

The University of Rome "Foro Italico" The German Sport University, Cologne The University of Southern Denmark, Odense The Norwegian School of Sport Sciences, Oslo The University of Vienna

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# "Sedentary behavior, overweight and obesity – a systematic literature review on direction of causality"

Kristine 1 ERCLE

Kristine Veddegjerde Candidate

Maria Hildebrand Supervisor

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#### Abstract

**Background:** Sedentary behavior has emerged as a new field of science, whereas it has been associated with several health problems such as obesity, independent of level of physical activity. However, it is unclear whether sedentary behavior is a cause or a result of overweight or obesity, or vice versa. To date, there is no review of prospective studies that systematically examine this relationship

**Objective:** To provide a systematic literature review of the existing literature of prospective populations-based studies investigating the bidirectional relationship between sedentary behavior and overweight and obesity among non-patient children to middle-aged adults, and to consider the directions of this causality

**Method:** This systematic literature review was conducted according to the PRISMA guideline, and searches were performed in four different databases; PsycINFO, EMBASE, PubMED and Web of Science, with search terms covering sedentary behavior and overweight and obesity.

**Results:** Out of 23,452 articles, 161 articles were assessed for eligibility, and 10 studies were included in the final sample. Most of the studies included children  $\leq$ 11 years old at baseline (n=4) or adults (n=4). Six studies use self-reported sedentary behavior, while the remaining four studies used objective measurements. Whether baseline weight was associated with change in sedentary behavior over time, four studies found no association, while one study found an unfavorable association in second half of the study, and five studies found an adverse association. Whether baseline sedentary behavior was associated with weight gain over time, seven studies found no association, while one study found mixed associations (between various exposure- and outcome variables), and two studies found an adverse association.

**Conclusion:** Current evidence suggests that baseline weight predicts later sedentary behavior, and that the evidence regarding a reverse- or bidirectional relationship to date is not of sufficient quality to determined such relationship. Future well-conducted prospective studies are therefore warranted to increase knowledge in this field as well as to enhance heath-promoting strategies.

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## Abbreviations

B(b)	Unstandardized regression coefficient
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CHD	Coronary Heart Disease
CI	Confidence Interval
CVD	CardioVascular Disease
DALY	Disability-Adjusted Life-Years
DEXA	Dual-Energy X-ray Absorptiometry
DOiT	Dutch Obesity Intervention in Teenagers
DVT	Deep Venous Thrombosis
ECW	ExtraCellular Water
EMA	Ecological Momentary Assessment
FFM	Fat Free Mass
FITT	Frequency, Intensity, Time (duration), Type of activity
FM	Fat Mass
FMI	Fat Mass Index
GLUT	GLUcose Transporter
GSHS	Global School-based student Health Survey
HBSC	Health Behaviour in School-aged Children
НС	Hip Circumference
HDL	High-Density Lipoprotein
HOYVS	Health of Young Victorians Study
HR	Heart Rate
ICAD	International Children Accelerometer Database
IPAQ	International Physical Activity Questionnaire
LPL	LipoProtein Lipase
MET	Metabolic Equivalent units
MVPA	Moderate to Vigorous Physical Activity
NCD	Non-Communicable Diseases
NIH	National Institute of Health
0	Objective
OR	Odd Ratio
PAEE	Physical Activity Energy Expenditure

PR	Parents-Report
RCT	Randomized Controlled Trial
SED	Sedentary behavior
SITT	Sedentary behavior frequency, Interruptions, Time (duration), Type (mode)
SR	Self-Report
TBW	Total Body Water
TV	Television
VO <sub>2</sub>	Oxygen uptake
WC	Waist Circumference
WHO	World Health Organization
z-BMI	Standardized BMI score
β	Standardized regression coefficient

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#### **1.0 Introduction**

Excessive weight and body fat, along with the associated health risks, affects more people worldwide, than underweight (Ng et al., 2014; WHO, 2014). Obesity has been developing as one of the greatest global health challenges in the 21st century (Ekelund, Brage, Besson, Sharp, & Wareham, 2008; Ng et al., 2014), and for the last two decades obesity has been considered a pandemic (Roth, Qiang, Marban, Redelt, & Lowell, 2004), with prevalence of obesity still increasing (WHO, 2014). The understanding of why people become more overweight and obese is still not fully known, but a combination of social, behavioral, cultural, physiological, metabolic and genetic factors are thought to cause the excessive weight gain (NIH, 1998).

Several prospective population-based cohort studies have observed an inverse association between change in physical activity, and follow-up physical activity, and weight gain over time (Fogelholm & Kukkonen-Harjula, 2000). However, the predictive association of physical activity on weight gain is somewhat inconsistent, and the literature on the observed association between physical activity and weight gain is rather uncertain (Fogelholm & Kukkonen-Harjula, 2000; Wareham, van Sluijs, & Ekelund, 2005). The amount of how much physical activity that is enough to prevent weight gain is still unknown, but a recent review of the prospective association of physical activity and weight gain implied that low levels of baseline physical activity only showed weak association with weight gain (Wareham et al., 2005), suggesting there is more than just inactivity affecting weight change. Several researchers have proposed that sedentary behavior is a great risk factor for weight gain or increased BMI (Hu, Li, Colditz, Willet, & Manson, 2003; Raynor, Phelan, Hill, & Wing, 2006), independent of physical activity (Hu et al., 2003).

Many cross-sectional studies have shown that sedentary behavior, and overweight or obesity, are inversely associated (Mortensen, Siegler, Barefoot, Gronbaek, & Sorensen, 2006; Must & Tybor, 2005). Studies have reported that sedentary behavior, and especially TV viewing, is related to increased weight or risk of obesity in adults (Blanck et al., 2007; Hu et al., 2003; Raynor et al., 2006), although no relationship is also reported (Pulsford, Stamatakis, Britton, Brunner, & Hillsdon, 2013). Several reviewed studies have observed a relationship between TV viewing and obesity in young children, while most of the studies of older children are inconsistently (Rey-López, Vicente-Rodríguez, Biosca, & Moreno, 2007). On the other hand,

several studies show that BMI is adverse associated with inactivity, but not vice versa (Metcalf et al., 2011; Mortensen et al., 2006; Petersen, Schnohr, & Sorensen, 2004)

However, sedentary behavior is thought to be a risk factor for overweight and obesity (WHO, 2000), and overweight is thought to be a risk factor for sedentary behaviors (King et al., 1992). Because overweight and obese individuals are less likely to stay active, certainties concerned direction of causality has been lacking in observational studies (Wareham, et al, 2000). Therefor, whether sedentary behavior is a cause or a result of overweight or obesity, or vice versa, is still not fully understood. There is no doubt that both sedentary behavior and excessive weight are contributing to great health risks (Hamilton, Healy, Dunstan, Zderic, & Owen, 2008; WHO, 2014), and a better understanding of these factors could greatly benefit health promotion and –treatment strategies.

In line with emerged research focus on the effect of sedentary behavior (Hamilton, Hamilton, & Zderic, 2007), there is a lack of a systematic literature review of the bidirectional causality of sedentary behavior and weight outcome. Therefor, this paper sought to review the existing literature to better understand the causal relationship between these factors.

#### **1.2 Conceptual clarifications**

Definitions of relevant terms used in the current literature review are presented in table 1.1.

Definition	
"a disease in which excess body fat has accumulated to an	
extent that health may be adversely affected" (WHO, 1997, p 7).	
"waking behaviour characterized by an energy expenditure $\leq 1.5$ metabolic equivalent units (METs) while in a sitting or reclining	
posture" (Sedentary behavior research network, 2012, p).	
"comprises any bodily movement produced by skeletal mucles	
that results in an increase in metabolic rate over resting energy	
expenditure." (Bouchard et al, 2012, p 12.)	

 Table 1.1. Definition of terms used in the present systematic literature review.

#### 2.0 Theory

#### 2.1 Overweight and obesity

Obesity is a complex multifactorial chronic disease caused by a combination of genotype and environment (NIH, 1998). Even though the mechanism behind why people become fatter seems not to be fully understood, overweight and obesity appear to be caused by a combination of social, behavioral, cultural, physiological, metabolic and genetic factors (NIH, 1998). Children and adults all over the world, both in developed- and developing countries, are overweight and obese (Ng et al., 2014). The pandemic of obesity leads to death, mortality and accelerated aging (Roth et al., 2004), and it is undoubted one of the world's greatest health challenges (WHO, 2014).

#### 2.1.1 Prevalence and trends of overweigh and obesity

Obesity prevalence has increased dramatically worldwide since 1980, whereas 39 % of all adults above 18 years old (38% men and 40% women) were classified as overweight in 2014 (WHO, 2014). In the same year, more than half a billion adults were classified as obese, 11 % of all men and 15 % of all women worldwide (WHO, 2014). Between 1980 and 2013, the prevalence of overweight and obesity combined increased by 28 % for adults and 47 % for children (Ng et al., 2013). The proportions of adults being overweight or obese (BMI  $\geq$  25 kg/m2, both self-reported and objectively measured) increased from 29 % to 36 % in men and from 30 % to 38 % in women worldwide. Changes in weight are seen both in developed and developing countries, but with different sex pattern. Overweight and obesity combined seem to be more present in men in developed countries, but more present in women in developing countries. When obesity is observed alone, women seem to have higher prevalence regardless of country. However, the rates of overweight and obesity seem to have slowed down the past decade, especially in developed countries, while it had its steepest increase between 1992 and 2002 (Ng et al., 2013).

From 1980 until 2013, the prevalence of overweight and obesity among children and adolescents in developed countries has increased from 17 % to 24 % in boys and from 16 % to 23 % in girls (Ng et al., 2013). The changes in prevalence among children and adolescents in developing countries, during the same time period, increased from 8 % to 13 % in boys and from 8 % to 13 % in girls. Independent of country, levels and trends of overweight and

obesity have small sex differences (Ng et al., 2013). In 2013, 42 million children worldwide (6 %) younger than five years old were estimated to be overweight (WHO, 2014).

#### 2.1.2 Risk factors for overweight and obesity

As previously mentioned, obesity is a result of a complex combination of environmental factors, genetic predisposition, and human behavior (Nguyen & El-Serag, 2010). There is an agreed understanding that obesity develops as a result of a positive imbalance in energy intake and energy expenditure. Environmental factors are likely to be key determinants to obesity (Nguyen & El-Serag, 2010). There has been a great focus on the "Big Two" risk factors leading to obesity; food marketing practices and technology, and institution-driven reductions in physical activity (Keith et al., 2006). However, a positive imbalance is thought to be a result of a complexity of various factors, rather than one factor alone (WHO, 2000). This means, obesity is caused by more than simply just eating too much, or moving too little (WHO, 2000).

Reduced physical activity and specific food manufacturing and marketing practices, are established risk contributors to the development of obesity (Keith et al., 2006). Risk factors for being physically inactive is further described in the sedentary behavior section, chapter regarding "Determinants of sedentary behavior". Dietary habits, food selection and availability have the potential to alter energy intake (Nguyen & El-Serag, 2010). Kant and Graubard (2006) observed an increase in quantity and energy density of food in the past 30 years. Although results should be interpreted with caution, this increase happened at the same time as overweight and obesity also increased. People do not seem to eat more often, but the food consumed seems to have changed (Kant & Graubard, 2006). Vending machines in schools, increased portion size, increased availability of fast food, sugar-sweetened beverages and fruit juice, and use of high-fructose corn syrup, are examples of specific food manufacturing and marketing practices. Food consumption is affected, although not exclusively, by these aforementioned factors (Kant & Graubard, 2006). Obesity is not only developed because of environmental factors, but also affected by policies towards the availability of high-caloric dense food, the cost of fruits and vegetables, and the built environment (Nguyen & El-Serag, 2010).

 Table 2.1. Summary of established- (bold) and supposed contributors based on existing evidence.

#### CONTRIBUTORS

- > Inactivity
- Dietary and food-related factors
- ➤ Less sleep
- Endocrine disruption (lipophilic, environmentally stable, industrially produced substances that can affect endocrine function.)
- > Exposure to ambient temperatures above or below the Thermo-neutral zone
- Non-smoking (nicotine has a preventive effect on adiposity)
- Certain pharmaceuticals (e.g.
- Age (e.g. slower metabolism with age, potentially more inactive with age)
- Ethnic group
- ➤ Greater maternal age
- Inherited (oocytes affected during epigenetic events or environmental alterations in earlier generations)
- Extremes of energy imbalance in utero (overfeeding or low birth weight)
- Reproductive fitness (genetics)
- ➢ (Assortative mating)

(Keith et al., 2006)

In addition to the putative risk factors for obesity summarized in Table 2.1., socioeconomic status, social relations and genes are also contributors to obesity. Socioeconomic status, whereas low socioeconomic status is as a risk factor, can be explained by people wit high income and/or education tend to report higher level of physical activity, greater health protection activities, and lower levels of risk behaviors (Lopez, 2007). A better access to health care and insurance might also favor people with higher socioeconomic status (Lopez, 2007). Christakis and Fowler (2007) studied social relations and their impact on obesity over 32 years, and concluded that network phenomena seems to be important to the biological and behavioral aspect of obesity. They observed that obesity tended to evolve through social relations across friends, sibling and spouses. Having a friend, who developed obesity in a given timeframe, increased an individual's chance of becoming obese with 57 %. Among sibling-couples, were one of the siblings developed obesity, the other sibling increased their chance of developing obesity with 40 %. Married individual, were the spouse became obese, increased their chance of also becoming obese by 37 %. The phenomena of social relationships seem to have a greater impact on relations of same sex. However, neighborrelationships seem not to have impact on the likelihood of developing obesity (Christakis & Fowler, 2007).

The genetic contribution to obesity can be considered in four different areas; Food intake, adipocyte, exercise activity, and thermogenesis (McPherson, 2007). Food intake regulation, at the level of hypothalamus, is determined by protein coded by genes. Defects at this level, are likely to affect obesity unfavorably. As an example, leptin is produced proportionally with fat storage and affect processes on higher level leading to decreased food intake or increased energy expenditure. Genetic alterations can lead to leptin deficiency, which down regulate its function. At the level of the adipocyte, genetic differences in numerous genes that are part of the fat storing process and processes altering it, can affect obesity. An example is polymorphic variation in peroxisome proliferator-activated receptor gamma (PPAR-y, upregulate expression of numerous essential adipocyte genes regulating triglyceride synthesis and storage), which is associated with obesity and insulin sensitivity. The two last areas concern genetic impact on exercise activity and thermogenesis. Genetic impact on exercise activity is primarily through regulation of spontaneous and intentional activity. Any gene that alters these processes has the potential to affect the total physical activity energy expenditure (PAEE), whereas gene deficiencies in turn can lead to lower PAEE. Gene alterations can also occur in the processes of adaptive thermogenesis (energy regulation in form of heat in response to low temperature exposure or additional energy intake), resulting in variations in energy distribution (McPherson, 2007).

#### 2.1.3 Consequences of overweight and obesity

Obesity is associated with serious health consequences such as mortality, accelerated aging, and illness (Roth et al., 2004). In both men and women, when adiposity exceed beyond normal (e.g. BMI >24,9), there is a progressive increase in risk of death and illness. With BMI as adiposity measurement, the weight–mortality relationship curve show increased risk of mortality in under weighted, a plateau in normal weighted and then an exponentially increase in an adverse association after normal weight (Roth et al., 2004). Worldwide overweight and obesity were estimated to account for 3,4 million deaths in 2010, in addition to 3,9 % of years lost and 3,8 % disability-adjusted life-years (DALYs) (Ng et al., 2013).

Obesity is a risk factor for non-communicable diseases (NCD) such as diabetes type 2, metabolic syndrome and coronary heart disease (WHO, 1997). It is also associated with several life threatening chronic health problems, which can roughly be divided into four areas; cardiovascular problems, conditions associated with insulin resistance, certain types of

cancer, and gallbladder disease and other organ diseases (Roth et al., 2004; WHO, 1997). Other less fatal health problem associated with obesity, are related to respiratory difficulties, chronic muscle-skeletal problems, skin problems and infertility (WHO, 1997). The relative risk of health problems associated with obesity can further be classified as greatly increased (relative risk significantly greater than 3), Moderate increased (relative risk between 2 and 3), and slightly increased (relative risk between 1 and 2) (WHO, 1997).

Well-documented cardiovascular disorders associated with obesity are hypertension, myocardial infarction, and stroke (Roth et al., 2004), which have a moderate increased risk of obesity-related health problems (WHO, 1997). Especially adipose tissue seems to be important to the association between obesity and coronary heart disease (CHD), whereas the degree of abdominal obesity, particularly intra-abdominal fat accumulation, is observed to affect morbidity in general (WHO, 1997). Because intra-abdominal tissue has more cells per unit fat mass, higher blood flow, more glucocorticoid (cortisol) receptors, most likely more androgen (testosterone) receptors, and greater catecholamine-induced lipolysis, than subcutaneous adipose tissue, it is more prone to hormonal stimulation and alterations in lipid accumulation and metabolism. Abdominal obesity is also a major contributor to the progress of insulin resistance and metabolic syndrome (e.g. hyperinsulinaemia, dyslipidaemia, hypertension), which has a greatly increased risk of obesity-related health problems (WHO, 1997). Type 2 Diabetes is the key condition associated with insulin resistance (Roth et al., 2004). When obesity and diabetes are pared, obesity is associated with faster onset, greater prevalence, and a stronger severity of all major old-age related diseases (except osteoporosis), such as in creased risk of dementia (when obesity occurs together with hyperglycemia) (Roth et al., 2004).

A slightly increased risk of obesity-related health issues is seen for cancer and organ diseases (WHO, 1997). Common obesity-associated cancer types are breast cancer in postmenopausal women, endometrial cancer, and colon cancer (Roth et al., 2004; WHO, 1997), whereas typically reported organ diseases are gallbladder disease, digestive diseases (e.g. gastroesophageal reflux disease (GERD), colorectal polyps, and liver disease (Nguyen & El-Serag, 2010)) and hepatic steatosis (which in turn can lead to hepatic dysfunction and cirrhosis) (Roth et al., 2004). Other conditions associated with slightly increased risk of obesity-related health issues are pulmonary diseases like asthma and sleep apnea, osteoarthritis, complications during and after surgery, fertility problems, pregnancy, and

delivery, and an increase in depression and suicide (Roth et al., 2004).

