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„Inflammaging: A cross sectional study of the current inflammatory status of elderly in association with various health-, nutrition- and physical activity factors "

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I hereby declare that I have made this work independently and without any help from others and have not used any sources and aids other than those indicated. I also assure you that this work has not yet been available elsewhere as a thesis.

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ATP	adenosine-triphosphate
BCM	body cell mass
BIA	bioelectrical-impedance- analyzer
BMI	body mass index
bp	blood pressure
CRP	C-reactive protein
DACH	Germany-Austria-Switzerland
DGE	German Association for Nutrition
dias	diastolic
Dr	doctor
ECM	extracellular mass
Fc	fragment crystallizable
FFM	fat-free mass
FFQ	food-frequency- questionnaire
I. e.	id est
IgG	immunoglobulin G
IL	interleukin
L	lymphocytes
Max	maximum
MET	metabolic equivalents
Min	minimum
MIPA	moderate intensity aerobic physical activity
N	neutrophil granulocytes
NAD	nicotinamide adenine dinucleotide
NaF	sodium- florid
NF-kB	nuclear factor 'kappa-light-chain-enhancer' of activated B-cells
NLR	neutrophil to lymphocyte ratio
P	platelet count
PA	physical activity
PLR	platelet-to-lymphocyte ratio
ROS	reactive oxygen species
SII	systemic immune-inflammation index
Sys	systolic
TNF-α	tumor- necrosis- factor alpha
VIPA	vigorous intensity aerobic physical activity
WHO	World Health Organization
WHR	waist-to-hip-ratio

V. List of units and symbols

℃	degrees Celsius
dL	deciliters
g	gram
hr	hour
kg	kilogram
KI	hour
mg	milligram
min	minute
mL	milliliter
mmHg	milliliters of mercury
nmol	nanomole
p	significance
pg	picogram
r	rho
µg	microgram
µmol	micromole

1 Introduction

Due to higher quality standards in hygiene, health care and an adequate food supply network, there is a substantial expansion in life expectancy among the world's population (Lunenfeld and Stratton 2013). It is estimated, that the world's population of over 60-year-old people, will be increased up to 22% by 2050 (Steverson 2018). With this increase in elderly people, new challenges arise including increased prevalence in aging-associated diseases, such as cardiovascular disease, Alzheimer's- and Parkinson's disease (Campisi et al. 2011). Therefore, the prevention of age-related diseases, perseverance of health and independency of the older population has become a public health priority (National Research Council (U.S.) 2001).

But why is it, that certain diseases are associated with aging and what processes may be the underlying causes? One potential explanation for the increase in those diseases are changes in the immune system (Fulop et al. 2017). Although it was long believed that a down regulated immune system is found only in unhealthy individuals, evidence now shows that is also found in healthy elderly indicating that the underlying modifications, that induce a down regulation of the immune system, are likely to be a physiological phenomenon which comes with aging (Campisi et al. 2011). Furthermore, in 1993, Fagiolo and colleagues reported that another reason for those age-related disorders may be alterations in the cytokine composition within the human body (Fagiolo et al. 1993). During in vitro tests, they observed higher concentrations of inflammation promoting cytokines like interleukine-6, tumor necrosis factor-α and interleukin-1β in cells of elderly people with a mean age of 80,2 years, when compared to selected cells of younger individuals with a mean age of 26,8 years (Fagiolo et al. 1993).
In this context, the term "*inflammaging*" was first described (C. Franceschi et al. 2000). Nowadays, it is recognized that the phenomenon of inflammation, which was believed as a pure immunological phenomenon, also involves non immune cells such as adipocytes, muscle fibers, senescent cells and endothelial cells (Campisi 2013; Prattichizzo et al. 2016; Kalinkovich and Livshits 2017).

A crucial point in the research of this topic is to understand why not only immune but also non-immune cells produce unusual high amounts of some inflammatory mediators, as the organism grows older, and if there are any ways to counteract those age-related changes.
Since every individual will age differently, it is important to note, that the progress of inflammation appears to be a pattern of remodeling due to a response of the organism on unpredictable long-time exposures to external and/or internal stressors. This concept was described by Grignolio et. al 2014 and termed *"immunobiography"* (Grignolio et al. 2014). It states that everyone has their own individual *immunobiography,* resulting in an individual aging- and therefore *inflammaging* process.

This process can be more or less severe with a wide spectrum of possible outcomes ranging from age-related diseases where inflammation plays a pathogenic role up to successful aging (Grignolio et al. 2014; Claudio Franceschi et al. 2017).

A huge impact on the individual aging process are having external lifestyle factors like nutrition and physical activity (vel Szic et al. 2015; Nimmo et al. 2013). As stated in the guidelines of the German Association for Nutrition (DGE) there are specific nutrients, that show a critical role when it comes to an adequate supply status in elderly individuals. This include vitamins like vitamin C, -D, -E, -B12 and folic acid as well as minerals like calcium, magnesium and iron (DGE 2019a). Results from the National Consumption Survey II (2008) show an inadequate nutrient supply of vitamin D, folic acid and calcium in people aged 51 to 80 (figure 1) (BMEL 2008).

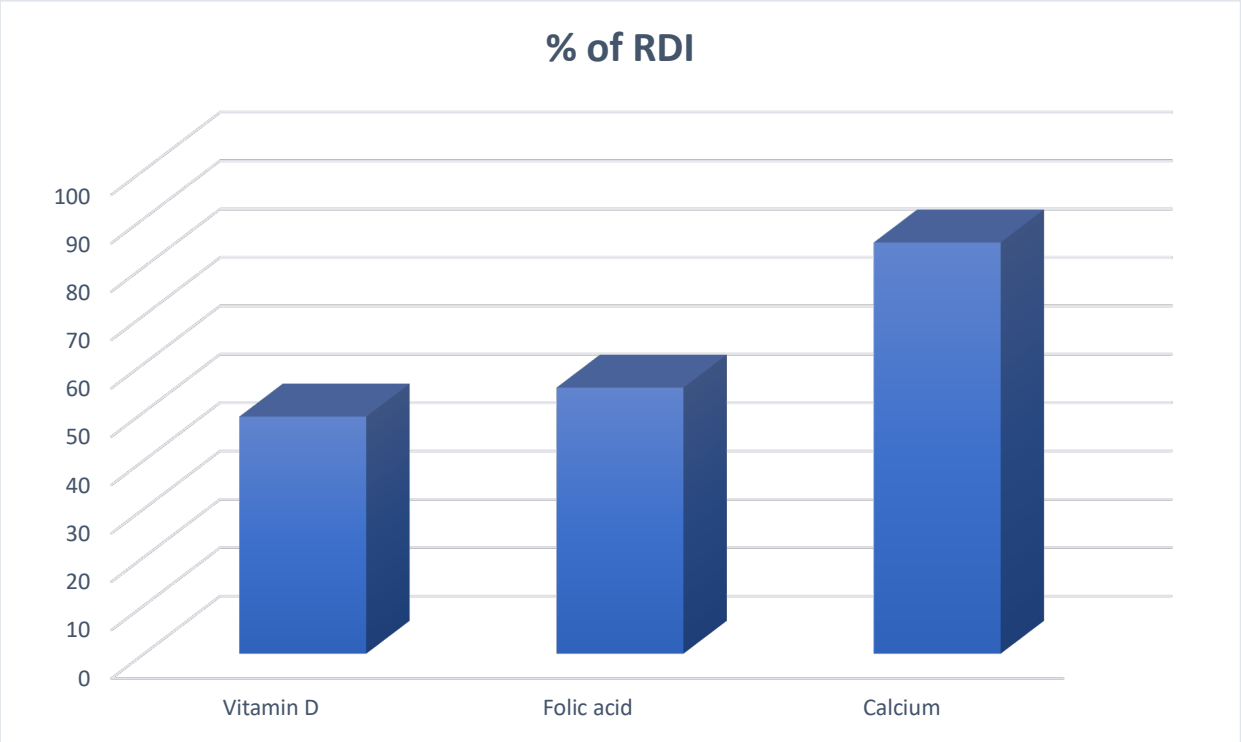

Figure 1. Nutrient intake of vitamin D, folic acid and calcium in relation to the recommended daily intake, prescribed by the DGE. (BMEL 2008)
RDI: Recommended daily intake

Additionally, physical activity provides health benefits for elderly, including lower rates of coronary heart disease, high blood pressure, stroke, type 2 diabetes, colon cancer and breast cancer (WHO 2020). In 2014, the Center of Disease Control and Prevention examined the physical activity status in adults aged 50 years and older living in the United States. The survey showed that 27.5% of participants aged ≥50 years reported no physical activity outside of work and that the inactivity prevalence significantly increased with age (Watson et al. 2016). They showed an 25.4% decrease in

physical activity among adults aged 50–64 years and further, a 26.9% decrease in physical activity among adults aged 65–74 years (Watson et al. 2016).

Taken together these data reinforce the importance of adequate physical activity and nutrient supply for elderly adults, to counteract the already described changes that come with aging.

1.1 *Inflammaging* as a chronic low-grade inflammation

Inflammaging is a chronic low-grade inflammatory state in the absence of any triggers, which is significantly associated to morbidity and also overall mortality in elderly (Ferrucci et al. 2010; H. J. Cohen et al. 1997). The difference between a chronic- low grade inflammation in comparison to an innate acute inflammation is that an acute inflammation is a direct response to an infection or an injury and leads to a short-term inflammatory response which results in prevention of a disease. A chronic-low-grade inflammation on the other hand is induced by ongoing lifestyle factors, like poor nutrition and inadequate physical activity levels, which leads to a lighter, but long-termed inflammation process and results in a continuing pathogenic progression (Capuron et al. 2008). Those differences are illustrated in figure 2 (Adaes 2016).

Low-grade inflammation is caused by a dramatically increased inflammatory profile in the bloodstream of "healthy" older people in comparison to younger individuals (Henrique 2019). This altered inflammatory profile includes raised blood levels of C-reactive protein, interleukin-6, tumor necrosis factor-α and interleukine-1β (Henrique 2019) and results in a pro-inflammatory state of aging individuals (Ferrucci and Fabbri 2018). In addition, the effectiveness of inflammatory response to immunogenic stimulations is reduced (Ferrucci et al. 2010). These changes are directly linked to changes in body composition, that naturally occurs with aging, which include a reduction in muscle mass and a higher quantity in fat mass (Henrique 2019).

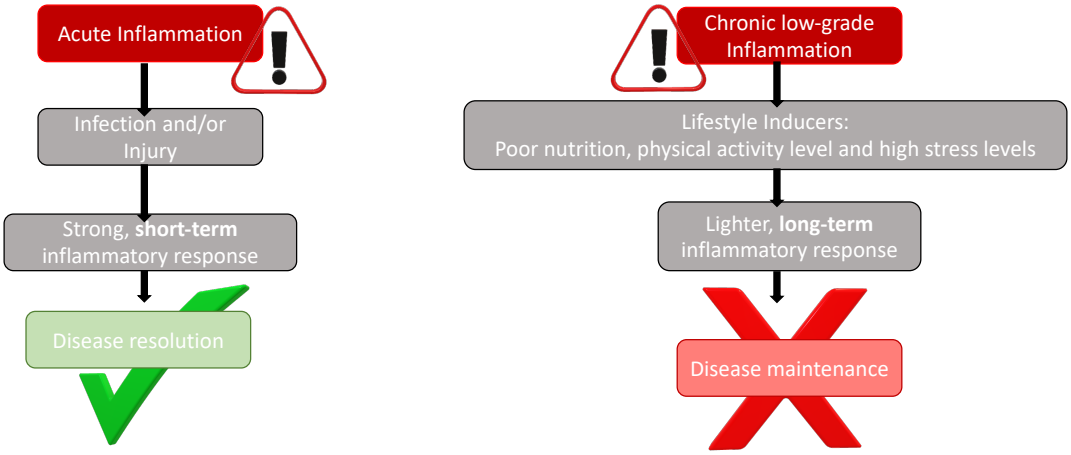

Figure 2. Difference between an innate (acute) inflammation and a chronic low-grade inflammation. (Adaes 2016)

1.1.1 Markers of Inflammation

1.1.1.1 C-reactive protein

C-reactive protein (CRP) is an acute-phase protein and a sensitive marker for systemic inflammation (Visser et al. 2001). Principally, it is synthesized in hepatocytes (Rahman and Bagchi 2014), and is working as a mediator of the innate immunity (Kim et al. 2015) but the molecular mechanism, that regulates the expression of CRP, is still not well understood. Studies suggest, that CRP concentrations are regulated directly or indirectly by cytokines including interleukin-1β, interleukin-6 and tumor-necrosis-factor alpha, during an acute-phase response, (Vermeire, Van Assche, and Rutgeerts 2005) illustrated in figure 3 (Vermeire, Van Assche, and Rutgeerts 2005). CRP is a stable plasma marker for systemic inflammation (Kim et al. 2015) thanks to its half-life of 19 hours and during infection or inflammation, it increases up to 1,000-fold at sites of inflammation (Rahman and Bagchi 2014) with a normal upper limit of 0.5mg/dL found in blood plasma of healthy individuals (LADR Laboratory). Furthermore, a variety of factors including age, gender, smoking status, bodyweight, blood lipid levels and blood pressure can alter CRP levels (Fadi G. Hage and Szalai 2007).

As already mentioned above, CRP is the main downstream mediator of the acute-phase response in reaction to an inflammatory event (Pradhan 2001).

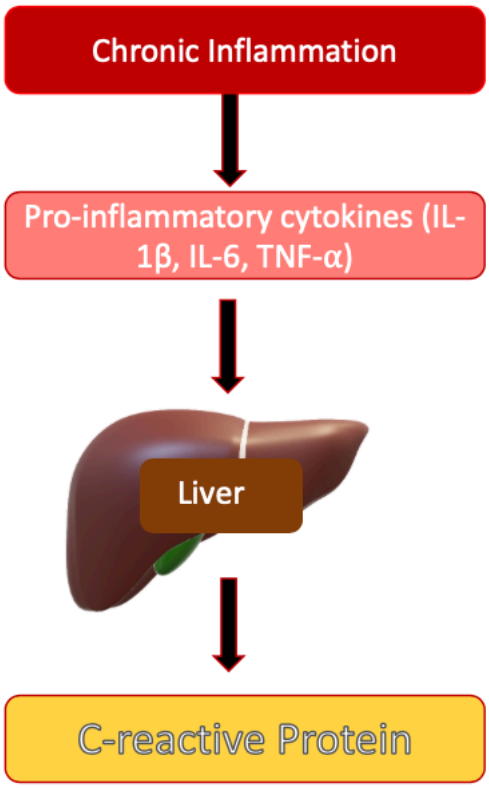

Figure 3. Activation pathway of C-reactive protein during chronic inflammation. (Vermeire, Van Assche, and Rutgeerts 2005)
IL: Interleukin

1.1.1.2 Cytokines

Cytokines are small signaling proteins. that affect a broad range of biological functions such as the activation, proliferation, and differentiation of several cells. Furthermore, they are capable of regulating the antibody production and the secretion of other cytokines (Arai et al. 1990) and therefore, the inflammatory status of the human body. With regards to their mechanisms of actions, there are different pathways through which cytokines may exert their effects. In one of these, they are acting on the cells that secreted them (autocrine action) or on proximate cells (paracrine action), while in another, they react on distant cells (endocrine action). Cytokines are secreted at local high concentrations by different cell types, were some of them can enhance inflammation (pro-inflammatory), while other can decrease inflammation (anti-inflammatory) (J.-M. Zhang and An 2007).

1.1.1.2.1 Pro-inflammatory cytokines

Proinflammatory cytokines are primarily produced by activated macrophages and are very important for up regulation of inflammatory reactions. Interleukin 1β (IL1-β), interleukin 6 (IL6) and tumor-

necrosis factor- α (TNF-α) are of special interest for low- grade inflammation which is described below (Windsor et al. 2018)(J.-M. Zhang and An 2007).

IL-1β is released during inflammation, cell injury and infection, primarily by monocytes and macrophages as well as by non-immune cells, such as fibroblasts and endothelial cells (J.-M. Zhang and An 2007). In healthy individuals the usual functions of IL-1β are homeostatic functions, including the regulation of hunger, sleep, and body temperature (Dinarello 1996). However, an overproduction of IL-1β indicates pathophysiological changes in the human body, that mainly occur during inflammation (Ren and Torres 2009).

TNF-α is a cytokine, involved in almost every known inflammatory process (Bradley 2008). Together with IL-6 and IL-1β, TNF-α is also involved in the acute phase response by synthetizing acute phase proteins like CRP. It is the first cytokine released during the signaling cascade of activated macrophages.(J.-M. Zhang and An 2007) TNF-α causes fever and lethargy and has an impact on fat metabolism, insulin resistance and blood clotting. Its most important function is the activation of various immune cells. Further, TNF-α stimulates cell differentiation and the release of other cytokines (Bradley 2008)(J.-M. Zhang and An 2007).

Lastly **IL-6,** plays a key role in the acute phase response and is a mediator of fever. By changing the nature of infiltrating leucocytes, IL-6 dictates the transition from acute to chronic inflammation. Additionally, it supports the chronic inflammatory response by initiating the growth of B-cells and as antagonist of regulatory T cells (Gabay 2006). Furthermore, interleukin-6 release into the blood circulation can be triggered by hormones like cortisol, which are released in human body while experiencing psychological stress (H. J. Cohen et al. 1997). IL-6 has a special status because of its inflammatory and anti-inflammatory properties depended from its origin of synthesis. When produced by monocytes, macrophages or adipocytes, IL-6 shows inflammatory properties, by for example acting in acute phase response and elevating CRP concentrations in the blood circulation (Bastard et al. 1999). On the other hand, it has extensive anti-inflammatory functions when secreted by muscle cells as response to muscle concentration (Febbraio and Pedersen 2005).

1.1.1.2.2 Anti-inflammatory cytokines

Anti-inflammatory cytokines are a series of immunoregulatory molecules, that control the pro-inflammatory cytokine response during inflammation (J.-M. Zhang and An 2007). Among all anti-inflammatory cytokines, **IL-10** has the most potent anti-inflammatory properties, for example the repression of the expression of inflammatory cytokines such as TNF-α, IL-6 and IL-1. Furthermore, IL-10 can increase the synthesis of endogenous anti-cytokines and decrease the expression of pro-

inflammatory cytokine receptors. Thus, it is capable of counter-regulating the production and function of pro-inflammatory cytokines (Barry et al. 2016).

1.1.1.3 Inflammation indices

To enhance health screenings which will help to understand the status of inflammation and therefore inflammation linked disease, researchers aim to determine parameter from simple blood tests and associate them with systemic inflammation.

To determine the prognosis in clinical situations the neutrophil-lymphocyte ratio (NLR) was shown to be a reliable and cost-effective parameter (Ulu et al. 2013) (Huang et al. 2015), as it is calculated from a large hemogram. More precisely, NLR is calculated as neutrophil count divided by lymphocyte count (NLR=N/L) (Lee et al. 2018). Several studies were able to show, that NLR is a potent marker for systematic inflammation (Bhat et al. 2013) (Zahorec 2001) (Proctor et al. 2012) (Kuyumcu et al. 2012) (Rembach et al. 2014). Another marker which can be used to measure the degree of systemic inflammation is the platelet-lymphocyte ratio (PLR). Usually, this ratio is used to determine the prognosis in critically ill patients, especially during postoperative and intensive care (Hudzik et al. 2016) (You et al. 2016). It also is obtained from large hemogram by calculating the ratio of platelet count to lymphocytes (PLR=P/L) (Lee et al. 2018). To ensure validity of the accuracy for the prediction of inflammation, another novel index, the systemic inflammation index (SII) was introduced (Hu et al. 2014). This marker combines the NLR and the PLR by putting neutrophil (N), platelet (P) and lymphocyte (L) counts in perspective (SII= NxP/L) (Chen et al. 2017). This might qualify SII as a noninvasive, reproducible and cost-effective indicator for the balance of immune and inflammatory status in patients with different inflammation linked diseases (Chen et al. 2017; Hong et al. 2015; Hu et al. 2014; Feng, Chen, and Yang 2017).

1.1.2 Influence of age, gender and anthropometric measurements on inflammation

1.1.2.1 Age

There are various definitions for the term "age" with two of them being: chronological age, which describes the timespan from the moment of birth to the present day in years (Cameron 2015) and the biological age, which is characterized by the functional capacity of every individual (Jackson, Weale, and Weale 2003). Furthermore, there is the maximal lifespan, which is defined by the average lifespan of the oldest member of a population (for the human species it is 125 years) (Weon and Je 2009) and life expectancy at birth (or at 40,65,… Years) which is described as the average number of years that a person can be expected to live at a specific point in their lifetime (Organization for Economic Co-operation and Development). The life expectancy depends of various external stimuli,

such as the country and year of birth, the gender and where that individual has lived the majority of his or her lifetime plays a key role.

1.1.2.2 Gender

Gender differences are evident in chronic inflammatory diseases and include for example, worse scores in pain and quality of life measurements due to genetic and hormonal factors in patients with rheumatoid arthritis, inflammatory bowel disease and psoriasis (Lesuis et al. 2012). Another study confirmed greater differences in frequency of complications during the disease progression in females, proposing that chronic inflammation may induce major damage in targeted organs and functions of women in comparison to men (Maric-Bilkan 2017). Furthermore, sex hormones affect body composition, such as amount of body fat mass or fat- free body mass and therefore, are indirectly linked to the inflammatory response (Kautzky-Willer, Harreiter, and Pacini 2016).

1.1.2.3 Body composition

Aging of the human body is not only accompanied by alterations in the immune system, but also in body composition. Those changes, described and summarized in figure 3 and encompass an increase in body fat and a decrease in muscle mass and body water (St-Onge and Gallagher 2010).

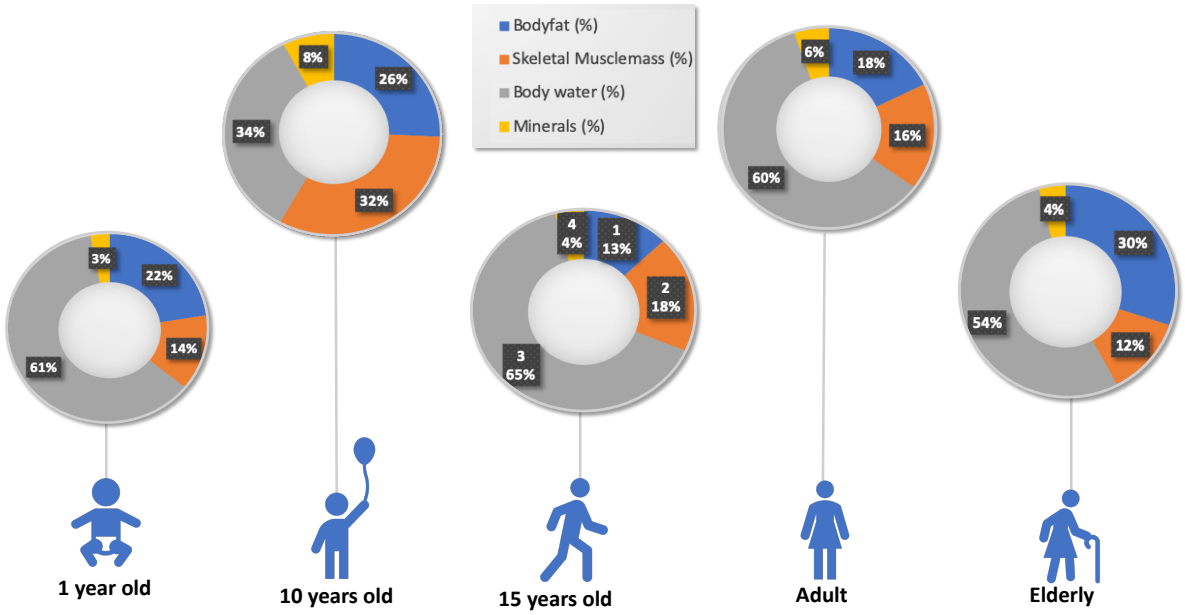

Figure 4. Overview of Body composition over the human life span. (St-Onge and Gallagher 2010)

Interestingly it was already shown, that the changes in body composition are also associated with the inflammatory state of the human body (Calvani et al. 2017). Adipose tissue, which is increased in elderly people, acts as a secretory organ, capable of both, sending and receiving signals. These signals modulate energy expenditure, appetite, insulin sensitivity, inflammation and more. Epidemiological studies have confirmed an increases of acute phase proteins, such as CRP, in obese subjects. This protein (CRP), produced principally in the liver in response to IL-6, is considered as marker for inflammation and insulin resistance (Gentile et al. 2010). In addition, further acute phase reactants were elevated in obese individuals, including TNF-α, IL-1β and IL-6 (Sam et al. 2009). Hypertrophic adipocytes may overproduce those proinflammatory cytokines which results in a local, and later, overall chronic inflammatory state of the human body (Pellegrinelli et al. 2015).

