Non-invasive detection of risks in and outside the body for metabolic syndrome in office workers

Bachelor thesis Biomedical Engineering
Shaldon Ingmar Hartman: s4069099
Date:
Department: DTPA
Supervisor: dr. Elisabeth Wilhelm
Second supervisor: dr. Taraneh Mokkaber

Summary

In today's society 22% of the population seem to suffer from metabolic syndrome (MetS), especially office workers have a high prevalence between 7-58% (Strauss et al., 2020) (Chini et al., 2014). So far research has proven its effectiveness in diagnosing and determining risk factors, the correlation establishing causalities, however, remains unknown. In order to help office workers and society to bring down this vastly increasing number of one out of five incidences in office workers, this thesis aim was to investigate why certain biomarkers (namely triglyceride, high density lipoprotein cholesterol (HDL-c) and blood sugar) are important and how these levels could potentially help detection before the syndrome progresses. This thesis also investigated which non-invasive detection devices and mechanisms are present outside of the body. The research concluded, stating that all levels, and especially blood sugar levels, play a central role in the development of MetS. However, the non-invasive technology that is available to directly measure these levels needs to be further developed to allow for early detection. Meaning that the key in early detection in the nearby future lies in non-invasive monitoring of food intake.

Table of Contents

Introduction

Metabolic syndrome (MetS) is an increasing public health concern that describes a cluster of several medical conditions that often concern office workers (Alavi et al., 2015). The incidence of MetS, has been increasing in well developed countries of the past fifty years mainly due to the rise of office jobs (Kelishadi, 2007). Nowadays the prevalence of MetS in office workers ranges between 7.4% and 48.6% (Strauss et al., 2020) (Chini et al., 2014), these figures account for 30% of the total 71% of deaths from non-communicable diseases (World Health Organization, 2022). Since MetS contributes to a large number of worldwide deaths, research has (with no success) focused on identifying the cause of the syndrome. However, research has identified the risk factors of MetS and the symptoms.

In order to classify as patients with MetS, patients should have at least three of the following conditions (these can be also found in table 1): abdominal obesity, hypertension, hypertriglyceridemia, low HDL-cholesterol level, high fasting blood sugar (Reaven, 2005). Since abdominal obesity is common under MetS patients, it is used a main pillar for identification. According to research abdominal obesity is defined as having a waist circumference larger or equal to 90^{th} percentile, which is gender dependant (Park et al., 2005). As for hypertension, clinicians often use the guidelines from 2018 from the ESH/ESC to measure arterial hypertension, these levels can be seen in the table below ("2018 Practice Guidelines for the Management of Arterial Hypertension of the European Society of Hypertension and the European Society of Cardiology," 2019). High fasting blood sugar is measured from the blood and detected with levels above 110mg/dl (Ludwig & Ebbeling, 2005), which are most easily caused by food containing simple carbohydrate levels (Goldberg & Mather, 2012). Low HDL-cholesterol levels are measured from the blood plasma, levels below 40 mg/dl in man and 50 mg/dl in women are considered for MetS (Ryu & Chin, 2016). Examples of food containing high HDL levels are eggs, walnuts, and spinach (Pagano & Strait, 2009). The last parameter that is measured is the hypertriglyceridemia level from blood serum. Normal levels of triglyceride are less 150 mg/dL (Yilmaz et al., 2006). Triglycerides are mainly found in food and drinks that contain alcohol, sugars, saturated and trans fats, high calorie foods and refined grains or starchy good. On the other hand, avocado's, fatty fish, and whole grains are known to lower hypertriglyceridemia (Wilson et al., 2022).

Table 1: Conditions of people suffering from MetS, compared to normal levels.

Condition	**MetS Level**	**Normal Level**
Abdominal obesity	>90^{th} percentile	< 90^{th} percentile
Hypertension	Systolic blood pressure: Grade I: ≥140mmHg Grade II: ≥160mmHg Grade III: ≥180mmHg	Systolic blood pressure: 120-130mmHg
High fasting blood sugar	>110 mg/dl	70-100 mg/dl
Low HDL-cholesterol	<40 mg/dl	45 mg/dl
Hypertriglyceridemia	>150 mg/dl	<150 mg/dl
Lipodystrophy	Has no firm diagnostic criteria, often a combination of several factors such as skinfold and imaging	-

Several risk factors for MetS have been determined which are categorized into unmodifiable and modifiable, the category depends on whether or not they can be changed through lifestyle modifications (see table 2). One example of a modifiable risk factor is stress. According to research, chronic distress compromises the homeostasis of the brain and nervous system, leading to several psychopathologic conditions that contribute to the development of obesity and other comorbid states (Pervanidou & Chrousos, 2011). Another example of a modifiable risk factor is a sedentary lifestyle. Research in this topic suggests that physical inactivity and poor eating habits in office workers increases the odds of MetS three times compared to that of active office workers (Ryu & Chin, 2016). An example of an unmodifiable risk of MetS is age. According to research, age influences physical activity, cholesterol levels, increased glucose levels, etc. (Lévesque et al., 2009). The last example of an unmodifiable risk factor is a genetic mutation causing lipodystrophy. In lipodystrophies the body continuously severely loses adipocytes by apoptosis, which leads to an insufficient metabolism of free fatty acids, thereby accumulation which leads to MetS (Mansilla et al., 2011).

Table 2: Examples of modifiable and unmodifiable risks.

Modifiable Risk factors	Unmodifiable risk factors
Stress due to imbalanced brain and nervous system	Age
Sedentary lifestyle due to poor eating habits and physical activity.	Lipodystrophy

Beside modifiable and unmodifiable risk factors, there are also diseases that are associated with MetS. One of these correlations of MetS is obesity. Obesity correlates in a way that it results into insulin resistance, increased blood pressure, high cholesterol, and triglyceride levels. These levels are used as indicators to diagnose MetS (Ross, 2017). Another correlation of MetS is Diabetes mellitus type 2, which is also seen as a complication. If patients have an impaired fasting glucose or impaired glucose tolerance the risk of developing DM-2 doubles if MetS is diagnosed (Goldberg & Mather, 2012). Rheumatic diseases are also associated with MetS, especially psoriatic rheumatism (Luime et al., 2016). The third indication or associative factor is Chronic obstructive pulmonary disease (COPD). Metabolic syndrome is found to be twice more common in COPD patients, compared to the general population. According to research almost 50% of the patients with COPD has at least one MetS condition, this might have partly to do with physical inactivity (Chan et al., 2019). The last factor is coronary artery disease, research has shown that apolipoprotein C-III is marker of increases triglyceride levels which is increased in both Mets and coronary artery disease (Yilmaz et al., 2006).

Research has proven effectiveness in terms of diagnosing patients suffering from Mets and in pinpointing the risk factors that are involved. This research focuses not necessary on diagnosing patients, but more on discovering what and why certain levels are important and how these levels can help early detection before the syndrome progresses. The factors this study research are triglyceride-, HDL-c and blood sugar levels. From a scientific point of view, this literature research will contribute in a way that it helps to steer further research in detecting potential poor eating habits before office workers actually suffer from the disease. For society, screening as a precaution could help reducing the amount of people getting the disease, thereby preventing disabilities and deaths. From a clinical point of view preventing the disease from happening reduces the healthcare costs and the amount of money/time clinicians spend on the patients suffering from the disease.

The main research problem of the research comes from the fact that diagnosing and determining the main factors behind MetS are well investigated. However, the amount of material present to detect the consequences of the risk factors is not overabundantly present and has not been verified with traditional diagnostics. With the main question “Which parameters that can be measured with sensors allow to identify people at risk of developing MetS?” This report will start with investigating the three measurable biomarkers, namely HDL-c, blood sugar and triglycerides, since according to research these biomarkers are correlated with MetS. These variables often require invasive measures, they might not be convenient for long term monitoring in the context of prevention. Therefore, the report will end with a review of indirect detection methods for monitoring food intake which is intricately linked to changes in these biomarkers.

