Biomarkers and age-related diseases
An overview of how biomarkers can be used to prevent age-related diseases.

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Abstract

Medical devices are becoming more and more implemented for use at home and in parallel, the interest from humans in their own health is increasing. Age-related diseases such as diabetes, cancer, and dementia, to name a few, are examples of diseases that with an early diagnosis could be prevented. To find out if there are early indications of the disease in the body, it is necessary to measure biomarkers. These can be measured either invasive or non-invasive and today they are often measurable only clinically at a hospital, but how can people measure these at home by themselves?

To investigate this, a literature study has been done with focus on age-related diseases. A total of 49 abstracts were read through to determine relevance to the questions of inquiry and three articles were mainly used in the literature study. It was found that there is research focusing on the use of biomarkers to identify and do earlier diagnosing of age-related diseases. Methodology and technology for measuring glucose to identify diabetes are implemented, and a change in lifestyle can prevent a person from being affected by type 2 diabetes. With this knowledge, it is easier to see opportunities for other diseases by using the same type of method and technology further on. A previously conducted study regarding diabetes focus on dietary variations and physical activity for non-diabetic people. Meanwhile in the cancer and dementia area, where the developments are not as successful, the focus is on earlier diagnosing by combining technologies.

In the future, the technology should be developed so that biomarkers can be used as indicators of the diseases cancer and dementia, and not just as a complement to already applied technology such as imaging techniques that are available today.
Populärvetenskaplig sammanfattning

Medicintekniska produkter implementeras alltmer för användning i hemmet samtidigt som människans intresse för sin hälsa ökar. Åldersrelaterade sjukdomar så som diabetes, cancer och demens, är exempel på sjukdomar som med en tidig diagnos hade kunnat förhindras. För att kunna ta reda på om indikationer på sjukdomen finns i kroppen, krävs det identifiering av biomarkörer. Dessa mätningar kan vara antingen invasiva eller icke-invasiva och är i dagsläget ofta mätbara kliniskt på ett sjukhus, men hur kan mätningen ske hemifrån?


I framtiden bör man utveckla tekniken så att biomarkörerna kan användas som indikatorer på de åldersrelaterade sjukdomarna, och inte bara som komplement till den redan tillämpade tekniken så som avbildningstekniker som finns att tillgå idag.
Preface

This thesis could not have been done without help from people with expertise. I would like to thank my supervisor, Ismail Elouafiq, for being supportive and giving me new ideas when needed.

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1. Introduction

1.1 Background

The development of medical devices is becoming more and more noticeable today. All types of products from disposable to advanced technology are developed and manufactured. It is not only the demand of new medical devices that accelerates the development, but also the interest in tracking health individually for research, development, and self-interest. As we begin to become more aware of our own mental and physical health, it becomes possible to move the focus of diseases from hospitals to the home, and therefore save time, resources, and money in healthcare.

According to the Institute for Health Metrics and Evaluation (IHME), diseases such as Alzheimer’s disease, cancer and diabetes were some of the most common causes of deaths in Sweden the year of 2019. The relevant risk factors of these diseases are high blood pressure, dietary risks, high fasting plasma glucose and non-optimal temperature. Therefore, it is relevant to study biomarkers connected to the risks to be able to prevent the diseases causing death.(1)

Sleep and daily activity are two of the most interesting parameters for people when finding out their state of health. These parameters are not only easy to track but also give a good indication of the general state of health. The user can either track them with devices at home like a smart watch, smartphone or other technical devices for consumers or the parameters can be tracked at a hospital.(2)

1.1.1 Biomarkers

When we track ourselves with electronic devices, we measure different biomarkers. Biomarkers are therefore measurable mechanisms in different forms in our body that we can measure with different techniques. For example, glucose is a biomarker when detecting diabetes.

The biomarkers can be measured invasively or non-invasively. To make people aware of their health, it is important to simplify measurements of these biomarkers, so people do not have to make invasive measurements and visit the hospital for tracking their health.

1.1.2 Aging

When discussing aging it is common to confirm it by detecting various age-related diseases. The diseases which are associated with aging occur when the functions of the organs in our bodies deteriorate. Since every human being is unique, changes in physical and mental health will arise in different ways at different ages.(3)
1.2 Problem description
An aging population together with an increasingly digitalized world mean that we need to take advantage of new technologies for detecting and preventing age related diseases.

1.3 Purpose
The purpose of this thesis is to find out how different biomarkers can be relevant in applications for age related diseases like dementia, diabetes, and cancer. This is done by a literature study where implemented solutions for anticipating and preventing diabetes are discussed to see if the same methods can be used in the future for dementia and cancer.

1.4 Question of inquiry
In this thesis, a literature study about age-related diseases and relevant biomarkers has been done. The thesis focuses on the following questions.

1. What biomarkers can be used to not only diagnose but prevent the occurrence of age-related diseases?
2. Can implemented methods for diabetes prevention be used for other diseases?
3. How is the user experience for people using already implemented techniques?

1.5 Limitations
This work is delimited to only look at these biomarkers:

1. Glucose by continuous glucose monitoring
2. Sleep by Oura ring
3. Heart rate by Oura ring
4. Temperature by Oura ring

and to focus on these specific age-related diseases:

1. Diabetes
2. Cancer
3. Dementia

This to get a better overview of the knowledge of health and the interest in individual state of health in individuals. The reason for giving an overview of the diseases dementia and cancer is because it is in interest to see if the already implemented devices for tracking and preventing diabetes can be implemented in diseases like dementia and cancer as well. This thesis is limited to give an overview of the biomarkers and diseases mentioned above through a literature study. Since no experiment has been done, the result, analysis and conclusion are based on the literature study.
2. Theory

Today, humans are increasingly invested in their own health, both physical and mental. The interest of electronic equipment to monitor physical activity such as heart rate, steps, sleep and other factors affects the interest in buying these. Many of the world’s public diseases are related to aging, and many of these can often be indications of aging. Although the concept of aging itself is not measurable, we can decide whether a person is old or not by identifying diseases, physical or mental conditions. However, typical age-related diseases do not necessarily indicate that a person is old, one can also be young and still suffer from these diseases.

2.1 Biomarkers

Biomarker is a term that describes various measurable factors that can indicate a state of health. The concept is widespread and can be anything from parameters related to sleep to measurements of proteins in the human body, invasively. In this thesis, biomarkers related to diabetes, cancer and dementia will be presented.