As already mentioned above, aging comes with an increasing body fat mass and decreased muscle mass. At the age of 40, the decline of the muscle mass begins. About ten percent of the total muscle mass for each ten-year period (Goodpaster et al. 2006). This reduction in muscle mass, in particular skeletal muscle mass, is associated with decreased levels of anti-inflammatory myokines such as IL-6 and changes in Interleukin 10 and TNF-α levels. This inflammatory imbalance culminates in *inflammaging* and causes several alterations and dysfunction in many tissues, including skeletal muscle, gut, blood vessels and many others (Orzechowski 2017).
Additionally, studies suggest that CRP levels also are significantly linked to sarcopenia, especially age-linked sarcopenia, an age-related decrease in muscle mass (Wang et al. 2017).

1.1.3 Inflammation and nutritional aspects

The importance of nutrition on inflammatory processes in the human body has long been acknowledged (Galland 2010). While some foods and nutrients may promote inflammation, others can help to reduce it (Kiecolt-Glaser 2010). In industrialized countries the most common diet is the "Western diet" which is characterized by a low intake of vegetables, fruits and whole grain products while the intake of highly processed foods such as sweets, convenience foods, chips etc. is too high. Taken together, this form of diet is high in refined sugar, saturated and trans-fats, high intake of pro-inflammatory omega-6 fatty acids, sodium and potassium and low in dietary fiber, complex carbohydrates, vitamins, including vitamin D and folic acid and minerals, including calcium and iron, especially in women (BMEL 2008).

Although the importance of a balanced and nutrient rich diet is evident, results from the German National Consumption Survey 2 (Nationale Verzehrsstudie 2) show, that the current dietary behavior and nutrient intake of people of the age of 51 to 80 years is not ideal (table 1). Regarding the consumption of specific food groups it was found, that intake of meat, sweets and alcohol consumption are too high while the cereal and vegetable consumption are too low (BMEL 2008). However, when compared among genders, women showed better dietary patterns than men. Concerning the intake of vitamins, most adults reached intakes as recommended by the German Nutrition Society et al. (DACH-Referenzwerte, 2013). Only the supply of vitamin D and folic acid seems to be insufficient especially in older people. 79% of the men and 86% of the women fall below the recommended intake value for folic acid and 80-90% do not reach the estimated values for the vitamin D intake (BMEL 2008).

Tabel 1. Food intake of different food groups in two age groups in Germany (BMEL 2008).

Food group		51-64 years	65-80 years
Cereal and cereal products	men	29 (g/day)	27 (g/day)
	women	28 (g/day)	23 (g/day)
Potatoes	men	81 (g/day)	97 (g/day)
	women	65 (g/day)	78 (g/day)
Vegetables	men	122 (g/day)	123 (g/day)
	women	125 (g/day)	106 (g/day)
Fruits	men	275 (g/day)	298 (g/day)
	women	330 (g/day)	317 (g/day)
Milk and milk products	men	219 (g/day)	210 (g/day)
	women	227 (g/day)	223 (g/day)
Meat and meat products	men	98 (g/day)	79 (g/day)
	women	54 (g/day)	46 (g/day)
Fish	men	19 (g/day)	21 (g/day)
	women	17 (g/day)	16 (g/day)
High processed foods: sweets	men	48 (g/day)	44 (g/day)
	women	41 (g/day)	39 (g/day)
High processed foods: salty snacks	men	6 (g/day)	3 (g/day)
	women	4 (g/day)	2 (g/day)
Alcohol	men	348 (g/day)	306 (g/day)
	women	101 (g/day)	70 (g/day)

1.1.3.1 Critical vitamins in elderly and inflammation

There are some nutrients, that are of special interest in elderly adults. Those include vitamin C, vitamin D, vitamin E, folic acid and vitamin B12. As mentioned in the following table (table 2) (DGE 2019a), vitamin C is important for the structure of connective tissue, bones and teeth, is protective against cell damage and promote wound healing. Vitamin D regulates calcium and phosphate exchanges and plays an essential role in bone formation. Vitamin E has a protective effect against cell damage and vitamin B12 is important for degradation of individual fatty acids and blood formation. Furthermore, folic acid acts in various ways including cell division and cell formation, blood formation, protein metabolism and more (DGE 2019a).

Tabel 2. Critical nutrients in elderly (DGE 2019a).

Critical nutrients (Vitamins)	Function	Deficiency	Sources
Vitamin C	Structure of connective tissue, bones & teeth, protection against cell damage, wound healing,	Poor wound healing, joint pain, infections, high bleeding tendency	Peppers, blackcurrant, parsley, sea buckthorn, citrus fruits, potatoes, cabbage, spinach, tomatoes,
Vitamin D	Regulation of calcium and phosphate change, bone formation	Disorder of bone formation, descaling, bone softening, Osteomalacia in adults	Fatty fish, Vit. D-enriched margarine
Vitamin E	Protection against cell damage and oxidation of other nutrients	Disruption of membrane functions, muscle metabolism and the nervous system	Plant oils (wheat germ oil. sunflower oil, corn germ oil, rapeseed oil), wheat germ, hazelnuts
Folic acid	Cell division and cell formation, blood formation, protein metabolism, nerve tissue, reduction of homocysteine concentration in the blood	Disruption of blood count, anemia	Vegetables (tomatoes, spinach, cabbages, cucumbers), oranges, grapes, whole grain baked goods, wheat germ, potatoes, soybeans
Vitamin B12	Degradation of individual fatty acids, blood formation	Anemia, permanent damage to the spinal cord	Liver, meat, plant-based foods produced by means of fermentation (sauerkraut)

Of the critical nutrients mentioned above, vitamin A, vitamin C and vitamin D are also involved in inflammation. As shown in table 2, vitamin A boost immune response in elderly (Rumore 1993) whereas deficiency induces inflammation and aggravates existing inflammatory states (Reifen 2002). Further, vitamin C acts as antioxidant by acting as electron donor for enzymes and neutralizes free radicals to protect cells from damage (Ellulu et al. 2015). When deficient, poor wound healing, joint pain, infections and high bleeding tendency, respectively, increases. Lastly, vitamin D is important for the modulation of the inflammatory system by regulating the production of inflammatory cytokines and immune cells (Liu et al. 2018), while deficiency leads to bone softening and Osteomalacia in elderly (Elmadfa 2009).

1.1.4 Influence of physical activity in inflammation

1.1.4.1 Physical activity

Together with nutrition, physical activity (PA) is the most studied intervention when it comes to counteract and/or slow down the aging process by decreasing the inflammation processes (Claudio Franceschi et al. 2018). Therefore, it is a widely recommended tool to treat inflammatory-related diseases (B. K. Pedersen and Saltin 2015). The anti-inflammatory effects are based on hundreds of myokines which are secreted by skeletal muscle fibers during and after exercise training. (Claudio Franceschi et al. 2018) Those secreted factors show potential drug-like effects on i.e. proteins, growth factors and cytokines (Bente K. Pedersen 2013). Acute physical activity induces an early release of IL-6 in the skeletal muscle, which initiates the production of anti-inflammatory cytokines such as IL-10 and also inhibit the pro-inflammatory cytokine TNF-α. (Bente Klarlund Pedersen 2012) Some of the further reasons, why PA shows anti-inflammatory properties are:

- reduction of visceral fat mass and therefore decreased release of inflammatory adipokines and reduced chronic activation of the hypothalamic–pituitary–adrenal axis (Henrique 2019)
- inhibition of TNF-α by monocytes caused by acute activation of the sympathetic nervous system
- downregulation of Toll-like Receptor, which causes deactivation of inflammatory pathways (Garatachea et al. 2015)
- reduced macrophage infiltration in tissues (Henrique 2019)
- increased antioxidant capacity by reducing activity of redox-depended nuclear factors like NF-κB (Henrique 2019)

2005, Petersen and Pedersen showed, that regular exercise enables the formation of an anti-inflammatory environment by reducing basal inflammatory and increasing anti-inflammatory cytokine concentrations in elderly (Petersen and Pedersen 2005). When performed regularly, these modifications in circulating cytokines become long term changes with long term health benefits on inflammation (Reihmane and Dela 2014). IL-6 for example, plays a dominant role during prolonged endurance exercise (Shephard 2002). Although various types of cells can produce cytokines, the main source of the exercise-induced IL-6 production is released by the exercising muscle (Shephard 2002). Acute increases in IL-6 by physical activity have been proposed to suppress proinflammatory TNF-α (Starkie et al. 2003) and increase anti-inflammatory cytokines such as IL-10 (Steensberg et al. 2003) which creates an anti-inflammatory milieu that lasts for several hours after the exercise session (Mendham et al. 2015). Unlike the anti-inflammatory benefits, of temporary increased IL-6 from skeletal muscle due to acute exercise, raises in IL-6 from other sources such as adipose tissue or hepatocytes are associated with elevated pro-inflammatory TNF-α and CRP (Windsor et al. 2018). Kohut et al. showed that higher levels of cardiorespiratory fitness are associated with decreased concentrations of circulating IL-6 and CRP at rest which strengthens the necessity of regular physical activity in every age category and in particular for older people (Kohut et al. 2006).

1.1.4.2 Recommendations

Physical activity is defined as "any bodily movement produced by skeletal muscles that requires energy expenditure" – WHO (WHO 2019b). It is more than exercising the body to build or maintain muscles and/or condition and therefore should not be mistaken with the term "exercise". (WHO 2019)

Physical activity can be classified in three main groups and is expressed by metabolic equivalents (METs). MET is the ratio of a person's working metabolic rate relative to their resting metabolic rate (WHO 2019).

The three physical activity categories are:

- "**moderate intensity aerobic physical activity**" which describes movements with moderate amount of effort and a noticeably accelerated heart rate. Those are exercises like dancing, gardening, walking, … which requires approximately 3-6 METs. (WHO 2019b)
- "**vigorous intensity aerobic physical activity**" which are movements that commands a large amount of effort and furthermore causes rapid breathing and a significantly increased heart rate. Those are exercises like running, spinning, aerobics,… which requires approximately more than 6 METs. (WHO 2019b)
- "**resistance training**" which are movements that causes the skeletal muscle to contract against an external resistance with the expectation to increase muscle mass and muscle strength, which requires approximately 3 METs (Phillips and Ziuraitis 2004). Above mentioned resistance can be dumbbells, rubber bands, bodyweight,… . (Weil n.d.)

The WHO defined for each of the above-mentioned PA categories minimal recommendations, to provide their health benefits. To ensure the minimum of benefits for disease prevention, 150 min of moderate intensity aerobic physical activity (MIPA) or 75min of vigorous intensity aerobic physical activity (VIPA) should be achieved per week. For additional health benefits it´s recommended to absolve 300 min. MIPA or 150 min. VIPA per week (WHO 2010).

2 Objective

The aim of this master thesis was to examine the current inflammation status of elderly people between the ages of 50 to 70 years. Therefore, CRP levels, IL-6, -10, -1β and TNF-α levels as well as NLR, PLR and SII were analyzed. Moreover, different lifestyle factors, including nutrition, physical activity and body composition measurements, were evaluated to reveal possible correlations between those factors and the chosen marker of inflammation.

This cross-sectionals analysis was part of an intervention study (BEGInn Study, Leibnitz University Hanover), which examined the impact of exercise alone compared to exercise combined with nutrition on health parameters of physical inactive, elderly people.

3 Material and Methods

Data used for this thesis was obtained from the BEGinn Study (Bewegung, Ernährung und Gesundheit) which was conducted at the Gottfried Willhelm Leibniz University of Hannover from October 2018 to August 2019. This study was an interdisciplinary project realized by the institute of food science and human nutrition and the institute of sports science.

The aim of this study was to investigate the effects of physical activity alone or in combination with an additional nutritional intervention on various immunological-, nutritional- and sport scientific parameters.

3.1 Study design

BEGinn is a randomized controlled human intervention study investigating the effects of a 12-weeks Intervention program including physical activity, nutrition and supplementation with omega-3 on immunologic-, nutritional- and physical activity parameter.

The study was conducted in accordance with the guidelines of the Declaration of Helsinki.

It was approved, in July 2018, by the Ethic Commission Hannover, of the medical council of Lower Saxony. This study is registered in the German Clinical Trial Register (DRKS00014322).

This master thesis evaluated the study as a cross- sectional study, with the aim to investigate the current inflammatory status in elderly people and possible correlations between age, body composition, physical activity state, nutrition and inflammation markers.

3.2 Participants

Participants were recruited between August 2018 and March 2019 by the institute of food science and human nutrition and the institute of sports science of the Gottfried Wilhelm Leibniz University Hannover.

135 healthy men (n=38) and women (n=96), ages between 50 and 70 years, participated in this study. All participants were physically inactive for at least two years prior; did not have any known chronic disease; did not take any medication that would alter immune function; did not abuse alcohol or drugs; are capable to exercise; and agree to complete the 12- week exercise- and nutrition program, and supplement intake schedule. Further inclusion and exclusion criteria are shown in table 3 (BEGinn Study protocol).

Tabel 3. Inclusion and exclusion criteria for the recruiting of study participants (Study protocol, BEGinn- Study).

Inclusion criteria	Exclusion criteria
Age 50 to 70 years	Manifested coronary heart disease, renal insufficiency, liver disease, chronic gastrointestinal disease
Physically inactive for at least the past two years	Blood clotting disorder
Capable of physical exercising	Immunologic diseases
Agree to a 12-week Exercise Program	Regular Laxans intake
Agree to adapt diet along DGE guidelines	Chronic intake of immunosuppressive drugs
Stable weight for the past 6 months at least (weight ± 5kg)	Simultaneously participation in other studies
Omnivore diet	Mineral- and/or Vitamin supplement Intake
	Not able to give consent

DGE: German Association for Nutrition

3.3 Process

The participants came on examination day, at morning and in fasting state. Anthropometric data were collected, by measuring body composition with the bioelectrical-impedance- analyzer (BIA) and by height and body weight. Furthermore, blood pressure was measured, and blood samples were taken. Next, the food- frequency- questionnaire (FFQ) and Freiburger questionnaire for physical activity were filled out, to access the dietary habits and physical activity levels of the participants. Also, the three-day food diary, which was send in beforehand and had to be completed three days in prior to the record day, was collected.

3.3.1 Measurement of body composition

Body mass index (BMI) and body composition, including body fat, fat-free mass (FFM) subdivided in body cell mass (BCM) and extracellular mass (ECM); total body water subdivided in intra- and extracellular water; and phase angle were measured by bioelectrical impedance analyzer (BIACOR-PUS RX 4004M, Manufactory: MEDI CAL HealthCare GmbH, Karlsruhe).

Participants arrived in the morning, rested and after an overnight fast (≥ 10 h). During the measurement, the participants lay on a chaise with arms away from the body, no shoes, socks, or any jewelry on. Two electrodes were placed on the left hand and foot as instructed by the manufacture 's procedure (Data Input GmbH, n.d.). The participants remained lying and still, without moving or talking, until the completion of the analysis. Resistance and reactance of different body tissues were measured, by passing 5kHz, 50kHz and 100kHz alternating current through the body tissues. Measurements were recorded, and later used, to estimate the above-mentioned measurements, using the NutriPlus© 5.4.1 software (Data Input Company, Darmstadt, Germany). Furthermore, height, body weight, waist-to-hip-ratio (WHR) and blood pressure (bp) were measured. The reference ranges for blood pressure and anthropometric data, including BMI, BCM, body fat and WHR are shown in the following table (table 4).

Tabel 4. Guidelines for systolic blood pressure (mmHg), diastolic blood pressure (mmHg), heartrate, BMI, Body cell mass (BCM, %), total bodyfat (%) and waist-to-hips-ratio (WHR) for woman and men (Elmadfa 2009; Mutschler et al. 2007).

	Women	Men
Blood pressure systolic (mmHg)	110-130	
Blood pressure diastolic (mmHg)	≦84	
Heartrate (bpm)	50-100	
BMI (kg/m2)	19,0-25,0	
BCM (%)	50-56	53-59
Bodyfat (%)	20-30	10-20
WHR	<0,85	<1

BMI: Body mass Index, BCM: Body cell mass, WHR: waist-to-hip ratio

3.3.2 Blood sample collection and assessment of biochemical parameters

80 ml of overnight fasting (10–12 hr) blood were taken to examine immunological parameters, nutrient status, omega-3-index and the large hemogram. Of special interest for this work are results of nutrient status for vitamin B12, vitamin D and folic acid; the large hemogram (neutrophils, lymphocytes, thrombocytes, leucocytes, CRP) and immunologic parameters (TNF-α, IL-6, IL-10, IL-1β). Therefore, venous blood from the antecubital vein was collected into serum- tubes, EDTA-tubes and sodium- florid (NaF)- tubes (Sarstedt AG & Co. KG, Nümbrecht, Germany) and remained at room temperature for 20 min to be clotted. Then, to separate the serum, it was centrifuged (1,000 g) at 4°C for 20 min. Serum and erythrocyte samples were allocated into 1.5 mL tubes and immediately frozen at −80°C for further analyzing cytokines, omega-3 index and other. Furthermore, blood samples were sent in EDTA- tubes to LADR laboratory (Laborärztlichen Arbeitsgemeinschaft für Diagnostik und Rationalisierung e.V.) and Labor Dr. von Froreich Bioscientia for analysis. The cytokines including IL-6, IL-10, IL-1β and TNF_α were analyzed by "*Bio-Plex pro human cytokine screening*" (Bio-Rad Laboratories GmbH, Feldkirchen, Germany). table 5 is an overview of the evaluated blood parameters and their reference values.

Tabel 5. Reference range for blood parameters of vitamin B12 (ng/l), folic acid in erythrocytes (µmol/l), vitamin D (nmol/l), leucocytes (G/l) and C-reactive Protein (CRP, mg/l) (LADR, Bioscientia).

Blood parameters	Reference value
Vitamin B12 [ng/l]	200-1000
Folic acid in erythrocytes [µmol/l]	523-1260
Vitamin D[nmol/l]	30-100
Leukocytes [G/l]	3.5-9.8
CRP [mg/l]	≦5

CRP: C-reactive protein

3.3.2.1 Biomarkers

For this thesis, chosen inflammatory markers are C- reactive protein, IL- 6, IL-10, and TNF- α. Furthermore, the systemic inflammation state was determined by SII, PLR and NLR evaluating leukocytes, platelet count and neutrophil granulocytes. The reference values for those biomarkers of inflammation, used to determine the inflammatory status, are listed in table 6 and table 7.

Tabel 6. Reference values for blood parameters of selected cytokines including interleukin-6 (IL-6), intereukin-10 (IL-10), interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) (Bio-Plex™- Cytokine Assay).

Cytokine	Reference value (pg/ml)
Interleukin-6	<6.557
Interleukin-10	<22.284
Interleukin-1β	<4.457
Tumor necrosis factor- α	<51.852

Tabel 7. Guidelines for neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and systemic immune inflammation index (SII) for woman and man (Lee et al. 2018; Fest et al. 2018).

Inflammatory indices	Reference value
Neutrophil-to-lymphocyte ratio (NLR)	0.78-3.53
Platelet-to-lymphocyte ratio (PLR)	<150 (60-268)
Systemic immune inflammation index (SII)	186-1131

3.3.3 Measurements of food consumption and nutritional supply

3.3.3.1 Food frequency questionnaire (FFQ)

To evaluate the frequency and portion size of food and beverage consumption over a specific time period, food- frequency- questionnaires (FFQ), created by the *Robert Koch Institute* and applied at the "DEGS"- Study (Study about the health of German adults) (appendix 10.3) were used. FFQs are common dietary assessment tools to use in large epidemiological studies of diet and health. They consist of various questions about the consume pattern of different food groups with the goal to assess the overall dietary pattern. These questionnaires are self- administered which means that they were filled out without additional monitoring by trained supervisors (Robert Koch Institut 2011).
After the evaluation, results were converted in servings per day for better comparison with each other and with dietary guidelines of the DGE, listed in the table 8 below.

Tabel 8. DGE-Guidelines for the consumption of different food groups in servings per day. (DGE 2019b)

Food groups	Guideline (servings per day)
Fruit consumption	2
vegetable consumption	3
Meat consumption	0.14
Potatoes, rice and cereal products	5
High processed food	0.14
Dairy and dairy products	2
Fish consumption	0.29
Alcohol consumption	0.14

3.3.3.2 Dietary records

To collect data, about the regular dietary behavior, 3-day- dietary records were used. Dietary records, also known as food diaries, collect the exact meals consumed during at least three consecutive days. They can be utilized to estimate current dietary pattern of individuals, as well as to identify groups with an inadequate nutritional supply status, by comparing results to dietary guidelines (Deutsch-, Österreichische-, Schweizerische Gesellschaft für Ernährung) for nutrient intake, shown in table 7 (Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, and Schweizerische Gesellschaft für Ernährungsforschung 2013). It is more precise about the exact nutrient intake, but only for a short period of time. In this study, a 3-day- food diary was utilized, exemplary template in appendix (appendix 10.2). The collected data is self-recorded at the time the food and beverages were consumed, thus, minimizing reliance on subject's memory, in contrast to FFQs (Ortega 2015). To evaluate the collected data, PRODI® software (Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart) was used.

Tabel 9. DACH-Guidelines for energy intake and nutrient for woman and men from the age of 50 years (Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, and Schweizerische Gesellschaft für Ernährungsforschung 2019).

	Women		Men
Energy consumption (kj/ day)	6900-7400		8300-9200
Energy consumption (kcal/ day)	1600-1800		2000-2200
Dietary Carbohydrates (g/ day)		>315*	
Dietary protein (g/ day) (51-56 years old)	47**		55**
Dietary protein (g/ day) (>56 years old)	57**		67**
Dietary fat (g/day)		<75*	
Dietary fiber (g/ day)		>30	
Vitamin B12 (µg/Tag)		3	
Vitamin C (mg/day)	95		110
Vitamin D (µg/day)		20	

(Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, and Schweizerische Gesellschaft für Ernährungsforschung 2013)
*) Calculated with 2000kcal/day, **) Calculated with reference measurements for body height derived from results of the DEGS1- Study (Studie zur Gesundheit Erwachsener in Deutschland) (DGE et. al, 2019)

3.3.4 Measurements of physical activity level

3.3.4.1 Freiburger questionnaire for measuring the physical activity level

The Freiburger questionnaire for measuring the physical activity level, is a questionnaire to assess health related physical activity (appendix 10.4). It is a self-assessment questionnaire for people between the ages of 18 to 78 (Frey et al. 1999) and consists of general questions about gender, age, height and body weight, furthermore, questions about "basic physical activities", "leisure time physical activities" and "(classic) physical activities" per week. Also, daily relaxation- and sleep phases are evaluated. The participants further had to rate, how much more or less active they are in comparison to their contemporaries. The following figure 6, illustrate the guidelines of WHO for physical activity of elderly people (WHO 2010).

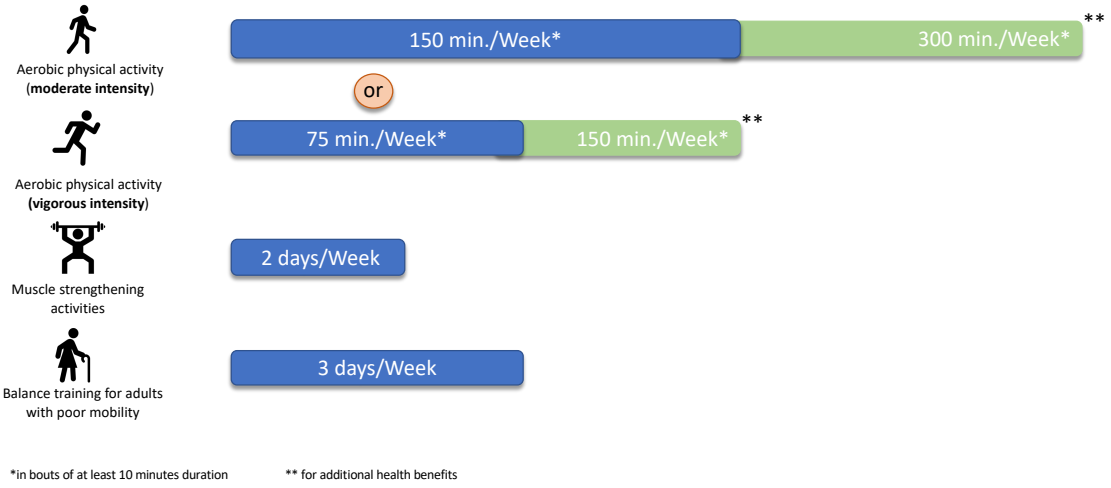

Figure 5. Recommendations for elderly on physical activity for health. (WHO 2020)

3.4 Data analysis

All statistical analyses were calculated and illustrated with SPSS- Statistics 26 software (IBM SPSS Statistics 26. Ink) and Microsoft Excel ® (Microsoft Deutschland, Unterschleißheim, Germany). The descriptive analysis was conducted for the study collective exploring gender and age distribution as well as the results of blood tests, anthropometric measurements, supply of nutrients, food intake and physical activity levels. This data is shown as mean ± standard deviation.