#### 2.1.4 Measurements of overweight and obesity

Body composition can be measured at three different levels (Table 2.2.) (Duren et al., 2008). Simple elements of carbon, calcium, potassium, and hydrogen can be measured *at* the *atomic level*, the extent of water, protein and fat can be assessed at *the molecular level*, and the distribution of adipose, skeletal and muscle tissue can be obtained at *the tissue level*. Measurements performed at atomic- and molecular level are obtained with direct body composition methods, and create the base of indirect measurements, which are used at tissue level. Indirect measurements can also be estimated based on criteria methods, which assess a property of the body (e.g. density, skeletal volume and distribution, muscle, adipose tissue) with x-ray or magnetic imaging techniques. Because indirect measurement methods are based on biological interrelationship between body components measured by direct or criteria methods, and how tissue-measurements are distributed among normal individuals, the methods are usually more prone to predictive errors (Duren et al., 2008).

Independent of measurement method, all body composition methodologies are based on the same assumption (Duren et al., 2008). Methodological assumptions are made from healthy individuals as a reference group concerning density of body tissue, concentrations of water and electrolytes, and/or biological interrelationship about the existence and distribution of body components and body tissues. This in turn makes body composition measurements most suitable for normal healthy individual, whereas the same assumptions are not accurate in individual that are obese or have certain chronic diseases (Duren et al., 2008). Obese individuals have increased total body hydration and adversely affected extracellular water (ECW)- intracellular water ratio, which makes certain body composition measurements less suitable since the assumptions for the assessment tools are not comparable to this population group (Beechy, Galpern, Petrone, & Das, 2012).

	Metho	ods of measurement
CT	$\triangleright$	Dilution technique (Total Body Water, TBW)
	$\triangleright$	Total Body Potassium (TBP) (Total Body Counting/Whole Body Counting)
	$\triangleright$	Neutron activation techniques
RE	$\triangleright$	Near-infrared interactance
DI	$\triangleright$	Three-dimensional photonic scanning
	$\triangleright$	Quantitative magnetic resonance
	$\triangleright$	Multi-compartment methods
A	$\triangleright$	Hydrodensitometry (hydrostatic weighing/underwater weighing)
RL	$\triangleright$	Air Displacement Plethysmography (ADP)
ΤE	$\triangleright$	Dual energy x-ray absorptiometry (DEXA)
RI	$\triangleright$	Computerized tomography scan (CT)
C	$\triangleright$	Magnetic resonance imaging (MRI)
	$\triangleright$	Anthropometrics
INDIRECT		• Body weight and height
		• Body mass index (BMI)
		• Abdominal circumference ("Waist" Circumference, WC)
		Skinfold thickness
	$\triangleright$	Bioelectrical Impedance Analysis (BIA)
	$\succ$	Bio Impedance Spectroscopy (BIS)
		(December at al. 2012)

 Table 2.2. Overview of methods to measure body composition.

(Beechy et al., 2012)

Measurement methods for body composition assessments are entirely performed objectively, except measurements of height and weight, which can also be subjectively obtained (Duren et al., 2008). Self- and proxy reported- and interview reported weight and height are frequently used in research (Atkin et al., 2012). Self- or proxy reported questionnaires are beneficial for their low distribution cost, low participation- and researcher burden and potential to reach many participants. However, subjective reports are limited by reporting bias, whereas subject might not know their weight and height accurate, or they report a socially desired weight (Atkin et al., 2012).

#### **Direct measurements**

The most common direct measurement methods are total body water (TBW), total body counting (whole body counting) and neutron activation (Duren et al., 2008). TBW is assessed by isotope dilution. Since water and fat free mass stay relative stably associated with each other, FFM and fat mass (e.g. total body weight minus FFM) can be predicted from the water/isotope-dilution volumes measured. A weakness, as with other method based on certain assumption of water, fat- and FFM relationships, is increased risk of estimating bias in overweighed individuals. The theory behind this method assume that 73 % of FFM is TBW,

even though the proportion can range between 67 -80 % depended on weight, and that around 15-30 % of TBW is located in adipose tissue (as extracellular fluid). These associations are altered with excess weight, whereas the proportion of TBW in adipose tissue increase with increased weight. Another limitation that can cause measurement bias is the equilibration time for the isotope concentration among different body types. The relationship between equilibration time and fatness is not fully understood, but theoretically the isotope dilution is though to have a longer equilibration time in obese individuals compared with normal weight individuals. However, the method could be considered for use in obese individual when used with caution. The low participant burden is a major strength, whereas the subjects only drink an isotope mix and obtain a urine sample (Duren et al., 2008).

#### Total body counting measure

Total body counting measure naturally radioactive potassium (most present intracellular ion) in the body using a whole body counter (Beechy et al., 2012; Duren et al., 2008). Potassium is almost exclusively found in body cell mass, which is the metabolically active part of the human body. By quantifying the amount of potassium present in the body, it is possible to estimate FFM (based on an assumption of constant amount of potassium present in FFM) and metabolism. This method has some limitations whereas the counting equipment is very expensive, limited to few holder (e.g. in America) and lack of strong support for accuracy. Estimation of FFM, and thereby fat mass, is dependent on an assumption of water-content in FFM, and can be altered with changes in hydration (especially in severe obese individuals) (Beechy et al., 2012; Duren et al., 2008)

#### Neutron activation

Neutron activation is a measurement method where the participants get exposed to a neutron field so that the cell nucleus can react on the exposure and produce gamma radiation (Duren et al., 2008). The gamma output is measured by a body scan assessed as the cell nucleus' return to normal state. The measurement method is considered as of high accuracy, with a broad variation of potentially measurements. Carbon, nitrogen, sodium and calcium are among elements that can be measured. FFM is calculated by the amount of protein in the body predicted by measured nitrogen. A key limitation is concerned the high level of neutron radiation that the participants are exposed to (Duren et al., 2008).

#### Criteria measurements

#### Hydrodensitometry

Hydrodensitometry and dual-energy x-ray absorptiometry (DEXA are two of the most common measurement methods used as criteria methods (Duren et al., 2008). Hydrodensitometry (underwater weighing) is a method that estimates body composition by using assessments of body weight, body volume, and residual lung volume. The models of estimating body composition have evolved, and more recently a multi-compartment model is used. This model includes body density combined with assessments of bone density and TBW to estimate body fatness, which is more accurate that previous used models. A key limitation is the dependence of participant performance on the results. Especially children and obese individuals might have difficulties with submerge completely under water. In addition, obese individuals might not be comfortable with the less clothing required to perform the measurement (Duren et al., 2008).

#### Dual-energy x-ray absorptiometry (DEXA)

DEXA is the most popular measurement method for quantifying fat tissue, fat free soft tissue and bone mineral (Beechy et al., 2012; Duren et al., 2008). X-ray at high and low energy level is used at the individuals in order to scan the body (Beechy et al, 2012). Great advantages of this method is the possibility to determine abdominal obesity, predict intraabdominal fatness, and provide regional body composition measurement (distinguish between android and gynoid obesity) in addition to low participant burden. Limitations are related to high cost, trained technicians required, equipment and the actual estimation of body composition (Beechy et al, 2012). DEXA estimates biases can be caused by variations between manufacturers in the technology, models, and software offered, methodological difficulties, and intra-and inter-machine variations (Duren et al., 2008). The DEXA machine has normally physical limitations regarding the participant's body weight, length, and body size, and the machine's details (e.g. pencil or fan beam). These limitations prevent obese individuals (children and adults) to perform a DEXA scan, if not the entire mass of the individual can be scanned (Duren et al., 2008).

#### **Indirect measurements**

Indirect measurements consist of anthropometric measurements and bioelectrical impedance analysis (BIA) (Duren et al., 2008). The most basic method for assessing body composition is measuring anthropometric measures, including assessments of weight, height, BMI, abdominal circumference (frequently referred to as waist circumference), and skinfolds. Because body size is influenced by weight gain, these assessments give acceptable measurements of an individual's overall adiposity (Duren et al., 2008). Anthropometric assessments are considered being easy, safe, and have low cost for measuring body composition (Beechy et al., 2012). However, the measurements are depended on the skills and training of test-personnel (Beechy et al., 2012).

#### Body weight

Body weight (e.g. kg, lbs) is the most used measurement to assess overweight and obesity, and is assessed using different types of scales (Duren et al., 2008). Normally, there is an association between body weight and body fat, whereas individuals who have a high body weight tend to also have a high percentage of body fat. Changes in body water, fat and/or lean tissue are reflected in changes in body weight. However, using only body weight as a measure for overweight has its limitations. Body weight is also associated with height, whereas tall individuals tend to weigh more than shorter individuals. Body weight as a measurement lack specificity. Further limitations might occur as a product of inaccurate scales, and therefor calibrations are important to avoid such inaccuracy (Duren et al., 2008).

#### Body mass index (BMI)

BMI, expressed as weight divided by height squared (kg/m2), can be explained as a descriptive index (table X) of both lean and obese individual's health related body-appearance (Duren et al., 2008). In adults overweight is classified with a BMI  $\geq$  25 kg/m2, while obesity is classified as a BMI  $\geq$  30 kg/m2 (Duren et al., 2008). Importantly, overweight and obesity are not mutually exclusive, whereas an obese person is also overweight (NIH, 1998). WHO (1995) has earlier identified obesity as having a body fat percentage  $\geq$ 25% for men, and  $\geq$ 35% for women However, most recent literature comparing BMI-measurements for obesity with more accurate assessments of adiposity, use cut-off values for body fat equal >25% for men and >30% for women (Okorodudu et al., 2010). BMI uses weight in relation to height to overcome the lack of specificity concerning body composition (Duren et al., 2008). Height can easily be measured using different wall-

mounted equipment. A strength concerning this method is the great evidence of large national reference data (Duren et al., 2008). Further, BMI has a well-documented relationship with level of body fatness, morbidity, and mortality in adults, and it is especially beneficial when monitoring obesity and tracking weight over time (Beech et al., 2012; Duren et al., 2008).

Classification	<b>BMI</b> (kg*m <sup>-2</sup> )	
Underweight	< 18,5	
Normal weight	18,5-24,9	
Overweight	$\geq$ 25	
Pre-obese	25-29,9	
Obese class I	30-34,9	
Obese class II	35-39,9	
Obese class III	$\geq 40$	

 Table 2.3. Classification of overweight in adults according to Body Mass Index (BMI).

(WHO, 1997)

An important limitation is that BMI does not differ between body compartments (fat-free mass vs. fat mass) (Beech et al., 2012), and for example athletic individuals or people with special types of medical conditions (e.g. sarcopenia) might have altered proportion of fat mass and fat-free mass (Duren et al., 2008). Therefor, in people with these conditions BMI is not strongly associated with fat mass, and other assessment methods for overweight should be chosen. Whether BMI has the same implications in different ethnical groups beside Europeans (white) has been discussed as a potential limitation. WHO expert consultation (2004) addressed this issue with regard to Asian populations. In general, Asian men and women have a lower BMI compared with their white European counterparts with same age and percentage fat (Duren et al., 2008). A higher risk of cardiovascular diseases is observed in the Asian populations compared to Western population at any give BMI (Low, Chin, Ma, Heng, & Deurenberg-Yap, 2009). The differences are not only observed between Asian and Western population, but within the Asian population (Low et al., 2009). Even difference between European population and white Americans is observed (WHO Expert WHO Expert Consultation, 2004). In Asia, Hong Kong Chinese, Indonesians, Singaporeans, urban Thai, and young Japanese were observed having lower BMI at a given percentage body fat compared with Europeans, whereas Beijing (northern) Chinese and rural Thai were observed having similar values compared with Europeans. Further, white Americans are generally observed having lower percentage of body fat at a certain BMI compared to Europeans. These differences cannot exclusively be explained by methodological differences in

measurements, but importantly differences in body built and lifestyle factors such as physical activity (WHO Expert WHO Expert Consultation, 2004).

Another key limitations concerns the fact that classifying children and adolescents as overweight or obese, is a little more complicated than with adults (WHO, 1997). Children and adolescents are still growing, and height and body composition are constantly changing. The onset and rate of growth is rather individual at this time, making a simple universal class system of adiposity of less value for this population group. Therefore other classification system has been proposed (WHO, 1997). A frequently used definition uses BMI in relation to reference centiles, where overweight equals having a BMI $\geq$  85th percentile, and obesity equals a BMI  $\geq$  95th percentile, based on US reference-data (Kuczmarski et al., 2002). Importantly, as discussed earlier concerned different ethnical groups, cautions of interpretations should be highlighted related to the potentially limitation of using US-reference data.

#### Abdominal circumference

Abdominal circumference (often referred to as waist circumference, WC) measurements are related to abdominal fat storage (Duren et al., 2008), has been shown to correlate well with BMI, and is used to define abdominal obesity (Misra, Wasir, & Vikram, 2005; WHO Consultation on Obesity, 1998). Clinical accepted cutoff points for WC are  $\geq$ 94 cm for men and  $\geq$ 80 cm for women at action level I (increased risk of obesity associated metabolic complications), and  $\geq$ 102 cm for men and  $\geq$ 88 cm for women at action level II (substantially increased risk of obesity-associated metabolic complications (WHO, 1997). Waist circumference (WC) Action level I equals BMI for overweight and action level II equals BMI for obesity, and the cutoff values for WC are based on white Caucasian adults living in European country (Misra et al., 2005). As highlighted for BMI, any interpretation to other ethnical groups should be further evaluated, whereas the cutoff values might not be valid beyond European population (Misra et al., 2005).

Since intra-abdominal tissue has an increased adverse association with health risk, this measurement method is more specific to intra-abdominal fat storage than measurements measuring total percentage body fat (e.g. BMI, BIA) (Duren et al., 2008). However, it is important to note that abdominal circumference does include subcutaneous fat accumulation and visceral adipose tissue, meaning it is not exclusively a representation of intra-abdominal

fat storage. However, abdominal circumference is still an important and often used method (Duren et al., 2008), since it is associated with several health risks, including cardiovascular diseases and other forms of chronic diseases (WHO Consultation on Obesity, 1998).

#### Skinfolds

Skinfolds measurements are performed to measure subcutaneous fat thickness at different regions of the body (Duren et al., 2008). The measurements are performed using skinfold calipers, usually at triceps and subscapular locations. Data are read from the caliper, and used in equations to estimate total body fat. A key limitation with this method is that calipers usually have an upper assessment limit of 45-55 mm, and therefor this method is suitable for modest overweight or thinner individuals, and not people with severe obesity. Another challenge is measurement bias, which can occur because of the test-person's skills or training, but also because of increased fat making the measurement more difficult. The more fat accumulation in one area, the harder it is for the caliper to grasp and hold the skinfold. Also, the skinfold at the triceps location differs across gender, and can also be a result of change in muscle mass rather than fat mass. A major strength is that the method is especially useful in observing children's variations in body fat, whereas children are small of size and most of their fat is subcutaneous (even in obese children) (Duren et al., 2008).

#### Bioelectric impedance analyses (BIA)

Bioelectric impedance analyses (BIA) measure the resistance in the body using an alternating electrical stream (Duren et al., 2008). Based on the resistance measured, body composition is presented as estimated TBW, FFM and fat mass. The body composition estimates are derived from a regression equation including an impedance index (height squared divided by resistance at a certain frequency, e.g. usually 50 Hz.), which is proportional with TBW, as an independent variable. A key limitation is that the regression equation used to predict body composition only explains statistical relationships, which are derived for biological associations for a particular population. This in turn, limits the use of the analysis to individuals that match the reference population regarding body size and shape (Duren et al., 2008). The used resistance 's ability to penetrate all tissues (Beechy et al., 2012). However, the method is thought to be easy to use, inexpensive, and safe with no risk related to frequent use. It is also a strength that the method is noninvasive, whereas it has no or little participant burden, and has no height or weight limitations (Beechy et al., 2012).

#### 2.2 Sedentary behavior

Sedentary behavior is often used to describe the lower end of the physical activity continuum, and refers to activities done in sitting or lying, with a low energy expenditure (Tremblay, Colley, Saunders, Healy, & Owen, 2010). It is crucial to mention that sedentary behavior differs greatly from inactivity and light physical activity. Inactivity is defined as insufficient level of moderate to vigorous physical activity (MVPA) (i.e., not meeting specified physical activity guidelines) (Sedentary Behaviour Research Network, 2012), while light physical activity is defined by activity that involves energy expenditure between 1.6-2.9 METs, such as slow walking, sitting and writing, cooking food, and washing dishes (Pate, O'Neill, & Lobelo, 2008). The construct of sedentary behavior does not replace the construct of inactivity, or vice versa (Neville Owen, Healy, Matthews, & Dunstan, 2010). It is possible for a person to meet the specified physical activity guidelines, and be categorized as physically active, but still spend a great amount of the remaining time of the day being sedentary. Opposite, it is possible for a person categorized as inactive to spend a lot of time in light physical activity. Accumulated sedentary behavior compromises an individual's metabolic health, and it is therefor important to differ between those two constructs (Neville Owen et al., 2010).

#### 2.2.1 Prevalence of sedentary behavior

Overall, 41,5 % of adults worldwide report spending four or more hours per day sitting (a comparison of 66 countries) (Hallal et al., 2012). Amount spent sitting per day varied across WHO regions, whereas the prevalence was 37,7 % in Africa, 55,2 % in Americas, 41,4 % in Mediterranean, 64,1 % in Europe, 23,8 % in South-East Asia and 39, 8 % in Western Pacific. The observations of persons spending four or more hours sitting per day were similar for adult (15-59 years) men and women, but increased for older individuals ( $\geq$  60 years old) (ibid.). Available data from around 49,500 adults (18-65 years old) across 20 countries, observed median reported sitting time to be 300 min/day (interquartile range 180-480 min/day) (Bauman et al, 2011). The lowest observed sitting time was reported in Portugal, Brazil and Colombia (medians 180 min/day), whereas the highest prevalence was observed in Taiwan, Norway, Hong Kong, Saudi Arabia, and Japan (medians 360 min/day) (Hallal et al., 2012). Contrary to Hallal and colleagues (2012), Bauman and co-workers (2011) observed a higher risk of reporting higher sitting time among adults (18-39 years old) than older adults (40-65 years old).

