust).
– isiksuseomadustest meisterlikkuse mediaanskoor oluliselt madalam ($p<0,05$).
– elustiili teguritest suitsetamise levimus oluliselt madalam ($p<0,05$).
– tervisenäitajatest rasvumuse levimus oluliselt kõrgem ($p<0,001$).

Logistiline regressioonmudel näitas, et rasvumus (KMI≥30,0 kg/m²) ennustas neli korda kõrgemat šanssi (OR=4,03, 95%CI 1,63−10,01, p=0,03) AH kujunemiseks võrreldes normkaalus uuritavatega (KMI≤24,9 kg/m²).

Kardiovaskulaarne suremus ning selle riskitegurid mitte-kardiovaskulaarse ja üldsuremuse kontekstis SWESTONIA põhiuuringus (III artikkel)

II uuringulaine alguseks oli Eestis ja Rootsis I uuringulaines osalenud 137 mehest surnud 30 (neist Eestist 86,7%). Surmapõhjuste järgi olid 13 (43,3%) KV ja 17 (56,7%) mitte-KV surmad. KV suremuse rühmas suri 76,9% ISH tõttu. Cox'i võrdeliste riskide mudeli tulemustest selgus, et tõenäosus surra KV haigustesse oli 6,4 (95% CI 1,7−23,1) korda suurem suitsetajatel ja 2,1 (95% CI 1,4−3,1) korda suurem kõrge interleukiin-6 tasemega isikutel; mitte-KV suremuse korral olid vastavad riskide suhted 4,6 (95% CI 1,6−13,2) ja 1,7 (95% CI 1,4−2,1).

Järeldused

SWESTONIA põhiuuringus leiti, et pärast 13-aastast jälgimisperioodi oli AH levimus oluliselt kõrgem Eestis kui Rootsis. Mõlemas riigis oli AH seotud mitmete psühhosotsiaalsete tegurite ja isiksuseomadustega. Eesti alamuuringu II laines leiti, et 55-aastaste kohordis oli rasvumine peamine AH teket ennustav riskitegur. KV suremus Eesti ja Rootsi 55-aastaste meeste kohordis oli SWESTONIA põhiuuringu jälgimisperioodi lõpus oluliselt kõrgem Eestis kui Rootsis.

Tööl põhinevad täpsemad järeldused on järgmised:

1. AH diagnoositi 55-aastaste kohordis enam kui pooltel eestlastel, kuid enam kui kolmandikul rootslastel 13-aastase jälgimisperioodi lõpus. Mõlemas vanuskohordis oli eestlastel võrreldes rootslastega oluliselt kõrgem depressiivne meeleolu ja NSES-st mõju, kuid madalam üldine elukvaliteet mõle-

mas uuringulaines. Võrreldes 55-aastaste AH-ga rootslastega oli eestlastel NSES-st mõju oluliselt kõrgem ja meisterlikkus oluliselt madalam.
2. AH levimus suurenes oluliselt Eesti 55-aastaste kohordis 13 aasta jooksul. Mitmed psühhosotsiaalsed ja elustiili tegurid ning tervisenäitajad näitasid sõltumatut seost AH-ga, kuid lõplikus regressioonmudelis oli AH-ga seotud vaid rasvumine.
3. Üks viiendik Eesti ja Rootsi 55-aastaste meeste kohordist suri 13 aasta jooksul. Ligi pooled surmadest olid tingitud KV haigustest ja nendega seotud surmade arv oli Eestis kuus korda kõrgem kui Rootsis. Eesti ja Rootsi meeste kohordis ennustasid KV suremust suitsetamine ja vereplasma interleukiin-6 kõrgem tase.

Praktilised soovitused

SWESTONIA uuringu tulemused on kasulikud primaarseks ja sekundaarseks ennetuseks. Riskitegurite jätkusuutlik käsitlus on oluline AH haigestumuse ja sellega seotud KV suremuse vähendamiseks Eestis.

Tööl põhinevad täpsemad praktilised soovitused on järgmised:

1. Psühhosotsiaalsed tegurid ja isiksuseomadused võiks välja sõeluda AH primaarse ja sekundaarse ennetuse vältel.
2. Pearlini meisterlikkuse skaala on soovitav lisada AH käsitluse ravijuhendisse, et hinnata indiviidi eneseusku toime tulla psühho-sotsiaalse stressiga.
3. Elustiili teguritest tuleb erilist tähelepanu pöörata rasvumise ja suitsetamise ennetamisele ning suitsetamisest loobumisele indiviidi-, rühma- ja rahvastikupõhise lähenemise abil.
4. AH riskirühma kuuluvaid isikuid tuleb avastada ja ravida varakult kasutades selleks terviklikku lähenemist kõigi riskitegurite osas ning rakendades erinevaid e-tervise strateegiaid ravi jälgimiseks.
5. Tõhus, pikaajaline ja keskselt koordineeritud valdkondadevaheline lähenemisviis peab olema AH ennetuses keskne, sealhulgas tuleb keskenduda haavatavatele elanikkonna rühmadele ja järgida naaberriikide (nt Rootsi, Soome) parimaid praktikaid.

ACKNOWLEDGEMENTS

This study was granted by Estonian Research Council (BF109) and by Estonian Centre of Excellence (TAR16013DB).

The author of the doctoral thesis would like to thank all those who contributed to the present study and my doctoral studies generally. In particular, I wish to express my gratitude to the following persons:

- my supervisor Professor Margus Viigimaa for his long-term and strong support throughout my doctoral studies. I am thankful to Professor Margus Viigimaa for provision of detailed overview of conducting the first wave of this longitudinal study. I appreciate his accuracy in the mentorship and in writing of the articles.
- my supervisor Associate Professor Kersti Pärna who joined the process of the supervision from the beginning of the thesis' writing. I am grateful to her for good thoughts and instructions, and relevant questions at the time of writing of the dissertation. I would like to thank Kersti Pärna for having shown great commitment to the revision of my doctoral thesis.
- my former supervisor Professor Raul-Allan Kiivet for his support and relevant recommendations until the end of his life.
- Heti Pisarev for thoughts of statistical analysis, and Karin Mets for provision of instructions upon performance of statistical analysis.
- reviewers Associate Professor Marje Oona and Research Fellow Tiia Ainla for giving effective feedback on this manuscript.
- Ilmar Part for English language revision of the doctoral thesis.
- all members of SWESTONIA study's team outside Estonia: Professor Mats Jensen-Urstad and dr. Hanna Lenhoff from Sweden, and Professor Jan Johansson from USA for their advices throughout the research process and for the contribution to scientific articles.
- all the study subjects who took part in the SWESTONIA study.
- Institute of Family Medicine and Public Health in University of Tartu for support throughout my doctoral studies.
- my colleaques from Tartu Health Care College for their support.
- my Mother for her strong support during my doctoral studies until the end of her life.
- other very close people in my life who expressed their motivational support to me throughout my doctoral studies.

APPENDIX: Questionnaire

KÜSIMUSTIK SÜDAME-VERESOONKONNA HAIGUSTE RISKIFAKTORITE VÄLJASELGITAMISEKS

Osalesite aastatel 1997-1998 SWESTONIA uuringus. SWESTONIA 13-aasta järeluuringus soovime taas selgitada Teie südame-veresoonkonna haiguste riskitegurid. Palume Teil täita küsimustik oma harjumuste ja eluolu kohta (nt toitumine, füüsiline koormus, suitsetamine, elukvaliteet).

Antud uuring on heaks kiidetud Tallinna Inimuuringute Eetika Komitee poolt (2007).
Andmete töötlemisel ei kasutata Teie nime ega isikukoodi ja uuringutulemused avaldatakse summaarselt kõigi uuritute kohta.

- **Ees- ja perekonnanimi** _____
- **Pikkus** _____
- **Kaal** _____

Vererõhk (kui Teil on võimalik määrata)

parem käsi	_____	_____
	Süstoolne (ülemine näit)	*Diastoolne (alumine näit)*
vasak käsi	_____	_____
	Süstoolne (ülemine näit)	*Diastoolne (alumine näit)*

TAUSTA KÜSIMUSED

1. **Sugu**
   - ☐ mees
   - ☐ naine

2. **Vanus ____ aastat**

3. **Elukutse** _____
   Tööülesanded
   _____

4. **Haridus**
   - ☐ põhikool
   - ☐ gümnaasium/keskkool
   - ☐ 1-2 aastat õppimist pärast gümnaasiumi/keskkooli
   - ☐ vähemalt 3-4 aastat õppimist pärast gümnaasiumi, kaasa arvatud kõrgem haridus

5. **Perekonnaseis**
   - ☐ abielus/vabaabielus
   - ☐ vallaline/lesk/lahutatud

6. **Mitu alla 16. aastast last elab teil kodus?** _____

KÜSIMUSED TOITUMISTAVADE KOHTA <u>viimase nelja nädala jooksul</u>

7. Kui tihti on Teil kombeks süüa nii hommiku-, lõuna- kui ka õhtusööki?

□ harva
□ mõnikord
□ enamasti

8. Kui tihti on Teil kombeks süüa hommikusööki?

□ 1 kord nädalas
□ 2-3 korda nädalas
□ 4-5 korda nädalas
□ 6-7 korda nädalas

9. Kui tihti on Teil kombeks süüa lõunasööki?

□ 1 kord nädalas
□ 2-3 korda nädalas
□ 4-5 korda nädalas
□ 6-7 korda nädalas

10. Kui tihti on Teil kombeks süüa õhtusööki?

□ 1 kord nädalas
□ 2-3 korda nädalas
□ 4-5 korda nädalas
□ 6-7 korda nädalas

11. Mitu võileiba (leib, või/ margariin ja leivamääre) Te päevas sööte?

□ mitte ühtegi
□ kõige rohkem 2 võileiba
□ 3-5 võileiba
□ vähemalt 6 võileiba

12. Mida Te tavaliselt leiva peale määrite?

□ või, taluvõi, Võideks või Bregott (80% rasva)
□ lahja või ja/või lauamargariin Lätta, Bordseve, Flora, Rama, Voimix, Allround (60% rasva)
□ Nytta, Vigor, Keiju või Aroma (40% rasva)
□ ma ei määri mingit rasvainet (leivamääret) leiva peale