Distribution of the data was analyzed using, Kolmogorov-Smirnov test. To find associations between the chosen inflammation marker and possible pro-inflammatory factors, Spearman's rho correlation was used. Furthermore, variables were categorized in following nominal groups:

- BMI (overweight (BMI≧25) and normal weight (BMI≦25))
- Age (age ≦ 65 and age ≧65)
- Gender (already was nominal)
- CRP (CRP levels ≦ 0.5mg/dL and levels ≧0.5mg/dL)
- Cytokines (cytokines levels above the reference values and reaching the reference values)
- Inflammation indices (inflammation index ratio above the reference values and reaching the reference values)
- Food groups (food intake above the dietary guidelines and reaching the dietary guidelines)
- Physical activity level (levels above the guidelines and reaching the guidelines)

All nominal categories were analyzed with cross-tables and testes for significance with pearson-chi2 test. Results were illustrated in histograms.

To examine a connection between possible pro-inflammatory factors and inflammation markers, multifactorial regression analysis was used by evaluating the nominal data sets, described above. Statistical significance always was set at $p<0.05$ and highly statistical significance at $p<0.01$.

4 Results

4.1 Characteristics of the study participants

A total of 134 people participated in this study. Of those 96 (71.6%) were women and 38 (28.4%) were men. On average they were 59±0.5 years old [95%KI 58; 60], had a bodyweight of 78,17±1,93kg [95% KI 74,34kg;82,00kg] for women and 95,66±3,34 [95% KI 88,86kg;102,47kg] for man, and had no known chronic diseases. As shown in table 11 and table 12, the mean waist-to-hip-ratio in woman was 0.80±0.01 [95% KI 0.80; 0.82] and in men was 0.96±0.01 [95% KI 0.94; 0.97]. Furthermore, table 10 shows, that the mean systolic blood pressure (133.5± 1.7 mmHg [95% KI 130; 137mmHg]), diastolic blood pressure (78.6±0.8 mmHg [95% KI 77;80mmHg]) and heartrate (73.3±0.81 bpm [95% KI 72; 75]) were overall slightly increased.

Tabel 10. Explorative data analysis of age, systolic blood pressure (sys. bp), diastolic blood pressure (diast. bp) and heartrate.

		Age (years)	sys. Bp. (mmHg)	diast. Bp. (mmHg)	Heartrate (bpm)
mean		59±0,5	133,5±1,7	78,6±0,8	73,3±0,81
95% confidence interval	min.	58,3	130	77	72
	max.	60,4	137	80	75
median		58	135	80	72
standard deviation		5,8	18	9	9
minimum		50	80	60	52
maximum		72	190	120	96
range		22	110	60	44

Sys. Bp.: systolic blood pressure
Diast. Bp.: diastolic blood pressure

Tabel 11. Explorative data analysis of weight (kg), height (cm) and WHR of woman.

		weight (kg)	height (cm)	WHR
mean		78,17±1,93	167,44±0,64	0,80±0,01
95% confidence interval	min.	74,34	166,16	0,80
	max.	82,00	168,72	0,82
median		76,10	166,00	0,81
standard deviation		18,51	6,18	0,06
minimum		51,80	156,00	0,65
maximum		156,40	188,00	0,94
range		104,60	32,00	0,29

WHR: waist-to-hip ratio

Tabel 12. Explorative data analysis of weight (kg), height (cm) and WHR of man.

		weight (kg)	height (cm)	WHR
mean		95,66±3,34	179,71±1,22	0,96±0,01
95% confidence interval	min.	88,86	177,21	0,94
	max.	102,47	182,20	0,97
median		89,50	179,00	0,97
standard deviation		19,50	7,15	0,05
minimum		70,80	165,50	0,84
maximum		147,70	194,90	1,03
range		76,90	28,50	0,19

WHR: waist-to-hip ratio

4.1.1 Anthropometrics

As shown in table 13 and table 14, the mean body-mass-index (BMI) in women was 27,84 ± 0.64 kg/m² [95% KI 26,57-29,10 kg/m²] with a basal metabolic rate of 1353±15 kcal/d [95% KI 1324;1383 kcal/d]. The mean anthropometric results of men, presented in table 14, showed even more increased measurements for body-mass-index (BMI) 29,45 ± 0.82 kg/m² [95% KI 27,82-31,17 kg/m²]. This BMI puts the participants in the overweight range. Additionally, the body cell mass (BCM) of women, with 48,39% of the total body weight (23,10± 0.38 kg [95% KI 22,35;23,85 kg]), was below the recommendations. Body fat was increased in women, with 36,21% of total body weight (29,60

kg [95% KI 26,8;32,40kg]), as well as in men, with 26,44% of total body weight (26,06±1.83 kg [95% KI 22,34;29,78 kg]).

Tabel 13. Explorative data analysis of the body-mass-index (BMI), basal metabolic rate (BMR), body water, body cell mass (BCM) and bodyfat of woman.

		BMI (kg/m²)	BMR (kcal/d)	Body water (l)	BCM (kg)	BCM (%)	Bodyfat (kg)	Bodyfat (%)
mean		27,84±0,64	1353,92±15,02	35,60±0,47	23,10±0,38	48,39±0,64	29,60±1,41	36,21±0,83
95% confidence interval	min.	26,57	1324,07	34,66	22,35	47,13	26,80	34,57
	max.	29,10	1383,78	36,54	23,85	49,65	32,40	37,85
median		26,99	1330,00	35,00	22,45	47,55	27,90	37,20
standard deviation		6,10	144,17	4,53	3,63	6,10	13,51	7,92
minimum		18,57	1150,00	28,50	16,90	35,70	11,40	21,90
maximum		49,36	2200,00	50,20	37,80	77,12	94,60	60,48
range		30,79	1050,00	21,70	20,90	41,42	83,20	38,59

BMI: Body mass Index
BMR: Basal metabolic rate
BCM: Body cell mass

Tabel 14. Explorative data analysis of the body-mass-index (BMI), basal metabolic rate (BMR), body water, body cell mass (BCM) and bodyfat of man.

		BMI (kg/m²)	BMR (kcal/d)	Body water (l)	BCM (kg)	BCM (%)	Bodyfat (kg)	Bodyfat (%)
mean		29,45±0,82	1747,53±28,64	51,00±1,37	35,74±0,96	55,72±1,78	26,06±1,83	26,44±0,98
95% confidence interval	min.	27,82	1689,26	48,21	33,74	52,11	22,34	24,44
	max.	31,17	1805,80	53,79	37,69	59,34	29,78	28,44
median		28,64	1710,00	48,45	33,95	52,20	23,10	25,75
standard deviation		4,81	167,00	8,00	5,57	10,36	10,67	5,74
minimum		21,03	1540,00	40,20	28,00	41,70	11,60	15,40
maximum		41,35	2279,00	72,90	54,80	80,43	57,90	39,70
range		20,32	739,00	32,70	26,80	38,73	46,30	24,30

BMI: Body mass Index
BMR: Basal metabolic rate
BCM: Body cell mass

As presented in table 15 and table 16, similar results are shown when divided by age. BMI was too high in both categories. BCM (up to 65 years: 26,91±0,71kg [95% KI 25,50;28,33kg], from 65 years: 25,57±1,30kg [95% KI 22,92;28,22kg]) and Bodyfat (up to 65 years: 29,07±1,34kg [95% KI 26,41;31,73kg], from 65 years: 27,52±2,10kg [95% KI 23,22;31,81kg]) reached the estimated reference values for their age groups.

Tabel 15. Explorative data analysis of the body-mass-index (BMI), basal metabolic rate (BMR), body water, body cell mass (BCM) and bodyfat of women and men from 50years to 65years.

		BMI (kg/m²)	BMR (kcal/d)	Body water (l)	BCM (kg)	BCM (%)	Bodyfat (kg)	Bodyfat (%)
mean		28,34±0,60	1474,20±23,52	39,82±0,86	26,91±0,71	51,17±0,85	29,07±1,34	33,81±0,89
95% confidence interval	min.	27,15	1427,52	38,11	25,50	49,49	26,41	32,05
	max.	29,52	1520,89	41,52	28,33	52,85	31,73	35,58
median		27,39	1395,00	37,85	24,50	49,40	24,85	33,70
standard deviation		5,91	232,84		7,04	8,40	13,26	8,79
minimum		18,57	1150,00	28,50	16,90	35,70	11,40	15,40
maximum		49,36	2279,00	72,90	54,80	80,43	94,60	60,49
range		30,79	1129,00	44,40	37,90	44,73	83,20	45,09

BMI: Body mass Index
BMR: Basal metabolic rate
BCM: Body cell mass

Tabel 16. Explorative data analysis of the body-mass-index (BMI), basal metabolic rate (BMR), body water, body cell mass (BCM) and bodyfat of women and men over 65years.

		BMI (kg/m²)	BMR (kcal/d)	Body water (l)	BCM (kg)	BCM (%)	Bodyfat (kg)	Bodyfat (%)
mean		28,33	1425,50±40,95	40,05±1,88	25,57±1,30	47,73±1,15	27,52±2,10	32,79
95% confidence interval	min.	26,30	1341,75	36,21	22,92	45,37	23,22	29,78
	max.	30,37	1509,25	43,89	28,22	50,08	31,81	35,79
median		27,79	1350,00	36,40	22,95	47,10	26,40	31,35
standard deviation		5,44	224,28	10,27	7,10	6,32	11,50	8,04
minimum		20,52	1180,00	28,80	17,80	41,70	13,00	18,20
maximum		41,63	2100,00	72,10	46,90	73,97	58,80	49,00
range		21,11	920,00	43,30	29,10	32,27	45,80	30,80

BMI: Body mass Index
BMR: Basal metabolic rate
BCM: Body cell mass

4.1.2 Inflammation marker

4.1.2.1 Parameters of the immune system

We examined the blood parameters of immune cells including leukocytes (5.88± 0.13 G/l [95% KI 5.61;6.14]), thrombocytes (264.8±5.6 G/l [95% KI 253.8;275.7]), lymphocytes (1.95 ±0.06 G/l [95%KI 1.84; 2.07]) and neutrophil granulocytes (3.16± 0.11 G/l [95% KI 2.94; 3.37]). Also, C-reactive protein (3.08±0.36 mg/l [95%KI 2.38;3.78]) was tested and the results are summarized in table 17.

Tabel 17. Explorative data analysis of leucocytes, thrombocytes, C-reactive protein (CRP), neutrophil granulocytes and lymphocytes.

		Leucocytes (G/l)	Thrombocytes (G/l)	Neutrophil Granulocytes (G/l)	Lymphocytes (G/l)	CRP (mg/l)
mean		5.88±0,13	264.75±5.55	3.16±0.11	1.95±0.06	3.08±0.36
95% confidence interval	min.	5.61	253.76	2.94	1.84	2.38
	max.	6.14	275.74	3.37	2.07	3.78
median		5.80	249.00	3.04	1.85	1.65
standard deviation		1.48	61.32	1.18	0.63	3.90
minimum		3.10	129.00	0.00	0.78	0.00
maximum		11.80	485.00	6.85	4.33	24.20
range		8.70	356.00	6.85	3.56	24.20

CRP: C-reactive Protein

4.1.2.2 Inflammation Indices

We selected three inflammation indices, listed in table 18. Neutrophil-to-lymphocyte- ratio (NLR), platelet-to-lymphocyte- ratio (PLR) and systemic inflammation index (SII), which are calculated on basis of leucocytes, thrombocytes and neutrophil granulocytes. During this study, all three indices, NLR (1,75±0,07 [95%KI 1,61;1,89]), PLR (147±4,7 [95%KI 137,7;156,3]) and SII (468±22 [95%KI 424;512]), lay within the given parameters.

Tabel 18. Explorative data analysis of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune inflammation index (SII).

		Neutrophil-to-lymphocyte-ratio	Platelet-to-lymphocyte-ratio	Systemic inflammation Index
mean		1.75±0.07	146.96±4.69	468.02±22.05
95% confidence interval	min.	1.61	137.67	424.36
	max.	1.89	156.25	511.68
median		1.63	138.77	418.64
standard deviation		0.80	51.82	243.59
minimum		0.00	64.40	0.00
maximum		4.95	367.89	1257.99
range		4.95	303.49	1257.99

4.1.2.3 Cytokine concentrations

Four cytokines were examined, which are listed in table 19. On average, IL-6 (5.62±0.57pg/ml [95% KI 4.45;6.78]), IL- 10 (12.27±0.6pg/ml [95%KI 11.05;13.49]) and IL- 1β (1.77±0.07pg/ml [95%KI 1.63;1.92]) were in reference range, however, tumor- necrosis- factor- alpha (101.89±3.71pg/ml [94.3;109.47]) was twice as high as the reference value.

Tabel 19. Explorative data analysis of interleukin 6 (IL-6), interleukin 10 (IL-10), interleukin 1beta (IL-1β) and tumor necrosis factor alpha (TNF-α).

		Interleukin-6 (pg/ml)	Interleukin-10 (pg/ml)	Interleukin-1β (pg/ml)	Tumor-necrosis factor- α (pg/ml)
mean		5.62±0.57	12.27±0.6	1.77±0.07	101.89±3.71
95% confidence interval	min.	4.45	11.05	1.63	94.30
	max.	6.78	13.49	1.92	109.47
median		4.95	11.83	1.76	99.93
standard deviation		3.12	3.27	0.39	20.31
minimum		2.10	5.87	1.15	65.32
maximum		14.66	23.61	3.17	161.85
range		12.56	17.74	2.02	96.53

4.1.3 Food consumption and nutritional state

4.1.3.1 Food consumption

To examine the food- frequency- questionnaires, we identified eight food groups and calculated the food consumption in portions per day. The identified food groups were the same as used by the DGE (DGE 2019b) for a better comparison purpose, illustrated in figure 6. The fruit (1.8±0.1 servings per day [95%KI 1.5;2.1]) and vegetable (1±0.1 servings per day [95%KI 0.8;1.2]) consumption is to low, meat- (1.6±0.1 servings per day [95%KI 1.3; 1.8]) and highly processed food (3.2±0.1 servings

per day [95%KI 1;1.5]) consumption on the other hand were elevated. As demonstrated in the following diagram (figure 7) the main food groups consumed on average were cereal products, potatoes and rice (3.2±0.2 servings per day [95%KI 2.9;3.6]) ; and dairy/-products (2.9±0.2 servings per day [95%KI 2.5;3.3]).

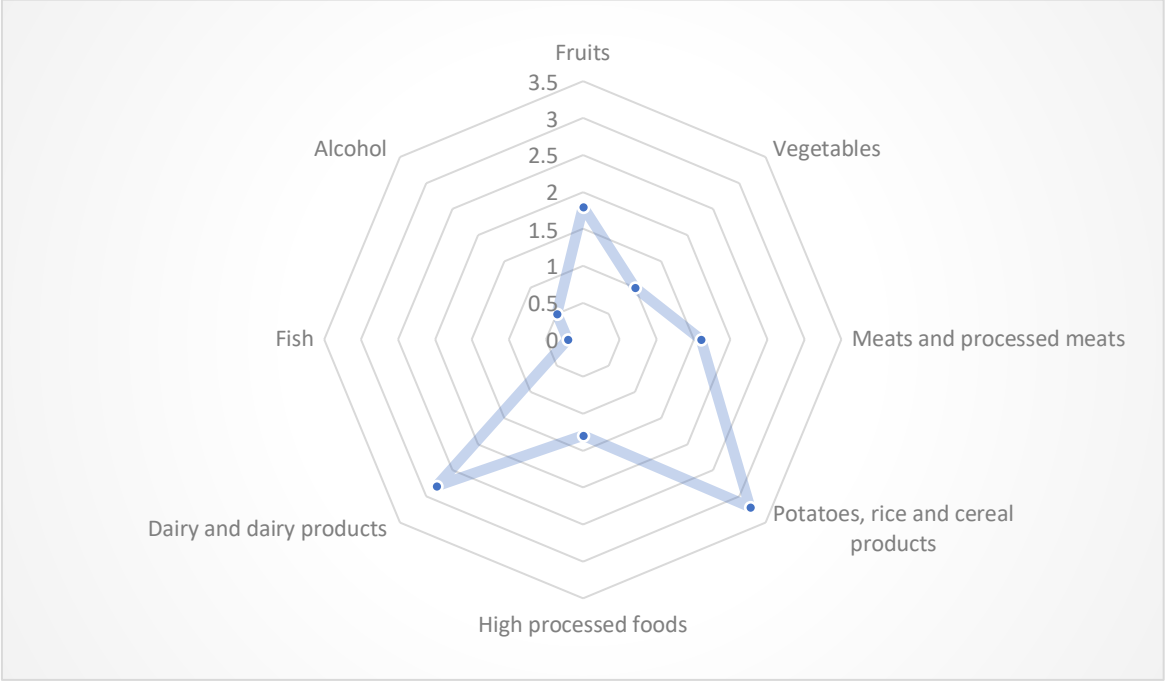

Figure 6. Mean dietary pattern of the study participants in servings per day for fruits, vegetables, meat/-products, cereal products, potatoes, rice, high processed foods, dairy-/products, fish and alcohol.

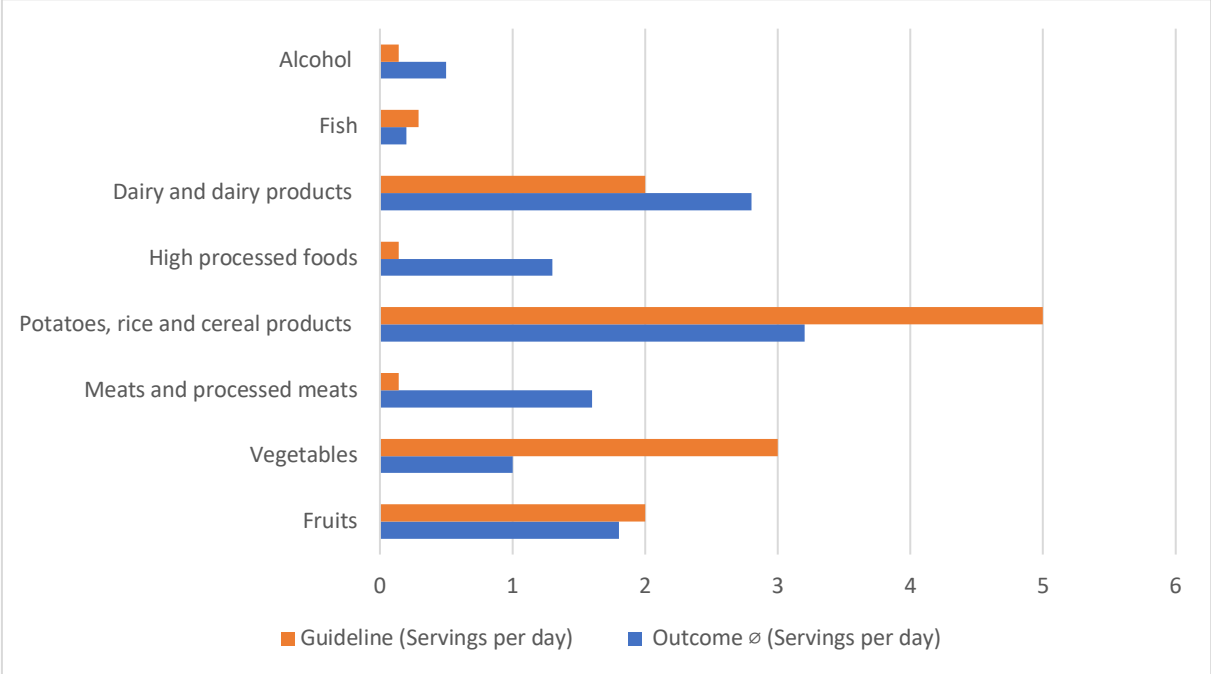

Figure 7. Overview of the servings per day of different food groups in comparison to the recommended servings per day.

4.1.3.2 Nutrient intake

We reviewed the three-day food diaries and focused on macronutrients, energy consumption and three vitamins important in aging and inflammatory processes, including vitamin B12, vitamin C and vitamin D. The following tables (table 20, table 21, table 22, table 23) display the nutrient- and energy consumption per day classified by women and men. It shows an insufficient intake of dietary fiber in both, women (20,79±0.75g/d [95%KI 19.29;22.28g/d]) and men (21,98±1,24g/d [95%KI 19.45;24,51g/d]). Energy consumption (women: 1867±43kcal/d [95%KI 1781;1952kcal/d], men: 1937±88kcal/d [95%KI 1759;2116kcal/d],), carbohydrate intake (women: 190±5,3g/d [95%KI 180,1;201,4g/d], men: 191,9±7,8g/d [95%KI 175,1,1;207,8g/d]), the supply of dietary fats (women: 77±2,8 g/d [95%KI 71,5;82,5 g/d], men: 80,3±5,7g/d [95%KI 68,7;81,8g/d]), and the intake of vitamin D (women: 3,77±0,54µg/d [95%KI 2.69;4.87µg/d], men: 2,53±0,36µg/d [95%KI 1,80;3,25g/d]) and vitamin B12 (women: 5,15±0.4µg/d [95%KI 4.35;5.96µg/d], men: 4,68±0.37µg/d [95%KI 3,91;5.44µg/d]) were according to the dietary guidelines. Furthermore, vitamin C- (women: 132,51±7,64mg/d [95%KI 117,34;147,68mg/d], men: 119,4±0,5mg/d [95%KI 99,55;129,25mg/d]) and dietary protein (women: 74,29±2,09g/d [95%KI 70,14;78,44g/d], men: 80,02±4,02 g/d [95%KI 71,83;88,21g/d]) consumption were elevated.

Tabel 20. Explorative data analysis of nutrient intake of women.

		Energy (kj/d)	Energy (kcal/d)	Dietary carbohydrates (g/d)	Dietary protein (g/d)	Dietary fat (g/d)	Dietary fiber (g/d)	Dietary fiber (g/1000kcal)
mean		8113,34±366,83	1937,45±87,63	191,89±7,81	80,02±4,02	80,28±5,67	21,98±1,24	11,38
95% confidence interval	min.	7367,01	1759,15	175,10	71,83	68,74	19,45	
	max.	8859,67	2115,74	207,78	88,21	91,81	24,51	
median		7885,62	1883,46	183,58	75,61	77,88	20,98	
standard deviation		2138,98	510,99	45,55	23,47	33,05	7,25	
minimum		4574,49	1092,23	111,82	46,42	36,26	7,07	
maximum		13695,00	3272,52	302,30	145,87	189,48	39,93	
range		9120,51	2180,20	190,48	99,45	153,22	32,86	

Tabel 21. Explorative data analysis of nutrient intake of men.

		Energy (kj/d)	Energy (kcal/d)	Dietary carbohydrates (g/d)	Dietary protein (g/d)	Dietary fat (g/d)	Dietary fiber (g/d)	Dietary fiber (g/1000kcal)
mean		7815,86±181,12	1866,56±43,24	190,74±5,34	74,29±2,09	77,02±2,78	20,79±0,75	11,12
95% confidence interval	min.	7456,09	1780,67	180,13	70,14	71,50	19,29	
	max.	8175,62	1952,46	201,35	78,44	82,53	22,28	
median		7618,80	1819,88	177,42	73,60	72,37	20,55	
standard deviation		1737,20	414,77	51,25	20,05	26,65	7,22	
minimum		4418,31	1054,72	56,62	29,80	28,84	7,75	
maximum		12699,11	3032,54	320,65	126,15	160,71	41,25	
range		8280,80	1977,82	264,03	96,35	131,87	33,50	

Tabel 22. Explorative data analysis of vitamin B12, vitamin C and vitamin D consumption of women.

		Vitamin B12 (µg/d)	Vitamin C (mg/d)	Vitamin D (µg/d)
mean		5,15±0,40	132,51±7,64	3,77±0,54
95% confidence interval	min.	4,35	117,34	2,69
	max.	5,96	147,68	4,87
median		4,25	118,34	2,29
standard deviation		3,89	73,25	5,26
minimum		1,03	14,81	0,38
maximum		29,97	429,72	27,88
range		28,94	414,91	27,50

Tabel 23. Explorative data analysis of vitamin B12, vitamin C and vitamin D consumption of men.