Literature review

Triglyceride: a biomarker for metabolic syndrome

Causes of hypertriglyceridemia

Causes of hypertriglyceridemia can be divided into primary and secondary. Primary causes hypertriglyceridemia arises from a group of familial disorder with genetic variants that impair lipoprotein lipase deficiency (LPL) metabolism that lead to mild to moderate hypertriglyceridemia with levels of about 200-500mg/dl (Schaefer, 2008). Higher levels of hypertriglyceridemia may be caused by loss of function mutations (Dron et al., 2019).

Secondary hypertriglyceridemia is caused by factors that exclude genetics. The most common factors are metabolic disorders, certain medications, and sedentary lifestyle. Other less common factors include alcohol intake, nephrotic syndrome, hyperthyroidism, and certain drugs (Bazarbashi & Miller, 2022).

Structure and metabolism

Triglycerides are ester molecules that are derived from a glycerol with three fatty acids. Triglycerides are a self-contained macromolecule in the body but are mainly found in so-called triglyceride rich lipoproteins (TRL). TRL are macromolecules structures composed of triglycerides and cholesteryl esters that are enclosed by a single layer of phospholipids, free cholesterol and apolipoproteins (Ginsberg, 2002). TRLs consist mainly of chylomicrons, very-low-density lipoprotein (VLDL), their remnants and intermediate-density lipoproteins. VLDLs are produced by hepatocytes and secreted in the circulation. In the circulation lipoprotein lipase-mediates hydrolysis results in the release of three fatty acids which are taken up by peripheral muscle or stored in adipose tissue for the use of energy (Dallinga-Thie et al., 2010).

Mechanisms for metabolic syndrome with hypertriglyceridemia

Research regarding the mechanisms of how high levels of triglycerides result into MetS are still under investigation. What is known is that triglycerides play a crucial role in energy usage and storage via beta oxidation, cholesterol production and insulin resistance (Li et al., 2013).

Beta oxidation

During beta-oxidation, which occurs in the Krebs-cycle, fatty acyl-CoA is oxidised into CoA and acetyl CoA. This process is responsible for ATP production. Hypertriglyceridemia ensures that more energy is produced, using beta oxidation, than needed. This excess of energy is then stored for later use, leading to obesity (Li et al., 2013).

Cholesterol production

According to research, hypertriglyceridemia may cause hypocholesterolaemia (Li et al., 2013). Although the actual mechanisms leading to this condition are still unclear, research hypothesized that hypertriglyceridemia impairs the conversion from VLDL to LDL with unknown consequences (Schaefer, 2008).

HTG and insulin resistance

Much research indicates that hypertriglyceridemia is closely related to insulin resistance. Research has found that primary hypertriglyceridemia causes an elevated turnover rate of non-esterified fatty acids. This elevation suggests that patients with primary hypertriglyceridemia to have an insulin resistance at the level of adipose tissue. In hypertriglyceridemia from secondary causes, there is an increase in the secretion of non-esterified fatty acids by adipose tissue, which creates an extra supply of excess fatty acids to the liver for the synthesis of triglycerides. These elevated levels of non-esterified fatty acids in the plasma are due to excess adipose tissue, primary insulin resistance in adipose tissue or due to abnormal fat distribution, flood the liver with lipids. The liver may then engender both prothrombotic and atherogenic dyslipidaemia. If the skeletal muscles are exposed to an excess of non-esterified fatty acids, they automatically increase their insulin resistance. Eventually, these processes predispose people to MetS (Grundy, 1999).

Mechanisms for cardiovascular disease with hypertriglyceridemia

In addition to MetS, triglycerides in the long term are also related to additional cardiovascular diseases, which regresses the state of disease in people already suffering from MetS. Four mechanisms caused by hypertriglyceridemia are known to affect cardiovascular disease. The first one is unregulated TRL-remnants, which cause atherosclerosis through plaque formation ((Varbo et al., 2013) (Bazarbashi & Miller, 2022). The second is through an increased levels of apolipoproteins that promote plaque formation vascular inflammation and worsen cardiac outcomes (Ooi et al., 2008). In the third mechanism, elevated levels of TRL lead to triglyceride hydrolysis, leaving dense TRL particles behind that are susceptible to a proatherogenic milieu, oxidative modification, and the incorporation of cholesterol into the vascular wall. These factors all lead to increased atherosclerosis (Chait et al., 1993). During the fourth mechanism increased triglyceride levels magnify the discordancy between LDL-p and LDL-c thereby increasing the atherosclerotic risk (Otvos et al., 2002). An overview of all factors concerning HTG can be found in figure 1.

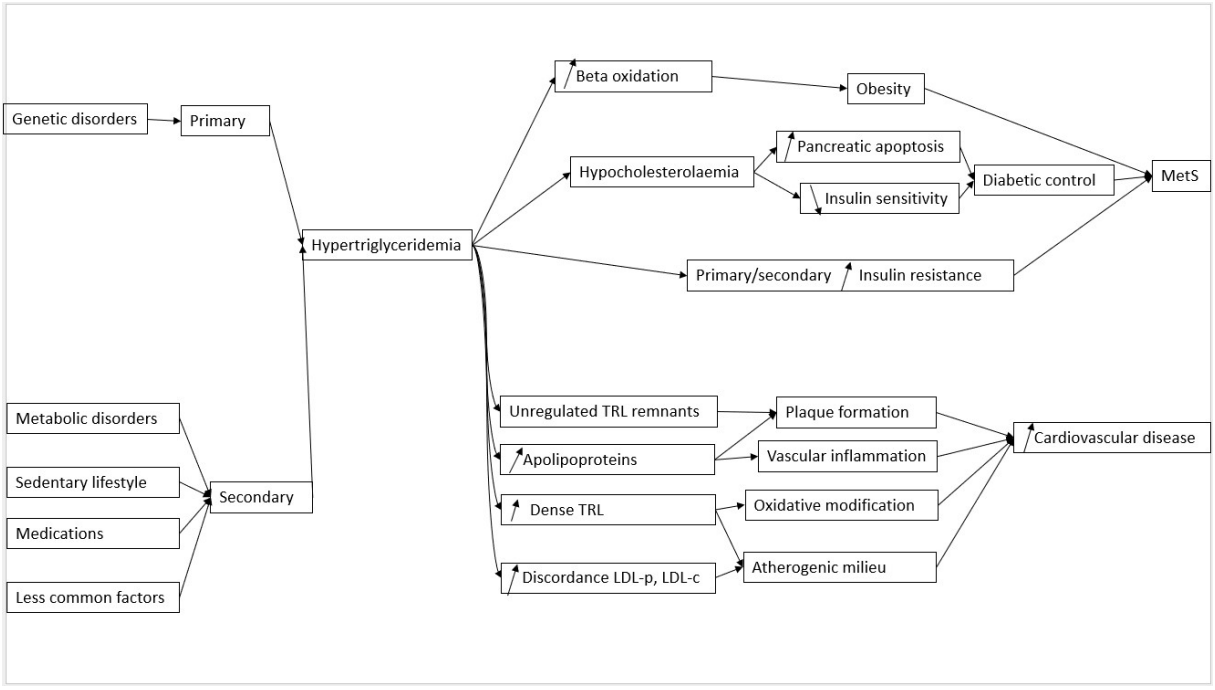

Figure 1: An overview of all causes, mechanisms, and outcomes of hypertriglyceridemia.

Detecting hypertriglyceridemia

As described above, triglycerides are tightly related to MetS and cardiovascular diseases. Research has shown that moderately overweight, non-diabetic man with an insulin resistance have higher plasma insulin and triglyceride levels, with low HDL concentrations. From these studies one can derive that the triglyceride to HDL ratios are the best markers to insulin resistance. Also, increased plasma triglyceride and reduced HDL ratios are crucial markers to determine MetS (Li et al., 2013). Nowadays, only blood samples are used to determine the triglyceride levels, meaning that no other detection methods are present (Medical Nutritional Institute, 2021).

Blood glucose: a correlating biomarker

In metabolic syndrome all conditions are related to one another. As described above for example, hypertriglyceridemia is related to insulin resistance, which on its own contributes to hyperglycaemia (Grundy, 1999). Elevated levels of blood glucose are not only related to insulin resistance but several factors. These will be discussed in this sub-chapter.