13. Kui palju võid või margariini Te ühe võileiva peale panete?

□□palju (umbes 10 g)
□□mõõdukalt (umbes 5 g)
□□veidi (alla 5 g)
□□ei kasuta üldse

14. Kui palju juustu-, vorsti- või maksapasteediga leivaviile Te päevas sööte?

□□Vähemalt 6
□□3-5
□□1-2
□□Mitte ühtegi

15. Kui palju juustuviile Te võileiva peale panete?

□□3 või rohkem viilu
□□2 viilu
□□1 viilu
□□ma ei söö juustu

16. Misssugust piima, keefiri või jogurtit Te eelistate?

□□tavalist (3% rasvasisaldusega)
□□võipiima (2,5% rasvasisaldusega)
□□väldin piimaprodukte

17. Kui sageli Te sööte puuvilju või marju?

□□harva
□□mõni kord nädalas
□□iga päev
□□mitu korda päevas

18. Kui sageli Te sööte praetud kartuleid, friikartuleid või kartulihautist?

□□paar korda nädalas
□□1 kord nädalas
□□paar korda kuus
□□peaaegu mitte kunagi

19. Kui sageli Te sööte juurvilju või aedvilja (välja arvatud salat, tomat, kurk)?

□□paar korda nädalas või veel harvemini
□□peaaegu iga päev
□□rohkem kui üks kord päevas

20. Kui sageli Te sööte rasvast kala (heeringas, räim, lõhe, makrell)?

□□harva
□□1-2 korda nädalas
□□3 korda nädalas või sagedamini

21. Kui sageli Te sööte praevorsti, pizzat, hamburgerit või peekonit päeva kõige tugevamaks söögikorraks?

□□paar korda nädalas või sagedamini
□□1 kord nädalas
□□paar korda kuus
□□peaaegu mitte kunagi

22. Kas Te lõikate peki liha küljest ära?

□□ei
□□mõnikord
□□jah

23. Kui palju Te sööte mune?

□□1 muna päevas või rohkem
□□4-6 muna nädalas
□□2-3 muna nädalas
□□1 muna nädalas või vähem

24. Kui sageli Te kasutate toidus (valmistamisel, lisate lauas) vähese rasvasisaldusega margariini, Nyttat, Vigöri, vedelat margariini või õli?

□□harva
□□umbes 1 kord kuus
□□iga päev

25. Kui sageli Te kasutate toidus rõõska koort, vahukoort, võid, Bregotti või Hushall margariini?

□□iga päev
□□umbes 1 kord nädalas
□□harva või üldse mitte

26. Kui sageli Te sööte tshipse, šokolaadi, saiakesi, torte, dessertjuustu?

□□paar korda nädalas või sagedamini
□□1 kord nädalas
□□paar korda kuus
□□peaaegu mitte kunagi

27. Kui sageli Te ostate spetsiaalselt madalakalorilist ja vähe küllastanud rasvhappeid sisaldavat toitu?

□□mitte kunagi
□□harva
□□tihti
□□alati

KÜSIMUSED ALKOHOLI JA SUITSETAMISE KOHTA <u>viimase kuu jooksul</u>

28. Kui palju lahjat õlut Te olete joonud viimase kuu jooksul?

□□1 purk või pudel (a´330 ml) päevas või rohkem
□□4-6 purki nädalas (a´ 330 ml)
□□2-3 purki nädalas (a´ 330 ml)
□□1 purk nädalas või vähem (a´ 330 ml)
□□pole üldse joonud

29. Kui palju kanget/keskmise kangusega õlut Te olete joonud viimase kuu jooksul?

□□1 purk päevas või rohkem (a´ 330 ml)
□□4-6 purki nädalas (a´ 330 ml)
□□2-3 purki nädalas (a´ 330 ml)
□□1 purk nädalas või vähem (a´ 330 ml)
□□pole üldse joonud

30. Kui palju veini (sh kanget veini) Te olete joonud viimase kuu jooksul?

□□4 pudelit (4x750 ml) nädalas või rohkem
□□2-3 pudelit nädalas (2-3x750 ml)
□□½ pudelit nädalas (375 ml)
□□vähem kui ½ pudelit nädalas (<375 ml)
□□pole üldse joonud

31. Kui palju kanget alkoholi (viski, liköör, viin) Te olete joonud viimase kuu jooksul?

□□1 pudel (750 ml) nädalas või rohkem
□□350-750 ml nädalas
□□150-350 ml nädalas
□□vähem kui 150 ml nädalas
□□pole üldse joonud

32. Kas Te suitsetate käesoleval ajal?

□□ei
□□jah

Kui ***jah***, siis sigarettide arv päevas on: _____
Piibutubaka pakkide arv päevas on: _____
Suitsetan _____ aastat

33. Kas Te kunagi varem olete suitsetanud?

□□ei
□□jah

Kui ***jah***, siis millal lõpetasite? _____

34. Kas Te kasutate nuusktubakat?

□□ei
□□jah

Kui ***jah***, siis dooside arv nädalas on: _____
Kasutan nuusktubakat _____ aastat

35. Kas Te kunagi varem olete kasutanud nuusktubakat?

□□ei
□□jah

Kui ***jah***, siis millal lõpetasite? _____

KÜSIMUSED KEHALISE LIIKUMISE KOHTA <u>viimase kuu jooksul</u>

36. Kui palju kordi Te olete viimase kuu jooksul tegelenud järgmiste spordialadega?

	Kordade arv	Kui kaua (minutites)?
Jalgrattasõit	_____	_____
Tervisejooks	_____	_____
Jooksmine	_____	_____
Liikumisvõimlemine	_____	_____
Suusatamine	_____	_____
Sulgpall, squash	_____	_____

Tennis, lauatennis	_____	_____
Jalutuskäik	_____	_____
Aiatöö jm füüsiline töö	_____	_____
Tantsimine	_____	_____
Jäähoki/uisutamine	_____	_____
Jalgpall	_____	_____
Jõutreening	_____	_____
Aeroobika ja sellega sarnane	_____	_____
Ujumine	_____	_____
Muu (mis nimelt)	_____	_____

37. Kas midagi sellist, mis on järgnevalt kirjas, on Teiega <u>viimase kuue kuu jooksul</u> juhtunud ja kui tugevasti see Teile mõjus? Palun hinnake, kuidas juhtum Teile mõjus ja <u>märkige joonele rist</u>.

	jah	ei	ei mõjunud üldse → → → → mõjus väga tugevalt
Lähedase inimese surm	☐	☐	_____
Oma haigus	☐	☐	_____
Lähedase haigus	☐	☐	_____
Töötaolek	☐	☐	_____
Probleemid väike-/teismelise/ täiskasvanud lapsega	☐	☐	_____
Muutunud suhted abikaasaga	☐	☐	_____
Majandusprobleemid	☐	☐	_____
Mure/kurbuse perioodid	☐	☐	_____

Teised juhtumid, mis Teile mõjusid .....
(palun nimetage need juhtumid)

☐ ☐ _____

KÜSIMUSED VAIMSE ENERGIA KOHTA

38. Kas Teil on <u>viimase kuue kuu jooksul</u> olnud mõni allpool mainitud probleemidest?

	jah	ei
1. On puudunud entusiasm midagi ette võtta	☐	☐
2. Söögiisu on kadunud	☐	☐
3. Olete tundnud end üksikuna	☐	☐
4. Olete tundnud end väsinuna või Teil pole olnud huvi midagi teha	☐	☐
5. On olnud raskusi uinumisega või enda virgena hoidmisega	☐	☐
6. Olete olnud nutuvalmis või on Teil olnud kerge nutma hakata	☐	☐
7. Olete tundnud end masendatuna või kurvana	☐	☐
8. Olete tundnud end jõuetuna või ilma energiata	☐	☐
9. Olete tundnud lootusetust tuleviku ees	☐	☐

KÜSIMUSED ISELOOMU KOHTA

39. Mil määral nõustute <u>iga</u> järgmise väitega iseenda kohta?

		olen nõus	osaliselt nõus	ei ole nõus
1.	Vihastun kergesti	☐	☐	☐
2.	Tahan, et kõik saaks tehtud kiiresti	☐	☐	☐
3.	Inimesed ütlevad mulle sageli „Võta vähe tempot maha”	☐	☐	☐
4.	Elan kiire tempoga ja piitsutan end tagant	☐	☐	☐
5.	Muutun kannatamatuks, kui inimesed teevad midagi aeglaselt	☐	☐	☐
6.	Ärritun inimeste peale, kes on kohmetud ja hooletud	☐	☐	☐
7.	Mul on alati kiire	☐	☐	☐
8.	Katsun töötada oma tavalise tempoga isegi siis, kui olen väsinud ja tujutu	☐	☐	☐
9.	Ärritun kuulates põhjalikke inimesi	☐	☐	☐
10.	Usun, et inimesed tahavad mulle halba teha, kui neil ainult selleks võimalus avaneb	☐	☐	☐

KÜSIMUSED ENESETUNDE KOHTA

40. Mil määral nõustute või ei nõustu üldse <u>iga</u> järgmise väitega iseenda kohta?

		üldse mitte	üsna vähe	üsna palju	palju
1.	Tunnen, et olen väärtuslik inimene, vähemalt võrdne teistega	☐	☐	☐	☐
2.	Tunnen, et mul on palju häid omadusi	☐	☐	☐	☐
3.	Lõppkokkuvõttes kaldun alati tundma end ebaõnnestununa	☐	☐	☐	☐
4.	Suudan kõike teha sama hästi kui teised	☐	☐	☐	☐
5.	Tunnen, et minus ei ole palju sellist, mille üle uhke olla	☐	☐	☐	☐
6.	Suhtun endasse positiivselt	☐	☐	☐	☐
7.	Üldkokkuvõttes olen endaga rahul	☐	☐	☐	☐
8.	Mõnikord tunnen end tõesti väärtusetuna	☐	☐	☐	☐
9.	Sooviksin, et suudaksin tunda suuremat austust enda vastu	☐	☐	☐	☐
10.	Mõnikord ma arvan, et minus pole midagi head, minuga on lood kehvad	☐	☐	☐	☐

