Preliminary Phases of DMT2 Early Diagnosis within MST a Secondary Healthcare System.

[John Scott, 2022].

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Summary

In 2019 there were up to 1,2 million people with the diagnosis of diabetes mellitus (DM) within the Netherlands. DMT2 is a disease that requires complex and frequent healthcare and therefore has a significant impact on the Dutch healthcare system. As these patients are a part of Dutch society and many are part of the Dutch working population, they also impact the Dutch economy directly and indirectly through significant healthcare consumption, both in primary and secondary healthcare.

DMT2 cannot yet be cured, making early diagnosis and prevention essential. In comparison to DMT2, its preliminary phases, hyperinsulinemia, and prediabetes can be reversed. As these phases are present years to decades before the onset of DMT2 early diagnosis and treatment of these preliminary phases of DMT2 could prevent the development of DMT2. This would increase the QALYs of the individual, relieve the Dutch healthcare system of the DMT2 burden, and minimize its impact on the Dutch economy. Therefore, this Master Thesis research will map to which extent this early diagnosis initiative is applied within MST, a secondary healthcare system. The research question is as follows: To what degree do medical doctors of MST perform early diagnosis for preliminary phases of diabetes mellitus type 2 within their patient population and which factors influence this implementation process?

The Master Thesis does consist of literature research and an empirical study. Literature was used to build early diagnoses intervention criteria, and to indicate and understand the essential building blocks for a preliminary phases of DMT2 early diagnoses intervention. By comparing DMT2 and the Dutch secondary healthcare system to these criteria, their fit for early diagnoses was analyzed and current implementation limitations and impediments were identified. These findings did portray the current early diagnoses implementation in Dutch secondary healthcare to be in the first stage of implementation according to Wensing and Grol: Orientation. The recommended pathophysiology to test for is insulin resistance, but more medical trials are required to indicate the most valid testing method. Most importantly, more research has to be conducted to provide the required insights into the preliminary phases of DMT2 early diagnoses its cost-effectiveness, its eligible patient population, and prediabetes treatment cost-effectiveness.

The empirical study does answer questions aiming at exploring the early implementation stage within MST a secondary healthcare system, by the usage of a survey and interview with internist Mattijs Out. An online survey conducted in Qualtrics explored the knowledge of, basal support for and experienced impediments to prediabetes early diagnosis by internists in MST. Eleven internists responded in total. Four internists(users) stated to test for insulin resistance within their patient population and seven(non-users) stated not to test for insulin resistance. Among all users, the knowledge was declared to be moderate to excellent. For the non-users this reached from limited to excellent, with the majority stating mediocre or sufficient, and more education on this matter was requested. The basal support is present. All internists test for glucose regulation and all internists, but one, who are not yet testing for insulin resistance are willing to test for insulin resistance. Who should be responsible for prediabetes early diagnosis is debated upon. Their opinions are distributed between primary and secondary care. There is however consensus on prediabetes early diagnosis within secondary healthcare being a task for internal medicine and optionally for interfering medical specializations. Important impediments to early diagnosis implementation stated by internists are lack of evidence of its cost-effectiveness, lack of time, lack of healthcare budget, lack of education, and lack of protocols. These impediments seem to be a nationwide problem within secondary healthcare. Other impediments stated by the literature are a lack of evidence on testing method accuracy, on the effectiveness of prediabetes early diagnosis and prediabetes treatments, and on indications for prediabetes risk patient populations. Many impediments, such as lack of time, budget, and protocols are a result of the lack of cost-effectiveness evidence. These stagnations can be explained by the need for evidence, before the providence of budgets and time by health insurance. Therefore, health insurance support and intervention implementations are often years behind scientific findings. This implies more research must be conducted on the cost-effectiveness of testing methods, prediabetes early diagnosis, prediabetes treatments, and eligible risk patient population selection, before hospitals and health insurance will provide the required budgets enabling prediabetes early diagnosis to become implemented within the Dutch secondary healthcare system.

Table of Content.

Acknowledgments.
Teacher P.J. Klok and internist Mattijs Out provided great support during this Master Thesis. Internist G. Laverman did provide great feedback to improve the Master Thesis Survey Results. Internist Y. Sijpkens provided me with progressive insights into the essence and potential of prediabetes early diagnosis and has motivated me to develop a healthier diet.

1.1 Public Health Problem.

In 2019 there were up to 1,2 million people with the diagnosis of diabetes mellitus (DM) within the Netherlands. Of these approximately 1,1 million were diagnosed with diabetes mellitus type 2(DMT2) [1]. Although there are more types of diabetes mellitus, the most common are diabetes mellitus type 1(DMT1), which distinguishes itself by the destruction of beta cells by the immune system, and DMT2, which is developed by insulin resistance of cells and depletion of beta cells. This Master Thesis does focus on DMT2.

DMT2 is more susceptible for people with genetic risk factors. The risk for disease is however highly dependent upon lifestyle, such as diet and the extent of an individual's mobility. Due to the increasing availability of processed foods, the development of the Western diet, and the low mobility pattern of a large proportion of Western society an increasing number of people are being at risk. In 2019 the incidence of DM was estimated to be up to 52.000 new cases per year, with an expected prevalence of 1,33 million in 2040, while maintaining a similar distribution between DMT1 and DMT2 [2]. Both incidence and prevalence increase as age progresses, with an average age of DMT2 diagnosis at 61 years of age [3]. On average DMT2 patients develop three comorbidities besides DMT2. The main comorbidities are cardiovascular diseases (49% of the cases), metabolic diseases (45%), related to airways (33%), eye diseases (25%), and digestion-related diseases (21%). DMT2 is a progressive disease, and the number of comorbidities increases as the disease progresses [Reference]. The risk of dying after age 45 is twice as high for patients with DMT2 compared to healthy individuals of the same age [3]. Its increase in prevalence and health burden can partially be explained by the 'vergrijzing' of the Dutch population [6].

DMT2 is a disease that requires complex and frequent healthcare and therefore has a significant impact on the Dutch healthcare system. As these patients are part of Dutch society and many of them are part of the Dutch working population, they also impact the Dutch economy directly and indirectly. Directly through their decreased labour. Indirectly, through significant healthcare consumption, both in primary and secondary healthcare [6] [7].

In 2017 up to 1,6 billion euros was spent directly on DMT1 and DMT2 healthcare. This was 1,8 percent of the total health care costs within the Netherlands[8]. In 2016, the estimated total economic burden of DM was € 6.8 billion. Healthcare costs (excluding costs of complications) were € 1.6 billion, direct costs of complications were € 1.3 billion, and indirect costs due to productivity losses, welfare payments, and complications were € 4.0 billion[9]. Comorbidities are not yet considered within these calculations. Cardiovascular disease (CVD) is one of the most prevalent comorbidities within the DMT2 population and can already be developed during the preliminary phase of DMT2. Patients with DMT2 have over twice the risk of occurrence of CVD compared to patients without DMT2[10]. Cardiovascular disease [11] being one of the biggest burdens within Dutch healthcare [12], with 6 cents of every euro within the total healthcare budget spent on it [11], provides more insight into the extent of DMT2 its burden upon the Dutch healthcare system. Not to mention the impact on the individual and the Dutch population. To provide insights into the potential of this budget, the opportunity costs of this € 6,8 billion is half of the Dutch Governmental budget spent on Defense (€ 11,2 billion) or Justice and Safety (€ 12,7 billion) in 2021[13].

Because DMT2 cannot yet be cured, early diagnosis and prevention are essential. In comparison to DMT2, its preliminary phases, hyperinsulinemia, and prediabetes can be reversed. As these phases are present years to decades before the onset of DMT2, early diagnosis and treatment of these preliminary phases of DMT2 could prevent the development of DMT2. This would increase the Quality Adjusted Life Years (QALY) of the individual, relieve the Dutch healthcare system of its burden, and minimize its impact on the Dutch economy. People suffering from the preliminary phases of DMT2 and DMT2 are present both diagnosed and undiagnosed within multiple educational and ethnic layers of the Dutch population. They are either not a patient yet or are present in primary healthcare and secondary healthcare. No information is available yet on the preliminary phases of DMT2 early diagnosis in secondary healthcare. This Master Thesis research will map to which extent preliminary phases of DMT2 early diagnosis are applied within Medisch Spectrum Twente (MST), a secondary healthcare system.

Multiple healthcare professionals can be the head practitioner of a patient. The extent to which MST implements preliminary phases of DMT2 early diagnosis does significantly depend on their medical doctors as they make up the majority of the head practitioners and file most of the requests for blood samples and diagnostics. Therefore, this Master Thesis does focus on medical doctors performing preliminary phases of DMT2 early diagnosis. MST requested to limit this study population to medical doctors with high subject interference. This request and limited time for this Master Thesis resulted in the study population of internists within MST.

The extent to which early diagnosis is implemented within MST will depend on multiple factors within the MST environment. These factors can either accelerate or complicate the implementation process. The Master Thesis will investigate which factors are considered impediments by internists within MST preventing them from performing or expanding their performance of preliminary phases of DMT2 early diagnosis. The Meetinstrument van Determinanten voor Innovatie (MIDI) categorizes these factors into four domains, which will be further elaborated upon in the theoretical framework.

MST has been chosen for this Master Thesis due to their experience with research and collaboration with University students. Besides, MST as a secondary healthcare system, in comparison to the primary healthcare system, has a high density of medical professionals within one micro healthcare system. Primary healthcare consists of many independent professionals, complicating the Master Thesis research. This decision also provides the convenience of the availability of a high number of medical diagnostics and interference with a large heterogenic proportion of the Dutch population.

1.2 Master Thesis Research Question

The broad and severe impact of DMT2 upon the Dutch population and healthcare system has been displayed within 1.1 Public Health Problem. This Master Thesis will focus on a small part of this problem.

Problem*:*

Many patients suffering from the preliminary phases of diabetes mellitus type 2 *are not yet diagnosed.* Patients suffering from the preliminary phases of DMT2 are at high risk of developing DMT2 and becoming part of this economic and healthcare burden. Diagnosis of DMT2 and its preliminary phases can be performed within the healthy population and both primary and secondary healthcare. This Master Thesis will focus on Medisch Spectrum Twente (MST), a secondary healthcare system. The following research aim has been stated.

Research Aim:

Map to which degree medical doctors within MST implement early diagnosis for preliminary phases of diabetes mellitus type 2 within their patient population and investigate which factors influence the implementation process.

Research Question:

The aim of this Master Thesis has been converted to the following research question.

To what degree do medical doctors of MST perform early diagnosis for preliminary phases of diabetes mellitus type 2 within their patient population and which factors influence this implementation process?

Sub questions

This is an explorative study and will try to portray the current situation of preliminary phases of DMT2 early diagnosis within MST as well as possible. To answer the Master Thesis research question multiple sub-questions have been stated. These are divided into literature research and empirical study. The literature sub-questions provide a base for the empirical study and are therefore performed first.

Sub-questions answered by literature

To be able to conduct research on the preliminary phases of DMT2 early diagnosis, and to understand this disease its potential for early diagnosis, the preliminary phases of DMT2 and their definition should be clarified. Also, the definition and framework of early diagnosis used within this Master Thesis should be defined.

1. What are the preliminary phases of DMT2.?
2. What are the symptoms of and risk factors for the preliminary phases of DMT2?
3. By which method can the preliminary phases of DMT2 be diagnosed.?
4. What are early screening and early detection?
5. Is the early diagnosis of prediabetes early screening or early detection?

To create an adequate framework for the empirical research and provide a valid survey the current status of prediabetes early diagnosis implementation within Dutch secondary healthcare is being analysed. The general phase of the Dutch secondary healthcare system can suggest which implementation stage MST is at. Hereby the empirical study can focus on evaluating the current implementation stage status. Every implementation phase requires tailored focus and has its additional challenges. This phase will be investigated by an interview with progressive internist Y. Sijpkens of Haaglanden MC, conversations with internist Mattijs Out from MST, and literature research.

6. In which implementation stage is the preliminary phases of DMT2 early diagnosis within Dutch secondary healthcare.?

7. Do the preliminary phases of DMT2 comply with the set criteria for early diagnosis.?

8. Does Dutch secondary healthcare comply with the early diagnosis criteria set for this Master Thesis.?

An early diagnosis intervention will have to be effective and affordable to be sustainable. Before implementation and during implementation the disease screened for and the healthcare system in which this is performed should be checked for their fitness for early diagnosis. This can be done by checking both the disease and healthcare system on early diagnosis criteria. The extent to which preliminary phases of DMT2 and DMT2 do comply with the set criteria for the early diagnosis will indicate its potential in Dutch healthcare. The extent to which the Dutch secondary healthcare system does provide a fertile healthcare system for the preliminary phases of DMT2 early diagnosis can be investigated by its compliance with the set criteria. The literature review will focus on the compliance of the general Dutch secondary healthcare. The empirical study will provide more insights into the compliance of MST with these criteria.

Sub-questions answered by empirical research

During the literature research and discussions with internists in the early phase of the Master Thesis, it did turn out that prediabetes early diagnosis is still in a very early stage of implementation within the Dutch Healthcare system. Hyperinsulinemia is a preliminary phase before prediabetes and is not yet considered to be ready for early diagnosis, both due to lack of scientific proof as to its low medical professional support base. Therefore, the empirical study of this Master Thesis will further focus on the early diagnosis of the preliminary phase of DMT2: prediabetes.

The following sub-questions are stated to identify the current implementation phase of prediabetes early diagnosis within MST.

9. Is there a protocol for early diagnosis of the preliminary phases of DMT2 within MST.?

The presence of a protocol provides insights into the availability of tools and organizational support to perform preliminary phases of DMT2 early diagnosis. This will explore whether there is a protocol for either of the preliminary phases of DMT2 to analyze the extent of the implementation.

10. To what degree do medical doctors in MST know about the preliminary phases of DMT2.?

To enable medical doctors to perform prediabetes early diagnosis, they require physiological and pathophysiological knowledge of the preliminary phases of DMT2 and its progression to DMT2. This will enable them to recognize the risk patients and choose the right tools for diagnosis.

11. What pathophysiology do medical doctors in MST test for to diagnose preliminary phases of DMT2.?

11.1 Which testing methods/ diagnostics are used?

11.2 Which preliminary phase of DMT2 can these testing methods diagnose?

Multiple tests provide insights into glucose regulation. They do however not provide accurate information on each preliminary phase of DMT2. Diagnosis of preliminary phases of DMT2 and DMT2 requires a careful testing method selection process to identify the current pathophysiological phase of the patient. Also, the pathology tested for will indicate which phase of DMT2 progression can be diagnosed.

12. Do medical doctors within MST provide basic support for prediabetes early diagnosis.?

Even if a protocol and organizational support are present, no early diagnosis will be performed if the medical doctors do not support this initiative themselves. Basic support depends on the knowledge of medical doctors, their expectations for the need for prediabetes early diagnosis, and the impediments they experience during implementation. The effectiveness and speed of the implementation process do also depend on experienced impediments. To potentially improve and accelerate the implementation process these impediments will have to be identified.

13. Which prediabetes early diagnosis impediments do medical doctors in MST experience.?

After setting the theoretical framework, the literature research is performed first. Literature research does provide essential information for building the Master Thesis survey for the empirical study and interview. Therefore, both the literature method and results, answering the literature sub-questions, are elaborated upon first. Hereafter, the empirical study method and results, answering the empirical sub-questions, are elaborated upon. These will be followed by the conclusion, discussion, recommendation, and Master Thesis evaluation, respectively.

2 Theoretical Framework Master Thesis.

To answer the Master Thesis research question both a literature review and a survey will be performed. The theoretical framework for both the literature review and the empirical study will be elaborated upon within this chapter. Both models and instruments are used to build this framework. First, the framework for the literature research is explained. Hereafter, the framework for the empirical study is discussed.

First, the literature review will discuss the definition of early diagnosis and whether prediabetes early diagnosis is early screening or early detection. Eight corresponding criteria are set based on the literature. Hereafter, the literature research does follow the structure of the eight early diagnoses criteria set for this Master Thesis. Not every disease is fit for early diagnosis. To provide insights into the fit of prediabetes and DMT2 for early diagnosis this fitness is elaborated upon per criterion. To analyze whether Dutch secondary healthcare is fit for prediabetes early diagnosis the compliance of Dutch secondary healthcare will be discussed per criterion. Both fits are based on literature and the interview with internist Y. Sijpkens. Per criterion, corresponding uncertainties and impediments concerning early diagnosis implementation are stated. These factors together can explain the current implementation phase. The impediments are organized according to the Meetinstrument voor Determinanten van Innovaties (MIDI)[14], which distinguishes four domains of innovation impediments: innovation, user, organization, and social-political environments.

The findings of the literature research do indicate in which implementation stage prediabetes early diagnosis is, in secondary healthcare within the Netherlands. The model of Wensing and Grol (2017) [15] recognizes phases of implementation and will be used to distinguish which aspects are of relevance for the present implementation state and what to focus upon in the empirical study, the Master Thesis survey.

The survey is an explorative study and is conducted and analyzed within Qualtrics. The survey will investigate within which stage of implementation prediabetes early diagnosis is within MST, as to Wensing and Grol. The survey questions will be based on the literature review and will be developed in elaboration with internist Mattijs Out from MST. The survey questions will explore the implementation status, using the implementation model of Wensing and Grol, the behavior model of Balm, and the Meetinstrument voor Determinanten van Innovaties (MIDI).

Wensing and Grol do focus on the complete organizational setting. To identify to which extent the medical doctors are motivated and found basic support for early diagnosis, the behavior model of Balm [16] is used to understand and display these results. This behavior model is commonly applied to patients to represent their therapy adherence process, though proves to be utile in this setting. The model recognizes three phases: melting, change, and freezing. During the melting process, the individual becomes aware of the current behavior. The individual will gain insights into the value of performing other behavior and becomes open to behavior change. During the change phase the required knowledge, attitude and skills will be gained. This will enable the individual to implement behavior change. During the freezing phase, the newly developed and improved behavior will be part of the daily behavior. These three phases are made up of six steps, which together represent the behavior change process: being open to, understanding, being willing to, being able to, doing, maintenance. The behavior change can stagnate at any step. The model does support anticipating and adequately responding to these stagnations. Only after recognizing the present stage of the medical doctors, individually and as a group, adequate and applicable interventions can be developed to promote a successful early diagnosis initiative. It can also result in recognition of fair motives not to implement early diagnosis in secondary care or possibly inform about external factors stagnating the implementation process. Within innovation implementation, there is always a group that is ahead of the others, according to the five customer segments of technology adoption [17]*: innovators, early adaptors, early majority, late majority, and laggards.* These groups have different motives and will require different and corresponding approaches to initiate innovation implementation. Recognition of these groups can provide insights into the influence of and relations between impediments and will increase the acceleration of the implementation process. A similar group distribution is expected within the respondent group of medical doctors.

3 Method

This Master Thesis is explorative qualitative research and consists of both desk research and field research. The empirical cycle (Zante, 2004) displayed in Figure 1 does show the phases of this Master Thesis research.

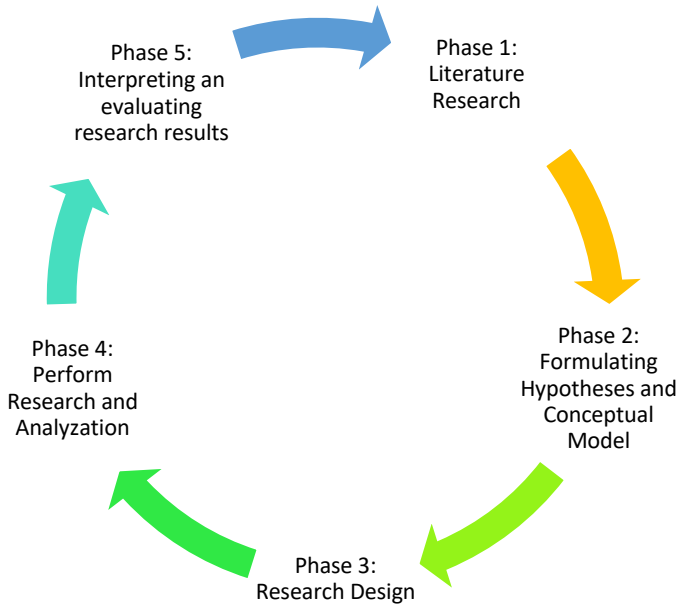


Figure 1. Empirical Cycle for Research.

First, the method for the literature study is elaborated upon followed by the literature study results. The empirical study framework is based upon the literature study, wherefore the empirical study method will follow the literature study results. After, the results of the empirical study will be stated.

3.1 Method Literature study

The literature research will focus on the Dutch secondary healthcare system. Wherefore, the following inclusion criteria have been set, Dutch secondary healthcare system, Dutch study population, publishing date between 2018 and 2022, and published in English or Dutch. The search engines PubMed, University of Twente Library, and Google Scholar are used. Large proportions of information about Dutch secondary healthcare and related factors are only retrievable through organizational and governmental websites and can be found through Google. Therefore, the websites of Google, Rijksinstituut voor Volksgezondheid en Milieu(RIVM), and Centraal Bureau voor Statistiek(CBS) are used. National study results are checked upon their representability for the Dutch secondary healthcare population.