Table 1. Biomarkers, how they can be measured and what they prove.

<table>
<thead>
<tr>
<th>What</th>
<th>How</th>
<th>Result</th>
<th>Biomarker</th>
</tr>
</thead>
<tbody>
<tr>
<td>OGTT</td>
<td>Blood test</td>
<td>Glucose tolerance</td>
<td>Glucose</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>Blood test</td>
<td>Insulin resistance</td>
<td>Insulin</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
<td>Blood test</td>
<td>Diabetes</td>
<td>Glucose</td>
</tr>
<tr>
<td>Resting heart rate</td>
<td>Pulse measuring</td>
<td>Heart related diseases</td>
<td>Pulse</td>
</tr>
<tr>
<td>Heart rate variability</td>
<td>ECG</td>
<td>Heart related diseases</td>
<td>HRV</td>
</tr>
<tr>
<td>Amino acid profiling</td>
<td>Protein measuring</td>
<td>Status on protein</td>
<td>Protein</td>
</tr>
</tbody>
</table>

In table 1, an overview of different biomarkers and which conditions or disease they can indicate is given. In this thesis, delimitations have been made, and the most relevant and measurable biomarkers have been chosen to answer the questions of inquiry.

OGTT, an oral glucose tolerance test, is a blood test used for detecting how good the human body is to take care of glucose. Thus testing the ability to metabolize glucose of a quantity that is standardized by letting the person drink glucose and then measure the glucose levels continuously by taking blood samples. Then, the results can be classified between normal and abnormal to later be used to diagnose all types of diabetes, which of course is advantageous. The test can also predict pre-
diabetes, show gestational diabetes for pregnant women, show insulin resistance, and give us information about reactive hypoglycemia.(4)

HOMA-IR is a Homeostasis Model Assessment resistance test for insulin, to detect how much added insulin the pancreas needs to have a normal function and therefore control the glucose levels in the body.(6) This biomarker is important when detecting diabetes type 2 since resistance against insulin can give obvious consequences. It is common to identify insulin resistance when disorders like hyperglycemia, hypertension and endothelial dysfunction are shown, since these are metabolic consequences. For sure, insulin resistance can in worst case lead to diabetes mellitus type 2.(7)

A fasting blood glucose is a glucose blood sample where the person fasted before the test.(8) There are many clinical studies with using mice to model different age-related diseases connected to abnormal glucose levels.(9)

Resting heart rate is the heart rate of a human at rest, when the heart works at the lowest possible level for the body to keeps its functions.(10) Heart rate variability is when variations in time between every heartbeat is found, so the rhythm is rubbed.(11) These variations can be found by doing an electrocardiogram, ECG.(3) Amino acid profiling is a way to measure and control how much of what proteins a person got in their blood. Thus taking blood samples and then analyse them.(12)

2.2 Invasive biomarkers

The possibilities of measuring different biomarkers are big and we can measure them with different types of sensors. The sensors used can be based on measuring pressure, flow, motion and force, temperature, bioelectricity, and chemical concentrations or reactions.

Here, the invasive biomarker discussed most is glucose, and one example of a device to measure glucose is the FreeStyle libre sensor. This is a glucose sensor that sends information to the participants' smartphone. The sensor can be used up to 14 days before it needs to be replaced which makes it easier for the user since the needle stick part for every measurement disappears. The user should also read the measured value on the sensor at least once every eight hours. This is therefore a more comfortable way to measure glucose levels in the body and the user gets an overview of the glucose levels during the day, and not only in momentary moments.(13)
The glucose monitoring sensor is connected to an application through IOS or Android for the user to follow the measuring of glucose continuously. Since the sensor has a needle to reach the interstitial fluid, glucose is an invasive biomarker in this case.(13)

2.3 Non-invasive biomarkers

It can also be of interest to measure biomarkers non-invasively. One example of a device to measure different biomarkers non-invasively is an Oura ring. It is a device that can measure sleep, heart rate and body temperature to give feedback on the person’s well-being. The ring is connected via Bluetooth to the participants' smartphone. Through seven temperature sensors the ring gives an overview of the person's body temperature during a period. In figure 2, the Oura ring is shown with its sensors. The sensors can provide sleep analysis, monitoring of heart rate and guided sessions for the user as well. The user can easily put in their own goals for daily activity to get information on what to do to reach their daily goals.
With the help of different types of devices, we can measure our sleep. Analysing sleep is connected to many diseases, not necessarily relevant to finding diseases, but we can for sure see a connection between how we sleep and how we feel, and a good well-being can prevent different diseases.\(^\text{(14)}\)

During the sleep cycle we have different states. We have REM sleep which is also known as the dream state. REM stands for rapid eye movement and during this phase the brain behave just like when you are awake, and therefore this state is the one when the sleep is as light as possible.\(^\text{(15,16)}\)

Then we have NREM sleep which stands for non-rapid eye movement. This state can be either light or deep, but it is the phase of entering the deep sleep. The non-REM sleep phase got three stages. The first stage where the muscle activity starts to slow down, and the eyes are closing. In this state it is a very light sleep. Then, we get into stage two where the heart rate and the body temperature decrease, and the body prepares for the deep sleep phase which is the next stage. Stage 3, deep sleep, is the stage where we are in such a mode that it is hard to wake us up. The eye movements and muscle activities are completely gone in this stage. Of course, we also have the state when we are awake.\(^\text{(2)}\)

For elderly, it is important to reach the stage of deep sleep. The reason for that, is that when humans are in the stage of deep sleep, the immune system, tissues, bones and muscles repairs and strengthens.\(^\text{(17)}\)

2.4 Age related diseases

2.4.1 Diabetes

Diabetes is a chronic disease that exists in different types, type 1 and 2. Diabetes affects a person when he or she has hyperglycemia, increased concentration of glucose in the blood. In the normal state, the kidneys reabsorb glucose, but for a person with diabetes, this ability has been exceeded and a large part of the glucose that normally should have been reabsorbed is now excreted in the urine instead. The reason why a person then suffers from diabetes is because he or she has a reduced production of
insulin or because of insulin resistance. Regardless of whether the person has suffered from decreased insulin production or resistance against it, the concentration of glucose will increase in the bloodstream and the cells will not be supplied with the same amount of glucose.