KÜSIMUSED PROBLEEMIDE LAHENDAMISE KOHTA

41. Mil määral nõustute või ei nõustu üldse iga järgmise väitega iseenda kohta?

	üldse mitte	üsna vähe	üsna palju	palju
1. Ma ei oska kohe tõesti mingit moodi oma probleeme lahendada	☐	☐	☐	☐
2. Mõnikord tundub mulle, et ma vaid hõljun elus ringi	☐	☐	☐	☐
3. Mul on puudulik kontroll asjade üle, mis minuga juhtub	☐	☐	☐	☐
4. Ma viin ellu peaaegu kõik, mida ma olen otsustanud	☐	☐	☐	☐
5. Tunnen end elus tihti probleemide ees abitult	☐	☐	☐	☐
6. See, mis minuga tulevikus juhtub, sõltub suurel määral minust enesest	☐	☐	☐	☐
7. Mina ise ei saa midagi erilist teha, et oma elus tähtsaid asju muuta	☐	☐	☐	☐

KÜSIMUSED ELUKVALITEEDI KOHTA

42. Märkige ristiga see kast, mis sobib kõige paremini sellega, kui rahul Te olete oma eluga 7-palli skaalal käesoleval ajal.

	väga halvasti			→ → →			suurepärane, ei saa parem olla
1. kodu ja perekond	☐	☐	☐	☐	☐	☐	☐
2. elukoht	☐	☐	☐	☐	☐	☐	☐
3. töö	☐	☐	☐	☐	☐	☐	☐
4. majanduslik seis	☐	☐	☐	☐	☐	☐	☐
5. vaba aeg	☐	☐	☐	☐	☐	☐	☐
6. kuulmine	☐	☐	☐	☐	☐	☐	☐
7. nägemine	☐	☐	☐	☐	☐	☐	☐
8. mälu	☐	☐	☐	☐	☐	☐	☐
9. kehalised võimed, „vorm”	☐	☐	☐	☐	☐	☐	☐
10. isu	☐	☐	☐	☐	☐	☐	☐
11. meeleolu	☐	☐	☐	☐	☐	☐	☐
12. energia	☐	☐	☐	☐	☐	☐	☐
13. kannatlikkus	☐	☐	☐	☐	☐	☐	☐
14. eneseusk	☐	☐	☐	☐	☐	☐	☐
15. uni	☐	☐	☐	☐	☐	☐	☐
16. kas Te tunnete end väljaspool kodu olulise ja hinnatud inimesena?	☐	☐	☐	☐	☐	☐	☐
17. kas Te tunnete end kodus olulise ja hinnatud inimesena?	☐	☐	☐	☐	☐	☐	☐

Palju tänu Teile vastamise eest!

PUBLICATIONS

CURRICULUM VITAE

Name: Sirje Sammul
e-mail: sirje.sammul.001@mail.ee

Education:

2010−…	University of Tartu, Faculty of Medicine, Institute of Family Medicine and Public Health, Doctoral programme in Medical Sciences
2003−2006	University of Tartu, Faculty of Medicine, Institute of Public Health, Master's programm in Public Health, evaluation of Master's thesis: *cum laude*
2001−2002	Tartu Medical School, Bachelor's programme in Nursing, *cum laude*
1994−1997	Tartu Medical School, Diploma in Nursing, with honors

Professional career:

2021−…	Tartu Health Care College, senior lecturer
2016−2020	Tartu Health Care College, lecturer
2015−2016	Tartu Health Care College, assistent
1999−2015	Family Doctor Maire Nirk LLC, family nurse

Membership:

2020−…	European Association of Preventive Cardiology
2020−…	International Family Nursing Association
2007−…	Society of Health Nursing, suborganisation of Estonian Nurses Union
1995−…	Estonian Nurses Union

Scientific work:
Main field of research: publik health; preventive cardiology (particularly arterial hypertension), risk factors, assessment and management of health behaviour.

Three scientific papers were published in international peer-reviewed journals based on the study of doctoral dissertation. The results of the study based on doctoral dissertation have been presented at two (one oral presentation and one e-poster) international congress and one Estonian scientific conference (oral presentation).

Publications:

Sammul, S., Jensen-Urstad, M., Johansson, J., Lenhoff, H., & Viigimaa, M. (2019). Psychosocial Factors and Personality Traits and the Prevalence of Arterial Hypertension Among 35- and 55-Year-Old Men and Women in Sweden and Estonia: a SWESTONIA Longitudinal Study. *High Blood Pressure and Cardiovascular Prevention*, *26*(6), 475–482. doi:10.1007/s40292-019-00348-y

Sammul, S., & Viigimaa, M. (2018). Rapid socio-economic changes, psycho-social factors and prevalence of hypertension among men and women aged 55 years at baseline in Estonia: a 13-year follow-up study. *Blood Pressure*, *27*(6), 351–357. doi:10.1080/08037051.2018.1476054

Jensen Urstad, M., Lenhoff, H., Johansson, J., Viigimaa, M., & Sammul, S. (2014). Impact of smoking: All-cause and cardiovascular mortality in a cohort of 55-year-old Swedes and Estonians. *Scandinavian Journal of Public Health*, *42*(8), 780–785. doi:10.1177/1403494814550177

Professional development:

22.05–23.05.2022	Association of Cardiovascualr Nursing & Allied Professions, congress. Madrid, Spain. Online
18.06.2021	The ’what‘ and ’how‘ of supporting behaviour change in clients: skills training workshop. European Society of Cardiology. Online
15.04−17.04.2021	European Association of Preventive Cardiology, congress. Praque, Czech. Online
10.06−12.06.2020	The course ‘Cardiovascular risk factors – assessment and management’. European Society of Cardiology. E-learning platform
14.05−16.05.2015	European Association for Cardiovascular Prevention and Rehabilitation's congress. Lisbon, Portugal

ELULOOKIRJELDUS

Nimi: Sirje Sammul
e-post: sirje.sammul.001@mail.ee

Haridus:

2010−…	Tartu Ülikool, Meditsiiniteaduste valdkond, Peremeditsiini ja rahvatervishoiu insituut, doktoriõpe arstiteaduses
2003−2006	Tartu Ülikool, Arstiteaduskond, Rahvatervishoiu instituut, magistriõpe rahvatervises, magistritöö kaitstud hindele *cum laude*
2001−2002	Tartu Meditsiinikool, bakalaureuseõpe õenduses*, cum laude*
1994−1997	Tartu Meditsiinikool, õe põhiõpe, kiitusega

Teenistuskäik:

2021−…	Tartu Tervishoiu Kõrgkool, vanemlektor
2016−2020	Tartu Tervishoiu Kõrgkool, lektor
2015−2016	Tartu Tervishoiu Kõrgkool, assistent
1999−2015	OÜ Perearst Maire Nirk, pereõde

Liikmelisus:

2020−…	Euroopa Preventiivkardioloogia Ühing
2020−…	Rahvusvaheline Pereõenduse Ühing
2007−…	Terviseõdede seltsing, Eesti Õdede Liidu allorganisatsioon
1995−…	Eesti Õdede Liit

Teadustöö:

Peamine uurimisvaldkond: rahvatervis; preventiivkardioloogia (eriti arteriaalne hüpertensioon), riskifaktorid, tervisekäitumise hindamine ja juhtimine.

Kolm teaduspublikatsiooni, mis baseeruvad doktoriväitekirja teemal, publitseeriti rahvusvahelise levikuga eelretsenseeritud ajakirjades. Antud uuringu tulemusi esitleti kahel rahvusvahelisel kongressil (üks suuline ettekanne ja üks poster-ettekanne) ja ühel Eesti-sisesel teaduskonverentsil (suuline ettekanne).

Publikatsioonid:

Sammul, S., Jensen-Urstad, M., Johansson, J., Lenhoff, H., & Viigimaa, M. (2019). Psychosocial Factors and Personality Traits and the Prevalence of Arterial Hypertension Among 35- and 55-Year-Old Men and Women in Sweden and Estonia: a SWESTONIA Longitudinal Study. *High Blood Pressure and Cardiovascular Prevention*, *26*(6), 475–482. doi:10.1007/s40292-019-00348-y

Sammul, S., & Viigimaa, M. (2018). Rapid socio-economic changes, psychosocial factors and prevalence of hypertension among men and women aged

55 years at baseline in Estonia: a 13-year follow-up study. *Blood Pressure*, *27*(6), 351–357. doi:10.1080/08037051.2018.1476054

Jensen Urstad, M., Lenhoff, H., Johansson, J., Viigimaa, M., & Sammul, S. (2014). Impact of smoking: All-cause and cardiovascular mortality in a cohort of 55-year-old Swedes and Estonians. *Scandinavian Journal of Public Health*, *42*(8), 780–785. doi:10.1177/1403494814550177

Erialane enesetäiendus

22.05–23.05.2022	Association of Cardiovascualr Nursing & Allied Professions, congress. Madrid, Spain. Online
18.06.2021	The 'what' and 'how' of supporting behaviour change in clients: skills training workshop. European Society of Cardiology. Online
15.04−17.04.2021	European Association of Preventive Cardiology, congress. Praque, Czech. Online
10.06−12.06.2020	The course 'Cardiovascular risk factors – assessment and management'. European Society of Cardiology. E-learning platform
14.05−16.05.2015	European Association for Cardiovascular Prevention and Rehabilitation's congress. Lisbon, Portugal

DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS

1. **Heidi-Ingrid Maaroos**. The natural course of gastric ulcer in connection with chronic gastritis and *Helicobacter pylori*. Tartu, 1991.
2. **Mihkel Zilmer**. Na-pump in normal and tumorous brain tissues: Structural, functional and tumorigenesis aspects. Tartu, 1991.
3. **Eero Vasar**. Role of cholecystokinin receptors in the regulation of behaviour and in the action of haloperidol and diazepam. Tartu, 1992.
4. **Tiina Talvik**. Hypoxic-ischaemic brain damage in neonates (clinical, biochemical and brain computed tomographical investigation). Tartu, 1992.
5. **Ants Peetsalu**. Vagotomy in duodenal ulcer disease: A study of gastric acidity, serum pepsinogen I, gastric mucosal histology and *Helicobacter pylori*. Tartu, 1992.
6. **Marika Mikelsaar**. Evaluation of the gastrointestinal microbial ecosystem in health and disease. Tartu, 1992.
7. **Hele Everaus**. Immuno-hormonal interactions in chronic lymphocytic leukaemia and multiple myeloma. Tartu, 1993.
8. **Ruth Mikelsaar**. Etiological factors of diseases in genetically consulted children and newborn screening: dissertation for the commencement of the degree of doctor of medical sciences. Tartu, 1993.
9. **Agu Tamm**. On metabolic action of intestinal microflora: clinical aspects. Tartu, 1993.
10. **Katrin Gross**. Multiple sclerosis in South-Estonia (epidemiological and computed tomographical investigations). Tartu, 1993.
11. **Oivi Uibo**. Childhood coeliac disease in Estonia: occurrence, screening, diagnosis and clinical characterization. Tartu, 1994.
12. **Viiu Tuulik**. The functional disorders of central nervous system of chemistry workers. Tartu, 1994.
13. **Margus Viigimaa**. Primary haemostasis, antiaggregative and anticoagulant treatment of acute myocardial infarction. Tartu, 1994.
14. **Rein Kolk**. Atrial versus ventricular pacing in patients with sick sinus syndrome. Tartu, 1994.
15. **Toomas Podar**. Incidence of childhood onset type 1 diabetes mellitus in Estonia. Tartu, 1994.
16. **Kiira Subi**. The laboratory surveillance of the acute respiratory viral infections in Estonia. Tartu, 1995.
17. **Irja Lutsar**. Infections of the central nervous system in children (epidemiologic, diagnostic and therapeutic aspects, long term outcome). Tartu, 1995.
18. **Aavo Lang**. The role of dopamine, 5-hydroxytryptamine, sigma and NMDA receptors in the action of antipsychotic drugs. Tartu, 1995.
19. **Andrus Arak**. Factors influencing the survival of patients after radical surgery for gastric cancer. Tartu, 1996.

20. **Tõnis Karki**. Quantitative composition of the human lactoflora and method for its examination. Tartu, 1996.
21. **Reet Mändar**. Vaginal microflora during pregnancy and its transmission to newborn. Tartu, 1996.
22. **Triin Remmel**. Primary biliary cirrhosis in Estonia: epidemiology, clinical characterization and prognostication of the course of the disease. Tartu, 1996.
23. **Toomas Kivastik**. Mechanisms of drug addiction: focus on positive reinforcing properties of morphine. Tartu, 1996.
24. **Paavo Pokk**. Stress due to sleep deprivation: focus on $GABA_A$ receptor-chloride ionophore complex. Tartu, 1996.
25. **Kristina Allikmets**. Renin system activity in essential hypertension. Associations with atherothrombogenic cardiovascular risk factors and with the efficacy of calcium antagonist treatment. Tartu, 1996.
26. **Triin Parik**. Oxidative stress in essential hypertension: Associations with metabolic disturbances and the effects of calcium antagonist treatment. Tartu, 1996.
27. **Svetlana Päi**. Factors promoting heterogeneity of the course of rheumatoid arthritis. Tartu, 1997.
28. **Maarike Sallo**. Studies on habitual physical activity and aerobic fitness in 4 to 10 years old children. Tartu, 1997.
29. **Paul Naaber**. *Clostridium difficile* infection and intestinal microbial ecology. Tartu, 1997.
30. **Rein Pähkla**. Studies in pinoline pharmacology. Tartu, 1997.
31. **Andrus Juhan Voitk**. Outpatient laparoscopic cholecystectomy. Tartu, 1997.
32. **Joel Starkopf**. Oxidative stress and ischaemia-reperfusion of the heart. Tartu, 1997.
33. **Janika Kõrv**. Incidence, case-fatality and outcome of stroke. Tartu, 1998.
34. **Ülla Linnamägi**. Changes in local cerebral blood flow and lipid peroxidation following lead exposure in experiment. Tartu, 1998.
35. **Ave Minajeva**. Sarcoplasmic reticulum function: comparison of atrial and ventricular myocardium. Tartu, 1998.
36. **Oleg Milenin**. Reconstruction of cervical part of esophagus by revascularised ileal autografts in dogs. A new complex multistage method. Tartu, 1998.
37. **Sergei Pakriev**. Prevalence of depression, harmful use of alcohol and alcohol dependence among rural population in Udmurtia. Tartu, 1998.
38. **Allen Kaasik**. Thyroid hormone control over β-adrenergic signalling system in rat atria. Tartu, 1998.
39. **Vallo Matto**. Pharmacological studies on anxiogenic and antiaggressive properties of antidepressants. Tartu, 1998.
40. **Maire Vasar**. Allergic diseases and bronchial hyperreactivity in Estonian children in relation to environmental influences. Tartu, 1998.
41. **Kaja Julge**. Humoral immune responses to allergens in early childhood. Tartu, 1998.

42. **Heli Grünberg**. The cardiovascular risk of Estonian schoolchildren. A cross-sectional study of 9-, 12- and 15-year-old children. Tartu, 1998.
43. **Epp Sepp**. Formation of intestinal microbial ecosystem in children. Tartu, 1998.
44. **Mai Ots**. Characteristics of the progression of human and experimental glomerulopathies. Tartu, 1998.
45. **Tiina Ristimäe**. Heart rate variability in patients with coronary artery disease. Tartu, 1998.
46. **Leho Kõiv**. Reaction of the sympatho-adrenal and hypothalamo-pituitary-adrenocortical system in the acute stage of head injury. Tartu, 1998.
47. **Bela Adojaan**. Immune and genetic factors of childhood onset IDDM in Estonia. An epidemiological study. Tartu, 1999.
48. **Jakov Shlik**. Psychophysiological effects of cholecystokinin in humans. Tartu, 1999.
49. **Kai Kisand**. Autoantibodies against dehydrogenases of α-ketoacids. Tartu, 1999.
50. **Toomas Marandi**. Drug treatment of depression in Estonia. Tartu, 1999.
51. **Ants Kask**. Behavioural studies on neuropeptide Y. Tartu, 1999.
52. **Ello-Rahel Karelson**. Modulation of adenylate cyclase activity in the rat hippocampus by neuropeptide galanin and its chimeric analogs. Tartu, 1999.
53. **Tanel Laisaar**. Treatment of pleural empyema — special reference to intrapleural therapy with streptokinase and surgical treatment modalities. Tartu, 1999.
54. **Eve Pihl**. Cardiovascular risk factors in middle-aged former athletes. Tartu, 1999.
55. **Katrin Õunap**. Phenylketonuria in Estonia: incidence, newborn screening, diagnosis, clinical characterization and genotype/phenotype correlation. Tartu, 1999.
56. **Siiri Kõljalg**. *Acinetobacter* – an important nosocomial pathogen. Tartu, 1999.
57. **Helle Karro**. Reproductive health and pregnancy outcome in Estonia: association with different factors. Tartu, 1999.
58. **Heili Varendi**. Behavioral effects observed in human newborns during exposure to naturally occurring odors. Tartu, 1999.
59. **Anneli Beilmann**. Epidemiology of epilepsy in children and adolescents in Estonia. Prevalence, incidence, and clinical characteristics. Tartu, 1999.
60. **Vallo Volke**. Pharmacological and biochemical studies on nitric oxide in the regulation of behaviour. Tartu, 1999.
61. **Pilvi Ilves**. Hypoxic-ischaemic encephalopathy in asphyxiated term infants. A prospective clinical, biochemical, ultrasonographical study. Tartu, 1999.
62. **Anti Kalda**. Oxygen-glucose deprivation-induced neuronal death and its pharmacological prevention in cerebellar granule cells. Tartu, 1999.
63. **Eve-Irene Lepist**. Oral peptide prodrugs – studies on stability and absorption. Tartu, 2000.

64. **Jana Kivastik**. Lung function in Estonian schoolchildren: relationship with anthropometric indices and respiratory symptomas, reference values for dynamic spirometry. Tartu, 2000.
65. **Karin Kull**. Inflammatory bowel disease: an immunogenetic study. Tartu, 2000.
66. **Kaire Innos**. Epidemiological resources in Estonia: data sources, their quality and feasibility of cohort studies. Tartu, 2000.
67. **Tamara Vorobjova**. Immune response to *Helicobacter pylori* and its association with dynamics of chronic gastritis and epithelial cell turnover in antrum and corpus. Tartu, 2001.
68. **Ruth Kalda**. Structure and outcome of family practice quality in the changing health care system of Estonia. Tartu, 2001.
69. **Annika Krüüner**. *Mycobacterium tuberculosis* – spread and drug resistance in Estonia. Tartu, 2001.
70. **Marlit Veldi**. Obstructive Sleep Apnoea: Computerized Endopharyngeal Myotonometry of the Soft Palate and Lingual Musculature. Tartu, 2001.
71. **Anneli Uusküla**. Epidemiology of sexually transmitted diseases in Estonia in 1990–2000. Tartu, 2001.
72. **Ade Kallas**. Characterization of antibodies to coagulation factor VIII. Tartu, 2002.
73. **Heidi Annuk**. Selection of medicinal plants and intestinal lactobacilli as antimicrobil components for functional foods. Tartu, 2002.
74. **Aet Lukmann**. Early rehabilitation of patients with ischaemic heart disease after surgical revascularization of the myocardium: assessment of health-related quality of life, cardiopulmonary reserve and oxidative stress. A clinical study. Tartu, 2002.
75. **Maigi Eisen**. Pathogenesis of Contact Dermatitis: participation of Oxidative Stress. A clinical – biochemical study. Tartu, 2002.
76. **Piret Hussar**. Histology of the post-traumatic bone repair in rats. Elaboration and use of a new standardized experimental model – bicortical perforation of tibia compared to internal fracture and resection osteotomy. Tartu, 2002.
77. **Tõnu Rätsep**. Aneurysmal subarachnoid haemorrhage: Noninvasive monitoring of cerebral haemodynamics. Tartu, 2002.
78. **Marju Herodes**. Quality of life of people with epilepsy in Estonia. Tartu, 2003.
79. **Katre Maasalu**. Changes in bone quality due to age and genetic disorders and their clinical expressions in Estonia. Tartu, 2003.
80. **Toomas Sillakivi**. Perforated peptic ulcer in Estonia: epidemiology, risk factors and relations with *Helicobacter pylori*. Tartu, 2003.
81. **Leena Puksa**. Late responses in motor nerve conduction studies. F and A waves in normal subjects and patients with neuropathies. Tartu, 2003.
82. **Krista Lõivukene**. *Helicobacter pylori* in gastric microbial ecology and its antimicrobial susceptibility pattern. Tartu, 2003.