		Vitamin B12 (µg/d)	Vitamin C (mg/d)	Vitamin D (µg/d)
mean		4,68±0,37	119,40±0,50	2,53±0,36
95% confidence interval	min.	3,91	99,55	1,80
	max.	5,44	139,25	3,25
median		4,08	123,22	1,85
standard deviation		2,19	56,89	0,47
minimum		1,44	17,36	9,05
maximum		10,76	222,10	8,58
range		9,32	204,74	1,90

Furthermore, figure 8 and figure 9 show the energy-% distribution divided by consumed macronutrients. In both, women and men, the distribution was not according to the recommendations. Protein- (women: 15%, men: 16%), fat- (women:33%, men: 36%) and alcohol (women:14%, men: 11%) consumption was too high, while the consumption of carbohydrates (women: 38%, men: 37%) was too low.

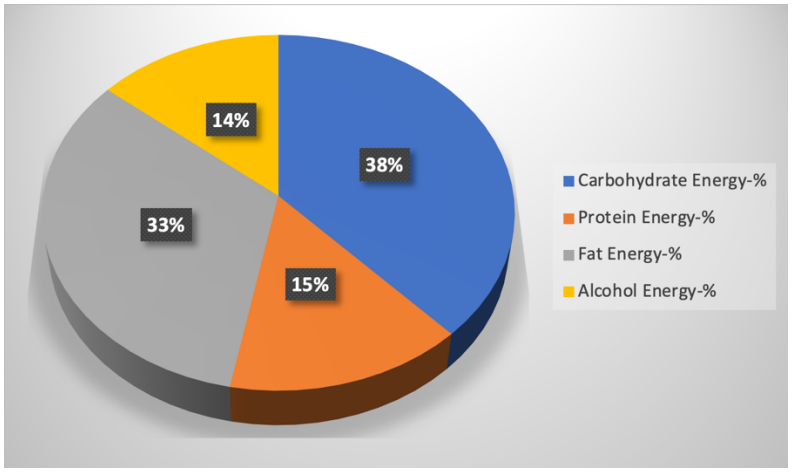

Figure 8. Proportion of macronutrients in total energy intake (E%) in women.

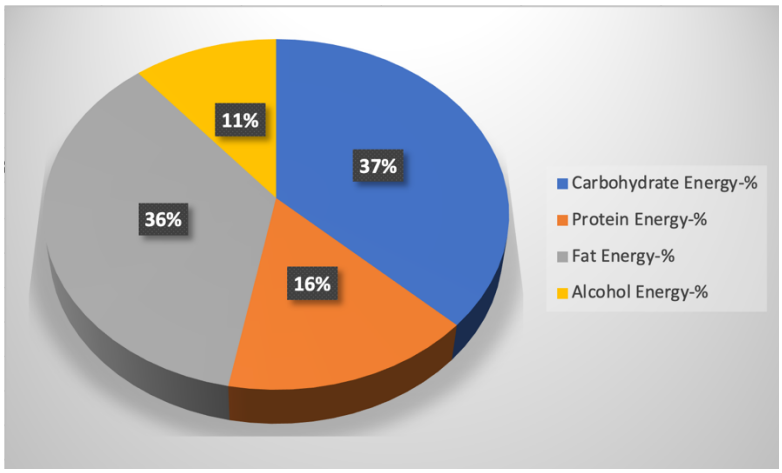

Figure 9. Proportion of macronutrients in total energy intake (E%) in men.

4.1.3.3 Vitamin B12-, folic acid- and vitamin D- levels

Additionally, vitamin B12- (387.8± 15.1ng/l [95%KI 357.9;417.7]), vitamin D- (47.1±2.4nmol/l [95%KI 42.4;51.9]) and folic acid levels (791.6±16µmol/l [95%KI 760;823] from blood tests, were evaluated and demonstrated in Table 24.

Tabel 24. Explorative data analysis of blood parameters of vitamin B12, folic acid and vitamin D.

		Vitamin B12 (ng/l)	Folic acid (µmol/l)	Vitamin D (nmol/l)
mean		387.81±15.1	791.6±15.94	47.12±2.4
95% confidence interval	min.	357.9077	760.0	42.42
	max.	417.7153	823.10	51.93
median		362.0	771.50	42.63
standard deviation		166.8373	176.10	26.52
minimum		134.0	502.0	10.75
maximum		1,533.0	1,520.0	195.50
range		1,399.0	1,018.0	184.75

4.1.4 Physical activity level

To determine the overall physical activity level, movement of the participants was subdivided in basic physical activity (3.37±0.35 [95% KI 2.67;4.07]), leisure time physical activity (2.01±0.24 [95% KI 1.53;2.48]) and vigorous intensity aerobic physical activity (0.36±0.07 [95%KI 0.21;0.50]) in hours per week shown in table 25.

Tabel 25. Explorative data analysis of physical activity accomplished in the period of one week.

		Basic physical activity (h/week)	leisure time physical activity (h/week)	vigorous intensity aerobic physical activity (h/week)
mean		3.37±0.35	2.01±0.24	0.36±0.07
95% confidence interval	min.	2.67	1.53	0.21
	max.	4.07	2.48	0.5
median		2.25	1	0
standard deviation		3.9	2.68	0.81
minimum		0	0	0
maximum		29	14	5
range		29	14	5

4.2 Correlation analysis

The selected Inflammation markers, including CRP, inflammation indices and cytokines were correlated with various health-, nutrition- and physical activity measurements including arthrometric measurements, blood parameters and dietary parameters, to examine their impact on inflammation.

4.2.1 Correlations of CRP with health and nutritional parameters

4.2.1.1 Correlations of CRP with anthropometric measurements

Blood concentration of CRP correlated strongly with body weight (p=0.000, r=0.534), waist-to-hip-ratio (p=0.006, r=0.239), systolic blood pressure (p=0.008, r=0.233), body-mass-index (p=0.000, r=0.605) and body fat (p=0.000, r0.557). Furthermore, but weaker, CRP correlated with diastolic blood pressure (p=0.020, r=0.020). These findings, demonstrated in table 26, show an overall frequent correlation of CRP with various anthropometric measurements. Higher CRP concentrations led to a negative shift of anthropometric measurements mentioned above.

Tabel 26. Correlation of C-reactive protein (CRP) and various anthropometric measurements like height, body weight, blood pressure and BMI.

		CRP [mg/l]
age (years)	correlation coefficient	0.012
	Sig. (2-tailed)	0.896
weight (kg)	correlation coefficient	0.534**
	Sig. (2-tailed)	**0,000**
height (cm)	correlation coefficient	0.025
	Sig. (2-tailed)	0.776
waist-to-hip-ratio	correlation coefficient	0.239**
	Sig. (2-tailed)	**0.006**
blood pressure systolic (mmHg)	correlation coefficient	0.233**
	Sig. (2-tailed)	**0.008**
blood pressure diastolic (mmHg)	correlation coefficient	0.203*
	Sig. (2-tailed)	**0.020**
heartrate (bpm)	correlation coefficient	0.044
	Sig. (2-tailed)	0.617
body mass Index	correlation coefficient	0.605**
	Sig. (2-tailed)	**0,000**
fat-free mass (kg)	correlation coefficient	0.319**
	Sig. (2-tailed)	**0,000**
bodyfat (kg)	correlation coefficient	0.557**
	Sig. (2-tailed)	**0,000**

Significant correlation (*) p≦0,05, highly significant (**) p≦0,01.
CRP= C-reactive protein

4.2.1.2 *Correlations of CRP with food consumption and physical activity state*

While assessing the dietary data, only one food group showed correlation with CRP (dairy/-products, p=0.035)), shown in Table 27. The negative correlation coefficient implies an inverse correlation between CRP and dairy/-products (r= -0.185). No further relation between CRP and food groups, nutrients such as vitamin B12, nutritional fatty acids and energy consumption per day, were indicated. CRP showed no correlations with nutrient intake and the physical activity state.

Tabel 27. Correlation of C-reactive protein (CRP) and food consumption in servings per day.

		CRP [mg/l]
Fruit consumption	correlation coefficient	-0.139
	Sig. (2-tailed)	0.114
Vegetable consumption	correlation coefficient	-0.03
	Sig. (2-tailed)	0.732
Meat/-products consumption	correlation coefficient	0.116
	Sig. (2-tailed)	0.187
Cereal products, potatoes, rice	correlation coefficient	0.048
	Sig. (2-tailed)	0.587
High processed food consumption	correlation coefficient	0.107
	Sig. (2-tailed)	0.227
Dairy/-products consumption	correlation coefficient	-0.185*
	Sig. (2-tailed)	**0.035**
Fish consumption	correlation coefficient	-0.084
	Sig. (2-tailed)	0.34
Alcohol consumption	correlation coefficient	-0.001
	Sig. (2-tailed)	0.987

Significant correlation (*) p≦0,05
CRP= C-reactive protein

4.2.1.3 *Correlations of CRP with inflammation indices*

The evaluation of three selected inflammation indices showed two correlations with CRP, listed in table 28. NLR correlated strongly with CRP (p=0.002, r=0.278) as well as with SII (p=0.004, r=0.252). PLR on the other hand showed no significant correlation.

Tabel 28. Correlation of C-reactive protein (CRP) and inflammation indices including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune inflammation index (SII)

		CRP [mg/l]
Neutrophil-to-lymphocyte ratio (NLR)	correlation coefficient	0.278**
	Sig. (2-tailed)	**0.002**
Platelet-to-lymphocyte ratio (PLR)	correlation coefficient	0.15
	Sig. (2-tailed)	0.093
Systemic Inflammation Index (SII)	correlation coefficient	0.252**
	Sig. (2-tailed)	**0.004**

Highly significant correlation (**) p≦0,01

4.2.2 Correlations of inflammation indices with health- and nutritional measurements

4.2.2.1 Correlations of Inflammation indices with anthropometric parameters

Amongst the correlation of inflammation indices (NLR, PLR and SSI) and anthropometric measurements, presented in table 29, only NLR showed a significant correlation with systolic blood pressure (p=0.002, r= 0.270). PLR correlated with BMI (p=0.040, r=0.182) and fat-free mass (p=0.044, r=0.181); and SII correlated with systolic blood pressure (p= 0.015, r= 0.215) and heartrate (p=0.024, r= 0.200).

Tabel 29. Correlation of inflammation indices and anthropometric measurements.

		Neutrophil-to-lymphocyte ratio (NLR)	Platelet-to-lymphocyte ratio (PLR)	Systemic Immune Inflammation Index (SII)
Age (years)	correlation coefficient	0.157	0.131	0.11
	Sig. (2-tailed)	0.077	0.14	0.215
weight (kg)	correlation coefficient	0.167	-0.003	0.09
	Sig. (2-tailed)	0.061	0.977	0.312
height (cm)	correlation coefficient	0.066	-0.035	-0.052
	Sig. (2-tailed)	0.462	0.696	0.564
WHR	correlation coefficient	0.08	-0.126	0.019
	Sig. (2-tailed)	0.373	0.157	0.834
Blood pressure systolic (mmHg)	correlation coefficient	0.270**	0.09	0.215*
	Sig. (2-tailed)	**0.002**	0.315	**0.015**
Blood pressure diastolic (mmHg)	correlation coefficient	0.069	-0.082	-0.002
	Sig. (2-tailed)	0.441	0.361	0.978
Heartrate (bpm)	correlation coefficient	0.114	0.117	0.200*
	Sig. (2-tailed)	0.202	0.19	**0.024**
BMI	correlation coefficient	0.017	0.182*	0.022
	Sig. (2-tailed)	0.845	**0.04**	0.805
Fat-free mass (kg)	correlation coefficient	-0.041	0.181*	0.005
	Sig. (2-tailed)	0.652	**0.044**	0.954
BCM (%)	correlation coefficient	0.149	-0.012	-0.081
	Sig. (2-tailed)	0.096	0.897	0.37
Bodyfat (kg)	correlation coefficient	-0.003	0.155	0.057
	Sig. (2-tailed)	0.978	0.085	0.525
Bodyfat (%)	correlation coefficient	0.005	0.095	0.059
	Sig. (2-tailed)	0.96	0.291	0.512

significant correlation (*) p≦0.05, highly significant correlation (**) p≦0,01
WHR= waist-to-hip ratio
BMI= body mass index
BCM= body cell mass

4.2.2.2 Correlations of inflammation indices with vitamin B12, folic acid and vitamin D levels

Each inflammation index correlated with a different blood vitamin level, demonstrated in table 30. NLR showed an inverse correlation with folic acid in erythrocytes (p= 0.012, r= -0.223), while SII showed a strong inverse correlation with folic acid in erythrocytes (p=0.007, r= -0.238). PLR on the other hand correlated with vitamin D levels in blood samples (p=0.029, r=0.194).

Tabel 30. Correlation of Inflammation indices and blood vitamin levels.

		Neutrophil-to-lymphocyte ratio (NLR)	Platelet-to-lymphocyte ratio (PLR)	Systemic Immune Inflammation Index (SII)
Vitamin B12 [ng/l]	correlation coefficient	-0.034	0.013	0.018
	Sig. (2-tailed)	0.709	0.889	0.839
Folic acid [µmol/l]	correlation coefficient	-0.223*	-0.096	-0.238**
	Sig. (2-tailed)	**0.012**	0.285	**0.007**
Vitamin D[nmol/l]	correlation coefficient	0.062	0.194*	0.054
	Sig. (2-tailed)	0.486	**0.029**	0.546

Significant correlation (*) p≦0.05, highly significant correlation (**) p≦0,01

The evaluation of the food groups showed no correlation with inflammation indices except for meat consumption which correlated with neutrophil-to-lymphocyte ratio (NLR) (p= 0.030, r =0.191). (Appendix 10.1) Furthermore, there is no relation between inflammation indices and nutrient intake, energy intake or the physical activity state.

4.2.3 Correlations of cytokines with health- and nutritional measurements

4.2.3.1 Correlations of cytokines

There is a strong correlation between TNF-α levels and the three other cytokines, such as IL-6 (p=0.003, r =0.523), IL-10 (p=0.000, r=0.712)) and IL-1β (p=0.000, r=0.532), demonstrated in table 31. Furthermore, IL-1β correlated strongly with IL-10 (p=0.000, r=0.593). IL-6 and IL-10 (p=0.049, r =0.362) also indicated a significant correlation, but less powerful.

Tabel 31. Correlation of cytokines levels.

		IL6 (pg/ml)	IL10 (pg/ml)	Il1-β (pg/ml)	TNF-α (pg/ml)
IL6 (pg/ml)	correlation coefficient	-	-	-	-
	Sig. (2-tailed)	-	-	-	-
IL10 (pg/ml)	correlation coefficient	0.362*	-	-	-
	Sig. (2-tailed)	**0.049**	-	-	-
Il1-β (pg/ml)	correlation coefficient	0.293	0.593**	-	-
	Sig. (2-tailed)	0.116	**0.000**	-	-
TNF-α (pg/ml)	correlation coefficient	0.523**	0.712**	0.532**	-
	Sig. (2-tailed)	**0.003**	**0.000**	**0.000**	-

Significant correlation (*) p≦0.05, highly significant correlation (**) p≦0,01
IL= Interleukin
TNF= Tumor necrosis factor

4.2.3.2 Correlations of Cytokines with anthropometric measurements

While investigating the correlation between cytokine levels and anthropometric measurements, shown in table 32, interleukin-6 correlated with several parameters, such as weight (p=0.023, r=0.415), waist-to-hip-ratio (p=0.019, r=0.427), body water (p=0.022, r=0.417) and BCM (%) (p=0.029, r= 0.400). Further, IL-6 correlated invers with gender (p=0.047, r= - 0.366). Interleukin-10 correlated invers with height (p=0.042, r= - 0.331) and interleukin-1β levels showed significant correlation with heartrate (p=0.018, r= 0.377). TNF-α levels showed no significant correlations at all.

Tabel 32. Correlation of cytokines and anthropometric measurements.

		IL6 (pg/ml)	IL10 (pg/ml)	Il1-β (pg/ml)	TNF-α (pg/ml)
Gender	correlation coefficient	-0.366*	0.28	0.181	0.067
	Sig. (2-tailed)	**0.047**	0.089	0.27	0.687
weight (kg)	correlation coefficient	0.415*	-0.075	-0.021	0.211
	Sig. (2-tailed)	**0.023**	0.656	0.897	0.197
height (cm)	correlation coefficient	0.23	-0.331*	-0.213	-0.075
	Sig. (2-tailed)	0.221	**0.042**	0.192	0.649
WHR	correlation coefficient	0.427*	-0.197	-0.182	-0.017
	Sig. (2-tailed)	**0.019**	0.236	0.266	0.919
Blood pressure systolic (mmHg)	correlation coefficient	0.067	0.046	0.175	0.045
	Sig. (2-tailed)	0.726	0.784	0.287	0.785
Blood pressure diastolic (mmHg)	correlation coefficient	0.088	-0.072	0.059	0.07
	Sig. (2-tailed)	0.646	0.668	0.721	0.671
Heartrate (bpm)	correlation coefficient	0.093	0.296	0.377*	0.216
	Sig. (2-tailed)	0.624	0.071	**0.018**	0.188
BMI	correlation coefficient	0.322	0.114	0.091	0.27
	Sig. (2-tailed)	0.082	0.494	0.583	0.096
Body water (l)	correlation coefficient	0.417*	-0.238	-0.103	0.043
	Sig. (2-tailed)	**0.022**	0.15	0.533	0.794
BCM (%)	correlation coefficient	0.400*	-0.25	-0.075	-0.01
	Sig. (2-tailed)	**0.029**	0.13	0.65	0.954
BCM (%)	correlation coefficient	-0.028	-0.191	-0.063	-0.111
	Sig. (2-tailed)	0.882	0.25	0.705	0.503
Bodyfat (kg)	correlation coefficient	0.107	0.152	0.134	0.253
	Sig. (2-tailed)	0.573	0.362	0.418	0.119
Bodyfat (%)	correlation coefficient	-0.16	0.229	0.149	0.198
	Sig. (2-tailed)	0.398	0.168	0.364	0.228

Significant correlation (*) p≦0.05
IL: Interleukin
TNF: Tumor necrosis factor
WHR: Waist-to-hip ratio
BMI: Body mass Index
BCM: Body cell mass

4.2.3.3 Correlations of cytokine levels with immune cell concentration

Investigating the correlation between cytokine levels and blood parameters revealed one significant result, which was between IL-6 and C-reactive protein levels (p=0.034, r=0.389), shown in table 33.

Tabel 33. Correlation of cytokines and blood parameters.

		IL6 (pg/ml)	IL10 (pg/ml)	Il1-β (pg/ml)	TNF-α (pg/ml)
Leucocytes (G/l)	correlation coefficient	0.172	0.186	-0.144	0.062
	Sig. (2-tailed)	0.364	0.263	0.383	0.707
Thrombocytes (G/l)	correlation coefficient	-0.214	-0.093	-0.176	-0.107
	Sig. (2-tailed)	0.257	0.578	0.283	0.516
Neutrophil granulocytes [G/l]	correlation coefficient	0.314	0.109	-0.141	-0.028
	Sig. (2-tailed)	0.091	0.515	0.392	0.865
Lymphocytes [G/l]	correlation coefficient	-0.133	0.003	0.056	0.041
	Sig. (2-tailed)	0.483	0.986	0.737	0.806
CRP (mg/l)	correlation coefficient	0.389*	0.19	0.007	0.087
	Sig. (2-tailed)	**0.034**	0.252	0.965	0.598

Significant correlation (*) p≦0.05
IL: Interleukin
CRP: C-reactive Protein

4.2.3.4 Correlations of cytokine levels with inflammation indices

One of three examined inflammation indices showed a significant correlation, when compared with cytokine levels. More precisely, NLR with IL-6 levels (p=0.028, r=0.407), demonstrated in table 34.

Tabel 34. Correlation of cytokines and inflammation indices.

		IL6 (pg/ml)	IL10 (pg/ml)	Il1-β (pg/ml)	TNF-α (pg/ml)
Neutrophil-to-lymphocyte ratio (NLR)	correlation coefficient	0.407*	0.071	-0.096	-0.051
	Sig. (2-tailed)	**0.028**	0.677	0.568	0.762
Platelet-to-lymphocyte ratio (PLR)	correlation coefficient	0.136	0.021	-0.043	0.004
	Sig. (2-tailed)	0.481	0.901	0.797	0.979
Systemic Immune Inflammation Index (SII)	correlation coefficient	0.272	0.05	-0.122	-0.073
	Sig. (2-tailed)	0.154	0.768	0.467	0.665

Significant correlation (*) p≦0.05
IL: Interleukin

4.2.3.5 Correlations of cytokine levels with vitamin B12, folic acid and vitamin D levels

In table 35, the possible correlations between cytokine levels and blood concentrations of vitamin B12, folic acid and vitamin D were examined. One vitamin, vitamin B12, showed a significant correlation with one of the cytokines, TNF-α (p=0.022, r=0.366).

Tabel 35. Correlation of cytokines and vitamin levels in blood samples.

		IL6 (pg/ml)	IL10 (pg/ml)	Il1-β (pg/ml)	TNF-α (pg/ml)
Vitamin B12 [ng/l]	correlation coefficient	0.107	0.317	0.204	0.366*
	Sig. (2-tailed)	0.574	0.053	0.214	**0.022**
Folic acid [µmol/l]	correlation coefficient	-0.076	0.138	0.112	0.19
	Sig. (2-tailed)	0.691	0.408	0.499	0.247
Vitamin D[nmol/l]	correlation coefficient	0.095	0.021	0.234	-0.031
	Sig. (2-tailed)	0.618	0.898	0.152	0.853

Significant correlation (*) p≦0.05
IL: Interleukin

4.3 Prevalence of inflammation

In the following, we evaluated the distribution of CRP and the inflammation marker in various groups like age, gender, food intake, physical activity and BMI. Classification criteria for each group is described in "Material and Methods" (3.4 "Data analysis").

4.3.1 Prevalence of inflammation measured by CRP

We have divided the age category in two groups - people under 65 years old and over 65 years old. While comparing with the occurrence of CRP there is no significant difference between both groups.

Next, CRP distribution between men and women was evaluated showing no significant difference between gender. Further evaluated groups were, physical activity status, fruit consumption, vegetable consumption, meat consumption, cereal product consumption, energy consumption, milk consumption and fish consumption. All of them, showed no significant differences in CRP- concentrations.

However, increased CRP prevalence in connection with BMI was investigated and revealed significant results (Chi^2= 4.521, p=0.033). 86.4% of the participants with increased CRP value were also overweight, as illustrated in figure 10.

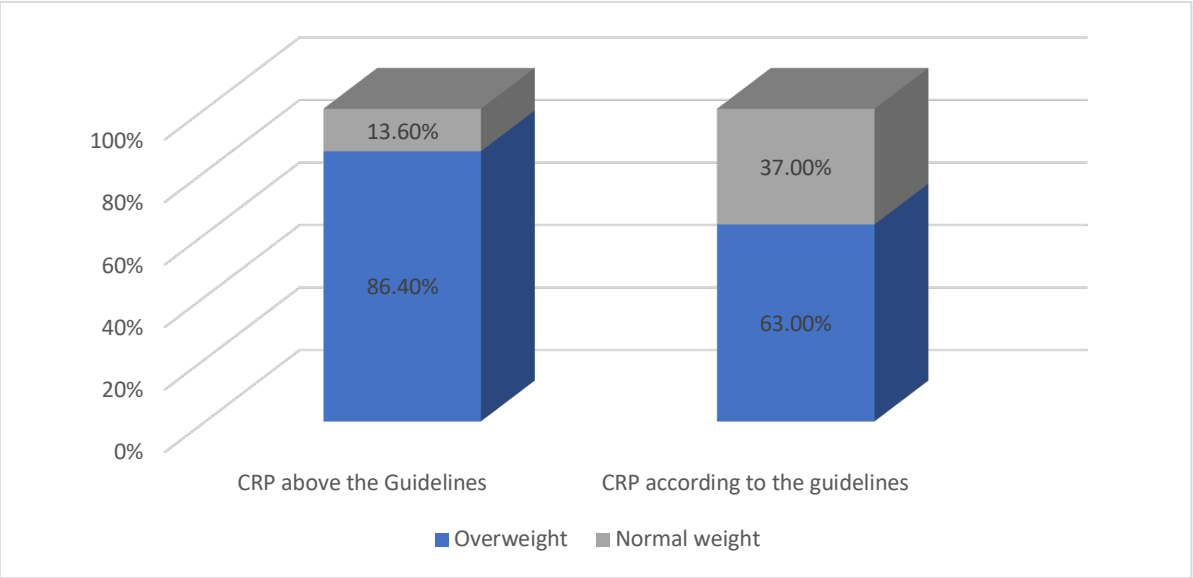

Figure 10. Prevalence of overweight in proportion to CRP

CRP: C-reactive protein

While investigating the CRP occurrence in participants with in-/adequate PLR levels it showed, that higher CRP levels were found in patients with inadequate PLR levels (60%,) and healthy CRP levels in participants with adequate PLR levels (63.6%) (Chi^2= 3.889, p=0.049), as described in figure 11.

