A Wireframe Representation of a Prototype Clinical Decision Support Tool

For the Management of Cardiometabolic Disorder and Diabetes Type 2

Gregory Don Aeschliman

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Committee:

Peter Tarczy-Hornoch

Michael Leu

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Abstract

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Gregory Don Aeschliman

Chair of the Supervisory Committee:

Peter Tarczy-Hornoch

Department of Biomedical Informatics and Medical Education

This research developed a wireframe representation of a prototype Clinical Decision Support Tool that enables the comprehensive, efficient and efficacious management of patients with Cardiometabolic Disorder and Diabetes Mellitus Type 2. This research took place in the Eastside Health Network, an Accountable Care Organization and employed user-centered, iterative design principles to create both the user interface and the backend decision support logic. The design process took place in the context of a cross-functional team of physicians, pharmacists, diabetic nurse educators, care managers and administrators.

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Abstract

The goal of this research is to develop a wireframe representation of a Clinical Decision Support Tool that will enable the comprehensive, efficient and efficacious management of patients with Cardiometabolic Disorder, CMD and Diabetes Mellitus Type 2, DM2 who are receiving their care in the Eastside Health Network, an Accountable Care Organization, ACO. This wireframe will serve as the model for developing the launch version of the Clinical Decision Support Tool, CDST. This research took place within the Eastside Health Network, EHN, an ACO in Washington State where the trainee serves on the Patient Quality and Contracting Committees. The wireframe was created based on user-centered design principles that created the success measures involved in caring for those patients with DM 2 who are enrolled in the ACO. The wireframe also incorporates the on-going experience gleaned from a cross-functional team of physicians that includes the trainee, pharmacists, diabetic nurse educators and care managers who are addressing the needs of individuals whose DM2 is severely out of control. This cross-functional team comprehensively addresses the spectrum of the care of these individuals, including blood sugar, lipid, and blood pressure control as well as any identified psychosocial needs. Based on a review of the literature and the expert opinions of the members of the Patient Quality Committee and the cross-functional team, a set of clinical care rules regarding the care of patients with Diabetes Mellitus Type 2, DM 2 was agreed to. These rules will be realized using conditional logic in the launch version of the Clinical Decision Support Tool, CDST. This logic is directed at the personalized care of the individual patient being cared for, based on the unique healthcare attributes of that individual. The logic assigns patient's level of risk, and addresses the patient's psychosocial needs as well as blood sugar, lipid, blood pressure control. The user interface was iteratively improved to reflect the user group's consensus via input from a

structured meeting with the entire Patient Quality Committee and multiple interactions with a subset of the committee involving clinical pharmacists, care managers and clinicians.

Preface

Caregivers providing care for patients with CMD and DM 2, are faced with three related, crosscutting issues. These include the disease complexity represented by these patients(1-3), the proliferation of new medications used for treating them(4-6), and the market pressures clinicians who are working within an ACO face as they are forced to change practice workflow patterns in order to deliver more value in the in the care delivery process(7-10). A measure of the cognitive load placed on these Caregivers can be illustrated by looking at the number of papers recently published concerning DM2. A PubMed search "Diabetes mellitus type two medications" limited to 2018 returned 440 references(2), and a similar search of "diabetes mellitus type 2" returned 7997 references(11); keeping up with the literature focused on DM2 alone is an impossible task for a busy Caregiver. These crosscutting issues create the context for the development of the Clinical Decision Support Tool directed at the care of individuals with CMD and DM2(12-15) that will be presented in this Thesis.

This context is expanded in the next few paragraphs where the themes of these crosscutting issues are introduced more fully. These include the complexity and increasing prevalence of CMD and DM2, the proliferation of medications available to treat these diseases, and marketplace pressures caregivers face as they work to deliver more value. After these issues are introduced, the core themes of this Thesis are presented, followed by an outline of the Thesis itself.

Common, Complex and Increasingly Prevalent

Cardiometabolic Disorder and DM 2 are common, complex diseases, their prevalence is increasing(16-18) and the sequalae of these diseases are creating an ever-increasing burden on those delivering care for these patients(19-22) These sequalae include conditions like a myocardial infarction(23, 24), stroke(25, 26), visual impairment(27, 28) and diabetic nephropathy(29, 30), including the need for renal dialysis(22, 31, 32) and renal transplant(33, 34).

New Medications

Several new medications have become available for treating patients with CMD and DM2(8, 35). Keeping track of these medications and when to use them, (these patients are often prescribed several of them together to manage their disease)(36), presents an ever-increasing cognitive and emotional load on Caregivers who are managing these and other chronic conditions(37-41)

One of the functions of a Clinical Decision Support Tool is to support the Caregivers in the clinical setting as medication management decisions are made(12). There is a need to increase the efficiency and efficacy of the care being delivered to patients with CMD and DM2(42-46).

In summary, Cardiometabolic Disease, CMD and Diabetes Mellitus Type 2, DM2, are prevalent, complex, costly diseases that require a disproportionate amount of care relative to other common conditions requiring treatment. Caregivers are under progressively increasing financial pressure to increase the value of the care they deliver, and several new medications for the care of patients with CMD and DM 2 are available, further adding cognitive load to a Caregiver's daily work. A Clinical Decision Support Tool aimed at addressing the care of these patients is presented as a potential solution.

The Pressures of the Marketplace

Marketplace pressures are requiring caregivers to address both the cost and quality(47, 48) of care they are delivering while also delivering this care in a manner that is well-received by patients (49, 50). These factors, (cost, quality and patient experience), are collectively referred to as the "Triple Aim," and represent the value, (as defined by those entities that pay for healthcare), of the care being delivered(51-53). Generally speaking, the objectives of the Triple Aim, combined with financial incentives, is referred to as "Managed Care"(54, 55). In this model, Caregivers can earn either extra revenue for excellent care management or be faced with severe financial penalties if these factors are not well-managed. An Accountable Care Organization, (ACO)(56), is an example of a Managed Care Organization. The Eastside Health Network, an ACO in the greater Seattle region, provides the context for the development of the Clinical Decision Support Tool mentioned above.

Within an ACO, the quality of care as it is defined by the healthcare payers involves a broad array of measurements such as the number of mammograms, colonoscopies or adolescent well-child exams have been done by the ACO. Given the prevalence, complexity and cost of care associated with CMD and DM 2, caregivers in an ACO have incentives to manage these disorders aggressively in order to either receive additional performance-based payments from the insurance company, or to avoid financial penalties for not managing these patients cost-effectively. Within the various ACO contract with payers, there are several outcomes metrics associated with the care of patients with CMD and DM2 including such values as their hemoglobin A1c, (HbA1c), levels, their LDL cholesterol levels, and their blood pressure and the expected clinical outcomes associated better management of these disorders(57, 58).

Core Themes in this Thesis

As noted above and as will be covered in detail in Section 1.2, CMD and DM2 are complex disorders that require a comprehensive approach to managing patients with these disorders. Throughout this Thesis the theme of a comprehensive approach to the care of these patients, enabled by a web-based Clinical Decision Support Tool will repeatedly surface in two distinct ways.

First, from a comprehensive medication management perspective, the successful treatment of patients with CMD and DM2 will focus not only on the patient's blood sugar(59), but also on blood pressure(60), lipid levels(61) and abnormal renal function when present(62).

Second, from a more global perspective, comprehensive care includes a personalized(63), patient-centered(64, 65) approach within a clearly-defined, team-based integrated healthcare delivery system, which in the present context is an Accountable Care Organization, ACO(66). The role played by PCP's in the care of diabetics is increasing(67) and other healthcare team members including diabetic nurse educators(68), pharmacists(69), case managers(70) and medical specialists in endocrinology, cardiology and nephrology are needed(71-74).

The web-based Clinical Decision Support Tool, CDST, presented in this Thesis supports this bifid comprehensive approach by gathering an extensive set of patient data, (including biometric data, psychosocial data, laboratory data and medications focused on blood pressure, lipid and blood sugar management), infers an assessment of the patient's status, generates management recommendations and creates an action plan for both lifestyle and medication management, and a team based approach to care, based on which recommendations the patient is decides to follow. This functionality is covered in Section 4.4 below.

In summary, CMD and DM2 are complex, common, increasingly prevalent disorders that more frequently need to be managed within the context of an ACO. The number of medications available to treat these disorders is increasing and a comprehensive medication management approach, within the context of a comprehensive, integrated healthcare delivery system is required to manage these patients successfully. The web-based Clinical Decision Support Tool presented in this Thesis is designed to efficiently support the workflow involved in a comprehensive approach to the care patients with CMD and DM2. The layout and divisions of this Thesis are covered in the following section.

Overview of this Thesis

This Thesis is divided into five chapters. Chapter 1 describes CMD and DM2 in some detail, reviews certain aspects of the pathophysiology involved in the sequelae of these disorders, while also delving into the societal impacts caused by the disease burden associated with these diseases. It will examine what we know about these diseases, why we should care about them, what gaps exist in the care being delivered, and what we can do to improve on these care gaps as care is delivered.

Chapter 2 discusses the delivery of healthcare value. The Triple Aim, as mentioned above, measures the per capita cost of care, the health of the population being cared for, and how the patient experiences the delivery of the healthcare process. The Triple Aim framework is a source of professional stress among Caregivers as they attempt to meet the entailed requirements. This associated stress gave rise to the Quadruple Aim where Caregiver experience is also attended to.