Data from the Global School-based student Health Survey (GSHS) including 34 countries, observed that more than half of the countries reported that more than 1/3 of adolescents (13-15 years old) spent three or more hours per day in self-reported sedentary activities (Guthold, Cowan, Autenrieth, Kann, & Riley, 2010). Data on time spent watching TV in adolescents (13-15 years old), using the Health Behaviour in School-aged Children (HBSC) comparing 40 countries, observed that 66% of the boys and 68% of the girls spent two or more hours per day watching TV in 2002 (Hallal et al., 2012). Data from 2010, show that the trend in time spent watching TV is decreasing slightly in most countries (Bucksch et al., 2016).

Using self-reported data do not always cover the whole spectrum of sedentary lifestyle (Atkin et al., 2012). Data available from big national mapping studies using objective measurements originate from Norway (Hansen et al., 2015), Sweden (Hagstromer, Oja, & Sjostrom, 2007), Portugal (Baptista et al., 2012), US (Matthews et al., 2008), and China (Peters et al., 2010), and give a small picture of prevalence worldwide. Americans ( $\geq 6$  years old) spent on average about 55 % of their waking hours in sedentary behavior (7,7 hours/day) (Matthews et al., 2008). There was observed a significant linear trend by age. The youngest children, aged 6-11 years old, were less sedentary than the rest of the population, spending on average 6 hours/day in sedentary behavior. Older adolescents (16-19 years old) and older adults (60-85 years old) spent the most time in sedentary behavior, reaching more than 8 hours/day or 60 % of their waking time (Matthews et al., 2008). Baptista and colleagues (2012) observed almost similar trends, whereas boys under 17 years old were less sedentary that other male age groups and men over 64 years were the most sedentary. Boys aged 10-11 spent on average 502 min/day in sedentary behaviors and men over 65 years old spent on average 612 min/day being sedentary. Lowest sedentary behavior was observed for women between 18 and 64 years old (Baptista et al., 2012).

Further, Peters and co-workers (2010) observed sedentary behavior in Chinese adults over 40 years old. Sedentary behavior ranged from 491 min/day to 540 min/day across age, whereas it seemed that older adults spent more time in sedentary behaviors (Peters et al., 2010). Hagstromer and colleagues (2007) observed an average of 459 min/day spent in sedentary behavior, in a Swedish cohort including men and women aged 18-74 years old. Sedentary behavior in this group did not differ from gender, age or BMI (Hagstromer et al., 2007). Numbers from Norway indicate a slightly higher prevalence of sedentary behavior (Hansen et al., 2015). In 2008-09, the Norwegian population reported an average of 545 min/day and six

years later the average reported time in sedentary behavior was 549 min/day, both occasions exceeding 9 hours/day (Hansen et al., 2015).

#### **2.2.2 Determinants of sedentary behavior**

In the beginning of human history, humans evolved over hundreds of millenniums to become standing, two-legged, walking individuals (Levine, 2015). Humans evolved to explore, invent, think and respond. Living thousands of years ago was dynamic. People hunted or gathered food by foot to survive. Right before the industrial revolution, 90 % of the world's population lived in agricultural communities, being physical active most of the day (Levine, 2015). With time, there has been a noticeably change in the environmental demands for being physical active, resulting in a more sedentary lifestyle (Owen et al., 2010). Especially since the middle of the last century, changes have occurred in transportation, communication, workplace and domestic-entertainment technologies resulting in a progressing sedentary lifestyle (Owen et al., 2010).

Even though sedentary behavior is distinct different from lack of sufficient physical activity, it can be seen as a set of behaviors that can coexist with and also compete with physical activity (Owen, Leslie, Salmon, & Fotheringham, 2000). Therefor, many of the risk factors for not being sufficient physically active, are the same factors instead increasing the risk of choosing to be sedentary. Sedentary behaviors are performed in the domains of community, home, occupation, education or transport (Owen et al., 2000). From an ecological model, interpersonal factors, perceived environment, behavioral settings (access and characteristics), policy environment, information environment, social- and cultural environment, and natural environment are all thought to impact the different domains, as determinants for sedentary behavior (Owen, Sugiyama, Eakin, Gardiner, Tremblay & Sallis, 2011). Many of the same factors influencing sedentary lifestyle are thought to affect children and adults across age (Owen et al., 2011).

Intrapersonal factors include demographics, biology, psychology and family situation (Owen et al., 2011). Gender has been shown to be a determinant for vigorous physical activity, but when light and moderate activity are included, gender is no longer associated with physical activity level (King et al., 1992). This suggests that gender is not so important for level of sedentariness. Age is another possible demographic determinant, whereas the prevalence

seems to vary across age (Matthews et al., 2008). Among the demographic factors affecting sedentary behavior, through less activity, socioeconomic status and level of education might be the most pronounced factors (King et al., 1992).

The intrapersonal factors act upon a social-cultural environment. Social norms and perceived crime in people's environment as well as interpersonal modeling, social support, prompts to sit, and awkwardness of standing affect the decision of being sedentary (Owen et al., 2011). Moreover, the access and characteristics of social climate, safety, crime, norms and culture as behavior settings, and the context of policies in which advocacy by individuals and organization, also determines level of sedentariness. People's perceptions of their environment affect level of sedentariness. In the context of transportation, if people have negative perceptions of active transport facilities or positive perceptions of "active" environments (unsafe-, uncomfortable-, unattractive- or inconvenient environment) affect whether or not people are sedentary during leisure time. While people being sedentary at home, might perceive their home to be comfortable, with convenience of laborsaving devices, or to have an attractiveness of sedentary entertainment. At work, perceived cues for sitting or purpose of furniture and desks determine people's sedentary behaviors (Owen et al., 2011).

Behavior setting is the physical and social context where sedentary behaviors occur (Owen et al., 2011). The access and characteristics of the behavior setting determine people's level of sedentary behavior. Behavior settings affecting level of sedentariness in leisure time are poor walking/bike facilities, aesthetics, and traffic safety in people's neighborhood, and seating in parks, park design to promote sitting, screen-based entertainment (movies, game arcades etc.), and sports spectatorship in the recreation environment. Home environment with electronic entertainment (passive/active), remote controls, laborsaving devices and furniture for sitting/reclining all promote sedentary behavior. Whether people chose sedentary promoting transport depends on neighborhood, walkability, walking/biking facilities, parking, transit and traffic. It also depends whether there is information promoting sedentary behavior during transportation, safe signage, radio ads and news, and billboards (Owen et al., 2011).

Workplace environment, and its behavioral setting, determines sedentariness (Owen et al., 2011). Furniture designed for sitting, neighborhood walkability, parking, transit access, building design, stair design and walking/bike facilities affect people's behavior. Most of the

same factors affect sedentary behavior in the context of school environment, but also physical education- and walk-to-school programs. Other behavior settings determining level of sedentary behavior are related to information (health care, counseling, media, etc) and nature (weather, topography, air quality etc.). Along with how policies are made and distributed, people's motivation and preferences influence their choice of behavior. Families and larger social settings, neighborhood climate, social networks, material resources and other factors determine the act of sedentary behavior (Owen et al., 2011).

#### 2.2.3 Consequences of being sedentary

#### Physiological mechanisms and effects of sedentary behavior

The history of research used to understand sedentary behavior and inactivity as one. However, research has now suggested that sedentary behavior is distinctive from inactivity, which often is defined as lack of moderate to vigorous physical activity. In a health promoting perspective, more attention was long focused on the preventive effect of being physical active (including the study of the effect of less inactivity), rather than the potential adverse effects of being sedentary (Hamilton et al., 2007). This perspective has been challenged, whereas some studies have indicated that there is a distinct difference between inactivity and sedentary behavior (Healy, Dunstan, Salmon, Cerin, Shaw, Zimmet & Neville, 2007; Healy, Dunstan, Salmon, Shaw, Zimmet & Owen, 2008). The characteristics of sedentary behavior have independent and qualitatively different effects on human metabolism, physical function, and health outcome (Tremblay et al., 2010).

Healy and colleagues (2007) observed that light physical activity was favorable associated with blood glucose, whereas sedentary behavior was adversely associated with blood glucose. If inactivity was measured instead of light intensity activity and sedentary behavior, the latter constructs would have been combined, whereas the beneficial effect of light activity could potentially been missed. This highlight the importance of having several intensity constructs in the lower end of the activity scale. Healy and co-workers (2008) later demonstrated that healthy Australians who met the physical activity guidelines, but spent great amount of time watching television, had higher level of a number of metabolic risk variables. Therefor, a new paradigm has emphasized the importance of studying the effect of a sedentary lifestyle, to better understand the cellular signals, physiological responses, and disease outcome related to this behavior, (Hamilton et al., 2007).

The underlying rationales of a new paradigm build upon four beliefs (Hamilton et al., 2007). From the relationship between mortality and fitness, it is observed that the least fit people has the highest risk of mortality, whereas the relative risk decrease significantly with small changes in activity level, and without big changes in relative risk when fitness level is further increased. Therefore, the first belief is that a more sedentary lifestyle could potentially push the relationship-curve upward or shift it to the left, resulting in allover higher risk of mortality, whereas the behaviors can be prevented in future health interventions. The second belief concerns that sitting time and various sedentary behaviors, and other activities are distinct different classes of behavior, with different determinants and effects on risk of diseases. An important belief in the new paradigm is the inactivity physiology and exercise physiology is different, as to having different responses due to specific cellular and molecular processes. The fourth, and last, belief concerns the idea that in inactive populations, age-adjusted rates of cardio-metabolic diseases cannot be caused by additional exercise deficiency (Hamilton et al., 2007).

The research of sedentary behavior and consequences is just in the beginning, starting to identify and understand the molecular processes linked to diseases caused by sedentary behavior (Hamilton et al., 2007). A great body of evidence regarding the physiological and biological mechanisms of sedentary behavior is obtained by bed rest studies, animal studies and immobilization studies (voluntary or after accidents) (Tremblay et al., 2010). Metabolic dysfunction, described as increased plasma triglyceride levels, decreased levels of highdensity lipoprotein (HDL) cholesterol, and decreased insulin sensitivity, has been demonstrated as a consequence of having a sedentary lifestyle. These conclusions are made from bed rest studies and injury induced immobilization. The harmful consequences on metabolic health caused by a sedentary lifestyle, seem to be at least partially mediated by alterations in lipoprotein lipase (LPL) activity (Tremblay et al., 2010). LPL is a protein that assists the uptake of free fatty acids into skeletal muscle and adipose tissue, by controlling plasma triglyceride catabolism, HDL cholesterol, and other metabolic risk factors (Hamilton et al., 2007). LPL activity seems to be lowered in response to both acute and chronic sedentary behavior (Tremblay et al., 2010). Summarized by Hamilton and colleagues (2007), low LPL has been associated with reduced plasma triglyceride uptake and lowered plasma HDL levels. Further, they state that LPL might have some effects on hypertension, diabetesinduces dyslipidemia, metabolic problems in aging, human metabolic syndrome, and

coronary artery disease (both severity and incidental) (Hamilton et al., 2007).

Results from denervation of muscles and immobilization caused by injury, suggest that sedentary behaviors affect carbohydrate metabolism through alterations in muscle glucose transporter (GLUT) protein content (Tremblay et al., 2010). These studies observe that when the muscles are not used, GLUT content drops fast. GLUT proteins are essential to glucose uptake stimulated by basal (GLUT-1), insulin (GLUT-4) and exercise (GLUT-4). Among other factors, low levels of GLUT-protein can contribute to insulin resistance at muscular level (Bergouignan, Rudwill, Simon, & Blanc, 2011).

A reduction in bone mineral density caused by sedentary behavior is also documented though studies on animals and human in space (time spent in orbit), bed rest and injury induced immobilization (Tremblay et al., 2010). The mechanism behind such relationship between sedentary behavior and bone health, is thought mediated by changes in the balance between bone resorption and deposition. It is further suggested that there is a fast increase in bone resorption without any parallel alterations in bone formation caused by sedentary behavior, and this effect is thought to reduce bone mineral content and increase risk of osteoporosis (Tremblay et al., 2010).

Sedentary behavior seems to have a negative effect in vascular health, although less scientific evidence available (Tremblay et al., 2010). Tremblay and colleague (2010) summarize the effect of bed rest studies on vascular health. Vascular changes seem to be related to reactive hyperemia (peripheral vascular function), increase in blood pressure and decrease in brachial artery diameter. Although, these changes can be altered by exercise, which means these changes might be caused by a mechanism both related to inactivity physiology and exercise physiology (Tremblay et al., 2010). Further, deep venous thrombosis (DVT), whereas blood clots occur deep in idle leg muscles, is associated with too much sitting independent of exercise (Hamilton et al., 2007).

#### Sedentary behavior and risk for diseases

Most of the studies regarding the effects of sedentary behaviors are obtained from cross sectional studies focusing on inactivity (Hamilton et al., 2007). While inactivity is well established as a major contributor to most of chronic diseases (Booth, Roberts, & Laye,

2012), it is important to remember that inactivity is distinct different from sedentary behavior (Hamilton et al., 2004). To establish a causal relationship between sedentary behavior and health outcome, it is necessary to evaluate intervention studies (Hamilton et al., 2007). Sedentary behavior has mostly been measured prospectively by self-reported methods (Thorp, Owen, Neuhaus, & Dunstan, 2011).

Proper and colleagues (2011) reviewed the literature of the longitudinal relationship between sedentary behavior and health outcomes in adults, published between 1989 and 2010. They identified 19 articles, whereas 14 were of high methodological quality. They found that there were insufficient evidence for the relationship between sedentary behavior and body weight/BMI, risk for overweight or obesity, waist gain, various cardiovascular disease (CVD) risk factors, and endometrial cancer respectively. There were no evidence for a relationship between sedentary behavior and mortality for cancer, but moderate evidence for a relationship with sitting time and risk of diabetes type 2, and strong evidence for a relationship with sedentary behavior and mortality from all causes and from CVD. However, more evidence was warranted to better conclude in the causal relationships (Proper et al., 2011). Thorp and co-workers (2011) also review the literature, more or less in the same timeframe as Proper and colleagues (2011), but with a larger inclusion, which support Proper and colleagues' (2011) findings. Thorp and co-workers (2011) also observed that sedentary behavior was associated with weight gain from childhood into adult years. A potential reverse causality between obesity markers and sedentary behavior was also highlighted (Thorp et al., 2011).

#### 2.2.4 Measurements of sedentary behavior

In order to identify causal relationship with different health outcome, to quantify accurately the extent of the relationship, and to determine a dose-response relationship, it is necessary to have high-quality exposure assessments (Atkin et al., 2012). Further, it is crucial to have precise measurements to be able to document patterns of, and changes in, sedentary behavior within and between individuals over time (ibid.). Physical activity is often described by frequency, intensity, time (duration), and type of activity (FITT) (Tremblay et al., 2010). Even though physical activity behaviors are distinct different from sedentary behaviors, it is argued that there should be little difference when sedentary behavior is measured. Because sedentary behaviors vary little in intensity the SITT formula is proposed, where the different

acronyms describe; Sedentary behavior frequency (number of bouts of a certain duration), Interruptions (e.g. breaks in sedentary behavior), Time (duration), and Type (mode of sedentary behavior) (Tremblay et al., 2010).

Sedentary behavior can be assessed both with subjective- and objective measurements. Several measurements methods are useful to assess the different aspects of SITT (Tremblay et al., 2010). Sedentary bout frequency (S) can be assessed by any objective measurement method, continuously measuring pattern of sedentary behavior throughout the day over a given time line. Interruptions (I) are also measured by objectively measurement tools, where breaks, change in position or energy expenditure can be conceptualized and derived. Both objective- and subjective measurements are suitable for assessing total time spent in sedentary behavior (T), while subjective methods are better fit to assess type of engaged sedentary behavior (T). Although, recent technology gives possibilities for assessing type with cameras and photographic images through direct observations (Tremblay et al., 2010).

#### Subjective measurements of sedentary behavior

Several surrogate behaviors are used to define sedentary behavior when subjective measurements (questionnaire, interview, and activity-recall instruments) are used (Kang & Rowe, 2015). In a review performed by Thorp and colleagues (2011) self-reported sedentary behavior was measured, in a combination or alone, as sitting time, TV viewing, other screen-time behaviors, or other sedentary behaviors. Tremblay and colleagues (2010) describe car time, chair time or sitting time, indoor time, and screen time, as part of population approaches when measuring sedentary behavior. Importantly, with all measurements that assess surrogate behaviors, none of these behaviors are representative for the total time spent in sedentary activities (Tremblay et al., 2010).

#### Self-and proxy reported questionnaires

Self-reported questionnaires are common approaches for assessing sedentary behavior (Kang & Rowe, 2015). The questionnaires can consist of a single-item question or multiple questions with different time frame (e.g., past day, past week, usual week, past year). Asking a single-item question (e.g. screen time, TV viewing, sitting time etc.) concerning the total amount spent sitting of lying down has been commonly used over the past years. However, only general information about sedentary lifestyle is possible to obtain, which may not be a

complete representation of sedentary behavior. Therefor, researchers have recently developed multiple-items questionnaires measuring multiple sedentary behaviors and domain-specific sedentary behaviors for better to understand the broader spectrum of a sedentary lifestyle (Kang & Rowe, 2015). The Sedentary Behavior Questionnaire, Marshall Sitting Questionnaire, International Physical Activity Questionnaire (IPAQ) and the Occupational Sitting and Physical Activity Questionnaire are examples of multiple-items questionnaires (Kang & Rowe, 2015; Rosenberg, Bull, Marshall, Sallis, & Bauman, 2008). The three first mentioned questionnaires assess sedentary behavior separate from weekdays and weekend days, both over a great range of domains (e.g. watching TV, sitting and talking on the phone, driving/riding in a car, bus or train, while at work, while using a computer at home, etc.) (Kang & Rowe, 2015). These questionnaires give a good picture of sedentary patterns throughput an entire week, and potentially gives room for differences in sedentary domains and weekends and weekdays. The last mentioned questionnaire is specific to sedentary behavior at work (Kang & Rowe, 2015).