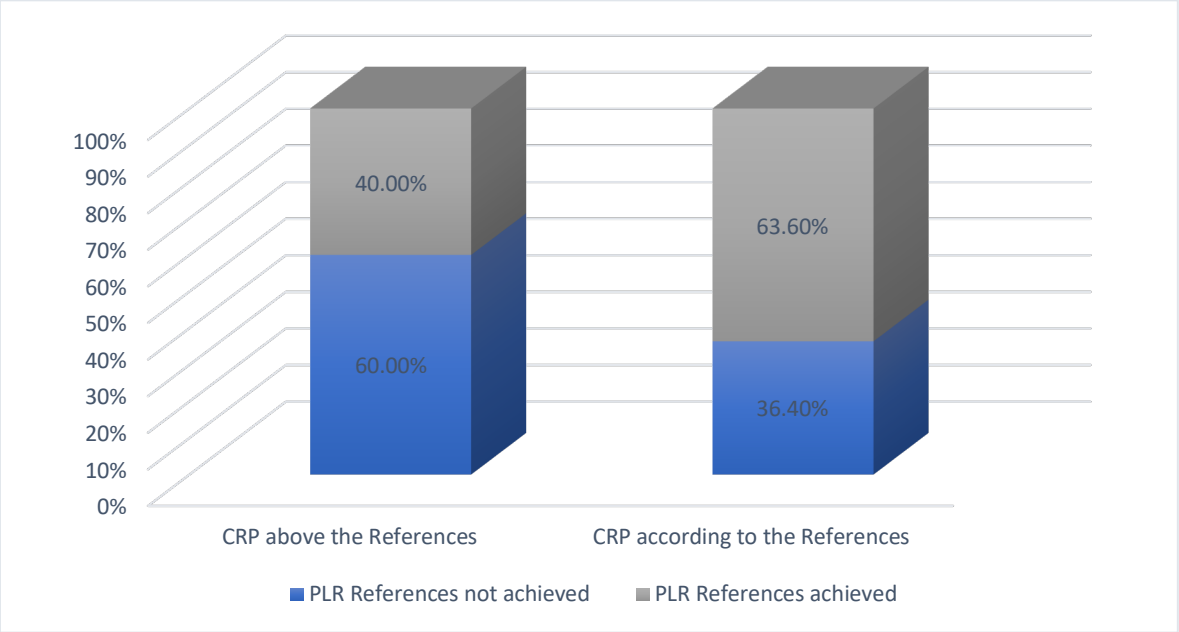

Figure 11. Prevalence of platelet-lymphocyte-ratio in proportion to CRP

CRP: C-reactive protein

PLR: platelet-to- lymphocyte ratio

4.3.2 Prevalence of Inflammation measured by inflammation index scores

The same groups as tested with CRP, also were used to evaluate the prevalence of inflammation by inflammation indices. Of all tested groups, only two results where significant and are presented in the following.

Figure 12 illustrates that 93.5% of the participants that did not achieved recommendations for cereal (-product), rice and potato intake, nonetheless achieved an NLR score within recommended reference range (Chi²= 5.759, p=0.016).

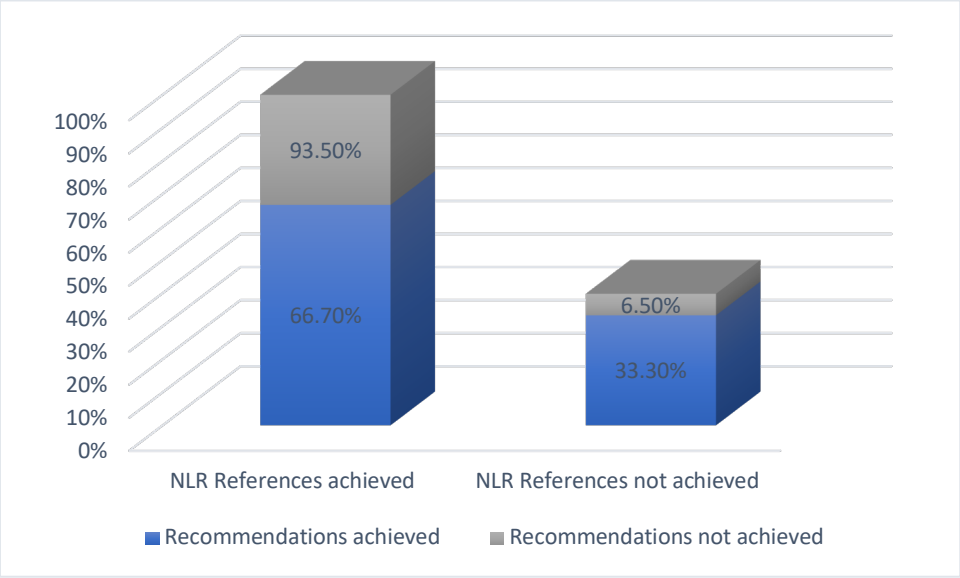

Figure 12. Prevalence of neutrophil- to- lymphocyte- ratio (NLR) and achievement of the recommended intake of cereal (-products), rice and potato.

NLR: Neutrophil-to-lymphocyte ratio

SII showed similar results. As shown in figure 13, 92.7% of the participants who did not achieve the recommendations for cereal (-product)-, potato- and rice consumption, still archived the recommended SII scores (Chi²= 4.964, p=0.026).

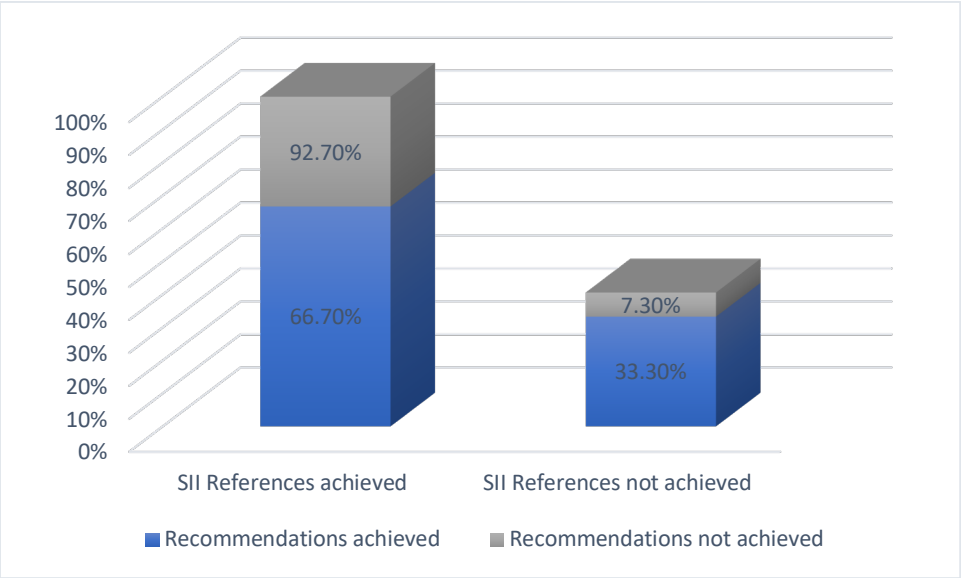

Figure 13. Prevalence of systemic-inflammation index (SII) and achievement of the recommended intake of cereal (-products), rice and potato.

SII: Systemic inflammation marker

4.4 Effects of age, BMI and gender on inflammatory markers

Three possible factors for increased inflammation, including age, BMI and gender, were evaluated by logistic regression. To measure inflammation, CRP concentrations, inflammation index scores and cytokine concentrations from blood samples were chosen as inflammatory markers.

4.4.1 Effects of age, BMI and gender on CRP concentrations

Age and gender showed no significant influence on inflammation markers including CRP- concentration, NLR, PLR and SII. Only weight, in particular overweight showed a significant increase, but only in CRP- concentrations (Shown in table 36).

Tabel 36. Logistic regression evaluating BMI, grouped in overweight and underweight category, and inflammatory markers including CRP [mg/l], neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and systemic immune inflammation index (SII).

	Regression coefficient B	Standard error	Wald	df	Sig.	Exp(B)
CRP [mg/l]	-0.739	0.204	13,074	1	**0.000***	0.477
Neutrophil-to-lymphocyte ratio (NLR)	0.199	0.619	0.103	1	0.748	1,220
Platelet-to-lymphocyte ratio (PLR)	0.011	0.007	2,433	1	0.119	1,011
Systemic Immune Inflammation Index (SII)	-0.004	0.003	1,816	1	0.178	0.996
constant	0.417	0.801	0.271	1	0.602	1,518

Significant correlation (*) p≦0.05

CRP: C-reactive protein

4.4.2 Effects of age, BMI and gender on cytokine concentrations

While assessing the influence of gender, BMI and age on IL-6, -10, -1β and TNF-α, demonstrated in table 37, only gender showed significant results by influencing IL-10 status (p=0.023, r^2=0.956) and IL-6 status inversely (p=0.046, r^2=-0.724). BMI and age did not show any significant outcomes.

Tabel 37. Logistic regression evaluating gender, grouped in female and male, and interleukin levels.

	Regression coefficient B	Standard error	Wald	df	Sig.	Exp(B)
Interleukin-6 (pg/ml)	-0.724	0.363	3,985	1	**0.046***	0.485
Interleukin-10 (pg/ml)	0.956	0.42	5,186	1	**0.023***	2,602
Interleukin-1β (pg/ml)	0.711	1,281	0.308	1	0.579	2,036
Tumor-necrosis-factor- α (pg/ml)	-0.065	0.05	1,730	1	0.188	0.937
constant	-1,971	3,293	0.358	1	0.55	0.139

Significant correlation (*) p≦0.05

5 Discussion

Inflammaging, a condition that occurs in aging bodies, is a problem recently described in several studies (Henrique 2019.; Minciullo et al. 2016; Prattichizzo et al. 2016; Franceschi et al. 2018). Although, its effects have been described already, the term *inflammaging* was implemented in 2000 by Franceschi and his colleagues (C. Franceschi et al. 2000). It is described as a negative shift in inflammatory markers such as cytokines and C-reactive protein (Ferrucci and Fabbri 2018). Literature explains these changes on the basis of alterations in the human body occurring during aging. Those alterations include differences in the body composition like increased body fat tissue and, at the same time, decreased skeletal muscle mass. Since the population is getting older, and the life expectancy at birth is increased during the last centuries, *inflammaging*, and more so its negative consequences like heart disease (Strandberg and Tilvis 2000), diabetes (Barzilay et al. 2001), cancer (Il'yasova 2005), and Alzheimer's disease (Akiyama 2000), are becoming an crucial public health problem now and in the future (National Research Council (U.S.) 2001).

The aim of this study was to investigate the inflammatory state in elderly people by examining their current status of various anthropometric measurements, nutritional supply, dietary patterns and physical activity levels as well as their possible influence on selected inflammatory markers, such as CRP levels and cytokine levels of IL-6,-10-,-1β and TNF-α and with inflammation indices like NLR, PLR and SII.

First, it is important to define the current overall state of health of the collective and which one of the measured variables are linked to inflammation and may be precursor during inflammatory processes. Based on the mean BMI of 28kg/m^2 in women and 29g/m^2 in men, the study participants can be classified as overweight. In line with that, analysis of the body composition showed an elevated body fat percentage and an increased waist-to-hip ratio in both, women and men. (Elmadfa 2009).
It was already shown, that increased body fat with lower lean body mass are also linked to raised blood pressure (Staessen, Fagard, and Amery 1988). A slightly elevated blood pressure was also found in our study collective. It is interesting to note, that the inflammation indices were according to the reference values and showed no presence of inflammation.
Further, all evaluated cytokine levels were according to the reference values, except TNF-α levels which were increased (101.89±3.71pg/ml). The mean was twice as high as the recommended reference value of <51.85pg/ml. Even the person with the lowest TNF-α value showed increased results (65.32pg/ml). Chronically increased TNF-α levels have been shown to be linked to inflammatory

diseases such as rheumatoid arthritis, psoriasis and inflammatory bowel disease (Esposito and Cuzzocrea 2009). These disorders are known to be frequent in elderly people and therefore are part of the inflammaging process (Zuo et al. 2019; Grimm and Friedman 1990).

5.1 Influence of gender and anthropometric measurements on inflammation

Obesity is linked to inflammation due to an overexpression of pro-inflammatory cytokines (Hotamisligil 2006). This overexpression is a result of the progressive adipocyte enlargement due to excessive nutrient intake. Because of hyperplasia and hypertrophy of adipocytes, the blood supply to fat tissue may be reduced, resulting in hypoxia (Cinti et al. 2005). Hypoxia is a condition were parts of the body are deprived of sufficient oxygen supply. This can further lead to necrosis of the affected body part and macrophage infiltration into adipose tissue (Ellulu et al. 2015), resulting in overproduction of pro-inflammatory mediators, including TNF-α and IL-6 (Ellulu et al. 2015). Furthermore, Zhang *et. al.* described in 2009, that an increased secretion of CRP in hepatocytes, is strongly stimulated due to elevated IL-6 levels (S. Zhang et al. 2009).

In the present examination, CRP prevalence was higher in overweight and obese people in comparison to participants with normal weight. Also, higher CRP concentrations showed significant correlations with total body weight, body fat mass and waist-to-hip ratio. This was also confirmed by the research of Timpson *et al.* in 2011, concluding that circulating CRP is likely to be a marker for adiposity, therefore they confirmed the positive outcome of higher CRP levels in overweight and obese people (Timpson et al. 2011).

Since poor lifestyle choices, such as an unhealthy, unbalanced diet and inadequate physical activity, are highly associated with increased body fat and in conclusion with an increased body weight, those lifestyle factors are indirectly an important cause for influencing the inflammatory state in the human body (Leigh, Byles, and Jagger 2016), although they didn't show any significant direct impact on CRP levels in this study.

In addition, our study confirmed the correlation between CRP levels and blood pressure, which is influenced by a high bodyweight and body fat mass (Staessen, Fagard, and Amery 1988). CRP levels are clinically exerted to predict the manifestation of cardiovascular events (F G Hage 2014). 2014, Hage stated, that CRP levels in hypertensive individuals are associated with atherosclerosis, vascular stiffness and cardiovascular events (F G Hage 2014).

Besides the anthropometric measurements mentioned above, only gender showed significant results for a possible effect on inflammation by influencing the IL-10 (p=0.023, r^2=0.956) and IL-6 status (p=0.046, r^2=-0.724). This might be due to the fact, that sex hormones show great impact on possible pro- and anti-inflammatory effects because of differences in the body composition, such as

amount of body fat mass or fat- free body mass and furthermore, directly on inflammatory response (Kautzky-Willer, Harreiter, and Pacini 2016).

5.2 Influence of nutrition and physical activity on inflammation

Our observations of the dietary pattern concluded a highly increased consumption of meat, processed meat, overall highly processed foods and alcoholic drinks. Studies show, that red meat and processed meat may increase inflammation by boosting IL-6 and CRP levels (Azadbakht and Esmaillzadeh 2009). However, most studies disprove that by adjusting for BMI, suggesting that the influence of meat consumption is no longer significant (Damião et al. 2006; Montonen et al. 2013; Chai et al. 2017). Similar findings exist for the consumption of highly processed foods and alcohol resulting in elevated levels of pro-inflammatory markers including CRP and IL-6 (Lopez-Garcia et al. 2004).

Furthermore, the consumption of cereal, rice and potatoes, vegetable and fruit in this study were below the recommendations of the DGE (DGE 2019b). This inadequacy of consumption has been shown to be important for the progression of inflammation in the human body. Studies demonstrate, that cereal and rice significantly reduce inflammation in human bodies (Kazemzadeh et al. 2014; Vitaglione et al. 2015), preferably consumed as whole grain for its beneficial effects (Xu et al. 2018). Processed grains on the other hand may increase inflammation due to their increased glycemic index, reduced vitamin and mineral levels and lesser amount of dietary fiber (Izadi and Azadbakht 2015). The consumption of potatoes showed possible beneficial effects on inflammation and are even described as possible potent anti-inflammatory staple crop in the future (Reddivari et al. 2019; McGill, Kurilich, and Davignon 2013). While assessing the latest studies, some showed the positive properties of a diet rich in fruit and vegetable on the prevention and improvement on inflammatory processes by influencing markers of inflammation and oxidative stress (Holt et al. 2009; Lopez-Garcia et al. 2004).

Overall, diets high in meat, processed food, refined sugar and sugar-sweetened beverages as well as low in whole-grain wheat, potatoes, vegetables and fruits, result in a negative shift in nutrient supply, which includes an increased dietary protein and -fat consumption while carbohydrate and dietary fiber intake is inadequate (Calle and Andersen 2019; Bailey and Holscher 2018; Vitaglione et al. 2015; Vermeulen et al. 2018). Interestingly, the present study collective showed dietary patterns that match the described unfavorable dietary pattern. This included not only a high protein and fat intake but also insufficient intake of carbohydrates and fiber. The overall negative shift in dietary pattern might result in a pro-inflammatory state in the human body. *Vermeulen and colleagues*

suggest, that dietary pattern characterized by high intakes of processed meat and refined sugar are related to inflammatory markers including CRP and IL-1β (Vermeulen et al. 2018).
In contrast to the findings mentioned above, this study showed, that more participants, whose cereal, rice and potato intake were below the recommendations, reached an anti-inflammatory score of SII and NLR compared to those with an adequate intake.
At first glance, these results may be conflicting with the previous findings of other studies, where an adequate carbohydrate intake showed anti-inflammatory properties. While examining the results of this study we noticed, that only the group of starchy vegetables displayed a significant association with SII and NLR. The group of *Khosroshanhi* however, demonstrated the effects of resistant high amylose starch on inflammation and stated, that starch had anti-inflammatory properties (Tayebi Khosroshahi et al. 2018). In 2020, these findings were furthermore supported in a randomized, double-blind, placebo-controlled crossover studies by *Esgalhado and colleagues* (Esgalhado et al. 2020).
Another crucial impact on our outcome might stem from gluten, a substance found in wheat and other cereal grains and which is capable of activating pro-inflammatory pathways in "gluten-sensitive" people or people with celiac disease (de Punder and Pruimboom 2013), which might be another potential reason for this studies outcome.

Also, a possible reason for above mentioned results might be the fact, that we did not distinguished between whole grain and refined grain consumption during the evaluation of the food diaries. *Malik and colleagues* were able to observe an increase in CRP levels when white rice was consumed compared to brown rice consumption (Malik et al. 2019).
Also, *Vitaglione et al.* showed, that whole grain consumption seems to have protective effects against inflammation. Their data on inflammation markers, including IL-6 and TNF-α, demonstrated a significant reduction after 8 weeks and an increase of IL-10 after 4 weeks of whole grain consumption (Vitaglione et al. 2015). These findings are supported by further studies (Katcher et al. 2008; Martínez et al. 2013).

Not only cereals, rice and potatoes showed significant results while examining the impact of nutrition on inflammation. Further statistical tests showed an inverse correlation between CRP levels and the consumption of milk and dairy products. This outcome is supported by a systematic review of 52 clinical trials which reported about the relation between inflammatory markers and dairy products by defining and evaluating an inflammatory score. They came to the conclusion that consumption of dairy products might have anti-inflammatory activity in humans (Bordoni et al. 2017). This is further supported in a systematic review by Labonté and colleagues (Labonté et al. 2013).

Despite adequate intake of vitamin D, the examination of circulating vitamin D-levels showed already detectable Vitamin D- deficiencies in the blood stream of the participants. Blood tests revealed, that circulating vitamin D-levels were at the lower end of the recommended reference values. This might be the consequence if insufficient outdoor exercise. Furthermore, inadequate vitamin D-status are a global health issue (Holick 2017) and highly linked to increased pro-inflammatory markers, including TNF-α (Berridge 2017; Holick 2017).

While analyzing the amount of vigorous intensity of physical activity per week, results showed, that participants accomplished less than 50% of the recommended time per week. These results are unsatisfactory and may be one of the reasons for the elevated CRP values in our participants. Various studies confirm the protective effects of physical activity on systemic low-grade inflammation, especially by reducing concentrations of CRP (Milani, Lavie, and Mehra 2004; Plaisance and Grandjean 2006; Mora et al. 2007). Moderate and vigorous physical activity can attenuate multisystem declines, including loss of skeletal muscle and changes in cardiorespiratory and vascular system, due to aging (Sam et al. 2009).

6 Conclusion

This study investigated the current inflammatory status in elderly people and potential influences of nutritional aspects, body composition and physical activity on chronic low-grade inflammation.
It is important to note, that although the participants may not show an evident increased inflammatory state, an influence of body weight, body fat and fat- free mass as well as various dietary compounds, including vitamin D, milk and dairy products on inflammatory markers could be found.

This study supports already existing findings in most parts, predominantly when body composition measurements were correlated with inflammatory markers and indices. However, it is hard to define the specific influences of body composition, nutrients, food and physical activity on inflammation, due to constantly ongoing interactions with other nutrients and lifestyle factors. The only conflicting outcome was found regarding the influence of cereals, rice and potatoes on inflammatory markers. Results showed higher SII and NLR ratios in participants who consumed those according to the dietary guidelines of the DGE (DGE 2019), which might be due to the fact, that during the evaluation, there was not made any differences between whole grains and refined grains. Other studies have been able to show anti-inflammatory properties of whole grain products (Vitaglione et al. 2015; Xu et al. 2018) while refined grains (e.g. white rice), showed pro-inflammatory properties (Malik et al. 2019).

In conclusion, this study supports the scientific consensus, that a high body weight and body fat mass, a nutrition high in meat and processed foods and low in fruits and vegetables and insufficient physical activity are important factors that promote inflammatory processes in the human body, which can result in chronic low-grade inflammation in the long run (Calvani et al. 2017; Nimmo et al. 2013; Rahman and Bagchi 2014). Identifying a single important factor is difficult and inadequate, since low-grade inflammation is a complex pathogenic condition and is caused by the interplay of various health- and lifestyle factors. This is important to consider, while developing potential prevention- and therapy treatments. Furthermore, additional research is needed, to support current findings and investigate the underlying cause for the influence of lifestyle factors mentioned above, on the inflammatory process during aging.

7 Summary

During the last decades, life expectancy increased substantially and implicates new challenges for the public health, for example, age-associated diseases like cardiovascular disease, Alzheimer's- and Parkinson's disease, respectively. Most of these diseases origin from down-regulations of the immune system, which leads to a pro-inflammatory state in the human body. This phenomenon is described as "*inflammaging*".

Inflammaging is the chronic low-grade inflammatory state in elderly people, in absence of any triggers and is significantly associated with morbidity and also overall mortality.

The aim of this master thesis was to investigate the current inflammatory state of elderly people and possible correlations of inflammation with age, body composition, physical activity state and nutrition.

The study collective was analyzed for gender and age distribution as well as results of blood tests, anthropometric measurements, supply of nutrients, food intake and physical activity levels.

To find associations between inflammatory markers, such as CRP, IL 6, -10, -1β, TNF-α, SII, NLR, PLR and possible pro-inflammatory factors, including body composition, nutrition, nutrient supply and physical activity, correlation analysis was used.

Results show no evident increased inflammatory state in the participant, still there are significant results, that show the influence of body weight, body fat and fat- free mass and of various dietary compounds, including vitamin D and milk and dairy products on inflammatory markers, such as CRP, IL-6, IL-10, SII and NLR.

In conclusion, this study supports the scientific consensus, that a normal BMI and an adequate body fat mass, a diet rich in unprocessed, plant-based foods and sufficient physical activity are important factors, that can prevent or even decrease inflammatory processes in elderly people and therefore, decelerate the *Inflammaging* process. Identifying a single important factor is problematic, since the combination of various health and lifestyle factors lead to this complex process of a systemic- low-grade inflammation. This should always be considered, while developing potential prevention and therapy treatments.

8 Zusammenfassung

In den letzten Jahrzehnten ist die Lebenserwartung erheblich gestiegen, was zu neuen Herausforderungen für den Bereich der öffentlicher Gesundheitsförderung führt. Dazu gehören altersbedingte Erkrankungen, wie Herz-Kreislauf-Erkrankungen, Alzheimer und Parkinson. Die meisten dieser Krankheiten haben ihren Ursprung in einer Herunterregulierung des Immunsystems. Diese Veränderung führt zu einem entzündungsfördernden Milieu im menschlichen Körper, welche in der Literatur als "*inflammaging*" definiert wird.

„*Inflammaging*" beschreibt eine chronische Entzündung bei älteren Menschen, welche auf keinen externen oder internen Auslöser zurückzuführen ist. Darüber hinaus wirkt sich dieser Vorgang signifikant auf die Morbidität und auch Gesamtsterblichkeit im Alter aus.

Ziel dieser Masterarbeit ist es, den aktuellen Entzündungszustand älterer Menschen zu ermitteln und mögliche Zusammenhänge zwischen Entzündungen und Lebensalter, Körperzusammensetzung, körperlicher Aktivität und Ernährung zu untersuchen.