No complete Dutch early diagnosis criteria are available, wherefore both international and national literature are utilized. Some early diagnosis criteria are internationally concurrent, wherefore both international and national literature and study results are used.

Interview

A semi-structured interview with internist Y. Sijpkens does provide additional insights into the implementation of early diagnosis of preliminary phases of DMT2 and DMT2 within the secondary healthcare system. Internist Y. Sijpkens has a progressive attitude towards preliminary phases of DMT2 and DMT2 early diagnosis and is one of the only internists known to test for these diseases. Mattijs Out recommended this internist due to the progressive attitude and extensive knowledge of this subject. The semi-structured interview questions are based on the literature review and publicly available information on the work of internist Y. Sijpkens. Those questions are available in Appendix 4a and the transcribed script of the part of the interview used for the Master Thesis is available in Appendix 4b. The interview was coded using open coding, axial coding, and selective coding.

4 Literature Research Results

To perform valid and effective research on early diagnosis a clear early diagnosis framework should be stated. Also understanding the physiology of insulin and the pathophysiology of preliminary phases of DMT2 and their risk factors is essential. Understanding early screening and early detection, both tools for early diagnosis, could support in deciding which method to focus on within the early diagnosis framework. This framework will be built by the eight set criteria for early diagnosis. In both the preliminary phases of DMT2 and the Dutch secondary healthcare system, their compliance with the set criteria will be elaborated upon. This chapter will answer sub-questions 4: *What are early screening and early detection?* and *5: Is the early diagnosis of prediabetes early screening or early detection?*

4.1 Physiology and Pathophysiology of Diabetes Mellitus Type 2

As obesity and DM reach epidemic proportions in the developed world, the role of insulin resistance and its consequences are gaining prominence. Understanding the role of insulin in wide-ranging physiological and pathophysiological processes and the influences on its synthesis and secretion do show its significant implications for many chronic diseases present in Western populations and the susceptibility of a large proportion of the Western population to this disease[18]. To distinguish to which extent early diagnosis of preliminary phases of DMT2 could be applied and by mean of which testing method, both the physiology and pathophysiology related to DMT2 should be understood. The physiology and pathophysiology are important for understanding the relation of preliminary phases of DMT2 and DMT2 to their risk factors, risk population, and the fitness of testing methods. This chapter will answer sub-question 1: *What are the preliminary phases of DMT2.?* and sub-question 2: *What are the symptoms of and risk factors for the preliminary phases of DMT2*? First, it will elaborate upon the physiology of blood glucose regulation to provide a basic understanding.

4.1.1 Physiology

Both preliminary phases of DMT2 are a progression toward DMT2. In both preliminary phases of DMT2, hyperinsulinemia, and prediabetes, the function of the hormone insulin is highly important. Therefore, this chapter will elaborate upon the initiation, secretion, and function of insulin.

Hormone insulin

Insulin is a hormone, meaning it is synthesized in one location of the human body and acts like a messenger molecule to affect other parts of the human body, without these parts being located directly beside the cell which produces the hormone[19]. The homeostasis of the human body is accomplished by a highly sophisticated network of various hormones and neuropeptides released mainly from the brain, pancreas, liver, and intestine as well as adipose and muscle tissue. Within this network, the pancreas represents a key player by secreting the blood sugar-lowering hormone insulin and its opponent glucagon[20]. The pancreas is located as shown in the picture.

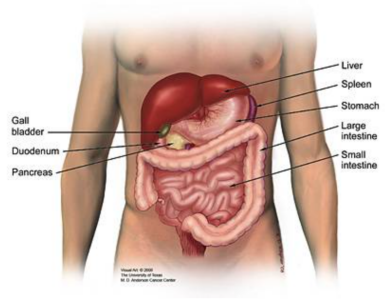


Figure 2. The pancreas within the human body[pancan, n.d.].

Islet cells and beta cells.

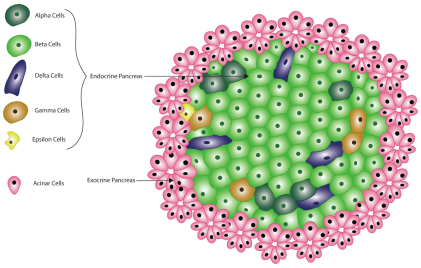


Figure3. A human islet cell.

Within the pancreas, endocrine cells are clustered together, thereby forming the islets of Langerhans, which are small, island-like structures within the exocrine pancreatic tissue [21]. The islets of Langerhans account for only 1–2% of the pancreatic tissue. There are five different cell types within these islets releasing various hormones from the endocrine system: glucagon-producing α-cells, which represent 15–20% of the total islet cells; amylin-, C-peptide- and insulin-producing β-cells, which account for 65–80% of the total cells; pancreatic polypeptide (PP)-producing γ-cells, which comprise 3–5% of the total islet cells; somatostatin-producing δ-cells, which constitute 3–10% of the total cells; and ghrelin-producing ε-cells, which comprise <1% of the total islet cells. Each of the hormones has distinct functions. Glucagon increases blood glucose levels, whereas insulin decreases them. Somatostatin inhibits both, glucagon and insulin release, whereas PP regulates the exocrine and endocrine secretion activity of the pancreas.

The Islet cells have a high number of veins running through them, enabling the beta cells to react rapidly to the fluctuations in blood glucose. [21]. Though insulin has multiple functions, two are best known and relevant for this Master Thesis. Firstly, insulin regulates healthy glucose levels within the blood together with somatostatin, and glucagon. Insulin induces the uptake of glucose, which is the primary energy source for mammalian cells[22]. Insulin signaling in skeletal muscle is critical in glucose disposal, accounting for almost 90% of whole-body glucose disposal in humans [23] [22]. Secondly, It does inhibit lipolysis within the adipose cells enabling fat storage. Insulin is mainly known for its influence on glucose uptake by muscle cells[22]. Insulin, however, does influence almost every organ in the human body, including adipose tissue, liver, brain, kidneys, and vasculature[24] and promotes cell multiplication. Altogether, these hormones tightly regulate[25] glucose homeostasis in humans.

Beta cells.

Insulin concentrations are regulated by a variety of mechanisms affecting insulin clearance and secretion. These are carefully coordinated [26] through signals from the hypothalamic–pituitary–adrenal axis, the liver–pancreas axis, the bone–pancreas axis, and the entero–osseous axis. The beta cells do produce and secrete the hormone insulin. There are two types of Insulin secretion, namely; static insulin and dynamic insulin secretion. Static insulin secretion is also referred to in the literature as basal insulin secretion [27] and postprandial insulin secretion as dynamic insulin secretion.

Basal insulin secretion consists of several complex secretory patterns: the circadian rhythm, the ultradian rhythm, and pulsatile insulin secretion. These rhythms do occur standardly and are not influenced by nutrient intake. Circadian regulation[28[of insulin secretion is critical for the healthy regulation of beta cell functioning, due to its significance to restrain insulin secretion during the inactive (sleep) phase, and to optimize insulin production and release during the active (feeding) phase of the circadian cycle, a daily cycle. The pulsatile rhythm has the highest frequency and occurs every few minutes. Secretion in a pulsatile manner prevents insulin resistance. Together rhythms ensure there is enough insulin in the blood system to maintain homeostasis. Dynamic insulin secretion is initiated by the increase of blood glucose, for instance after a meal or after an increased release of glucose by the liver. Together the static and dynamic insulin secretion maintains healthy blood glucose levels and provides homeostasis.

4.1.2 Pathophysiology

Multiple internal and external factors can influence blood glucose levels. In the case of continuous hyperglycemia, a continuous demand arises for insulin to maintain homeostasis. As a result, insulin levels in the blood will rise and insulin receptors within the body will be exposed to high levels of insulin, and hyperinsulinemia. Hyperinsulinemia will result in a decrease in insulin sensitivity by the cells and can progress into insulin resistance. Insulin resistance is defined as the incapability of cells to respond to insulin [29] and therefore the inability of insulin-dependent cells to take up glucose for energy. The development of insulin resistance is a natural process and happens every day to a minimal extent due to nutrient intake and glucose release by the liver. During fasting at night, the insulin resistance diminished again to a basal level in the morning. In the case of hyperinsulinemia, insulin resistance is maintained and can slowly increase in severity if glucose levels remain high.

This pathophysiological insulin resistance is a slow progressive process that can take up to years. To counter the low insulin response of cells the beta cells do elevate their insulin production and secretion. This can suffice and maintain homeostasis for a while but will prove insufficient in case the beta cells become depleted and lose their function or in case the body cells eventually become insulin resistant. Due to insulin resistance, the beta cells must produce insulin in profound quantities, in the long run depleting the beta cells. This provides a cycle of beta cell depletion and insulin resistance. Insulin resistance in skeletal muscle tissues can be regarded as the initiating defect and is present decades before impaired β-cell function [30]. Impaired β-cell function and increased insulin resistance are two pathological pathways that lead to prediabetes, and subsequently, DMT2. Either path can ultimately result in the presence of both.

Preliminary phases of Diabetes Mellitus Type 2.

This sub-chapter will answer sub-question 1 *What are the preliminary phases of DMT2.?* The progression of DMT2 can be divided into two preliminary phases, hyperinsulinemia, and prediabetes. Hyperinsulinemia can be defined as dysregulated insulin secretion and/or clearance resulting in a chronically elevated insulin level without hypoglycemia. During this phase, insulin levels are above normal, and the increase in insulin production and secretion can counter insulin resistance to maintain homeostasis. The onset of increased insulin resistance starts years before DMT2 and pre-diabetes, somewhere in the phase of hyperinsulinemia.

Prediabetes[31] is a term used to describe the buffer period before the onset of DMT2, with blood glucose levels being higher than normal but lower than the diagnostic criteria of DMT2. At which health stage and corresponding blood values the phase of hyperinsulinemia transitions into prediabetes differs within literature and between health care organizations.

Prediabetes' definition varies within the literature and the WHO's definition of prediabetes has been changed regularly. Since 1965, the WHO has at least changed the definition of prediabetes five times [32]. Currently, prediabetes [33] is defined as *'Prediabetes comprising Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) represents an intermediate stage of altered glucose metabolism between normal glucose levels and type 2 diabetes mellitus and is associated with an increased risk for the development of diabetes and cardiovascular disease.*' It is also mentioned there is considerable evidence that glucose levels lower than those meeting the current definition of prediabetes may also be associated with similar health risks, particularly in high-risk individuals. Prediabetes, therefore, is often unrecognized and constitutes a major public health problem. The need for an earlier intervention than is currently recommended by WHO is needed. Proving the demand for recognition of an earlier preliminary phase of DMT2, hyperinsulinemia.

Risk factors

This subchapter will answer sub-question 2 *What are the symptoms of and risk factors for the preliminary phases of DMT2*? As hyperinsulinemia and prediabetes are progressive preliminary phases of DMT2 their risk factors are the same. There are multiple risk factors for the development of preliminary phases of DMT2 and DMT2 and are comprised of both external factors, such as lifestyle, including diet, and environmental factors and internal factors, which can be both physiological and pathophysiological. The main drivers of the DMT2 epidemic are the global rise in obesity, sedentary lifestyles, high-caloric diets, and population aging[34]. Other risk factors are hypertension, visceral fat, ethnicity, low socioeconomic status[35], high caloric diet, genetics/ familiarity [3], deficient metabolic clearance of insulin, low insulin sensitivity, and degressive beta cell function or mass [34]. Some of these risk factors do form a chain reaction.

Sedentary lifestyle, unhealthy eating habits, and stress increase dysregulation of the metabolic system and an increased risk in people who are genetically susceptible to metabolic dysregulation. High caloric intake stimulates fat resources and stimulates inflammatory responses. These inflammatory responses deregulate insulin functioning. Adipose tissue promotes insulin resistance through various inflammatory mechanisms, including increased free fatty acid (FFA) release and adipokine deregulation.

Aging is a risk factor. The average age of DMT2 diagnosis within the Netherlands is set at 61 years of age [3]. DMT2 is suspected to have an average onset of 4 to 7 years before diagnosis, resulting in an estimation of 51 of age for the onset of DMT2. Prediabetes does precede DMT2 and should therefore be screened even earlier. How much earlier is heavily debated upon but could reach up to 20 to 5 years before 51 years of age. Internist Y. Sijpkens implies up to 20 years prior.

More risk factors including environmental factors are related to DMT2 development, though the factors previously mentioned are stated by literature to be most relevant. Besides, some diseases are risk factors for the preliminary phases of DMT2 and DMT2, elaborated upon in the following subchapter.

Diabetes Mellitus Type 2 Comorbidities

The study of Hossain et al does elaborate on the progression of DMT2 comorbidities and their interaction [34]. The study shows there is a high relation between DMT2 comorbidities and risk factors and suggests the exponential burden of patients diagnosed with both DMT2 and CVD. Patients with both DMT2 and CVD represent a higher hospital admission burden, more transitions between comorbidities, and a more complex progression structure over subsequent hospital admissions compared to DMT2 patients without CVD. The figure shows risk factors and the comorbidities and corresponding relations. Multiple comorbidities mentioned within the study of Hossain et al. have a significantly higher prevalence within the DMT2 population compared to nondiabetic patients [36].

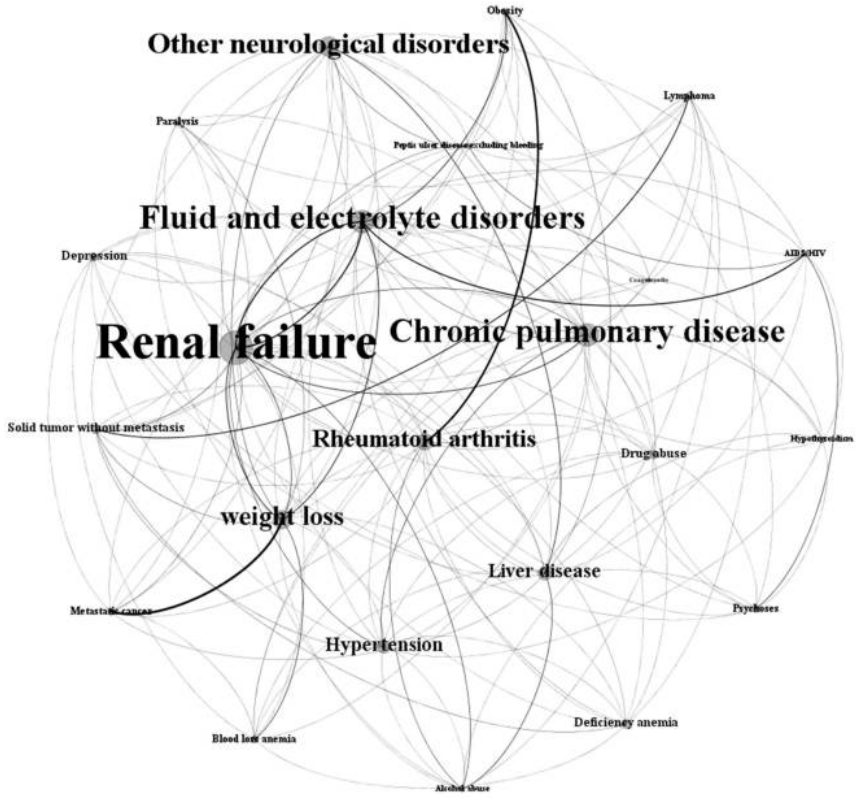


Figure 4. Comorbidities DMT2. [Hussein et al., 2020]

The nodes in the figure indicate the comorbidities or diseases. The size of the nodes and labels are proportional to the prevalence of the corresponding comorbidity. Renal failure, fluid and electrolyte disorders, chronic pulmonary disease and hypertension dominate the final disease network; this reflects the fact that these comorbidities can be risk factors of progressing towards CVD in patients with T2DM. The large number of edges in the network represents the transitions from one disease to another disease. The thickness of an edge is proportional to its weight.

4.2 Early Screening or Early Detection.

Often the words 'early screening' and 'early detection' are used intertwined. However, there is a distinctive difference. According to WHO, concretely, screening is performed on asymptomatic people and early detection on symptomatic people. Though being distinctively different and being part of secondary and primary prevention, respectively, both methods can highly contribute to the overall prevention of DMT2. Definitions do slightly differ within the literature and will be elaborated upon within this chapter. To conduct a specific Master Thesis research, it is essential to define the meaning of early diagnosis. The following definitions picture the current conception of early screening and early detection in literature.

Early detection as an early diagnosis method according to WHO is *'Early diagnosis focuses on detecting symptomatic patients as early as possible while screening consists of testing healthy individuals to identify those having cancers before any symptoms appear'*.

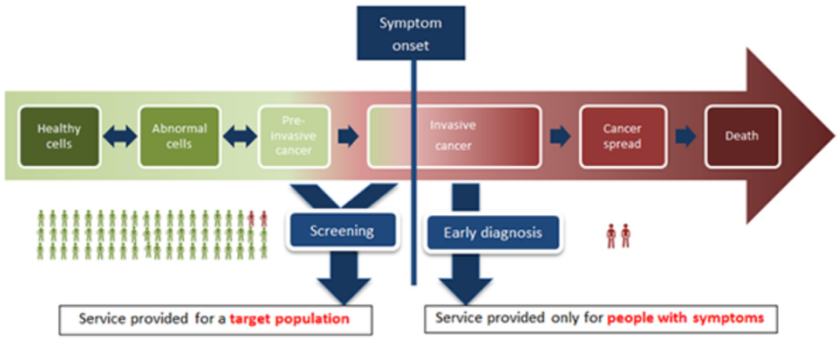
J. Dillner: *'Early detection has two major components: screening and education to recognize symptoms and promote an early diagnosis. '*

H Theodore et al.[37]: '*Secondary prevention is early diagnosis and management to prevent complications from a disease*.'

WHO[38]:*' Screening refers to the use of simple tests across a healthy population to identify those individuals who have a disease, but do not yet have symptoms.'*

According to Johns Hopkins Medicine[39]: *'A screening test is done to detect potential health disorders or diseases in people who do not have any symptoms of the disease. The goal is early detection and lifestyle changes or surveillance to reduce the risk of disease, or to detect it early enough to treat it most effectively. Screening tests are not considered diagnostic but are used to determine the presence or absence of disease.'*

Figure 5. Screening and early detection. [WHO, n.d.]



Early screening and early detection can both support preventing DMT2. If an early diagnosis intervention will include asymptomatic patients for either prediabetes or DMT2 it is early screening. Many prediabetes and DMT2 patients have slight symptoms or are asymptomatic. These patients would be detected during screening. Eligibility for these screening interventions would be based on DMT2 risk factors, not symptoms. Early diagnosis of the symptomatic patient will be early detection, wherefore eligibility will be based upon DMT2 risk factors and symptoms. Prediabetes symptoms are similar to DMT2 symptoms. Limiting early detection to only prediabetes or DMT2 would therefore be complex and maybe even impossible. It should be mentioned symptomatic prediabetes patients do not comply with DMT2 diagnosis criteria yet and it could therefore be considered screening, even though they are symptomatic. It is, however, impossible to state beforehand, before the test, whether this does concern prediabetes or DMT2 patients. This does complicate the situation. The definition of early diagnosis does not have to be limited to either early screening or early detection. As to Harvard, early diagnosis means: 'Methods to determine in patients the nature of a disease or disorder at its early stage of progression. Generally, early diagnosis improves PROGNOSIS and TREATMENT OUTCOME' [40]. It does not mention limitations of eligibility to asymptomatic or symptomatic patients. An intervention can include both if its aim will allow it.

Definition Early Diagnosis Master Thesis.

The following definition has been stated for early diagnosis within this Master Thesis. This combination of multiple aspects of both screening and early detection explains the aim of the Master Thesis Study. Early diagnosis: *Early diagnoses focuses on detecting prediabetes early enough to effectively prevent DMT2 and can be applied as a secondary prevention measure for DMT2 to prevent further complications and comorbidities.*

The definition of this Master Thesis for early diagnosis does neither rule early screening nor early detection out. Also, the early diagnosis should not be limited to prediabetes patients but should include DMT2 patients. The combination of both early screening and early detection for both prediabetes and DMT2 patients would increase the yield and cost-effectiveness of the intervention. Even though DMT2 cannot be reversed, early diagnosis could stimulate the stabilization of the disease and prevent further complications and comorbidities, complying with the aim of the early diagnosis as to its definition.

4.3 Criteria for Early Diagnosis.

This Master Thesis focuses on the early diagnosis of prediabetes as DMT2 prevention within MST, a secondary health care system. The definition of early diagnosis for this Master Thesis has been set. In this chapter, the compliance of prediabetes early diagnosis and Dutch secondary healthcare with the early diagnosis criteria will be discussed. Thereby this chapter does answer sub-questions 7 *Do the preliminary phases of DMT2 comply with the set criteria for early diagnosis.?* and 8 *Does Dutch secondary healthcare comply with early diagnosis criteria set for this Master Thesis.?* Some criteria only apply to either the disease or the secondary healthcare system.