Metabolism of blood glucose

The metabolism of blood glucose is shown in the figure 2 below. The Figure shows that pancreatic cells are responsible for either producing blood sugar lowering insulin or blood sugar elevating glucagon. Metabolism of blood glucose is mainly regulated by the pancreatic islets and done by the liver (Marieb & Hoehn, 2018).

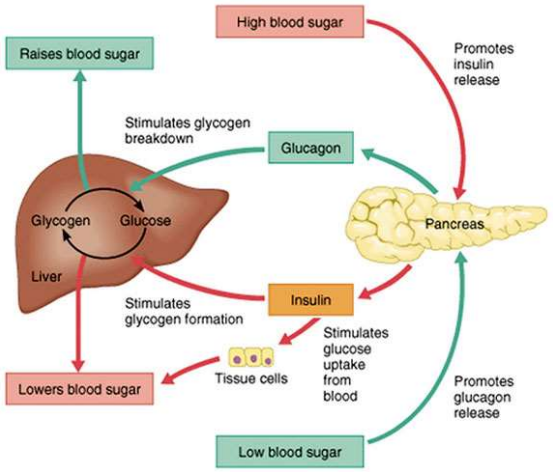

Figure 2: The metabolism of blood glucose[A]

Causes and mechanisms of hyperglycaemia

Hyperglycaemia knows three causes, namely, endocrine pathophysiology, stress, and medications. An overview of all processes can be found in figure 3**.** According to research drugs like corticosteroids, beta blockers and others all have the ability to permanently raise the level of blood glucose (Luna & Feinglos, 2001).

Research related to stress induced hyperglycaemia concludes several pathophysiological causes. It often is a combination of several of these causes that induce hyperglycaemia. One of the causes lies in the physiology that stress leads to hypercortisolaemia, which promotes hepatic gluconeogenesis and glycogenolysis. The elevated levels of cortisol also enhance transcription of the genes that are involved in gluconeogenesis from non-carbohydrate sources. Hypercortisolaemia also leads to increased levels of amino acids (the result from increased protein catabolism), these amino acids serve as precursors for gluconeogenesis. Another effect of stress is that it leads to increased secretion of pro-inflammatory cytokines, which increase insulin resistance by interfering with the insulin signalling pathway. These inflammatory cytokines also cause elevated levels of growth hormone secretion which lead to increased lipolysis, generating free fatty acids and glycerol, and increased insulin resistance. The last effect of stress on hyperglycaemia is that stress causes noradrenaline and adrenaline release form the pancreas, leading to increased insulin resistance. If the pancreas does not compensate by overproducing insulin, the net effect of stress is hyperglycaemia (Mifsud et al., 2018).

The third cause of hyperglycaemia is endocrine pathophysiology. Endocrine dysfunctions can be categorized into diabetes and insulin resistance. Insulin resistance and the mechanisms behind it comprises different topics such as hypertriglyceridemia and others that are described in the text

above. Diabetes is known as chronic hyperglycaemia resulting from malfunctions in insulin action, insulin secretion or both. The process leading to the development of diabetes are beta-cell failure, insulin resistance, inappropriate hormone release and decreased incretin effect. During beta-cell failure, the beta cells of the pancreas are no longer able to produce enough insulin to meet the body's needs, leading to greater amounts of glucose and thus hyperglycaemia. Insulin resistance leads to lessened glucose uptake and thus higher blood glucose. In inappropriate hormone release the feedback systems for hepatic glucose production and glucagon secretion are malfunctioning. This leads to unbalanced glucagon release from the alpha cells of the pancreas and inappropriate glucose release from the liver. Decreased incretin levels ensures that the body does not feel satiated and poor carbohydrate absorption (Kreider et al., 2018).

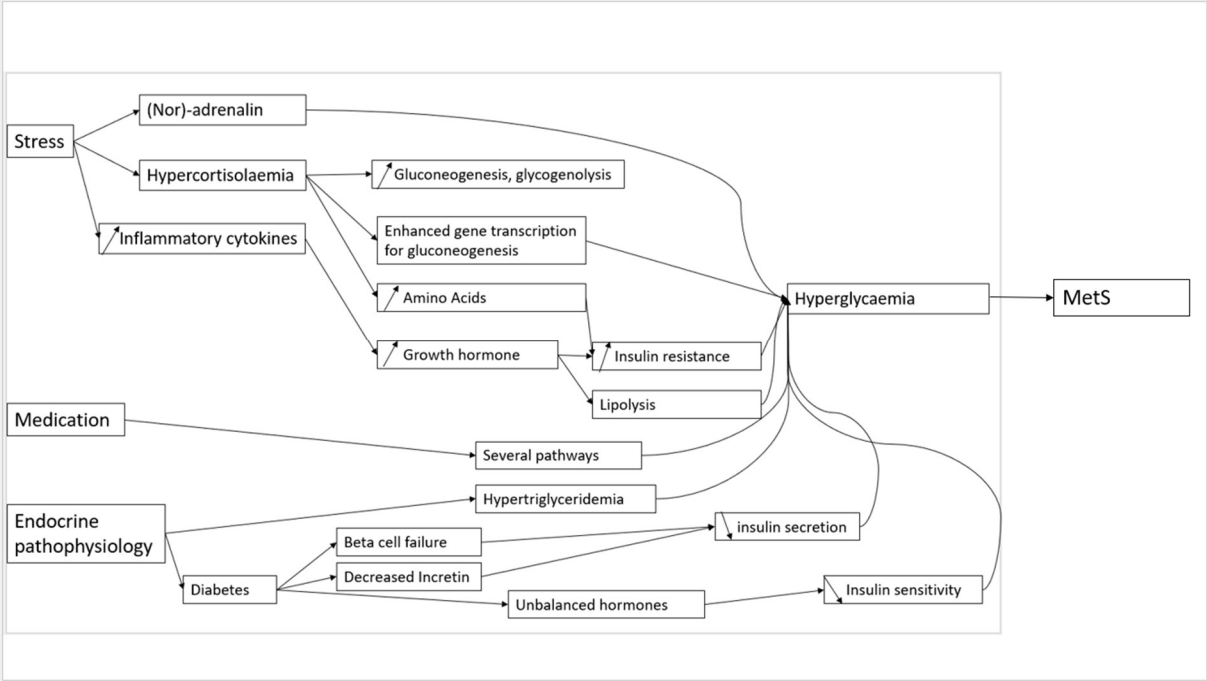

Figure 3: An overview of the mechanisms causing hyperglycaemia

Detection of blood glucose

Detection of blood glucose has shifted in the past few years from invasive to non-invasive because of the increase in number of patients suffering from infections and pain of invasive methods. Non-invasive blood glucose detection can be divided into three categories: electrochemistry, microwave and optical (Tang et al., 2020). An overview of these methods and their advantages and disadvantages can be found in table 3

Optical monitoring

Optical methods often include but are not limited to polarized optical rotation, near-infrared spectroscopy, Raman spectroscopy, optical coherence fluoroscopy, fluorescence (Tang et al., 2020).

In spectroscopy of the human body, light is absorbed that is closely related to the wavelength of the tissue. In near infrared (680-2500nm) spectroscopy (NIR) light has a strong ability to penetrate soft tissues and biofluids, making it possible to sense and measure through reflection and transmission (Sakudo, 2016). The wavelength windows for NIR are 700-1100nm, 1500-1850nm, and 2000-2400nm, can be used to measure glucose (Tang et al., 2020). Even though the windows of glucose are known, a

complex algorithm is necessary in order to differentiate glucose from other biofluid substances and internal structure of human tissues (Zanon et al., 2011).

In optical polarimetry, the stable optical rotation of glucose is used to measure a deflection angle, which is proportional to the amount of glucose, when a polarized beam is send through a sample. Although this method is not complicated, thus easy to obtain results and directly detectable with visible light, this method is not yet accurate enough for home and personal use (Purvinis et al., 2011).

Raman scattering occurs when a laser of a specific frequency hits a samples' surface, causing the molecules inside the materials to absorb the energy and to vibrate in different ways and degrees, causing scattering of light in different frequencies. The variation in frequency depends on the material, making it possible to identify a substance by Raman spectroscopy (Tang et al., 2018). Advantages are little interference, accurate, less overlap. The main disadvantage of this method is masking by environmental noise (Tang et al., 2020).