Since type 2 of diabetes is the most common diabetic disease, and especially among the elderly, this will be addressed in the thesis. Nearly 90 percent of all cases of diabetes include type 2 which is also called insulin-independent diabetes, which means that it is not the reduced production of insulin that causes the disease, but the reduced effect of insulin on the cells.(3)

The peptide hormone insulin is secreted from beta cells which break down the so-called proinsulin into two parts, active insulin, and inactive c-peptide. Due to the slow degradation of the c-peptides, their concentration is used to measure the secretion of insulin, which is an important part when determining diabetes.(3)

2.4.1.1 Continuous glucose monitoring

Continuous glucose monitoring, CGM, is a method to measure glucose levels in the blood continuously during a period to not have to measure it with a stick in the finger several times a day. With this method, individuals will get direct feedback on their choices throughout the day, in food and physical activity.(18)

Since high blood sugar levels affect many of the diseases that occur in older age, the continuous glucose monitoring is a relevant biomarker when discussing age related diseases. Even if high blood sugar does not directly affect cancer, people with that condition are more likely to get any form of cancer.

2.4.2 Cancer

Another disease that is connected to aging is cancer. There are no clear connections between cancer and aging but there is a bigger risk for older people since the immune system deteriorates. There are also small noticeable parallels between bad sleep habits and cancer.(19)

In the human body, cells die, and new cells are created by mitosis, which is the name for cell division. When this adjustment does not work as normal, and new cells creates faster than the degradation of old cells, tumours are created. Tumours are basically lumps of cells and can be either benign or malignant. If a tumour is benign, it means that it is not dangerous, but if the tumour is malignant, it is dangerous and risks spreading into other organs and tissues in the body, which is also called cancer.(3)

When we are getting older, our immune system deteriorates, and features such as mitosis might not work as good as it should.(3) Therefore, there is a major risk of being affected by uncontrolled cell changes in older age and since the changes takes place over long periods of time there is larger risks of cancer the older, we get.(3,20)
2.4.3 Dementia

Dementia is one of many diseases that affects people in older age, and the most common disease in the group of dementia is Alzheimer's disease. Dementia includes many diseases where the neurological condition for a person is affected negatively through changes in brain capacity and since it is a chronic disease it also affects society and the healthcare. (21–23)

Since there is still no cure for dementia, a lot of money is spent on research and of course in caring for those who have dementia today, either by medications or living in a retirement home. Dementia do not only affect the person who got the disease, but also their family and relatives. (23)

The neurological effect dementia has on a person is shown with different symptoms. The most common one and probably the one everyone can relate to is memory loss. Also, problems related to communication occur. Dementia can be shown in different diseases and what symptoms a person gets depends on which part of the brain that gets affected. (24)

2.4.3.1 Alzheimer’s disease

Dementia can as mentioned be shown in different diseases and the most common one is Alzheimer’s disease, around 50 percent of the people with dementia have Alzheimer’s disease. In this case, it is the nerve cells in the temporal lobe and parietal lobe that are damaged. Alzheimer’s disease occurs when a protein called beta-amyloid is stored in the brain. This protein is harmful and the reason why it is stored in the brain can be hereditary. The reason why nerve cells are destroyed may also be due to changes in the neurofibrils, the small nerve threads. (25)

2.4.3.2 Blood vessel related dementia

The second most common type of dementia is the one called blood vessel related dementia which is also known as blood vessel dementia or vascular dementia. It is common to have a mixture between Alzheimer’s disease and blood vessel dementia. Blood vessel dementia arises when nutrient deficiency and oxygen deficiency occurs in the nerve cells of the brain. Damage in the temporal lobes affects the memory, frontal lobe damage can affect the personality and parietal lobe damage can affect analytical ability, interpretive ability, and the ability to understand their surroundings.

There are several reasons for oxygen deficiency in the brain. The blood vessels may have narrowed because of fat, blood cells and connective tissue stuck on the inner vessel wall. The narrowed blood vessels prevent the blood from circulating properly. Since the blood is a carrier of oxygen, oxygen deficiency may occur in the brain. Also, high blood pressure, blood clots and bleeding in the brain can be a cause of oxygen deficiency. (26)
2.4.3.3 Lewy body dementia
Lewy body dementia is an unusual type of dementia that in some ways is similar to Alzheimer’s and Parkinson’s disease and the condition can change from day to day for the person affected. There is not as much knowledge about this disease, and it is discovered after the person’s death since the changes in the brain are so small. (27)

2.4.3.4 Frontal lobe dementia
Frontal lobe dementia is also an unusual type of dementia, but its symptoms are nothing like the other types. For example, the memory loss does not come up until far into the disease, which means that memory loss is probably not the first indicator of frontal lobe dementia, it is more common to notice the disease by the person's personality change. Just like the name tells us, frontal lobe dementia is when changes in the frontal lobe occur, but it is not known what the exact cause of this disease is, but it might depend on metabolism of certain proteins in nerve cells. Around 50 percent of people with frontal lobe dementia have a relative that also had the disease. (28)

As a result, actions and thoughts controlled from this part of the brain will function worse and worse. The anterior parts of the brain will affect the personality and the function in social contexts. The frontal lobe enables expression such as speech and language, it also controls the person's judgment and ability to discern. For the person with frontal lobe dementia, it might be a problem with controlling impulsivity and aggression. (29)

2.5 Previous work
There are many studies on relevant biomarkers to find connections between diseases such as cancer and how it is connected to aging and bad habits due to health in life. There are also many studies about whether cancer is connected to the person’s quality of sleep, and if the risk of getting cancer in older age increases with bad sleep. (30)

Even if it seems like the connection between bad habits and diseases like cancer does exist, it is hard to see an obvious connection about getting cancer, but we know for sure that bad habits in our everyday lives do affect us and accelerate diseases.

Song C. et al. say that there are connections between bad sleep quality and increased risk of cancer diseases. But they also conclude that there are many factors that affect the increased risk, such as genetic risks of cancer. According to the authors, they have identified a new risk of being affected by cancer that includes bad sleep habits. (30)
3. Method

During this project, a literature study was implemented. The first five weeks consisted of researching and reading articles combined with doing the literature study. When the thesis started, the focus was to do a project together with Biohackeri. Since the project was not started in time, a complete literature study was done to be able to answer the questions of inquiry.