83. **Helgi Kolk**. Dyspepsia and *Helicobacter pylori* infection: the diagnostic value of symptoms, treatment and follow-up of patients referred for upper gastrointestinal endoscopy by family physicians. Tartu, 2003.
84. **Helena Soomer**. Validation of identification and age estimation methods in forensic odontology. Tartu, 2003.
85. **Kersti Oselin**. Studies on the human MDR1, MRP1, and MRP2 ABC transporters: functional relevance of the genetic polymorphisms in the *MDR1* and *MRP1* gene. Tartu, 2003.
86. **Jaan Soplepmann**. Peptic ulcer haemorrhage in Estonia: epidemiology, prognostic factors, treatment and outcome. Tartu, 2003.
87. **Margot Peetsalu**. Long-term follow-up after vagotomy in duodenal ulcer disease: recurrent ulcer, changes in the function, morphology and *Helicobacter pylori* colonisation of the gastric mucosa. Tartu, 2003.
88. **Kersti Klaamas**. Humoral immune response to *Helicobacter pylori* a study of host-dependent and microbial factors. Tartu, 2003.
89. **Pille Taba**. Epidemiology of Parkinson's disease in Tartu, Estonia. Prevalence, incidence, clinical characteristics, and pharmacoepidemiology. Tartu, 2003.
90. **Alar Veraksitš**. Characterization of behavioural and biochemical phenotype of cholecystokinin-2 receptor deficient mice: changes in the function of the dopamine and endopioidergic system. Tartu, 2003.
91. **Ingrid Kalev**. CC-chemokine receptor 5 (CCR5) gene polymorphism in Estonians and in patients with Type I and Type II diabetes mellitus. Tartu, 2003.
92. **Lumme Kadaja**. Molecular approach to the regulation of mitochondrial function in oxidative muscle cells. Tartu, 2003.
93. **Aive Liigant**. Epidemiology of primary central nervous system tumours in Estonia from 1986 to 1996. Clinical characteristics, incidence, survival and prognostic factors. Tartu, 2004.
94. **Andres, Kulla**. Molecular characteristics of mesenchymal stroma in human astrocytic gliomas. Tartu, 2004.
95. **Mari Järvelaid**. Health damaging risk behaviours in adolescence. Tartu, 2004.
96. **Ülle Pechter**. Progression prevention strategies in chronic renal failure and hypertension. An experimental and clinical study. Tartu, 2004.
97. **Gunnar Tasa**. Polymorphic glutathione S-transferases – biology and role in modifying genetic susceptibility to senile cataract and primary open angle glaucoma. Tartu, 2004.
98. **Tuuli Käämbre**. Intracellular energetic unit: structural and functional aspects. Tartu, 2004.
99. **Vitali Vassiljev**. Influence of nitric oxide syntase inhibitors on the effects of ethanol after acute and chronic ethanol administration and withdrawal. Tartu, 2004.

100. **Aune Rehema**. Assessment of nonhaem ferrous iron and glutathione redox ratio as markers of pathogeneticity of oxidative stress in different clinical groups. Tartu, 2004.
101. **Evelin Seppet**. Interaction of mitochondria and ATPases in oxidative muscle cells in normal and pathological conditions. Tartu, 2004.
102. **Eduard Maron**. Serotonin function in panic disorder: from clinical experiments to brain imaging and genetics. Tartu, 2004.
103. **Marje Oona**. *Helicobacter pylori* infection in children: epidemiological and therapeutic aspects. Tartu, 2004.
104. **Kersti Kokk**. Regulation of active and passive molecular transport in the testis. Tartu, 2005.
105. **Vladimir Järv**. Cross-sectional imaging for pretreatment evaluation and follow-up of pelvic malignant tumours. Tartu, 2005.
106. **Andre Õun**. Epidemiology of adult epilepsy in Tartu, Estonia. Incidence, prevalence and medical treatment. Tartu, 2005.
107. **Piibe Muda**. Homocysteine and hypertension: associations between homocysteine and essential hypertension in treated and untreated hypertensive patients with and without coronary artery disease. Tartu, 2005.
108. **Külli Kingo**. The interleukin-10 family cytokines gene polymorphisms in plaque psoriasis. Tartu, 2005.
109. **Mati Merila**. Anatomy and clinical relevance of the glenohumeral joint capsule and ligaments. Tartu, 2005.
110. **Epp Songisepp**. Evaluation of technological and functional properties of the new probiotic *Lactobacillus fermentum* ME-3. Tartu, 2005.
111. **Tiia Ainla**. Acute myocardial infarction in Estonia: clinical characteristics, management and outcome. Tartu, 2005.
112. **Andres Sell**. Determining the minimum local anaesthetic requirements for hip replacement surgery under spinal anaesthesia – a study employing a spinal catheter. Tartu, 2005.
113. **Tiia Tamme**. Epidemiology of odontogenic tumours in Estonia. Pathogenesis and clinical behaviour of ameloblastoma. Tartu, 2005.
114. **Triine Annus**. Allergy in Estonian schoolchildren: time trends and characteristics. Tartu, 2005.
115. **Tiia Voor**. Microorganisms in infancy and development of allergy: comparison of Estonian and Swedish children. Tartu, 2005.
116. **Priit Kasenõmm**. Indicators for tonsillectomy in adults with recurrent tonsillitis – clinical, microbiological and pathomorphological investigations. Tartu, 2005.
117. **Eva Zusinaite**. Hepatitis C virus: genotype identification and interactions between viral proteases. Tartu, 2005.
118. **Piret Kõll**. Oral lactoflora in chronic periodontitis and periodontal health. Tartu, 2006.
119. **Tiina Stelmach**. Epidemiology of cerebral palsy and unfavourable neurodevelopmental outcome in child population of Tartu city and county, Estonia Prevalence, clinical features and risk factors. Tartu, 2006.

120. **Katrin Pudersell**. Tropane alkaloid production and riboflavine excretion in the field and tissue cultures of henbane (*Hyoscyamus niger* L.). Tartu, 2006.
121. **Külli Jaako**. Studies on the role of neurogenesis in brain plasticity. Tartu, 2006.
122. **Aare Märtson**. Lower limb lengthening: experimental studies of bone regeneration and long-term clinical results. Tartu, 2006.
123. **Heli Tähepõld**. Patient consultation in family medicine. Tartu, 2006.
124. **Stanislav Liskmann**. Peri-implant disease: pathogenesis, diagnosis and treatment in view of both inflammation and oxidative stress profiling. Tartu, 2006.
125. **Ruth Rudissaar**. Neuropharmacology of atypical antipsychotics and an animal model of psychosis. Tartu, 2006.
126. **Helena Andreson**. Diversity of *Helicobacter pylori* genotypes in Estonian patients with chronic inflammatory gastric diseases. Tartu, 2006.
127. **Katrin Pruus**. Mechanism of action of antidepressants: aspects of serotoninergic system and its interaction with glutamate. Tartu, 2006.
128. **Priit Põder**. Clinical and experimental investigation: relationship of ischaemia/reperfusion injury with oxidative stress in abdominal aortic aneurysm repair and in extracranial brain artery endarterectomy and possibilities of protection against ischaemia using a glutathione analogue in a rat model of global brain ischaemia. Tartu, 2006.
129. **Marika Tammaru**. Patient-reported outcome measurement in rheumatoid arthritis. Tartu, 2006.
130. **Tiia Reimand**. Down syndrome in Estonia. Tartu, 2006.
131. **Diva Eensoo**. Risk-taking in traffic and Markers of Risk-Taking Behaviour in Schoolchildren and Car Drivers. Tartu, 2007.
132. **Riina Vibo**. The third stroke registry in Tartu, Estonia from 2001 to 2003: incidence, case-fatality, risk factors and long-term outcome. Tartu, 2007.
133. **Chris Pruunsild**. Juvenile idiopathic arthritis in children in Estonia. Tartu, 2007.
134. **Eve Õiglane-Šlik**. Angelman and Prader-Willi syndromes in Estonia. Tartu, 2007.
135. **Kadri Haller**. Antibodies to follicle stimulating hormone. Significance in female infertility. Tartu, 2007.
136. **Pille Ööpik**. Management of depression in family medicine. Tartu, 2007.
137. **Jaak Kals**. Endothelial function and arterial stiffness in patients with atherosclerosis and in healthy subjects. Tartu, 2007.
138. **Priit Kampus**. Impact of inflammation, oxidative stress and age on arterial stiffness and carotid artery intima-media thickness. Tartu, 2007.
139. **Margus Punab**. Male fertility and its risk factors in Estonia. Tartu, 2007.
140. **Alar Toom**. Heterotopic ossification after total hip arthroplasty: clinical and pathogenetic investigation. Tartu, 2007.