In fluorescence optical monitoring, the decay of a molecule an excited state back to the ground state can be used to measure several substances in the blood. To measure glucose levels, fluorescent materials such as quantum dots and carbon dots are used as probes for detection. The enzymatic reaction between glucose and certain fluorescence substances causes the dots to quench, the degree of quenching is used to measure the amount of glucose on a macro level. The advantages of fluorescence are its high sensitivity, selectivity, and stability. The main disadvantage of this method is the large set-up of equipment. (Cho & Park, 2019).

Optical coherence tomography (OCT) provides depth-oriented capabilities based on low coherence interference. In OCT, the contrast results from spatial variations in optical reflection properties within the biological tissue or material. In OCT, the distinction of glucose concentrations leads to different dermal tissue coefficients. These coefficients result in the OCT slope change, which declines with the increase of blood glucose concentration. Advantages of OCT are reduced interference factors, high signal to noise ratio, high resolution, and penetration depth. Disadvantages are temperature and movement sensitivity and the need for continuous calibration (Tang et al., 2020).

Microwave monitoring

In microwave monitoring, the interaction between biological tissues and electromagnetic waves is used to measure properties such as reflection, transmission and absorption that are closely related to the dielectric properties of the tissues which vary with glucose fluctuations (Villena Gonzales et al., 2019). Many researchers favour microwave monitoring due to its non-ionization, high penetration depth, portability, and low cost. However, the sensitivity of this method is influenced by many factors such as dielectric loss, transmission loss and parasitic loss of the measured substance (Tang et al., 2020).

Electrochemical methods

In electrochemical methods, the electrical charge of particles is used to separate substances in the blood to make it easier to measure them. An example of an electrochemical method is reverse iontophoresis technology (RI). There are two mechanisms behind RI: electromigration, in which there is a direct interaction between the charged ions and an applied electric field, and electroosmosis in which a connective solvent flows from the anode to the cathode. The electrochemical gradient that is created by electromigration promotes osmotic flow of water with neutral molecules to the cathode.

These then can be measured (Giri et al., 2017). Taking account for skin thickness, current intensity, constant/pulsed current, current duration, and electrode material, one could measure the glucose in the interstitial fluid, sweat, tears and saliva (Tang et al., 2020).

Table 3: Overview of the non-invasive detection methods used for blood glucose

Optical method	**Mechanism**	**Advantages**	**Disadvantages**
Spectroscopy	Infrared	Has the same precision as standard clinical procedures (Han et al., 2021)	Complex algorithm needed; the set-up is too complex to use in the office setting
Optical polarimetry	Polarized beam	Method can be used in the office setting	The accuracy to measure blood glucose in an office setting is low
Raman Scattering	Laser	In small cohorts it has proven to be adequate enough in measuring blood glucose (Pandey et al., 2017)	Sensitive to environmental noise, no hand-held format for in the office of this device is available, requires more validation to prove effectiveness (Tang et al., 2020
Fluorescence optical monitoring	Excitation and de-excitation	Accurate enough compared to standard clinical procedures (Cho & Park, 2019)	Requires a large set-up with advanced knowledge to operate
OCT	Energy waves	Approaches standard clinical procedures in terms of accuracy (Kuranov et al., 2007)	Affected by several factors such as temperature and movement, also difficult to operate in the office setting (Tang et al., 2020)
Microwave method	**Mechanism**	**Advantages**	**Disadvantages**
General method	Electromagnetic waves	Portable.	Affected by selectivity and poor sensitivity
Electrochemical method	**Mechanism**	**Advantages**	**Disadvantages**
RI	Cathode and anodes	Detect levels accurately	Not easy to operate in office setting due to continuously maintenance

HDL levels

Research related to biomarkers of MetS indicated that at least 25% of the people suffering from the syndrome have low HDL-cholesterol levels (Vorgucin et al., 2011). HDL is a high density lipoprotein and is part of one of the five major groups of lipoproteins. Functions of HDL include antimicrobial, antiglycation, antioxidant, antithrombotic, anti-inflammatory, antiplatelet, cell membrane protective, antiatherogenic and immune modulatory functions (Soran et al., 2012).

Metabolism of HDL

The synthesis of HDL is complex and still not completely known. What is known is that the precursors of mature and circulating HDL molecules are likely to be disc-shaped bilayers, largely composed of proteins (apoA-I and apoA-II) and phospholipids that are secreted by the gut and liver. Matured HDL is formed by the acquisition of extracellular apolipoproteins, lipids and phospholipids and always contains apoA-I, whereas apolipoproteins are only present on subset of HDL particles (Soran et al., 2012).

Causes and mechanisms of low HDL cholesterol (HDL-c) in metabolic syndrome

Studies show that several factors correlate to low HDL-c, these include elevated triglyceride levels, obesity, cigarette smoking, sedentary lifestyle, type 2 diabetes, high carbohydrate diet, medications, and genetic factors (Barter, 2011). The overview of the factors and mechanisms can be found in figure 4.

From the factors given above, medication, genetic factors and cigarette smoking are only of indirect significance for office workers, these mechanisms are therefore not further explained. On the other hand, triglyceride levels, obesity, sedentary lifestyle, diabetes and carbohydrate diets are explained below. The mechanisms of triglycerides on HDL-c have already been explained in the triglyceride part above. Research has suggested that the effect of increased carbohydrates affect the body in the same way and mechanisms as those for triglycerides (Siri & Krauss, 2005). For obesity, the underlying mechanism between body weight and HDL-c concentration is still unclear. In sedentary lifestyle research mainly found that an increase in physical activity causes increased levels of HDL-c which is secondary to an increased activity of the lipoprotein lipase and the reduction of plasma triglyceride. In terms of diabetes the main effects of HDL-c are that it affects glucose homeostasis by regulating pancreatic beta cell function and plasma glucose disposal. In pancreatic cells, HDL levels have shown beneficial effect since they inhibit apoptosis. Also, research has shown that the major HDL proteins (apoA-1 and apoA-II) increase insulin synthesis and secretion up to five fold. Meaning that low HDL-c levels decrease the amount of insulin being secreted by these cells, elevating the blood glucose levels and their consequences, MetS included. In terms of glucose disposal, research has proven that HDL is responsible for an increase in cellular glucose uptake by skeletal muscle, thereby improving diabetic control (Barter, 2011).

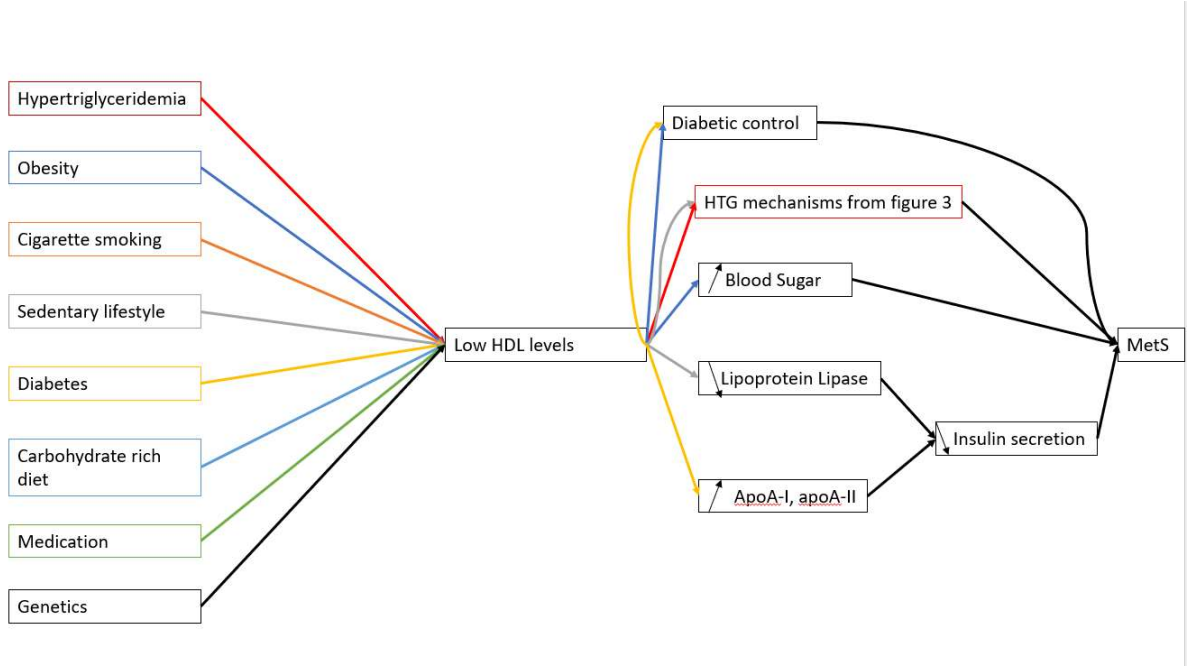

Figure 4 overview of factors and mechanisms involved in low HDL levels.