The main study of the thesis is the literature study. At first, the plan was to do a complementing interview study to the literature one, to give an overview of the user perspective. Due to a time limit and difficulties by getting in contact with enough users of the two devices FreeStyle Pro and the Oura ring, the interview study was limited to only give answers from two users.

The literature study is made in three categories, with focus on three different age-related diseases that all are described in the theory part of the thesis. First, a searching on PubMed with interest of collecting information about diabetes was made. The keywords for this search were “continuous glucose monitoring”, “self-monitoring” and “non-diabetic”. The reason for adding a key word of non-diabetic was to narrow down the results, and since continuous glucose monitoring is a device made for diabetics, adding the keyword “non-diabetic” narrowed down the search to relevant articles for this thesis. The same method was used for finding articles about cancer and dementia as well, and an overview of the search method is presented in table 2.

When searching in PubMed, the goal was to narrow down every search so that less than 25 articles was found. In table 2, an overview of the different diseases, how many articles that were found in every disease and how many that are used in the thesis is presented. The reason why between 11 and 21 abstracts was read but only 1-3 full texts was read is because many articles could be excluded since they were not relevant for this thesis. Some were not available in full text, some articles had requirements of underlying diseases or performed surgeries of the participants which made them irrelevant. For example, there was some articles with studies on pregnant women only, which was not relevant.
Table 2. Overview of the articles of the three diseases, how many read abstracts, full texts and how many used in the thesis.

<table>
<thead>
<tr>
<th>Date</th>
<th>MESH terms and keywords</th>
<th>Specifications</th>
<th>Articles found</th>
<th>Abstract read</th>
<th>Full text read</th>
<th>Used in thesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-05-10</td>
<td>Continuous glucose monitoring</td>
<td>None</td>
<td>21</td>
<td>21</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Self-monitoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-diabetic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22-05-10</td>
<td>Blood-based biomarkers Cancer Monitoring</td>
<td>Articles published within 1 year</td>
<td>11</td>
<td>11</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>22-05-10</td>
<td>Alzheimer's disease</td>
<td>Articles published within 1 year</td>
<td>17</td>
<td>17</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Blood-based biomarkers Monitoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For the interview study, which can be found in appendix 1, questions to ask the candidates were formulated together with the supervisor for the thesis. The candidates were found through an online group for people that uses devices like Oura ring and continuous glucose monitoring and some of the candidates were contacted with help from the supervisor.

The questions used in the interview study was formulated to be relevant in terms of the questions of inquiry as previously stated in the thesis. The goal with the interviews was to collect information about the use of both Oura ring and continuous glucose monitoring and how good usability both devices got. Why only interviews regarding the Oura ring and continuous glucose monitoring have been done, is because devices tracking cancer and dementia diseases are not applied for self-monitoring or even implemented.
4. Result

For the literature study, three articles are used. They all describe how each disease can be tracked by using different biomarkers. The interview study gave two interest perspectives of the usability of non-diabetic people using devices for tracking their glucose levels. In general, both candidates had a positive experience of using the non-invasive Oura ring, while they disagreed on the view of the CGM device due to differences in the felt discomfort of the needle. For more detailed answers, see appendix 2.

4.1 Diabetes

Fechner et al. discuss in an article the results of their randomized crossover trial where non-diabetic people use continuous glucose monitoring. According to the authors, studies of non-diabetic persons from dietary perspective have never been done before. The participants in the trial are both men and women between 50 and 70 years old that are overweight according to the BMI scale. None of them was diabetic or had any other disease that could affect the results when starting the trial, in general they assumed to be healthy except the overweight. The trial was formed for the participants to follow a schedule for diet and activity, so that the authors would be able to prove their hypothesis.

They describe the importance of non-diabetics to measure their plasma glucose levels as well since vascular complications and diabetes can be prevented. The reason for doing the diets compared in glycemic load is because variations in glucose levels depend on glycemic load. The glycemic load varies with the glycemic index. Therefore, both are measured in account to the body’s consumption of carbohydrates. The differences of high and low glycemic foods are described and compared in the article. High glycemic food such as fast carbohydrates and low glycemic food such as whole grains are compared in the aspect of how much effect it has on glucose levels in the body. The purpose of the study was to “assess the ability of the continuous glucose monitoring device to detect differences in estimated plasma glucose concentrations during the consumption of two different diets – one with a low and another with a high GL – in non-diabetic, free-living participants”. The authors therefore had a hypothesis that the device for continuous glucose monitoring, Abbott FreeStyle Libre Pro, could detect the differences in glucose levels while being on the different diets.

The design of the trial was that the participants were given a diet, either with low or high glycemic load, with random order to consume for three days. On the fourth day, the participants were given the standard meal challenge of three hours where they were supposed to do fasting and some blood tests after eating. Every participant was supposed to do both a low and high glycemic load diet but with a “washout period” of two and a half days to be off from any strict diet before starting the other intervention and at the same time, keep a food diary. The day before starting the three-day diet, the participants consumed a low-fat dinner and were asked to not do any kind of vigorous physical activity or drinking more than one glass of alcoholic beverage and this was suggested during the whole trial as
well. During the trial, the participants wore a continuous glucose monitor and a device for measuring physical activity.

When the participants were on their diet, they had every meal and snack in between prepared. One set was made of low glycemic load food and the other set was high glycemic load food. They got breakfast, lunch and dinner and snack in between scheduled 2 hours after each meal and therefore they were not allowed to add any drinks or food except water, tea and plain coffee. During the trial, each participant got help from a dietician to keep up the strict diets. Every 15 minutes the glucose was measured continuously in every participant to be able to catch any noticeable differences between the two different diets.

Different methods were used to calculate the glucose value and the glucose variability, “area under glucose curve (tAUC)” and “overlapping net glycemic action method with a 4-hour interval (CONGA-4)”. The device for tracking activity, a belt placed around the hip, were worn by the participants every day of the trial. Just like the continuous glucose monitoring, this device also measured every 15 minutes, and the results of measurements were used in the trial if the participant used it for more than 12 hours a day.

In the article, it is mentioned that the blood samples were tested in “NaF and EDTA-containing vacutainer tubes”. They also describe the process of cooling the tubes and centrifuge them and how they stored the samples in liquid nitrogen which measured a temperature of -80 degrees Celsius. The reason for storing the samples after the first tests, was to be able to test all samples from every person at the end and therefore analyse them during the same analytical run.