Das Studienkollektiv wurde auf Geschlechts- und Altersverteilung untersucht. Des Weiteren wurden die Blutuntersuchungen, anthropometrischen Messungen, die Nährstoffversorgung und Nahrungsaufnahme sowie die körperliche Aktivität ausgewertet und analysiert.

Um Assoziationen zwischen Entzündungsmarkern wie CRP, IL 6, -10, -1β, TNF-α, SII, NLR, PLR und möglichen entzündungsfördernden Faktoren, einschließlich Körperzusammensetzung, Ernährung, Nährstoffversorgung und körperlicher Aktivität, zu finden, wurde eine Korrelationsanalyse durchgeführt.

Die Ergebnisse zeigen keinen offensichtlich erhöhten Entzündungszustand bei den Teilnehmer, jedoch gab es signifikante Ergebnisse, die den Einfluss der Körperzusammensetzung, wie Körpergewicht, Körperfett und fettfreie Masse und verschiedenen Nährstoffen und Lebensmitteln, einschließlich Vitamin D, Milch und Milchprodukte auf entzündliche Marker, wie CRP, IL-6, IL-10, SII und NLR zeigten.

Zusammenfassend unterstützt diese Studie den wissenschaftlichen Konsens, dass ein normaler BMI und eine angemessene Körperfettmasse, eine ausgewogene Ernährung und körperliche Aktivität wichtige Einflussfaktoren sind, die entzündliche Prozesse im menschlichen Körper und damit eine chronische Entzündung verhindern oder verringern können. Die Identifizierung eines einzelnen relevanten Faktors ist jedoch problematisch, da eine chronische Entzündung ein komplexer Prozess ist, bei dem eine Kombination aus verschiedenen Gesundheits- und Lebensstilfaktoren eine Rolle dafür spielen. Dies sollte immer, während der Entwicklung potenzieller Präventions- und Therapiebehandlungen, berücksichtigt werden.

9 References

- Adaes, Sara. 2016. "CHRONIC LOW-GRADE INFLAMMATION – A COMMON GROUND FOR MODERN EPIDEMICS."
- Akiyama, H. 2000. "Inflammation and Alzheimer's Disease." *Neurobiology of Aging* 21 (3): 383–421. https://doi.org/10.1016/S0197-4580(00)00124-X.
- Arai, K, F Lee, A Miyajima, S Miyatake, N Arai, and T Yokota. 1990. "Cytokines: Coordinators of Immune and Inflammatory Responses." *Annual Review of Biochemistry* 59 (1): 783–836. https://doi.org/10.1146/annurev.bi.59.070190.004031.
- Azadbakht, Leila, and Ahmad Esmaillzadeh. 2009. "Red Meat Intake Is Associated with Metabolic Syndrome and the Plasma C-Reactive Protein Concentration in Women." *The Journal of Nutrition* 139 (2): 335–39. https://doi.org/10.3945/jn.108.096297.
- Bailey, Melisa A, and Hannah D Holscher. 2018. "Microbiome-Mediated Effects of the Mediterranean Diet on Inflammation." *Advances in Nutrition* 9 (3): 193–206. https://doi.org/10.1093/advances/nmy013.
- Barry, Julianne C., Soroush Shakibakho, Cody Durrer, Svetlana Simtchouk, Kamaldeep K. Jawanda, Sylvia T. Cheung, Alice L. Mui, and Jonathan P. Little. 2016. "Hyporesponsiveness to the Anti-Inflammatory Action of Interleukin-10 in Type 2 Diabetes." *Scientific Reports* 6 (1): 21244. https://doi.org/10.1038/srep21244.
- Barzilay, J. I., L. Abraham, S. R. Heckbert, M. Cushman, L. H. Kuller, H. E. Resnick, and R. P. Tracy. 2001. "The Relation of Markers of Inflammation to the Development of Glucose Disorders in the Elderly: The Cardiovascular Health Study." *Diabetes* 50 (10): 2384–89. https://doi.org/10.2337/diabetes.50.10.2384.
- Bastard, J. P., C. Jardel, J. Delattre, B. Hainque, E. Bruckert, and F. Oberlin. 1999. "Evidence for a Link between Adipose Tissue Interleukin-6 Content and Serum C-Reactive Protein Concentrations in Obese Subjects." *Circulation* 99 (16): 2221–22.
- Berridge, Michael J. 2017. "Vitamin D Deficiency Accelerates Ageing and Age-Related Diseases: A Novel Hypothesis: Vitamin D Deficiency and Ageing." *The Journal of Physiology* 595 (22): 6825–36. https://doi.org/10.1113/JP274887.
- Bhat, Tariq, Sumaya Teli, Jharendra Rijal, Hilal Bhat, Muhammad Raza, Georges Khoueiry, Mustafain Meghani, Muhammad Akhtar, and Thomas Costantino. 2013. "Neutrophil to Lymphocyte Ratio and Cardiovascular Diseases: A Review." *Expert Review of Cardiovascular Therapy* 11 (1): 55–59. https://doi.org/10.1586/erc.12.159.
- BMEL. 2008. "Nationale Verzehrsstudie 2."
- Bordoni, Alessandra, Francesca Danesi, Dominique Dardevet, Didier Dupont, Aida S. Fernandez, Doreen Gille, Claudia Nunes dos Santos, et al. 2017. "Dairy Products and Inflammation: A Review of the Clinical Evidence." *Critical Reviews in Food Science and Nutrition* 57 (12): 2497–2525. https://doi.org/10.1080/10408398.2014.967385.
- Bradley, Jr. 2008. "TNF-Mediated Inflammatory Disease." *The Journal of Pathology* 214 (2):

149–60. https://doi.org/10.1002/path.2287.

- Cabral-Santos, Carolina, Edson Alves de Lima Junior, Isabela Maia da Cruz Fernandes, Rafael Zambelli Pinto, José César Rosa-Neto, Nicolette Charllote Bishop, and Fábio Santos Lira. 2019. "Interleukin-10 Responses from Acute Exercise in Healthy Subjects: A Systematic Review." *Journal of Cellular Physiology* 234 (7): 9956–65. https://doi.org/10.1002/jcp.27920.
- Calle, Mariana C., and Catherine J. Andersen. 2019. "Assessment of Dietary Patterns Represents a Potential, Yet Variable, Measure of Inflammatory Status: A Review and Update." *Disease Markers* 2019 (January): 1–13. https://doi.org/10.1155/2019/3102870.
- Calvani, Riccardo, Federico Marini, Matteo Cesari, Thomas W. Buford, Todd M. Manini, Marco Pahor, Christiaan Leeuwenburgh, Roberto Bernabei, Francesco Landi, and Emanuele Marzetti. 2017. "Systemic Inflammation, Body Composition, and Physical Performance in Old Community-Dwellers." *Journal of Cachexia, Sarcopenia and Muscle* 8 (1): 69–77. https://doi.org/10.1002/jcsm.12134.
- Cameron, Noël. 2015. "Can Maturity Indicators Be Used to Estimate Chronological Age in Children?" *Annals of Human Biology* 42 (4): 302–7. https://doi.org/10.3109/03014460.2015.1032349.
- Campisi, Judith. 2013. "Aging, Cellular Senescence, and Cancer." *Annual Review of Physiology* 75: 685–705. https://doi.org/10.1146/annurev-physiol-030212-183653.
- Campisi, Judith, Julie K. Andersen, Pankaj Kapahi, and Simon Melov. 2011. "Cellular Senescence: A Link between Cancer and Age-Related Degenerative Disease?" *Seminars in Cancer Biology* 21 (6): 354–59. https://doi.org/10.1016/j.semcancer.2011.09.001.
- Capuron, Lucile, Shaoyong Su, Andrew H. Miller, J. Douglas Bremner, Jack Goldberg, Gerald J. Vogt, Carisa Maisano, Linda Jones, Nancy V. Murrah, and Viola Vaccarino. 2008. "Depressive Symptoms and Metabolic Syndrome: Is Inflammation the Underlying Link?" *Biological Psychiatry* 64 (10): 896–900. https://doi.org/10.1016/j.biopsych.2008.05.019.
- Chai, Weiwen, Yukiko Morimoto, Robert V. Cooney, Adrian A. Franke, Yurii B. Shvetsov, Loïc Le Marchand, Christopher A. Haiman, Laurence N. Kolonel, Marc T. Goodman, and Gertraud Maskarinec. 2017. "Dietary Red and Processed Meat Intake and Markers of Adiposity and Inflammation: The Multiethnic Cohort Study." *Journal of the American College of Nutrition* 36 (5): 378–85. https://doi.org/10.1080/07315724.2017.1318317.
- Chen, Li, Ying Yan, Lihua Zhu, Xiliang Cong, Sen Li, Shubin Song, Hongjiang Song, and Yingwei Xue. 2017. "Systemic Immune–Inflammation Index as a Useful Prognostic Indicator Predicts Survival in Patients with Advanced Gastric Cancer Treated with Neoadjuvant Chemotherapy." *Cancer Management and Research* 9 (December): 849–67. https://doi.org/10.2147/CMAR.S151026.
- Cinti, Saverio, Grant Mitchell, Giorgio Barbatelli, Incoronata Murano, Enzo Ceresi, Emanuela Faloia, Shupei Wang, Melanie Fortier, Andrew S. Greenberg, and Martin S. Obin. 2005. "Adipocyte Death Defines Macrophage Localization and Function in Adipose Tissue of Obese Mice and Humans." *Journal of Lipid Research* 46 (11): 2347–55. https://doi.org/10.1194/jlr.M500294-JLR200.
- Cohen, H. J., C. F. Pieper, T. Harris, K M. K Rao, and M. S. Currie. 1997. "The Association of

Plasma IL-6 Levels With Functional Disability in Community-Dwelling Elderly." *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 52A (4): M201–8. https://doi.org/10.1093/gerona/52A.4.M201.

- Cohen, S., W. J. Doyle, and D. P. Skoner. 1999. "Psychological Stress, Cytokine Production, and Severity of Upper Respiratory Illness." *Psychosomatic Medicine* 61 (2): 175–80. https://doi.org/10.1097/00006842-199903000-00009.
- Cook, Chad M., Terje S. Larsen, Linda D. Derrig, Kathleen M. Kelly, and Kurt S. Tande. 2016. "Wax Ester Rich Oil From The Marine Crustacean, Calanus Finmarchicus, Is a Bioavailable Source of EPA and DHA for Human Consumption." *Lipids* 51 (10): 1137–44. https://doi.org/10.1007/s11745-016-4189-y.
- Coutts, Fiona, Alish B. Palmos, Rodrigo R. R. Duarte, Simone de Jong, Cathryn M. Lewis, Danai Dima, and Timothy R. Powell. 2019. "The Polygenic Nature of Telomere Length and the Anti-Ageing Properties of Lithium." *Neuropsychopharmacology* 44 (4): 757–65. https://doi.org/10.1038/s41386-018-0289-0.
- Dalpiaz, Orietta, Daniel Krieger, Georg C. Ehrlich, Kristof Pohlmann, Tatjana Stojakovic, Karl Pummer, Richard Zigeuner, Martin Pichler, and Georg C. Hutterer. 2017. "Validation of the Preoperative Platelet-to-Lymphocyte Ratio as a Prognostic Factor in a European Cohort of Patients with Upper Tract Urothelial Carcinoma." *Urologia Internationalis* 98 (3): 320–27. https://doi.org/10.1159/000452109.
- Damião, Renata, Teresa G. Castro, Marly A. Cardoso, Suely G. A. Gimeno, Sandra R. G. Ferreira, and Japanese-Brazilian Diabetes Study Group. 2006. "Dietary Intakes Associated with Metabolic Syndrome in a Cohort of Japanese Ancestry." *The British Journal of Nutrition* 96 (3): 532–38.
- Data Input GmbH. n.d. "Nutriguard_MS Gebrauchsanweisung." https://www.data-input.de/media/pdf_deutsch_2018/Gebrauchsanleitung_Nutriguard%20MS_2019.pdf.
- Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, and Schweizerische Gesellschaft für Ernährungsforschung, eds. 2013. *Referenzwerte für die Nährstoffzufuhr*. 1. Aufl., 5. korrigierter Nachdr. Neustadt an der Weinstraße: Neuer Umschau Buchverlag.
- DGE. 2019a. "Kritische Nährstoffe Im Alter."
- ———. 2019b. "Orientierungswerte Für Erwachsene."
- Dinarello, C. A. 1996. "Biologic Basis for Interleukin-1 in Disease." *Blood* 87 (6): 2095–2147.
- Ellulu, Mohammed S., Ismail Patimah, Huzwah Khaza'ai, Asmah Rahmat, and Yehia Abed. 2017. "Obesity and Inflammation: The Linking Mechanism and the Complications." *Archives of Medical Science* 4: 851–63. https://doi.org/10.5114/aoms.2016.58928.
- Ellulu, Mohammed S., Asmah Rahmat, Patimah Ismail, Huzwah Khaza'ai, and Yehia Abed. 2015. "Effect of Vitamin C on Inflammation and Metabolic Markers in Hypertensive and/or Diabetic Obese Adults: A Randomized Controlled Trial." *Drug Design, Development and Therapy*, July, 3405. https://doi.org/10.2147/DDDT.S83144.
- Elmadfa, Ibrahim. 2009. *Ernährungslehre: 101 Tabellen*. 2., überarb. Aufl. UTB 2509. Stuttgart: Ulmer.

- Esgalhado, Marta, Julie Ann Kemp, Bruna R. de Paiva, Jessyca Sousa Brito, Ludmila F. M. F. Cardozo, Renata Azevedo, Diana Barbosa Cunha, Lia S. Nakao, and Denise Mafra. 2020. "Resistant Starch Type-2 Enriched Cookies Modulate Uremic Toxins and Inflammation in Hemodialysis Patients: A Randomized, Double-Blind, Crossover and Placebo-Controlled Trial." *Food & Function* 11 (3): 2617–25. https://doi.org/10.1039/C9FO02939G.
- Esposito, E., and S. Cuzzocrea. 2009. "TNF-Alpha as a Therapeutic Target in Inflammatory Diseases, Ischemia- Reperfusion Injury and Trauma." *Current Medicinal Chemistry* 16 (24): 3152–67. https://doi.org/10.2174/092986709788803024.
- Fagiolo, U., A. Cossarizza, E. Scala, E. Fanales-Belasio, C. Ortolani, E. Cozzi, D. Monti, C. Franceschi, and R. Paganelli. 1993. "Increased Cytokine Production in Mononuclear Cells of Healthy Elderly People." *European Journal of Immunology* 23 (9): 2375–78. https://doi.org/10.1002/eji.1830230950.
- Febbraio, Mark A., and Bente K. Pedersen. 2005. "Contraction-Induced Myokine Production and Release: Is Skeletal Muscle an Endocrine Organ?:" *Exercise and Sport Sciences Reviews* 33 (3): 114–19. https://doi.org/10.1097/00003677-200507000-00003.
- Feng, Ji-Feng, Sheng Chen, and Xun Yang. 2017. "Systemic Immune-Inflammation Index (SII) Is a Useful Prognostic Indicator for Patients with Squamous Cell Carcinoma of the Esophagus." *Medicine* 96 (4). https://doi.org/10.1097/MD.0000000000005886.
- Ferenbach, David A., and Joseph V. Bonventre. 2016. "Chapter 27 - The Molecular Response to Renal Injury: How Does Chronic Renal Damage Suppress Normal Repair Processes?" In *Kidney Development, Disease, Repair and Regeneration*, edited by Melissa H. Little, 367–79. San Diego: Academic Press. https://doi.org/10.1016/B978-0-12-800102-8.00027-8.
- Ferrucci, Luigi, and Elisa Fabbri. 2018. "Inflammageing: Chronic Inflammation in Ageing, Cardiovascular Disease, and Frailty." *Nature Reviews Cardiology* 15 (9): 505–22. https://doi.org/10.1038/s41569-018-0064-2.
- Ferrucci, Luigi, Richard D. Semba, Jack M. Guralnik, William B. Ershler, Stefania Bandinelli, Kushang V. Patel, Kai Sun, et al. 2010. "Proinflammatory State, Hepcidin, and Anemia in Older Persons." *Blood* 115 (18): 3810–16. https://doi.org/10.1182/blood-2009-02-201087.
- Fest, Jesse, Rikje Ruiter, M. Arfan Ikram, Trudy Voortman, Casper H. J. van Eijck, and Bruno H. Stricker. 2018. "Reference Values for White Blood-Cell-Based Inflammatory Markers in the Rotterdam Study: A Population-Based Prospective Cohort Study." *Scientific Reports* 8 (1): 10566. https://doi.org/10.1038/s41598-018-28646-w.
- Foley, Nicole M., Graham M. Hughes, Zixia Huang, Michael Clarke, David Jebb, Conor V. Whelan, Eric J. Petit, et al. 2018. "Growing Old, yet Staying Young: The Role of Telomeres in Bats' Exceptional Longevity." *Science Advances* 4 (2): eaao0926. https://doi.org/10.1126/sciadv.aao0926.
- Franceschi, C., M. Bonafè, S. Valensin, F. Olivieri, M. De Luca, E. Ottaviani, and G. De Benedictis. 2000. "Inflamm-Aging. An Evolutionary Perspective on Immunosenescence." *Annals of the New York Academy of Sciences* 908 (June): 244–54. https://doi.org/10.1111/j.1749-6632.2000.tb06651.x.

- Franceschi, Claudio, Miriam Capri, Paolo Garagnani, Rita Ostan, Aurelia Santoro, Daniela Monti, and Stefano Salvioli. 2018. "Inflammaging." In *Handbook of Immunosenescence*, edited by Tamas Fulop, Claudio Franceschi, Katsuiku Hirokawa, and Graham Pawelec, 1–31. Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-64597-1_45-1.
- Franceschi, Claudio, Stefano Salvioli, Paolo Garagnani, Magda de Eguileor, Daniela Monti, and Miriam Capri. 2017. "Immunobiography and the Heterogeneity of Immune Responses in the Elderly: A Focus on Inflammaging and Trained Immunity." *Frontiers in Immunology* 8 (August). https://doi.org/10.3389/fimmu.2017.00982.
- Frey, Ingrid, Aloys Berg, Dominik Grathwohl, and Joseph Keul. 1999. "Freiburger Fragebogen zur körperlichen Aktivität-Entwicklung, Prüfung und Anwendung." *Sozial- und Präventivmedizin SPM* 44 (2): 55–64. https://doi.org/10.1007/BF01667127.
- Fulop, Tamas, Anis Larbi, Gilles Dupuis, Aurélie Le Page, Eric H. Frost, Alan A. Cohen, Jacek M. Witkowski, and Claudio Franceschi. 2017. "Immunosenescence and Inflamm-Aging As Two Sides of the Same Coin: Friends or Foes?" *Frontiers in Immunology* 8: 1960. https://doi.org/10.3389/fimmu.2017.01960.
- ———. 2018. "Immunosenescence and Inflamm-Aging As Two Sides of the Same Coin: Friends or Foes?" *Frontiers in Immunology* 8 (January): 1960. https://doi.org/10.3389/fimmu.2017.01960.
- Gabay, Cem. 2006. "Interleukin-6 and Chronic Inflammation." *Arthritis Research & Therapy* 8 (Suppl 2): S3. https://doi.org/10.1186/ar1917.
- Galland, Leo. 2010. "Diet and Inflammation." *Nutrition in Clinical Practice* 25 (6): 634–40. https://doi.org/10.1177/0884533610385703.
- Galle, Fernando Alexis, Diana Martella, and Guilherme Bresciani. 2018. "Modulación Antioxidante y Antiinflamatoria Del Ejercicio Físico Durante El Envejecimiento." *Revista Española de Geriatría y Gerontología* 53 (5): 279–84. https://doi.org/10.1016/j.regg.2018.03.003.
- Garatachea, Nuria, Helios Pareja-Galeano, Fabian Sanchis-Gomar, Alejandro Santos-Lozano, Carmen Fiuza-Luces, María Morán, Enzo Emanuele, Michael J. Joyner, and Alejandro Lucia. 2015. "Exercise Attenuates the Major Hallmarks of Aging." *Rejuvenation Research* 18 (1): 57–89. https://doi.org/10.1089/rej.2014.1623.
- Gentile, M, S Panico, F Rubba, A Mattiello, P Chiodini, F Jossa, G Marotta, P Pauciullo, and P Rubba. 2010. "Obesity, Overweight, and Weight Gain over Adult Life Are Main Determinants of Elevated Hs-CRP in a Cohort of Mediterranean Women." *European Journal of Clinical Nutrition* 64 (8): 873–78. https://doi.org/10.1038/ejcn.2010.69.
- Goldhammer, Ehud, Alon Tanchilevitch, Irit Maor, Yael Beniamini, Uri Rosenschein, and Michael Sagiv. 2005. "Exercise Training Modulates Cytokines Activity in Coronary Heart Disease Patients." *International Journal of Cardiology* 100 (1): 93–99. https://doi.org/10.1016/j.ijcard.2004.08.073.
- Goodpaster, B. H., S. W. Park, T. B. Harris, S. B. Kritchevsky, M. Nevitt, A. V. Schwartz, E. M. Simonsick, et al. 2006. "The Loss of Skeletal Muscle Strength, Mass, and Quality in Older Adults: The Health, Aging and Body Composition Study." *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 61 (10): 1059–64.

https://doi.org/10.1093/gerona/61.10.1059.

- Grignolio, Andrea, Michele Mishto, Ana Maria Caetano Faria, Paolo Garagnani, Claudio Franceschi, and Paolo Tieri. 2014. "Towards a Liquid Self: How Time, Geography, and Life Experiences Reshape the Biological Identity." *Frontiers in Immunology* 5 (April). https://doi.org/10.3389/fimmu.2014.00153.
- Grimm, I. S., and L. S. Friedman. 1990. "Inflammatory Bowel Disease in the Elderly." *Gastroenterology Clinics of North America* 19 (2): 361–89.
- Groten, Jenny, Anusha Venkatraman, and Roland Mertelsmann. 2018. "Chapter 12 - Modeling and Simulating Carcinogenesis." In *Precision Medicine*, edited by Hans-Peter Deigner and Matthias Kohl, 277–95. Academic Press. https://doi.org/10.1016/B978-0-12-805364-5.00012-3.
- Hage, F G. 2014. "C-Reactive Protein and Hypertension." *Journal of Human Hypertension* 28 (7): 410–15. https://doi.org/10.1038/jhh.2013.111.
- Hage, Fadi G., and Alexander J. Szalai. 2007. "C-Reactive Protein Gene Polymorphisms, C-Reactive Protein Blood Levels, and Cardiovascular Disease Risk." *Journal of the American College of Cardiology* 50 (12): 1115–22. https://doi.org/10.1016/j.jacc.2007.06.012.
- Hahn, Andreas, Alexander Ströhle, and Maike Wolters. 2016. *Ernährung Phsiologische Grundlagen, Pärvention, Therapie*. 3. Edition. Wissenschafltiche Verlagsgesellschaft Bremen.
- Henrique, Carlos. 2019. "Exercise Training for the Elderly: Inflammaging and the Central Role for HSP70." ResearchGate. 2019. https://www.researchgate.net/publication/334303259_Exercise_Training_for_the_Elderly_Inflammaging_and_the_Central_Role_for_HSP70.
- Holick, Michael F. 2017. "The Vitamin D Deficiency Pandemic: Approaches for Diagnosis, Treatment and Prevention." *Reviews in Endocrine and Metabolic Disorders* 18 (2): 153–65. https://doi.org/10.1007/s11154-017-9424-1.
- Holt, Erica M., Lyn M. Steffen, Antoinette Moran, Samar Basu, Julia Steinberger, Julie A. Ross, Ching-Ping Hong, and Alan R. Sinaiko. 2009. "Fruit and Vegetable Consumption and Its Relation to Markers of Inflammation and Oxidative Stress in Adolescents." *Journal of the American Dietetic Association* 109 (3): 414–21. https://doi.org/10.1016/j.jada.2008.11.036.
- Hong, Xuan, Baohong Cui, Meng Wang, Zhaoyang Yang, Li Wang, and Qingyong Xu. 2015. "Systemic Immune-Inflammation Index, Based on Platelet Counts and Neutrophil-Lymphocyte Ratio, Is Useful for Predicting Prognosis in Small Cell Lung Cancer." *The Tohoku Journal of Experimental Medicine* 236 (4): 297–304. https://doi.org/10.1620/tjem.236.297.
- Hotamisligil, Gökhan S. 2006. "Inflammation and Metabolic Disorders." *Nature* 444 (7121): 860–67. https://doi.org/10.1038/nature05485.
- Hu, Bo, Xin-Rong Yang, Yang Xu, Yun-Fan Sun, Chao Sun, Wei Guo, Xin Zhang, et al. 2014. "Systemic Immune-Inflammation Index Predicts Prognosis of Patients after Curative Resection for Hepatocellular Carcinoma." *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research* 20 (23): 6212–22. https://doi.org/10.1158/1078-0432.CCR-14-0442.