Mechanisms for detecting HDL levels

Since HDL and especially HDL-c levels are associated with cardiovascular diseases, as well as MetS, research has several ways to measure these levels. In clinical practice, the standard procedure to measure the amount of cholesterol in HDL is after precipitation of apoB-containing lipoproteins. Other more refined techniques include electrophoresis, ultracentrifugation (UTC), precipitation methods, high performance lipoprotein chromatography (HPLC) and nuclear magnetic resonance (NMR) (Hafiane & Genest, 2015). The overview of these methods can be found in table 4.

Electrophoresis

In electrophoresis the charge and mass ratio of the different substances (such as proteins, lipids, sugar etc.) in the blood plasma is used to separate and measure the quantity of HDL-c (Hafiane & Genest, 2015).

Ultracentrifugation

The main mechanisms measured in ultracentrifugation are vertical auto profile (VAP) and density gradient fractionation (DGF). In VAP in a single spin in an inverted rate zonal density sequentially measures the cholesterol content of all five lipoprotein classes (Chung et al., 1980). In density gradient fractionation, sequential flotation is used to separate lipoproteins into five major groups, based on the initial hydrated density range of each of the five groups (Movva & Rader, 2008).

Precipitation methods

During this process HDL-c is separated by precipitating apoB that contains lipoproteins from a serum using polyanions combinations. Then HDL is quantified as cholesterol in the supernatant. This method is easily reproduced, convenient and a fast. However, according to literature there are many factors such as experimental conditions etc. that drastically affect the results (Hafiane & Genest, 2015).

High performance lipoprotein chromatography (HPLC)

In this method, lipoproteins are separated by permeation columns, the lipid components, constituting of triglycerides and cholesterol, are detected with enzymes. Then various columns containing nonporous polymer-based gels are used to separate the major classes of lipoproteins in humans (Hirowatari et al., 2003).

Nuclear magnetic resonance (NMR)

All HDL subclasses have different characteristic lipid methyl groups, these groups broadcast a specific signal-amplitude which can be measured. This technique employs proton (hydrogen, carbon, and phosphor) spectroscopy to directly estimate the different sizes of lipoprotein subfractions and their quantity (Jeyarajah et al., 2006).

Table 4: Overview of the systems used to measure HDL levels.

Method	**Mechanism**	**Advantages**	**Disadvantages**
Electrophoresis	Mass-ratio substances	Simple, fast, effective, low cost	Not accurate enough compared to clinical setting (Boldura & Baltă, 2018)
Ultracentrifugation	VAP, DGF	Easy to operate, clear results (Barton et al., 2007)	Takes up a lot of time (Barton et al., 2007)
Precipitation	Precipitating apo-B using polyanions	Easily reproduced, convenient, fast	Results are strongly affected by measuring conditions, making it hard to measure in the office setting (Hafiane & Genest, 2015)
HPLC	Enzymes that detect lipid components	Rapid, easily reproduced, efficient	Expensive method to use as a monitoring tool (YOSHIDA et al., 1984)
NMR	Signal amplitude of lipid methyl groups	Precise and specific enough compared with the standard clinical procedure	High costs when used as a monitoring tool in the office (Rao, 2014)

Detection and measuring methods for outside the body

Up until here, this research has been focused on understanding the causes and consequences of the levels of triglyceride, HDL-c, and blood glucose. Also, detection methods and mechanisms to directly detect these levels inside the body have been explained. These detection methods often comprise of complex systems and detectors, which is difficult to implement for office workers. Therefore, it seems reasonable to further explore other options to detect poor eating habits, which is an indirect but non-invasive way to measure these risk factors. This detection is done manually, using an app, and automatically, using sensors, whom will be discussed in this part.

Manual monitoring of eating habits

Development in e-health in the past few years has made it possible to provide remote health care by mobile devices such as personal digital systems, mobile phones, patient monitoring devices and others (Tosi et al., 2021). Especially fitness- and health related mobile apps are used in all age groups and seems to have a positive effect on weight management and daily behaviour, which are of significance in MetS (Azar et al., 2013). Nutrition apps can be used to track dietary consumption with diaries, receive health tips based on daily behaviour and managing weight. Advantages of these apps are related to their direct and daily involvement in the life of the users, meaning that users can set their goals, thereby enhancing their motivation, and can get personal real-time feedback to correct, e.g., poor eating habits. Disadvantages of these apps are the fact that they can improper use can cause health problems and the apps could potentially trigger or maintain eating disorder symptomatology (Simpson & Mazzeo, 2017).

Automated monitoring of eating habits

Automated monitoring of eating habits nowadays is done using specific sensors. Since this research focuses on office workers, only on-body sensors are discussed in this part. On-body sensors measure food intake from at least one of the following responses of which an overview of these responses and sensors can be found in table 5:

Table 5**:** overview of the body's responses to food intake and their on-body sensors.

Food intake response	Dimensions of eating habits	Modalities for everyday use
Swallowing: measuring the swallowing reflex initiated during food intake	**Timing:** ability to recognize four bolus types **Food type:** open **Food amount:** ability to recognize low vs. high volume **Limit:** individual modalities caused by head and neck movements, speaking and chewing	**Modalities:** acoustic transducers, skin movement at the throat, throat impedance, capacitive sensing (Amft & Troster, 2006), textile capacitive collar sensors (Cheng et al., 2013), neck mounted EMG electrodes (Ono et al., 2009)
Chewing: measuring the sound that is produced during chewing strokes	**Timing:** ability to recognise two food categories **Food type:** so far 19 types of food **Food amount:** open **Limit:** environmental noise interferes with the measurement (Lear et al., 1965)	**Modalities:** ear-pad microphones (Amft & Troster, 2006), in-ear or neck-worn microphones (Pasler & Fischer, 2014)
Thermic effect: the body temperature increases after food intake at the liver region	**Timing:** ability to measure temperature rises 60 minutes after intake **Limit:** environment, physical activity and regularity of food intake influence the readings (Farshchi et al., 2004)	**Modalities:** skin-contacting temperature sensor (Amft & Troster, 2006)
Cardiac response; heart rate and blood pressure change related to food intake	**Timing:** effective readings 30 minutes after food intake up to 3 hours **Food type:** only the effect of salt and sugar is known **Limit:** environmental temperature, physical activity, time of the day (Parker et al., 1995)	**Modalities:** ECG, blood pressure monitors (Amft & Troster, 2006)
Gastric activity: sensors measure stomach activity and bowel sounds related to food intake	**Timing:** 15 minutes after food intake. **Limit:** has only been effective in laboratory settings (Amft & Troster, 2006)	**Modalities:** microphones, electrogastrography (EGG) (Abell & Malagelada, 1988)
Intake gestures: sensors measure the intentional arm movement to bring food to the mouth (Amft et al., 2005)	**Timing:** ability to distinguish four gestures **Limit:** long gestures and arbitrary arm movements (Junker et al., 2008)	**Modalities:** sensor at lower arms and upper back (Amft & Troster, 2006)
Body composition: changes related to food intake	**Timing:** impedance alters after 30 minutes **Limit:** body movements during measurement (Gualdi-Russo & Toselli, 2002)	**Modalities:** impedance meter with electrodes
Body weight; which increases after food intake (Amft & Troster, 2009)	**Timing:** directly after food intake (Amft & Troster, 2006)	**Modalities:** scale

Discussion and conclusions

This thesis focused on MetS by looking at three measurable biomarkers that are related to MetS to answer the research question "Which parameters that can be measured with sensors allow to identify people at risk of developing MetS?". To answer the research question, this thesis investigated what the effects of hypertriglyceridemia, low HDL-c and high fasting blood are, by researching two topics. The first topic to investigate and check is whether theses levels or other factors could be used to detect the development of MetS. The second topic to investigate is what type of devices could potentially help foresee the development of MetS by focusing on detecting one modifiable risk factor: poor eating habits. The results describe these topics.