Chapter 3 examines the goal of this Thesis in more detail, the sub aims of the Thesis, and my role in the development of the wireframe that will serve as a guide the development of a Clinical

Decision Support Tool, CDST directed at the management of patients with CMD and DM2. In this chapter we examine the desiderata associated with the design and implementation of a CSDT, the problems this CDST needs to address, how informatics in general can support increasing the value of the care we can deliver when caring for patients with CMD and DM2 and draws particular attention to the value of those CDST's that support personalized, comprehensive care.

Chapter 4 examines the vision and functionality of the CDST that will be implemented based on the wireframe that is presented in this Thesis. The Tools structure, function and knowledge base are discussed and this CSDT will be compared with other somewhat similar commonly-used web based tools. Based on this comparison, the need for a comprehensive, personalized CDST along the lines of what is presented in this Thesis is defended.

Chapter 5 lists and discusses some of the trainee's reflections and learnings regarding some of the topics in this Thesis, along with some of the experiences involved in creating it.

CHAPTER 1: Cardiometabolic Disease and Diabetes Mellitus Type 2

Section 1.1 Introduction

This Thesis is about a stand-alone web-based Clinical Decision Support Tool for use by Caregivers in the clinical setting who are delivering care for individuals with Cardiometabolic disease, CMD, and Diabetes Mellitus Type 2, DM 2. This chapter introduces CMD and DM 2, and why it is important of address these conditions. It moves on to explore various clinical, financial and psychosocial sequelae related to these disorders and locates the clinical management of these sequelae within the context of how a Clinical Decision Support Tool can assist Caregivers in decreasing the morbidity and mortality associated with these disorders.

As outlined in Section 1.2 below, CMD and DM 2 are highly-prevalent diseases, both internationally and with the United States of America. As of 2015, 9.4 percent of the US population has diabetes and 100 million individuals in the US have diabetes or prediabetes (75, 76). The cost of diagnosed diabetes in 2012 was approximately $245 billion(77) and estimated at $327 billion in 2017(78). Accounting for the exact cost of these disorders is difficult since there is a considerable overlap of CMD with other disorders such as cardiovascular disease, cerebrovascular disease, peripheral vascular disease and DM 2 as outlined in Section 1.1 below. Additionally, the costs involved in caring for patients with CMD and DM 2 include several categories. There are the costs of medications, outpatient visits, inpatient care, emergency department visits, the costs involved in the ongoing treatment of heart attacks and strokes, the costs of procedures, (including limb amputation, laser retinal surgery to decrease the progression of vision loss associated with diabetic retinopathy, the creation of an arteriovenous shunt and ongoing renal dialysis associated with diabetic nephropathy to name a few), that are sequalae of

CMD and DM 2 (27, 79-86). Allocating exact costs to these categories is difficult, if not impossible, but it remains clear that the costs of diabetic complications and comorbidities is substantial(87, 88).

Likewise, accounting for the psychosocial impact of CMD and DM2 is difficult (89). For example, the impact of amputations owing to peripheral vascular disease is significant. There are prostheses, the cost of physical therapy to regain ambulatory status, changes in the configuration of the driver's controls in an automobile, the impact on care delivery caused by an increased number of falls, and the depression and social adjustment associated with becoming obviously disfigured. There are the social costs of isolation and the increased dependence on caregivers owing to diminished visual capacity, including blindness that are significant. Renal dialysis, a common sequela of diabetic kidney disease, becomes a "center of gravity" in a patient's weekly schedule, often requiring a caregiver who orchestrates the processes involved in the patient's care.

In summary, it is hard to overestimate the financial and biopsychosocial costs of CMD and DM 2. In the following Sections 1.1-1.4 CMD and DM2 will be defined per the ICD-10 standard, and we will examine in more detail why we care about these disorders, what is known about them and where the gaps exist in treating them.

Section 1.2 The Diseases Defined: Cardiometabolic Disease and Diabetes Mellitus Type 2

Cardiometabolic Disease, (ICD-10 code E88.81), and Diabetes Mellitus Type 2, (ICD-10 code E11), are defined based on a composite or constellation of clinical findings: it is not necessary to have all of the clinical findings in the descriptor to make the diagnosis. This type of classification is both common in health care and is attended by a sense of nebulousness when

precision is required. As an example, the diagnosis of a transmural myocardial infarction(90) of the inferior wall of the heart, (a heart attack where cardiac tissue death involves the full-thickness death of the cardiac tissue), is relatively straightforward as referenced by the ICD-10 code I21.9. On the other hand, acute coronary syndrome (91) is caused by the blockage of a coronary artery has symptoms such as chest discomfort, shortness of breath, strange feelings in the arms, nausea or vomiting and is referenced by the ICD-10 code I24.9. Not all of these symptoms are required to make the diagnosis of acute coronary syndrome. Relatedly, if an instance of acute coronary syndrome is not aggressively managed, it can progress to myocardial infarction. Similarly, a stroke(92) , caused by the blockage of an artery supplying the brain that causes tissue death, (ICD-10 code I63.40), is fairly clear while a transient ischemic attack, (ICD-10 code G45.1) often caused by intermittent blockages in the arteries supplying the brain is somewhat more nebulous.

There are two reasons for choosing the above examples. First to illustrate the difference between those diagnoses that are relatively clearly demarcated and those that are somewhat more nebulous in their definition. Second, as will be seen repeatedly throughout this Thesis, the clinical sequelae of both CMD and DM2 can include a heart attack or a stroke, or the more nebulous composite symptoms of acute coronary syndrome or transient ischemic attack that are warning signs and symptoms that a heart attack or stroke is likely to occur.

With this background information, we can now explore both CMD and DM2 in more detail. Both of these diagnoses are made based on a composite of clinical findings as described above: some, but not all of the clinical findings are needed to make the diagnosis. There is an additional level of complexity: there is an intersection of clinical findings when comparing the CMD and DM2 diagnoses. Many of the clinical findings in CMD may not include the findings necessary

to diagnose DM2 while most of the time the clinical findings that make the diagnosis of DM2 are found in CMD. This overlap of clinical findings can blur the lines between these respective diagnoses.

Section 1.2.1: Cardiometabolic Disease

Cardiometabolic disease, (CMD), also referred to as Cardiometabolic Syndrome, is, from a population health perspective, an increasingly prevalent(17) (16, 18) disorder that is associated with excess morbidity and mortality(93). The components of CMD include:

- Excess abdominal fat
- Atherogenic dyslipidemia
- Hypertension
- Hyperglycemia
- Insulin resistance
- A proinflammatory state
- A prothrombotic (thrombosis) state(94).

A more recent definition of CMD is:

- "Metabolic syndrome is defined by a constellation of interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of cardiovascular disease, type 2 diabetes mellitus, and all-cause mortality. Insulin resistance, visceral adiposity, atherogenic dyslipidemia, endothelial dysfunction, genetic susceptibility, elevated blood pressure, hypercoagulable state, and chronic stress are the several factors which constitute the syndrome. Chronic inflammation is

> known to be associated with visceral obesity and insulin resistance which is characterized by production of abnormal adipocytokines such as tumor necrosis factor α, interleukin-1 (IL-1), IL-6, leptin, and adiponectin. The interaction between components of the clinical phenotype of the syndrome with its biological phenotype (insulin resistance, dyslipidemia, etc.) contributes to the development of a proinflammatory state and further a chronic, subclinical vascular inflammation which modulates and results in atherosclerotic processes. Lifestyle modification remains the initial intervention of choice for such population. Modern lifestyle modification therapy combines specific recommendations on diet and exercise with behavioral strategies. Pharmacological treatment should be considered for those whose risk factors are not adequately reduced with lifestyle changes. This review provides summary of literature related to the syndrome's definition, epidemiology, underlying pathogenesis, and treatment approaches of each of the risk factors comprising metabolic syndrome"(95).

As noted above, CMD is a "constellation of metabolic factors." From a clinical care perspective certain patterns involving some of these metabolic factors are seen in the daily work of a Primary Care Provider, PCP. Examples include the patient with hypertension, central obesity and an increased Body Mass Index, BMI, the patient with elevated fasting glucose, hypertriglyceridemia and hypertension, or the patient with DM 2, hypertension and dyslipidemia.

Section 1.2.2: Diabetes Mellitus Type 2

According to the American Diabetes Association in "Standards of Medical Care in Diabetes-2017" (96) and repeated in 2019(97) , the criteria for diagnosing diabetes include (with some reformatting added for the present context):

- A fasting plasma glucose of 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.

  OR

- A 2-hour post prandial plasma glucose of 200mg/dL, (11.1mmol/L), during an oral glucose tolerance test, (OGTT). The test should be performed as described by the World Health Organization, WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

  OR

- Hemoglobin A1C of 6.5%, (48mmol/mol), or greater. The test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program, NGSP certified and standardized to the Diabetes Control and Complications Trial, DCCT assay.

  OR

- In the inpatient environment with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose of 200 mg/dL (11.1 mmol/L).

The possible clinical sequelae of DM 2 are multiple as outlined and cited in Section 1.1 above, and include disorders such as diabetic retinopathy, which increases the risk of blindness, diabetic

nephropathy, which increases the risk of renal dialysis, myocardial infarction, stroke, and peripheral arterial disease which increases the risk of amputation.