141. **Lea Pehme**. Epidemiology of tuberculosis in Estonia 1991–2003 with special regard to extrapulmonary tuberculosis and delay in diagnosis of pulmonary tuberculosis. Tartu, 2007.
142. **Juri Karjagin**. The pharmacokinetics of metronidazole and meropenem in septic shock. Tartu, 2007.
143. **Inga Talvik**. Inflicted traumatic brain injury shaken baby syndrome in Estonia – epidemiology and outcome. Tartu, 2007.
144. **Tarvo Rajasalu**. Autoimmune diabetes: an immunological study of type 1 diabetes in humans and in a model of experimental diabetes (in RIP-B7.1 mice). Tartu, 2007.
145. **Inga Karu**. Ischaemia-reperfusion injury of the heart during coronary surgery: a clinical study investigating the effect of hyperoxia. Tartu, 2007.
146. **Peeter Padrik**. Renal cell carcinoma: Changes in natural history and treatment of metastatic disease. Tartu, 2007.
147. **Neve Vendt**. Iron deficiency and iron deficiency anaemia in infants aged 9 to 12 months in Estonia. Tartu, 2008.
148. **Lenne-Triin Heidmets**. The effects of neurotoxins on brain plasticity: focus on neural Cell Adhesion Molecule. Tartu, 2008.
149. **Paul Korrovits**. Asymptomatic inflammatory prostatitis: prevalence, etiological factors, diagnostic tools. Tartu, 2008.
150. **Annika Reintam**. Gastrointestinal failure in intensive care patients. Tartu, 2008.
151. **Kristiina Roots**. Cationic regulation of Na-pump in the normal, Alzheimer's and CCK_2 receptor-deficient brain. Tartu, 2008.
152. **Helen Puusepp**. The genetic causes of mental retardation in Estonia: fragile X syndrome and creatine transporter defect. Tartu, 2009.
153. **Kristiina Rull**. Human chorionic gonadotropin beta genes and recurrent miscarriage: expression and variation study. Tartu, 2009.
154. **Margus Eimre**. Organization of energy transfer and feedback regulation in oxidative muscle cells. Tartu, 2009.
155. **Maire Link**. Transcription factors FoxP3 and AIRE: autoantibody associations. Tartu, 2009.
156. **Kai Haldre**. Sexual health and behaviour of young women in Estonia. Tartu, 2009.
157. **Kaur Liivak**. Classical form of congenital adrenal hyperplasia due to 21-hydroxylase deficiency in Estonia: incidence, genotype and phenotype with special attention to short-term growth and 24-hour blood pressure. Tartu, 2009.
158. **Kersti Ehrlich**. Antioxidative glutathione analogues (UPF peptides) – molecular design, structure-activity relationships and testing the protective properties. Tartu, 2009.
159. **Anneli Rätsep**. Type 2 diabetes care in family medicine. Tartu, 2009.
160. **Silver Türk**. Etiopathogenetic aspects of chronic prostatitis: role of mycoplasmas, coryneform bacteria and oxidative stress. Tartu, 2009.

161. **Kaire Heilman**. Risk markers for cardiovascular disease and low bone mineral density in children with type 1 diabetes. Tartu, 2009.
162. **Kristi Rüütel**. HIV-epidemic in Estonia: injecting drug use and quality of life of people living with HIV. Tartu, 2009.
163. **Triin Eller**. Immune markers in major depression and in antidepressive treatment. Tartu, 2009.
164. **Siim Suutre**. The role of TGF-β isoforms and osteoprogenitor cells in the pathogenesis of heterotopic ossification. An experimental and clinical study of hip arthroplasty. Tartu, 2010.
165. **Kai Kliiman**. Highly drug-resistant tuberculosis in Estonia: Risk factors and predictors of poor treatment outcome. Tartu, 2010.
166. **Inga Villa**. Cardiovascular health-related nutrition, physical activity and fitness in Estonia. Tartu, 2010.
167. **Tõnis Org**. Molecular function of the first PHD finger domain of Autoimmune Regulator protein. Tartu, 2010.
168. **Tuuli Metsvaht**. Optimal antibacterial therapy of neonates at risk of early onset sepsis. Tartu, 2010.
169. **Jaanus Kahu**. Kidney transplantation: Studies on donor risk factors and mycophenolate mofetil. Tartu, 2010.
170. **Koit Reimand**. Autoimmunity in reproductive failure: A study on associated autoantibodies and autoantigens. Tartu, 2010.
171. **Mart Kull**. Impact of vitamin D and hypolactasia on bone mineral density: a population based study in Estonia. Tartu, 2010.
172. **Rael Laugesaar**. Stroke in children – epidemiology and risk factors. Tartu, 2010.
173. **Mark Braschinsky**. Epidemiology and quality of life issues of hereditary spastic paraplegia in Estonia and implemention of genetic analysis in everyday neurologic practice. Tartu, 2010.
174. **Kadri Suija**. Major depression in family medicine: associated factors, recurrence and possible intervention. Tartu, 2010.
175. **Jarno Habicht**. Health care utilisation in Estonia: socioeconomic determinants and financial burden of out-of-pocket payments. Tartu, 2010.
176. **Kristi Abram**. The prevalence and risk factors of rosacea. Subjective disease perception of rosacea patients. Tartu, 2010.
177. **Malle Kuum**. Mitochondrial and endoplasmic reticulum cation fluxes: Novel roles in cellular physiology. Tartu, 2010.
178. **Rita Teek**. The genetic causes of early onset hearing loss in Estonian children. Tartu, 2010.
179. **Daisy Volmer**. The development of community pharmacy services in Estonia – public and professional perceptions 1993–2006. Tartu, 2010.
180. **Jelena Lissitsina**. Cytogenetic causes in male infertility. Tartu, 2011.
181. **Delia Lepik**. Comparison of gunshot injuries caused from Tokarev, Makarov and Glock 19 pistols at different firing distances. Tartu, 2011.
182. **Ene-Renate Pähkla**. Factors related to the efficiency of treatment of advanced periodontitis. Tartu, 2011.

183. **Maarja Krass**. L-Arginine pathways and antidepressant action. Tartu, 2011.
184. **Taavi Lai**. Population health measures to support evidence-based health policy in Estonia. Tartu, 2011.
185. **Tiit Salum**. Similarity and difference of temperature-dependence of the brain sodium pump in normal, different neuropathological, and aberrant conditions and its possible reasons. Tartu, 2011.
186. **Tõnu Vooder**. Molecular differences and similarities between histological subtypes of non-small cell lung cancer. Tartu, 2011.
187. **Jelena Štšepetova**. The characterisation of intestinal lactic acid bacteria using bacteriological, biochemical and molecular approaches. Tartu, 2011.
188. **Radko Avi**. Natural polymorphisms and transmitted drug resistance in Estonian HIV-1 CRF06_cpx and its recombinant viruses. Tartu, 2011, 116 p.
189. **Edward Laane**. Multiparameter flow cytometry in haematological malignancies. Tartu, 2011, 152 p.
190. **Triin Jagomägi**. A study of the genetic etiology of nonsyndromic cleft lip and palate. Tartu, 2011, 158 p.
191. **Ivo Laidmäe**. Fibrin glue of fish (*Salmo salar*) origin: immunological study and development of new pharmaceutical preparation. Tartu, 2012, 150 p.
192. **Ülle Parm**. Early mucosal colonisation and its role in prediction of invasive infection in neonates at risk of early onset sepsis. Tartu, 2012, 168 p.
193. **Kaupo Teesalu**. Autoantibodies against desmin and transglutaminase 2 in celiac disease: diagnostic and functional significance. Tartu, 2012, 142 p.
194. **Maksim Zagura**. Biochemical, functional and structural profiling of arterial damage in atherosclerosis. Tartu, 2012, 162 p.
195. **Vivian Kont**. Autoimmune regulator: characterization of thymic gene regulation and promoter methylation. Tartu, 2012, 134 p.
196. **Pirje Hütt**. Functional properties, persistence, safety and efficacy of potential probiotic lactobacilli. Tartu, 2012, 246 p.
197. **Innar Tõru**. Serotonergic modulation of CCK-4- induced panic. Tartu, 2012, 132 p.
198. **Sigrid Vorobjov**. Drug use, related risk behaviour and harm reduction interventions utilization among injecting drug users in Estonia: implications for drug policy. Tartu, 2012, 120 p.
199. **Martin Serg**. Therapeutic aspects of central haemodynamics, arterial stiffness and oxidative stress in hypertension. Tartu, 2012, 156 p.
200. **Jaanika Kumm**. Molecular markers of articular tissues in early knee osteoarthritis: a population-based longitudinal study in middle-aged subjects. Tartu, 2012, 159 p.
201. **Kertu Rünkorg**. Functional changes of dopamine, endopioid and endocannabinoid systems in CCK2 receptor deficient mice. Tartu, 2012, 125 p.
202. **Mai Blöndal**. Changes in the baseline characteristics, management and outcomes of acute myocardial infarction in Estonia. Tartu, 2012, 127 p.

203. **Jana Lass**. Epidemiological and clinical aspects of medicines use in children in Estonia. Tartu, 2012, 170 p.
204. **Kai Truusalu**. Probiotic lactobacilli in experimental persistent *Salmonella* infection. Tartu, 2013, 139 p.
205. **Oksana Jagur**. Temporomandibular joint diagnostic imaging in relation to pain and bone characteristics. Long-term results of arthroscopic treatment. Tartu, 2013, 126 p.
206. **Katrin Sikk**. Manganese-ephedrone intoxication – pathogenesis of neurological damage and clinical symptomatology. Tartu, 2013, 125 p.
207. **Kai Blöndal**. Tuberculosis in Estonia with special emphasis on drug-resistant tuberculosis: Notification rate, disease recurrence and mortality. Tartu, 2013, 151 p.
208. **Marju Puurand**. Oxidative phosphorylation in different diseases of gastric mucosa. Tartu, 2013, 123 p.
209. **Aili Tagoma**. Immune activation in female infertility: Significance of autoantibodies and inflammatory mediators. Tartu, 2013, 135 p.
210. **Liis Sabre**. Epidemiology of traumatic spinal cord injury in Estonia. Brain activation in the acute phase of traumatic spinal cord injury. Tartu, 2013, 135 p.
211. **Merit Lamp**. Genetic susceptibility factors in endometriosis. Tartu, 2013, 125 p.
212. **Erik Salum**. Beneficial effects of vitamin D and angiotensin II receptor blocker on arterial damage. Tartu, 2013, 167 p.
213. **Maire Karelson**. Vitiligo: clinical aspects, quality of life and the role of melanocortin system in pathogenesis. Tartu, 2013, 153 p.
214. **Kuldar Kaljurand**. Prevalence of exfoliation syndrome in Estonia and its clinical significance. Tartu, 2013, 113 p.
215. **Raido Paasma**. Clinical study of methanol poisoning: handling large outbreaks, treatment with antidotes, and long-term outcomes. Tartu, 2013, 96 p.
216. **Anne Kleinberg**. Major depression in Estonia: prevalence, associated factors, and use of health services. Tartu, 2013, 129 p.
217. **Triin Eglit**. Obesity, impaired glucose regulation, metabolic syndrome and their associations with high-molecular-weight adiponectin levels. Tartu, 2014, 115 p.
218. **Kristo Ausmees**. Reproductive function in middle-aged males: Associations with prostate, lifestyle and couple infertility status. Tartu, 2014, 125 p.
219. **Kristi Huik**. The influence of host genetic factors on the susceptibility to HIV and HCV infections among intravenous drug users. Tartu, 2014, 144 p.
220. **Liina Tserel**. Epigenetic profiles of monocytes, monocyte-derived macrophages and dendritic cells. Tartu, 2014, 143 p.
221. **Irina Kerna**. The contribution of *ADAM12* and *CILP* genes to the development of knee osteoarthritis. Tartu, 2014, 152 p.