Self-reported questionnaires have strengths whereas they are cost-effective, easily accessible to the majority of the population, and have relatively low participant- and researcher burden. These questionnaires are widely used, with feasibility well established (Atkin et al., 2012). They measure and identify specific behaviors, and the environment and/or the social context they occur. The questionnaires assess valuable information, which can be used to design interventions. Important limitations of self-reported questionnaires include poor validity, subject to recall, reporting bias, and perception and understanding of language including translation to other languages. A great challenge in establishing validity for self-reported measurements lies in the lack of an accepted " gold standard" referent measure of sedentary behavior. Correlation errors are likely to occur if one self-reported measurement is used to validate another self-reported measurement, and therefor this would be inappropriate. This is problematic when self-reported measurements have dominated certain aspect of sedentary behavior research (e.g. type of sedentary behavior) (Atkin et al., 2012).

Both cultural norms and perceived social desirability have the potential to affect how people answer their questions (reporting bias) (Atkin et al., 2012). It is socially desirable to be active, and therefor it is possible that people report less sedentary behavior than what is actually the case (Atkin et al., 2012). On the other hand, recall biases could also occur. Sedentary behaviors are not usually structured and purposive (Kang & Rowe, 2015). They

occur throughout the day in the free-living environment, and are not always so easy to accurately remember and report (Kang & Rowe, 2015). Important to self-reported questionnaires are how people understand the questions (Atkin et al., 2012). It is not consistently that people perceive words and phrases different. Age, gender, socioeconomic status etc. might affect people's interpretations. Moreover, differences can occur when these questionnaires are translated to different languages, and should be used with caution when comparing studies across different populations (Atkin et al., 2012).

Because self-reported questionnaires are difficult to use in children, and in some cases older adults, proxy-reports are used instead (Atkin et al., 2012). Someone significant to the individual (e.g. parent, guardian, offspring etc.) report on the individual's behalf. This method has the same strength and limitations as self-reported measurements, in addition to give information about this particular population group (Atkin et al., 2012). Other subjective measurement tools are diary and ecological momentary assessment (EMA) in which are good for studying pattern of sedentary behavior (Kang & Rowe, 2015). Diaries are time-dependent records of behaviors, observations, thoughts or feelings (Atkin et al., 2012), whereas EMA are similar to diaries, but can capture behaviors and the factors that might influence it (report current activity, location, and social surroundings) (Kang & Row, 2015). Strengths of these methods are that they provide "real-world" information about sedentary behavior, are low on cost and easy to distribute to many subjects at the same time. On the other hand, these methods have a moderate participants- and researcher burden and are subject to recall- and reporting biases (Atkin et al., 2012).

#### **Objective measurements of sedentary behavior**

To address some of the limitation present with self- and proxy-reported measurements, more research include objective measurement tools (Atkin et al., 2012). When sedentary behavior is assessed with objective measurements the assessed sedentary behavior aspect is either energy expenditure or posture (Kang & Rowe, 2015). Objectively assessments can be accelerometers, posture monitors, heart rate (HR) monitoring and combined sensing, and multi-unit monitors (Atkin et al., 2012). Except for HR monitoring, most of the time the same technology with accelerometry underlies, but with different algorithmic approach (Kang & Rowe, 2015). Therefore, further only accelerometer, including posture monitors, and HR flex method will be more described.

#### Accelerometers

Accelerometers (e.g. ActiGraph) are small devices that are typically worn on the hip, lower back or wrist (Atkin et al., 2012; Kang & Rowe, 2015). They can be used to provide details about total amount, frequency, intensity, and duration of physical activity and sedentary behavior (Westerterp, 2009). Attached to an elastic belt or bracelet, these devices measure the frequency and amplitude of acceleration of the body part where they are worn (Atkin et al., 2012). Human movement is measured, and the magnitude of the acceleration is measured within fixed time periods (epochs; e.g. 60 seconds, 10 seconds etc.), or as a continuous data stream at a certain frequency (e.g. 50 Hz) (Kang & Rowe, 2015). The acceleration is thereafter translated into activity counts. Tailored algorithms and software are used to translate data stream at a certain frequency and acceleration magnitude within epochs to raw data (Kang & Rowe, 2015).

The threshold of activity counts that is equivalent to an energy expenditure level ( $\leq 1.5$  METs) related to sedentary behavior varies across studies (Kang & Rowe, 2015). There is no consensus on one threshold, as a result from lack of consistent validation studies, but most studies seem to agree on a cut-off level were < 100 counts per minutes (cpm) from vertical axis data is defined as sedentary behavior (Kang & Rowe, 2015). Although, there has been proposed a range of different cut-off levels among children, adolescents and adults (Atkin et al., 2012). Kozey-Keadle and co-workers (2011) investigated the validity of several cut-off levels used for ActiGraph (50, 100, 150, 200, and 250 cpm) against direct observation in a small sample of adult overweight individuals. They reported that ActiGraph underestimate directly observed sedentary behavior by 4,9 %, when cut-off levels of 100 cpm were used. Further, cut-off levels of 150 cpm showed the least bias, whereas it overestimated sedentary behavior by 1,8 %. When 50cpm, 200cpm and 250 cpm were used as cut-off levels, the percentage bias ranged from -22 % to 18 %, whereas all were reported higher than for 100cpm and 150cmp (Kozey-Keadle et al., 2011).

Validation studies performed in children and adolescent have proposed cut-off levels between 10 to 1592 cpm (Atkin et al., 2012). Treuth and colleagues (2004) investigated thresholds for accelerometer (ActiGrap) counts compared to oxygen consumption data for different activities in adolescent girls (12-14 years old). Threshold for sedentary behavior were observed within the range of 0 to 50 cpm (Treuth et al., 2004). Pulsford and co-workers Pulsford et al. (2011) investigated thresholds for ActiGraph comparing to energy expenditure

in different exercise intensities in seven years old children. The threshold for sedentary behavior were observed as >100 cpm, with a satisfying discriminating power (Pulsford et al., 2011). The main concerns when using accelerometer as measurement method for sedentary behavior relate to device initialization, post-processing, signal feature extraction and inference of specific outcome variables (Atkin et al., 2012). In addition to cut-off values, the researchers have to define non-wear time and minimum hours/day and days with valid measurements in their protocol. It is noticeable that children and adults differ in their patters of behavior. This is important to acknowledge in the protocol (e.g. children's behaviors are more sporadic than adult's, and a lower epoch might be more suitable for this group to differ sedentary behavior from light activity, or vice versa) (Atkin et al., 2012).

An important limitation of the use of accelerometer (use of only vertical axis) is that this method only measure intensity and therefor cannot differ between postures (Atkin et al., 2012). As a result, standing can be measured by the accelerometer as sedentary behavior, even though it would have higher energy expenditure than sedentary behaviors. Or opposite, measurements of sitting can be lost, and misclassified as activity of higher intensity (Atkin et al., 2012). The accelerometer can neither capture contextual information about the type of behaviors (Tremblay et al., 2010). Because error can occur throughout all stages of data collection and interpretation process, different choices across different studies, makes comparisons complicated (not impossible) (Kang & Rowe, 2015). The method is further of moderate cost, results in a moderate researcher burden, and might cause reactivity in subjects (Atkin et al., 2012; Kang & Rowe, 2015). A key strength of the use of accelerometer is that it can be used on a wide age-range, including children and adults (Atkin et al., 2012). Accelerometers have a low participation burden, and have a substantial literature on application and analysis of total sedentary behavior, including bouts and breaks in a free-living environment (Atkin et al., 2012).

#### **Posture monitors**

Posture monitors (e.g. ActivPAL) are small devices attached directly to the skin on the middle of the front side of the thigh (Atkin et al., 2012). Posture monitors are using the same acceleration technology as accelerometers. How the thigh is accelerating, gravity and use of suitable algorithms, determine the posture recorded; sitting or lying, standing or stepping. Data that can be provided by the posture monitors are number of step taken, cadence, sit-to stand and stand-to sit shifts, and estimates of energy expenditure. This method has been
shown to be reliable and valid for measuring steps and cadence, and emerging evidence has evaluated the reliability and validity of an equivalent conclusion for sitting time (Atkin et al., 2012).

Kozey-Keadle and co-worker (2011) examined the validity of ActivPAL, compared to direct observation in inactive office workers, for assessing sedentary behavior measured as sitting or lying. They observed that ActivPAl underestimated sitting time by 2,8 %, and correlated well with direct observation ( $R^2=0.94$ ). After a second measurement where the office-workers were instructed to decrease sitting time, the ActivPAL was observed able to detect this reduction, making it a rather good tool for measuring sedentary behavior (Kozey-Keadle et al., 2011). Steeves and colleagues (2015) observed how well ActivPAL measured sitting, standing, and stepping classifications in adults, in laboratory. The ActivPAL was observed to correctly classify 100 % of standing time, and more than 95 % of sitting time (in four of six postures; Stool sitting time was misclassified by 95 %, and 14 % for sitting with legs outstretched) and stepping time (Steeves et al., 2015). Further, Edwardson and colleague (2016) also found a good agreement, whereas ActivPAL correctly classified  $\geq 93\%$  of the time lying,  $\geq$ 91% of the time sitting, and  $\geq$ 93% of the time upright. As observed by others (Steeves et al, 2014), Edwardson and co-workers (2016) reported a misclassification of 58 % by ActivPAL when sitting on a chair with legs stretched out. Altogether, there seem to be a general good agreement on the validity of posture detection using ActivPAL in adults.

Validations studies are performed in children with varying results. De Decker and colleagues (2013) concluded that ActivPAL had low classification accuracy, compared to direct observation, to assess sedentary behavior in preschoolers (mean age 5,5 years old). When sedentary behavior where measured including sitting/lying, kneel up, kneel down, and no translocation of the body, a poor misclassification (ROC-AUC= 0,61) and low sensitivity (54%) were observed. Including standing still resulted in even worse results (De Decker et al., 2013). On the other hand, Aminian and Hinckson (2012) observed a satisfying validity when ActivPAL was used to measure sitting/lying, standing, and walking time, sit-to stand and stand-to-sit transition counts and step counts in slow and normal walking in children (mean age 10 years old) in a laboratory setting, compared to direct observation. Less satisfying validity was observed for steps taken during treadmill and fast walking and running (Aminian & Hinckson, 2012). This might imply that interpretations of behaviors measured by ActivPAL should be carefully evaluated based on age and specific behaviors.

Another limitation is that posture monitors do not directly use energy expenditure to support defining sedentary behaviors (Kang & Rowe, 2015). As a consequence, lying and sitting behaviors with higher energy expenditure (e.g. weight lifting) would be classified as sedentary, while they originally are of higher intensity (Kang & Rowe, 2015). However, it is a strength that the method can assess and distinguish between sitting and standing (Atkin et al, 2012). This method has similarities in strength and weaknesses as accelerometer, regarding cost, population, and participant- and researcher burden (Atkin et al., 2012).

## Flex HR

Flex HR is a method using heart rate (HR) measurements together with an individually established Flex HR point (a discriminatory threshold between rest and exercise) (Atkin et al., 2012). The underlying theory is that heart rate correlate well with oxygen uptake (VO<sub>2</sub>) at different intensities, and therefore is related to energy expenditure (Bassett, 2000). Heart rate methods alone are used to measure exercise intensities, based on a linear relationship between heart rate and intensity (Sirard & Pate, 2001). This relationship is not that linear when the intensities get low, and therefor is not appropriate for measuring sedentary behavior. This challenges is accounted for when a Flex HR point is included in the method (Sirard & Pate, 2001). The Flex HR method can measure sedentary behavior as frequency, interruption and total time spent in sedentary behavior (Atkin et al., 2012). To distinguish sedentary behavior from other types of behaviors, Flex HR has been used as threshold whereas all behavior resulting in a HR below Flex HR equals sedentary behavior (Atkin et al., 2012).

The strengths and limitations related to Flex HR method are linked to heart rate as method for assessing activity and behavior, and calculations of Flex HR point (Atkin et al., 2012). A key limitation is that heart rate is not exclusively determined by activity (Westerterp et al., 2009). There are other factors affecting heart rate such as stress, emotions, medications, smoking, and caffeine, to name some (Bassett, 2000; Sirad & Pate, 2001). This can cause biases when sedentary behaviors are determined by low heart rate. Further, age and fitness affect the heart rate-VO<sub>2</sub> relationship, resulting in absolute heart rate values being less comparable (Bassett, 2000). However, this situation might be more important assessing behaviors of higher intensity than sedentary behavior. In addition, Flex HR uses an individually calculated threshold value, which account for individual differences (Atkin, et al, 2012). However, the quality of the method used to estimating this threshold value, determine the overall quality of

the Flex HR method. Other limitations are related to moderate cost and researcher burden. Strengths include established relationship with energy expenditure, low participation burden and can be used in a wide age-range (children and adults) (Atkin et al., 2012).

# 2.3 Bidirectional relationship between sedentary behavior, and overweight and obesity

In the middle of 1900s the interest of investigating the relationship between physically active and inactive occupation with death rates arose. Bus drivers in London were observed to be more likely to die suddenly from coronary thrombosis, than the conductors working at the same double-decker bus, and Government clerks were more prone to suffer from rapidly fatal cardiac infarction than postmen (Morris, Heady, Raffle, Roberts, & Parks, 1953a, 1953b). This led to the general hypothesis that "*men in physically active jobs have a lower incidence of coronary (ischaemic) heart disease in middle-age than men in physically inactive jobs. More important, the disease is not so severe in physically active workers, tending to present in them in relatively benign forms*" (cited in Morris & Crawford (1958), p. 5111). Taylor and colleagues (1962) investigated deaths rates among physically active and sedentary workers of the railroad industry; clerks, switchmen, and section men. They showed that clerks generally had significant higher death rate of all causes, than the other work groups with higher work physical activity demands. Further, they observed that between switchmen and section men a difference excited both in total deaths and nonviolent deaths, but not in deaths caused by arteriosclerotic heart disease (Taylor et al., 1962).

Many studies report that sedentary behavior and overweight or obesity is inversely correlated in both children and adults (Must & Tybor, 2005; Mortensen et al., 2006). However, it is not possible to draw any conclusions about causality. Whether sedentary behavior leads to overweight and obesity, or overweight and obesity leads to sedentary behavior can only be determined by longitudinal analyses. Prospective population-based cohort studies investigating physical activity and obesity prevention, have observed a weakly association between baseline leisure time physical activity and weight gain at follow up (Wareham et al., 2005). However, the reviewed studies varied in their conclusions because of confounding variables, reverse causality and assessment error (Wareham et al., 2005). Hu and co-workers (2003) observed in the "Nurses' Health Study cohort" that American women's self-reported TV viewing at baseline was positively related to risk of self-reported obesity six years later. A study of American postmenopausal women followed up over seven years, showed that self-reported physical activity and non-occupational sedentary behavior independently were associated with risk of 10 pound weight gain among women reported not being overweight at baseline (Blanck et al., 2007). Pulsford and colleagues (2013) measured physical activity and sitting time in English adults when around 40 years, and the result showed that sitting time was not associated with obesity around five years later. However, consistently reported prior obesity, from the age of 25 years old, was prospectively associated with sitting during TV viewing and leisure time later in life (Pulsford et al., 2013). Rey-lópez and colleagues (2007) review the literature between 1990 and 2007 on sedentary behavior and obesity development in children and adolescents aged 2-18 years old. They found that about 70 % of studies investigating young children (<10 years) suggested an independent relationship between TV viewing and obesity development, while the rest reported a null relationship. However, a caution when interpretations are made should be noticed whereas the studies differed in measurement for outcome and exposure. The literature was further inconsistent on the relationship when children got older (Rey-López et al., 2007). A study conducted among Brits, showed that television viewing in adolescent and early adulthood (at 16 and 23 years old) was associated with changes in BMI at 33 years old and central adiposity at 45 years old (Parsons, Manor, & Power, 2008). Basterfield and co-workers (2012) showed that change in objectively measured SED (% time) was associated with change in fat mass index in English children, however not independent of MVPA.

Studies have also showed that BMI predict inactivity, but not vice versa (e.g. Petersen et al., 2004; Metcalf et al., 2011). Petersen and colleagues (2004) showed that self-reported physical inactivity was not associated with development of objectively measured obesity in a Danish adult population, when they observed that those who reported being more active had higher odds of being obese five years later. Over the same five years period, they observed that high BMI was consistently associated with high odds of inactivity (Petersen et al., 2004). This is consistent with Metcalf and co-workers' (2011) result. They demonstrated that objectively assessed fat mass at in English children 7 years at baseline predicted change in MVPA over three years, but not the other way around (Metcalf et al., 2011).

Mortensen and colleagues (2006) studied the bidirectional relationship between sedentary lifestyle and BMI in American adults 41 years old at baseline. They however, defined sedentary lifestyle as the absence of regular participation in programmed recreation sport or heavy physical activity (which compared to the literature, is referred to as inactivity). They showed that baseline BMI was consistently associated with sedentary lifestyle over several years. Contrary, they could not prove that sedentary lifestyle at baseline predicted BMI later in age (Mortensen et al., 2006).

## 2.4 The overall aim of the study

To provide a better understanding of the knowledge in this particular area, the aim of this thesis is: *To provide a systematic literature review of the existing literature of prospective populations-based studies investigating the bidirectional relationship between sedentary behavior and overweight and obesity among non-patient children to middle-aged adults, and to consider the directions of this causality.* 

## **3.0 Method**

In order to investigate the bi-direction association between overweight and obesity, and sedentary behavior, a systematic literature review was chosen as method. Using this design, compared to a field research, as method for this thesis is especially beneficial due to limited time frame and financial resources. The review sought to identify and evaluate the existing knowledge in this field, and was conducted according to the PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009).