As noted above, DM 2 is related to CMD:

- "Most patients with this form of diabetes are obese, and obesity itself causes some degree of insulin resistance. Patients who are not obese by traditional weight criteria may have an increased percentage of body fat distributed predominantly in the abdominal region. Ketoacidosis seldom occurs spontaneously in this type of diabetes; when seen, it usually arises in association with the stress of another illness such as infection. This form of diabetes frequently goes undiagnosed for many years because the hyperglycemia develops gradually and at earlier stages is often not severe enough for the patient to notice any of the classic symptoms of diabetes. Nevertheless, such patients are at increased risk of developing macrovascular and microvascular complications. Whereas patients with this form of diabetes may have insulin levels that appear normal or elevated, the higher blood glucose levels in these diabetic patients would be expected to result in even higher insulin values had their β-cell function been normal. Thus, insulin secretion is defective in these patients and insufficient to compensate for insulin resistance. Insulin resistance may improve with weight reduction and/or pharmacological treatment of hyperglycemia but is seldom restored to normal. The risk of developing this form of diabetes increases with age, obesity, and lack of physical activity. It occurs more frequently in women with prior GDM, (gestational diabetes mellitus), and in individuals with hypertension or dyslipidemia, and its frequency varies in different racial/ethnic subgroups. It is often associated with a strong genetic predisposition, more so than is the

autoimmune form of type 1 diabetes. However, the genetics of this form of diabetes are complex and not clearly defined" (98).

Section 1.3: Cardiometabolic Disease and DM2: Why Should We Care?

In the introduction to this chapter we covered both the financial and psychosocial costs associated with CMD and DM 2 and in Section 1.1 the complexity of these disorders was outlined. Taken together, these disorders are major causes excess mortality and morbidity. In this section we examine both the human costs in terms of illness and suffering and the financial costs involved in caring for these patients.

Section 1.3.1: Vascular and Kidney Disease

The arterial endothelium is, in a sense, the "target" of the CMD and DM2 disorders and damage to the endothelium of the heart, brain and kidneys caused by these disorders constitutes a major cause of excess morbidity and mortality(99-101). Coronary heart disease is the leading cause of death for both men and women in the United States, killing about 800,000 people annually(102) . About 735,000 people a year have a heart attack.(103)

There are about 795,000 stokes a year in the United States, killing about 140,000 people. Stroke costs about $35 billion a year and is a leading cause of serious long-term disability. (104) There are more than 385,000 people in the USA with Chronic Kidney Disease with end-stage renal failure and 19.2 million people with Chronic Kidney Disease(105), and diabetes is a major contributing cause of Chronic Kidney Disease(106, 107)

Section 1.3.2: Increasing Prevalence

The prevalence of Cardiometabolic Disease, CMD and Diabetes Mellitus Type 2, DM2 are increasing (96) (108) and if this trend continues it is difficult to project to total impact on society. Diabetes Mellitus Type 2, shares many of the attributes of CMD, and is included in the overall prevalence of CMD. In fact, DM 2 itself contributes(109) a lifetime cost of $82,500 per individual with DM 2. Per the American Diabetes Association, the cost of care of an individual with diabetes is approximately 2.3 times greater than an individual without diabetes(110). Caregiving costs are expected to rise dramatically(111).

Section 1.3.3: The Value of Prevention and Management

CMD and DM2 are both preventable and are composed of an aggregate of modifiable risk factors. Screening for these disorders(112, 113) and addressing these modifiable risk factors has the potential to decrease the associated morbidity and mortality for those with these disorders (18, 114) . Managing CMD efficiently will generate cost savings, not only for the patient with the disorder, but also for the involved healthcare business, (Payors and healthcare delivery systems like an Accountable Care Organization), (ACO)(115-117)

Section 1.3.4: Hospital Costs

Cardiometabolic Disease increases the risk of hospitalization in patients with DM 2, and generates a significant cost burden both in the USA and abroad(118-123) . The average cost of an admission for congestive heart failure was estimated at more than $37 billion in 2009(124), and as many as 20% of patients are readmitted in less than 30 days(125, 126), which generates

costs to healthcare organizations in the form of penalties from CMS, (Centers for Medicare and Medicaid Services).

Section 1.3.5: The Psychosocial Impact

The psychosocial costs associated with behavioral health issues, as noted above in Section 1.1, play a significant role in the cost of care. We know that CMD is associated with a progression towards depression and cognitive decline(127). We also know that biopsychosocial factors such as depression and marital status affect cardiovascular outcomes. In addition to direct cost of providing care for patients with CMD and DM2, there is a direct societal impact involving the economy and worker productivity(128-131).

Section 1.4: Cardiometabolic Disease and Diabetes Mellitus Type 2: What Do We Know?

We have known of the positive impact on the cost of care that is possible with evidence-based care of patients with DM2 for decades. Attention to lifestyle changes and compliance with correct medication regimens decreases the morbidity and mortality associated with DM2, and yet significant gaps in managing the care of diabetics continues to exist(132) as evidenced by the year 5 performance data for Medicare Pioneer ACO's. CMS, (Centers for Medicare and Medicaid Services), keeps performance scores via ACO measures.(133) Examining the data collected concerning year #5 on this page,(134) reveals that the best composite performance score with respect to care gaps and performance outcomes was 85.88% and the lowest was 17.1%. The column for the DM Composite score ranges from a low of 17.17% to 88.5%, with an arithmetic mean score of 47.03%. The ACO 28 metric measures the performance of hypertension management. The performance for this metric is better, ranging from 66.23% to 93.67% with an arithmetic mean of 77.79%. There is clearly work to be done to raise the quality

of care of diabetics in this ACO model This is true outside the ACO model as seen in both the United States and abroad(135-138).

We know that adherence to Evidence-Guided care suggestions improves clinical and financial outcomes. For example, treating hypertension effectively decreases cardiovascular events and death by 5,000-13,000 a year in the United States of America, USA(139-141). Adherence to evidence-guided care for hypertension not only decreased the incidence of acute cardiovascular events(142), post-screening follow-up resulted in new medications not only for hypertension, but also hyperlipidemia and diabetes, and prompted helpful lifestyle changes(143).

We know that the prevalence of cardiovascular disease and heart failure are decreasing in patients with diabetes as care improves, but still exceed rates found in non-diabetics(144). As noted above, the tight Blood Pressure, BP control in DM2 decreases the cost of care (145), and compliance with evidence-guided standards decreases the cost of medication(146). Congestive heart failure, a complication of DM2(147, 148) , management can be improved (149) We know that the incidence and mortality of hypertrophic cardiomyopathy, (a complication of poorly-controlled hypertension), is higher in diabetics, reinforcing the need for close attention to a patient's blood pressure management(150). Diabetic cardiomyopathy is also an issue (151, 152)

We know that an elevated LDL, Low Density Lipoprotein, cholesterol is an important factor for excess mortality and morbidity in both CMD and DM2(153). Overall, getting high-risk patients to an appropriate goal somehow seems to remain out of reach(154), while the anticipated cost of care is expected to increase dramatically in the future(155, 156) .

We know that diabetic nephropathy creates a significant burden on both patients and caregivers. Prevention and early treatment with an Angiotensin Receptor Blocker, ARB at the onset of microalbuminuria decreases the mortality and cost of End Stage Renal Disease when compared with control and later treatment(157).

It is evident from a systems-level perspective, that a multi-faceted approach to diabetes management improves diabetes control and process outcomes(66), and that integrated delivery systems and ACO's should focus on cardiometabolic syndrome. Screening, stratification and algorithm-based treatment of patients with cardiometabolic syndrome is recommended. The Cardiometabolic Health alliance presented several key findings (KF)(158), including:

- "KF.3: A new care model for patients with MetS (note that "MetS" or Metabolic Syndrome, the equivalent of CMD in the present context), is essential and should include screening, risk stratification, and algorithmic management of patients according to the specific subtype and stage."
- "KF.4: Structured lifestyle interventions are required to adequately treat MetS and reduce residual Atherosclerotic Cardiovascular Disease, ASCVD risk."
- "KF.5: Implementation of a new patient care model should focus on integrated care delivery, alternative reimbursement strategies (perhaps utilizing the emerging constructs of the Patient-Centered Medical Home, PCMH and ACO), and education that uses structured lifestyle intervention; optimal use of pharmaceuticals, including combination therapies; and appropriate consideration of surgery."

We know that Primary Care is a substantive component in an integrated healthcare delivery system(43, 159) , and more will be expected of these clinicians in the future,(115, 160) that

patient-centered approaches improve outcomes(161-163) , and that a shared decision-making decision aid for management of DM2 is well-received by clinical practice staff(164).

In summary, in Section 1.3 we saw why we should care about CMD and DM2, and in this section we reviewed what is known about CMD and DM 2 and how a comprehensive approach to treating patients with these disorders improves morbidity, mortality and decreases the cost of care. Despite this knowledge, we found that substantial gaps in care delivery, (as defined by the metrics published by those organizations that are paying for care), exist, and to this we now turn out attention.

Section 1.5: Cardiometabolic Disease and DM2: What Care Gaps and Challenges Exist?

A healthcare delivery system's care process improvement initiatives require assessing the current state of care and declaring the desired future state of care, thereby identifying care gaps. Examples include finding patients with care gaps in the control of their HbA1c, Hemoglobin A1c, lipid level or their blood pressure measurement. At the fundamental level there appears to be a decreased awareness of the disorder(158). Poor DM and blood pressure Medicare Pioneer ACO scores were cited in Section 1.4, and a study by the Veteran's Administration suggests blood pressure control in diabetics is suboptimal(165) , despite it being clear that blood pressure control is a crucial aspect of caring for those with CMD(166). Actual care gaps involved in the care of patients with diabetes mellitus type II appear substantial, with blood sugar control in the 60% of recommended range(167).

Specifically, caring for patients with CMD and DM2 is a complex, time-consuming process. More broadly, Primary Care Providers are faced with progressively increasing time-consuming administrative tasks that decrease the time available to spend with patients needing care for

CMD and DM2 in particular, as well as having to address multiple complaints other patients present with(168, 169).