222. **Ingrid Liiv**. Autoimmune regulator protein interaction with DNA-dependent protein kinase and its role in apoptosis. Tartu, 2014, 143 p.
223. **Liivi Maddison**. Tissue perfusion and metabolism during intra-abdominal hypertension. Tartu, 2014, 103 p.
224. **Krista Ress**. Childhood coeliac disease in Estonia, prevalence in atopic dermatitis and immunological characterisation of coexistence. Tartu, 2014, 124 p.
225. **Kai Muru**. Prenatal screening strategies, long-term outcome of children with marked changes in maternal screening tests and the most common syndromic heart anomalies in Estonia. Tartu, 2014, 189 p.
226. **Kaja Rahu**. Morbidity and mortality among Baltic Chernobyl cleanup workers: a register-based cohort study. Tartu, 2014, 155 p.
227. **Klari Noormets**. The development of diabetes mellitus, fertility and energy metabolism disturbances in a Wfs1-deficient mouse model of Wolfram syndrome. Tartu, 2014, 132 p.
228. **Liis Toome**. Very low gestational age infants in Estonia. Tartu, 2014, 183 p.
229. **Ceith Nikkolo**. Impact of different mesh parameters on chronic pain and foreign body feeling after open inguinal hernia repair. Tartu, 2014, 132 p.
230. **Vadim Brjalin**. Chronic hepatitis C: predictors of treatment response in Estonian patients. Tartu, 2014, 122 p.
231. **Vahur Metsna**. Anterior knee pain in patients following total knee arthroplasty: the prevalence, correlation with patellar cartilage impairment and aspects of patellofemoral congruence. Tartu, 2014, 130 p.
232. **Marju Kase**. Glioblastoma multiforme: possibilities to improve treatment efficacy. Tartu, 2015, 137 p.
233. **Riina Runnel**. Oral health among elementary school children and the effects of polyol candies on the prevention of dental caries. Tartu, 2015, 112 p.
234. **Made Laanpere**. Factors influencing women's sexual health and reproductive choices in Estonia. Tartu, 2015, 176 p.
235. **Andres Lust**. Water mediated solid state transformations of a polymorphic drug – effect on pharmaceutical product performance. Tartu, 2015, 134 p.
236. **Anna Klugman**. Functionality related characterization of pretreated wood lignin, cellulose and polyvinylpyrrolidone for pharmaceutical applications. Tartu, 2015, 156 p.
237. **Triin Laisk-Podar**. Genetic variation as a modulator of susceptibility to female infertility and a source for potential biomarkers. Tartu, 2015, 155 p.
238. **Mailis Tõnisson**. Clinical picture and biochemical changes in blood in children with acute alcohol intoxication. Tartu, 2015, 100 p.
239. **Kadri Tamme**. High volume haemodiafiltration in treatment of severe sepsis – impact on pharmacokinetics of antibiotics and inflammatory response. Tartu, 2015, 133 p.

240. **Kai Part**. Sexual health of young people in Estonia in a social context: the role of school-based sexuality education and youth-friendly counseling services. Tartu, 2015, 203 p.
241. **Urve Paaver**. New perspectives for the amorphization and physical stabilization of poorly water-soluble drugs and understanding their dissolution behavior. Tartu, 2015, 139 p.
242. **Aleksandr Peet**. Intrauterine and postnatal growth in children with HLA-conferred susceptibility to type 1 diabetes. Tartu. 2015, 146 p.
243. **Piret Mitt**. Healthcare-associated infections in Estonia – epidemiology and surveillance of bloodstream and surgical site infections. Tartu, 2015, 145 p.
244. **Merli Saare**. Molecular Profiling of Endometriotic Lesions and Endometria of Endometriosis Patients. Tartu, 2016, 129 p.
245. **Kaja-Triin Laisaar**. People living with HIV in Estonia: Engagement in medical care and methods of increasing adherence to antiretroviral therapy and safe sexual behavior. Tartu, 2016, 132 p.
246. **Eero Merilind**. Primary health care performance: impact of payment and practice-based characteristics. Tartu, 2016, 120 p.
247. **Jaanika Kärner**. Cytokine-specific autoantibodies in AIRE deficiency. Tartu, 2016, 182 p.
248. **Kaido Paapstel**. Metabolomic profile of arterial stiffness and early biomarkers of renal damage in atherosclerosis. Tartu, 2016, 173 p.
249. **Liidia Kiisk**. Long-term nutritional study: anthropometrical and clinico-laboratory assessments in renal replacement therapy patients after intensive nutritional counselling. Tartu, 2016, 207 p.
250. **Georgi Nellis**. The use of excipients in medicines administered to neonates in Europe. Tartu, 2017, 159 p.
251. **Aleksei Rakitin**. Metabolic effects of acute and chronic treatment with valproic acid in people with epilepsy. Tartu, 2017, 125 p.
252. **Eveli Kallas**. The influence of immunological markers to susceptibility to HIV, HBV, and HCV infections among persons who inject drugs. Tartu, 2017, 138 p.
253. **Tiina Freimann**. Musculoskeletal pain among nurses: prevalence, risk factors, and intervention. Tartu, 2017, 125 p.
254. **Evelyn Aaviksoo**. Sickness absence in Estonia: determinants and influence of the sick-pay cut reform. Tartu, 2017, 121 p.
255. **Kalev Nõupuu**. Autosomal-recessive Stargardt disease: phenotypic heterogeneity and genotype-phenotype associations. Tartu, 2017, 131 p.
256. **Ho Duy Binh**. Osteogenesis imperfecta in Vietnam. Tartu, 2017, 125 p.
257. **Uku Haljasorg**. Transcriptional mechanisms in thymic central tolerance. Tartu, 2017, 147 p.
258. **Živile Riispere**. IgA Nephropathy study according to the Oxford Classification: IgA Nephropathy clinical-morphological correlations, disease progression and the effect of renoprotective therapy. Tartu, 2017, 129 p.

259. **Hiie Soeorg**. Coagulase-negative staphylococci in gut of preterm neonates and in breast milk of their mothers. Tartu, 2017, 216 p.
260. **Anne-Mari Anton Willmore**. Silver nanoparticles for cancer research. Tartu, 2017, 132 p.
261. **Ott Laius**. Utilization of osteoporosis medicines, medication adherence and the trend in osteoporosis related hip fractures in Estonia. Tartu, 2017, 134 p.
262. **Alar Aab**. Insights into molecular mechanisms of asthma and atopic dermatitis. Tartu, 2017, 164 p.
263. **Sander Pajusalu**. Genome-wide diagnostics of Mendelian disorders: from chromosomal microarrays to next-generation sequencing. Tartu, 2017, 146 p.
264. **Mikk Jürisson**. Health and economic impact of hip fracture in Estonia. Tartu, 2017, 164 p.
265. **Kaspar Tootsi**. Cardiovascular and metabolomic profiling of osteoarthritis. Tartu, 2017, 150 p.
266. **Mario Saare**. The influence of AIRE on gene expression – studies of transcriptional regulatory mechanisms in cell culture systems. Tartu, 2017, 172 p.
267. **Piia Jõgi**. Epidemiological and clinical characteristics of pertussis in Estonia. Tartu, 2018, 168 p.
268. **Elle Põldoja**. Structure and blood supply of the superior part of the shoulder joint capsule. Tartu, 2018, 116 p.
269. **Minh Son Nguyen**. Oral health status and prevalence of temporomandibular disorders in 65–74-year-olds in Vietnam. Tartu, 2018, 182 p.
270. **Kristian Semjonov**. Development of pharmaceutical quench-cooled molten and melt-electrospun solid dispersions for poorly water-soluble indomethacin. Tartu, 2018, 125 p.
271. **Janne Tiigimäe-Saar**. Botulinum neurotoxin type A treatment for sialorrhea in central nervous system diseases. Tartu, 2018, 109 p.
272. **Veiko Vengerfeldt**. Apical periodontitis: prevalence and etiopathogenetic aspects. Tartu, 2018, 150 p.
273. **Rudolf Bichele**. TNF superfamily and AIRE at the crossroads of thymic differentiation and host protection against *Candida albicans* infection. Tartu, 2018, 153 p.
274. **Olga Tšuiko**. Unravelling Chromosomal Instability in Mammalian Preimplantation Embryos Using Single-Cell Genomics. Tartu, 2018, 169 p.
275. **Kärt Kriisa**. Profile of acylcarnitines, inflammation and oxidative stress in first-episode psychosis before and after antipsychotic treatment. Tartu, 2018, 145 p.
276. **Xuan Dung Ho**. Characterization of the genomic profile of osteosarcoma. Tartu, 2018, 144 p.
277. **Karit Reinson**. New Diagnostic Methods for Early Detection of Inborn Errors of Metabolism in Estonia. Tartu, 2018, 201 p.