23 participants started the trial but 21 finished it due to different circumstances including one where the participant had detachment of the sensor. According to the results of the trial, the concluding meal challenge affected the glucose responses more after having the low glycemic load diet than having the high one.

With this trial, the authors demonstrated the use of continuous glucose monitoring and its possibilities to detect differences in glucose levels when consuming two different diets with different glycemic loads. Since the Abbott FreeStyle Libre Pro was giving different results for the period of low glycemic load and high glycemic load, Fechner et al. accepts their hypothesis that “diet-induced differences between the two intervention periods could be detected by the Abbott FreeStyle Libre Pro”. Since the used device for continuous glucose monitoring is meant for diabetics with an insulin dependent, they present with this trial that it can be used for non-diabetics as well to identify differences in glucose levels. For the continuous glucose monitoring and plasma glucose concentrations there are noticeable differences. Continuous glucose monitoring measures the glucose levels in the interstitial fluid while plasma glucose is measured in the plasma. Changes in glucose levels measured by continuous glucose monitoring are delayed in relation to how the plasma glucose detect, and the delay time depends on
how long the diffusion of glucose from capillary endothelium to the interstitial fluid which in turn is affected by the blood flow and the permeability of the capillaries.

In what rate subcutaneous tissue cells can take up glucose affects the continuous glucose monitoring. In the trial, the blood samples were taken at specific times right after the meal challenge and directly compared with the glucose levels on the device at the same time. The regression analysis in the trial showed that the mean concentration of glucose was an influencing factor in the variance between continuous glucose monitoring method and the plasma method. If the concentrations of glucose were less or equal to 7.0 mmol/L the continuous glucose monitoring levels were lower than the plasma ones, but if the glucose concentrations were higher, the continuous glucose monitoring levels was higher. Measuring the glucose levels showed noticeable higher concentrations of glucose after the low glycemic load diet comparing to the high glycemic load diet, after the meal challenge.

In the trial, the structure of the different diets was extreme, 70% carbohydrate energy for the high glycemic load diet vs the low at 16%. According to the authors, the study could present the functionality of the sensor, “but do not reflect habitual dietary patterns in a free-living situation”. Since the device for continuous glucose monitoring, Abbott FreeStyle Libre Pro, do not have to be calibrated by the user, and has a period of use of 14 days before changing the sensor, the manual glucose measuring with using fingerstick becomes needless. The participants of the trial had different experiences regarding the sensor attached to the arm. One experienced irritation at the beginning and one during both periods and two had to restart because of bad attachment between the sensor and the arm. The detachments of the sensor were solved by a transparent film, Tegaderm™.

To conclude, Fechner et al. accepted their hypothesis of detecting glucose level differences in non-diabetics with a device developed for diabetics. For future studies, the authors suggest that the focus should be on the sensor’s sensitivity when detecting differences in glucose levels with less extreme diets than this trial and do this with a varying group of participants.(31)

In appendix 1, questions of the interview study are listed. Since diabetes is the only disease of these three where tracking the biomarker at home is possible, the user experience is interesting when discussing future devices for other diseases as well. As seen in appendix 2, two user experiences are presented where both users were non-diabetic and still used a device for tracking their glucose levels. Both candidates describe their overall experience, upcoming problems, and behavioural changes with using continuous glucose monitoring and give different answers apart from the changes in their behaviour. Candidate 1 did not state any problems with using continuous glucose monitoring, while candidate 1 felt discomfort due to the needle of the sensor. They both had the same experience with their behavioural changing, and mostly according to their eating habits and getting direct feedback of glucose levels while eating.
4.2 Cancer

In an article by Ali et al. from 2021 gliomas are discussed which leads us into how to prevent different cancer diseases. It is discussed how effectful blood-based biomarkers are for diagnosing cancer and how they can be used to predict cancer cells before the person even notices any side effects that can be connected to glioma. People who were assumed to be healthy were compared to patients with glioma to measure the diagnostic marker.

Ali et al. believe that certain criteria should be fulfilled for the promising blood-based biomarkers. They wrote about three criteria. The blood-biomarkers should have a high accuracy. It should also have a resistance to factors depending on the patient itself, for example gender, body temperature, medication and more. The last criterion for the biomarkers is that they should be “tested in several (preferably independent) studies”. There are also wishes on how the device that analyses the biomarkers should be, “relatively cheap, easy to operate, sensitive in determining low concentrations of biomarker and specific for the biomarker” and at the same time avoid any test results that might be false positive.

One of the most harmful tumors in the central nervous system is called gliomas and when it is diagnosed, it depends on the “tumor tissue assessment”, even though it is not desired to collect the tumor tissue repetitive to track the evolution of the tumor in the body. Today, advanced imaging techniques are used to monitor gliomas but the research of using blood-based biomarkers for monitoring the tumors has already started. Blood-based biomarkers are relevant for early diagnosis and other application like prognostic and predictive. Because of the possibilities of using the biomarkers to detect gliomas in an early stage, patients that are at risk of getting gliomas can be tested without having any symptoms.

The article discusses different biomarker terms and one of them are “diagnostic marker” which according to the authors describes biomarkers that are used to be able to compare healthy individuals and patients with glioma. The second biomarker discussed is the predictive markers which are used for the therapy part to choose the right one and the third biomarker is the monitoring marker which are used for measuring the volume of the tumor or for monitoring the progression of the tumor.

The purpose of the review that Ali et al. have done was to bring forward “the most promising and well-researched blood-based biomarkers for patients with glioma”. For the review, they used PubMed and Embase with keywords like “glioma”, “blood” and “biomarkers”. In total, the search gave 7919 articles in the two databases and 262 of them were used. Many of the biomarkers described in the references included at most two studies and Ali et al. suggested that it was relevant to look at the results with at least four studies, in their opinion they were the most promising biomarkers. They also suggest that many of the articles and their studies had very few participants did not have any validation group. Also, the accuracy of the biomarkers was often not mentioned in the studies. The
markers used in the review are presented in four groups of biomolecules: proteins, nucleic acids, circulating cells and metabolomics. “We decided to report the diagnosis as provided in the referenced studies.”

In the discussion part of the article, Ali et al. discuss how much impact glioma has on the human body and therefore how important it is to collect information about the tumor and its characteristics. They do not think that any of the biomarkers that has been studied in the article should be implemented clinically yet.