Many Primary Care Providers work either in solo practice or in small groups(170) and are less likely to leverage the care coordination resources available caregivers who have access to a multidisciplinary team approach that is available in large integrated healthcare systems(171). In small primary care groups diabetes care gaps are not closed (172). An ACO provides a mechanism for Caregivers in small groups to access these multidisciplinary resources(173).

Another existing gap in the care of patients with CMD and DM2, and the central theme in this Thesis, is the availability an electronic Clinical Decision Support Tool that comprehensively addresses the needs of these patients. This topic is addressed by Wilkinson et al(12) and will be discussed in Section 3.6 below, dealing with Clinical Decision Support Tools.

Section 1.6: The Value of Health Information Technology

Health Information Technology can play an important part in a learning healthcare organization's performance in CMD management by making evidence-guided CMD information available at the point of care. By necessity, and Accountable Care Organization, ACO must become a learning organization in order to improve the quality of the care they deliver, as measured by outcomes metrics(158, 174, 175). Financial performance is central to an ACO's success and some of this performance is tied to the efficient management of Cardiometabolic Disease(176-178).

There is an increased interest in using artificial intelligence in Clinical Decision Support Tools that are directed towards the care of diabetic patients(179), as well as plans for developing

mobile Clinical Decision Support Tools to support primary care clinicians who care for diabetics(180). An example of how a Clinical Decision Support Tool, CDST, for selecting diabetic medications is found in(181), revealing an 85% concordance rate with what an endocrinologist would have chosen as a diabetic medication in a given clinical setting. Using a Clinical Decision Support Tool to interpret a patient's self-monitoring of blood sugar shows promise(182). Providing personalized care(183), based on a diabetic patient's healthcare preferences when using a CDST improves participation and outcomes yet only 30% of the CDST's used in diabetic care include patient preferences(12).

Section 1.7: Chapter Summary and Context

In this chapter we have covered what Cardiometabolic Disease, CMD and Diabetes Mellitus Type 2, DM2 are. They are interrelated disorders that are "syndromic" in nature. Individuals may have some, but not all the listed attributes of these disorders and some may have CMD and not DM2 and vice versa, in a formal sense, yet their wellbeing is at risk. We know why we should care about these diagnoses: they are associated with potentially devastating personal wellbeing consequences such as stoke, myocardial infarction, renal failure and along with the entailed person financial burdens, while also representing significant societal and financial consequences and an increasing burden on the healthcare delivery system. We know there are care gaps in the healthcare delivery system: closing them will increase personal wellbeing and drive down the cost of care. We have seen the value of health information technology: we can improve patient care outcomes using Clinical Decision Support Tools.

The ultimate end of this project's roadmap is the launch of a comprehensive CDST that aids Caregivers who are managing all of the aspects of CMD within the context of care being

delivered in an ACO, where the per capita costs of care, and population health, must be managed efficiently and efficaciously to promote the health and wellbeing of the population being cared for, while also avoiding potentially adverse financial consequences. We now turn our attention to various types of healthcare delivery systems that operate within the financial pressures of the marketplace.

CHAPTER 2: Addressing the Healthcare Value Delivery Problem

Section 2.1: Introduction

The value of the care that is delivered by a given healthcare system can be measured via the triad known as "The Triple Aim," a construct introduced by the Institute for Healthcare Improvement(53). The Triple Aim attends to the quality of care that is delivered, the patient's experience of the healthcare delivery process and the per capita cost of that care are assessed as a single construct. From an international perspective, when comparing the value of care being delivered in the major industrialized countries, the quality of the care that is delivered, is severely lacking.

The United States Healthcare Delivery System is under considerable pressure to reform itself both in terms of population-based health outcomes and the cost of healthcare delivery. Two commonly mentioned reports that reference healthcare outcomes in the US include the Institute of Medicine's, IOM's "Crossing the Quality Chasm (184) in 2010 that called attention to the prevalence and consequences of medical errors, and the 2014 Commonwealth's Fund report (185), that ranked the US as 10^{th} out of the 10 for healthcare outcomes among the major industrialized countries in the world. Per capita healthcare costs in the US are over double the average of the industrialized nations, healthcare costs comprise over 20% of the Federal budget and the cost of care has grown faster than the Consumer Price Index, CPI for at least a decade (186-189). The progressive increase in healthcare costs is considered unsustainable(1) (190).

A broad range of initiatives is emerging to address these accelerating costs. The initiatives are coming from Government, Insurers, Employers, Providers and Consumers. As mentioned above, the Triple Aim, (again the quality of the care being delivered to a given population, as defined by

a set of metrics, the per capita cost of care of that given population, and the patient's experience of the care delivery process), has emerged as a comprehensive metric for assessing the value of healthcare delivery systems. The updated Quadruple Aim(37) adds Provider experience, acknowledging the fact that meeting the demands of the triple aim generates a considerable amount of caregiver stress, and recognizes that caregiver experience is an important perspective to maintain while trying to improve the value of healthcare delivery.

The Market is responding to these outcome and cost issues on both the Payor and Provider sides of the healthcare system. Payors include the Federal and State governments, Employers, Insurers and Individuals. Providers include Health Maintenance Organizations, HMO's, not-for-profit Integrated Delivery Systems, Healthcare Foundations, Private Practices and Accountable Care Organizations, ACO's. The market interface is defined by the agreements that are entered into between Payors and Providers. These agreements define the expected healthcare outcomes, the total cost of care, and how funds will flow based on the level of financial risk the Provider is willing to take.

It is likely that as the future unfolds and Clinicians, Hospitals, ACO's and other types of Integrated Delivery Systems will have to balance the conflicts inherent within the Quadruple Aim. Controlling per capita costs means increasing business costs to implement new software and spending time training to create new workflows. Following guidelines, care pathways and protocols that are evidence-based may be interpreted by patients as withholding care, affecting patient experience outcomes. The professional stress created by following guidelines more closely, managing the cost of care and increasing patient satisfaction will impact Clinician experience. Balancing the conflict created by the Quadruple Aim is necessary for a healthcare entity to successfully navigate the changing marketplace.

In what follows various types of responses aimed at addressing the US healthcare delivery system are briefly and broadly sketched in order to add background and context to this research project. These responses fall into government responses, insurer responses, employer responses and provider responses.

Section 2.2: Government Responses

At the Federal level, the Centers for Medicare and Medicaid Services, CMS, is playing an active role. Examples include bundled payments for certain procedures such as total hip replacement or a coronary vascular intervention, rewarding some Healthcare Delivery Systems that are providing high-quality, cost-effective care, while penalizing other Systems for substandard quality and excess cost(191-193). CMS, Centers for Medicare and Medicaid Services, now publishes the Hospital Consumer Assessment of Healthcare Providers and Systems, HCAHPS Star Rating that ranks hospitals based on quality(194-196). The stated intent of this publication is to incentivize patients to use hospitals that deliver high-quality care. Similar Star Ratings exist for nursing homes and home health entities (195, 197, 198). The Affordable Care Act, ACA(199), created access to millions of individuals who did not have insurance coverage. These plans generally have high deductibles, forcing consumers to be cost-conscious. The ACA also formalized the development of Accountable Care Organizations, ACO's.

Medicaid contracts are entered into at the State level. The State also sets the laws concerning how Payors will behave, what types of Healthcare entities exist in the State, and who is licensed to practice professionally in the State. The State can also enter into cost-containing, outcomes-driven agreements with Providers. As an example, in the State of Washington the Healthcare Authority, HCA(200), has entered into agreements with Providers, including ACO's (201, 202),

that call for the delivery of certain healthcare outcomes within a total-cost-of-care budget. The healthcare delivery system is required to accept downside risk, (as opposed to upside gainsharing), for the cost of care. Cost overruns can result in millions of dollars of loss annually to these delivery systems.

Section 2.3: Insurer Responses

Healthcare insurance companies are playing an active role in the Market with several types of offerings which, in effect, stipulate which healthcare is and how it will be paid for. Insurers stipulate what healthcare services consumers are allowed to access, what price Insurers will pay the Providers for their services, and what costs consumers are expected to bear. There are several categories of offerings made by Insurers.

Section 2.3.1: Preferred Provider Organizations

Preferred Provider Organizations, PPO's(203), charge consumers less if they use the given network of Providers that is covered by the contract. Consumers can use Providers outside the network, generally without a referral for an additional cost. PPO's negotiate lower fees for services with networks in order to decrease cost.

Some Payors include Exclusive Provider Networks, EPO's (128), or "narrow networks." These plans are similar to PPO's, but consumers are required to use only the given network for general care. Care outside the EPO is generally not covered. Referrals from a PCP are often required for specialty care.

Section 2.3.2: Health Maintenance Organizations

A Health Maintenance Organization, HMO(204) (205), is an insurance plan and provider network that emphasizes preventive care services such as routine physicals, health risk assessments, immunizations, and cancer screening services such as mammograms and colonoscopies. A fixed amount is paid to the HMO each month, and this amount is expected to cover all of the costs incurred in the healthcare delivery process. Most care outside the network, much like in the case of an EPO, is not covered. Since HMO's receive a fixed payment, they have created the resources they need to deliver care cost effectively. These plans generally require the selection of a PCP who becomes responsible for most of the preventive services and care management outcomes. The PCP also coordinates a patient's care when specialty services are required. HMO's often require that consumers live and work in the area where the HMO is offered.

A broad distinction between two types of HMO can be drawn. The "Insurance Model HMO" is actually a contracted arrangement with an EPO-like network. The criteria required to qualify as an HMO are met at the insurance company level, and the actual delivery of care occurs via the delivery network. Alternatively, a "Provider-Model HMO" has an insurance function, but healthcare services are delivered by Providers who are employed by the HMO itself. This type of model, using its insurance function, can also contract with other providers of its choosing who are not employed by the HMO.