278. **Mari-Anne Vals**. Congenital N-glycosylation Disorders in Estonia. Tartu, 2019, 148 p.
279. **Liis Kadastik-Eerme**. Parkinson's disease in Estonia: epidemiology, quality of life, clinical characteristics and pharmacotherapy. Tartu, 2019, 202 p.
280. **Hedi Hunt**. Precision targeting of intraperitoneal tumors with peptide-guided nanocarriers. Tartu, 2019, 179 p.
281. **Rando Porosk**. The role of oxidative stress in Wolfram syndrome 1 and hypothermia. Tartu, 2019, 123 p.
282. **Ene-Ly Jõgeda**. The influence of coinfections and host genetic factor on the susceptibility to HIV infection among people who inject drugs. Tartu, 2019, 126 p.
283. **Kristel Ehala-Aleksejev**. The associations between body composition, obesity and obesity-related health and lifestyle conditions with male reproductive function. Tartu, 2019, 138 p.
284. **Aigar Ottas**. The metabolomic profiling of psoriasis, atopic dermatitis and atherosclerosis. Tartu, 2019, 136 p.
285. **Elmira Gurbanova**. Specific characteristics of tuberculosis in low default, but high multidrug–resistance prison setting. Tartu, 2019, 129 p.
286. **Van Thai Nguyeni**. The first study of the treatment outcomes of patients with cleft lip and palate in Central Vietnam. Tartu, 2019, 144 p.
287. **Maria Yakoreva**. Imprinting Disorders in Estonia. Tartu, 2019, 187 p.
288. **Kadri Rekker**. The putative role of microRNAs in endometriosis pathogenesis and potential in diagnostics. Tartu, 2019, 140 p.
289. **Ülle Võhma**. Association between personality traits, clinical characteristics and pharmacological treatment response in panic disorder. Tartu, 2019, 121 p.
290. **Aet Saar**. Acute myocardial infarction in Estonia 2001–2014: towards risk-based prevention and management. Tartu, 2019, 124 p.
291. **Toomas Toomsoo**. Transcranial brain sonography in the Estonian cohort of Parkinson's disease. Tartu, 2019, 114 p.
292. **Lidiia Zhytnik**. Inter- and intrafamilial diversity based on genotype and phenotype correlations of Osteogenesis Imperfecta. Tartu, 2019, 224 p.
293. **Pilleriin Soodla**. Newly HIV-infected people in Estonia: estimation of incidence and transmitted drug resistance. Tartu, 2019, 194 p.
294. **Kristiina Ojamaa**. Epidemiology of gynecological cancer in Estonia. Tartu, 2020, 133 p.
295. **Marianne Saard**. Modern Cognitive and Social Intervention Techniques in Paediatric Neurorehabilitation for Children with Acquired Brain Injury. Tartu, 2020, 168 p.
296. **Julia Maslovskaja**. The importance of DNA binding and DNA breaks for AIRE-mediated transcriptional activation. Tartu, 2020, 162 p.
297. **Natalia Lobanovskaya**. The role of PSA-NCAM in the survival of retinal ganglion cells. Tartu, 2020, 105 p.

298. **Madis Rahu**. Structure and blood supply of the postero-superior part of the shoulder joint capsule with implementation of surgical treatment after anterior traumatic dislocation. Tartu, 2020, 104 p.
299. **Helen Zirnask**. Luteinizing hormone (LH) receptor expression in the penis and its possible role in pathogenesis of erectile disturbances. Tartu, 2020, 87 p.
300. **Kadri Toome**. Homing peptides for targeting of brain diseases. Tartu, 2020, 152 p.
301. **Maarja Hallik**. Pharmacokinetics and pharmacodynamics of inotropic drugs in neonates. Tartu, 2020, 172 p.
302. **Raili Müller**. Cardiometabolic risk profile and body composition in early rheumatoid arthritis. Tartu, 2020, 133 p.
303. **Sergo Kasvandik**. The role of proteomic changes in endometrial cells – from the perspective of fertility and endometriosis. Tartu, 2020, 191 p.
304. **Epp Kaleviste**. Genetic variants revealing the role of STAT1/STAT3 signaling cytokines in immune protection and pathology. Tartu, 2020, 189 p.
305. **Sten Saar**. Epidemiology of severe injuries in Estonia. Tartu, 2020, 104 p.
306. **Kati Braschinsky**. Epidemiology of primary headaches in Estonia and applicability of web-based solutions in headache epidemiology research. Tartu, 2020, 129 p.
307. **Helen Vaher**. MicroRNAs in the regulation of keratinocyte responses in *psoriasis vulgaris* and atopic dermatitis. Tartu, 2020, 242 p.
308. **Liisi Raam**. Molecular Alterations in the Pathogenesis of Two Chronic Dermatoses – Vitiligo and Psoriasis. Tartu, 2020, 164 p.
309. **Artur Vetkas**. Long-term quality of life, emotional health, and associated factors in patients after aneurysmal subarachnoid haemorrhage. Tartu, 2020, 127 p.
310. **Teele Kasepalu**. Effects of remote ischaemic preconditioning on organ damage and acylcarnitines' metabolism in vascular surgery. Tartu, 2020, 130 p.
311. **Prakash Lingasamy**. Development of multitargeted tumor penetrating peptides. Tartu, 2020, 246 p.
312. **Lille Kurvits.** Parkinson's disease as a multisystem disorder: whole transcriptome study in Parkinson's disease patients' skin and blood. Tartu, 2021, 142 p.
313. **Mariliis Põld.** Smoking, attitudes towards smoking behaviour, and nicotine dependence among physicians in Estonia: cross-sectional surveys 1982–2014. Tartu, 2021, 172 p.
314. **Triin Kikas**. Single nucleotide variants affecting placental gene expression and pregnancy outcome. Tartu, 2021, 160 p.
315. **Hedda Lippus-Metsaots**. Interpersonal violence in Estonia: prevalence, impact on health and health behaviour. Tartu, 2021, 172 p.

316. **Georgi Dzaparidze.** Quantification and evaluation of the diagnostic significance of adenocarcinoma-associated microenvironmental changes in the prostate using modern digital pathology solutions. Tartu, 2021, 132 p.
317. **Tuuli Sedman.** New avenues for GLP1 receptor agonists in the treatment of diabetes. Tartu, 2021, 118 p.
318. **Martin Padar.** Enteral nutrition, gastrointestinal dysfunction and intestinal biomarkers in critically ill patients. Tartu, 2021, 189 p.
319. **Siim Schneider.** Risk factors, etiology and long-term outcome in young ischemic stroke patients in Estonia. Tartu, 2021, 131 p.
320. **Konstantin Ridnõi.** Implementation and effectiveness of new prenatal diagnostic strategies in Estonia. Tartu, 2021, 191 p.
321. **Risto Vaikjärv.** Etiopathogenetic and clinical aspects of peritonsillar abscess. Tartu, 2021, 115 p.
322. **Liis Preem.** Design and characterization of antibacterial electrospun drug delivery systems for wound infections. Tartu, 2022, 220 p.
323. **Keerthie Dissanayake.** Preimplantation embryo-derived extracellular vesicles: potential as an embryo quality marker and their role during the embryo-maternal communication. Tartu, 2022, 203 p.
324. **Laura Viidik.** 3D printing in pharmaceutics: a new avenue for fabricating therapeutic drug delivery systems. Tartu, 2022, 139 p.
325. **Kasun Godakumara.** Extracellular vesicle mediated embryo-maternal communication – A tool for evaluating functional competency of preimplantation embryos. Tartu, 2022, 176 p.
326. **Hindrek Teder.** Developing computational methods and workflows for targeted and whole-genome sequencing based non-invasive prenatal testing. Tartu, 2022, 138 p.
327. **Jana Tuusov.** Deaths caused by alcohol, psychotropic and other substances in Estonia: evidence based on forensic autopsies. Tartu, 2022, 157 p.
328. **Heigo Reima.** Colorectal cancer care and outcomes – evaluation and possibilities for improvement in Estonia. Tartu, 2022, 146 p.
329. **Liisa Kuhi.** A contribution of biomarker collagen type II neoepitope C2C in urine to the diagnosis and prognosis of knee osteoarthritis. Tartu, 2022, 157 p.
330. **Reeli Tamme.** Associations between pubertal hormones and physical activity levels, and subsequent bone mineral characteristics: a longitudinal study of boys aged 12–18. Tartu, 2022, 118 p.
331. **Deniss Sõritsa.** The impact of endometriosis and physical activity on female reproduction. Tartu, 2022, 152 p.
332. **Mohammad Mehedi Hasan.** Characterization of follicular fluid-derived extracellular vesicles and their contribution to periconception environment. Tartu, 2022, 194 p.
333. **Priya Kulkarni.** Osteoarthritis pathogenesis: an immunological passage through synovium-synovial fluid axis. Tartu, 2022, 268 p.

334. **Nigul Ilves.** Brain plasticity and network reorganization in children with perinatal stroke: a functional magnetic resonance imaging study. Tartu, 2022, 169 p.
335. **Marko Murruste.** Short- and long-term outcomes of surgical management of chronic pancreatitis. Tartu, 2022, 180 p.
336. **Marilin Ivask.** Transcriptomic and metabolic changes in the WFS1-deficient mouse model. Tartu, 2022, 158 p.
337. **Jüri Lieberg.** Results of surgical treatment and role of biomarkers in pathogenesis and risk prediction in patients with abdominal aortic aneurysm and peripheral artery disease. Tartu, 2022, 160 p.
338. **Sanna Puusepp.** Comparison of molecular genetics and morphological findings of childhood-onset neuromuscular disorders. Tartu, 2022, 216 p.
339. **Khan Nguyen Viet.** Chemical composition and bioactivity of extracts and constituents isolated from the medicinal plants in Vietnam and their nanotechnology-based delivery systems. Tartu, 2023, 172 p.
340. **Getnet Balcha Midekessa.** Towards understanding the colloidal stability and detection of Extracellular Vesicles. Tartu, 2023, 172 p.
341. **Kristiina Sepp.** Competency-based and person-centred community pharmacy practice – development and implementation in Estonia. Tartu, 2023, 242 p.
342. **Linda Sõber.** Impact of thyroid disease and surgery on patient's quality of voice and swallowing. Tartu, 2023, 114 p.
343. **Anni Lepland.** Precision targeting of tumour-associated macrophages in triple negative breast cancer. Tartu, 2023, 160 p.