Internationally there are no concurrent criteria available for early diagnosis. Some adequate criteria have been mentioned by MD C. Herman for early screening[41] which for the majority would apply to the definition of early diagnosis for this Master Thesis. The United Kingdom Government [42] has set the UK National Screening Committee Criteria. The objectives and criteria set for early diagnosis within this Master Thesis will consist of an adjusted set of MD C Herman's criteria, the UK Government, and WHO criteria with some additions from a performed study by Obuchowski et al[43]. In both objectives, the disease can be read as DMT2.

Objective 1: *'detection of disease at a preliminary stage when treatment can be more effective than it would be after the patient develops the actual disease[41]].*

Objective 2: *'identification of risk factors that increase the likelihood of developing the disease and use of this knowledge to prevent or lessen the disease by modifying the risk factors.' [41].*

Objective 1 is met. Prediabetes is a preliminary phase of DMT2. Prediabetes is reversible and its treatment can prevent DMT2. Objective 2 is met. Early diagnosis and treatment of prediabetes and related risk factors are more effective than treating DMT2. Besides early diagnosis of DMT2 can prevent further progression of the disease and the development of comorbidities.

Criteria:

1. *constitute a significant public health problem. [41]*

   Meaning it is a common condition with significant morbidity and mortality. The disease should be one that, if not found in its detectable preclinical phase before the critical point, will become life-threatening or cause significant morbidity. If the critical point occurs soon after the start of the detectable preclinical phase, screening may be too late to be helpful.

2. *not be a pseudo-disease [44].*

   There are two types of pseudo diseases. In the first type, the disease never progresses and may regress naturally. Screening tests cannot distinguish type I pseudo disease from true disease, so the patient undergoes unnecessary and sometimes risky tests and procedures. In type II pseudo disease, the disease progresses so slowly that the patient never develops symptoms and dies from another cause. Type II pseudo disease is common in diseases with long detectable preclinical phases or among patients with short life expectancies [5]. Patients with type II pseudo disease also undergo unnecessary tests and treatment but derive no benefit from the treatment. Screening tests that detect a high frequency of pseudo disease cannot be cost-effective.

3. *have a readily available treatment* with a potential for cure that increases with early diagnoses *[41]*. There should be an agreed policy on the further diagnostic investigation of individuals with positive test results and the choices available to those individuals.

4. *be capable of detecting a high proportion of disease* in its preclinical state*[41]*.

   The preclinical phase of disease starts with the onset of the disease process and lasts until signs and symptoms appear, which is when the clinical phase begins. The detectable preclinical phase is the interval during which the disease is detectable by screening, but the patient is still asymptomatic. During this period, there is a critical point at which intervention is more effective than if started after the clinical phase begins. Sensitivity is usually increased at the expense of specificity when the disease is serious and curable in its preclinical phase. However, high specificity may be desired over sensitivity when the costs or risks of further testing are significant, as they are, for example, with surgical biopsy. Patients must be informed that a negative screening result does not mean the disease is not present, but rather the likelihood of the disease is low. Since few tests have both high sensitivity and high specificity, multiple tests are often used to aid in the detection of disease in the preclinical phase.

5. *the testing method should be safe, precise, and validated [41][42].*

   The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed upon. The tests must not have associated morbidity or mortality—even minor side effects may offset the benefits of screening.

6. *be reasonable in cost [41].*

Otherwise, insurers may not provide coverage, and patients may be unable or unwilling to pay for the tests themselves.

7. *lead to demonstrated improved health outcomes[41].*

   There should be evidence from high-quality randomized controlled trials that the screening program is effective.

8. *be widely available* as must the interventions that follow a positive result*[41]*.

   They must not discriminate in availability between any subpopulations. There should be evidence that the complete screening program (test, diagnostic procedures, treatment/ intervention) is clinically, socially, and ethically acceptable to health professionals and the public[42].

Though the following is not considered a criterion the following aim mentioned by WHO[38] is considered relevant and should be striven for and not just be aftermath: *increased awareness* of first signs, among physicians, nurses, and other health care providers as well as among the general public.

4 .4 Early Diagnosis Criteria Compliance Prediabetes.

The extent to which prediabetes early diagnosis as DMT2 prevention will comply with those criteria is elaborated upon in this subchapter. The numbers correspond to the criteria mentioned in 4.3 Criteria for Early Diagnosis. Hermans states the early screening program and disease should comply which each of the criteria to meet the objectives. The UK Government demands an early screening program to comply with each of their criteria. This chapter aims to map to which extent prediabetes early diagnosis comply with the set criteria. The following information applies to the Netherlands unless stated differently.

1. *constitute a significant public health problem*.Morbidity covers the burden caused by a disease[5] its incidence, and its prevalence[reference]. The severity of the DMT2 epidemic and its impact on the population has been described in the introduction. So have the incidence and prevalence. DMT2 Mortality and patient morbidity will be elaborated upon in this subchapter. DMT2 patients[48] between 45-70 years of age have a twice as high risk of dying early and on average live four years shorter compared to healthy people. The life expectancy of DMT2 patients is highly related to glucose regulation and the occurrence of complications, such as CVD and renal problems. This difference in mortal risk decreases as age progresses. Between 2012 and 2019 each year approximately 34.000 DMT2 patients died. For 7 percent of these patients, DMT2 was indicated as the cause of death. In many cases, this was related to comorbidities[49]. The table shows the absolute number of deaths between 2012-2019, including non-diabetes, DMT1 patients, and DMT2 patients, and the percentage of DM being the cause of death.

	Geen DM*	DM 1*	DM 2*	DM als doodsoorzaak**	% mensen met DM bij wie DM doodsoorzaak was
45-49	14.170	442	1.117	256	16%
50-54	23.376	717	2.792	447	13%
55-59	34.818	1.463	5.708	689	10%
60-64	49.021	2.035	10.949	1.070	8%
65-69	67.127	3.304	20.285	1.739	7%
70-74	80.554	4.426	30.783	2.180	6%
75-79	96.902	5.240	40.074	2.951	7%
80-84	126.868	7.491	54.716	4.050	7%
85-89	151.347	7.942	56.229	4.668	7%
90-94	124.829	4.887	37.597	3.137	7%
95+	60.860	1.475	12.975	998	7%
Totaal	829.871	39.421	273.225	22.185	7%

Figure 6 . [Nivel 2021.]

Besides incidence and prevalence [50] morbidity can also mean the burden caused by a disease. For DMT2 this consist of complications, comorbidities, and overall burden caused by the treatment and daily limitations for the patient. These aspects combined can be measured in Disability Adjusted Life Years (DALY). A DALY measures the number of years a person has died more early plus the years lived with the disease. 85 percent of the DALY's for DMT2 are based upon the years lived with the disease. DMT2 is the third highest disease burden within the Netherlands, with 201.000 DALYs in 2018[51]

DMT2 has an increased risk of comorbidities, such as CVD which also has a high mortality and morbidity rate causing it to be the highest disease burden [52][51]. The complex and broad-ranging interrelation between the comorbidities explained during the pathophysiology of DMT2 and the high prevalence of the comorbidities within the DMT2 patient population suggest prediabetes and DMT2 impact on healthcare and patients themselves should not be underestimated.

Though most studies focus on DMT2, prediabetic patients also declare to experience a lower quality of health compared to healthy individuals [53] The increased risk of comorbidities and their development begins in the stage of hyperinsulinemia [54], wherefore the preliminary phases of DMT2 impact the Dutch economy and health care system making it a multidisciplinary and therefore profound problem. The preliminary phases of DMT2 in contradiction to DMT2 can be reversed. Altogether, DMT2 does comply with this criterion.

2. *not be a pseudo disease*

There are two types of pseudo diseases. Prediabetes can be considered a pseudo disease type I and II. Prediabetes can be reversed by a healthy lifestyle. This is however still an intervention. DMT2 patients can grow old with the disease, therefore causing a high healthcare burden. Prediabetes, however, does not necessarily cause high healthcare costs and its detection can be cost-effective, due to DMT2 and comorbidity prevention. This criterion is not met for DMT2. This criterion aims to keep the early diagnosis intervention cost-effectively. In the case of a big eligible population, diagnosis and treatment of pseudo diseases would rapidly become unaffordable. However, the burden of pseudo disease types 1 and 2 are neither counterweight for the severity of progression to DMT2 nor undetected DMT2. Therefore, this criterion is considered inferior and not applicable for DMT2 in cases of a highly cost-effective intervention.

3. have a readily available treatment with a potential for cure that increases with early diagnoses.

This early diagnosis is a DMT2 prevention method and focuses on early diagnosis of prediabetes. However, patients could unnoticedly have DMT2. The patients can therefore be diagnosed either with prediabetes or DMT2. This criterion focuses on prediabetes. The common treatment option for prediabetes consists of lifestyle intervention. This can be prescribed by a secondary healthcare professional but will mainly be provided outside of the hospital. According to Rijksinstituut van Volksgezondheid en Milieu (RIVM) [55], the combined lifestyle intervention(GLI) for prediabetes is defined as an intervention aimed at decreasing the caloric intake, increasing physical activity, and if needed providing additional individualized phycological interventions as a support for behavior change (Latta & van der Meer, 2018).'The effectiveness of this intervention is stated to be high[56], but maintenance proves to be difficult[57]. The effectiveness shown in the study is in practice not guaranteed.

GLI has been recently introduced and lifestyle coach is stated to be a new profession. The provided interventions differ extensively [58] and no protocol has yet been developed [59].The background and experience of the lifestyle coaches are highly variated. Internist Y. Sijpkens van Haaglanden MC did describe this situation as well during the interview. GLI is included within the basic healthcare package [60].

Internist M. Out mentioned the lack of effective studies for these types of interventions. There are indeed a low number of studies performed within the Netherlands. More research should be conducted on the effectiveness and cost-effectiveness of these prediabetes interventions before this criterion could comply with DMT2. Due to the same reasons, it is difficult for secondary care medical doctors after prescribing an adequate intervention to refer the patient to an adequate treatment program. This criterion is not yet met for secondary healthcare.

4. be capable of detecting a high proportion of disease in its preclinical state.

For prediabetes, this criterion is met. For DMT2 this criterion is not met within the Dutch population due to the low rate of undiagnosed DMT2 patients within the Netherlands. This will be further elaborated upon in the chapter *Early Diagnosis Implementation within the Netherlands.* Testing methods with high sensitivity and specificity and the capability to diagnose prediabetes and DMT2 patients with high accuracy are available in secondary healthcare.

5. Many testing methods are available. Although inconcurrent definitions of prediabetes do complicate the situation. Many factors, such as population determinants and diets, do influence testing accuracy and cut-off values. Therefore accurate, precise and valid prediabetes tests for the Dutch population are available but not yet optimal. There is no superior testing method appointed yet. More emphasis will be provided on the subject by the literature review and will be elaborated upon in the subchapter of the Results: *Testing methods.*

6. This is a complex criterion and will consist of two estimated budgets: costs per performed test and costs of the early diagnosis program. This reimbursement will be a trade-off to other healthcare interventions due to the limited healthcare budget. It is paramount the intervention is both effective and affordable.

Prediabetes testing costs depend on the applied testing method. These testing methods can be considered reasonable in unit price [44]. The early diagnosis method will be reimbursed by the healthcare insurance and include no out-off pocket costs for the patient. The prevalence of prediabetes is expected to be high. A big eligible population can result in an unaffordable early diagnosis intervention, as mentioned in criterion 2. Tight eligibility criteria are essential. By limiting the intervention to secondary healthcare, the target population declines in proportion. In 2020 secondary healthcare reported up to 2,7 million hospital submissions [61] [62], including resubmissions of individuals. 43.490 of these are related to endocrinology. Though this population could be expected to have a higher eligible density, diagnosed DMT2 patients are excluded. To be able to justify prediabetes early diagnosis, accurate and nationally concurring prediabetes definitions, eligibility criteria and testing cut-off points must be indicated to guarantee affordability. All but the prediabetes definition has not yet been stated. Therefore, this criterion is not met yet.

7. *lead to demonstrated improved health outcomes*

Currently, there are no controlled trial studies providing insights into the effectiveness of early screening or detection of prediabetes simply due to ethics. It is not ethical to withhold a diagnosis from an early-detected prediabetes or DMT2 patient. Besides four other common problems exist when comparing the survival of screened patients [43] with unscreened patients: Lead-Time Bias, Length bias, Overdiagnosis Bias and Stage Migration Bias. On the other hand, insulin and glucose dysregulation in prediabetes patients are reversible. For DMT2 this is not the case. Effective treatments are not widely available yet as stated in criteria 3. Therefore, this criterion is only partially met.

8. *be widely available* as must the interventions that follow a positive result

Everyone who lives or works in the Netherlands is legally obligated to take out health insurance [46]. Early diagnosis of prediabetes in asymptomatic and symptomatic patients on an indication by a medical doctor can be performed within the healthcare budget. This will enable any eligible patient to participate in the early diagnosis initiative when indicated by a medical doctor, without out-of-pocket costs. In these cases, the additional healthcare budget provided for by the health insurance is complex and is currently not to be expected. The medical doctor must perform treatment within a limited budget, which will not be enlarged by indication of prediabetes early diagnosis. Though prediabetes early diagnosis is not yet widely recognized or indicated within the Netherlands, the Dutch healthcare system has the tools to provide the availability to every layer and part of the Dutch population, if eligible.

Compliance impediments prediabetes early diagnosis and Dutch secondary healthcare system.

Compliance impediments of prediabetes early diagnosis in secondary healthcare to the early diagnosis criteria, according to literature, can be categorized into four MIDI domains. Table 1 shows where the impediments mentioned within this chapter fit within the four MIDI domains.

MIDI domain	Impediment.
Innovation	Lack of evidence on effectiveness treatment No-superior testing method
User	-
Organisation	Lack of prediabetes treatment protocols Lack of prediabetes early diagnosis protocols No cost-effectiveness indication No affordability indication. No eligibility criteria stated.
Socio-political environment.	Lack of national treatment protocols.

Table 1. By Literature stated prediabetes early diagnosis impediments categorized into four MIDI domains.

Summary criteria compliance

Early diagnosis of prediabetes as DMT2 prevention has potential and the need for DMT2 prevention is obvious. Prediabetes early diagnosis does not comply with each criterion yet more research has to be conducted and progression has to be made on prediabetes testing methods and treatment. This evidence could provide reimbursements by the Health Insurance which enlarges the ability and probability of medical doctors to include prediabetes early diagnosis within the treatment. When these aspects are met, adequate prediabetes early diagnosis could potentially provide a big support in DMT2 prevention and savings on the healthcare budget.

4.5 Early Diagnosis Population for Prediabetes.

To analyze which medical doctors should be included in the Master Thesis survey the patient population for prediabetes early diagnosis should be identified. The patient population is also important for the framework of prediabetes early diagnosis. Within MST, secondary healthcare, medical doctors are categorized into multiple medical specializations. Each interferes with a different patient population. This difference does indicate a variance in their interference with the prediabetes early diagnosis eligible population. MST requested to include medical doctors within the survey with a high interference of the study subject. To indicate which medical doctors would be included in the study sample, an estimation of the eligible patient population is made.

In practice, a tight eligibility protocol is essential for the cost-effectiveness of an early diagnosis intervention. This is however not part of the chapter's aim, as this is an explorative study.

The patient population can be identified by the presence of risk factors for prediabetes. These risk factors have been stated in the chapter Pathophysiology. Patient categories with a high prevalence of these risk factors and related diseases will make up the eligible early-diagnosis population.

Risk factors.

The literature does mention the following risk factors for prediabetes to be high in prevalence:

- Obesity (max.) [45].
- Visceral fat(max.)
- High caloric diet (max.)
- Age(max.)
- Ethnicity [3]
- Mobility (min.)
- Hypertension(max.)
- Smoking and alcohol(max.)
- Genetics/ Familiarity [3].
- Metabolic syndrome(max.) [68]

Maximum(max) will imply the higher the value the higher the risk. Minimum (Min) will imply the lower the value the higher the risk.

Literature review indicated patients with CVD, liver disease (such as fatty liver), renal dysfunction, and elderly. To indicate medical departments fit for early diagnosis of prediabetes, these medical departments will be analyzed upon their presence of these risk factors and related diseases. High caloric diet is tough to identify without a thorough patient conversation and will be excluded. Ethnicity is tough to relate to a patient group or medical department and is indirectly represented by the high risk of related diseases and thus will be excluded. Obesity and visceral fat are highly correlated with diseases such as CVD and fatty liver, causing overlap. To which extent each medical department does have obese patient is tough to analyze and will therefore be excluded.

Table 2 shows which medical departments are likely to include a high rate of the eligible population. The medical departments have been selected upon common knowledge and the presence of the risk factors is based on the literature review and common knowledge. In collaboration with medical doctors, the actual departments for early diagnosis can be indicated during further research.

Department **Risk factor**	Cardiology	Internal medicine	Nephrology	MDL	Vein surgery	Neurology	Gynaecology
CVD	X	X	X		X	X	
Liver Disease	X	X	X	X	X		
Renal dysfunction	X	X	X				
Age	X	X	X	X	X	X	
Mobility	X	X	X		X	X	
Hypertension	X	X	X		X	X	X
Smoking/ alcohol	X	X	X	X	X	X	
Genetics	X	X					X
Metabolic syndrome	X	X	X		X	X	X

Table 2. Medical department to DM risk matrix.

Multiple risk factors are highly correlated such as genetics, age, hypertension, and mobility, therefore often being all present or not present within patient categories. Patient categories with the highest prevalence of risk factors and associated diseases are cardiology, internal medicine, nephrology, neurology, and vein surgery. Observational evidence[32] shows associations of prediabetes with early states of nephropathy, small fiber neuropathy, diabetic retinopathy, chronic kidney disease, atherosclerosis, and increased risk of macrovascular disease. Each of those diseases is related to micro and macro vasculature diseases. Hyperglycemia and dyslipidemia hurt vasculature health [69]. The vein surgery department and renal dysfunction in the nephrology department relate to these micro and macro vasculature dysfunction and are a far-developed stage. The chance of these patients being screened for prediabetes and DMT2 is significant. In case these departments could have been included in the survey their inclusion could be elaborated upon with the corresponding medical doctors. Internist Mattijs Out indicates cardiology, rheumatology, gynecology, and internal medicine. Due to the request of MST and the duration of this Master Thesis the survey is conducted with internists in MST.

4.6 Testing methods for Preliminary Phases of DMT2.

This chapter will answer sub-question 3 *By which method can the preliminary phases of DMT2 be diagnosed.?* Early diagnosis of a disease can be performed using any type of diagnostics. The most efficient testing method and pathophysiology to test for during prediabetes early diagnosis will be elaborated upon within this chapter. These results can be compared to the used testing methods by the internists in MST. This could clarify their decision and verify to which extent the currently applied testing methods are applicable for early diagnosis. It can also map to which extent internists in MST are informed about the available testing methods for prediabetes early diagnosis.

Multiple testing methods have been and are being developed to diagnose prediabetes and DMT2. The accuracy of those testing methods is being studied by means of a wide range of study designs and a wide variety of study populations. Currently, there is not one single test that has been proven to be superior for prediabetes nor DMT2. The testing methods test for different aspects of DMT2 pathophysiology, such as hyperglycemia, hyperinsulinemia, or an insulin-to-glucose index which can show the stage of insulin resistance development. Therefore, these tests are tough to compare. Maybe a better question would be what pathophysiological factor is most capable of diagnosing prediabetes.

Firstly, requirements for an adequate testing method and present complications for the representability of study results will be elaborated upon. After prediabetes testing methods will be elaborated upon. By providing insights into the testing methods, their fit for early diagnosis can be stated. After, the most adequate pathophysiological factor will be discussed to provide another perspective on the adequacy of testing methods.

Multiple aspects of a testing method will influence its applicability for early diagnosis, such as costs, easiness in usage, invasiveness, safety, and accuracy. Many are stated within the early diagnosis criteria. Accuracy is elaborated upon as this chapter aims to show to which extent these testing methods can diagnose prediabetes. Costs will not be stated as the intervention costs are based upon much more than the costs for one single test. Precision, sensitivity, and specificity are related to accuracy. Accuracy means a testing method does measure what it is supposed to measure, meaning it is capable to measure the true concentration or amount of a substance within a sample. A precise testing method can reliably reproduce its measurement, with only a small amount of random variation. Specificity and sensitivity reveal the likelihood of false negatives and false positive testing results. An effective pathology test is expected to detect abnormalities within the patient with certainty. Specificity and sensitivity do depend on cut-off points. Each of these aspects should be available to provide an effective testing result. Information about these aspects is not available yet for each testing method discussed within this chapter. Available information, expected to be representative for the Dutch population will be mentioned.

Multiple studies are conducted on these qualities of prediabetes tests. Studies state efficiency for their eligible population and do not guarantee representability for other populations. Multiple factors provide difficulty in comparing testing methods, let alone justifying a superior testing method. The accuracy, specificity, and sensitivity rates of the testing methods do differ per cut-off value[70]. Those cut-off values vary between organizations and countries and might be a result of the variety in prediabetes definitions within healthcare. A major comparison difficulty is the lack of concurring study designs, and concurring cut-off values. Most of these studies are performed within the United States. Environmental factors and public health within the United States are not representative for the Dutch population. The study's eligibility criteria can minimize this gap, though many risk factors for prediabetes are tough to identify during the study population selection and can intervene with the results, such as the American diet. Therefore, the results of these studies cannot guarantee to be representative for the Dutch population. Due to these complications, these testing methods will be described and their applicability according to studies will be elaborated upon. Found effectiveness rates will be stated but cannot be considered representable.