- Huang, Wanjing, Jinhua Huang, Qingxing Liu, Fuchuan Lin, Zhihao He, Zhenhua Zeng, and Lei He. 2015. "Neutrophil-Lymphocyte Ratio Is a Reliable Predictive Marker for Early-Stage Diabetic Nephropathy." *Clinical Endocrinology* 82 (2): 229–33. https://doi.org/10.1111/cen.12576.
- Hudzik, Bartosz, Janusz Szkodziński, Andrzej Lekston, Marek Gierlotka, Lech Poloński, and Mariusz Gąsior. 2016. "Mean Platelet Volume-to-Lymphocyte Ratio: A Novel Marker of Poor Short- and Long-Term Prognosis in Patients with Diabetes Mellitus and Acute Myocardial Infarction." *Journal of Diabetes and Its Complications* 30 (6): 1097–1102. https://doi.org/10.1016/j.jdiacomp.2016.04.010.
- Il'yasova, D. 2005. "Circulating Levels of Inflammatory Markers and Cancer Risk in the Health Aging and Body Composition Cohort." *Cancer Epidemiology Biomarkers & Prevention* 14 (10): 2413–18. https://doi.org/10.1158/1055-9965.EPI-05-0316.
- Izadi, Vajihe, and Leila Azadbakht. 2015. "Is There Any Association between Rice Consumption and Some of the Cardiovascular Diseases Risk Factors? A Systematic Review." *ARYA Atherosclerosis* 11 (Suppl 1): 109–15.
- Jackson, Stephen H. D, Martin R Weale, and Robert A Weale. 2003. "Biological Age—What Is It and Can It Be Measured?" *Archives of Gerontology and Geriatrics* 36 (2): 103–15. https://doi.org/10.1016/S0167-4943(02)00060-2.
- Kalinkovich, Alexander, and Gregory Livshits. 2017. "Sarcopenic Obesity or Obese Sarcopenia: A Cross Talk between Age-Associated Adipose Tissue and Skeletal Muscle Inflammation as a Main Mechanism of the Pathogenesis." *Ageing Research Reviews* 35 (May): 200–221. https://doi.org/10.1016/j.arr.2016.09.008.
- Katcher, Heather I, Richard S Legro, Allen R Kunselman, Peter J Gillies, Laurence M Demers, Deborah M Bagshaw, and Penny M Kris-Etherton. 2008. "The Effects of a Whole Grain–Enriched Hypocaloric Diet on Cardiovascular Disease Risk Factors in Men and Women with Metabolic Syndrome." *The American Journal of Clinical Nutrition* 87 (1): 79–90. https://doi.org/10.1093/ajcn/87.1.79.
- Kautzky-Willer, Alexandra, Jürgen Harreiter, and Giovanni Pacini. 2016. "Sex and Gender Differences in Risk, Pathophysiology and Complications of Type 2 Diabetes Mellitus." *Endocrine Reviews* 37 (3): 278–316. https://doi.org/10.1210/er.2015-1137.
- Kazemzadeh, Mahdieh, Sayyed Morteza Safavi, Shahrzad Nematollahi, and Zeinab Nourieh. 2014. "Effect of Brown Rice Consumption on Inflammatory Marker and Cardiovascular Risk Factors among Overweight and Obese Non-Menopausal Female Adults." *International Journal of Preventive Medicine* 5 (4): 478–88.
- Kiecolt-Glaser, Janice K. 2010. "Stress, Food, and Inflammation: Psychoneuroimmunology and Nutrition at the Cutting Edge:" *Psychosomatic Medicine* 72 (4): 365–69. https://doi.org/10.1097/PSY.0b013e3181dbf489.
- Kim, Yoonseo, Nicole Noren Hooten, Douglas F. Dluzen, Jennifer L. Martindale, Myriam Gorospe, and Michele K. Evans. 2015. "Posttranscriptional Regulation of the Inflammatory Marker C-Reactive Protein by the RNA-Binding Protein HuR and MicroRNA 637." *Molecular and Cellular Biology* 35 (24): 4212–21. https://doi.org/10.1128/MCB.00645-15.

- Koelman, Liselot, Olga Pivovarova-Ramich, Andreas F. H. Pfeiffer, Tilman Grune, and Krasimira Aleksandrova. 2019. "Cytokines for Evaluation of Chronic Inflammatory Status in Ageing Research: Reliability and Phenotypic Characterisation." *Immunity & Ageing: I & A* 16: 11. https://doi.org/10.1186/s12979-019-0151-1.
- Koh, Yunsuk, Kyung-Shin Park, Yunsuk Koh, and Kyung-Shin Park. 2017. "Responses of Inflammatory Cytokines Following Moderate Intensity Walking Exercise in Overweight or Obese Individuals." *Journal of Exercise Rehabilitation* 13 (4): 472–76. https://doi.org/10.12965/jer.1735066.533.
- Kohut, M. L., D. A. McCann, D. W. Russell, D. N. Konopka, J. E. Cunnick, W. D. Franke, M. C. Castillo, A. E. Reighard, and E. Vanderah. 2006. "Aerobic Exercise, but Not Flexibility/Resistance Exercise, Reduces Serum IL-18, CRP, and IL-6 Independent of Beta-Blockers, BMI, and Psychosocial Factors in Older Adults." *Brain, Behavior, and Immunity* 20 (3): 201–9. https://doi.org/10.1016/j.bbi.2005.12.002.
- Kuyumcu, Mehmet Emin, Yusuf Yesil, Zeynel Abidin Oztürk, Cemal Kizilarslanoğlu, Sezgin Etgül, Meltem Halil, Zekeriya Ulger, Mustafa Cankurtaran, and Servet Arıoğul. 2012. "The Evaluation of Neutrophil-Lymphocyte Ratio in Alzheimer's Disease." *Dementia and Geriatric Cognitive Disorders* 34 (2): 69–74. https://doi.org/10.1159/000341583.
- Labonté, Marie-Ève, Patrick Couture, Caroline Richard, Sophie Desroches, and Benoît Lamarche. 2013. "Impact of Dairy Products on Biomarkers of Inflammation: A Systematic Review of Randomized Controlled Nutritional Intervention Studies in Overweight and Obese Adults." *The American Journal of Clinical Nutrition* 97 (4): 706–17. https://doi.org/10.3945/ajcn.112.052217.
- Lee, Jeong Soo, Na Young Kim, Se Hee Na, Young Hoon Youn, and Cheung Soo Shin. 2018. "Reference Values of Neutrophil-Lymphocyte Ratio, Lymphocyte-Monocyte Ratio, Platelet-Lymphocyte Ratio, and Mean Platelet Volume in Healthy Adults in South Korea." *Medicine* 97 (26). https://doi.org/10.1097/MD.0000000000011138.
- Leigh, L., J. E. Byles, and C. Jagger. 2016. "BMI and Healthy Life Expectancy in Old and Very Old Women." *British Journal of Nutrition* 116 (4): 692–99. https://doi.org/10.1017/S0007114516002403.
- Lesuis, Nienke, Ragnar Befrits, Filippa Nyberg, and Ronald F van Vollenhoven. 2012. "Gender and the Treatment of Immune-Mediated Chronic Inflammatory Diseases: Rheumatoid Arthritis, Inflammatory Bowel Disease and Psoriasis: An Observational Study." *BMC Medicine* 10 (1): 82. https://doi.org/10.1186/1741-7015-10-82.
- Liu, Wei, Lei Zhang, Hui-Jing Xu, Yan Li, Chuan-Min Hu, Jing-Yan Yang, and Mei-Yan Sun. 2018. "The Anti-Inflammatory Effects of Vitamin D in Tumorigenesis." *International Journal of Molecular Sciences* 19 (9): 2736. https://doi.org/10.3390/ijms19092736.
- Lone, Anna Mari, and Kjetil Taskén. 2013. "Proinflammatory and Immunoregulatory Roles of Eicosanoids in T Cells." *Frontiers in Immunology* 4 (June). https://doi.org/10.3389/fimmu.2013.00130.
- Lopez-Garcia, Esther, Matthias B Schulze, Teresa T Fung, James B Meigs, Nader Rifai, JoAnn

E Manson, and Frank B Hu. 2004. "Major Dietary Patterns Are Related to Plasma Concentrations of Markers of Inflammation and Endothelial Dysfunction." *The American Journal of Clinical Nutrition* 80 (4): 1029–35. https://doi.org/10.1093/ajcn/80.4.1029.

- Lunenfeld, Bruno, and Pamela Stratton. 2013. "The Clinical Consequences of an Ageing World and Preventive Strategies." *Best Practice & Research Clinical Obstetrics & Gynaecology* 27 (5): 643–59. https://doi.org/10.1016/j.bpobgyn.2013.02.005.
- Malik, V. S., V. Sudha, N. M. Wedick, M. RamyaBai, P. Vijayalakshmi, N. Lakshmipriya, R. Gayathri, et al. 2019. "Substituting Brown Rice for White Rice on Diabetes Risk Factors in India: A Randomised Controlled Trial." *British Journal of Nutrition* 121 (12): 1389–97. https://doi.org/10.1017/S000711451900076X.
- Marchioli Roberto, Barzi Federica, Bomba Elena, Chieffo Carmine, Di Gregorio Domenico, Di Mascio Rocco, Franzosi Maria Grazia, et al. 2002. "Early Protection Against Sudden Death by N-3 Polyunsaturated Fatty Acids After Myocardial Infarction." *Circulation* 105 (16): 1897–1903. https://doi.org/10.1161/01.CIR.0000014682.14181.F2.
- Maric-Bilkan, Christine. 2017. "Sex Differences in Micro- and Macro-Vascular Complications of Diabetes Mellitus." *Clinical Science* 131 (9): 833–46. https://doi.org/10.1042/CS20160998.
- Martínez, Inés, James M Lattimer, Kelcie L Hubach, Jennifer A Case, Junyi Yang, Casey G Weber, Julie A Louk, et al. 2013. "Gut Microbiome Composition Is Linked to Whole Grain-Induced Immunological Improvements." *The ISME Journal* 7 (2): 269–80. https://doi.org/10.1038/ismej.2012.104.
- McGill, Carla R., Anne C. Kurilich, and Jean Davignon. 2013. "The Role of Potatoes and Potato Components in Cardiometabolic Health: A Review." *Annals of Medicine* 45 (7): 467–73. https://doi.org/10.3109/07853890.2013.813633.
- Mendham, Amy E., Rob Duffield, Frank Marino, and Aaron J. Coutts. 2015. "Differences in the Acute Inflammatory and Glucose Regulatory Responses between Small-Sided Games and Cycling in Sedentary, Middle-Aged Men." *Journal of Science and Medicine in Sport* 18 (6): 714–19. https://doi.org/10.1016/j.jsams.2014.09.008.
- Mikkelsen, U. R., C. Couppé, A. Karlsen, J. F. Grosset, P. Schjerling, A. L. Mackey, H. H. Klausen, S. P. Magnusson, and M. Kjær. 2013. "Life-Long Endurance Exercise in Humans: Circulating Levels of Inflammatory Markers and Leg Muscle Size." *Mechanisms of Ageing and Development* 134 (11–12): 531–40. https://doi.org/10.1016/j.mad.2013.11.004.
- Milani, Richard V, Carl J Lavie, and Mandeep R Mehra. 2004. "Reduction in C-Reactive Protein through Cardiac Rehabilitation and Exercise Training." *Journal of the American College of Cardiology* 43 (6): 1056–61. https://doi.org/10.1016/j.jacc.2003.10.041.
- Minciullo, Paola Lucia, Antonino Catalano, Giuseppe Mandraffino, Marco Casciaro, Andrea Crucitti, Giuseppe Maltese, Nunziata Morabito, Antonino Lasco, Sebastiano Gangemi, and Giorgio Basile. 2016. "Inflammaging and Anti-Inflammaging: The Role of Cytokines in Extreme Longevity." *Archivum Immunologiae et Therapiae Experimentalis* 64 (2): 111–26. https://doi.org/10.1007/s00005-015-0377-3.
- M.M. Antunes, Bárbara, Fabrício E. Rossi, Jason M. Cholewa, and Fábio S. Lira. 2016. "Regular Physical Activity and Vascular Aging." *Current Pharmaceutical Design* 22 (24): 3715–29.

https://doi.org/10.2174/1381612822666160322144724.
- Montonen, Jukka, Heiner Boeing, Andreas Fritsche, Erwin Schleicher, Hans-Georg Joost, Matthias B. Schulze, Annika Steffen, and Tobias Pischon. 2013. "Consumption of Red Meat and Whole-Grain Bread in Relation to Biomarkers of Obesity, Inflammation, Glucose Metabolism and Oxidative Stress." *European Journal of Nutrition* 52 (1): 337–45. https://doi.org/10.1007/s00394-012-0340-6.
- Mora, Samia, Nancy Cook, Julie E. Buring, Paul M Ridker, and I-Min Lee. 2007. "Physical Activity and Reduced Risk of Cardiovascular Events: Potential Mediating Mechanisms." *Circulation* 116 (19): 2110–18. https://doi.org/10.1161/CIRCULATIONAHA.107.729939.
- Morrisette-Thomas, Vincent, Alan A. Cohen, Tamàs Fülöp, Éléonor Riesco, Véronique Legault, Qing Li, Emmanuel Milot, Françis Dusseault-Bélanger, and Luigi Ferrucci. 2014. "Inflamm-Aging Does Not Simply Reflect Increases in pro-Inflammatory Markers." *Mechanisms of Ageing and Development* 139 (July): 49–57. https://doi.org/10.1016/j.mad.2014.06.005.
- Mutschler, Ernst, Hans-Georg Schaible, Peter Vaupel, and Gerhard Thews. 2007. *Anatomie, Physiologie, Pathophysiologie des Menschen: 140 Tabellen*. 6., völlig überarb. und erw. Aufl. Stuttgart: Wiss. Verl.-Ges.
- National Research Council (U.S.), ed. 2001. *Preparing for an Aging World: The Case for Cross-National Research*. Washington, D.C: National Academy Press.
- Nimmo, M. A., M. Leggate, J. L. Viana, and J. A. King. 2013. "The Effect of Physical Activity on Mediators of Inflammation." *Diabetes, Obesity & Metabolism* 15 Suppl 3 (September): 51–60. https://doi.org/10.1111/dom.12156.
- Olovnikov, Alexey M. 1996. "Telomeres, Telomerase, and Aging: Origin of the Theory." *Experimental Gerontology* 31 (4): 443–48. https://doi.org/10.1016/0531-5565(96)00005-8.
- Ortega, Rosa M. 2015. "Métodos de Evaluación de La Ingesta Actual: Registro o Diario Dietético." *NUTRICION HOSPITALARIA*, no. 3 (February): 38–45. https://doi.org/10.3305/nh.2015.31.sup3.8749.
- Orzechowski, Arkadiusz. 2017. "Cytokines in Skeletal Muscle Growth and Decay." In *The Plasticity of Skeletal Muscle*, edited by Kunihiro Sakuma, 113–39. Singapore: Springer Singapore. https://doi.org/10.1007/978-981-10-3292-9_5.
- Pedersen, B. K., and B. Saltin. 2015. "Exercise as Medicine - Evidence for Prescribing Exercise as Therapy in 26 Different Chronic Diseases." *Scandinavian Journal of Medicine & Science in Sports* 25 Suppl 3 (December): 1–72. https://doi.org/10.1111/sms.12581.
- Pedersen, Bente K. 2013. "Muscle as a Secretory Organ." *Comprehensive Physiology* 3 (3): 1337–62. https://doi.org/10.1002/cphy.c120033.
- Pedersen, Bente Klarlund. 2012. "Muscular Interleukin-6 and Its Role as an Energy Sensor." *Medicine and Science in Sports and Exercise* 44 (3): 392–96. https://doi.org/10.1249/MSS.0b013e31822f94ac.
- Pellegrinelli, Vanessa, Christine Rouault, Sergio Rodriguez-Cuenca, Victorine Albert, Frédérique Edom-Vovard, Antonio Vidal-Puig, Karine Clément, Gillian S. Butler-Browne, and Danièle Lacasa. 2015. "Human Adipocytes Induce Inflammation and Atrophy in Muscle

Cells During Obesity." *Diabetes* 64 (9): 3121–34. https://doi.org/10.2337/db14-0796.
- Petersen, Anne Marie W., and Bente Klarlund Pedersen. 2005. "The Anti-Inflammatory Effect of Exercise." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 98 (4): 1154–62. https://doi.org/10.1152/japplphysiol.00164.2004.
- Pfeifer, Klaus, and Alfred Rütten. 2017. "Nationale Empfehlungen für Bewegung und Bewegungsförderung." *Das Gesundheitswesen* 79 (S 01): S2–3. https://doi.org/10.1055/s-0042-123346.
- Phillips, Wayne T., and Joana R. Ziuraitis. 2004. "Energy Cost of Single-Set Resistance Training in Older Adults." *Journal of Strength and Conditioning Research* 18 (3): 606–9. https://doi.org/10.1519/1533-4287(2004)18<606:ECOSRT>2.0.CO;2.
- Plaisance, Eric P, and Peter W Grandjean. 2006. "Physical Activity and High-Sensitivity C-Reactive Protein:" *Sports Medicine* 36 (5): 443–58. https://doi.org/10.2165/00007256-200636050-00006.
- Pradhan, Aruna D. 2001. "C-Reactive Protein, Interleukin 6, and Risk of Developing Type 2 Diabetes Mellitus." *JAMA* 286 (3): 327. https://doi.org/10.1001/jama.286.3.327.
- Prattichizzo, Francesco, Valeria De Nigris, Lucia La Sala, Antonio Domenico Procopio, Fabiola Olivieri, and Antonio Ceriello. 2016. "'Inflammaging' as a Druggable Target: A Senescence-Associated Secretory Phenotype—Centered View of Type 2 Diabetes." *Oxidative Medicine and Cellular Longevity* 2016. https://doi.org/10.1155/2016/1810327.
- Proctor, M. J., D. C. McMillan, D. S. Morrison, C. D. Fletcher, P. G. Horgan, and S. J. Clarke. 2012. "A Derived Neutrophil to Lymphocyte Ratio Predicts Survival in Patients with Cancer." *British Journal of Cancer* 107 (4): 695–99. https://doi.org/10.1038/bjc.2012.292.
- Rahman, Irfan, and Debasis Bagchi, eds. 2014. *Inflammation, Advancing Age and Nutrition: Research and Clinical Interventions*. 1st ed. Amsterdam ; Boston: Academic Press.
- Reddivari, Lavanya, Tianmin Wang, Binning Wu, and Shiyu Li. 2019. "Potato: An Anti-Inflammatory Food." *American Journal of Potato Research* 96 (2): 164–69. https://doi.org/10.1007/s12230-018-09699-z.
- Reifen, Ram. 2002. "Vitamin A as an Anti-Inflammatory Agent." *Proceedings of the Nutrition Society* 61 (3): 397–400. https://doi.org/10.1079/PNS2002172.
- Reihmane, Dace, and Flemming Dela. 2014. "Interleukin-6: Possible Biological Roles during Exercise." *European Journal of Sport Science* 14 (3): 242–50. https://doi.org/10.1080/17461391.2013.776640.
- Rembach, Alan, Andrew D. Watt, William J. Wilson, Stephanie Rainey-Smith, Kathryn A. Ellis, Christopher C. Rowe, Victor L. Villemagne, et al. 2014. "An Increased Neutrophil-Lymphocyte Ratio in Alzheimer's Disease Is a Function of Age and Is Weakly Correlated with Neocortical Amyloid Accumulation." *Journal of Neuroimmunology* 273 (1–2): 65–71. https://doi.org/10.1016/j.jneuroim.2014.05.005.
- Ren, Ke, and Richard Torres. 2009. "Role of Interleukin-1β during Pain and Inflammation." *Brain Research Reviews* 60 (1): 57–64. https://doi.org/10.1016/j.brainresrev.2008.12.020.
- Robert Koch Institut. 2011. "DEGS-Ernährungsfragebogen."
- Rogers, Robert S., E. Matthew Morris, Joshua L. Wheatley, Ashley E. Archer, Colin S.

McCoin, Kathleen S. White, David R. Wilson, et al. 2016. "Deficiency in the Heat Stress Response Could Underlie Susceptibility to Metabolic Disease." *Diabetes* 65 (11): 3341–51. https://doi.org/10.2337/db16-0292.

- Rumore, M. M. 1993. "Vitamin A as an Immunomodulating Agent." *Clinical Pharmacy* 12 (7): 506–14.
- Salamat, Khalid Mohamadzadeh, Mohammad Ali Azarbayjani, Ashril Yusof, and Firouzeh Dehghan. 2016. "The Response of Pre-Inflammatory Cytokines Factors to Different Exercises (Endurance, Resistance, Concurrent) in Overweight Men." *Alexandria Journal of Medicine* 52 (4): 367–70. https://doi.org/10.1016/j.ajme.2015.12.007.
- Sam, S., S. Haffner, M. H. Davidson, R. B. D'Agostino, S. Feinstein, G. Kondos, A. Perez, and T. Mazzone. 2009. "Relation of Abdominal Fat Depots to Systemic Markers of Inflammation in Type 2 Diabetes." *Diabetes Care* 32 (5): 932–37. https://doi.org/10.2337/dc08-1856.
- Shephard, Roy J. 2002. "Cytokine Responses to Physical Activity, with Particular Reference to IL-6: Sources, Actions, and Clinical Implications." *Critical Reviews in Immunology* 22 (3): 165–82.
- Staessen, J., R. Fagard, and A. Amery. 1988. "The Relationship between Body Weight and Blood Pressure." *Journal of Human Hypertension* 2 (4): 207–17.
- Starkie, Rebecca, Sisse Rye Ostrowski, Sune Jauffred, Mark Febbraio, and Bente Klarlund Pedersen. 2003. "Exercise and IL-6 Infusion Inhibit Endotoxin-Induced TNF-Alpha Production in Humans." *FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology* 17 (8): 884–86. https://doi.org/10.1096/fj.02-0670fje.
- Steensberg, Adam, Christian P. Fischer, Charlotte Keller, Kirsten Møller, and Bente Klarlund Pedersen. 2003. "IL-6 Enhances Plasma IL-1ra, IL-10, and Cortisol in Humans." *American Journal of Physiology. Endocrinology and Metabolism* 285 (2): E433-437. https://doi.org/10.1152/ajpendo.00074.2003.
- Steverson, M. 2018. "Aging and Health." World Health Organization (WHO). https://www.who.int/news-room/fact-sheets/detail/ageing-and-health.
- St-Onge, Marie-Pierre, and Dympna Gallagher. 2010. "Body Composition Changes with Aging: The Cause or the Result of Alterations in Metabolic Rate and Macronutrient Oxidation?" *Nutrition* 26 (2): 152–55. https://doi.org/10.1016/j.nut.2009.07.004.
- Strandberg, Timo E., and Reijo S. Tilvis. 2000. "C-Reactive Protein, Cardiovascular Risk Factors, and Mortality in a Prospective Study in the Elderly." *Arteriosclerosis, Thrombosis, and Vascular Biology* 20 (4): 1057–60. https://doi.org/10.1161/01.ATV.20.4.1057.
- Szic, Katarzyna Szarc vel, Ken Declerck, Melita Vidaković, and Wim Vanden Berghe. 2015. "From Inflammaging to Healthy Aging by Dietary Lifestyle Choices: Is Epigenetics the Key to Personalized Nutrition?" *Clinical Epigenetics* 7 (1): 33. https://doi.org/10.1186/s13148-015-0068-2.
- Tayebi Khosroshahi, Hamid, Nosratola D. Vaziri, Behzad Abedi, Bahlol Habibi Asl, Morteza Ghojazadeh, Wanghui Jing, and Amir Mansur Vatankhah. 2018. "Effect of High Amylose Resistant Starch (HAM-RS2) Supplementation on Biomarkers of Inflammation and Oxidative Stress in Hemodialysis Patients: A Randomized Clinical Trial: Use of Dietary Amylose in

ESRD Patients." *Hemodialysis International* 22 (4): 492–500. https://doi.org/10.1111/hdi.12653.