According to the authors, biomarkers in groups is more accurate than biomarkers individually and their analysis shows that biomarker levels come to be more and more dysregulated when the tumour become malignant. The reason for this is that there is a connection between biomarker levels and tumour grade. They suggest that multi-biosource should be implemented for patients with glioma. Multi-biosource is a blood test based on multi biomolecules. The authors hopes that other body fluids than blood is good enough to use as a tracer for glioma and they believe that today, blood-based biomarkers only work as a complement to the methods that is already implemented for diagnosing gliomas, and not works for themselves.

The authors, suggest that it is important to report future research and studies of biomarkers, so it is easy to find and reproduce the results. If that is not possible, they think that it should be mandatory to include a branch of blood-based biomarkers when doing any clinical trial. It is also of interest to let blood-based biomarkers work as complement to already implemented techniques to identify progression of tumours. They think that future studies should highlight the clinical use.(32)

4.3 Dementia

Teunissen et al. wrote an article about Alzheimer’s disease and biomarkers.(33) They describe how important biomarkers are and how they can be detected. Methods such as different PET scans and CSF are described as expensive and non-invasive and therefore the article focus on however it is possible to discover biomarkers that is more effective in a cost perspective. They then suggest that biomarkers that are blood-based meets those requirements. The authors refer to other studies with results of how blood-biomarkers acts in people with Alzheimer’s disease and why they are important for, for example, early diagnosis. Three different biomarkers are in focus in this article: amyloid, pTau and NfL, but GFAP is also mentioned. A roadmap for clinical implementation of the blood-based biomarkers is also presented in the article.

To get the best possible results when measuring the biomarkers, it is important to understand how and what factors that influence. Since many studies including blood-based biomarkers are done in “well characterised populations” the analysis of the blood-based biomarkers and its influencing factors are important in “population-based” and “community-based” groups. In primary care, this is particularly important since the blood-based biomarkers suits better than CSF and neuroimaging markers that are
invasive and expensive. Clinical analysis of blood-based biomarkers is affected by many factors: age, gender, and lifestyle factors to name a few.

Teunissen et al. mentions five phases when implement new fluid biomarkers. The first phase includes an initial exploratory study followed by phase two which is the development and validation of the biomarkers clinically. Phase three includes a study of the biomarkers use in retrospective and longitudinal groups. Then, evaluation of “prospective validation studies in real-world settings” of the biomarkers is done, which is the fourth phase. Lastly, phase five is the clinical implementation.

They also mentioned that the development of how-to storage and process biomarkers is a relevant criterion when implementing the blood-based biomarkers clinically.

Because of the limited availability of amyloid PET and CSF biomarkers, testing of biomarkers related to Alzheimer’s disease is limited, but it is possible to use blood-based biomarkers to make it possible to do tests for Alzheimer’s. Today, the only measuring method for amyloids is either with CSF or PET. A cause for implement the blood-based biomarkers clinically could be the antibody aducanumab, which probably will be approved in some parts of the world.

Teunissen et al. used PubMed for research with the keyword “Alzheimer’s disease” together with any of “amyloid”, “Tau”, “pTau”, “NfL”, “GFAP”, and “plasma”, “serum”, “blood”. They conclude their trial with suggestions on future work with blood-based biomarkers in use for diagnosing Alzheimer’s disease and thinks that the next step in the process is to develop techniques to be able to use the biomarkers for individuals. They believe that it will be possible to use the biomarkers clinically in a few years. “Validation and implementation of blood-based biomarkers will facilitate the development of precision medicine”.

4.4 Microneedles for continuous glucose monitoring

In an article written by Chien et al. discusses the possibilities of using microneedle sensors for continuous glucose monitoring instead of the conventionally needles used today. The medical continuous glucose monitoring device with microneedles must be inserted under the skin to be able to measure the glucose levels continuously in the body. The device was tested on two candidates and the article is therefore an analysis of this test. Chien et al. discuss the reason for why it is so important for people with diabetes to be able to do continuous glucose monitoring and simultaneously reduce pain and risks with traditional needles. They also discuss other articles with research about non-invasively methods for continuous glucose monitoring. They mentioned Caduff et al.(35) whose team done the first human experiments with non-invasive and non-optical methods for continuous glucose monitoring and Lahdesmaki et al.(36) which in turn discuss however it is possible to use a contact lens for continuous glucose monitoring and therefore use the molecules in tears as a biomarker.
Chien et al. (34) uses an electrochemical sensor for their project which can be connected to a smartphone. Since the microneedle patch that is inserted has a minimally invasive effect the skin will be minimally affected after use as seen in figure 3.

![Image](image.png)

*Figure 3 The skin when removing the microneedle device (34)*

In the article, Chien et al. also mentioned different well known continuous glucose monitoring systems that all uses a needle with length from 5 mm up to 13 mm. The microneedle in the continuous glucose monitoring device they use is only 1 mm long and has a thickness of 0.1 mm which means that the needles does not reach long enough into the skin to have a bad impact on blood vessels. (34)
5. Discussion

This part involves a discussion regarding the questions of inquiry of the thesis and a discussion about the used method and improvements.

5.1 Discussion regarding questions of inquiry

The reason for discussing dementia and cancer in this thesis, even though only devices for sleep habits, body temperature and glucose are represented in the interviews and literature study, is because it was of interest to see if it is possible to use a device like continuous glucose monitoring for preventing cancer and dementia diseases as well.

Applications in the field of diabetes are constantly evolving and there is a lot of research on continuous glucose monitoring and how to develop methods to improve the quality of life for people affected by different types of diabetes. The concept of self-monitoring is becoming increasingly common for people who are not affected by any disease. The opportunities to be able to prevent and predict diseases such as diabetes, cancer and dementia in the future are big. It is important to find the right type of biomarker to be able to use self-monitoring as a process where you can detect these diseases at an early stage, which is a big part of all deaths in the world. How do you motivate someone who is not ill to spend time and money on medical devices to be able to detect diseases before it is too late? I believe that we are at a very early stage of self-monitoring and that aspects such as cost, time and discomfort prevent many people from using a product that is not originally intended for the healthy individuals.

Continuous glucose monitoring is an excellent example of a product where diabetes can be predicted and prevented at an early stage, for diabetes type 2 where a changed lifestyle can make the person do healthier choices and get normal glucose levels again. Being able to monitor other biomarkers than glucose at home in the future to be able to predict other diseases like cancer and dementia feels like a great opportunity.