Testing methods for Prediabetes

The testing methods measure different aspects of glucose regulation, wherefore not all measure similar blood substances and use similar methods. This does influence the invasiveness, presence of protocol user-friendliness, and patient friendliness of the testing method. These aspects are represented within the early diagnosis criteria and will be elaborated upon per testing method. Invasiveness, user friendliness, and patient friendliness are scaled in very low – low – intermediate – high - very high.

Fasting plasma glucose test (FGT).

Blood sampling after an overnight fast (at least 8–12 h) [71]. Values and protocols are nationally stated and available.

This test can be performed using one single blood draw. It requires an overnight fast (at least 8–12 h) and is less sensitive than the OGTT.[72]. This is the most commonly used testing method and the majority of the global diabetes prevalence epidemiology studies are based on the FGT. It can be considered low in invasiveness, intermediate for patient friendliness, and high for user-friendliness.

Oral glucose tolerance test (OGTT).

Includes assessment of both FPG and the two-hour post loading glucose(PLG). Its assessment of the glucose response after an oral glucose intake [73]. Two blood samples are required. Values and protocols are nationally stated and available.

In studies, the OGTT has been combined with the FGT and Hb1Ac. Combination with FGT proves the highest accuracy [72]. Multiple mathematical representations calculating insulin sensitivity from glucose and insulin excursions after oral glucose ingestion have been developed, which potentially can influence the effectiveness and application. The OGTT could be confounded[74] by physiologic factors separate from insulin resistance itself.

This testing method identifies more individuals with dysglycemia than a single FGT or HbA1c[72]. It does, however, require an overnight fast, administration of glucose causes nausea and vomiting in a small proportion of the population (~2-5%) and the test has a two-hour duration. Its sensitivity does vary day-to-day due to diet or exercise. Besides the values vary according to the time of day of testing, according to the circadian rhythm and reproducibility is not as good as the FGT or HbA1c. Around 10% of patients cannot be diagnosed based solely on the two-hour PLG value [75]. The 1-hour PG has a sensitivity of up to 0.95 and a specificity of up to 0.94[76].

It can be considered to be intermediate in invasiveness, between intermediate and low for patient friendliness and intermediate for user friendliness.

Oral Glucose Challenge Test (OGCT).

The OGCT is similar to the OGTT. No fasting is required. After the intake of glucose, only one blood sample is taken. This test is usually performed in pregnant women but is stated to be a promising screening method for non-pregnant patients. No concurrent cut-off values or protocol for non-pregnant patients are stated yet.

The OGCT test has proven to be as sensitive and specific as the OGTT [77]. For the OGCT only a few studies have been performed within a non-pregnant study population [72]. The sensitivity was up to 92% and specificity up to 87% for diabetes. Only 40% of the at-risk population were indicated for a follow-up OGTT for confirmatory diagnosis, of whom 45% had either prediabetes or DMT2. This method would be adequate for targeted diagnostic testing in a high-risk subset of the at-risk population.

The test is convenient as it can be conducted at any time of day, without prior fasting. It only requires one blood sample, an optional second sample, and has a duration of one hour. By reducing the OGTT to one blood sample this testing method is more cost-effective.

It is considered to be low in invasiveness, high in patient friendliness, and high in user-friendliness.

Hemoglobin A1c test.

The HbA1C blood test provides insights into the average blood glucose levels for the past two to three months [78]. When glucose enters the bloodstream, it attaches to hemoglobin, a protein in the red blood cells. In healthy individuals, there is a small amount of glucose attached to the hemoglobin. When blood glucose levels rise a higher amount of glucose attaches to a red blood cell. The HbA1C test measures the percentage of red blood cells that have glucose-coated hemoglobin and requires one blood sample. Values and protocols are nationally stated and available. It is considered to be low in invasiveness, high for patient friendliness, and high for user-friendliness.

The testing method is low in invasiveness and is convenient. It does not require fasting or patient preparation. It has a high reproducibility (precision) and is less day-to-day influential during stress and illness compared to OGTT and FGT.

On the other hand, it is less sensitive than the FPG and OGTT and the accuracy and interpretation can be affected by the presence of hemoglobin variants, iron deficiency anemia, chronic kidney failure, differences in red blood cell lifespan, and differences in age and race. Further elaborated upon in figure 7. The figure shows influential factors. Besides, it is weakly associated with the DMT2 pathophysiology of insulin sensitivity and ß-cell function, and its results may be high or low relative to underlying average glucose levels. Meaning the accuracy – HbA1c can provide "mismatches" as a reflection of average glucose levels [72]. In brief, its ability to predict the preliminary phases of diabetes is poor in comparison with the OGTT. The HbA1c is a valuable method for dysglycemia diagnosis, but in screening, for high-risk individuals, the HbA1c alone may be insufficient to substitute for OGTT.

Main Non-Glycemic Factors Affecting HbA1c Measurement

Elevates HbA1c	**Reduces HbA1c**
Iron deficiency anemia	Pregnancy
Chronic kidney disease	Hemolytic anemia
Vitamin B12 deficiency	Erythropoietin therapy
Severe hypertriglyceridemia	Iron/vitamin B12 replacement
Aging	Chronic liver disease
Black race, Asian race, Hispanic ethnicity	Antiretrovirals
Hemoglobinopathies	Hemoglobinopathies
Genetic factors	Genetic factors

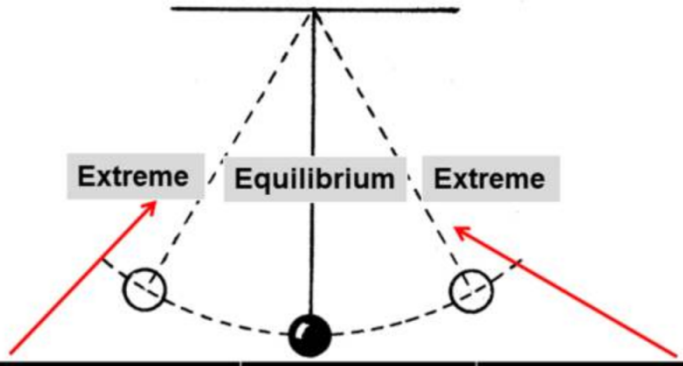
Figure 7. HbA1c affecting factors [72].

HOMA Index. Fasting glucose Fating insulin ratio.

A blood sample of both fasting glucose and fasting insulin is taken, after a 12-hour fast [81]. The laboratory can decide if both can be measured by means of one single blood draw. The G: I ratio between glucose and insulin is measured by a calculation. Lower values depict higher degrees of insulin resistance. No adequate and concurrent values have been set yet for prediabetes. The current research stated sensitivity is not concurrent, reaching from 0.60 and specificity of 0.66 [79] up to 95% sensitivity and 84% specificity. [80]

The cut-off value does depend on some factors including ethnicity. More research should be conducted for the values for non-diabetics, before it can be a screening tool [87]One weakness of this model is that it does assume the G: I relationship is linear when in fact it is parabolic. This testing method can measure blood glucose, insulin, and insulin resistance and can therefore be used for testing for hyperinsulinemia, prediabetes, and DMT2. It can be considered to be low in invasiveness, intermediate for patient friendliness, and high for user-friendliness.

The described testing methods can all diagnose prediabetes, though Hb1Ac is not as adequate. The accuracy of these tests for diagnosing prediabetes does depend on the set cut-off values, which do differ between health organizations and countries. The most promising testing methods would be OGCT and the G: I index. OGCT due to the combination of high accuracy. For G: I index due to its low invasiveness, user-friendliness, potential accuracy, and low costs. OGCT is still in development and studies are being performed to identify the most effective cut-off values and glucose administrations. Figure 8 does show some major steps of OGCT protocol developments. The HOMA-Index is promising but would need more research before it could be used as a prediabetes screening tool.



	Historic (Complex testing)	Future ? (Realistic)	Current (Over simplification)
Testing	2-hour OGTT (various glucose doses)	1-hour 75-gram OGTT	2-hour 75-gram OGTT
Time points	0, 30, 60, 90, and 120 min.	60 min	0 and 120-min
Cut-off values	No. Based on the shape of the glucose curve	Yes. 1-h PG>155 mg/dl	Yes
No. of specimen	> 2	1	2
Clinical Applicability	Not practical	Practical	Intermediate
Pathophysiology	Early	Early	Late
Primary prevention studies	Not available	Emerging	Evidence established
Cost-effective for screening	No	Yes	No

Figure 8. OGTT protocols evolution.

An additional pre-screening tool for high-risk individuals is recommended by multiple studies [76]. Its effectiveness is shown in the ADDITION and FINDRISK study. [67] The study of M. Visser does mention [82] prediction models often do not fare as well in extern populations compared to the population the model is based upon. It should therefore be developed for the Dutch population or a similar population. Even though a lot of pathophysiological patient information is available within the patient dossier, screening this file and picking those patients by hand for present risk factors would be inefficient. This tool can be developed to speed up this process and can be designed to be a low burden to the patient. This tool can be used to select the eligible population and could also be used to verify handpick patients on eligibility. This would increase the cost-effectiveness of the early diagnosis intervention. It can be considered to be low in invasiveness, high in patient friendliness, and high in user-friendliness.

4.7 Pathophysiological factor for Prediabetes Diagnosis

Though there is no test decided upon to be superior, evidence suggests the most relevant pathophysiological factor to test for is insulin resistance.

Insulin resistance.

Hyperinsulinemia is the cause of insulin resistance and in most cases is caused by hyperglycemia. The extent to which insulin resistance is occurring, however, is the pathological measurement most representable for the progression of DMT2. Currently, the hyperinsulinemic euglycemic clamp is regarded as the “gold standard” for determining insulin resistance. The modified insulin suppression test also is an accurate method. Both methods have, however, a complicated nature and need to be performed in a clinical setting, due to the risk of potential hypoglycemia, limiting their applicability in routine usage. Research is being done to find more adequate biomarkers for the diagnosis of insulin resistance and prediabetes[83].

Lipids

Some other adequate indicators for prediabetes are lipid values in the blood. Changes in the number of circulating lipids, including triglycerides and LDL cholesterol as well as the HDL are frequent during the development of DMT2 [84] An increase in lipid blood values is present due to the saturated adipose tissues not taking up any more fat molecules. The surplus in lipids will be stored in the muscle, liver, or heart tissue or will be present in the blood increasing the lipid blood values. Triglycerides are accurate in diagnosing hyperinsulinemia and insulin resistance. The triglycerides to glucose ratio's highest achieved sensitivity are 96% using HIEC, and the highest specificity is 99% with reference to the HIEC and HOMA test [MT40]. This test can be performed by one single blood draw and a protocol is present. Triglycerides to glucose ratio would be an addition to OGCT. The invasiveness is low. Patient friendliness is considered low to intermediate as it might require an additional blood draw and user friendliness is high.

Influential Factors for Testing

Multiple external and internal factors can influence testing results. For instance, iron deficiency can cause an overestimation in measured HbA1c. One major physiological factor is the circadian rhythm, which influences insulin secretion. Any blood test targeting blood glucose or insulin will be influenced. The moment of blood sampling is therefore highly important. Internist Y. Sijpkens does agree with these statements.

The testing method according to internists

The most accurate testing factor would be insulin resistance according to internist Mattijs Out, using the glucose to insulin index, optionally with an additional lipids test. The fasting glucose to fasting insulin(G: I) ratio has shown to be a promising sensitivity and specificity measurement[80] of insulin sensitivity, with lower values depicting higher degrees[81] of insulin resistance. It has up to 95% sensitivity and 84% specificity. This testing accuracy does depend on the set ratio value and the study population, therefore needing more research to identify its applicability and usefulness.

Progressive internist Y. Sijpkens of Medical Centre Haaglanden in the Hague, the Netherlands agreed on conducting a semi-structured interview for the Master Thesis. The results are discussed within this subchapter. Early detection of prediabetes should be applied in both primary and secondary health care. The prevalence of metabolic diseases is increasing and occurs within younger populations. The method applied within current general screening is however limited. There should be a transition within the screening process from glucose disease to insulin resistance disease and preferably even further to metabolic dysfunctions (MD). Not to confuse metabolic syndrome with MD. Metabolic syndrome is limited to five factors and is very much restrained to the cardiovascular disease detection which it was created for. MD should extend further and include all dysfunction of the metabolic system, including for instance fatty liver disease. Metabolic dysfunctions are highly related and can have high interaction rates. Prediabetes and DMT2 are a result of metabolic dysfunction. By extending the testing to MD the root cause of the disease can be diagnosed and treated, instead of treating its consequences of cardiovascular disease and DMT2 separately. More information on the impediments to implementation of prediabetes early detection according to internist Y. Sijpkens is displayed in chapter Results.

Internist Y. Sijpkens, does progressively test for prediabetes, according to another definition, metabolic dysfunctions (MD). MD does recognize a wider variety of metabolic dysfunctions than metabolic syndrome. Simplified, MD does include every dysfunction of metabolism. MD does state insulin resistance to be one of the multiple MD factors, which together form a web of metabolic dysfunctions, which can highly influence one another's progression. When using a definition such as metabolic syndrome, which includes only five risk factors, there is a risk of the medical doctor searching for the root cause of the disease within this definition, searching within a box. This often results into symptom treatment and not into the treatment of the root cause. This is also called 'uitsluit geneeskunde' and is a common phenomenon within the present health care system. The web of MD does reach a wide variety of medical specialism, thereby promoting diagnosis outside of this box. To find and treat the root cause, not symptoms. Therefore, internist Y. Sijpkens does not just test for insulin resistance but also for its risk factors/ comorbidities, the other MD. MD testing applied by Internist Y. Sijpkens does consist of: Fasting insulin, fasting glucose, HbA1c, fasting lipids, triglyceride: HDL ratio, ALAT Gamma GT, ferritin, vitamin D, uric acid, albumin:creatine, visceral fat, stomachcircumference: length, testesteron, estrogen, echo liver, CT calcium score(cardiac CT calcium score). This is a wide variety of testing methods and could be considered to be an impact on the health care budget. However, internist Y. Sijpkens does mention this method has already saved a lot of money and has the potential to minimize the healthcare costs spend on DMT2 comorbidity treatment and according to 'draaideur patienten' due to DMT2 prevention. A very essential remark is internist Y. Sijpkens does perform this prediabetes early diagnosis within own time.

Internist Mattijs Out does agree those tests do provide some interesting results. To which extent they do provide additional value for diagnosis is mentioned to be uncertain, due to lack of study evidence. Internist Mattijs Out does therefore limit testing to symptomatic and high-risk patients. Mainly by means of blood tests. This does provide insights into the experienced impediments by an internist and their influence on prediabetes early diagnosis implementation. It proves again, more research has to be done on the cost-effectiveness of prediabetes testing methods and eligible prediabetes risk patient population to make it applicable.

4.8 Early Diagnosis Implementation within the Netherlands.

Multiple factors will facilitate the success of early diagnosis initiatives within a population or healthcare system. Some major factors are the population deterministic, type of disease, healthcare structure, screening method composition, and applied testing method. Dutch early diagnosis study results can provide insights into the status of these factors. These factors are expected to apply to this Master Thesis research and will therefore be discussed within this chapter and will answer sub-question 6 *In which implementation stage is the preliminary phases of DMT2 early diagnosis within Dutch secondary healthcare.?*

There is insufficient information on the determinants of the Dutch prediabetes patient population within secondary healthcare. Therefore, the determinants of the Dutch population will be used to test the applicability of prediabetes early diagnosis on. A large proportion of the Dutch population is represented within the hospital patient population [61] [62] [63]. Also, every inhabitant might potentially require a form of hospital care. The words screening and early detection are used intertwined within the literature used for this chapter. Therefore, these words will also be used intertwined within this chapter.

Early Diagnosis of Prediabetes internationally.

This study focuses on the Netherlands. Internationally some study results might be applicable to the Netherlands and potentially be useful for the development of Dutch early diagnosis studies. Besides these impediments show why the development of these programs is so slow. Prediabetes and DMT2 screening methods are internationally being developed and applied. Internationally, studies identifying the benefits of DMT2 screening do show contradictory results. I do suspect this has to do with the large heterogeneity between international studies in publishing date -with studies reaching from 2013 to 2022- study populations, and quality and types of study designs [64]. The heterogeneity between those studies can partially be explained by the differences between countries' healthcare systems, population deterministic, quality of healthcare, and presence of prevention programs. Nevertheless, this heterogeneity causes difficulty in generalizing those study results, wherefore some study results might not be utile for early detection programs for the Dutch population.

Tijdschrift voor Praktijondersteuner en Praktijkverpleegkundigen(TvPO)[65] does base this indecisiveness within international literature upon some other relevant factors. Firstly, there is a problem with the definition of DM. The diagnosed blood values of DM are originally based on the occurrence of retinopathy. The biggest health burden, however, is caused by cardio- and vascular diseases. The main cause of DM screening should be to prevent cardiovascular diseases. Therefore, it would be more efficient and beneficial to not solely measure blood glucose values but include cardiovascular risk profiles. The latter also being highly recommended by internist Y. Sijpkens. Another reason would be there not being an obvious superior diagnostic test to diagnose DMT2. Especially when including cost-effectiveness and patient friendliness.

Study results within the Netherlands.

No studies or initiatives are found within the consulted databases for Dutch screening initiatives solely aiming at prediabetes. The mentioned initiatives were focused on DMT2 and performed in primary health care or within the Dutch population. No early diagnosis initiatives for prediabetes in Dutch secondary healthcare are stated, wherefore preliminary phases of DMT2 early diagnosis is expected to be in the first phase of the implementation model of Wensing and Grol: orientation. Within the Netherlands DMT2 screening initiatives are being performed. These will be elaborated upon, as they provide important information proving the potential and complications for prediabetes early diagnosis in secondary healthcare.

The Dutch attitude towards the effectiveness of prediabetes and DMT2 screening remains skeptical. In contradiction to some international studies, such as in Sweden [66], Dutch opportunistic population DM screening has a low yield. This is suspected to be due to low rates of undiagnosed DMT2 patients as a result of case findings. In the mid 90s an estimation of half of the DM patients were suspected to be undiagnosed, causing an increase in case finding within General Practitioner (GP) practices. This was reflected into a high increase in DMT2 cases within the late 90s. Case findings consist of GP practices testing the blood glucose of high-risk patients during 'spreekuur'. The NHG-Guideline Diabetes Mellitus Type 2 for GPs does recommend limiting the conduction of screening methods to once every three years for patients who are 45 years or older and have at least one or more risk factors for DMT2[65]. An American study shows conducting screening more often or for younger populations is unnecessarily costly.

The Dutch ADDITION-Research proved those high rates of undiagnosed DM patients are no longer the case. The study consisted of case finding within GP practices and provided some other interesting results. The rate of DM-diagnosed patients was a bit lower when conducted by younger GPs, showing experience does have an influence, but is not significant. Besides, no significant difference was shown for GPS with high interest in DM[67]. In brief, they concluded opportunistic population screening is ineffective within the Netherlands, and case findings would be a more effective method. In the first place because the Dutch Healthcare system contains some necessary features for case findings. In the Netherlands (almost) every inhabitant is subscribed to a GP practice, the diabetic care is highly developed and structured- partly due to the presence of the GP assistant and diabetic nurses- and the GP practices provide a healthcare structure in which screening can be a continuous process [67].

The attitude towards the Dutch healthcare structure being fertile for early detection of prediabetes is uncertain and underexplored. The Dutch secondary healthcare system provides a continuous process through polyclinical consults. However structural problems do emerge such as lack of time and working pressure, hospital care budget restrain, and lack of proof of cost-effectiveness. These factors are recognized both by Internist Y. Sijpkens of MC Haaglanden and Internist Mattijs Out of MST. All three factors prove to be major arguments for Dutch internists to not yet apply early detection. Besides among medical professionals, there are expectations of a low yield for undiagnosed DMT2 patients and possibly also for undiagnosed prediabetes patients in secondary care, again showing a low yield. These expectations are not based on study results. There might however be a satisfying yield for prediabetes patients due to the lack of prediabetes screening, this argument being supported by Internist Y. Sijpkens. Internist Y. Sijpkens is in the fifth phase of the implementation model of Wensing and Grol, Maintaining, but is suspected to be an innovator as to the five customer segments of technology adoption, and ahead of most internists. This will therefore not be representable for internists in secondary healthcare.

5 Method Empirical Study

The Empirical study will exist out of a survey and an interview with internist Mattijs Out. The framework of the survey is built upon the literature research results. First, some hypothesis will be stated, after which their relevance is explained and their measurement tool. After the hypothesis, the survey framework will be elaborated upon. MST requested to limit the survey to medical doctors with a high interference with the Master Thesis subject. This resulted in a limitation to internists in MST for the Master Thesis survey. The literature research has been conducted resulting in the following hypotheses for the empirical field study. Hypothesis 1 will be referred to as H1 and as followed.