Section 2.3.3: Point of Service Plans

A Point of Service Plan, POS(206), has characteristics of both a PPO and an HMO. A PCP is usually required and referrals from the PCP are often needed for specialty care. The network of

providers is not as restrictive as an HMO and access to providers outside the network is permitted for an additional cost.

Section 2.3.4: High Deductible Health Plans

High Deductible Health Plans(207) have lower premiums than other health plans which saves the consumer money on a monthly basis. The co-pays and deductible are higher, creating higher out-of-pocket costs for the consumer. According to the IRS, the minimum annual deductible for these plans is $1,300 for an individual and $2,600 for a family. The maximum annual out of pocket costs are $6,650 for an individual and $13,100 for a family. These plans are available to consumers individually via the Exchange or via employers who may also tie these plans to a Health Savings Account.

Section 2.4: Employer Responses

Employers are also playing an active role to increase quality and decrease cost(208). Each year, Employers reassess the cost and coverage they provide by changing Insurers. Deductibles and copays are increasing, narrow network plans are being used, the cost of premiums are shared with employees and Health Savings Accounts are being offered. Employers are also promoting employee wellness by rewarding smoking cessation, weight loss programs and going for screening exams. An important subset of an employer response is found where the healthcare delivery system is itself the employer of the patient, and that healthcare delivery system is self-insured. All savings realized by the healthcare delivery system are “hard-dollar” savings to the healthcare organization and employees are often heavily incentivized to seek their care by using the system’s clinicians, ancillary services and hospital since this utilization is “at the margin” where fixed expenses for these services already exist.

Direct Business-to-Business contracting is increasing. As an example, Boeing has entered into contracting relationships with Healthcare Delivery Systems in the Northwest(209, 210) and require that certain healthcare outcomes are met, and costs contained. This is a down-side risk agreement; Providers will suffer financial losses if cost and quality targets are not met. Other self-insured employers are using Third Party Administrators, TPA's, to address healthcare quality and cost by making agreed-upon payments to a network of Providers for specific outcomes.

Section 2.5: Accountable Care Organizations

This research is being conducted within an Accountable Care Organization(207) (211). ACO's which have been formalized as part of the Affordable Care Act, ACA (199) (212) foster the development of Integrated Delivery Systems, IDS. Clinicians and Hospitals are incentivized to form businesses that have the authority to deliver care, are responsible for the outcomes of care, and have financial responsibility for the cost of care(213). This financial responsibility can be either gain-sharing(214) if cost and quality targets, known as "care gaps" (215) are met, or at-risk agreements, bearing what can be substantial losses if cost and/or quality targets are not met. As an example, in a Medicare-based Pioneer ACO(134) a first-year reported loss of $2,548,911 was realized by the Genesys PHO that covered only 15,668 lives in the contract, (also known as "the population"). By contrast the highest profit of $14,001,887 was realized by Montefiore ACO which had a population of 20,107 covered lives. There were 32 healthcare systems represented in this year. Eighteen of them had no shared savings. In the most recent report, year 5, there were only 8 participating organizations, of which 6 were profitable and 2 had no shared savings. Banner Health Network earned the most at $10,940,821 with a population of 42,040

patients. Montefiore realized $7,412,870 with 40,825 covered lives. Clearly there are financial incentives attached to becoming a performant healthcare organization in the Pioneer ACO model. It is also the case that only one-fourth of the organizations who signed on to the model are still participating, and one-fourth of the organizations that are still in business did not show a profit, despite the hard work involved in administering an ACO.

Health Maintenance Organizations, discussed in Section 2.3.2, take a fixed amount of money on a monthly basis to care for each enrollee. This care includes preventive care, immunizations and a structured disease management system. HMO's have been in existence since perhaps 1910 when a pre-paid plan was founded in Tacoma Washington(216). In 1973 employers with more than 25 employees were required to offer an HMO options for healthcare to their employees.

There are similarities between ACO's with full-risk agreements and HMO's. A fixed amount is paid per member per month, PMPM, to an ACO. The ACO then becomes accountable for delivering outcomes-measured care within the fixed budget. All of the enrollees in an ACO are referred to as the "enrolled population" and the mechanism for delivering care is called "population health management." In full-risk agreements when care is carefully coordinated in order to achieve the required measurable outcomes, i.e., close care gaps, while also finding more efficient ways to coordinate care, substantial financial rewards can be realized by the ACO. Again, there is the potential for substantial losses.

Section 2.6: Summary and Tool's Relevance to the Healthcare Value Problem

This section has outlined several of the types of organizational responses that are focused on increasing the value of the health care we deliver in the United States. The last response type, the ACO, Accountable Care Organization, forms the context for this project. The Eastside Health

Network, EHN, is an Accountable Care Organization, ACO that is formed and integrated delivery network involving Overlake and Evergreen Hospital and approximately 1000 physicians. Currently the ACO is responsible for approximately 20,000 covered lives. Majority of the contracts involved in these covered lives are “upside-only” where the payers distribute savings to the ACO if clinical outcomes have been met. There is an important concept here: It is possible to deliver outstanding care, as measured by the closure of care gaps, not save money and receive no distributed savings. It is also possible to deliver cost-effective care and not close care gaps, also resulting in no distribution. In full-risk contracts, it is possible to lose literally millions of dollars on a contract if care is not sufficiently cost-effective, despite closing care gaps.

As noted in Sections 1.1-1.4, patients with Cardiometabolic Disease, CMD or Diabetes Mellitus Type 2, DM2 are at high risk regarding their personal wellbeing. These disorders also generate a significant cost burden to society at large. This cost burden has significant financial implications in an ACO whether in an upside-only or at-risk contract: an ACO cannot share gains in upside contract if there are cost overruns, and also suffer significant financial loss if there are cost overruns in an at-risk contract. Said differently, patients with CMD and DM2 represent a substantial risk to an ACO both from a population health perspective and from a per capita cost of care perspective. Additionally, caring for these complex patients is taxing in the daily life of the clinician, making outstanding patient experience more difficult to achieve. The purpose of the Tool presented in this Thesis is to comprehensively address the value of the care being delivered both at the personal patient level and at the ACO level by offering Clinical Decision Support in the office at the point of care that guides the patient and caregiver through the

involved clinical workflow more efficiently and effectively. This is the topic of following chapter.

CHAPTER 3 Thesis Goal

Section 3.1: Introduction

The goal of the MS work is to develop a wireframe of a Clinical Decision Support Tool, CDST, that will enable the comprehensive, efficient and efficacious management of patients with Cardiometabolic Disorder and Diabetes Mellitus Type 2 who are receiving their care in the Eastside Health Network, an ACO. This wireframe will serve as the model for developing the launch version of the CDST.

Within this goal there are three sub-aims.

1. Understand the types of resources the Caregivers in the ACO need in order to more efficiently and efficaciously care for patients with CMD and DM2.
2. Work collaboratively with the members of the ACO's Patient Quality Committee to define the scope and desired attributes of the CDST described in this Thesis.
3. Review the literature to find the best clinical practices that should be adopted which will enable the ACO Caregivers to efficaciously care for patients with CMD and DM2, review the web-based tools that already exist to support this care, and review the desiderata required to successfully design and launch a CDST.

The underlying assumption of this project is that a web-based comprehensive Clinical Decision Support Tool is required to effectively address the triad of challenges faced by Caregivers working in the ACO. These challenges, as introduced in the Preface, include the complexity of the CMD and DM2 disorders, the proliferation of new medications used for treating patients with

these disorders, and the market pressures clinicians who are working within an ACO face as they attempt to deliver more value in the care delivery process. It is expected that this Tool will evolve iteratively as more is learned about what users need.

The launch version of this Tool will be based on the wireframe presented in this Thesis and will focus specifically on the decision support Caregivers need as they choose the appropriate medical therapy for managing a given diabetic patient's blood sugar. As we saw in Sections 1.1-1.4, Cardiometabolic Disease, CMD and Diabetes Mellitus Type 2, DM2 are complex disorders involving not only blood sugar management. There are, among other things, potential cardiac central nervous system and renal sequelae involved as this disease progresses. Section 2.1.2.1 of Appendix 1 details the need for medications that manage not only the blood sugar of patients with DM2. Medications that manage lipids and blood sugar are also required as part of a comprehensive approach to the management of CMD and DM2.

Future iterations of the Tool that support this comprehensive approach will be developed iteratively and collaboratively by healthcare knowledge workers in the ACO. In a future state, the Tool will more inclusively address issues such as the optimized management of treatment-resistant hypertension, complex dyslipemia management, chronic kidney disease, and congestive heart failure. Speed and ease of use are crucially important in the design of a CDST as noted in Section 4.2. An unavoidable limitation of this stand-alone Tool is that duplicate data entry, (the data already reside in the EMR used by that clinic, using the same screen as this CDST), is required by the Caregiver team, and this may impact adoption. This limitation but is an unavoidable consequence of the need to manage the care of CMD and DM2 across an ACO that has approximately 70 EHR's.

As envisioned, this Tool has the potential to increase both patient and caregiver engagement since it focuses on increasing the quality of care by closing accepted gaps and preventing or delaying the potential clinical sequelae of CMD and DM2 outlined in Sections 1.1 and 1.4 above , thereby decreasing the excess morbidity and mortality associated with these disorders. This Tool may increase the Caregiver's knowledge of the evidence-guided standards of care suggested in the care of patients with CMD and DM2 and Tool's user interface will lighten the load involved in achieving these standards. Perhaps patients will see the value of "knowing their numbers," and understand the evidence-guided reasons behind the recommendations generated by the tool. The use of the Tool in the clinical setting has the potential to enhance the patient's experience of their care and strengthen the patient-caregiver relationship as discussed below in Section 3.6.