The research regarding the first topic concluded that the levels of triglyceride, HDL-c and blood sugar are factors that could be used to identify people with MetS. The results in this thesis highlighted the correlation and influence that these biomarkers have in the further development of MetS, but they do not explain how they correlate with the onset of syndrome. Biomarkers are helpful to identify the disease and further development, but they do not help identify the risk of development since they look at the body's response to a stimuli instead of looking at the onset of the stimuli. On the other hand, detection methods outside the body look at the onset of a stimuli that has the potential to increase the risk of developing MetS. It seems that sensors outside the body help identify whether risk factors are present and thus help to identify people at risk of developing the syndrome. Outside the body detection seems best-suited for measuring risk factors.

The research about the second topic concluded that there are multiple devices present to measure poor eating habits. Of these devices it seems that devices that detect chewing and swallowing reflexes have modalities that have been researched the most. Moreover, these devices have the ability to collect the most data and are therefore have the highest potential to foresee the development of MetS.

The results that are found and described give an overview of mechanisms and methods that may help steer research towards finding the solution for early detection of MetS. However, this thesis also contains limitations. One limitation of the thesis is that although it describes several devices and techniques to measure, they are only a small part of a larger population of devices. The devices that are described were selected based on how frequently they were cited in big publications, meaning that there are many more devices present and available for further research. Another limitation comes from the tables in the results, which try to compare the different types of devices. However, not all papers contain the information necessary to compare the different assessment techniques, also, due to time constraints, a selection of most frequently cited or most informative papers was made. For both reasons it implies that there is a gap in the data to fully compare the devices and to produce an objective consideration with regards to selecting the best parameter. The third limitation of this thesis has to do with current state of knowledge in the papers that were used. Some of the papers used in this thesis claim causality between pathophysiological mechanisms in MetS and detection devices. However, these papers used small groups of stereotype participants, e.g., participants with the same ethnicity from the same country. While this is the case, the papers claim causality while the method is not verifying this. Another limitation of this thesis is that is focused on detection of levels that are already present in the body, thereby neglecting the fact that it could take days, weeks, months or even longer for these levels to develop. This implies that the presented systems have a diagnostic function as well, meaning that it could be they could be too late in detecting and thus in early prevention of MetS. The exact information about the timespan in which these levels develop was not present in the papers, in the future further research is needed before deciding which technique is best to use.

To conclude: the levels of triglyceride, HDL-c and blood sugar could all be used to give information and diagnose patients with MetS. However, further research is needed to support and further realise these methods to be used for detecting the risk of developing MetS. For now, the best parameters that allow identification are outside the body detection of chewing and swallowing reflexes. To select between these techniques and devices and how they can be implemented, there are two important factors that need to be considered to make the device available for monitoring the public. In order to make these devices effective, invasiveness and costs need to be considered, specifically, non-invasiveness and low costs are necessary. Future research should also take these factors in account.

Reference list

Literature

- 2018 Practice Guidelines for the management of arterial hypertension of the European Society of Hypertension and the European Society of Cardiology. (2019). Journal of Hypertension, 37(2), 456. https://doi.org/10.1097/hjh.0000000000002026

- Abell, T. L., & Malagelada, J. R. (1988). Electrogastrography. Digestive Diseases and Sciences, 33(8), 982–992.

- Alavi, S., Makarem, J., Mehrdad, R., & Abbasi, M. (2015). Metabolic Syndrome: A Common Problem among Office Workers. The International Journal of Occupational and Environmental Medicine, 6(1), 34–40. https://doi.org/10.15171/ijoem.2015.492

- Amft, O., Junker, H., & Troster, G. (2005). Detection of eating and drinking arm gestures using inertial body-Worn sensors. Proc. IEEE Int'l Symp. Wearable Computers (ISWc), 160–163.

- Amft, O., & Troster, G. (2006). Methods for Detection and Classification of Normal Swallowing from Muscle Activation and Sound. 2006 Pervasive Health Conference and Workshops. https://doi.org/10.1109/pcthealth.2006.361624

- Amft, O., & Troster, G. (2009). On-Body Sensing Solutions for Automatic Dietary Monitoring. IEEE Pervasive Computing, 8(2), 62–70. https://doi.org/10.1109/mprv.2009.32

- Azar, K. M., Lesser, L. I., Laing, B. Y., Stephens, J., Aurora, M. S., Burke, L. E., & Palaniappan, L. P. (2013). Mobile Applications for Weight Management. American Journal of Preventive Medicine, 45(5), 583–589. https://doi.org/10.1016/j.amepre.2013.07.005

- Barter, P. J. (2011). The Causes and Consequences of Low Levels of High Density Lipoproteins in Patients with Diabetes. Diabetes & Metabolism Journal, 35(2), 101. https://doi.org/10.4093/dmj.2011.35.2.101

- Barton, P., Austin, R., & Fessey, R. (2007). In Vitro Models for Plasma Binding and Tissue Storage. Comprehensive Medicinal Chemistry II, 321–340. https://doi.org/10.1016/b0-08-045044-x/00129-2

- Boldura, O. M., & Baltă, C. (2018). Electrophoresis - Life Sciences Practical Applications. IntechOpen.

- Bazarbashi, N., & Miller, M. (2022). Tri g ly cer id es How to Manage Patients with Elevated Triglycerides and When to Refer? Medical Clinics of North America, 106(2), 299–312. https://doi.org/10.1016/J.MCNA.2021.11.006

- Chait, A., Brazg, R. L., Tribble, D. L., & Krauss, R. M. (1993). Susceptibility of small, dense, low-density lipoproteins to oxidative modification in subjects with the atherogenic lipoprotein phenotype, pattern B. The American Journal of Medicine, 94(4), 350–356. https://doi.org/10.1016/0002-9343(93)90144-e

- Chan, S. M., Selemidis, S., Bozinovski, S., & Vlahos, R. (2019). Pathobiological mechanisms underlying metabolic syndrome (MetS) in chronic obstructive pulmonary disease (COPD): clinical significance and therapeutic strategies. Pharmacology & Therapeutics, 198, 160–188. https://doi.org/10.1016/j.pharmthera.2019.02.013

- Cheng, J., Zhou, B., Kunze, K., Rheinländer, C. C., Wille, S., Wehn, N., Weppner, J., & Lukowicz, P. (2013). Activity recognition and nutrition monitoring in every day situations with a textile capacitive neckband. Proceedings of the 2013 ACM Conference on Pervasive and Ubiquitous Computing Adjunct Publication. https://doi.org/10.1145/2494091.2494143

- Chini, L. S. N., Greffin, S., & Lugon, J. R. (2014). Prevalence of metabolic syndrome among workers from the Company of Generation and Distribution of Energy in Rio de Janeiro, Brazil. Cadernos Saúde Coletiva, 22(4), 359–364. https://doi.org/10.1590/1414-462x201400040009

- Cho, M. J., & Park, S. Y. (2019). Carbon-dot-based ratiometric fluorescence glucose biosensor. Sensors and Actuators B: Chemical, 282, 719–729. https://doi.org/10.1016/j.snb.2018.11.055

- Chung, B. H., Wilkinson, T., Geer, J. C., & Segrest, J. P. (1980). Preparative and quantitative isolation of plasma lipoproteins: rapid, single discontinuous density gradient ultracentrifugation in a vertical rotor. Journal of Lipid Research, 21(3), 284–291. https://doi.org/10.1016/s0022-2275(20)39807-2

- Dallinga-Thie, G. M., Franssen, R., Mooij, H. L., Visser, M. E., Hassing, H. C., Peelman, F., Kastelein, J. J., Péterfy, M., & Nieuwdorp, M. (2010). The metabolism of triglyceride-rich lipoproteins revisited: New players, new insight. Atherosclerosis, 211(1), 1–8. https://doi.org/10.1016/j.atherosclerosis.2009.12.027