Hypotheses

Based upon the literature review and interview with internist Y. Sijpkens, secondary health care is suspected to be within the first or second stage of the model of Wensing and Grol: informing medical doctors about the innovation, and stir up inquisitee, gaining knowledge of the innovation. The corresponding first and second step of the behavior model of Balm is being open to and understanding, requiring knowledge about the innovation. As a result, the survey will focus on the extent of the medical doctors their knowledge of the preliminary phases of DMT2 and their performance of preliminary phases of DMT2 early diagnosis.

H1: Medical doctors are not informed about the preliminary phases of DMT2 or insulin resistance.

To be capable of implementing an innovation and wielding the innovation a person requires knowledge about the innovation. Therefore, the internists of MST are requested to declare their state of interfering knowledge.

H1 will be rejected if the predictive value is >0.5 for medical doctors to know about the preliminary phases of DMT2. Meaning, 50% of the respondents state their knowledge of the preliminary phases of DMT2 is 'voldoende' or higher. No P-value will be used due to the small sample size [85].

H2: Medical doctors in MST do not perform prediabetes early diagnosis.

The survey consists of two branches, users and non-users of prediabetes early diagnosis. To identify to which category they belong they are asked whether they do apply early diagnosis. The answer does imply in which stage the individual doctor is within the model of Balm and the total group response does imply in which stage the MST is within prediabetes early diagnosis implementation.

H2 will be rejected in case the predictive value is >0.5 for medical doctors performing early diagnosis. This is the case when >50 percent declare to test for prediabetes or insulin resistance on a 'regelmatig'(regularly) base or more often. The pathophysiology of insulin resistance is fit for prediabetes diagnosis.

H3: Medical doctors do use an adequate testing method to test for insulin resistance.

There is no superior prediabetes testing method appointed. Literature and internist Mattijs Out of MST do recommend the pathophysiological factor to test for, insulin resistance. This is set as a pathophysiological golden standard to test for prediabetes within this Master Thesis. Any testing method capable to diagnose either insulin resistance or prediabetes according to the literature is marked adequate. The applied testing method will provide insights into the blood values tested for and the corresponding preliminary phase of DMT2 tested for. This will show whether their early diagnosis initiative does comply with the testing method criteria. Besides, it will explore their application and can provide new insights into (effective) early diagnosis applications.

H3 is rejected in case the predictive value is >0.5 for internists not testing for insulin resistance or prediabetes. Meaning >50 percent of internists do not apply an adequate testing method to test for insulin resistance or prediabetes. Adequate testing methods will be elaborated upon in the subchapter Testing Methods.

H4: There are no external factors providing stagnation of prediabetes early diagnosis in MST.

To provide a successful implementation of early diagnosis within MST support within the four domains of MIDI will have to suffice. Insufficient availability of factors within any of these domains will influence or even stagnate the early diagnosis implementation in MST. It can also provide insights into genuine reasons not to apply preliminary phases of DMT2 early diagnosis in MST. The experience of an individual's impediments can depend on the individual's capacities. Therefore, H4 will be rejected in case more than 50 percent of medical doctors mention an impediment.

H5: There is no basal support for prediabetes early diagnosis by medical doctors in MST.

The internists will be asked whether they test for or are willing to test for insulin resistance, the most accurate pathophysiological factor for prediabetes diagnosis. In case the majority, meaning >50 percent of internists in MST, do test or are willing to test for insulin resistance H5 will be rejected.

Survey Study Population

The Master Thesis research aim is to provide insights into which extents medical doctors in MST apply early diagnosis. The study population would therefore preferably consist of medical doctors within MST and will consist of non-probability sampling. MST has proposed to only send the survey to medical specialisms having a high interface with the Master Thesis subject, due to high working pressure. In consultation with internist Mattijs Out this resulted in cardiology, rheumatology, gynecology, and internal medicine. Though due to the previous statement and limited time for this Master Thesis this has been narrowed to internists in MST.

Survey Inclusion Criteria.

To guarantee the feasibility and validity of the survey, the medical doctors will have to be able to read Dutch with a B2 degree [MT60]. This is suspected to apply to all medical doctors within MST.

Survey Design

The qualitative cross-sectional survey has been conducted online in the Dutch language using Qualtrics [MT61]. Qualtrics does comply with the privacy standards set by the University of Twente. The survey is a combination of an explorative and descriptive survey design [88] and is therefore mostly qualitative in nature, seeking input from respondents using open-ended questions focused on why and/or how the respondents perceive prediabetes early diagnosis implementation, with some additional questions on their perception, such as their attitudes, behavior and reported interactions with prediabetes early diagnosis. The latter questions merely use quantified Likert scales and matrix designs.

The MIDI does provide a questionnaire. The size was considered burdensome and multiple questions could be answered by documents or were expected to be irrelevant to the implementation phase of the early diagnosis in MST. Therefore, questions were based on literature and in cooperation with internist Mattijs Out. The MIDI domains were applicable and therefore applied to the survey results.

Only the medical specialism had been requested as respondent deterministic. Other deterministic, such as years of experience and sub-specialization are considered valuable. However, due to the small study population and number of medical doctors per medical specialism, any other deterministic could identify the respondent and were therefore not requested. This deterministic was not necessary due to the narrowing of the study population from medical doctors within MST to internists in MST. The Master Thesis survey was, however, already developed, preserving this question. The survey was divided into two cohorts or branches: users and non-users of prediabetes early diagnosis. Respondents who declared they do not, 'nooit' test for insulin resistance, the golden standard, are considered non-users of prediabetes early diagnosis. This resulted in two introduction questions and eight questions per branch. The number of questions and combinations of types of questions was predicted to provide a balance between a low respondent burden and high survey validity.

The validity and reliability of the survey were estimated and improved by pilot testing its content on the flow and the understandability of instructions also called face validity. Content validity assessments, meaning comparing the survey to similar tools, were not conducted as this is an explorative cross-sectional survey and has no aim to be used structurally. Neither are similar tools for this subject available yet.

Within survey designs, four biases are recognized, as to F. Lau. Coverage bias occurs when the sampling frame is not representative of the study population such that certain segments of the population are excluded or under-represented[88. In case of sampling bias, the study is not representative of the population such that the sample values cannot be generalized to the broader population. Both are expected due to the narrowing of the study population. The results will not be representable for medical doctors in MST but are validly representable for internists in MST. Eleven out of the internists. A slight presence of measurement bias is expected due to the limited time for the Master Thesis and short pilot testing, which could result in low understandability of some questions or instructions. Jargon was avoided, response options were simplified by using verbal Likert scales and pilot testing was conducted to minimize this bias. Pilot testing was done with internist Mattijs Out. Besides two fellow students at the University of Twente performed a pilot test. The study results will be checked for completeness by applying the checklist of Kelly, Clark, Brown, and Sitzia (2003) for survey reports.

Data Collection and Analyzation.

The survey is conducted and analyzed using Qualtrics (2022). The respondents were invited by internist Mattijs Out, to prevent healthy user bias and increase accuracy. Healthy user bias, for this study, means internists which have a high affinity with innovation and this subject and are likely to be overrepresented. Non-users could avoid attendance. An attendance reminder was sent to the internists to minimize this bias. The questions are shown in Appendix 2.

Qualitative responses are thematically analyzed. Open questions are coded [89]. By coding answers from multiple medical specializations and medical sub-specializations can be compared and combined. The matrixes and Likert verbal scale results are quantified, after which they are descriptively analyzed. Before allocating the impediments mentioned in the survey and interview into the MIDI domains, they are checked for overlap and independence. In case of a slight overlap or slight dependence, both impediments are mentioned. It does not indicate the magnitude of the impediments, only exploring the presence of impediments.

Data Quality Assessment.

Data quality is defined as data being fit for its intended purpose and having a close relationship with the construct it is intended to measure[90] The five main criteria for data quality are accuracy, relevancy, completeness, timeliness, and consistency[91].

Accuracy in data quality assessment identifies how close the data is to the true value. The usage of 5 point-Likert scales is expected to suffice in accuracy. The data collected by the survey is ought to be relevant as they answer the research question and sub-questions. A complete picture of medical doctors' application of prediabetes early diagnosis is striven for but not essential for this Master Thesis, as this is an explorative study. The coverage bias and sampling bias are expected. A high respondent rate of internists would increase the representability of the study population for internists of MST and therefore the accuracy of this subpopulation. Due to the proactive attitude of Mattijs Out, a high respondence rate is provided. Due to the recentness of the response timeliness does comply. Due to the slow innovation process within secondary healthcare, the responses are not expected to change within the upcoming two months. Consistency will be checked per respondent, to see whether their responses are not controversial. Cronbach Alpha can be used to calculate the consistency. Due to the small study population, this was not applied. Control questions were not applied to minimize the respondent burden. Respondent consistency will be checked using common sense.

The data is expected to be corrupted due to high working pressure, and they might or might not be motivated to answer the survey. This can influence the quantity and quality of provided data. Verification of the survey results by conducting brief interviews with multiple internists in MST would increase the data quality. This could however be considered burdensome for the internist, due to high working pressure. Therefore, the results are verified with the interview conducted with internist Mattijs Out and literature. The data is qualified to answer the Master Thesis research question by enabling an inventory of the state of prediabetes early diagnosis implementation in MST. Further research could increase the quality and completeness of data necessary for the successful implementation of prediabetes early diagnosis.

Interview

A semi-structured interview has been conducted with internist Mattijs Out of MST. The interview results will provide more information on the experienced prediabetes early diagnosis impediments. The semi-structured interview, which allowed further questioning as a response to provided answers, provided more valid information than a single survey. The survey results of the internists are verified with these interview results. Due to a nonfunctional MST Ipad and therefore an interview without sound, the interview results were verified with internist Mattijs Out. The results on impediments are categorized as to MIDI and provided in a table.

5.1 Empirical Results

The Master Thesis survey had 11 internist respondents. Four users and seven non-users of prediabetes early diagnosis. One user only responded to a small number of questions. The empirical study will answer the empirical study sub-questions, meaning sub-questions 9 to 13. The sub-questions are categorized into basic support, knowledge of prediabetes early diagnosis, and implementation status. The corresponding hypotheses used to answer the sub-questions are mentioned. The survey results provide insights into whether these hypotheses are rejected or justified. These hypotheses have been altered by medical doctors into internists within MST.

This part will answer the following sub-question:

Is there basic support for early diagnosis of the preliminary phases of DMT2 in MST.?

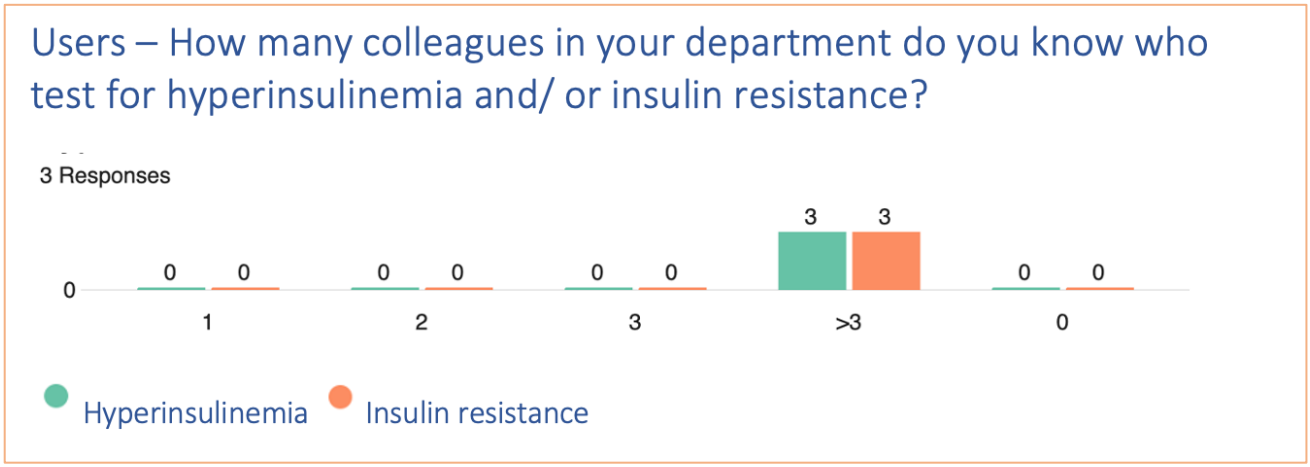
Five of the survey questions were related to basic support for prediabetes early diagnosis. Hypothesis H2 and H5 are related to this subject. The results will state whether these two hypotheses will be rejected or justified.

H2: Medical doctors in MST do not perform early diagnosis for prediabetes.

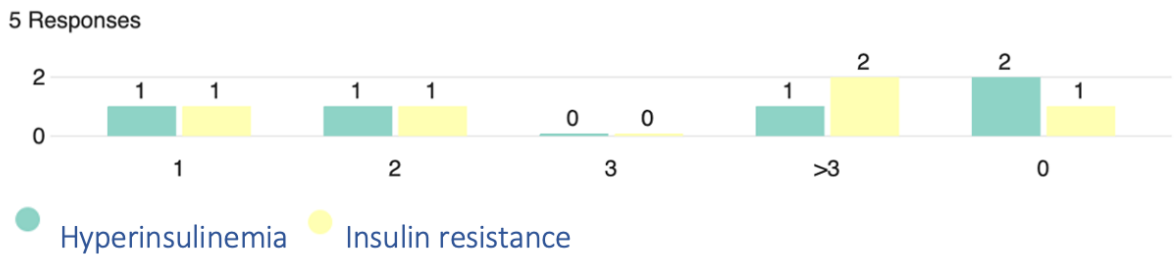
H5: There is no basal support for prediabetes early diagnosis by internists in MST.

7 out of 11 respondents do not test for insulin resistance. Only 1 stated to test for insulin resistance often, 1 once in a while and 1 seldom. All internists test for glucose regulation. 4 out of 11 state they are not testing for prediabetes. 4 out of 11 of the internists, or 36 percent, are <50 percent of the respondents. This statement will be justified. Internal medicine in MST does not yet perform early diagnosis for prediabetes. Insulin resistance can be used to diagnose both prediabetes and DMT2. This would be an inconsistent answer, or they limit its use to DMT2 diagnosis. This inconsistency also applies to the following question about responsibility.

None of the users denied it to be their responsibility to test for prediabetes. Glucose regulation and insulin resistance were evenly distributed from indecisive 'noch mee eens, noch mee oneens' to very much agree. These distributions were similar for non-users, with only one statement for 'niet mee eens' for insulin resistance and prediabetes. Insulin resistance can be used to diagnose both prediabetes and DMT2. This would be an inconsistent answer or they limit its use to DMT2 diagnosis. All three users replied they expected more than 3 internal medicine colleagues to be testing for hyperinsulinemia or insulin resistance. Both are shown in the following figures. Five of the seven non-users responded. Their answers do highly vary.



Non-Users: How many colleagues in your department do you know who test for hyperinsulinemia and/ or insulin resistance?



The users stated there should be more education and evidence on effectiveness for them to expand their prediabetes early diagnosis application. The non-users stated they did not early diagnosis yet due to a lack of knowledge and education, lack of protocol, lack of evidence, unusuality, and lack of reimbursement. Two respondents also stated it does not have a high interference with their medical sub-specialization. For non-users to start applying prediabetes early diagnosis they would require education, protocols, cost-effectiveness evidence, more time, and referrals for prediabetes. Prediabetes early diagnosis could be performed without a referral. This relates to the in-the-box treatment.

The majority of the users and non-users stated 'noch mee eens, noch mee oneens' on whether their medical specialism or MST should test more often for prediabetes. For users, only one statement of 'mee eens' for both within medical specialism and MST was made, and two statements disagreed with it being relevant for their medical specialism. For non-users, one statement for both medical specialism and MST was 'mee eens'.

The following was stated following the question of whether the non-users would want to perform prediabetes early diagnosis. Two respondents stated they would if indicated. One answered with 'yes'. One stated 'no' and one did not understand the question and was therefore invalid. Three out of four non-user respondents do show a support base. The users could be presumed to be a support base as they are already performing early diagnosis. Even though they might use the testing for DMT2 diagnosis it is applicable for prediabetes. Meaning >50 percent of the internists show support base for prediabetes early diagnosis.

Statements implying which department should perform this and to which extent this should be applied are varied. The non-user stated the following medical doctors should perform early diagnosis: medical doctors focusing on CVD risk, endocrinologists, internists, gynecologists, cardiologists, MDL, and rheumatologists. One stated 'do not know' and one did misunderstand the question stating the eligible patient population: unstable DM patients. The users mentioned, any medical doctor in MST if urged to by the diagnosis, general practitioner, or medical doctors frequently prescribing dexamethasone. Six respondents provided a valid answer, two an invalid, and two no answer. Even though their answers are not highly concurring the majority, 2/3 of users and 3 /5 of non-users, mentioned medical doctors present within secondary healthcare. One user mentioned primary care. Their answer might have been steered towards secondary care, in MST, due to the survey subject.

In brief, prediabetes early diagnosis is not yet widely applied within internal medicine of MST, wherefore it is in the first stage of Wensing and Grol. Although, the internists do show basic support for prediabetes early diagnosis.

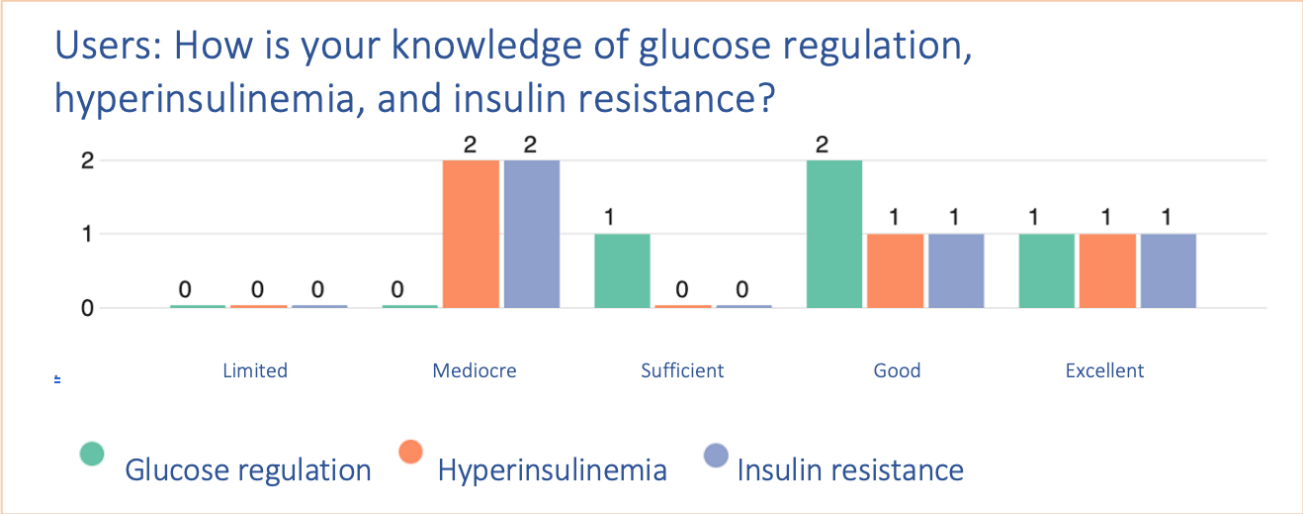
Prediabetes Knowledge

1. *To what degree do medical doctors in MST know about the preliminary phases of DMT2.?*

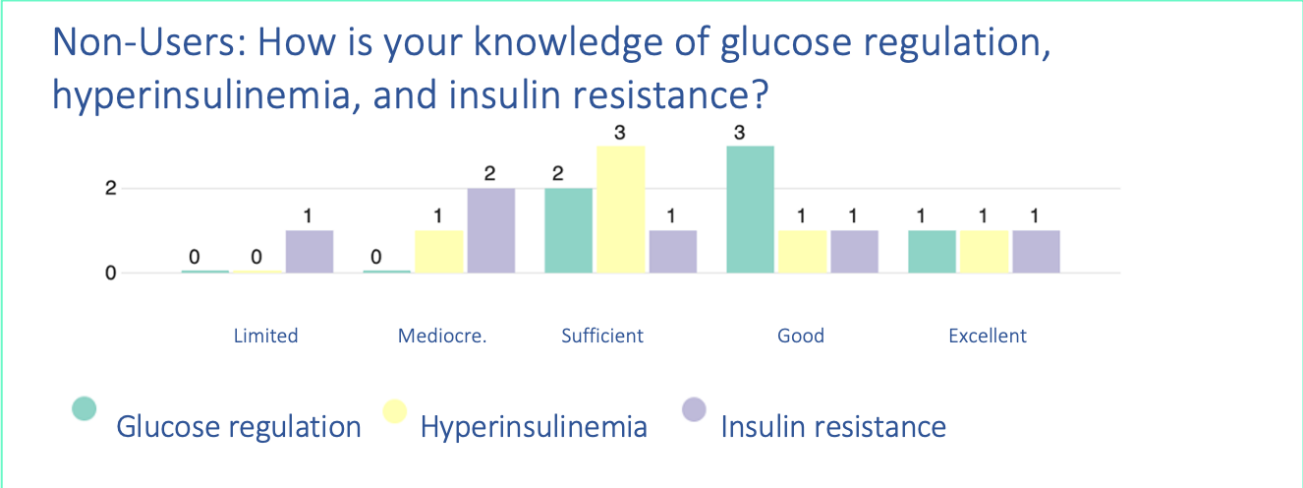
Hypothesis H1 and H3 are related to prediabetes knowledge among medical doctors. Two questions were related to this subject.