In summary the Tool that is envisioned by the wireframe in this Thesis has the potential to improve the well-being of patients with CMD and DM2 when used in the clinical setting. In what follows we touch on the Trainee's role in guiding the creation of the wireframe and then examine the problems this Tool is trying to address, how informatics can address these problems, and then examine Clinical Decision Support tools in some detail.

Section 3.2: My Role

Drawing on my training in informatics, my daily work as a PCP over the last 39 years who cares for individuals with CMD and DM2, and as a member of the Contracting and Quality Committees of our Accountable Care Organization, ACO, I proposed and am spearheading the development of a Web-based Clinical Decision Support Tool that stratifies the risk of a given individual with respect to CMD DM2, analyzes the medications being administered and where

appropriate, suggests medication changes, and recommends a set of clinical interventions and clinical management strategies based on the individual's unique clinical status. The Executive Director of our ACO has agreed to develop my idea and proposal as a pilot proof of concept that is part my MS work in Biomedical Health Informatics. If this pilot is successful and the ACO is interested in operationalizing or commercializing the work that results from this pilot, I will have no personal financial interest in the resulting commercial product.

In the context of this Thesis, I served as the project's Physician Lead and was responsible for directing the workflows necessary to create the Tool's content. I was directly responsible for the work in progress that involved generating the rule set that analyzes the inputs and derives the suggested management strategies. The project proceeded via a User-Centered iterative design process. The inference rules, (work in progress that is demonstrated in Appendix 1 Sections 3.5.1-3.5.3,3.7.1, 4.1.1-4.1.7-4.4.1, 4.5.1,4.6.1,5.1.2-5.1.8), were written by the Trainee as learning continued via participation in the Patient Quality Committee, working subgroups and the multi-disciplinary team, (of which the Trainee is a member), that comprehensively address the care of patients whose DM2 is severely out of control as represented by their elevated HbA1c. All of the research and literature review for this Thesis, as evidenced by the attached bibliography was done exclusively by the Trainee.

Cardiometabolic Disorder and Diabetes Mellitus are complex disorders as was noted in Sections 1.2-1.2.2. In what follows next, we examine the problems this Tool will address, followed by an analysis of the attributes of a functional Clinical Decision Support Tool, CDST along with the associated potential pitfalls to avoid when developing an CDST. We then examine some of the CDST's that are available to aid with the management of patients with DM2.

Section 3.3: What Problems is this Tool Trying to Address?

1. The need for a centralized, standardized, evidence-guided digital resource that enables ACO Caregivers to optimize and personalize an individual patient's care with respect to CMD and DM2 without the need to manage the requirements of HIPAA, Health Insurance Portability and Accountability Act, integrate the ACO's approximately 70 instances of Electronic Health Records, EHR's bidirectionally. This is a major driver for a stand-alone system.
2. The perceived lack of both patient and caregiver knowledge of existing evidence-guided standards for managing patients with CMD and DM2 as evidenced by the substantial variation in diabetes outcome measurements across the ACO as generated by the ACO's population health management application.
3. The lack of patient and clinician engagement in managing Cardiometabolic Disease(217-220).
4. The heterogeneity that exists across the Eastside Health Network and the need for an easily-accessible diabetes management tool.
    a. There are 267 PCP's, 44 Cardiologists, 7 nephrologists and 10 Endocrinologists in EHN
    b. There are 2 large multispecialty groups of 362 and 260 caregivers that are employed by EvergreenHealth and Overlake Hospital respectively.
    c. There is a total of 92 private practices in Eastside Health Network, EHN, ranging in size from 1 caregiver, (23 private practices have 1 caregiver), to 92 caregivers in these practices.

d. EHN's Population Health Tool is not yet accepting feeds from all the practices, making it impossible to provide a centralized, accurate tool that addresses every patient's needs comprehensively using a data feed from the Population Health Tool where substantial patient-specific data exist.

Section 3.4: How Can Clinical Informatics Address CMD and DM 2 Care Gaps?

1. Create an application that addresses the clinical concerns involved in caring for patients with diabetes mellitus type II for use across ACO, following user centered design principles.
2. Create algorithms that logically assign risk and recommendations in a personalized fashion at the individual patient level.
3. Engender patient and caregiver engagement.
    a. Patients who use the tool before a clinical encounter will have to "know their numbers" and will receive concrete recommendations that they can print out and carry to the visit as a way of focusing their care.
    b. Empowered Medical Assistants can enter data before the patient sees the caregiver, allowing this individual to work at a higher level and become invested in the patient's CMD and DM2 disease management.
    c. Create an evidence-guided action plan that can be given to the patient as a concrete next step in care.

4. Create a method to immediately update Caregivers on changes in evidence-base standards of care by maintaining a single source of clinical rules in the algorithm that can be changed efficiently.
5. Create a method that assesses the risks and care gaps involved in an individual's care clearly explains why to change the vector of care involved in the recommendations that are made.

Section 3.5: CDS Tools: A Potential Solution to Addressing Care Gaps

Section 3.5.1: Introduction

In a broad sense a CDST is a form of Expert System, ES. Marshall outlines several components of an ES(221). These include a knowledge base specific to the domain of discourse, a data base, an inference engine and a natural language human interface. The inference engine uses IF THEN statements in the rules, which can number in the thousands, that operate on the knowledge base and data base. Building an ES involves a human domain expert who works closely with a knowledge engineer to create the ES. The domain expert and the user interact with the ES via the same natural language human interface. Schnupp et al (222) describe similar components in an ES as stated by Marshal and Klar(223), and echoes a similar model in the design of an ES/CDST that is directed towards the care of individuals needing pulmonary care. Darlington(224) goes a step further, and indeed, this is an important step, by emphasizing the value of building explanation facilities into a healthcare CDST: "explanation facilities can lead to greater adherence to the recommendations of the expert system," that "opaque programs such as neural networks are clinically doubtful as compared with the transparency offered by

explanation facilities," and that "Empirical research has consistently shown that user acceptance of expert systems increases for nonexpert users when this justification knowledge is present and that justification is the most effective type of explanation to bring about positive changes in user attitudes toward the advice-giving system."

In the present context, the CDST described in this Thesis is an ES that is directed towards managing the care of individuals with CMD and DM2 more safely(225, 226), efficaciously (227) and efficiently(228). It is important to note that the explanation facilities described by Darlington in the preceding paragraph are a central design element in the Tool under discussion. The Assessment and Recommendation pages, as described in Section 1.2 below and in detail in Section 3 of Appendix 1 clearly demonstrate, for both the patient and the Caregiver, how assessments are made with respect to the patient's CMD and DM2 status, and why the subsequent recommendations are made.

There are several perspectives in the literature concerning how to define a CDST, what the purpose of a CDST is, the value a CDST can bring, best practices and important design considerations to follow when designing a CDST in order to realize that value. There are also design and performance barriers that may cause the implementation of a CDST to fail. In what follows, we examine these themes more closely.

Section 3.5.2: The AHRQ

The AHRQ, Agency for Healthcare Research and Quality, defines a CDST and comments on its purpose and implementation: (229)

- “Clinical decision support (CDS) provides timely information, usually at the point of care, to help inform decisions about a patient's care. CDS tools and systems help clinical teams by taking over some routine tasks, warning of potential problems, or providing suggestions for the clinical team and patient to consider.”
- “The main purpose of CDS is to provide timely information to clinicians, patients, and others to inform decisions about health care. Examples of CDS tools include order sets created for particular conditions or types of patients, recommendations, and databases that can provide information relevant to particular patients, reminders for preventive care, and alerts about potentially dangerous situations. CDS can potentially lower costs, improve efficiency, and reduce patient inconvenience. In fact, CDS can sometimes address all three of these areas at the same time—for example, by alerting clinicians about possible duplicate tests a patient may be about to receive.”
- “CDS can be used on a variety of platforms (such as the Internet, personal computers, electronic medical record networks, handheld devices, or written materials). Planning for a new health information technology (IT) system to support electronically-based CDS includes a number of key steps, such as identifying the needs of users and what the system is expected to do, deciding whether to purchase a commercial system or build the system, designing the system for a clinic's specific needs, planning the implementation process, and determining how to evaluate how well the system has addressed the identified needs. In the case of CDS, issues around design and implementation of the system are often interconnected.”

Section 3.5.3: HealthIT.gov

The HealthIT.gov resource(230) states:

- "A CDS is a sophisticated health IT component. It requires computable biomedical knowledge, person-specific data, and a reasoning or inferencing mechanism that combines knowledge and data to generate and present helpful information to clinicians as care is being delivered. This information must be filtered, organized and presented in a way that supports the current workflow, allowing the user to make an informed decision quickly and take action. Different types of CDS may be ideal for different processes of care in different settings."
- "Health information technologies designed to improve clinical decision making are particularly attractive for their ability to address the growing information overload clinicians face, and to provide a platform for integrating evidence-based knowledge into care delivery. The majority of CDS applications operate as components of comprehensive EHR systems, although stand-alone CDS systems are also used."
- "Clinical decision support (CDS) provides clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care. CDS encompasses a variety of tools to enhance decision-making in the clinical workflow. These tools include computerized alerts and reminders to care providers and patients; clinical guidelines; condition-specific order sets; focused patient data reports and summaries; documentation templates; diagnostic support, and contextually relevant reference information, among other tools."