## 3.1 Study inclusion criteria

The aim was to identify all eligible longitudinal, prospective population-based cohort studies in this area of research. Even though randomized controlled trials (RCT's) are considered the "gold standard" for observation, these studies might be unnecessary, inappropriate, impossible or inadequate in some situations (Black, 1996). In these situations, such as the current reviewed bidirectional relationship, challenges might be overcome by theory, but the practical implications for the researchers and/or access to financial funds might affect the possibility of conducting RCTs (Black, 1996). Therefor, cohort studies are considered the highest level of evidence in the current review. Further, only studies including minimum one follow-up measurement on a non-patient population, including both measurements of sedentary behavior and overweight and/or obesity was selected for eligibility assessment.

In cases were there were uncertainties whether or not the inclusion criteria were met, the article were saved for further eligibility assessment. Of the articles considered for eligibility, only studies measuring a bi-directional association, where both directions were assessed at the same time period, were included. After selecting those articles meeting inclusion criteria, the reference list of these articles were in turn, as the last procedure towards the final result, used for a backward-forward tracking to potentially include more relevant studies.

## 3.2 Study exclusion criteria

No exclusions were made regarding age, type of sedentary behavior or weight variable, or measurement method (objective vs. self-report). The review protocol allowed for modifications (Moher et al., 2009), based on scope and quality of included articles, even though no modifications were made in this case. Articles were excluded if they only studied one direction of the relationship, did not measure an independent prospective relationship between sedentary behavior and overweight or obesity, were a review article, did not measure sedentary behavior (only measure physical activity), or included a population being diagnosed, disadvantaged, of higher risk- or predisposed to obesity, or too specific (hence, offshore workers and menopausal women were excluded).

## **3.4 Search strategy**

The literature search was conducted in four different databases; PsycINFO(21<sup>st</sup> of January) EMBASE (27<sup>nd</sup> of January), PubMED (27<sup>nd</sup> of January), and Web of Science (29<sup>th</sup> of January). The investigated relationship is mainly based in sports science, but can be interpreted through medicine and interdisciplinary towards health. The chosen databases were therefore thought to sufficient cover the field of this relationship. Because some of the databases have different categories and terms related to their search engines, different search terms were used in the different databases (Table 3.1.). Web of Science's search engine is the only database that does not include pre-made categories or terms. Therefore, the search words used in this database were used to find relative terms for the other databases. If the original search word from Web of Science did not exist as a category or term, the word was used as an independent keyword to determine if it would benefit the final search.

Sedentary behavior	Overweight and obesity
PsycI	NFO <sup>1</sup>
Computer usage or human computer interaction or internet usage or television viewing or computer games or <i>sedentary or</i> <i>physical inactivity or physically inactive</i>	Overweight or obesity or body weight or body size or weight gain or body fat or body mass index or weight control or adipose tissue or adipocytes
EMB	$ASE^1$
Sitting or body position or physical inactivity or television viewing or human computer interaction or sedentary lifestyle or <i>sedentary</i>	Obesity or abdominal obesity or body mass or "weight, mass and size" or body weight or lean body weight or weight change or weight control or weight gain
PubM	$\text{IED}^2$
Sedentary lifestyle or sedentary lifestyles or television or internet or game, video or <i>computer</i>	Obesity or overweight or adiposity or body weight or body mass index or body size or circumference, waist or body weight or body weight change or body weight changes

 Table 3.1. Overview of search terms related to the different databases used.

 Sedentory behavior

<sup>&</sup>lt;sup>1</sup> Thesaurus chosen as search tool; words in *italics* are searched as keywords

<sup>&</sup>lt;sup>2</sup> Search conducted through MeSH terms; words in *italics* are searched as "Other terms".

Web of	Science
Sedentary, "sitting", "physical* inactiv*",	Obes*, overweight, "body weight", BMI,
"screen time", television, TV, computer, PC,	"body mass index", adiposity, "fat mass",
"video game*", videogame*	"fat free mass", "body size", "waist
	circumference", "weight gain"

## Table 3.1. Overview of search terms related to the different databases used. (continued). Web of Science

All search were limited to English language only, and article document type. Limiting search to human was possible through search function in all, but Web of Science. Latter was therefore performed in most of the databases. Search conducted in Web of science, was further refined by research areas. Hence, only including the areas of physiology, family studies, endocrinology metabolism, public environmental occupational health, sport science, behavioral science, and health care science services.

All the identified references were exported to EndNote (X7.5.1.1), for better handling the search result across the databases. The references were exported to the computer –based reference program the same day as the searches were completed, and removals of duplicates were then possible. Further, one reviewer performed the whole search, whereas studies were screened by title and abstract to determine their eligibility for inclusion, full-text articles were screened for final inclusion, and forward and backward tracking were conducted based on reference lists of the final included articles.

## **3.5 Data extraction**

Data were extracted from all the included studies into a table created with regard to reference, population (country, age, number of participants, and gender contribution), follow-up duration, data analyses, type and measurements of sedentary behavior, type and measurements of overweight or obesity, result and cofounding variables. One reviewer, who was not blinded to the authors or journal during the extraction process, performed all the data extraction.

## 3.6 Risk of bias assessment

Longitudinal, prospective population-based cohort studies are considered to be of the highest level of evidence, since RCT's are not feasible in this field (Burns, Rohrich, & Chung, 2011). To evaluate the risk of bias, all selected studies were quality assessed. The "QualSyst"(Table), a pragmatic systematic review tool from the "Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields" (Alberta Heritage Foundation for Medical Research) was used (Kmet, Lee, & Cook, 2004). This tool aim to assess the internal validity of the chosen articles, and therefore evaluated to what extend the research is planed, performed and analyzed in a way to minimizes risk of biases and errors. The checklist, developed for quantitative studies, included 14 items to be scored according to if the specific criteria was met or reported ("yes"=2, "partial"=1, "no"=0). "QualSyst" gives room for removing items that is not applicable for the assessed design. Therefore, three items was removed (*5. If interventional and random allocation was possible, was it described? 6. If interventional and blinding of investigators was possible, was it reported? 7. If interventional and blinding of subjects was possible, was it reported?). Total quality score, ranging from 0-1, was calculated for each article by dividing total score by possible score (e.g. total score 19/ possible score 22 = 0,86) (Kmet et al., 2004).* 

Table 3.2. Checklist for assessing the quality of quantitative studies (QualSyst).

## QualSyst assessment criteria

- 1. Question or objective sufficiently described?
- 2. Design evident and appropriate to answer study question?
- 3. Method of subject selection (and comparison group selection, if applicable) or source of information/input variables (e.g., for decision analysis) is described and appropriate.
- 4. Subject (and comparison group, if applicable) characteristics or input variables/information (e.g., for decision analyses) sufficiently described?
- 8. Outcome and (if applicable) exposure measure(s) well defined and robust to measurement / misclassification bias? Means of assessment reported?
- 9. Sample size appropriate?
- 10. Analysis described and appropriate?
- 11. Some estimate of variance (e.g., confidence intervals, standard errors) is reported for the main results/outcomes (i.e., those directly addressing the study question/ objective upon which the conclusions are based)?
- 12. Controlled for confounding?
- 13. Results reported in sufficient detail?
- 14. Do the results support the conclusions?

(Kmet et al., 2004)

## 4.0 Results

## 4.1 Search and selection

Final search identified 23,452 articles (Figure 4.1.) across the four databases (PsycINFO, n= 1,935; EMBASE, n=926; PubMED, n= 3,358; and Web of Science, n=17,233). After removing duplicates, a total of 19,837 articles were available for screening. Title and abstract were screened, and 19,675 records did not meet the inclusion criteria. Remaining 161 articles were assessed for eligibility, through full-text examination, and in total 153 of these articles were excluded according to previously described exclusion criteria. Forward-backward tracking did not resulted in more eligible articles, making the final sample ten articles.



Figure 4.1. Flowchart outlining the study selection.

## 4.2 Study characteristics

Of the ten studies included (Table 4.1.), five were conducted in Australia (De Cocker, van Uffelen, & Brown, 2010; Fuller-Tyszkiewicz, Skouteris, Hardy, & Halse, 2012; Hesketh, Wake, Graham, & Waters, 2007; Pedisic et al., 2014; van Uffelen, Watson, Dobson, & Brown, 2010), four in Europe (Altenburg, Singh, van Mechelen, Brug, & Chinapaw, 2012; Ekelund et al., 2008; Ekelund et al., 2012; Hjorth et al., 2014) and one in USA (Butte et al.,

2014). The majority of the studies are published in 2012 or later (Altenburg et al., 2012; Butte et al., 2014; Ekelund et al., 2012; Fuller-Tyszkiewicz et al., 2012; Hjorth et al., 2014; Pedisic et al., 2014), whereas no studies were published before 2007. One study (Ekelund et al., 2012) has a meta-analytic approach, and included data published between 2001-2009. Four studies included children ≤11 years old at baseline (Butte et al., 2014; Fuller-Tyszkiewicz et al., 2012; Hesketh et al., 2007; Hjorth et al., 2014), one study examined adolescents (Altenburg et al., 2012), one study covered both children and adolescents (4-16 years old) (Ekelund et al., 2012), while the remaining studies included adults (De Cocker et al., 2010; Ekelund et al., 2008; Pedisic et al., 2014; van Uffelen et al., 2010). Follow-up duration ranged from 200 days as the shortest (Hjorth et al., 2014) and six years as the longest (De Cocker et al., 2010; van Uffelen et al., 2010) follow-up. Median follow-up time was 3,2 years. About half of the selected study sample had two or more follow-up waves (Altenburg et al., 2012; Butte et al., 2012; De Cocker et al., 2010; Fuller-Tyszkiewicz et al., 2012; van Uffelen et al., 2010). Sample size ranged from 282 (Butte et al., 2012) to 31,787(Pedisic et al., 2014) participants. The median sample size was 4,340, when the two cohorts in the "Longitudinal Study of Australian Children" (Fuller-Tyszkiewicz et al., 2012) were used as independent study samples. All, but two studies (De Cocker et al., 2010; van Uffelen et al., 2010) included both genders in their population.

All, but two studies (Pedisic et al., 2014; van Uffelen et al., 2010), report objective overweight and/or obesity measurements. Except two studies (Hjort et al., 2014; Ekelund et al., 2012), all studies include BMI measure for weight status. Other weight related measurements included are WC (Altenburg et al., 2012; Ekelund et al., 2008; Ekelund et al., 2012), skinfold thickness and HC (Altenburg et al., 2012), body weight and FM (Ekelund et al., 2008), and FMI (Hjorth et al., 2014). Six of the studies use self-reported (Altenburg et al., 2012; De Cocker et al., 2010; Pedisic et al., 2010; van Uffelen et al., 2010) and parent-reported (Fuller-tyszkiewicz et al., 2012; Hesketh et al., 2007) sedentary behavior, measured as TV viewing (Altenburg et al., 2012; Fuller-Tyszkiewicz et al., 2012), computer use (Altenburg et al., 2010; van Uffelen et al., 2007), and siting time (De Cocker et al., 2010; Pedisic et al., 2010). Four studies use objective measurements (accelerometer: Hjorth et al., 2014; Butte et al., 2012; Ekelund et al., 2012, HR Flex: Ekelund et al., 2008) for assessing sedentary behavior. The latter studies had objective measurements for both variables.

verweight and Qualit	eneral Specific	BMI, 0,91 WC, HC, and skinfold thickness	BMI 0,91	BMI 0,91	BW, 0,91 BMI, FM, and WC	WC 0,95	BMI 0.50
y behavior O	Specific G	TV O viewing and computer	%SED 0	Sitting O time	SED 0	SED 0	TV 0
Sedentar measure	General	SR	0	SR	0	0	PR
	Age at baseline	12-14	×	22-27	49-50	4-16	0-1
pants	Proportion <sup>1</sup>	53 % M 47 % F	47 % M 53 % F	100% F	45 % M 55 % F	Not specified	51 % M
Particiļ	Total	465	282	5562	393	6413	$4340^{a}$
Follow- up	duration	20 months <sup>c</sup>	2 years <sup>c</sup>	6 years <sup>c</sup>	5,6 years (median)	2,1 years (median)	4 years <sup>c</sup>
Statistical analyses		Multilevel linear regression	Cross- lagged panel model	Linear regression	Linear regression	Linear regression	Auto-
Country		Netherlands	USA	Australia	UK	UK, Switzerland, Denmark, and Portugal	Australia
Author (year)	,	Altenburg et al., (2012)	Butte et al., (2014)	De Cocker et al., (2010)	Ekelund et al., (2008)	Ekelund et al., (2012)*	Fuller- Tvszkiewicz

<b>Table 4.1.</b> Des	scriptive characte	eristics of the i	ncluded art	icles (cor	ntinued).						
Hesketh et al., (2007)	Australia	Linear regression, logistic regression and and variance variance analyses	3 years	1278	49 % M 51 % F	5-10	Ы	Screen time	0	z-BMI and BMI category	0,82
Hjorth et al., (2014)*	Denmark	Linear mixed model	200 days	708	52 % M 48 % F	8-11	0	SED	0	FMI	0,91
Pedisic et al., (2014)	Australia	Linear regression and binary logistic regression	3,4 years (mean)	31787	42,5 % M 57,5 % F	45-65	SR	Sitting time	SR	BMI	0,86
Van Uffelen et al., (2010)	Australia	Repeated measure regression models	6 years°	8,233	100 % F	50-55	SR	Sitting time	SR	BMI	0,82
1=gender; 2=y *=Ekelund et a prospective an *= Hjort et al, a= Cohort B; b years, De Cocl et al (2010); fc Abbreviations: circumference, data", FMI; fai	tears; $3=QualSyi$ al. (2012); Meta- alysis only when 2014; gender pr $=$ Cohort K; ${}^{\circ}=A$ ker et al. (2010); bllow up waves $i$ ; M; male, F; fen , BW; body weig t mass index, SE	st (Leanne et al -analysis, relev reas proportion oportion is rep Altenburg et al t 3 and 6 years nale, PR; parei at 2. BMI; sta 2D; sedentary b	l, 2004); sco ant include of gender ' orted eligib (2012); foll (2012); foll 'es at 3 and 'es at 3 and 's. trs-report, S ndardized F ndardized F	a articles d articles vas not s le popula ow-up w 6 years, R; self-r SMI scor SED; sed	/een 0 and 1. is published bet pecified for th ation, includin aves at 8, 12 a Fuller-Tyszkid eport, O; objec e based on "U lentary behavi	ween 2001 le prospecti g 77 indivio und 20 mon ewicz et al. ctive, BMI; S Centers f or expresse	and 2009, ve studies. Juals lost to ths, Butte e (2012); fol body mass or Disease d as a perce	further char o follow-up at al (2014); low-up wav index, WC Control and ent of awake	acteristics a not include follow-up es at 2 and ; waist circ ! Prevention e time.	are describe d in the anal waves at 1 a 4 years, Van umference, 1 2000 grow	l for ysis. nd 2 n Uffelen HC; Hip th chart

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Table 4.2. Sum	mary of main results and con	nfounding variables of the included articles.		
Author (year)		Summary of main results		Confounding*
	Predictor <sup>a</sup>	Outcome	Result <sup>b</sup>	
Altenburg et	Fatness*	Changes in TV viewing and computer use	0	Outcome at baseline, ethnicity, aerobic
al., (2012)	TV viewing	Change in BMI and HC in boys	+	fitness
		Change in body fatness* in girls	0	
	Computer use	Change in skinfold thickness in both gender,	+	
		and BMI in girls.		
Butte et al.,	BMI	%SED at FU1 (both genders)	0	Gender, age, time-lagged pubertal
(2014)	BMI at FU1	%SED at FU2 (both genders)	+	status
	%SED	BMI at FU1 among boys	+	
	%SED at FU2	BMI at FU2 (both gender)	0	
De Cocker et	BW	Change in sitting time	0	Outcome a baseline, age, area of
al., (2010)	Early change in BW	Late change in sitting time	0	residence, educations, occupations, work
	Sitting time	Change in BW	0	load, partner, numbers of birth, smoking,
	Early change in sitting	Late change in BW	0	alcohol, physical activity, energy intake,
	time			BMI
Ekelund et al.,	SED	Change in weight-variables	0	Age, gender, PAEE, follow-up duration,
(2008)	BW, BMI, FM, and WC	Change in SED	+	outcome at baseline, smoking,
				socioeconomic status
Ekelund et al.,	SED	Change in WC	0	Age, smoking, outcome at baseline,
(2012)	WC	Change in SED	+	follow-up duration, monitor wear time
Fuller-	TV viewing	BMI at FU1 for both cohorts	+	Not noted
Tyszkiewicz et	TV viewing at FU1	BMI at FU2 for both cohorts	+	
al., (2012)	BMI	TV at FU1 for both cohorts	+	
	BMI at FU1	TV at FU2 for both cohorts	+	

e	z-BMI and BMI category	+	Age
	Change in z-BMI	0	
<b>BMI</b> category	Screen time	+	
<b>BMI</b> category	Change in screen time	0	
	Change in FMI	0	Age, gender, pubertal status, sex-pubertal
	Change in total sedentary time.	+	status interaction, month of first
			measurement (baseline), follow-up
			duration, outcome at baseline
	Change in BMI	0	Age, gender, educational level, area level
0	Increased sitting time	+	socio-economic status, employment
	Change in total sitting time	+	status, outcome at baseline, chronic
	(<8 hours/day)		illnesses, risk of psychological distress,
			self-reported general health, MVPA
	Change in BMI (energy balance-model)	+	Exercise status, energy intake, smoking
	Change in BMI (fully adjusted-model)	0	status, alcohol intake, depression, number
	Change in sitting time	0	of chronic diseases, marital status, country
			of birth, area of residence, education, job
			status.
I variables are b	aseline measurements.	ibern neem	otor and outcome. ()
	variables are b	Change in FMI Change in total sedentary time. Change in BMI Increased sitting time Change in total sitting time (<8 hours/day) (<8 hours/day) ( 8 hours/day)<br (<8 hours/day) (<8 hours/day	Change in total sedentary time. () Change in total sedentary time. () Change in BMI Increased sitting time (As hours/day) (<8 hours/day)

variables of the included articles (continued) ممنامستم لمقو 11 q ΰ 

<sup>2</sup> = significant association between predictor and outcome:+, No significant association between predictor and outcome. υ. Abbreviations: BMI; body mass index, WC; waist circumference, BW; body weight, z-BMI; standardized BMI score based on "US Centers for Disease Control and Prevention 2000 growth chart data", FMI; fat mass index, SED; sedentary behavior, %SED; sedentary behavior expressed as a percent of awake time, MVPA; moderate to vigorous physical activity, FU1 (2); follow-up 1 (2), HC; hip circumference

## 4.5 Methodological quality assessment

Overall, the included studies showed good quality (Table 4.2.). Seven of the studies had a quality score above 0,85, with 0,95 being the highest score. Of the three studies with lowest score only one study had a score less than 0,82, with the lowest score reported being 0,59. All studies reported sufficient described and/or appropriate research question or objective, sample size and analysis. Further, estimate of variance was reported sufficiently in all, but one study. Of criteria most often not met, only three studies The most common limitation was reported for method of subject selection, where only three articles were sufficient described, and for appropriate outcome- and exposure measures, where four articles reported well-defined and robust assessments.