- Dron, J. S., Wang, J., Cao, H., McIntyre, A. D., Iacocca, M. A., Menard, J. R., Movsesyan, I., Malloy, M. J., Pullinger, C. R., Kane, J. P., & Hegele, R. A. (2019). Severe hypertriglyceridemia is primarily polygenic. Journal of Clinical Lipidology, 13(1), 80–88. https://doi.org/10.1016/j.jacl.2018.10.006

- Farshchi, H. R., Taylor, M. A., & Macdonald, I. A. (2004). Decreased thermic effect of food after an irregular compared with a regular meal pattern in healthy lean women. International Journal of Obesity, 28(5), 653–660. https://doi.org/10.1038/sj.ijo.0802616

- Fathallah, N., Slim, R., Larif, S., Hmouda, H., & ben Salem, C. (2015). Drug-Induced Hyperglycaemia and Diabetes. Drug Safety, 38(12), 1153–1168. https://doi.org/10.1007/s40264-015-0339-z

- Ginsberg, H. N. (2002). New perspectives on atherogenesis: Role of abnormal Triglyceride-Rich lipoprotein metabolism. Circulation, 106(16), 2137–2142. https://oce-ovid-com.proxy-ub.rug.nl/article/00003017-200210150-00023/HTML

- Giri, T. K., Chakrabarty, S., & Ghosh, B. (2017). Transdermal reverse iontophoresis: A novel technique for therapeutic drug monitoring. Journal of Controlled Release, 246, 30–38. https://doi.org/10.1016/j.jconrel.2016.12.007

- Goldberg, R. B., & Mather, K. (2012). Targeting the Consequences of the Metabolic Syndrome in the Diabetes Prevention Program. Arteriosclerosis, Thrombosis, and Vascular Biology, 32(9), 2077–2090. https://doi.org/10.1161/atvbaha.111.241893

- Grundy, S. M. (1999). Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. The American Journal of Cardiology, 83(9), 25–29. https://doi.org/10.1016/s0002-9149(99)00211-8

- Gualdi-Russo, E., & Toselli, S. (2002). Influence of various factors on the measurement of multifrequency bioimpedance. HOMO, 53(1), 1–16. https://doi.org/10.1078/0018-442x-00035

- Hafiane, A., & Genest, J. (2015). High density lipoproteins: Measurement techniques and potential biomarkers of cardiovascular risk. BBA Clinical, 3, 175–188. https://doi.org/10.1016/j.bbacli.2015.01.005

- Han, G., Chen, S., Wang, X., Wang, J., Wang, H., & Zhao, Z. (2021). Noninvasive blood glucose sensing by near-infrared spectroscopy based on PLSR combines SAE deep neural network approach. Infrared Physics & Technology, 113, 103620. https://doi.org/10.1016/j.infrared.2020.103620

- Hirowatari, Y., Yoshida, H., Kurosawa, H., Doumitu, K. I., & Tada, N. (2003). Measurement of cholesterol of major serum lipoprotein classes by anion-exchange HPLC with perchlorate ion-containing eluent. Journal of Lipid Research, 44(7), 1404–1412. https://doi.org/10.1194/jlr.d300003-jlr200

- Jeyarajah, E. J., Cromwell, W. C., & Otvos, J. D. (2006). Lipoprotein Particle Analysis by Nuclear Magnetic Resonance Spectroscopy. Clinics in Laboratory Medicine, 26(4), 847–870. https://doi.org/10.1016/j.cll.2006.07.006

- Junker, H., Amft, O., Lukowicz, P., & Tröster, G. (2008). Gesture spotting with body-worn inertial sensors to detect user activities. Pattern Recognition, 41(6), 2010–2024. https://doi.org/10.1016/j.patcog.2007.11.016

- Kelishadi, R. (2007). Childhood Overweight, Obesity, and the Metabolic Syndrome in Developing Countries. Epidemiologic Reviews, 29(1), 62–76. https://doi.org/10.1093/epirev/mxm003

- Kuranov, R. V., Sapozhnikova, V. V., Prough, D. S., Cicenaite, I., & Esenaliev, R. O. (2007). Prediction Capability of Optical Coherence Tomography for Blood Glucose Concentration Monitoring. Journal of Diabetes Science and Technology, 1(4), 470–477. https://doi.org/10.1177/193229680700100404

- Kreider, K. E., Gabrielski, A. A., & Hammonds, F. B. (2018). Hyperglycemia Syndromes. Nursing Clinics of North America, 53(3), 303–317. https://doi.org/10.1016/j.cnur.2018.04.001

- Lear, C., Flanagan, J., & Moorrees, C. (1965). The frequency of deglutition in man. Archives of Oral Biology, 10(1), 83-IN15. https://doi.org/10.1016/0003-9969(65)90060-9

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

- Li, Z., Deng, M. L., Tseng, C. H., & Heber, D. (2013). Hypertriglyceridemia Is a Practical Biomarker of Metabolic Syndrome in Individuals with Abdominal Obesity. Metabolic Syndrome and Related Disorders, 11(2), 87–91. https://doi.org/10.1089/met.2012.0090

- Ludwig, D. S., & Ebbeling, C. B. (2005). Overweight Children and Adolescents. New England Journal of Medicine, 353(10), 1070–1071. https://doi.org/10.1056/nejmc051637

- Luime, J. J., Buisman, L. R., Oppe, M., Hazes, J. M. W., & Rutten-van Mölken, M. P. M. H. (2016). Cost-Effectiveness Model for Evaluating New Diagnostic Tests in the Evaluation of Patients With Inflammatory Arthritis at Risk of Having Rheumatoid Arthritis. Arthritis Care & Research, 68(7), 927–935. https://doi.org/10.1002/acr.22776

- Luna, B., & Feinglos, M. N. (2001). Drug-Induced hyperglycemia. Journal American Medical Association, 286(16), 1945–1948. https://doi.org/10.1001/jama.286.16.1945

- Mansilla, E., Díaz Aquino, V., Zambón, D., Marin, G. H., Mártire, K., Roque, G., Ichim, T., Riordan, N. H., Patel, A., Sturla, F., Larsen, G., Spretz, R., Núñez, L., Soratti, C., Ibar, R., van Leeuwen, M., Tau, J. M., Drago, H., & Maceira, A. (2011). Could Metabolic Syndrome, Lipodystrophy, and Aging Be Mesenchymal Stem Cell Exhaustion Syndromes? Stem Cells International, 2011, 1–10. https://doi.org/10.4061/2011/943216

- Marieb, E., & Hoehn, K. (2018). Human Anatomy & Physiology (11th ed.). Pearson.

- Medical Nutritional Institute. (2021, September 29). What Are Triglycerides? | Measurements & Methods Of Improvements. Retrieved September 28, 2022, from https://mnilifestyle.co.za/screening-guidelines/triglycerides/

- Mifsud, S., Schembri, E. L., & Gruppetta, M. (2018). Stress-induced hyperglycaemia. British Journal of Hospital Medicine, 79(11), 634–639. https://doi.org/10.12968/hmed.2018.79.11.634

- Movva, R., & Rader, D. J. (2008). Laboratory Assessment of HDL Heterogeneity and Function. Clinical Chemistry, 54(5), 788–800. https://doi.org/10.1373/clinchem.2007.101923

- Ono, T., Hori, K., Masuda, Y., & Hayashi, T. (2009). Recent Advances in Sensing Oropharyngeal Swallowing Function in Japan. Sensors, 10(1), 176–202. https://doi.org/10.3390/s100100176

- Ooi, E., Barrett, P., Chan, D., & Watts, G. (2008). Apolipoprotein C-III: understanding an emerging cardiovascular risk factor. Clinical Science, 114(10), 611–624. https://doi.org/10.1042/cs20070308

- Otvos, J. D., Jeyarajah, E. J., & Cromwell, W. C. (2002). Measurement issues related to lipoprotein heterogeneity. The American Journal of Cardiology, 90(8), 22–29. https://doi.org/10.1016/s0002-9149(02)02632-2

- Pagano, I. S., & Strait, N. B. (2009). HDL and LDL Cholesterol: Physiology and Clinical Significance (Biochemistry Research Trends Series) (UK ed.). Nova Biomedical.