Cancer and dementia can be predicted today by the person undergoing treatments at the hospital in case of suspicion that the person has been affected. The question is how one could simplify these methods, by using the same types of biomarkers, to make it easier to predict this. The problem is that dementia is neurological and complex and cancer diseases can occur anywhere in the body, which makes it more difficult to measure without suspicion of disease.

The strategies of measuring biomarkers to make sure whether a person has dementia or not are very complex and in need of specific competence and therefore it seems hard to measure them outside a hospital without experts today. The research in this field is getting more and more common and even the use of blood samples in hospitals to diagnose and prevent dementia are in an early stage. With that knowledge, we can assume that a monitoring system for self-monitoring dementia and diseases
connected to dementia may not be possible today, but if the development in different treatments at hospitals are coming through, we may see a device for dementia that works just as good as the glucose monitor for diabetes.

Both Teunissen et al. with the article about Alzheimer’s disease and Ali et al. with the article of cancer describes blood-based biomarkers.

5.2 Method discussion
During the first phase of this thesis, it was planned to follow a project together with Biohackeri. Therefore, the purpose, questions of inquiry and method was developed with this in mind. Since the project did not start on time as planned, the original plan needed to be adjusted and at first a setup for an interview study was made. In consultation with the supervisor of the thesis, relevant questions were formulated and then contacted people that used the devices. The interviews were not succeeded as planned and therefore a new adjustment was done which was to focus on a literature study. If the first adjustment of the project had been done earlier, more time could have been dedicated for the interview study and later the literature study. By that, better searching for the articles could have been done and perhaps, more than one article per disease could have been useful in the thesis.

The goal with doing the interviews was to get the users thoughts on their experience and be able to connect what the literature says and the user perspective.
6. Conclusion

The conclusion of this thesis is that research has already begun on whether one can proceed to find solutions for making an early diagnosis of diseases such as cancer and dementia. Today this is possible for diabetes since there are devices for the measurement of glucose available for everyone to use.

It seems that the research so far has not reached the stage where biomarkers are used as indicators of the diseases, but more as a complement to previous technology. This means that in the future it is important to focus on developing methods and techniques to be able to measure these biomarkers and determine if there are indicators of the disease.

People without diabetes can use the same device that a diabetic use to measure their glucose levels, and then adjust their everyday choices with food and activity to avoid the risk of developing diabetes. We should therefore in the future be able to see new technology and new methods of measuring other biomarkers as well to be able to do early diagnoses and perhaps even prevent the development of various types of cancer and dementia diseases.

6.1 Future work

Getting healthy people to use products that cost them both time and money can be problematic. I do believe that invasive methods such as needle sticks or manual methods can be difficult to implement as self-monitoring devices. With this approach, it is conceivable that in the future we should focus on developing simple, cheap, and non-invasive methods that work in all applications, where the primary focus should be on diabetes as this disease already has developed technology to measure its biomarker, glucose.

More studies on healthy individuals should also be carried out to be able to demonstrate the effect this can have. Both diabetes, cancer and dementia are diseases that affect many in society and individuals can prevent getting these diseases with a different lifestyle and reduce the contributing causes of the diseases.
7. References


9. Fasting blood glucose as a predictor of mortality: Lost in translation - ScienceDirect


17. Sleep Basics: REM & NREM, Sleep Stages, Good Sleep Habits & More [Internet]. Cleveland Clinic. [cited 2022 Apr 24]. Available from: https://my.clevelandclinic.org/health/articles/12148-sleep-basics


23. The worldwide economic impact of dementia 2010 - Wimo - 2013 - Alzheimer’s & Dementia - Wiley Online Library


Appendix

Appendix 1. Interview study questions

Questions Oura ring experience:

1. How was your overall experience with the Oura ring?
2. Did you get any problems with the devices?
3. Did you notice any behavioural changes while using the devices? I am interested in changes due to your health and habits.
4. Is it okay to maybe look at your data if you have it saved? It would have been great for my thesis to have some examples. Of course, it will be anonymized.
5. What made you choose to use the Oura ring?
6. What could have been better with either the devices or the functions in the application?
7. How long did you use the Oura ring?
8. Would you use the monitor again? Why or why not?
9. Did you improve any aspect of your health after using any of these devices?
10. Did you feel watched or judged while using it?
11. Did any of these devices make your habits worse?
12. What did you learn using the Oura ring?
13. Do you have any kind of disease or else that could affect the result?

Questions Continuous glucose monitoring experience:

1. How was your overall experience with the continuous glucose monitoring?
2. Did you get any problems with the devices?
3. Did you notice any behavioural changes while using the devices? I am interested in changes due to your health and habits.
4. Is it okay to maybe look at your data if you have it saved? It would have been great for my thesis to have some examples. Of course, it will be anonymized.
5. What made you choose to use the continuous glucose monitoring?
6. What could have been better with either the devices or the functions in the application?
7. Was it okay to do the CGM or was it uncomfortable?
8. Would you rather have used microneedles or something else that does not hurt? Something else than a traditional needle?
9. How many times did you use the continuous glucose monitoring?
10. Would you use the monitor again? Why or why not?
11. If you would like to use the glucose monitor again in the future, how often would you want to use the device?
12. What did you learn using the continuous glucose monitoring?
13. Did you improve any aspect of your health after using any of these devices?
14. Did you feel watched or judged while using it?
15. Did any of these devices make your habits worse?
16. Do you have any kind of disease or else that could affect the result?
Appendix 2. Interview study answers

In this thesis, an interview study with two candidates has been made. Both candidates have used both Oura ring and continuous glucose monitoring. Since the interview study was not as successful as desired, the answers from the two candidates are presented here to be able to discuss the answers in the discussion part of the report.

The first candidate to interview, in this thesis called candidate 1, have used both the Oura ring and the Continuous glucose monitoring. For the CGM, the candidate has used the FreeStyle libre, and no previous diseases is known that could have affect the results or the use of these devices. The candidate used the FreeStyle libre with the corresponding application and they also used another application with the motivation that the FreeStyle libre application is very simple and not very specific.

The second candidate to interview, candidate 2, have used both the Oura ring and the Continuous glucose monitoring. This candidate did not have any previous diseases that could affect the result or the use of the devices.

Oura ring

Two candidates have used or uses the Oura ring. Out of these candidates y used the CGM as well. The candidates were asked to participate in an interview in person, but one out of two could not make it and therefore all candidates were also asked to answer the questions by email.