## 5.6 Does sedentary behavior cause overweight and obesity?

Of the ten included studies, seven studies found no association between baseline sedentary behavior and change in overweight/obesity over time, while one study found mixed associations between different surrogates of sedentary behavior at baseline and change in various fatness variables at follow-up between gender (e.g. baseline TV viewing predicted change in BMI over time in boys, and computer use at baseline was adverse associated with change in BMI over time in girls only), and two studies found an adverse association between baseline sedentary behavior and change in weight over time.

Pedisic and colleagues (2014) showed that self-reported baseline sitting time (categories) was not significant associated with change in self-reported BMI category several years later in middle-aged adults (p=0,292). Similarly, De Cocker and colleagues (2010) were unable to show any effect of baseline self-reported sitting time on objectively assessed body weight, in female young adults. Sitting time at baseline was not associated with change in body weight after six years, neither change in sitting time from the three first years of measurements were associated with change in body weight from the last three years of measurement (p > 0,05) (De Cocker et al., 2010)

Van Uffelen and co-workers (2010) showed that self-reported sitting time at baseline was not associated with self-reported percentage weight change the three first years or the three last years. However, for those who reported being normal weight or overweight at baseline,

sitting time at baseline was associated with change in weight when only exercise status and energy intake were adjusted for (normal weight, E=0,08, 95% CI= 0,02; 014 and overweight, E=-0,09, 95% CI=-0,16; -0,01) (van Uffelen et al., 2010).

Altenburg and coworkers (2012) showed that minutes of self-reported TV viewing at baseline predicted measures of objectively measured BMI (b= 0,001, 95% CI = 0,001; 0,001) and HC (b= 0,002, 95% CI = 0,000; 0,004) after 20 months, adjusted for the outcome variable at baseline, in adolescent boys. Contrary, changes in body fatness (BMI, WC, HC and skinfold thickness) were not predicted by TV viewing at baseline, in adolescent girls (p> 0,05). In both genders, computer use (minutes/day) at baseline predicted change in skinfold thickness (boys: b= 0,008, 95% CI = 0,005; 0,016 and girls b= 0,015, 95% CI = 0,003; 0,027). This association was modified by time, in girls. Further, change in BMI was predicted by baseline computer use (minutes/day), in boys (b= 0,001, 95% CI = 0,001; 0,001) (Altenburg et al., 2012).

Hesketh et al (2007) demonstrated that baseline self-reported screen time predicted both objectively measured z-BMI ( $\beta = 0,02, 95\%$  CI = 0,01; 0,02) and BMI category: non-overweight or overweight/obese (OR = 1;03, 95% CI = 1,02; 1,05) after three years follow-up in children. Baseline screen time did not predict changes in z-BMI at follow up (level of significance not described)(Hesketh et al., 2007). Fuller-Tyszkiewicz and colleagues (2012) demonstrated that self-reported TV viewing had a small but significant prediction on objectively assessed BMI in young children. TV viewing at baseline predicted BMI after two years (both cohorts,  $\beta = 0,03$ , estimate of variance not described), and TV viewing at mid follow-up after two years predicted BMI two years later at the final follow-up (cohort B,  $\beta = 0,03$  and cohort K,  $\beta = 0,02$ , estimate of variance not described) (Fuller-Tyszkiewicz et al., 2012).

Ekelund et al (2008) found no effect of objective measured baseline SED on change in any of the objective assessed weight associated outcomes more than five years in average later, in middle-aged adults (level of significance not described). The school children examined by Hjorth and colleagues (2014) showed that baseline objective SED did not predict changes in objectively measured FMI after 200 days (p= 0,16). There was no association between changes in SED and changes in FMI (p= 0,15) (Ekelund et al., 2008)). Butte et al. (2014) demonstrated in their analyses that children's objective %SED at baseline explain children's

objectively measured BMI at follow-up at one year, for boys (b= -0,04, p= 0,01). %SED at mid follow-up after one year, did not predict BMI at the final follow-up at the second year of measurement, in either gender (p= 0,64) (Butte et al., 2014). Ekelund and colleagues (2012) showed no association between objectively measure baseline SED and objective measured WC several years later (p> 0,05) in European children and adolescents.

### 4.7 Does overweight or obesity cause sedentary behavior?

Of the ten included studies, four studies found no association between baseline weight and change in sedentary behavior over time, while one study only found an unfavorable association between mid-study weight and change in sedentary behavior over time in second half of the study, and five studies found an adverse association between baseline weight and change in sedentary behavior at follow-up.

Pedisic and co-workers (2014) showed that those who self-reported being obese (BMI  $\geq$  30 kg/m2) at baseline, compared to those self-reported being normal weighted (BMI 18,5-25), were association with having increased self-reported sitting time several years later (adjusted OR= 1.20, 95% CI= 1,11-1,30). BMI category at baseline was predictive of change in total sitting time at follow-up in all, but those who reported the highest siting time at baseline (obese and <4 hours total sitting at baseline, adjusted OR=1,05, 95% CI= 0,94-1,17; obese and 4-8 hours/day sitting at baseline, adjusted OR= 1,05 95% CI= 0,96-1,15) (Pedisic et al., 2014). There were no associations between body weight and sitting time in any of the situations (p >0,05) assessed by De Cocker and co-workers (2010). Baseline body weight, categorized by BMI (underweight= BMI <18.5 kg/m2; normal weight= BMI 18.5–24.9 kg/m2; overweight= BMI 25–29.9 kg/m2; and obese= BMI  $\geq$  30 kg/m2), did not predict change in sitting time after six years. Changes in body weight from baseline to mid follow-up after three years was not associated with changes in sitting time the last three years of measurements (De Cocker et al., 2010). Van Uffelen and colleagues (2010) showed that self reported BMI at baseline was not associated with changes in sitting time, neither the three first years of measurements or the three last years, in any of the BMI categories reported at baseline (p>0,05).

Altenburg and colleagues (2012) demonstrated that neither objectively measured BMI, WC, HC or skinfold thickness at baseline predicted change in self-reported TV viewing after 20

months (p> 0,05). Hesketh and colleagues (2007) showed that children with higher z-BMIs (based on age and gender specific US reference data; Kuczmarski et al, 2000) and those classified as overweight/obese (based on international age and gender specific cutoff points; Cole, Bellizzi, Flegal & Dietz, 2000) at baseline had higher screen time three years later, after adjusting for age (b = 1,59, 95% CI = 0,89; 2,29). Change in screen time at follow-up was not predicted by BMI category or z-BMI at baseline (level of significance not described) (ibid.). Fuller-Tyszkievicz and colleagues (2012) observed that objectively assessed BMI at baseline predicted self-reported TV viewing at mid follow-up after two years, in young children (cohort B,  $\beta$  =0,03 and cohort K,  $\beta$  =0,05, estimate of variance not described). From the second year of study at mid follow-up until last follow-up two years later, BMI only predicted follow-up TV viewing in cohort B ( $\beta$  =0,04, estimate of variance not described) (Fuller-Tyszkieviczet al., 2012).

Ekelund and colleagues (2008) observed that body weight, fat mass, BMI, and WC at baseline, were all significant and independent predicted by change in SED after more than an average five years later (body weight;  $\beta = 0,33,95\%$  CI = 0,15; 0,50, p= <0,001, fat mass;  $\beta = 0,59,95\%$  CI = 0,11; 0,40, p= <0,001, BMI;  $\beta = 1,10,95\%$  CI = 0,58; 1,63, p= <0,001, WC;  $\beta = 0,44,95\%$  CI = 0,23; 0,66, p= <0,005) in middle-aged adults. Change in body weight, BMI and fat mass were also associated with change in SED at follow-up (fully adjusted analyses:  $\Delta$  body weight;  $\beta = 0,43,95\%$  CI = 0,007; 0,79, p ≤0,019,  $\Delta$ BMI;  $\beta = 1,26$ , 95% CI = 0,27; 2,26, p ≤0,013 and  $\Delta$  fat mass;  $\beta = 0,49,95\%$  CI = 0,02; 0,96, p ≤0,041) (Ekelund et al., 2008).

Hjorth and co-workers (2014) showed that baseline objectively measured FMI sig. predicted change in total objective SED after 200 days (b = 0,42, 95% CI = 0,22; 0,63, p  $\leq$ 0,001), among school children. When only normal-weight children were accounted for in the analyses, the relationship still remained significant (p $\leq$  0,03)(Hjort et al., 2014). Butte and co-workers (2014) showed that objectively measured BMI at baseline did not predict objective %SED at follow-up after one year (boys, p=0,13 and girls, p=0,20). BMI at follow-up after one year predicted %SED at follow-up after two years, in both genders (b=0,29, p=0,03) (Butte et al., 2014). Ekelund and colleagues (2012) observed an overall association between objectively measured baseline WC and objectively measured SED several years later (b= 0,40, 95% CI= 0,19; 0,61), in European children and adolescents.

## **5.0 Discussion**

## 5.1 Summary of main results

The aim of the present paper was to review the prospective bidirectional relationship between sedentary behavior, and overweight and obesity among non-patient children to middle-aged adults, and to consider the directions of this causality. Ten articles were identified, and in the direction whether overweight/obesity cause sedentary behavior four studies found no association between baseline weight and change in sedentary behavior over time, while one study only found an unfavorable association between mid-study weight and change in sedentary behavior over time in second half of the study, and five studies found an adverse association between baseline weight and change in sedentary behavior at follow-up. In the opposite direction whether sedentary behavior cause overweight/obesity seven studies found no association between baseline sedentary behavior and change in overweight/obesity over time, while one study found mixed associations between different surrogates of sedentary behavior at baseline and change in various fatness variables at follow-up between gender (e.g. baseline TV viewing predicted change in BMI over time in boys, and computer use at baseline was adverse associated with change in BMI over time in girls only), and two studies found an adverse association between baseline sedentary behavior and change in weight over time.

## 5.2 Agreements and disagreements with existing literature

The results on whether sedentary behavior predicts overweight and/or obesity are somewhat supported by previous reviews (Chinapaw, Proper, Brug, van Mechelen, & Singh, 2011; Cox, Skouteris, Rutherford, & Fuller-Tyszkiewicz, 2012; Ekelund, Hildebrand, & Collings, 2014; Thorp et al., 2011). Chinapaw and co-workers (2011) found that there was insufficient evidence for a longitudinal relationship between self- or proxy-reported sedentary time and BMI, and indicators of adiposity in young people. However, it seemed to be no evidence for a relationship between sedentary behavior and BMI for girls, when measured alone (Chinapaw et al., 2011). The latter is consistent with what Altenburg and colleagues (2012) found, where TV viewing was adverse associated with BMI and HC in boys only. Cox and colleagues (2012) on the other hand, found that most studies observed an unfavorable association between hours spent watching TV and child adiposity measurements, with subjective assessments including observations. Latter is supported by Thorp and colleagues (2011), who reported that there were sufficient amount of evidence to determine that obesity during

adulthood was strongly predicted by sedentary behavior during childhood and adolescence. If this is the case, conflicting results can be explained by short follow-up time if the studies do not follow up into adulthood.

Thorp and co-workers (2011) found that there was limited evidence for a longitudinal relationship between self-reported sedentary behavior(s), weight gain, and risk of obesity in adults. Ekelund and colleagues (2014) on the other hand, found that objectively measured sedentary behavior seemed not to be associated with adiposity in children and adolescents when MVPA was accounted for, even though the result were not unambiguous. The latter is more in line with this review's results in adults, showing consistent result that self-reported sitting time and objectively measured sedentary behavior were not associated with BMI or other weight measurements, with the exception of one study showing averse associations in less adjusted models (van Uffelen et al., 2010).

The majority of the high quality studies (quality score above 0,85) observed no relationship between sedentary behavior and change in weight outcome, but an adverse association between weight predictors and sedentary behavior. That overweight and obesity lead to more sedentary behavior is consistent compared with literature dealing with inactivity outcomes (Metcalf et al., 2011; Mortensen et al., 2006, Petersen et al., 2004). Inactivity is distinct different from sedentary behavior (Hamilton et al., 2008), but would be the closest comparable measurement when literature on association with sedentary behavior is limited. Mortensen and colleagues (2006) observed that self-reported sedentary time (no reported leisure-time physical activity) was longitudinal predicted by self-reported weight status in adults. When BMI was calculated with objective assessment, an adverse relationship is also reported (Petersen et al., 2004). If only compared to the reviewed studies including adults using self-reported sedentary behavior, these results are conflicting. Both van Uffelen and colleagues (2010) and De Cocker and colleagues (2010) observed no association between baseline BMI and change in follow-up sitting time, only included women. If such an adverse relationship exists, the differences may be explained by self-reported measurement causing biases. Metcalf and co-workers (2011) used entirely objective measurements, and found that fatness variables predicted change in inactivity in children. This is consistent with findings in this review, and a possible similar association in adults is arguable whereas Ekelund and colleague (2008) also found such adverse association in adults.

All of the reviewed studies observed total time spent in sedentary behavior or any other surrogate behavior in association with weight measurement, and vice versa. Existing studies suggest that sedentary patterns (bouts and breaks related to sedentary behavior) are of interesting importance for metabolic health (e.g. Healy et. al., 2008; Peddie et al., 2013) Healy and colleagues (2013) observed that Australian adults who increased breaks in sedentary behavior, independent of total sedentary behavior and MVPA, had a beneficially association with WC, triglycerides and 2 hour plasma glucose. Other studies have also supported the beneficial association with other cardio metabolic risk factors (e.g. c-peptide, glucose and insulin levels) (Altenburg et al., 2013; Peddie et al., 2013; Dunstan et al., 2012). None of the included studies investigated sedentary behavior pattern because there was no such current literature on the bidirectional relationship between sedentary behavior pattern and weight variables.

## **5.3.** Rationales for a bidirectional relationship

## 5.3.1 Sedentary behavior cause overweight/obesity

The rationales for sedentary behavior to cause overweight and obesity are mainly linked to alterations of energy balance and physiological processes, which in turn affect weight gain (Hamilton et al., 2007). Time spent in sedentary behaviors is associated with a reduction in overall PAEE, whereas it displaces time spent in physical activity of higher intensities (Owen et al., 2010). Importantly, sedentary behavior does not only displace physical activity of high intensity (such as MVPA), but also activities with light intensity. This could be illustrated by replacement of two hours light physical activity (2,5 METs) by sedentary behaviors (1,5 METs) every day. Such replacement could be estimated to reduce PAEE by about two METhours/day, which in turn would result in approximately the same level of energy expenditure as walking 30 minutes per day (0,5 hours\* 3,5 METs= 1,75 MET-hours)(Owen et al., 2010). Further, a displacement of physical activity by sedentary behavior that result in a difference of 10 MET-hours/week, would equal approximately 1000 kcal/week (Garber et al., 2011). Based on energy expenditure alone, a reduced energy expenditure of 1000 kcal/week would result in 0,5 kg increase in body fat over three week (1 pound body fat equals 3500 kcal) (Hill, Wyatt & Peters, 2013), which over time would be a major risk of overweight and obesity.

The physiological processes induced by sedentary behavior seem to be different from those initiated by physical activity (Hamilton et al., 2007). Sedentary behavior result in less work performed by large skeletal muscles such as legs, back and trunk, which otherwise would have been used for upright movements. As an example, sedentary behavior is related to impaired lipid metabolism, whereas LPL activity in skeletal muscles is especially sensitive to activity. Loss of LPL activity at the vascular endothelium, caused by sedentary behavior, reduce the optimal tissue-specific uptake of lipoprotein-derived fatty acids. Lack of LPL activity impair hydrolysis of triglyceride within lipoproteins, which in turn could contribute to the risk of obesity and other cardio metabolic conditions (Hamilton et al., 2007).