H1: Medical doctors are not informed about the preliminary phases of DMT2 or insulin resistance

Three statements per respondent were provided within this question, one for glucose regulation, one for hyperinsulinemia, and one for insulin resistance.



Half of the users state to have enough knowledge of hyperinsulinemia and insulin resistance. All state to have adequate knowledge of glucose regulation.



The non-users stated a slightly lower degree of knowledge of the preliminary phases of DMT2 and a similar knowledge of glucose regulation. One respondent did not answer this question.

4/ 8 users and 8/ 12 non-users responses related to hyperinsulinemia and insulin resistance were 'voldoende' or higher. Meaning a predictive value of 0.5 and 0.67 for users and non-users respectively. For the total respondent group, the predictive value was 0.6, meaning >0.5, wherefore H1 is rejected. The alternative hypothesis is justified: *internists in MST have adequate knowledge about the preliminary phases of DMT2.*

Implementation status

This part will focus on answering the following sub-questions:

2. Is there a protocol for early diagnosis of the preliminary phases of DMT2 within MST.?
3. What pathophysiology do medical doctors in MST test for to diagnose preliminary phases of DMT2.?

3.1 Which testing methods/ diagnostics?

3.2 Which preliminary phase of DMT2 can these testing methods diagnose?

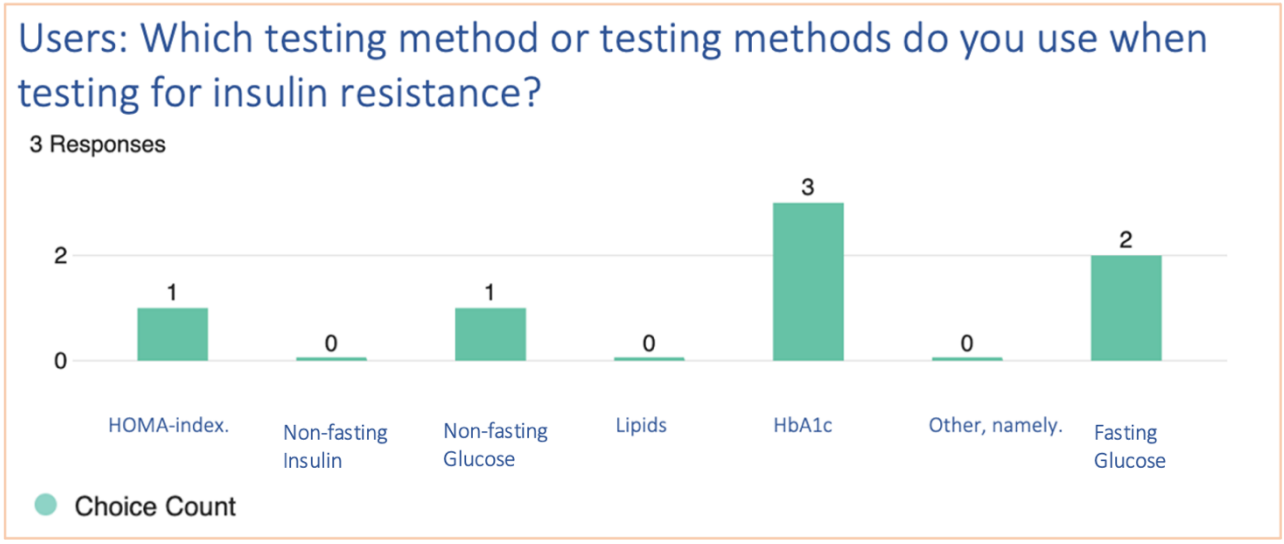
Four hypotheses are related to the implementation status of prediabetes early diagnosis. H2 has already been justified showing the implementation status is within the first phase of the model of Wensing and Grol.

H2: Medical doctors in MST do not perform early detection for prediabetes.

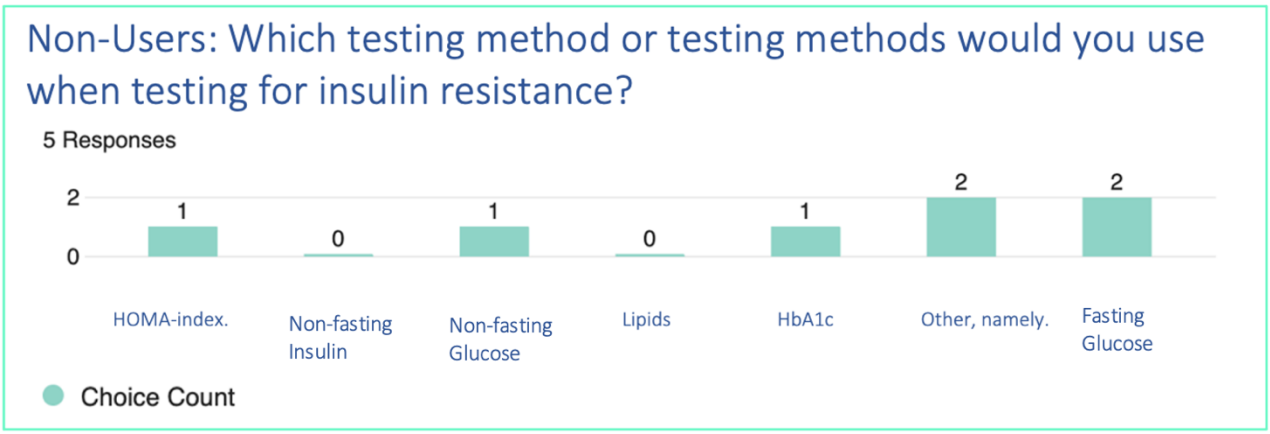
H3: Medical doctors do use an adequate testing method for insulin resistance diagnosis.

H4: There are no external factors influencing the stagnation of early diagnoses in MST.

The users stated to know one testing method each: OGTT, HOMA IR, and blood glucose test. The first two are adequate to test for insulin resistance. The latter might be an incomplete answer. Blood glucose on itself is inadequate. Two out of three respondents do state a valid testing method. The figure shows a multiple-choice question, with multiple answers possible.



Only one answer, the HOMA index, is valid. Therefore, the answers are inconsistent. HbA1c is one of the most common testing methods for DMT2 but is inadequate for insulin resistance and prediabetes. The non-users were firstly requested to state the testing methods they know and after a multiple choice question of which they would use in case of testing for insulin resistance. The first question had the following answers. One non-user stated 'glucose, HbA1c do diagnose DMT2 though maybe not prediabetes.' One stated OGTT. One stated HOMA, insulin, glucose, Hb1Ac and one respondent did not seem to know an answer. Two of the five respondents answered with a valid testing method. They were also provided the following multiple-choice question, with multiple answers possible. Five out of seven responded.



Only one out of the non-users did provide a valid answer: HOMA-index. Again, showing inconsistency. The two respondents supplying 'Anders, namelijk' stated they did not know which testing method to apply. Meaning one out of seven non-users provided a valid answer. Of all respondents, 4 out of 11 did reply with a valid testing method for insulin resistance. This has a predictive value of 0.364, which is <0.5, meaning H2 will be rejected. This does show there is a lack of knowledge for detecting prediabetes.

The external factors influencing the stagnation of early diagnosis in MST were measured by two questions for the non-users and one question for the users. The non-users were asked why they did not perform prediabetes early diagnosis yet, measured as impediments, and what should be done for them to perform this, stated as requirements for implementation. The users were requested to mention what should be done for them to expand their early diagnosis performance, stated as an impediment or requirement for implementation depending on their formulation. The stated impediments and requirements for implementation are shown in the following table. Three of the five responding non-users stated one or more impediments. Two did not respond. The other two stated they had a low interference with this subject. Each user stated one impediment. Six of the eleven respondents, 55 percent, stated one or more impediments. H3 is rejected due to 55 percent of medical doctors, meaning >50%, stating an impediment. Therefore, the alternative hypothesis is justified: Prediabetes early diagnosis impediments are present in MST and stagnate the prediabetes early diagnosis implementation.

Behavior Model of Balm and Implementation Stage

The survey had 11 respondents. One respondent did not answer enough questions to be included in this model. Four internists do state to test for prediabetes and three for insulin resistance. Only one user applied a valid prediabetes testing method within both the multiple choice and open questions and is therefore categorized as Doing. Two non-users stated a valid testing method and adequate knowledge and will be stated in the phase Willing to. The other internists will be categorized as Being open to, but one internist stated not to be willing to apply prediabetes early diagnosis.

Most internists in MST are in the stage of orientation within the Model of Wensink and Grol. The distribution as to the five customer segments of technological adoption is hard to apply, due to the small number of respondents. There is, however, a similar distribution.

Impediments Interview Internist Mattijs Out.

Including information provided by the interview and meetings within Internist Mattijs Out.

MIDI Domain	Impediments	Conditions for implementation
Innovation	• No superior testing method. • Lack of evidence cost-effectiveness testing method. • Lack of evidence cost-effectiveness of early detection. • Lack of evidence risk patient population.	• Strong evidence for cost-effectiveness for both the testing method and early detection. • Adequate and effective health behavior interventions
User	• Lack of knowledge about hyperinsulinemia, insulin resistance. • Experienced working pressure	• Education on preliminary phases of DMT2 and its early detection
Organization	• Lack of education • Lack of time • Lack of available hospital budget • No reimbursement early diagnosis (if not included within prior hypothetical diagnosis) • No protocol to guide adequate early detection.	• Required time and health care budget. • Education on preliminary phases of DMT2 and its early detection • Adequately founded protocols for preliminary phases of DMT2 early detection.
Socio-Political Environment.	• Lack of education • Lack of time No protocol to guide adequate early detection.	• Required time and health care budget. • Education on preliminary phases of DMT2 and its early detection

		• Adequately founded protocols for preliminary phases of DMT2 early detection.

The organization and sociopolitical environment have similar impediments. Protocols within an organization are often based on national or international protocols and evidence. Besides the lack of education provided by a hospital, the study of Medicine does also not provide enough education and is part of the socio-political environment. The hospital has a budget. However, the social-political environment is also part of budgeting, due to national health insurance regulations and health insurance reimbursements. The impediments stated by the internists of MST, by means of the survey, do comply with the stated impediments by internist Mattijs Out. Supporting the Alternative hypothesis as a verification: Prediabetes early diagnosis impediments are present in MST and stagnate the prediabetes early diagnosis implementation.

6. Conclusion

The physiology of prediabetes and DMT2 does merely comply with most early diagnosis criteria set for this Master Thesis. There is however not yet enough evidence on the effectiveness of available testing methods and prediabetes interventions to comply with set criteria. The general Dutch healthcare system including the secondary healthcare system does seem fertile, but not ready yet for implementation. This also relates to the lack of evidence on cost-effectiveness. Health insurance does not reimburse yet for prediabetes early diagnosis, resulting in a lack of time for medical doctors to include prediabetes early diagnoses within the treatment, which complicates the implementation of early diagnosis for medical doctors. As it is arranged at the moment, medical doctors will have to perform most prediabetes early diagnoses within the limited treatment budget and their own time.

Internists in MST do perform prediabetes early diagnosis to a minimal extent. Even though the motivation and basal support for prediabetes early diagnosis is present, users only perform prediabetes early diagnosis if requested by the stated hypothetical diagnosis or in presence of multiple obvious symptoms or high risks factors. Even then this is often limited to DMT2. Limiting the testing to highly symptomatic patients and focusing mainly on DMT2 is caused by the lack of evidence on cost-effectiveness, lack of education, and restrained healthcare budgets. This is highly related to the lack of reimbursements by health insurance.

The impediments of lack of time, budget, education, and protocols are a result of a lack of evidence of its cost-effectiveness. These stagnations can be explained by the need for evidence, before the providence of budgets and time by the health insurance. Therefore, implementations are often years behind scientific findings. Only after these steps are taken a successful implementation can be established.

In brief, prediabetes early diagnosis in MST is in the orientation and insight phase of the model of Wensink and Grol. The medical doctors are distributed as to the five customer segments for technological application. The innovators, such as Mattijs Out, are currently in the phase of willing to implement and doing, according to the behavior model of Balm, though are restrained by the health care budgets and hesitant due to lack of evidence on cost-effectiveness. The early and late majority are currently within the phase of understanding, due to the lack of information provided and gained about insulin resistance and corresponding testing methods. They seem to be slightly skeptical but open to discussion and are requesting evidence on cost-effectiveness. The openness could probably be explained by the presence of the continuous developments of the health care system and a tremendous amount of performed research. But uttermost by their willingness to perform the best possible healthcare for their patients. Though the motivation and knowledge of preliminary phases of DMT2 are heterogenous within the group of internists in MST, and impediments are present in all four domains of MIDI, the major impediments causing stagnation of prediabetes early diagnosis are located within the domains of innovation, organization and social-political environment and are highly related. They imply more research must be conducted on the cost-effectiveness of testing methods, set-risk patient population, and prediabetes treatments, before hospitals and health insurance will provide the required budgets and education. These steps should be taken nationally and internationally by governments and healthcare organizations. Only after performing these steps, MST can focus on the successful implementation of prediabetes early diagnosis.

7 Discussion.

The survey provides a small grasp of the current early diagnosis status within MST a secondary healthcare system. Important findings and limitations of the Master Thesis will be mentioned in this chapter.

7. 1 Limitation

The Master Thesis survey was not provided to each medical doctor in MST. This Master Thesis can therefore only partially answer the Master Thesis research question by mapping to which extent internists in MST perform prediabetes early diagnosis. Due to the lack of time of medical doctors, only a small number of questions have been included. These were highly sufficient to answer the research question. It is important to acknowledge the limitation of this resulting in a small amount of information potentially providing an incomplete picture of their motives for and attitude towards prediabetes early diagnosis. The results of the survey have been verified by comparing those to the interview with Mattijs Out and the literature. The conclusions drawn from the survey would have been stronger if more internists could have been consulted for verification. The results from the interview with Mattijs Out and surveys of internists in MST are, however, consistent in motives and experienced impediments. The same impediments are identified within MC Haaglanden by internist Y. Sijpkens and literature and seem to be a nationwide problem. This supports the validity of the survey and interview results.

In the first phase of the Master Thesis, the sub-specialisms within internal medicine were not recognized to be highly influential upon the performance of prediabetes early diagnosis. Recognizing this within further research would be recommended.

7. 2 Findings

The empirical study findings do merely comply with the literature study. The Master Thesis findings, both literature study findings, and empirical study findings, are elaborated upon per subject: knowledge, impediments, testing methods, and basal support. All survey results could be influenced by the work pressure, wherefore further research and verification of results are recommended to improve the validity.

Knowledge

There is a high positive relation between the stated knowledge of internists of hyperinsulinemia and insulin resistance and the performance of prediabetes early diagnosis. Internists of MST do declare to have sufficient to excellent knowledge of glucose regulation. Insulin resistance and hyperinsulinemia, however, are considered only low to excellent, with the majority leaning towards low to moderate. This underlines the impediments of lack of knowledge and corresponding education and proves the stagnation of prediabetes early diagnosis within the MIDI domain organization and user.

Impediments

The most important impediments seem to be a lack of evidence for cost-effectiveness, lack of time, lack of education, lack of protocols, and lack of reimbursement. Further research could provide a more complete picture of the impediments. However, this research provides enough prove for the need for evidence on cost-effectiveness of prediabetes early diagnoses. The stated impediments are all related to the domains of innovations, organization, and socio-political environment. The lack of knowledge, user domain, is not directly stated as an impediment, but most internists state a low to moderate knowledge of prediabetes and insulin resistance. It is considered an impediment as it will prevent effective implementation. The stated impediments are highly dependable and interactive and are part of a chain reaction. Lack of evidence on cost-effectiveness does provide a lack of reimbursement, protocols, and education. The lack of education prevents a wide implementation. Lack of evidence could initiate a chain reaction and is therefore the impediment to challenge first. The Master Thesis research provides insights into the current implementation status. This current implementation status and stagnation can be very well explained by the stated impediments.

Testing Methods

The testing methods used or proposed by most internists of MST do not comply with the literature. Most of the mentioned testing methods cannot diagnose prediabetes by insulin resistance or by any other pathophysiology. Most mentioned testing methods focus on glucose, which complies with the stated knowledge on glucose regulation being present and on insulin resistance being limited. This implies of knowledge of DMT2 is present but underlines the limitation of knowledge on the preliminary phases of DMT2.

Basal support

The survey proves the consensus concerning the importance of prediabetes early diagnosis, showing the internal medicine provides basal support for prediabetes early diagnoses. There is, however, a difference in opinion regarding whom should perform this. It should be considered, the Master Thesis does focus on the implementation within secondary healthcare, which could have steered the answers towards the secondary healthcare system. Verification of these answers with MST internists could provide more insights into this inconsistency. The GP, part of the primary health care system, has been mentioned. The majority of internists do declare to consider testing for insulin resistance and prediabetes to be part of their responsibility as internists. The majority of internists are either neutral or supportive towards performing prediabetes early diagnosis more often within MST, by interfering medical specializations. All, but one internist, who mentioned not to test for insulin resistance, declared to be willing to if conditions, such as more evidence of cost-effectiveness and education, are met. This proves internists are motivated and provide a support base for prediabetes early diagnosis.

8 Recommendation

A national wide cost-effectiveness research on prediabetes early diagnoses is needed. The patient target group should be identified and an effective treatment has to be stated. Based on these results nationally concurrent protocols for the prediabetes early diagnoses should be stated. Medical doctors can make initiatives to perform prediabetes early diagnoses within their own practice. To make a big and lasting impact on prediabetes population a wide implemented intervention is required which will only be achievable by more research.

Broadening the framework of DMT2 to metabolic dysfunctions could improve the effectiveness of treatments by locating the origin of diseases more specifically. Defining a concise protocol and providing education would be essential, to minimize costs and to guide medical doctors outside their own box. In brief, to maintain its cost-effectiveness. The metabolic treatments should aim at health behavior interventions as much as possible limiting their medicinal interventions. This could reverse prediabetes and could provide a well base for health maintenance. In case of DMT2 patients, it would prevent them from becoming 'draaideur patienten' and developing recurrences of the disease. Internist Y. Sijpkens states it would save on the healthcare budget.

In brief, more evidence is required to provide the required healthcare reimbursements by the health insurance and successfully implement prediabetes early diagnosis within Dutch secondary healthcare.

Evaluation Master Thesis.

I have learned a lot during this Master Thesis research. Mainly about the importance of interacting with the study population, the internists in MST. I interpreted the meetings with internist Mattijs Out would be included within the number of recommended meetings with the supervisors. In my opinion, this should not be the case. Interaction with the study population provides essential information for the research question, framework, methodology, and survey framework. Brief verification of the applicability of found literature to MST would have provided a more fitting survey and would have speeded up the Master Thesis progress. In the case of official research this would have been significantly more cost-effective.

Besides I have learned how to better organize this type of research. In future research, I would perform more explorative background research before setting up the study framework. During the literature review and after the interview with internist Y. Sijpkens I narrowed the Master Thesis framework many times. A lot of time on conducting the research could have been saved if I would have narrowed the framework earlier, thereby focusing the research more early in the right direction. This can merely be explained by this research being a voluntary Master Thesis subject set up by myself in cooperation with internist Mattijs Out. This resulted in a broad Master Thesis subject with a small amount of provided background information. Setting and narrowing the framework for this Master Thesis subject took a lot of literature research and meetings with internist Mattijs Out due to the lack of evidence within this field. More interaction with internists earlier in the literature review could have speeded up and steered the Master Thesis progress in the right direction. As a result, the Master Thesis chapters were very scattered during the early phase of the Master Thesis. This complicated the requests for feedback by university professors even though they were motivated to. Something which could have very much guided me within these phases of the Master Thesis. Organizing this more adequately could enable me to request feedback more early resulting in a more quick progression of the research and a more progressive learning curve.

Setting up the theoretical framework and method was tough for me until a meeting with P.J. Klok after my first Master Thesis submission. Highest likely due to the broad subject and minor amount of feedback as mentioned previously. Even though I have read through Thesis examples to learn about the thesis structure, a more thorough exploration would have saved me time in restructuring the Master Thesis. Structuring is also highly related to the framework, wherefore this can also be explained by the long search for this Master Thesis aspect.

Most importantly I have learned about my passion for research. And the importance of prediabetes research and the potential of DMT2 prevention by means of early diagnosis within Dutch healthcare.

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Appendix 1.

The ADDITION study:

The Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (ADDITION-Europe*)[TK18]* . The study design differed per country. Only the Dutch studies will be elaborated upon. The Dutch centres used two different types of screening programmes: a four-step programme and a three-step screening programme.