- "A CDS has a number of important benefits including: Increased quality of care and enhanced health outcomes, avoidance of errors and adverse events and improved efficiency, cost benefit and provider and patient satisfaction."

Section 3.5.4: Openclinical.org

The openclinical.org site (231) states that the benefits of a CDS include:

- "Improved patient safety e.g. through reduced medication errors and adverse events and improved medication and test ordering; Improved quality of care e.g. by increasing clinicians' available time for direct patient care, increased application of clinical pathways and guidelines, facilitating the use of up-to-date clinical evidence, improved clinical documentation and patient satisfaction; Improved efficiency in health care delivery e.g. by reducing costs through faster order processing, reductions in test duplication, decreased adverse events, and changed patterns of drug prescribing favouring cheaper but equally effective generic brands, and that a CDS can supply clinical information anytime, anywhere it's needed. In the last resort, widespread use of clinical decision support systems in clinical practice will not occur without electronic patient record systems using terminology and data standards that will allow them to be accessed effortlessly during routine patient care."

Some of the success factors listed on this site that are deemed particularly important in the present context include: attitude of targeted users: breadth and depth of commitment ,degree of user acceptance prior to and after installation, ease of use - time needed to learn to use and to use, ease of integration within organisational context and routine workflow, user interface:

design, structure, number of forms, and the quality and reliability of a system and its knowledge base which should be populated with trusted, up-to-date and maintainable knowledge.

Wright et al(232) conducted an extensive review of the clinical decision support literature since 1959, sequenced the progress of these systems and developed a model that consists of four evolutional phases of a CDST, quoted verbatim:

- Standalone decision support systems
- Decision support integrated into clinical systems
- Standards for sharing clinical decision support content
- Service models for decision support.

Four limitations that were common in each of the above phases included, again quote verbatim were that:

- Fixed knowledge representation systems inherently circumscribe the type of knowledge that can be represented in them
- There are serious terminological issues
- Patient data may be spread across several sources with no single source having a complete view of the patient
- Major difficulties exist in transferring successful interventions from one site to another.

Section 3.5.6: Bates et al

Bates et al(233) present Ten Commandments for effective clinical decision support, some of which include:

- “Speed is everything”

- “Fit into the user’s workflow”
- “Simple interventions work best”
- “Manage and maintain your knowledge-based systems.”

Section 3.5.7: Sittig and Bates

Sittig and Bates(234) present grand challenges in clinical decision support. These include:

- “Improve the human–computer interface”
- “Disseminate best practices in CDS design, development, and implementation”
- “Summarize patient-level information”
- “Prioritize and filter recommendations to the user”
- “Create an architecture for sharing executable CDS modules and services”
- “Combine recommendations for patients with co-morbidities”
- “Prioritize CDS content development and implementation”
- “Create internet-accessible clinical decision support repositories”
- “Use free text information to drive clinical decision support”
- “Mine large clinical databases to create new CDS’s”

The authors summarize by stating that the “Identification of solutions to these challenges is critical if clinical decision support is to achieve its potential and improve the quality, safety and efficiency of healthcare.”

Section 3.5.8: Sim et al

Sim et al(13) focus on the interplay of a CDDS and evidence-based medicine and identify 5 broad areas of concern:

- "Capture literature-based and practice-based evidence in machine-interpretable knowledge bases"
- "Develop maintainable technical and methodological foundations for computer-based decision support"
- "Evaluate the clinical effects and costs of clinical decision support systems and the ways clinical decision support systems affect and are affected by professional and organizational practices"
- "Identify and disseminate best practices for work flow–sensitive implementations of clinical decision support systems"
- "Establish public policies that provide incentives for implementing clinical decision support systems to improve health care quality."

In summary, we have seen that a CDST is a species of an ES, that there are several closely-related definitions of CDST's, that CDST's can add value to the quality of the healthcare delivery process, and that there are best practices and pitfalls involved in the design and implementation of a CDST. Electronic decision support directed at the care of patients with CMD and DM2 is a species of CDST and we now turn attention to the subject of CDST directed specifically at the care of patients with DM2.

Section 3.6: Clinical Decision Support Tools for Diabetes Mellitus Type 2

This Thesis is focused on the development of a wireframe of a future CDST that supports the comprehensive care of individuals with CMD and DM2 both at the personal level by accounting for the given patient's personal, laboratory and medication data as noted in detail in Section 2.1 of the Appendix, and at the comprehensive team-based level as noted above where the core

themes of this Thesis were introduced, and in Section 1.4 above. There are several widely-accepted tools that address some of the issues involved in the care of individuals with CMD and DM2 as detailed in Section 3 of the Appendix. To summarize these tools, they generally have a very narrow focus on the type and quantity of the data ingested, and present neither a comprehensive, personalized assessment of the patient's status, nor a platform for comprehensively managing that patient's care in the context of an ACO where the Triple Aim's constructs must be carefully attended to. Filling these gaps is the central thrust of this project. There is literature addressing these gaps, and to this we next turn our attention.

Wilkinson et al(12) examines personalized decision support in the care of individuals with DM2, defining "personalized" as:

- "We define decision support as personalized when a decision aid or tool incorporates patients' clinical characteristics and/or treatment preferences into the clinical decision-making process."

Wilkinson et. al. created two tables to summarize both personalized and non-personalized CDST's for managing diabetes. These tables (recreated below: tables 3.6.1, table 3.6.2) summarize the salient points of the work contained in the original publications referenced by the hyperlinks in the first column, and the reader is referred to these original publications for the details contained in these original publications. It is worth noting that the types of Clinical Decision Support Tools referenced in these tables is varied and is summarized in what follows.

There are tools that encourage shared decision-making without referencing the type of informatics tool being used, (Corser et al.), a printed aid that summarizes treatment burden issues that the clinician reviews in-person with the patient, (Mullen et. al), web-based tools that tailor

the decision about statin use to the individual patient, (Weymiller et. al., Nannenga et. al., Abadie et. al., Simmons), a web-based color coded “diabetes tracker,” (Holbrook et.al.), a decision support system embedded in an EHR, (Hunt et.al, O’Conner et. al), a laboratory-based registry with reporting mechanisms for both patients and clinicians to consume, a computer-based decision support system for patients using insulin pumps which includes telemedicine functionality, (Augstein et. al), a mobile phone personalized intervention system, (Quinn et. al), and unspecified computer application systems (Saenz et. al, Rodbard et. al).

The personalized support tools are summarized in Table 1 of (12), recreated below:

Table 3.6.1 Studies of decision support tools for type 2 diabetes mellitus which provide support for personalization

Primary author, study year	Target audience	Study characteristics	Goal	Intervention Type	Method and degree of personalization	Decisions and outcomes affected
Corser, et al. 2007	Physicians, patients	58 Patients, single-group, pretest-posttest study, 15-month study period.	Improve outcomes, documentation of management goals, and patient knowledge and empowerment regarding diabetes goals.	Printed aid that summarizes treatment	Encouraged patients to set goals to be considered in shared-decision making process.	Addressed care decisions using shared decision-making that incorporates patient's goals. Significantly increased patient goal-setting and knowledge (P= .001). Did not have a significant impact on HbA1c, weight, or BP.
Mullan, et al. 2009	Physicians, patients	40 Clinicians and 56 patients, cluster randomized trial, 12-month enrollment period.	Improve adherence and glycemic control.	Web-based decision support tool	Printed tool used to help personalize pharmacologic therapy for diabetes based on patient and physician preferences.	Affected decision of how to medically manage diabetes. Increased patient involvement and aspects of knowledge and acceptability. Did not improve adherence or HbA1c at 6 months.

Primary author, study year	Target audience	Study characteristics	Goal	Intervention Type	Method and degree of personalization	Decisions and outcomes affected
Weymiller, et al. 2007	Physicians, patients	98 Patients and 21 physicians, 2×2 clustered factorial design randomized trial, 4-month enrollment period.	Improve patient decision-making process.	Web-based decision support tool	Initiation of statin therapy was largely dependent on patient knowledge and preference.	Decision of whether to take statin. Increased patient knowledge and decreased decisional conflict. Increased medication adherence.
Nannenga, et al. 2009	Physicians, patients	16 Clinicians and 98 Patients, 2×2 clustered factorial design randomized trial, 4 month enrollment period.	Measure effect of the tool on patient knowledge, decisional conflict, participation and trust.	Web-based decision support tool	Initiation of statin therapy was largely dependent on patient knowledge and preference.	Decision of whether to take statin. Trend toward increased total trust in physician. Improved patient knowledge, decisional conflict, and participation, each of which increased the likelihood of total trust.
Abadie, et al. 2009	Physicians, patients	98 Patients, factorial-design randomized trial.	Examine decision aid use patterns by physicians.	Web-based decision support tool	Initiation of statin therapy was largely dependent on patient knowledge and preference.	Decision of whether to take statin. Tool was used as intended by physicians in 64% of the interventions.

Primary author, study year	Target audience	Study characteristics	Goal	Intervention Type	Method and degree of personalization	Decisions and outcomes affected
Mann, et al. 2010	Physicians, patients	150 Patients, randomized trial.	Improve elements of patient decision-making process in a largely minority population and determine effect of tool on medication adherence.	Web-based decision support tool	Initiation of statin therapy was largely dependent on patient knowledge and preference.	Decision of whether to take statin. Improved patient perception of risk, beliefs regarding the medication, and decisional conflict. Did not affect medication adherence.

HbA1c = hemoglobin A1c; BP = blood pressure.