- Pandey, R., Paidi, S. K., Valdez, T. A., Zhang, C., Spegazzini, N., Dasari, R. R., & Barman, I. (2017). Noninvasive Monitoring of Blood Glucose with Raman Spectroscopy. Accounts of Chemical Research, 50(2), 264–272. https://doi.org/10.1021/acs.accounts.6b00472

- Park, H. S., Han, J. H., Choi, K. M., & Kim, S. M. (2005). Relation between elevated serum alanine aminotransferase and metabolic syndrome in Korean adolescents. The American Journal of Clinical Nutrition, 82(5), 1046–1051. https://doi.org/10.1093/ajcn/82.5.1046

- Parker, D. R., Carlisle, K., Cowan, F. J., Corrall, R. J., & Read, A. E. (1995). Postprandial mesenteric blood flow in humans: relationship to endogenous gastrointestinal hormone secretion and energy content of food. European journal of gastroenterology & hepatology, 7(5), 435–440.

- Pasler, S., & Fischer, W. J. (2014). Food Intake Monitoring: Automated Chew Event Detection in Chewing Sounds. *IEEE Journal of Biomedical and Health Informatics*, *18*(1), 278–289. https://doi.org/10.1109/jbhi.2013.2268663

- Peake, J. M., Kerr, G., & Sullivan, J. P. (2018). A Critical Review of Consumer Wearables, Mobile Applications, and Equipment for Providing Biofeedback, Monitoring Stress, and Sleep in Physically Active Populations. Frontiers in Physiology, 9. https://doi.org/10.3389/fphys.2018.00743

- Pervanidou, P., & Chrousos, G. P. (2011). Stress and obesity/metabolic syndrome in childhood and adolescence. International Journal of Pediatric Obesity, 6(S1), 21–28. https://doi.org/10.3109/17477166.2011.615996

- Purvinis, G., Cameron, B. D., & Altrogge, D. M. (2011). Noninvasive Polarimetric-Based Glucose Monitoring: An in Vivo Study. Journal of Diabetes Science and Technology, 5(2), 380–387. https://doi.org/10.1177/193229681100500227

- Rao, K. D. (2014). Nuclear Magnetic Resonance Nmr: Theory, Applications and Technology (Physics Research and Technology) (UK ed.) [E-book]. Nova Science Pub Inc.

- Reaven, G. M. (2005). The Metabolic Syndrome: Requiescat in Pace. Clinical Chemistry, 51(6), 931–938. https://doi.org/10.1373/clinchem.2005.048611

- Ross, S. M. (2017). Obesity and Metabolic Syndrome. Holistic Nursing Practice, 31(5), 348–352. https://doi.org/10.1097/hnp.0000000000000232

- Ryu, H., & Chin, D. L. (2016). Factors associated with metabolic syndrome among Korean office workers. Archives of Environmental & Occupational Health, 72(5), 249–257. https://doi.org/10.1080/19338244.2016.1200004

- Sakudo, A. (2016). Near-infrared spectroscopy for medical applications: Current status and future perspectives. Clinica Chimica Acta, 455, 181–188. https://doi.org/10.1016/j.cca.2016.02.009

- Schaefer, J. R. (2008). Unraveling hyperlipidemia type III (dysbetalipoproteinemia), slowly. European Journal of Human Genetics, 17(5), 541–542. https://doi.org/10.1038/ejhg.2008.222

- Simpson, C. C., & Mazzeo, S. E. (2017). Calorie counting and fitness tracking technology: Associations with eating disorder symptomatology. Eating Behaviors, 26, 89–92. https://doi.org/10.1016/j.eatbeh.2017.02.002

- Siri, P. W., & Krauss, R. M. (2005). Influence of dietary carbohydrate and fat on LDL and HDL particle distributions. Current Atherosclerosis Reports, 7(6), 455–459. https://doi.org/10.1007/s11883-005-0062-9

- Soran, H., Salam, H., Yadav, R., & Durrington, P. N. (2012). HDL functionality. Current Opinion in Lipidology, 23(4), 353–366. https://doi.org/10.1097/MOL.0b013e328355ca25

- Strauss, M., Foshag, P., & Leischik, R. (2020). Prospective Evaluation of Cardiovascular, Cardiorespiratory, and Metabolic Risk of German Office Workers in Comparison to International Data. International Journal of Environmental Research and Public Health, 17(5), 1590. https://doi.org/10.3390/ijerph17051590

- Tang, L., Chang, S. J., Chen, C. J., & Liu, J. T. (2020). Non-Invasive Blood Glucose Monitoring Technology: A Review. Sensors, 20(23), 6925. https://doi.org/10.3390/s20236925

- Tosi, M., Radice, D., Carioni, G., Vecchiati, T., Fiori, F., Parpinel, M., & Gnagnarella, P. (2021). Accuracy of applications to monitor food intake: Evaluation by comparison with 3-d food diary. Nutrition, 84, 111018. https://doi.org/10.1016/j.nut.2020.111018

- Tang, Z., Barton, S. J., Ward, T. E., Lowry, J. P., Doran, M. M., Byrne, H. J., & Hennelly, B. M. (2018). Multicomponent analysis using a confocal Raman microscope. Applied Optics, 57(22), E118. https://doi.org/10.1364/ao.57.00e118

- Varbo, A., Benn, M., Tybjærg-Hansen, A., Jørgensen, A. B., Frikke-Schmidt, R., & Nordestgaard, B. G. (2013). Remnant Cholesterol as a Causal Risk Factor for Ischemic Heart Disease. Journal of the American College of Cardiology, 61(4), 427–436. https://doi.org/10.1016/j.jacc.2012.08.1026

- Villena Gonzales, W., Mobashsher, A., & Abbosh, A. (2019). The Progress of Glucose Monitoring—A Review of Invasive to Minimally and Non-Invasive Techniques, Devices and Sensors. Sensors, 19(4), 800. https://doi.org/10.3390/s19040800

- Vorgucin, I., Naumovic, N., Vlaski, J., Katanic, D., & Kostanstinidis, G. (2011). Predictive values of metabolic syndrome in children. Central European Journal of Medicine, 6(4), 379–385. https://doi.org/10.2478/s11536-011-0032-2

- Wilson, D. P., Williams, L., & Kavey, R. E. W. (2022). Hypertriglyceridemia in Youth. The Journal of Pediatrics, 243, 200–207. https://doi.org/10.1016/j.jpeds.2021.12.017

- World Health Organization. (2022, April 14). Https://Www.Who.Int/Activities/Preventing-Noncommunicable-Diseases/. Retrieved April 20, 2022, from https://www.who.int/activities/preventing-noncommunicable-diseases/

- Yilmaz, M. B., Guray, Y., Guray, U., Biyikoglu, S. F., Tandogan, I., & Korkmaz, S. (2006). Metabolic syndrome increases the risk of significant coronary artery involvement in patients with peripheral artery disease. Coronary Artery Disease, 17(6), 529–532. https://doi.org/10.1097/00019501-200609000-00006

- YOSHIDA, K., SETA, K., MIYAJIMA, E., & NAKAMURA, H. (1984). High performance liquid chromatography of fat-soluble components of human plasma lipoprotein fractions. BUNSEKI KAGAKU, 33(7), 371–376. https://doi.org/10.2116/bunsekikagaku.33.7_371

- Zanon, M., Riz, M., Sparacino, G., Facchinetti, A., Suri, R. E., Talary, M. S., & Cobelli, C. (2011). Assessment of linear regression techniques for modeling multisensor data for non-invasive continuous glucose monitoring. 2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society. https://doi.org/10.1109/iembs.2011.6090702

Figures

A. Figure 2: The metabolism of blood glucose. (2014, April 14). [Figure]. Insulin, and How the Body Controls Storage and Burning of Glucose and Fat. Retrieved on April 11, 2022 from https://www.fastday.com/fasting/science/insulin-and-how-the-body-controls-storage-and-burning-of-glucose-and-fat/