Centres in the Netherlands screened individuals aged 50 to 69 years, whereas other participating countries screened individuals aged 40 to 69 years. A total of 41 practices were included into the four-step screening programme and 38 practices into the three-step screening programme. Both types of programmes, conducted a Hoorn Symptom Risk Questionnaire, among the eligible patients, to identify those at high risk of DMT2. The questionnaire requested: age; sex; BMI; antihypertensive medication; parent or sibling with diabetes; history of frequent thirst; pain during walking, with need to slow down; shortness of breath when walking with people of the same age; or any reluctance to use a bicycle for transportation.

The four-step screening programme used a slightly modified questionnaire. Patients scoring ≥4 points were invited for further tests. Those with a random blood glucose(RBG) level of ≥5.5 mmol/l were further analysed in 1 week's time for Fasting Blood Glucose(FBG) level. Patients with a RBG level of ≥11.1 mmol/l and a FBG level of ≥6.1 mmol/l were categorised as having DMT2. If patients had a FBG level of ≥6.1 mmol/l and a RBG level of <11.1 mmol/l then they were invited for an Orale Glucose Tolerantie Test (OGTT) using venous blood. Similarly, patients with FBG level of between 5.2 and 6.0 mmol/l were invited for an OGTT. If a 2-hour OGTT level was ≥11.1 mmol/l then patients were invited for a second OGTT. No data on correlation between the two OGTTs is provided.

The three-step screening programme invited patients scoring ≥6 points on the risk questionnaire for measurement of FBG level. Those patients with a FBG level of ≥6.1 mmol/l, would undertake a OGTT. Patients with at least one diabetic value during an OGTT were considered diabetic.

For the four-step programme, a target population of 29,251 aged 50–69 years was identified. All were invited to complete the risk questionnaire. The number of patients invited for blood testing was not known. Approximately 11,000 (38% of the target population) attended the screening clinic for RBG testing. Of the patients invited for FBG, 91% attended the clinic. Out of 1209 patients invited for an OGTT, 75% attended.

A target population of 27,727 aged between 50 and 69 years was identified for the three-step screening programme. All were invited to complete a risk questionnaire. Again the number of patients invited for blood testing was not known; however, as per the target population, approximately 25% attended the clinic for FBG testing. Of those invited for an OGTT, approximately 81% attended.
The prevalence of known diabetes in the participating practices in the Netherlands was 3.1%. Using the four-step postal screening strategy, 285 patients were diagnosed with T2DM, which was 0.97% of the target population. A total of 301 (1.09% of the target population) patients were found to have T2DM using the three-step screening method.

In brief the program consisted of an early screening program, though some questions in the risk questionnaire are about the presence of DMT2 symptoms and therefore early detection: thirst. The Method further consisted of: risk questionnaire, random blood glucose(RBG), Fasting Blood Glucose(FBG), Orale Glucose Tolerance Test (OGTT).

Links. TK 18 https://diabetesjournals.org/care/article/38/8/1449/31344/Early-Detection-and-Treatment-of-Type-2-Diabetes

Appendix 3.

Study	Method	Multiple methods compared	Best result	Preliminary phase studied
P Whitley. et al. [11a]	A1c to standard	no	Hb1Ac.	Hyperinsulinemia
X Zue et al. [8a]	A1c to IFG and IGT	Yes	IFG and IGT	Diabetes and Prediabetes.
A. Khokar et al. [9a]	A1c and OGTT	Yes	OGTT or in combination	Prediabetes.
Sequiera. I et al. [70]	A1c	No	Hb1Ac.	Prediabetes

[11a] Whitley H.P., etb al. Systematic Diabetes Screening Using Point-of-Care HbA1c Testing Facilitates Identification of Prediabetes [Internet]. Available from: https://www.annfammed.org/content/annalsfm/15/2/162.full.pdf. [Accessed at 4th of November 2022].

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Appendix 4a Semi Structures Interview Internist Y. Sijpkens.

Test u naar hyperinsulinemie en insuline resistentie.?

Met welk doel testen naar hyperinsulinemie. Korte termijn doel. Lange termijn doel. Bij insuline resistentie.?
David Unwing Study. Firty Health.

Welke voordelen komt u tegen door naar hyperinsulinemie te testen.? Korter termijn. Lange termijn.

Welke symptomen gebruikt u als indicator.? Waarom deze. Mogelijk ook ziektebeelden. Hoe screent u uw patiënten.?

Welke testen gebruikt u om te testen naar hyperinsulinemie en Waar test u naar. ?

Welke voorfase focust u op.?
Hebben circadian rhythms of bepaalde factoren volgens u invloed op deze test.

Wat vind u van de FI/FG ratio test. ?

Vind je dat meer dokters moeten testen naar hyperinsulinemie.? Waarom.? Ook in Haaglanden.?

Waarom ook in de Haaglanden. ?

Is er volgens u voldoende oplevering om binnen het budget naar hyperinsulinemie te testen.?

Welke patiëntencategorieën komen voornamelijk bij u naar voren.?

Appendix 4b Transcribed interview internist Y. Sijpkens.

Transcriberen Gesprek Dokter Sijpkens op 13-10-2022.

Voorstadium van diabetes. Hoe we daar handen en voeten aan kunnen geven en uitrollen in de eerste en tweedelijns gezondheidszorg. **Ik weet dat u onderzoek doet naar de voorfases van diabetes maar doet u dit voornamelijk naar hyperinsuline als insulineresistentie. Of naar welke voorfases doet u met name onderzoek.** Ik trek het meteen breder. Voor mij de grote groep metabole ziektes daar gaat het uiteindelijk om. Daar is DM een onderdeel van. Maar ook obesitas en leververvetting. Ik ga zelfs zo ver dat sub klinische atherosclerose, aderverkalking, ook voor een groot deel een metabole ziekte is.
maar voor een deel ook maligniteiten, dementie, artrose, hormonale aandoeningen. Erectiestoornissen. PCOS. Die aandoeningen die vaak voorkomen en steeds vaker voorkomen. Steeds Vaker op jongere leeftijd voorkomen. Die kennen een gemeenschappelijke grondoorzaak en dat noem ik dan metabole dysfunctie. Dus je kan zeggen dat ik heb een hypertensie poli in Den haag. Je hebt een normale bloeddruk prehypertensie en hypertensie. Je hebt een normale bloedsuiker je hebt prediabetes en je hebt DM en je hebt DM. Dat is een beetje de oude manier van denken. Ik wil daar een ander paradigma aan koppelen. Dat de metabole ziekten in hun volle wagdom voorafgegaan worden door metabole dysfunctie. Dat is dus een opvolg term ten opzichten van het metabool syndroom. Want metabool syndroom is een hele oude term en de koppelingen van die ziektes en van atherosclerose is des tijds al gemaakt en de koppeling met insuline resistentie is ook al gemaakt. Want het heette voorheen syndroom x of zelf het insuline resistentie syndroom. Dus die basis die is er al alleen al in de praktijk heb. Ik gemerkt dat noch de huisarts noch de specialist werkt met de term metabool syndroom het is toch een beetje allergaatje en ik heb natuurlijk heel lang de componenten van het metabool syndroom overgewicht, wat hoge bloedsuiker, dyslipidemie heb ik als afzonderlijke entiteiten gewerkt. Vooral vroeg met farmacotherapie behandelt. Dus die samenhang dat kende onvoldoende en vertaalslag met de praktijk. Je gaat toch als snel met de onderdelen met medicatie gaat behandelen. Maar met de nieuwe inzichten. Ja kent het metabool syndroom kent die gemeenschappelijke grondoorzaak en ik vind dat de term metabole dysfunctie de term van de toekomst is en dat heeft er mee te maken voordeel dat het. Internationaal steeds meer gebruikt wordt. Nederland kijkt daar te weinig naar. Nederland zit wat dat betreft op een eiland en dat vind ik onterecht. Ik vind dat we ons als klein land een beetje moeten voegen hoe het internationaal gaat. Het grote voordeel is dus da het zich verbreed met leververvetting en atherosclerose entiteiten die je ook al heel goed kan herkennen voordat er ziektelast is bij patiënten. De inzichten in die gemeenschappelijke grondoorzaak komen dan ook beter tot hun recht en dat is veel complexer dan enkel wat koolhydraten gebruiken. He dus het een heel veranderde omgeving die we hebben. Met fijn stof en bestrijdingsmiddelen een heel ander een ander micromilieu waarmee we leven. Binnen zitten he veel stress die er is. Slaap tekort dat speelt allemaal een rol in die veranderde context en uh in ongunstige zin is ook nog eens het voedingsaanbod veranderd. Bewerkte voeding waardoor mensen veel te vaak eten dan krijg je dus een perfecte storm waardoor die metabole dysfunctie ontstaat als voorlopen van die ziektes kijk en de prediabetes is een van is een onderdeel uit maar dat is veel te veel in een hokje gedacht en vandaar die verbreding en dan kom ik dus op je antwoord uit. Hyperinsulinemie en insuline resistentie eigenlijk een veel betere parameter is om je daar op te richten omdat het een enorm voordeel ten opzichte van de suiker omdat het veel eerder op te pakken is de hyperinsulinemie is eigenlijk de eerste fase van de metabole ontregeling. Door de hyperinsulinemie blijven de glocose waardes lang goed. En pas na 10 jaar gaan die bloedsuiker waardes een beetje omhoog en nog eens 10 jaar verder heb je DM. Dus gemiddeld genomen is er een window van 20 jaar. **En is dat die 20 jaar mag ik hier even een vraagje stellen.** Ja wat wil je zeggen. **Ja die 20 jaar hoe komt u daar zo bij waarop is dat gebasseerd.** Nou je ziet bij voorbeeld in het NTVG artikel dat je bij kinderen al een hoge insuline spiegels en ziet en dat ja dat hoef je maar heel simpel te volgen. Dus als je gaat kijken longitudinaal wanneer gaan insuline spiegels stijgen in het leven. Dan zie je dat en dan is het dramatisch dat dat nou al bij kinder leeftijd is. Wanneer gaan de bloedsuiker stijgen. Nou wat is nou al het dramatische. Dat het nou op adolescentie. Dat wisselt dus per persoon. Ja. Dan hoe je dat maar te tracken en dan is dat ook niet verbazingwekkend dat DM op steeds jongere leeftijd voorkomt. En dat is dan dat hokje van suikers. Maar visceraal overgewicht staat op veel jongere leeftijd leververvetting op jongere leeftijd. Atherosclerose op jongere leeftijd en en en beelden als PCOS neemt toe. Ontstaat ook allemaal op jongere leeftijd het is een enorme pakket van ziekte last. En daar moeten we ons mee bezig houden. JA. **Het is dus eigen een soort van observatieve studie geweest waar het op gebaseerd is.** Ja ik vond het schokkend dat het in het NVTG dat kan ik me dan herinneren dat het dat de insuline spiegel ook een ander voorbeeld. In Den Haag hebben we vaak te maken met mensen uit andere culturen. En dan in het bijzonder zijn het vaak patienten met Surinaamse afkomst en het heeft dan niet zo veel te make met het geloof gebonden, hindoestaans of creools. Maarde mensen in Suriname de Zuid aZiatische afkomst daar is ook onderzoek over dat die groep de insuline spiegels aal vroeg in het leven hoog zijn. Het stomme is en ik hoop dat Mattijs en dit onderzoek daar aan bijdraagt is dat het de onderbouwing aanleveren dat we niet alleen de glucose moeten meten. Niet en Dat gebeurt ook nog niet eens een hba1c moeten meten dat we de transitie moeten maken van een glucose ziekte naar een insuline ziekte en dus is het ook logisch om zo een simpele goedkope maatregelen te nemen. Dus de afgelopen 4 jaar meet ik bij elke patiënt de FI waarde en dan zie natuurlijk met een enorme selectie die ik binnenkrijg aan patienten dat maar weinig mensen een normaal insuline hebben. En als ze een niet een hoge insuline hebben dan hebben ze een hoog glucose en dat is ook niet goed want dan hebben ze uh dan uh hebben ze een pancreas die niet zo goed functioneer den DM. Maar dat alles goed is en insuline laag en daarmee de gemiddelde bloedsuiker een hb1Ac laad en laag en een normaal lipide patroon en normale lever functie en een laag urine zuur en normaal vitamine D en op scan geen aderverkalking. Ja dat bij middelbaar leeftijd zijn. Maar weinig mensen die ik vang die op elk punt een groen vinkje scoren. Dus de meeste mensen van volwassen leeftijd min of meer metabool ongezond of hebben min of meer een metabole dysfunctie en het grote voordeel van dit paradigma is het heel goed in kaart te brengen is met een MB screening dat vind ik ook heel belangrijk woord. je screent niet op prediabetes maar je screent op MD met insuline waarden en je uhuh dat heb je het in een keer niet meer over primaire preventie hooguit maar secundaire preventie je hebt al een ontregeling. En dan ga je opweg naar de Metabole gezondheid en dat is dus heel goed meetbaar en de patiënt vind het geweldig om dat te zien van d ie metabole parameters allemaal die ik heb genoemd verbeteren en dan zijn ze blij en alleen het grote punt is voor het verbeteren van die metabole dysfunctie is naar metabole gezondheid is een leefstijl interventie nodig. En daar is het hele systeem niet op ingericht en daarom blijft achter en blijven we maar wachten en hopen dat we dit met medicijnen kunnen oplossen. **Ja. En even kijken want eigenlijk er is zijn 4 kenmerken voor MB en u heeft het al metabole dysfunctie. Welke beschouwd u daar binnen welke test op als u daar concreet in kan zijn.** Dat zeg ik net. Ik doe bij iedereen een MB screening een FI bepaling een nuchtere glucose bepaling een[19.04]. Hb1Ac. Nuchter panel in de lipiden met HDL triglyceriden ben eigenlijk veel minder geïnteresseerd in LDL dan trigelyceride :HDL ratio dat zou ook een enorme game changer betekenen als cardiologen bijvoorbeeld zich die daar op richten en niet blind staren op LDL dat wat met medicatie naar beneneden gehamerd moet worden met veel bijwerkingen. Een Een als je dat doet en je hebt geen aandacht voor de MD. Ja dan blijven die recidieven net zo makkelijk komen. Want die nou wat een rijtje af te maken. ALAT gamma GT dat doe ik als parameter voor de lever. Ferritine is ook een enorm onderschatte inflammatie marker die goed werkt. Ik neem vitamine D mee ,urine zuur mee, ik neem de albumine: creat ratio mee. Ik neem het viscerale de buikomvang mee met de ratio tussen buikomvang en lengte. En dan steeds vaker nu ook testesteron bij mannen en zelfs de oestrogeen bij mannen. Want mannen zijn vrouwen aan het worden en vrouwen zijn mannen aan het worden. **Mogelijk bijna.** Dat is toch niet de bedoeling van de natuur. Dus dat vang ik ook steeds meer problemen dus het is nogal een pakket. En dan in de beeldvorming een echo voor de leververvetting. Een CT calcium score ook een hele belangrijke die ik heel vaak doe. En dan heb ik het geluk dat ik de autonomie heb in mijn ziekenhuis dat ik dat gewoon mag aan vragen en dat zo een aanvraag gehonereerd wordt want dat staat onder druk want het wordt toch steeds meer een krapte model. En dan kun je op een gegeven moment die dingen niet aanvragen ook met een insuline bepaling mijn collega's doe het niet omdat het niet in de richtlijn staat omdat ze denken dat dat te duur is en omdat ze eigenlijk niet weten dat het zo'n een belangrijke parameter is en dat het ze niet geleerd. Dus die doen het allemaal niet dat is heel zwart wit. Ik doe het altijd en de rest doet het eigenlijk vrijwel nooit. Hooguit en dat is al nieuw in de diagnostiek van de DM. **U noemt nu best wel veel waarden die u meet. U zegt u meet het bij elke patiënt. Dan bij daadwerkelijk elke patiënt die binnen komt of enkel bij enkele symptomen of klachten.** Nou ik doe het bij elke patiënt. Dan gebruikt ik het eigenlijk ook als een nul meting want dan kan ik zien dat bij een jong persoon dat die nog metabool gezond is . Mensen komen bij mij altijd bij een klacht. Chroniche vermoeiheid is een goed voorbeeld dan een normale normaal gaat dan doe je een ijzer status dat is meestal goed. Een vit D dat doet ook niet lang niet iedereen nou ook niet zo laag Ik doe dan de schildklier bij 9 van 10 mensen met CV zijn die parameters goed en dan zegt men op mijn terrein hebt u geen klachten u bent gezond het gaat vanzelf over ga maar terug naar de huisarts. dat noem ik Uitsluit geneeskunde dat is de norm geworden van de gezondheidszorg. Ik wil het omdraaien omdraaien. Ik ben dus geïnteresseerd in wat die mensen wel hebben ik ben dus geïnteresseerd of op jonge leeftijd ook al een MB component te vangen is die verklaard dat er mensen mentaal een minder goed functioneren wat blijkt nu dat de leestijl interventie die nodig is voor MB gezondheid ook nodig is voor mentale gezondheid ook nodig is voor het herstel van de microbionme bijvoorbeeld . Het loopt allemaal over elkaar heen en dan heb ik het diee dat met een leefstijl interventie ik mensen meer help met CV ik geef ze zelf de regie en verantwoordelijk heid terug dat ze er ook zelf wat aan kunnen doen en dat maakt voor mij de manier van werken veel positiever. Dus ik zou nooit meer terug kunnen naar. Ja een beetje de mijn oude manier van doen. Ik ben niet oordelend naar mijn collega's ik weet waar ik vandaan kom ik ben nog steeds een echte mecijn man en zet medicijnen in waar nodig is. De lol is nu dat ik veel minder medicijnen hoef te starten en veel minder medicijnen. Hoef toe te voegen. En sterker nog. Ik ben u bezig met zoveel mogelijk aan het afbouwen aan het demedicaliseren en dat vind ik nou echt weer een mooie internistische taak om mensen van de medicijnen af te helpen dus ik heb jaren lang meer meer gegeven omdat ik als een pietje precies als een echte internist elke streefwaarde op orde wilde hebben en maar deed dat vooral met medicijnen. Nu met leefstijl ben ik gericht op MB gezondheid inplaats van dan ldl en ik heb veel minder medicijnen nodig en dat is heerlijk voor de patiënt daar gaat het uiteindelijk om en die is daar tevreden mee en ook nog dat je ook niet enkel de patiënt ermee behandeld maar ook de partner en de familie ik heb daarmee een brug naar hele gezinnen end omdat het goed werkt via mond op mond reclame heb ik denk ik de afgelopen 4 jaren in Den Haag al heel erg veel kunnen bereiken. En nemen geleidelijk aan meer zorgverleners deze manier van werken over maar dat loopt nog gigantisch achter. **En u even kijken u heeft eigenlijk al indirect enorm veel vragen beantwoord ik ben benieuwd omdat het kosten plaatje behoorlijk relevant is en er toch wel een behoorlijke druk staat op de kosten in het ziekenhuis en het budget waar artsen het mee moeten doen. U test dan bij elk van uw patiënten elk van die testen/. Naja U doet het dus u vind het kosten effectief. Vind U vind dus dat door binnen het budget van ziekenhuizen daar voldoende ruimte voor is.** Nou ja het zijn hooguit collegas die daar kritisch naar kijken. Die zeggen Het moet allemaal leaner. Je moet je beperken tot de vraagstelling van de huisarts, Als die iet met bloeddruk doet moet je de bloeddruk meten en niet suikers vaan meten. En dat is er is zoveel druk op de gezondheidszorg dus je ziet nu een tendens dat we nu eigenlijk minder mogen doen ook om sneller en meer patiënten te kunnen werken. En meer patiënt aan te kunnen. En daarmee komt de leefstijl nog meer onder druk te staan terwijl in het macro kader de manier waarop ik werk miljoenen al bespaard heeft en nog doet. Want bij uitstek is dit om een hartinfarct een beroerte een volle DM met insuline met maligniteiten dementie artrose met kunst knieën te voorkomen. In het buitenland in Engeland en in Amerika hebben ze dat netjes kosten effectief berekend maar wij zijn dan in Nederland lijkt het er inderdaad op dat we in het ziekenhuis niet meer mogen uitgeven en aan preventie mogen doen zodat bij die besparing niks terecht komt. EN we kunnen het niet aan. Dus dat is voor mij een belangrij motief. We worden overspoeld door zorgvragen die in prince te vermijden zijn 70 tot 80 procent van die Chronische Zieken zijn vermijdbaar als je er voor zorgt dat mensen vanaf jonge leeftijd metabool gezond blijven en als ze dan al als het al ontstaat om het dan in de kiem te smoren met een leefstijl interventie dan is het al moeilijke genoeg met laag sociale economische klasse en omgeving die er niet aan mee werk. He dus dat snap ik ook wel. Maar je kan veel meer bereiken dan mensen denken. Ook bijlage 6 en andere culturen. Mensen willen uiteindelijk gezond hun leven leiden en als ze dan ook weten. Hoe dan veel gemotiveerder dan ze denken. Als steeds meer mensen er naar vragen dat de omgeving hopelijk daar n aar veranderen omdat er meer vraag ik naar gezonde producten **Ja Ja. Eigenlijk beantwoord u al een beetje de volgende vraag Want U merkt dan ook daadwerkelijk dat mensen er wat mee gaan doen met de resultaten van de testen.** Ja **Dat is toch vaak het dilemma een beetje.** JA natuurlijk want omdat dit kijk waar hangt het nou van af. Wat ik net zei net. Da heb ik nog niet verteld dat de metabole gezondheid moet herstellen met een leefstijl. Interventie alleen een leefstijl interventie is een gekaapt begrip is een paraplu term wat iedereen met zijn eigen term in vult en er verschillende dingen onder verstaat. Ja daar probeer ik leiding aan te geven het gaat er om welke leefstijl interventie geschikt is voor de individuele persoon en dan kun je dus niet weg komen met hoe het ging en nog vaak gaat let maar een beetje op uw gewicht. en dat komt het dus goed. Ga maar naar de GLI en dan komt het wel goed ga maar naar uw dietiste dan komt het wel goed. Het denken van een zorgverlener hebben ze dan aan een leefstijl gedaan maar inhoudelijks stelt het niks voor mensen komen terecht met bij goed bedoelende zorgverleners met een enorm verschillende achtergronden en dan is er dus een variatie in praktijk variatie en dan zijn het vaak schadelijk adviezen die niet werken en dan ja de patiënt heeft geen resultaat en wat zegt vervolgens de zorgverlener de patiënt is niet gemotiveerd en omdat dit zo vaak is voorgekomen en dan denkt een zorgverlener ik vul het dan in voor anderen maar zo hoor ik het ook terug. Van nou een leefstijl interventie heeft geen zin omdat het A niet werkt en het werkt niet omdat er geen motivatie is en we hebben geen tijd en dan proberen we met motivational interviewing een beetje in te vullen maar dat is ook op hele onvolkomen manier omdat er geen. Tijd voor is. Omdat er geen training voor is. En daarin komt. Wat er aan leefstijl wordt gedaan is eigenlijk niet goed. Terwijl. Als je het goed doet dan pas werkt het en dan ontstaat de motivatie. Dus je moet het omdraaien. **Even een vraagje tussendoor. Kunt u mijn goed horen of hoort u veel achtergrond geluid.** Ja Ja. HA nee ik praat vaak heel vele ik ben blij als u mij hoort. **ja hoor duidelijk. U heeft dus geen last van de achtergrond geluiden.** Nee hoor nee. Nee. **Oh prima. Even kijken uhm. Naja ik had een vraag komen bepaalde patiënten categorien met name naar voren maar u test eigenlijk bij elke patiënt.** Bij jong en oud. Goed en laag opgeleid. Heel veel mensen hebben het idee dat ze goed leven . En als ik daarop doorvraag dan schrikken ze ervan dat welke majeuren verbeter punten zijn. Mensen vallen van hun stoel af dat het echt beter kan. Patiënten zitten in die beleving dat ze het goed doen. Er is heel vaak ruimte voor verbetering. **Uhm even kijken. Ja ik was ook nog benieuwd want ik heb onderzoek gedaan naar bloedwaarden en cortisol bijvoorbeeld en adrenaline hebben invloed op de insuline. En Ik was benieuwd of daar ook op let wanneer u etst. Met bijvoorbeeld de circadian Rhythm ik denk dat u bekend bent met die term.** Ja zeker zeker nou je moet het uhm dat zijn nieuwe invullingen. Je hebt helemaal gelijk. Er is een grote behoefte aan. Meten van stress alleen de cortisol waarden wat ik steeds vaker mee neem is dat niet zo een goede maat voor. En ook de catecholimines die we meten in mensen met hypertensie is ook niet zo een goede maat er voor. Ik gebruik dus steeds meer wearables. Nou hier een horloge waar de heartratevariability op staat en dus ik heb. Nu heel goed geslapen en dan kan ik nou dan klopt dat en op mijn. Body battery staat 95 dus ik heb een geweldig goede kwaliteit gehad en dus nou ondanks dat ik drukke dag had gisteren dus daar ben ik blij mee dus daarmee meet ik mijn stress niveau en voel ik nu ook de energie om een goed interview af te leveren waar je wat aan hebt en kan ik straks weer de hele dag poli doen en vanavond tennissen dus de hartrate variability die ik nu meet dan doen dat doen de mensen nog niet terwijl dit helemaal niet een heel kostbaar horloge is. Je hebt daar geen auraring voor nodig. Maar dat is een wens van mij om een stress meter te hebben en het leuke is dus de educatie ik opzoek al die biohack zitten daar in hoe meet je dan slaap hoe meet je je stressniveau en dan heb je daarmee als individu een feedback op hoe je je voelt. En dan de glucose Ik raad elke patiënt aan ik geef enkele een blaadje met de basis van de leefstijl interventie en daar staan ook bronnen bij en daar heb ik heel snel de insulinerevolutie van insjape LP bij aan gezet en dat vind ik heet heel belangrijk onderdeel van de strategie die ik waarschijnlijk de meeste kans geeft dat doormiddel van citizen sciences via mensen gewoon patiënt of mensen die het oppakken. Dat daar de mensen terecht kunnen. Om te leren hoe ze metabool gezond moeten worden. Omdat ze helaas bot vangen bij hun huisarts of specialist. Dus de nu zie ik dat specialisten en huisartsen links en recht ingehaald worden door coaches die een veel beter resultaat hebben. Omdat die met de leefstijl interventies zoals het hoort aan de gang gaan en die nemen dus die nieuwe ontwikkelingen en nieuwe boeken wel mee terwijl een zorgverlener wachten op de richtlijnen. Nou dan kun je lang wachten tot er iets verandert. **Wat u zegt nou. Cortisol af en toe wel mee af en toe niet. Maar als u kijkt naar het feit dat dus meerdere hormonen elkaar beïnvloeden en daarmee levels van insuline beïnvloeden. Als je kijkt naar cortisol. Die level zijn in de ochtend om 7 uur 8 uur het hoogst volgens de wetenschappen. Dan zou dus insuline wat dat betreft relatief onderdrukt worden. Wat ik ervan begrijp.** Nee nee. Fout. Helemaal niet. Het tegendeel. Cortisol is een aanjager van insuline. Mensen met stress hebben juist een hoge insuline. Het voedt de insuline resistentie natuurlijk. Dat kennen we van de ziekte van Cushion. Je moet altijd kijken naar een uitgebroken ziektebeeld nou wat een van de kenmerken is diabetes ontwikkeling en insuline resistentie. Met hoge insuline spiegels. Dat verbaast me dus. Hooge hoge maten dat de endocrinologen in Nederland zo weinig interesse hebben in insuline en zo weinig interesse hebben in vitamine D. Het gewoon niet meten en daardoor zijn die verbanden niet alom bekend. En dan kun je ook ineens zo een opmerking maken dat hoog cortisol insuline onderdrukt. Nou dat is totaal de verkeerde kant op. **Nou dat is dan fijn om bij deze te horen. Let u op welk moment van de dag u de insuline meet omdat bepaalde factoren de insuline waardes kunnen beïnvloeden.** Nee ik zei ik meet het circadiale rhythm is enorm van belang. Dus je moet erop letten op welk moment je dat meet. Testesteron ben ik vaak aan het meten en dat moet je in de ochtend meten. Dat zie ik dan als een soort marker voor metabole syndroom. Ik hoop dat de kennis zich ontwikkelt dat we ook iets met cortisol kunnen doen. Dat een hoog normaal cortisol of mogelijk een hoog normaal aldesteron vaker voorkomt bij mensen met een metabool dysfunctie. Maar die kennis die ken ik nog niet en ik hoop dat die kennis tot ons komt. Dat is gewoon nog heel veel onderzoek nodig naar al die verbanden. Maar als ik cortisol afneem houd ik rekening met. Behalve als een patiënt duidelijk dik in de stress zit dan en ik benieuwd wat doet die cortisol nou eens. En dan ja dan hoog normaal cortisol wat zegt me dat dan in die persoon. En als er dan beter tijden zijn voor die persoon daalt dan dat cortisol en daalt daarmee ook het insuline want dat is voor mij het belangrijkste deel van het werk dat ik aan de slag ga en dat ik dan de insuline controleer en vroeger dacht ik. Ik beperkt de koolhydraten of de mensen doen dat zelf en de insuline ermee naar beneden en alles komt. Goed maar dat is helemaal niet zo. Ik zie dat bij een groot deel van de mensen de insuline hoog blijft terwijl ze koolhydraten beperken en daaruit heb ik geleerd dat je een voeding en leefstijl interventie veel breder is om dat doel te bereiken dan neem maar wat minder suiker of eet geen brood meer. Dat is bij de categorie patiënten de gevorderde patiënten die ik zie is dat veel te simpel. En en mensen denken met de manier waarop ik werk dat het alleen maar dat doe. Maar ik heb het zo doorontwikkeld naar een volledig pakket aan maatregelen dat ik als dat ik maar dat insuline naar beneden krijg. **Het is eigenlijk een enorm bouwwerk dat elkaar beïnvloed. Wat dat betreft het metabool.** En veel ingewikkelder dan je denkt. Ik vind dit een veel grotere uitdaging om op deze manier. [42.05]Met dit concept te werken. Dus mijn internisten bleod stroomt als een dolle en ik werk op de top van mijn kunnen om bij de individuele patiënt die metabole gezondheid weer te krijgen en dat is zoveel mooier en uitdagender dan allen maar met pillen werken. Alleen het gezondheidssysteem is e rniet op ingericht. Vroeger dacht ik dat elke collega dat meot doen. Dat denk ik helemaal niet. Ik denk dat het echt specialisten werk is en dat het zorglandschap moet veranderen en dat je dit moet outsourcen naar toegeruste huisartsen. Leefstijlhuisartsen dat inderdaad die leefstijlcoaches met je leefstijl als medicijn. En daar ben ik dan bewust mee adviseur om die organisatie tre voeden met kennis zodat ik daar mensen naar toe kan verwijzen. Met dieet en leefstijl nieuws op de website elke twee weken en desgewenst een FB groep waar ze support krijgen. Daar bereik ik je veel meer mee dan als je als individuele dokter zonder tijd een half advies geeft. **En even kijken mijn vraag was eigenlijk ook of u vind dat meer artsen dit moeten doen. En dat is eigenlijk wel redelijk duidelijk ja.** Specialiscren wel specialeren bij. Je moet je er echt op toeleggen en hoe eerder je dar me begin als in de opleiding leefstijl dat echt de volwassen aandacht krijgt dan daar moet het mee beginnen. Dan moet het in de opleidingen een belangrijke rol spelen. Of je nou gyneacoloog bent er moeten specialisten komen op dit gebied. Dus als je als gynaecoloog met PCOS werkt dan moet ermee aan de slag maar ook een uroloog die met uritiele dysfunctie werkt of met prostaat hypertrofy nou daar ligt ook de wereld open. Als ik vraag aan een uroloog en ik vraag waarom is de prostaat groot bij die patiënt dan zeggen ze nou het zijn mannen en dze zijn wat