Overall experience

Candidate 1 and candidate 2 had a positive overall experience with the Oura ring. Both were impressed of the battery, and they felt it was very good that they did not have to recharge it often. Both candidate 1 and 2, felt like they were more

Both candidates were so impressed by the device, that they will continue to use the Oura ring in the future. None of the candidates felt watched or judged by using the device.

Problems and improvements

Candidate 1 experienced some problems with losing data on days when they forgot to open the application, something that candidate 2 had no problem with. A few times candidate 1 experienced that the quality of sleep increased even though no changes in behaviour were made. They felt like it showed a great sleeping quality on days when it should not be good at all, according to how the feeling was when waking up the morning after. For example, the sleep quality was very good even though the candidate consumed alcohol and only slept for a few hours. Candidate 1 also experienced problems while working out. The Oura ring seems to be more of a health device rather than a fitness device since it does not register anything when the user is doing some type of heart rate-boosting activity.

Candidate 1 would like to see a real time heart rate function with the Oura ring in the application.
Candidate 2 got improvements regarding however the Oura ring could integrate with other applications as well, and not only the corresponding application. For example, to connect the Oura ring with a smart watch.

Behavioural changes

Candidate 1 experienced a small behaviour change by just having the device before the start of use. During the first week they experienced a need of entering the application just to check through the parameters, a few times a day. When using the device for a period, the candidate felt more attentive and was questioning “why am I extra tired today” or “why was my body temperature so high last night” for example. One thing that was positive with the application connected to the Oura ring according to candidate 1, was that the device did not make they feel like they must do any kind of activity. Instead, they felt like the application suggested activities in a passive way more than in an urging way because of how the notifications were formulated.

Candidate 2 felt that they became more aware of its sleeping quality and was more likely to take time to rest during the days when the sleep quality was not good. They also thought that reminders and feedback such as notifications were very good, “the measuring and feedback is the valuable part of using an Oura ring”.

Continuous glucose monitoring

Candidate 2 wanted to see if there was some correlation between feeling tired and low blood sugar and therefor, they started to use CGM. Today, candidate 2 has experience of using CGM three times.

Overall experience

The overall experience for candidate 2 was not as good as with the Oura ring for several reasons.

Problems

Candidate 2 felt discomfort with using the CGM because of the needle while candidate 1 did not felt any discomfort at all. The differences in experience due to the needle itself obviously differ between users.

Behavioural changes

Both candidate 1 and 2 experienced behavioural changes according to eating between meals and what they ate. This because they got direct feedback on how their body was affected of what they were eating at the time.
## Appendix 3. Overview of the full text articles read

All articles were collected on May 10th, 2022, through the database PubMed.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Title</th>
<th>Author</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Diabetes</td>
<td>Diet-induced differences in estimated plasma glucose concentrations in healthy, non-diabetic adults are detected by continuous glucose monitoring-a randomized crossover trial</td>
<td>Eva Fechner et al.</td>
<td>In conclusion, we showed that the Abbott Freestyle Libre Pro was able to detect diet-induced differences in estimated plasma glucose concentrations in healthy individuals. Our results support the use of this CGM not only in clinical practice, but also for research purposes during dietary interventions in non-diabetic participants. Future studies are needed to assess the sensor's sensitivity to glucose changes induced by less extreme diets in different population groups.</td>
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<tr>
<td>Cancer</td>
<td>Blood-Based Biomarkers for Glioma in the Context of Gliomagenesis: A Systematic Review</td>
<td>Hamza Ali et al.</td>
<td>Panels of microRNAs and proteins are most promising biomarkers, while single biomarkers such as GFAP, IL-10 and individual miRNAs also hold promise. It is possible that panels are more accurate once these are involved in different, complementary cancer-related molecular pathways, because not all pathways may be dysregulated in cancer patients. As biomarkers seem to be increasingly dysregulated in patients with short survival, higher tumor grades and more pathological tumor types, it can be hypothesized that more pathways are dysregulated as the degree of malignancy of the glial tumor increases. Despite, none of the biomarkers found in the literature search seem to be currently ready for clinical implementation, and most of the studies report only preliminary application of the identified biomarkers. Hence, large-scale validation of currently identified and potential novel biomarkers to show clinical utility is warranted.</td>
</tr>
<tr>
<td>Cancer</td>
<td>Non-invasive early detection of cancer four years before conventional diagnosis using a blood test</td>
<td>Xingdon Chen et al.</td>
<td>None</td>
</tr>
<tr>
<td>Cancer</td>
<td>Early Detection of Cancer: Past, Present, and Future</td>
<td>Joshua D. Schiffman et al.</td>
<td>Although stage at diagnosis is the dominant prognostic factor for malignancies, the early diagnosis of a particular cancer type does not necessarily lead to higher rates of cure, and potential risks include overdiagnosis and/or overtreatment of cancers. It is presumed that for each primary cancer there will be a typical window from the point at which ctDNA is initially detectable to when the lesion is incurable, a window that may be only a few months or may be several years, and potentially may vary widely within a particular cancer type. There is much still to be learned. A multitude of blood-based biomarkers have previously been proposed as cancer screening tests, but none have yet proven to be clinically useful, demonstrating the many challenges of translating initially promising data to a clinical reality. ctDNA-based cancer screening tests would appear feasible, given the available data regarding sensitivity and specificity. From here, carefully conducted clinical studies are required to determine the risks and benefits of early diagnosis across a broad range of tumor types, the optimal frequency of testing, the most desired ctDNA panel, the most efficient algorithms for further investigation of any positive test, and the patient populations that will benefit most from screening.</td>
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<tr>
<td>Dementia</td>
<td>Blood-based biomarkers for Alzheimer’s disease: towards clinical implementation</td>
<td>Charlott e E Teunissen et al.</td>
<td>Use of blood-based biomarkers for diagnosis and prognosis of Alzheimer’s disease is nearing clinical use, both in specialist clinics and in the primary care setting, largely due to availability of ultrasensitive detection methods. A crucial next step is to define the use of these biomarkers at the individual patient level. In a few years, we expect that blood-based biomarkers of Alzheimer’s disease will be ready for clinical implementation—perhaps even earlier in clinical trials. These advances also hold promise for the development of novel neurospecific protein biomarkers…</td>
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