## 5.3.2. Overweight and obesity cause sedentary behavior

Rationales for overweigh and obesity to cause sedentary behavior might not be as established as for the opposite relationship, but is mainly concerned how overweight/obesity cause a behavioral displacement of physical activity of various intensities by sedentary behavior. Overweight individuals are less likely to stay physical active (Ekelund et al., 2014; Wareham et al., 2005). In general, healthy people are more active than individuals with medical issues and conditions (King et al., 1992). Therefore it is not unlikely to believe that obesity would lead lo less activity, whereas obesity is associated with serious health consequences such as mortality, accelerated aging and illness (Roth et al., 2004). Okosun and colleagues (2001) observed that obesity was adverse associated with self-rated general health. This is further supported by Wolk & Rössner (1996), which observed that obese individuals reported higher prevalence of sever pain in various joints, and physical impairment (particularly reduced mobility). It is somewhat easy to imagine how overweight, and particularly joint pain, could make sedentary behaviors more an appealing choice of behavior, but it could also be further explained by "The Fear-Avoidance Model" (Leeuw, Goossens, Linton, Crombez, Boersma & Vlaeyen, 2007)

It is somewhat easy to imagine that carrying excessive weight on your body would lead to less physical activity, whether it is because of the actual extra weight, or discomfort, pain or adverse psychological aspects. Goran and co-workers (2000) demonstrated that obese individuals had reduced sub-maximal aerobic capacity. It is important to notice that maximal VO<sub>2</sub> is not affected by excessive fat mass, but rather by FFM. Since relative cardiorespiratory fitness describe an individual's ability to perform exhaustive work, obese individuals would potentially perceive a given activity more exhausting than normal weighted individuals with higher relative cardiorespiratory fitness (Goran et al., 2000). Hypothetically, because overweight and obese people perceive an activity more exhausting the barrier for choosing to do that activity increase, and they might be more likely to choose a sedentary behavior instead. Imagine walking to the grocery store would be fast and easy for a normal weighted individual. The same walk would make the obese individual breath faster, increase body temperature, increase sweating, and feel tiring. The barriers for walking are potentially much higher for the obese individual, making it easier to choose to drive or even stay home and order what needed online.

Ball and colleagues (2000) observed in a population-based sample of Australian adults, that having a perception of being "too fat" to exercise was a barrier for being physically active among several overweight and obese individuals. Further, they also observed those who perceived themselves as being "too fat", also were more likely to have feelings of being "too shy" or embarrassed, and lazy or unmotivated (Ball et al., 2000). Overweight and obese individuals might have less self-efficacy and less positive experiences with activity, which are determinants for physical activity (King et al., 1992), and therefore potentially are more likely to choose sedentary behaviors instead of being physically active. Deforch and colleagues (2006) observed that overweight and obese adolescents had a less positive attitude towards physical activity, and perceived more barriers for leisure-time physical activity. These result are somewhat supported by Trost and co-workers (2001), which observed that obese children reported lower levels of physical activity self-efficacy compared with their non-obese counterparts.

## **5.4 Methodological limitations**

#### 5.4.1. Quality assessment of the Included studies

The present review included 10 studies published between 2007 and 2014 examining the bidirectional relationship between sedentary behavior, and overweight and obesity. The studies included children, adolescents or adults, and had a median sample size of 4,340 individuals with sample sizes ranging from 282 (Butte et al., 2014) to 31,787 (Pedisic et al., 2014) participants. The methodological quality assessment ranged between, 0,59 and 0,95, whereas seven studies were assessed having a score above 0,85. Overall, the general quality of the included studies were considered rather good. A great advantage is that all studies reported sufficient described and/or appropriate research question or objective, sample size,

and analysis. Except for one study, estimates of variance were also sufficient described for the main results across all studies.

## Method of subject selection

A key quality limitation of the included studies was frequent lack of sufficient described and appropriate method of subject selection, which could introduce selection bias. Seven out of the ten included articles were scored as insufficient because method of subject selection were reported elsewhere (Fuller-tyszkiewicz et al., 2012) or not sufficiently summarized (De Cocker et al., 2010), chronic illness was possibly present in study population (Pedisic et al., 2014; van Uffelen et al., 2010), or subject were recruited from study with conflicting aim (Altenburg et al., 2012; Hjort et al., 2014) or from an integrated health care delivery organization (Butte et al., 2014).

The reduced quality of method of subject selection has potential to produce selection bias. Factors that affect subject selection are not directly thought to create selection bias, besides when selection could affect both exposure and outcome (Grimes & Schulz, 2002). Internal controls are used in single cohort studies, and consist of those individuals that do not develop the outcome of interest (Mann, 2003). In this review, it is a matter whether those who are normal weight, and overweight or obese, differ in characteristic beside sedentary behavior, and whether those who are sedentary or less sedentary differ in important variables except overweight or obesity. It can be hypothesized that participants originated from another study with conflicting aim, might change their behavior in such way as affecting the potential development of an outcome. Example, children from the control croup in the "Dutch Obesity Intervention in Teenagers" (DOiT) study (Altenburg et al., 2012) could have been affected by the aim of preventing excessive weight gain. It is potentially crucial if individuals having a natural behavior towards the observed relationship change their behavior and reverse potential outcome of the original everyday behavior. However, it could be argued that the same potential impact would affect all participants, those developing the outcome and those who do not. If this is the case, the internal validity is not crucial decreased, but rather external validity could have been affected.

The quality assessment tool does not assess losses to follow-up, which could be important in turn of evaluating non-respondent bias, also known as attrition bias, as part of selection bias.

Of the reviewed articles, three studies (Butte et al., 2014; Ekelund et al., 2012; Fuller-Tyszkiewicz et al., 2012) did not specify missing data to follow-up. Two studies (Altenburg et al., 2012; De Cocker et al., 2010) report some numbers of missing data, but interpretations are somewhat challenging. Altenburg and colleagues (2012) describe range of missing data among the different measurements, example analyzed population consisted of 246 boys (not exclusively) and missing data sample size ranged from 247-177 among three different times of measurements for the boys. Because it is possible for different people to have missing data for the different measurements, it is not certain how many boys who were eligible for assessment at all times, and how many who were lost to follow-up because of one or more missing data. However, it seems that amount of missing data is rather high compared to analyzed population. De Cocker and co-workers (2010) account for data lost for weight and sitting time independent, but it is not stated whether it is possible that those who have missing values for one variable can have missing values for the other. If those with missing data only had missing data for either one of the variables, the analyzed sample is rather small (analyzed sample /(analyzed sample + numbers of missing weight data+ numbers of missing sitting time data) = 65 %) compared to eligible study sample.

The remaining five studies account for losses to follow-up; retention rate could be calculated based on provided study information as being 83 % for Pedisic et al. (2014), 87 % for van Uffelen et al. (2010), and 85 % for Hjort et al. (2014), and percentage analyzed of those eligible was provided in the remaining two articles being 87 % for Ekelund et al. (2008) and 81 % for Hesketh et al. (2007). As a general rule, no more than 20 % of the study sample should be lost to follow-up (Song & Chung, 2010). In cases where too many individuals are lost through the study, the internal validity is weakened (Song & Chung, 2010). Hence, it is reason to believe that the five latter described studies should not have their internal validity affected by non-respondent bias. Whether the remaining five studies are affected by attrition bias, should be taken in to account when interpretations are made.

In observational studies non-responders vary from responders (Grimes & Schulz, 2002). Those who smoke cigarettes are more likely to not respond to mail surveys (Grimes & Schulz, 2002). Shahar and colleagues (1996) investigated non-respondents in a populationbased cohort study of cardiovascular disease in terms of demographics and health characteristics. They observed that non-responders were less likely to be married, employed and well educated. The investigators reported their findings to be consistent with similar literature, whereas most evidence has been found for low education that has been shown to have a strong relationship with non-response in health surveys. Older age and less favorable described general health status were also reported among the non-responders. Other studies have suggested a higher mortality rate to be present among non-responders than responders. It can be debated whether non-responders are more likely to have more diseases (Shahar et al., 1996).

Hesketh and colleagues (2007) were the only investigators, among the reviewed studies, who compared responders and non-responders. In this study responders and non-responders were comparable with respect to gender, age, maternal- and paternal education levels, TV viewing (per/week), electronic game/computer use (per week), and total screen time. On the other hand, non-responders had significantly higher mean BMI than responders, and numbers of individuals classified as overweight or obese at baseline were higher among non-responders. Non-responders were more likely to be children of parents born in a non-English speaking country, and had a slight, but not significant, tendency to be resident in urban areas (Hesketh et al., 2007). It seems like the non-respondents are as sedentary as responders, but have higher BMI. If this difference is of importance, it is of especially value for understanding and confirming a potentially adverse relationship between excessive weight and sedentary behavior.

## **Outcome and exposure measurements**

Another frequent reported limitation was regarding whether outcome and exposure were well defined, and robust to measurement and misclassification bias. Only four of the included studies were considered meeting the criteria, whereas limitations reflected choice of measurement methods. Four studies reported objective measurements, and the remaining six studies reported self- or proxy reported sedentary behavior. If exposure or outcome is incorrectly determined, it can cause information biases (observation-, classification- or measurement bias) (Grimes & Schulz, 2002). Self-reported methods are considered more prone to recall and reporting biases, and are therefor a less accurate measurement method than objective assessments (Atkin et al., 2012). Self-reported BMI is generally based on an overestimation of height, and underestimation of weight (Hattori & Sturm, 2013; Krul, Daanen, & Choi, 2011). In addition differences in reporting are seen across ages, gender and countries (Krul et al, 2011).

In the adult population included in the current review, three articles reported using selfreported measurements for sitting time. All studies reported some indications about reliability and validity of used measurements, although varying precision. Two studies used questions similar to those included in IPAQ, which have high test-retest reliability but is shown to correlate rather weakly with accelerometer (Rosenberg et al., 2008). In children and adolescent, surrogate measurements of sedentary behavior were measured as self- or proxy reported TV viewing (with and without computer use) or screen time, which is problematic as it does not represent the total time spent sedentary (Atkin et al., 2012). Only Altenburg and colleagues (2012) reported indications for validity or reliability, whereas they described to have used a questionnaire that is comparable to a previous validated questionnaire with high test-retest reliability (r=0,94) (Robinson, 1999). Self- and proxy reported sedentary behaviors among children and adolescents have shown varying validity and reliability across studies (Atkin et al., 2012; Lubans et al., 2011), and a common way of establishing validity and/or reliability has been to compare one self-or proxy reported method against another self- or proxy reported method (Lubans et al., 2011). This is especially problematic since one measurement with unknown validity is compared with another measurement with unknown validity. In addition, studies using accelerometer as criteria measurement have showed lower levels of validity. However, there is a limitation in reporting these measurements whereas it lack a gold standards, which increase the importance of considering adjustments of higher correlation coefficient to attenuate for the reduced effect of assessment error (Lubans et al., 2011).

Another limitation could occur when different measurements are used at baseline and followup. Ekelund and colleagues (2008) report two different measurements for establishing Flex HR between baseline and follow-up. At baseline, the individual Flex HR was established based on a graded exercise test on a cycle ergometer, while the Flex HR was calculated based on a submaximal walking treadmill test at follow up. In order to calculate the Flex HR, each individual relationship between HR and oxygen uptake were measured. In general, people tend to reach higher maximal oxygen uptake during treadmill tests than cycling, and differences in lactate accumulation in local muscles as a result of lacking technique is more prone to affect the maximal oxygen uptake and heart rate in cycling (Millet, Vleck, & Bentley, 2009). Although, this might be more important when differing behaviors of higher intensities apart, compared when determining sedentary behaviors. Hesketh and co-workers (2007) also report using two different proxy-report of average screen time per day from baseline to follow-up, whereas a six-point ordinal response scale was used at baseline, and an open-ended continuous response scale was used at follow-up. This also has the potential to cause bias.

However, precision of exposure and outcome variable are also important to consider whereas measurement errors can introduce bias to an estimate of the association between exposure and outcome (Hutcheon, Chiolero, & Hanley, 2010). Assessment of adiposity, and physical activity and sedentary behavior, differ noticeably in measurement precision (Ekelund et al., 2014). Adiposity measurements are in generally more precise than what physical activity and sedentary behavior measurements are. This is the case even when physical activity and sedentary behavior are measured by objective measurements, whereas they only provide a snapshot of the true individual activity level because the assessments are limited to few days of recall or observation. Since adiposity and sedentary behavior are both exposure and outcome depending on the observed direction of this relationship, the varying precision has impact on the interpretation of the potentially bidirectional relationship (Ekelund et al., 2014). The influence of random measurement error vary depending on whether the error is concerned the outcome or the exposure variable (Hutcheon et al., 2010). If the error is in the exposure, the measure of effect is attenuated, while if the error is in the outcome, the error will have minimal effect on the attenuation, but the precision of the estimate would be decreased (increased standard error) (Ekelund et al., 2014; Hutcheon et al., 2010). Therefor, the direction where the least precise measurement (sedentary behavior) is used as the exposure, the measure of effect is more attenuated. This might explain why there in general is more consistent evidence that baseline weight cause later sedentary behavior, that what is seen for the reverse relationship.

Further, choice of adiposity marker would potentially affect how precisely the bidirectional relationship is measured. Especially the use of BMI could be further discussed. Ekelund and colleagues (2014) emphasize the challenge of using BMI as surrogate measure for adiposity in children. This is especially problematic because the relative contribution of fat mass and fat-free mass to body weight differ by sex, age and pubertal status, and during growth a positive change in BMI is mainly a result of increased fat-free mass rather then fat mass (Ekelund et al., 2014). However, all the included articles using BMI in children have taken growth, age and sex into account, whereas Butte and colleagues (2014) used US reference data related to the 85<sup>th</sup> (overweight) and 95<sup>th</sup> (obese) centiles of BMI (Kuczmarski et al.,

2002), Fuller-Tyszkiewicz and colleagues (2012) used internationally cut-off points (Cole et al., 2000), and Hesketh and co-workers used both previous mentioned methods. Using the 2000 CDC Growth Charts for the United States (Kuczmarski et al., 2002) to define BMI in children is especially questioned based on it generalizability and the validity of the used cut-off centiles, whereas the 90<sup>th</sup>, 91<sup>th</sup>, 97<sup>th</sup> or 98<sup>th</sup> centile are just as valid as the used 85<sup>th</sup> or 95<sup>th</sup> centile (Cole et al., 2000). The international cut-off points, on the other hand, are defined in BMI units in young adulthood, based on obesity prevalence, and extrapolated to childhood, in a wide international population. To what extend these methods reflect the individual or group-level maturation, affect the precision of BMI used in children.

This challenge could be argued to also apply for the study conducted by Altenburg and colleagues (2012), as no specific considerations were done regarding the use of BMI in adolescents. Another aspect of using BMI to identify adiposity, is related the older population. Both change in height and body composition can occur as a result of age, and differ from changes seen in adults (Roth et al., 2004; Sorkin, Muller & Andres, 1999). Sorkin and colleagues (1999) observed a modest effect of height loss on BMI. If older individuals only experience height loss, and no other differences in body composition, this change would lead to a higher BMI and an overestimation of fat mass. However, older individuals often experience an increase in fat mass and decrease in muscle mass (Roth et al., 2004). Hypothetically, an isolated change in body composition could occur in elderly individuals without any change in body weight, which in turn could lead to an unchanged BMI (given the height has not changed) and underestimated fat mass. The differences in the young and older population should be taken into account, and more precise measurement should be considered used.

Another aspect is how well BMI detect adiposity in general. Okoroduro and colleagues (2010) conducted a systematic review and meta-analysis of articles examining the performance of BMI to detect body adiposity. They concluded in their article that the cut-off values commonly used to diagnose obesity have high specificity, bot low sensitivity to assess adiposity, whereas it fails to recognize half of the individuals with excess percentage body fat. The result of low sensitivity is that less people are identified as having excess body fat (Okoroduro et al., 2010). Romero-Corral and co-workers (2010) observed normal weight obesity, defined as the combination of normal BMI and high percentage body fat in a representative American adult population. They observed that the highest tertiles within the

normal weight BMI group, equaled > 23 % body fat in men and > 33 % body fat in women. Interpreted, one out of three with normal BMI should potentially have been classified as overweight or obese by a more sensitive adiposity measure (% BF).

This could be critical when BMI is used as exposure, and individuals are categorized. Both Pedisic and colleagues (2014) and van Uffelen and co-workers (2010) classify their subjects by BMI at baseline. When the normal BMI group at baseline potentially includes individuals with excess body fat, which is the investigated exposure, this group is not entirely representative for a true non-exposed group. This is problematic when both the overweightand obese BMI group are compared to the normal weight BMI group. Because the investigated change now could occur in both the exposed and non-exposed group, the change in the exposed group would differ less from the non-exposed group than what would have been if the true exposed and non-exposed groups had been identified. This could potentially explain why Pedisic and colleagues (2014) found that only those classified as obese at baseline were associated with more sitting time later on. In addition, Okoroduro and colleagues (2010) further observed that BMI was sufficient specific to identify adiposity above 30 BMI.

#### **Confounding variables**

The included articles do overall report sufficient adjustments of cofounding variables. However, some report adjustment for more cofounding variables than other do. It is well established that physical activity prevent both overweight and obesity, and could result in less sedentary behavior as it has the potential to displaces time spent sedentary with higher intensities (Owen et al., 2010; WHO, 2014), and should therefor be adjusted for. Only five of the included studies reported adjusting for any measurements of physical activity. Aerobic fitness, PAEE, exercise status (non, low, moderate, and high) and MVPA. Although, it should be noted that it is statistically impossible to adjusting sedentary time for total physical activity since these to are perfectly inversely correlated by definition (Ekelund et al, 2014). Accounting for PAEE can therefor be problematic since PAEE should include the energy expenditure from sedentary behavior, and therefor be inversely associated. This become especially important if there is a balance between positive effect from physical activity and negative effect from sedentary behavior, which in turn determine the overall risk of health problem. Diet is another potentially confounding variable, affecting the relationship between sedentary behavior and weight outcome, which is less reported in the current review. Only three studies (De Cocker et al., 2010; Hjorth et al., 2014; van Uffelen et al., 2010) reported adjustments for diet or energy intake, while Fuller-Tyszkiewicz and colleagues (2012) investigated the mediating role of diet in the bidirectional relationship. The latter study did not observe any mediation role of diet in most of the cases studies between TV viewing and later BMI. Potentially, dietary intake or snacking during TV viewing could mediate the association between time spent watching TV and weight outcome (Ekelund et al, 2014). In order to control for differences in those who develop outcome and those who do not, cofounding variables such as age, gender, and socioeconomic status should be analyzed.