ouder. Veel verder komen ze niet. Dus een metabool invloed herkennen in zo een ziekte beeld nou dat die kennis is er nog helemaal niet. Dus over de gehele geneeskunde is er ruimte om dit op te pakken. Maar dan moet je dat goed odne en daarop studeren en specialiserren en dan kunnen de collegas die daar minder tijd voor hebben daarvan profiteren. Het systeem op orde hebt. Ik heb bijvoorbeeld eigen dietistes opgeleid. En die kunnen dezelfde adviezen geven die ik geef maar die zijn met een langepje te zoeken. En als je dat niet zelf organiseert dan wordt het niks. En daar gaat het om. **Oke even kijken. Ik denk dat u eigenlijk de meeste vragen al beantwoord heeft. Hm. Ja ik had de vraag dus wat zou de tweede lijn voor functie hierun kunnen hebben. Maar dat heeft u al behoorlijk beantwoord.** De arts en leefstijl ik commiteer me nou ook aan arts en leefstijl en ik denk en ik zie ik denk dat ik ook de eerste specialist was van die club. Het was eerst arts en voeding en toen arts en leefstijl dus ik volg alles. En dus daar zit nou bij Douwe artsma in het bestuur een cardioloog waar ik veel mee optrek. Dat vind ik een heel goede ontwikkeling en elk jaar zie ik meer specialisten landen bij die club. En als specialist neem je dan ook al snel de leiding en we proberen nou ook we hebben gister ook een arts en leefstijl werkgroep opgericht omdat concept verder handen voeten te geven en te communiceren via webinars en via de arts en leefstijl week. Nou en ik kan kijk Mattijs geeft nou een praatje op de internisten dagen. Dat vind ik geweldig. Zit ik ik nou is een handje vol specialisten die die kant op durft te gaan. En dat ik voor mij heerlijk he dat ik niet alleen ben want zo heb ik me jaren lang gevoeld. Er was Janno pel in leiden en ik verving als Janno het te druk had om in zijn naam een verhaal te houden. Het hoogte punt was het asecco health symposium Daar kun je ook naar kijken. Dat was in het Engels. Dat was in Juni afgelopen jaar. Daar heb ik echt een groot podium gepakt om metabole dysfunctie neer te zetten. En dat is heel goed om te ontvangen en internationaal heb ik ook al een aantal verhalen gehouden en daar pakken ze het veel makkelijker op. **Ja ik zou u nog concreet kunnen zeggen wat voor u het verschil is tussen het metabool syndroom en metabole dysfunctie.** Zeker. Het metabool syndroom is maar 5 items. Er zijn criteria voor opgesteld. Van het metabool spreken als je 3 van de 5 criteria hebt Dat is heel instrumenteel geweest omdat met die criteria goed onderzoek is gedaan. Om de gevolgen van het metabool nsyndroom goed in kaart kan brengen. Dat is dan ook dat ik hard kan maken dat atherosclerose een metabole ziekte is. Dat is algemeen bekend. Hard maken dat insuline resistentie gekoppeld is aan het metabool syndroom. Maar voor de clinicus vandaag de dag is het te eng dan ga je weer plussen en minnen met criteria en bij een patiënt werkt het zo niet. Met wat ik heb uitgelegd. Bij mij is een hyperinsulinemie dat geen onderdeel uitmaakt van de criteria is uh uh een belangrijke parameter voor de metabole dysfunctie. Zo is ook leverceatose een [48.26]. belangrijke parameter en zit niet in het metabool syndroom. Dus eigenlijk het een betere invulling en het is een betere prikkel om met patiënt op zoek te gaan naar de grondoorzaak waardoor je op een leefstijlinterventie komt. Met het metabool syndroom kom je eerder bij medicijnen terecht in plaats van dat je leefstijl interventie aan de slag gaat. **Dus dan is eigenlijk het eigenlijk het hele functioneren van het metabole functies end an daar de dysfunctie van . Zo breed als je bijna het maar kan maken dan eigenlijk.**

En kijk omdat je over dysfuncties spreekt dat geeft de brug naar metabole gezondheid. Nu weet je precies wanneer ik iemand metabool gezond kan verklaren. **Ik verwacht dat ik het wel begrepen heb nou. Ik wou nog proberen in kaart te brengen voor mezelf. Zou ik u misschien nog kunnen mailen. Om te kunnen kijken of het klopt hoe ik het heb opgevat.** Het enige wat je niet gevraag hebt is. Waar bestaat nou de leefstijl; interventie uit. Hoe doe je dat nou in de praktijk. [50.26].

Dat kun je niet in een consultnuitrollen over de patient. Dat moet stap voor stap. Er speelt verslaving een rol in voeding. Dat hoort er allemaal bij.

Te integreren met de huidige geneeskunde en dat het niet een aparte status wordt. **Geneeskunde daar hoort leefstijl bij.**

Welke blemmeringen ervaart u. Merkt u weerstand in het ziekenhuis mogelijk ook van de patiënten. Nee de patiënten willen het wel . zeker als ik vraag kan ik wat verder kijken naar je gezondheid iedereen is geïnteresseerd. Bij Collegas en ziekenhuizen loop ik met name vast op de kliniek hebben. We ook afspraken moeten maken en als ik dit ook in de kliniek ga doen dat kan het systeem niet aan. Collegas zijn er niet vertrouwd mee en assistenten moeten al zoveel leren. Op acuut gebied. En dan doe ik niet mD bij iemand ie opgenomen wordt voor ene erysitenlast terwijl ik dat wel nodig zou vinden. Als het aan mij ligt zou ik deze manier van werken ook in de kliniek doen. Met het argumentb bdat een opname van een patient een teachable moment is. Dus ook naja het hele voedingssysteem van een ziekenhuis is daarop niet ingericht. Het wordt er allemaal niet beter op. Dat is echt symptoom behandeling AB AB AB. Heel goed als he nodig is een boze bacterie van buiten behandel je met Ab. De gastheer speelt geen enkele rol in de behandeling. Dat is de wereld op zijn kop voor mij. Het begint voor mij b=nij de gastheer. Wat is er met de patiënt dat ik de bacterie krijgt. Wat is er niet gezond aan het immuunsysteem. Dat hebben we ook gezien bij corona dat oudere ondervoede mensen met weinig spiermassa de grote categorie en de jongere mensen die metabool ongezond zijn. Dat zijn de mensen die in het zienkenhuis komen tijdens de corona tijd maar ook buiten de corona tijd. En daar doen we niks mee. Dat is volgens mij echt het grote falen avn het huidge gezondheidssysteem. De koppel niet maken tussen de pandemien van MD en de infectie pandemie die er is. Dit ligt wat gevoeliger maar is wel echt mijn menig erover.

Enkel op de poli doet wordt MD screening gedaan. De kliniek niemand.
Zit daar een verschil in gebruik van budgetten. Mijn collegas en assistent zo druk dus daar moeten we focussen op wat prioriteit heeft en daar ben ik het mee eens en dan moet je de zorg niet moeilijker en duurder maken dan die is. Dus zo snel mogelijk de infectie behandelen en weer naar hius krijgen. Dat is nu een alles wat we aan extra aandahct hebben voor de gastheer hebben we de luxe niet meer voor. Daar begint de gezondheidszorg te imploderen. Daarmee voorkom je natuurlijk niet een komend recidief. Allemaal draaideur patiënten. Die met de een na de andere metabole ziekte aan de hand is. **U ervaart wel de ruimte dat te doen bij de poli patiënten.** Moet veel meer tijd erin stoppen tot 7 uur in de avond met bel spreekuren. Ik ga nu de mensen bellen die vanmmiddag op mijn spreekuur stana om met de behandeling over leefstijl te praten. 15 minuten poli en 20 minuten nodig. Bij de eerste afspraak heb ik een half uur terwijl ik drie kwartier tot een uur nodig heb. Die tijd is er helemaal niet. **Dus opzich is tijd daarin een belemmering. Ervaart u dat u dus wel die tijd weer ruimte doordat u dat erin steek op lange termijn dat het die mensen gezonder maakt.** Nou dat voordeel gaat naar de patiënt toe. Die tijd besparing zie ik niet rterug. **Dus dan doet u behoorlijk veel in uw eigen tijd.** Bijna iedereen heeft hier behoefte aan zo een gesprek. Ik vraag dan of de patiënt de behoefte aan heeft. Dan draai ik. Het plateau om. Ik ben een internist met veel ervaring en brede kijk., Waar zit u mee en dan komt er vaak een heel mooi gesprek en dat geeft veel voldoening. Het kost extra tijd en die is er in het systeem niet en die wordt er ook niet voor gemaakt. Dat gaat ten koste van de productie en dat zouden veel te veel patiënten zijn. Dan zou je opeen. S heel veel wachtlijsten krijgen. Dus we noeten eht buiten de gweone zorg om organiseren. Daar zijn dus ik en Mattijs voor nodig om daar leiding aan te geven. **Die tijd is dat dan u eigen tijd. Hoe maakt u daar tijd voor.** IN eigen tijd. 11 uur werk ik noon stop. Dat kan ik doen omdat mijn eigen metabole gezondheid goed is. Dat is te veel en niet gezond. Ik moet nu heel bewust mijn ontspanning momenten vinden op een dag om dit zelf vol te houden. En dan zie ik de meeste artsen niet doen en vooral lang volhouden. Dan komen ze in een burn out en dan krijg je een vicieuze cirkel dat zie ik ook veel ontstaan nou. **Wat betreft zou er ook al meer naar preventie gegaan moet dat mensen niet zo ver komen meer informatie zodat en dat als ze bij u komen dat ze gezonder zijn. U heeft de meeste vragen wel beantwoord. Heeft u zelf nog iets wat u wilt noemen of misschien aan Mattijs dat u nog wilt zeggen.** Ik heb net eigenlijk de belangrijkste aanvulling al gedaan wat de leefstijl interventie inhoud. Kennis is de informatie aan het exploderen. Moeten met een efficientere manier en kennis naar Nederland moeten halen zodat meer mensen ervan profiteren. Naja ik gebruik nu maar alle genia die voor mijn voeten komen. Met de podcastbereik je al veel meer mensen. Meestal een op een in gesprekken. Congressen en nascholingen om dit verhaal te vertellen. Dat valt me eerlijk gezegd nog ene beetje tegen gegeven het feit hoe belangrijk dit is.

Personeelstekort. Budgettekort zorginfarct wachtlijsten. Het is zo belanrgijk dat je dit als dokter wil. De mooiste manier om op dot manier te werken dat gun ik elke collega en dan moet je daar de voorwarden voor genereren.