- Timpson, N J, B G Nordestgaard, R M Harbord, J Zacho, T M Frayling, A Tybjærg-Hansen, and G Davey Smith. 2011. "C-Reactive Protein Levels and Body Mass Index: Elucidating Direction of Causation through Reciprocal Mendelian Randomization." *International Journal of Obesity* 35 (2): 300–308. https://doi.org/10.1038/ijo.2010.137.
- Ulu, Sena Memnune, Mustafa Dogan, Ahmet Ahsen, Abdullah Altug, Kasım Demir, Gürsel Acartürk, and Sibel Inan. 2013. "Neutrophil-to-Lymphocyte Ratio as a Quick and Reliable Predictive Marker to Diagnose the Severity of Diabetic Retinopathy." *Diabetes Technology & Therapeutics* 15 (11): 942–47. https://doi.org/10.1089/dia.2013.0097.
- Vella, Chantal, Matthew Allison, Mary Cushman, Nancy Jenny, Mary Miles, Britta Larsen, Susan Lakoski, Erin Michos, and Michael Blaha. 2017. "Physical Activity and Adiposity-Related Inflammation: The MESA." *Medicine & Science in Sports & Exercise* 49 (5): 915–21. https://doi.org/10.1249/MSS.0000000000001179.
- Vermeire, Séverine, Gert Van Assche, and Paul Rutgeerts. 2005. "The Role of C-Reactive Protein as an Inflammatory Marker in Gastrointestinal Diseases." *Nature Clinical Practice Gastroenterology & Hepatology* 2 (12): 580–86. https://doi.org/10.1038/ncpgasthep0359.
- Vermeulen, Esther, Ingeborg A. Brouwer, Karien Stronks, Stefania Bandinelli, Luigi Ferrucci, Marjolein Visser, and Mary Nicolaou. 2018. "Inflammatory Dietary Patterns and Depressive Symptoms in Italian Older Adults." *Brain, Behavior, and Immunity* 67 (January): 290–98. https://doi.org/10.1016/j.bbi.2017.09.005.
- Vijayaraghava, Ambarish, and Venkatesh Doreswamy. 2017. "Exercise and the Cytokines-Interleukin-6 (IL-6) and Tumor Necrosis Factor-α (TNF-α): A Review." *Annals of Medical Physiology* 1 (1): 3–8. https://doi.org/10.23921/amp.2017v1i1.263485.
- Visser, M., L. M. Bouter, G. M. McQuillan, M. H. Wener, and T. B. Harris. 2001. "Low-Grade Systemic Inflammation in Overweight Children." *PEDIATRICS* 107 (1): e13–e13. https://doi.org/10.1542/peds.107.1.e13.
- Vitaglione, Paola, Ilario Mennella, Rosalia Ferracane, Angela A Rivellese, Rosalba Giacco, Danilo Ercolini, Sean M Gibbons, et al. 2015. "Whole-Grain Wheat Consumption Reduces Inflammation in a Randomized Controlled Trial on Overweight and Obese Subjects with Unhealthy Dietary and Lifestyle Behaviors: Role of Polyphenols Bound to Cereal Dietary Fiber." *The American Journal of Clinical Nutrition* 101 (2): 251–61. https://doi.org/10.3945/ajcn.114.088120.
- Wang, Jinyu, Kwok-Sui Leung, Simon Kwoon-Ho Chow, and Wing-Hoi Cheung. 2017. "Inflammation and Age-Associated Skeletal Muscle Deterioration (Sarcopaenia)." *Journal of Orthopaedic Translation* 10 (July): 94–101. https://doi.org/10.1016/j.jot.2017.05.006.
- Watson, Kathleen B., Susan A. Carlson, Janelle P. Gunn, Deborah A. Galuska, Ann O'Connor, Kurt J. Greenlund, and Janet E. Fulton. 2016. "Physical Inactivity Among Adults Aged 50 Years and Older — United States, 2014." *MMWR. Morbidity and Mortality Weekly Report* 65 (36): 954–58. https://doi.org/10.15585/mmwr.mm6536a3.

- Weil, Richard. n.d. "Resistance Training Exercises: Benefits, Definition & Examples." EMedicineHealth. Accessed August 19, 2019. https://www.emedicinehealth.com/strength_training/article_em.htm.
- Weon, Byung Mook, and Jung Ho Je. 2009. "Theoretical Estimation of Maximum Human Lifespan." *Biogerontology* 10 (1): 65–71. https://doi.org/10.1007/s10522-008-9156-4.
- WHO. 2010. *Global Recommendations on Physical Activity for Health*. Genève: WHO.
- ———. 2019a. "Global Strategy on Diet, Physical Activity and Health." WHO. 2019. http://www.who.int/dietphysicalactivity/pa/en/.
- ———. 2019b. "What Is Moderate-Intensity and Vigorous-Intensity Physical Activity?" WHO. 2019. https://www.who.int/dietphysicalactivity/physical_activity_intensity/en/.
- ———. 2020. "Physical Activity and Older Adults Recommended Levels of Physical Activity for Adults Aged 65 and Above."
- Windsor, Mark T., Tom G. Bailey, Maria Perissiou, Lara Meital, Jonathan Golledge, Fraser D. Russell, and Christopher D. Askew. 2018. "Cytokine Responses to Acute Exercise in Healthy Older Adults: The Effect of Cardiorespiratory Fitness." *Frontiers in Physiology* 9 (March). https://doi.org/10.3389/fphys.2018.00203.
- Xu, Yujie, Qianyi Wan, Jinhua Feng, Liang Du, Ka Li, and Yong Zhou. 2018. "Whole Grain Diet Reduces Systemic Inflammation: A Meta-Analysis of 9 Randomized Trials." *Medicine* 97 (43): e12995. https://doi.org/10.1097/MD.0000000000012995.
- You, Jie, Gui-Qi Zhu, Linka Xie, Wen-Yue Liu, Liang Shi, Ou-Chen Wang, Zong-Hai Huang, Martin Braddock, Gui-Long Guo, and Ming-Hua Zheng. 2016. "Preoperative Platelet to Lymphocyte Ratio Is a Valuable Prognostic Biomarker in Patients with Colorectal Cancer." *Oncotarget* 7 (18): 25516–27. https://doi.org/10.18632/oncotarget.8334.
- Zahorec, R. 2001. "Ratio of Neutrophil to Lymphocyte Counts--Rapid and Simple Parameter of Systemic Inflammation and Stress in Critically Ill." *Bratislavske Lekarske Listy* 102 (1): 5–14.
- Zhang, Jun-Ming, and Jianxiong An. 2007. "Cytokines, Inflammation, and Pain:" *International Anesthesiology Clinics* 45 (2): 27–37. https://doi.org/10.1097/AIA.0b013e318034194e.
- Zhang, Songwen, Qiangyuan Liu, Juan Wang, and Douglas C. Harnish. 2009. "Suppression of Interleukin-6-Induced C-Reactive Protein Expression by FXR Agonists." *Biochemical and Biophysical Research Communications* 379 (2): 476–79. https://doi.org/10.1016/j.bbrc.2008.12.117.
- Zuo, Prather, Stetskiv, Garrison, Meade, Peace, and Zhou. 2019. "Inflammaging and Oxidative Stress in Human Diseases: From Molecular Mechanisms to Novel Treatments." *International Journal of Molecular Sciences* 20 (18): 4472. https://doi.org/10.3390/ijms20184472.

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10 Appendix

10.1 Tables

Tabel 38. Correlation of Inflammation Indices and food groups

		Neutrophil-to-lymphocyte ratio (NLR)	Platelet-to-lymphocyte ratio (PLR)	Systemic Immune Inflammation Index (SII)
Fruit consumption	correlation coefficient	0.045	0.096	0.05
	Sig. (2-tailed)	0.612	0.28	0.571
vegetable consumption	correlation coefficient	0.023	0.024	0.022
	Sig. (2-tailed)	0.799	0.789	0.801
Meat consumption	correlation coefficient	0.191*	0.016	0.093
	Sig. (2-tailed)	**0.030**	0.857	0.292
Cereals/-products, potatoes and rice	correlation coefficient	0.155	0.052	0.146
	Sig. (2-tailed)	0.08	0.557	0.099
Highly processed food consumption	correlation coefficient	0.05	0.01	0.066
	Sig. (2-tailed)	0.577	0.912	0.457
dairy and dairy products	correlation coefficient	-0.01	0.085	0.011
	Sig. (2-tailed)	0.908	0.34	0.905
fish consumption	correlation coefficient	-0.127	0.008	-0.122
	Sig. (2-tailed)	0.152	0.931	0.169
alcohol consumption	correlation coefficient	-0.144	0.095	-0.029
	Sig. (2-tailed)	0.104	0.284	0.747

Significant correlation (*) ≦0,05

10.2 Food diary

Exemplary extract of the 3-day food diary. The following template is the original one, used in the "*BEginn Study*", thus it is in German language.

Hinweise zur Erstellung eines Ernährungsprotokolls

- Bitte führen Sie das Ernährungsprotokoll über **3 Tage** und zwar an 2 Wochentagen und 1 Tag am Wochenende, Somit ergibt sich daraus:
Donnerstag, Freitag, Samstag vor dem jeweiligen Untersuchungstag

- **Ändern** Sie in diesem Zeitraum ihre **üblichen Ernährungsgewohnheiten nicht**

- Erfassen Sie in diesem Zeitraum **alles**, was Sie essen und trinken (auch Bonbons usw,)

- Tragen Sie, wenn möglich, alle Lebensmittel **sofort** in Ihr Protokoll ein, vermeiden Sie es, Ihre Angaben abends nachzutragen

- Angabe der Lebensmittelmengen in **Haushaltsmaßen** und/oder **Gramm** z, B, Teelöffel, Esslöffel, Tasse, Becher, Portion

- Bei abgepackten Lebensmitteln oder **Fertigprodukten** bitte den **Hersteller** (Marke, Firma) und die Menge in Gramm angeben (Jogurt, Pizza, Konserven, Abtropfgewicht...) - Achten Sie auf den **Fettgehalt** der Lebensmittel (z, B, Milch 1,5% oder 3,5%)

Beispiel

Tag: 1 Montag	Datum: 15,04,2000	Gewicht: 88kg

-

Uhrzeit	Menge (Gramm, Haushaltsmaße)	Lebensmittel, Getränk	Grund/Anlass
7,30	1 Becher (200 ml) 1geh, TL 1 1 gestrichener EL 1 Scheibe 1 Scheibe	Kaffee Zucker Brötchen Margarine Mortadella Gouda (45% F, i, Tr,)	Gewohnheit, selber gemacht
10,00	1 1 Glas	Banane Apfelschorle	Hunger
12,30	1 1 EL 3 kleine 1 Portion 2 Soßenkellen 1 Portion 1 Glas	Schweineschnitzel paniert Sonnenblumenöl Kartoffeln Blumenkohl Holländische Soße Schokopudding Cola	Hunger, Kantine
16,00	1 Stück 2 Tassen (150 ml)	Marmorkuchen Kaffee mit Milch (3,5%)	Lust auf Süßes, Dr, Oetker
19,00	2 Stück 1 Portion 1 Flasche	Pizza (Hackfleisch) Salat (Gurke, Tomate, Eisberg, Mais, Zwiebel) Essig/Öl Bier	Gäste zum Abendessen, TK
21,00-23,30	1 kleine Tüte (75 g) ½ Tafel 1 Flasche (0,7 l)	Kartoffelchips Schokolade Mineralwasser	s,o,

10.3 Food frequency questionnaire

Exemplary extract of the food-frequency-questionnaire used in the *BEGinn- Study*, thus it's in German language.

Food Frequency Questionnaire (FFQ)

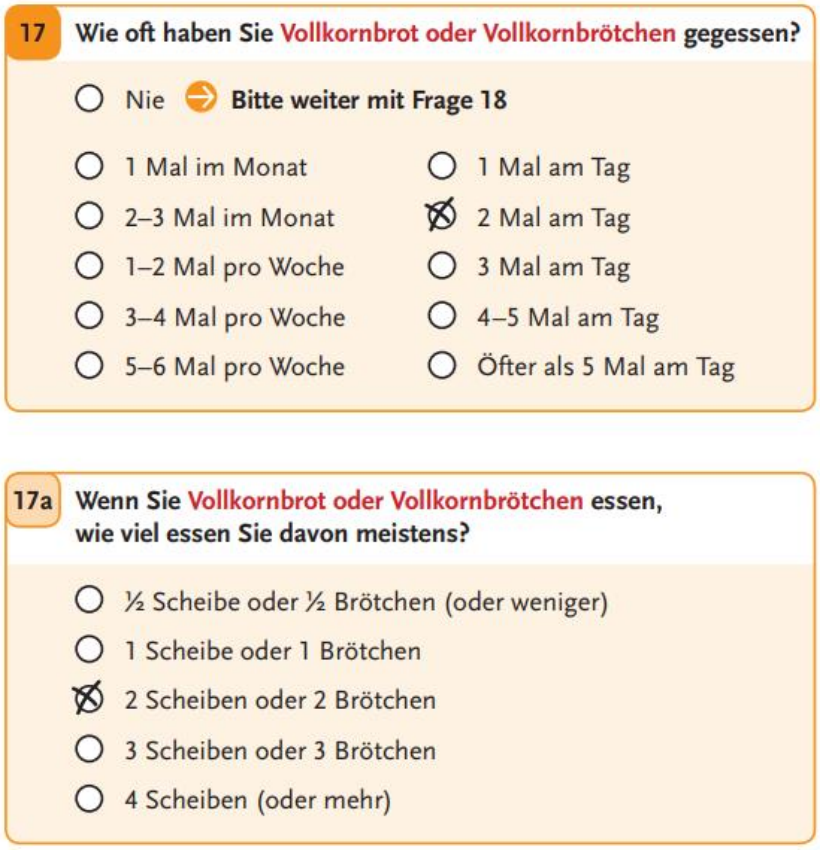
Wir freuen uns, dass Sie an unserer Studie teilnehmen!

Essen und Trinken haben viel mit Gesundheit zu tun. Um diese Zusammenhänge besser verstehen zu können, möchten wir Sie bitten, diesen Fragebogen auszufüllen. Bitte geben Sie den ausgefüllten Fragebogen am Untersuchungstag bei uns ab.

Wie wird's gemacht?

- • Bitte benutzen Sie zum Ausfüllen keinen Bleistift, sondern möglichst einen blauen oder schwarzen Kugelschreiber.
- • Sie werden gefragt, wie oft und in welcher Menge Sie in den letzten vier Wochen verschiedene Lebensmittel gegessen haben. Denken Sie dabei auch an Mahlzeiten, die Sie außer Haus (z. B. im Restaurant, in der Kantine) eingenommen haben.
- • Bitte beantworten Sie jede Frage. Wenn Sie sich nicht sicher sind, dann schätzen Sie. Eine ungefähre Schätzung ist besser als gar keine Antwort. t Denken Sie bitte nur an Ihre Ernährung in den letzten vier Wochen!

- • Es kommt vielleicht vor, dass Sie bestimmte Sachen nicht essen oder trinken. Kreuzen Sie dann bitte „nie“ an und gehen weiter zur nächsten Frage.
- • Bei den Mengenangaben geht es um die durchschnittliche Menge.
- • Bitte bei jeder Frage nur eine Antwort ankreuzen.
  Beispiel: Sie essen morgens 1 Vollkornbrötchen und abends 3 Scheiben Vollkornbrot. Bitte kreuzen Sie dann wie unten „2 Mal am Tag“ und als Menge „2 Scheiben“ (den Durchschnitt) an:

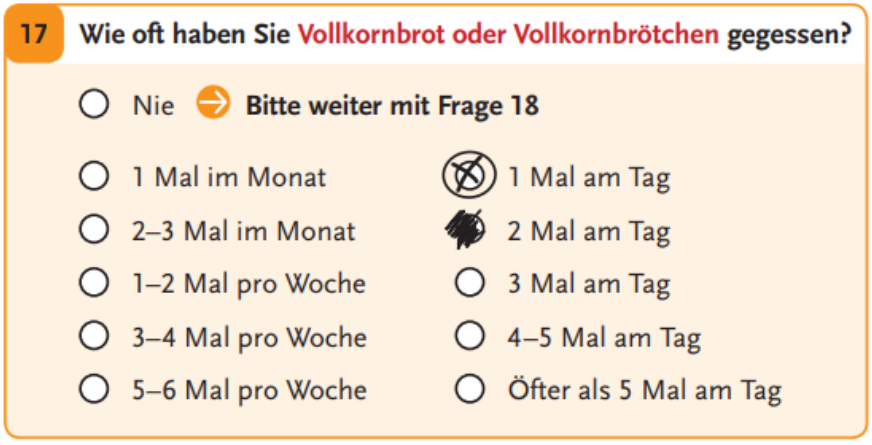


• Wenn Sie eine Antwort korrigieren möchten, schwärzen Sie die falsche Angabe, kreuzen Sie die richtige an und machen Sie zusätzlich einen Kreis um die richtige Antwort.

Beispiel: Sie essen nicht 2 Mal am Tag, sondern nur 1 Mal Vollkornbrot. Korrigieren Sie die Frage bitte wie folgt:

Die Einhaltung des Datenschutzes und die Wahrung der Vertraulichkeit sind uns wichtige Anliegen. **Bitte notieren Sie daher nicht Ihren Namen oder Ihre Telefonnummer auf dem Fragebogen.**

Wenn Sie Rückfragen zum Ausfüllen des Fragenbogens haben, wenden Sie sich bitte direkt an unser Studienteam. Die Mitarbeiterinnen und Mitarbeiter helfen Ihnen gern.



17 **Wie oft haben Sie Vollkornbrot oder Vollkornbrötchen gegessen?**

- ○ Nie → **Bitte weiter mit Frage 18**
- ○ 1 Mal im Monat
- ○ 2–3 Mal im Monat
- ○ 1–2 Mal pro Woche
- ○ 3–4 Mal pro Woche
- ○ 5–6 Mal pro Woche
- ⊗ 1 Mal am Tag
- ● 2 Mal am Tag
- ○ 3 Mal am Tag
- ○ 4–5 Mal am Tag
- ○ Öfter als 5 Mal am Tag

Der vorliegende Ernährungsfragebogen stammt aus der Studie zur Gesundheit Erwachsender in Deutschland (DEGS Studie) und wird mit freundlicher Genehmigung des Robert Koch- Instituts verwendet.

In den letzten 4 Wochen...

Bitte bei jeder Frage nur eine Antwort ankreuzen!

a **Wann sind Sie geboren?**

☐☐ Monat ☐☐ Jahr (1 9 ☐ ☐)

b **Welches Geschlecht haben Sie?**

- ○ Männlich
- ○ Weiblich

1 **Wie oft haben Sie in den letzten 4 Wochen Milch (einschließlich Milch für Kaffee, Müsli) getrunken?**

- ○ Nie → **Bitte weiter mit Frage 2**
- ○ 1 Mal im Monat
- ○ 2–3 Mal im Monat
- ○ 1–2 Mal pro Woche
- ○ 3–4 Mal pro Woche
- ○ 5–6 Mal pro Woche
- ○ 1 Mal am Tag
- ○ 2 Mal am Tag
- ○ 3 Mal am Tag
- ○ 4–5 Mal am Tag
- ○ Öfter als 5 Mal am Tag

1a **Wenn Sie Milch trinken, wie viel trinken Sie davon meistens?**

- ○ ½ Glas (oder weniger)
- ○ 1 Glas (200 ml)
- ○ 2 Gläser
- ○ 3 Gläser
- ○ 4 Gläser (oder mehr)

1b **Welche Art von Milch trinken Sie meistens?**

- ○ Vollmilch (mindestens 3,5 % Fett)
- ○ Fettarme Milch (1,5 % Fett)
- ○ Magermilch (max. 0,3 % Fett)
- ○ Sojamilch
- ○ Laktosefreie Milch
- ○ Andere

In den letzten 4 Wochen...

2 **Wie oft haben Sie in den letzten 4 Wochen zuckerhaltige Erfrischungsgetränke (z. B. Cola, Limonade, Eistee, Malzbier, Energiegetränke) getrunken?** Nicht gemeint sind Light-Getränke.

- ○ Nie → **Bitte weiter mit Frage 3**
- ○ 1 Mal im Monat
- ○ 2–3 Mal im Monat
- ○ 1–2 Mal pro Woche
- ○ 3–4 Mal pro Woche
- ○ 5–6 Mal pro Woche
- ○ 1 Mal am Tag
- ○ 2 Mal am Tag
- ○ 3 Mal am Tag
- ○ 4–5 Mal am Tag
- ○ Öfter als 5 Mal am Tag

2a **Wenn Sie zuckerhaltige Erfrischungsgetränke trinken, wie viel trinken Sie davon meistens?**

- ○ ½ Glas (oder weniger)
- ○ 1 Glas (200 ml)
- ○ 2 Gläser
- ○ 3 Gläser
- ○ 4 Gläser (oder mehr)

3 **Wie oft haben Sie kalorienreduzierte Erfrischungsgetränke (z. B. Light-Getränke) getrunken?**

- ○ Nie → **Bitte weiter mit Frage 4**
- ○ 1 Mal im Monat
- ○ 2–3 Mal im Monat
- ○ 1–2 Mal pro Woche
- ○ 3–4 Mal pro Woche
- ○ 5–6 Mal pro Woche
- ○ 1 Mal am Tag
- ○ 2 Mal am Tag
- ○ 3 Mal am Tag
- ○ 4–5 Mal am Tag
- ○ Öfter als 5 Mal am Tag

3a **Wenn Sie kalorienreduzierte Erfrischungsgetränke trinken, wie viel trinken Sie davon meistens?**

- ○ ½ Glas (oder weniger)
- ○ 1 Glas (200 ml)
- ○ 2 Gläser
- ○ 3 Gläser
- ○ 4 Gläser (oder mehr)

10.4 Freiburger Questionnaire to measure the physical activity status

Exemplary extract of the Freiburger questionnaire on physical activity used in the *BEGinn- Study*, thus it's in German language.

Freiburger Fragebogen zur körperlichen Aktivität

1. **Sind Sie berufstätig** (auch Hausfrau) **oder Ausbildung?** ❑ nein ❑ ja

Ihre berufliche Tätigkeit beinhaltet hauptsächlich:

❑ **sitzende Tätigkeit** (z.B. : Büro, Student ...)

❑ **mäßige Bewegung** (z.B.: Handwerker, Hausmeister, Hausfrau ...)

❑ **intensive Bewegung** (z.B.: Briefträger, Wald- u. Bauarbeiter ...)

2. **Waren Sie in der letzten Woche zu Fuß unterwegs.**

a) ... auf dem Weg zur Arbeit oder zum Einkaufen usw.? ❑ nein ❑ ja

Wenn ja, wie lange sind Sie dabei gegangen? **insgesamt** .....Minuten / Stunden

Wie würden Sie ihr „Gehtempo" beschreiben? ❑ gemächlich ❑ normal ❑ zügig

b) ... zum Spazieren gehen? ❑ nein ❑ ja

Wenn ja, wie lange waren Sie letzte Woche spazieren? **insgesamt**.....Minuten / Stunden

Wie würden Sie Ihr „Gehtempo" beschreiben? ❑ gemächlich ❑ normal ❑ zügig

3. **Sind Sie in der letzten Woche Fahrrad gefahren,**

a) ... zur Arbeit oder zum Einkaufen usw.? ❑ nein ❑ ja

Wenn ja, wie lange sind Sie dabei geradelt? **insgesamt** ..... Minuten / Stunden

In welchem Tempo? ❑ gemächlich ❑ normal ❑ zügig

b) ... auf dem Heimtrainer bzw. auf Radtouren? ❑ nein ❑ ja

(aber: **Radsport** unter **Frage 7** angeben)?

Wenn ja, wie lange sind Sie dabei geradelt? **insgesamt** ..... Minuten / Stunden

In welchem Tempo? ❑ gemächlich ❑ normal ❑ schnell

Seite 1 von 4

Freiburger Fragebogen zur körperlichen Aktivität

4. Haben Sie einen Garten? ☐ nein ☐ ja

Wenn ja, wie viel Stunden haben Sie letzte Woche in ihrem Garten verbracht?

..... Stunden pro Woche

Davon sind ..... Stunden Gartenarbeit

und ..... Stunden Ruhe und Erholung

5. Steigen Sie regelmäßig Treppen?

☐ nein

☐ ja, ... Stockwerke, ... mal am Tag

6. Sind Sie im letzten Monat geschwommen?

☐ nein

☐ ja, im Thermalbad ca. ..... Stunden im Monat (reine Schwimmzeit)

im Schwimmbad ca. ..... Stunden im Monat (reine Schwimmzeit)

7. Haben Sie im letzten Monat Sport betrieben? ☐ nein ☐ ja

(Jogging, Radsport, Fußball, Handball Federball, Squash, Gymnastik, Tennis, Tischtennis...)

wenn ja, welchen Sport?

Beispiel:

..... 1 .. Dauerlauf ..... ca. .. 30 .. Minuten / Stunden pro Woche / Monat

..... 2 .. Federball .... 2.. Minuten / Stunden pro Woche / Monat

1. ..... ca. ..... Minuten / Stunden pro Woche / Monat

2. ..... ca. ..... Minuten / Stunden pro Woche / Monat

3. ..... ca. ..... Minuten / Stunden pro Woche / Monat

4. ..... ca. ..... Minuten / Stunden pro Woche / Monat