#### **Other considerations**

Question could be raised whether the chosen quality assessment tool provided adequate information about the individual strength and weaknesses of the included studies, whereas this might not always be the case with quality assessment tools (Wright, Brand, Dunn, & Spindler, 2007). It is possible that a study could have fatal flaws, but still reaches a satisfying overall quality score (Wright et al., 2007). It should be mentioned that the article by Ekelund and colleagues (2012) were assessed having an overall good quality score. However, a bidirectional relationship was not included in the objective of the article, and therefor the quality of the study does not directly reflect the quality of the bidirectional relationship that was reported. Importantly this study had a meta-analytic approach, and did only show forest plot for the relation between WC and sedentary behavior at follow up. Further, the forest plot presented showed that the overall effect was significant and negatively associated, with a good heterogeneity. However, all, but one study showed non-significant relationships between WC and SED, whereas three showed a negative effect and four showed a positive effect. Awareness of this should further be included when interpretations are made.

## 5.4.2. Generalizability of the results?

Of the ten included studies in this literature review, six studies observed children and/or adolescents and four studies observed adults. To what extend these studies can be generalized to all children, adolescents and adults in the world, across all ages, will in the further be carefully discussed.

Observed data from children and/or adolescents are comprised from industrialized countries, covering Europe (Altenburg et al., 2012; Ekelund et al., 2014; Hjorth et al., 2014), Australia (Fuller Tyszkiewicz et al., 2012; Hesketh et al., 2007) and USA (Butte et al., 2014). An important difference in developing and developed countries is concerned the prevalence of obesity. Even though overweight and obesity is increasing in prevalence both in developed and developed countries, the prevalence in developing countries is lower compared to developed countries (Ng et al., 2014). Physical inactivity also differ from regions, whereas adolescents from WHO South-East Asia Region are observed having the lowest prevalence of inactivity and adolescents in the Eastern Mediterranean Region, the African Region and the Western Pacific Region are observed having the highest amount of time spent inactive (WHO, 2014). Since physical activity is a well-established protector of obesity (Hamilton et al., 2008), it should be considered whether the same risk of obesity is present in the different regions.

Data from Europe is derived from one study observing Danish children aged 8-11 years old (Hjorth et al., 2014), one study observing Dutch adolescent 12-14 years old (Altenburg et al., 2012) and one study based on meta-analysis from children and adolescents aged 4-16 years old from UK, Switzerland, Denmark and Portugal (Ekelund et al., 2012). The Eurothine project has observed large variations in the degree of health inequalities across countries in Europe (Erasmus MC, 2007). A consistency in rates of mortality and self-reported adverse health has been reported across countries whereas an adverse association has been observed with socioeconomic status. Larger inequalities have been observed in East and Baltic Regions have compared to the European average (Erasmus MC, 2007). The European countries covered in the included study sample can be considered as well-developed countries. However, a less inequality between Nordic countries compared to the rest of Europe, is not observed. In an extend to this, the included European studies in the current review might have external validity toward other European countries, but a further evaluation of socioeconomic status would be more relevant in terms of interpretations.

Hjorth and colleagues (2014) are the only investigators who reported the socioeconomic characteristics of their study population, whereas this study was reported to be large and greatly representative for Danish children. This leaves room for uncertainties regarding socioeconomic distribution. The Dutch adolescents (Altenburg et al., 2012) included in the present review, originated from the DOiT-study, which focused on adolescents with lower

socio-economic and educational level (Amika S. Singh et al., 2006). Finally, the sample covered by Ekelund and colleagues (2012) originate from the International Children Accelerometer Database (ICAD) having a great strength enhancing social and cultural diversity (Sherar et al., 2011). However, the bidirectional analyses included in present review do not necessarily have the same strength as ICAD, whereas they include less countries and these are not further described regarded socioeconomic status.

Observed data from Australia were reported for children aged 0 to 1 years old and 4 to 5 years old (Fuller-Tyszkiewicz et al., 2012), and 5 to 10 years old at baseline (Hesketh et al., 2007). None of the studies reported socioeconomic status of their study participants. However, Fuller-Tyszkiewicz and colleagues (2012) reported their study sample as nationally representative, based on gender and socioeconomic status of their subject, and Hesketh and colleagues (2007) described their population (conducted in 1997) whereto it was derived from the Health of Young Victorians Study (HOYVS) employed to cover a representative sample of children in the state of Victoria. Whether representativeness was fulfilled in the HOYVS or the study by Hesketh and colleagues (2007) is either presented or discussed by Hesketh and colleagues (2007). Mathers and colleagues (2007) have summarized the HOYVS 1997 sample to be similar to the Victorian population regarded children with parents born in Australia, and children from native backgrounds. Because the current included study (Hesketh et al., 2007) reported losses to follow up, although reasonable, cautions of interpretations should be made regarding representativeness to the state of Victoria. Also a further interpretation of representativeness to Australia should be considered with caution, based on the present information.

Children observed in USA were 8 years old at baseline, and were limited to one study (Butte et al., 2014). Importantly, this study only observed Latino Americans in San Francisco Bay Area. Obesity is observed to affect more Latino children in the US, making this group of high risk for weight gain, but also indicating that the different groups might not be comparable with regard to weight and weight related risk factors. Several studies have assessed physical activity level within and across region and population groups in the US (e.g. Mattews et al., 2008). Differences, among several influencing factors (e.g. study design, population, threshold definitions etc.), are observed in regional sociodemographic factors affecting pattern of physical activity (Butte et al, 2014). Example, in Houston 23 % of Latin and African American children satisfy the recommended amount of MVPA (Butte et al., 2014),

while in inner Philadelphia only 19 % of Latin children were classified as sufficient active (Stewart G. Trost et al., 2013). Because of differences in physical activity level based across regions, interpretations should be carefully made considered.

The remaining four articles included in the current review were comprised to adults. One study examined female young adults aged 22-27 (De cocker et al., 2010), whereas the remaining three articles observed mid-aged adults between 45 and 65 years old at baseline (Ekelund et al., 2008; Pedisic et al., 2014; van Uffelen et al., 2010). Only one study examined mid-aged adults in the UK (Ekelund et al., 2008), whereas the rest of the adult population observed were contained from Australia. There is a noticeable gap between the studied populations whereas no evidence for adults aged 28 and up to 44 is present. Therefor no conclusions should be interpreted in other populations with this age. Further, there is only one study examining female young Australian adults (De Cocker et al., 2010).

All researches examining adults, except Ekelund and colleagues (2008), report socioeconomic status. De Cocker and colleagues (2010) reported their study with the strength of having a large randomly sample of young adult woman in Australia, making it reasonable to believe it is comparable to the young Australian woman. Pedisic and co-workers (2014) included a large sample of middle-aged Australian adults, stratified by a number of possible moderation factors (e.g. sex, employment status, BMI etc.). The sample is limited to New South Wales, and whether this limit further interpretation to other population of same age can be questioned. Even though Ekelund and co-workers (2008) do not report socioeconomic status, they reported having such measurements. Their sample is randomized, but to what extend it can be generalized remains unknown.

Summarized, the current review has a general limited generalization to industrialized countries, and some disadvantage groups (with regard to ethnicity and socioeconomic), including children, adolescents, young adults and mid-aged adults. Further interpretations should be done with cautions concerned various ages studied in limited countries and their generalization.

## 5.4.3. Limitations with the review

Research on sedentary behavior is a relative new field (Hamilton et al., 2007), which also is reflected by the occurrence that none of the included articles are published before 2007. Further, all the included studies were obtained in Europe, USA and Australia, which shows a wide international range of studies, but rather limited to high-income countries. Even though the field has a great international concern, there are few studies done on the bidirectional relationship when conducted in the same population at the same time period. To the author's knowledge, there is no other review on this area. However, reviews aiming to investigate sedentary behavior and health outcome are mainly based on studies from high-income countries (e.g. Chinapaw et al., 2011; Must & Tybor, 2005; Proper et al., 2011). Gülmezoglu and colleagues (2004) emphasized an important overall challenge to identify available data from less developed countries when burden of disease is reviewed. This highlights the need for a greater quantum of studies and more studies from low-income populations. The current review is solely based on prospective studies, which substantiate the aim of investigating causality rather than only associations. However, the existing literature examining the bidirectional relationship between sedentary behavior, and overweight and obesity, is rather small. Yet, the quality of the included studies is overall good.

## **5.4.4.** Potential biases in the review process

Major strengths with the current review are its systematic approach and that it is thought to contain the highest level of evidence possible. In order for the systematic review to provide meaningful conclusions and be of high-level evidence, it is dependent on the level of evidence of the articles selected for assessment (Wright et al., 2007). Randomized control trials (RCT's) are considered to be of the highest level of evidence (Burns, et al, 2011). Systematic reviews are therefore often based on RCT's (Wright et al., 2007). However, studying the bidirectional relationship between sedentary behavior and overweight and obesity, seems rather impossible. It is hard to blind people to control- and intervention groups. In this case, it is difficult having people not knowing whether they are sedentary or not, or knowing they are overweight or obese. Ethically, it is also challenging having an intervention group where outcome preferably is sedentary behavior, or overweight or obesity. The latter is of great concern when both outcomes are considered to be harmful for general health (WHO, 2014). Longitudinal prospective population-based cohort studies, is therefore considered as the highest level of evidence towards better understand this causal relationship (Burns et al., 2011).
A key limitation is concerned that only one reviewer participated throughout the whole process of this systematic literature review. Any potential situations where subjectivity could be used for interpretations could lead to bias, and it can be thought that these biases are more likely not to occur if two or more reviewers have the possibility to discuss differences. Decisions made in relation to the actual literature search are vulnerable to bias. In the process of finding search terms, it is critical for the final search result to cover all potential articles. Because some of the used databases had different categories and terms related to their search engines, different search terms were used in the different databases. The process of finding these terms acquired several "try and fail" search in order to revile potential terms, and questions could be raised whether the used search terms covered all eligible literature aimed to find.

Limitations were also performed different across databases. In all databases, but Web of Science, it was possible to limit search to human. It should be questioned whether a search term including "human" or "NOT animal", or specific age terms (e.g. children, adolescents, adults, etc), should have been included in terms of reducing the final search to more relevant articles. During search, even though not documented, the final search result included several articles concerned animals. This in turn is thought to have lead to a greater workload, meaning more articles are screen and therefor more potential article to misjudge. Another limitation regarding limiting search could be identified when choosing areas of research in Web of Science. The search was limited to areas of physiology, family studies, endocrinology metabolism, public environmental occupational health, sport science, behavioral science, and health care science services. Whether these areas are sufficient or not could further be questioned. Another limitation that could have potentially effects on the final result, is that only English-published articles were included. Only including English-published articles could potentially limited study sample to industrialized countries. Gülmezoglu and coworkers (2004) emphasis that studies from developing countries are more prone to be published in non-indexed and non-English journals.

When identifying potential articles, only electronic databases were used. A limitation concerns that no search were done through bibliographies. Reviewing bibliographies is of special importance for detecting published articles of new date (previous six months), because these might not yet be included in the electronic databases (Wright et al., 2007). On the other hand, including four electronic databases would be considered a great strength,

whereas the used databases are thought to cover the literature relevant for this review. For example, including both EMBASE and PubMed result in a greater coverage of potential literature, since the databases are observed to have a 34 % overlap of journals (Wright et al., 2007).

Both subjective interpretations of the search results and concentration, accuracy and stamina could affect the final included result. In order to develop a comprehensive list of potentially relevant studies it is important to be exhaustive enough to carefully assess final search result (Wright et al., 2007). The process of screening is monotonic and time assuming and human errors are possible to occur. How the inclusion and exclusion criteria are read and interpreted could be affected by subjective understanding. However, a forward-backward tracking of the included articles' reference lists reduce the potential limitation of not identifying all relevant articles, giving a second chance of detecting potentially missed relevant articles. This does not make up for the fact that articles could have been systematically missed, and the benefit of being more than one reviewer would have contributed to reduce the risk of systematic errors.

Further, publication bias remains a challenge in systematic review, and therefor also in the current review (Wright et al., 2007). Publication bias occurs when only positive or considerable differences are published, and there is a potential for unpublished results to affect the reviewed result. Moreover, it could be questioned whether the participation of authors across the included studies could potentially create bias. Both Jannique G.Z. van Uffelen (De Cocker et al., 2010; van Uffelen et al., 2010) and Ulf Ekelund (Ekelund et al., 2008; Ekelund et al., 2012) are participating in two studies respective.

This review had only one reviewer to assess quality of the included studies, and this might contributes to bias. Wright and colleagues (2007) highlight the need of minimum two independent reviewers in the process of measuring study-quality. It might be that some interpretations made are mistaken, or that the assessed items might not always be considered consistent across studies. A great strength with being two or more researchers is the possibility to discuss any discrepancies, whereas mutual agreement can resolved any differences there might be (Wright et al., 2007). It has been suggested that quality assessments should include blinding, whereas journal name, study title, authors, and institution are unknown for the reviewer. However, this is time consuming, and has not been

linked to a better overall result of the systematic review (Wright et al., 2007).

The quality scoring system is further possibly limited by subjectivity when rating. However, Kmet and co-workers (2004) report that the final version of the quality assessment tool is revised to overcome a difference inter-rate agreement between to reviews in an earlier version, mostly caused by differences in judgments of the applicability of certain items regarding study design and the differentiation of scoring "yes" versus "partial" to meet the criteria. The final version had an inter-rate agreement ranging from 73-100 % (by-item), and any differences between reviewers were caused by different judgment whereas scoring "yes" versus "partial" to meet the applicability to meet in the criteria item. However, the quality tool was considered to have a suitable reproducible (Kmet et al., 2004).

### **5.5 Future direction**

#### 5.5.3. Implications for research

The potential bidirectional relationship between sedentary behavior and, overweight and obesity, is still not fully understood. Although the present evidence suggests that baseline weight could predict later sedentary behavior, it does not rule out the possibility of a revers or bidirectional relationship. In order to better understand the directions of these relationships future research should continue using prospective longitudinal population-based studies, but include more precise measurements of exposure and outcome variables performed more frequently repeated over the studied time line (Ekelund et al., 2014). In order to understand more about this association in children, there is a need for the research to start early, potentially before fat accumulation inhibit physical activity (Ekelund et al., 2014). Since youth overweight and obesity is a great risk factor for staying overweight or obese when adult, health interventions targeting children are of special value (Singh, Mulder, Twisk, van Mechelen & Chinapaw, 2008). However, this does not exclude the need for health interventions to other age groups. Therefor, more research should target populations across all age ranges. Especially adults and older adults are understudied at the moment, in addition to populations in developing countries.

Moreover, there is a wanted need for well-performed cohort studies, investigating the potential bidirectional relationship, controlling for well-considered confounding variables (Ekelund et al., 2014). Dietary intake, change in pubertal maturation, physical activity and socioeconomic status are of great interest, and should especially be further considered.

Further, Hamilton and colleagues (2008) emphasis the need of a better understanding of the biological mechanisms of sedentary behavior and health outcomes. To this extend, experimental studies might be beneficial to better understand biomarkers and disease outcome potentially caused by sedentary behavior-mechanisms.

#### 5.5.4. Implication for practice

There is no doubt that sedentary behavior and, overweight and obesity, are great threats to good human health (WHO, 2014). As the evidence, provided in the current review, does not rule out the potential for a bidirectional relationship and suggest that baseline weight predict later sedentary behavior, health promotion should be aware of the potential mutual association between both sedentary behavior and, overweight and obesity.

Health promoting strategies should therefor not only promote obesity-reducing interventions and recommendations, but also promote reduced sedentary behavior as a health promoting strategy. Several countries, like Australia, Norway and Canada, have already acknowledged the need for reducing sedentary behavior as national communicated recommendation for better health, which here is emphasized as an important national strategy. Sedentary behavior is distinct from physical activity, and should therefor be promoted as an additional target behavior together with existing promoted physical activity. The challenge for health practice lies in communicating these perspectives. As people in general do not have a common perception of what is "sedentary behavior", it could be beneficial to promote less sitting, as this is a common behavior that is easy to relate to (Hamilton et al., 2008). As people are more aware of their posture, than what they are about their energy expenditure and metabolic profile, promoting less sitting would be of great potential to reduce the health related problems associated with sedentary behavior.

## **6.0 Conclusion**

Prospective population-based studies investigating the bidirectional relationship between sedentary behavior, and overweight and obesity among non-patient children to middle-aged adults are systematically reviewed. The current evidence suggests that baseline weight predicts later sedentary behavior, and that the evidence regarding a reverse or bidirectional relationship to date is not of sufficient quality to determined such relationship. Future wellconducted prospective studies are therefore warranted to increase knowledge in this field as well as to enhance heath-promoting strategies.

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# Attachment

Criteria	1.	2.	3.	4.	8.	9.	10.	11.	12.	13.	14.	Total
Study												score
Altenburg et al.,	2	2	1	2	1	2	2	2	2	2	2	20/22
(2012)												0,91
Butte et al.,	2	2	1	2	2	2	2	2	2	2	1	20/22
(2014)												0,91
De Cocker et al.,	2	2	1	2	1	2	2	2	2	2	2	20/22
(2010)												0,91
Ekelund et al.,	2	2	2	1	2	2	2	2	2	1	2	20/22
(2008)												0,91
Ekelund et al.,	2	2	2	2	2	2	2	2	2	1	2	21/22
(2012)												0,95
Fuller-	2	1	0	2	1	2	2	0	0	2	1	13/22
Tyszkiewicz et												0,59
al., (2012)												
Hesketh et al.,	2	2	2	1	1	2	2	2	1	1	2	18/22
(2007)												0,82
Hjorth et al.,	2	1	1	2	2	2	2	2	2	2	2	20/22
(2014)												0,91
Pedisic et al.,	2	2	1	1	1	2	2	2	2	2	2	19/22
(2014)												0,86
Van Uffelen et	2	2	1	1	1	2	2	2	2	2	1	18/22
al., (2010)												0,82

 Table A.1. Quality assessment scoring (QualSyst) for the included articles.