Non-personalized support tools in table 2 of (12), recreated below:

Table 3.6.2 Studies of decision support tools for type 2 diabetes mellitus which provide support for standard diabetes care without personalization

Primary author, study year	Target audience	Study characteristics	Goal	Intervention Type	Decisions and outcomes affected
Cleveringa, et al. 2008	Physician, nurse	3,391 Patients, cluster-randomized trial.	Improve clinical markers (A1c, BP, cholesterol).	Computerized decision support and feedback	Targeted at overall management. Decreased total cholesterol, LDL, BP. No significant change in HbA1c.
Holbrook, et al. 2009	Physicians, patients	46 Clinicians, 511 Patients, cluster-randomized trial, 1 year enrollment period.	Improve frequency and ease of assessing diabetes markers.	Web-based color-coded "diabetes tracker"	Targeted at overall management and frequency of certain assessments. Improved quality of monitoring. Resulted in lower BP and HbA1c.
Hunt, et al. 2009	Physician	4,265 continuously enrolled patients. Pre-post intervention, two year study period.	Improve clinical markers (HbA1c, BP, cholesterol), and process of care.	Decision support system embedded in an EHR	Targeted at overall management. Decreased LDL, BP. Improved LDL and HbA1c testing. Did not reduce mean HbA1c, but did improve percent of patients at HbA1c goal.
MacLean, et al. 2009	Physicians, patients	7,412 patients, cluster-randomized trial, 32 month study period.	Evaluate the effect of support system on processes of care and outcomes.	Laboratory-based registry with reporting mechanisms	Targeted at overall management. Improved likelihood of testing for cholesterol, creatinine, and proteinuria, but not HbA1C. Did not impact HbA1c or LDL levels.

Primary author, study year	Target audience	Study characteristics	Goal	Intervention Type	Decisions and outcomes affected
Augstein, et al. 2010	Physician	359 Patients, retrospective, observational study.	Improve glycemic control.	Laboratory-based registry with reporting mechanisms	Targeted at overall management, emphasis on glycemic control. Decreased HbA1c, mean sensor glucose, and glucose variability.
O'Connor, et al. 2011	Physician	41 Clinicians, 2,556 Patients, cluster-randomized trial, 9 month study period.	Reduce HbA1C, BP, LDL	Decision support system embedded in an EHR	Targeted at overall management. Improved HbA1c and SBP, not LDL.
Quinn, et al. 2011	Physicians, patients	163 Patients, cluster-randomized trial, 1-year treatment period.	Reduce HbA1c.	Mobile phone personalized intervention	Targeted at overall management. Certain forms of the intervention reduced HbA1c over 1 year compared with usual care.
Saenz, et al. 2012	Physician	66 Clinicians and 697 Patients, Cluster-randomized trial, 18-month study period.	Reduce HbA1c	Unspecified computer application	How to use insulin in type II diabetes. Reduced HbA1c.
Leal, et al. 2009	Not specified.	Development of life expectancy tables based on the United Kingdom Prospective Diabetes.	Develop a tool to help predict life expectancy.	Risk-stratified ables reporting life-expectancy	Study describes tool. Presumably the decision relates to addressing modifiable risks in an attempt to improve life expectancy.
Rodbard, et al. 2011	Physician, patients	Development of computerized clinical decision support tool for patients with type 2 diabetes.	Improve glycemic control.	Unspecified computer application	Targeted at glycemic management. Currently being tested.

HbA1c = hemoglobin A1c; BP = blood pressure; SBP = systolic blood pressure; LDL = low-density lipoprotein cholesterol.

The theme of a comprehensive, personalized approach to the care of patients with CMD and DM2 recurs throughout this Thesis, and Wilkinson et al summarize the advantages of this approach as captioned in the tables immediately above. At the risk of over-simplification, these tables show that CDST's directed at the care of patients with DM2 support improvement in measured outcomes, and specifically, those CDST's that take the personalized approach also engendered a deeper knowledge that patients have concerning their disease and its entailed risks, better acceptance of goals regarding their care and increased trust in the Caregiver.

Section 3.7: Chapter Summary

The aim of this research is to develop the wireframe representation of a web-based Clinical Decision Support Tool, CDST, that will assist caregivers as they manage individuals with Cardiometabolic Disorder, CMD, and Diabetes Mellitus Type 2, DM2. This wireframe will serve as the model for developing the launch version of the CDST. We have the Trainee's role in the process, which involved suggesting the development of a web based CDST directed at the management of blood sugar medications in patients with DM2. We then looked at the problems this Tool is directed at solving, how informatics in general can address these problems, and then turned to an in-depth review of CDST's in general and finished our review by looking at existing tools for managing DM2. We now turn out attention to the vision behind the development of the Tool presented in this Thesis and look at its functional requirements.

CHAPTER 4: Vision and Functional Requirements for the Tool

Section 4.1: Introduction

This Chapter builds upon the themes developed in Chapter 3 where we examined the problems this Tool is trying to address, how a clinical informatics solution can be used to address evidence-based gaps in care, several perspectives and opinions concerning what a CDST is, along with the desiderata for an ideal CDST, Clinical Decision Support Tool, along with the potential pitfalls to avoid when designing one. We also saw how a CDST can improve care, and then focused directly on Clinical Decision Support Tools that address CMD and DM2.

This Chapter begins by reiterating several aspects of an Expert System that were examined in Sections 3.5-3.5.1 and apply these aspects that are relevant to the Tool's design. Focus then shifts to the Tool's functionality, it's structure, knowledge base, inference model, and its user interface. We then move on to discusses the risk analysis involved in choosing appropriate care of patients with CMD and DM2 and compare several web-based risk-assessment tools that are currently available.

Section 4.2: An Expert System

This Tool is a Clinical Decision Support Tool and is a species of an Expert System, ES, as was noted in Section 3.5.1 where we reviewed the contributions made by Marshall, Schuup, Klar and Darlington concerning the components of an ES. For our immediate purposes we will cover three of these components, including the Tool's inference model, addressed in Section 4.6 and in more detail in Sections 3.5.1-3.5.3,3.7.1, 4.1.1-4.1.7-4.4.1, 4.5.1,4.6.1,5.1.2-5.1.8 of Appendix 1,

the Tool's user interface, addressed in Section 4.7 and the Tool's knowledge base, addressed in Section 4.8. We then apply several of the attributes of successful CDST's

The definitions and advantages of a CDST are referenced and discussed in Sections 3.5.2-3.5.4 and several of the desiderata necessary to implement a successful CDST that were covered in Sections 3.5.6-3.5.8. Several of these desiderata are relevant to this Tool's design and are recapitulated and briefly commented on next, followed by reiterating and applying some of Wright's comments before moving on the Tool's design. These desiderata include:

- Speed is everything
    - Categorical and ordinal data are used to speed up data input, there will be no scrolling down a page, and moving between pages will be essentially instantaneous.
- Fit into the user's workflow
    - The Tool will be used in the clinical setting and will support the conversation Caregivers and patients need to have anyway. The tool provides focus in this conversation.
- Simple interventions work best
    - This is a relatively light-weight Tool. Each page is clearly laid out and logically linked to the next page.
- Manage and maintain your knowledge-based systems and capture literature-based and practice-based evidence in machine-interpretable knowledge bases
    - Evidence-guided standards and expert opinion are a central design feature.
- Summarize patient-level information

    - The Tool's rules-based engine presents a comprehensive, personalized summary of the patient's status on the Assessments Page.
- Prioritize and filter recommendations to the user
    - This is the function of the Recommendations Page.
- Combine recommendations for patients with co-morbidities
    - This Tool will address obesity, dietary choices, exercise, emotional wellbeing, hyperlipidemia, hypertension and chronic kidney disease.

Returning to Wright(232), the Tool under discussion in this Thesis is, in Wright's model, the most basic type of CDST. In his words it is a "standalone decision support system."

Wright also mentions four common limitations of CDST's three of which are mentioned and commented on next:

- Fixed knowledge representation systems inherently circumscribe the type of knowledge that can be represented in them
    - This is not a limitation concerning the Tool under development since it is narrowly focused to address the knowledge involved in caring for patients with CMD and DM2. The circumscribed type of knowledge that the Tool represents is exactly what is desired: patient-centered personalized knowledge about the patient's status with respect to CMD and DM2 as represented on the Assessments Page, and inference-driven patient-centered personalized circumscribed knowledge regarding what should be done in terms of secondary and tertiary prevention as represented on the Recommendation Page.

- Patient data may be spread across several sources with no single source having a complete view of the patient
    - Patient data is indeed spread across all of the Electronic Health Records, EHR's in the ACO as well as the ACO's population health management application. This limitation is addressed by developing a web-based Tool that is used in the clinical setting where the patient's data reside in the associated EHR. Since this tool is narrowly-focused on CMD and DM2 a "complete view of the patient" outside of the data required to address CMD and DM2 is not necessary, while at the same time creating a "complete view of the patient" from the perspective of managing CMD and DM2 is necessary.
- Major difficulties exist in transferring successful interventions from one site to another
    - Each of the sites in the ACO will use the same web-based CDST. The Caregiver and patient are presented with personalized, patient-centered recommendations which are unrelated to the site of care delivery. Since all clinics in the ACO will use the same CDST, the issue of "transferring successful interventions from one site to another" is addressed.

In Section 3.6 we reviewed Wilkinson's analysis of CDST's that are directed at the care of patients with DM2. He demonstrated improved clinical outcomes when the tools were personalized. While not explicitly addressed, is possible that the noted decrease in LDL Cholesterol, HbA1c and better use of insulin was correlated with better medication adherence, since these lab values are correlated with medication use, and using insulin correctly also suggests improved medication compliance. Enhanced trust in the clinician was also demonstrated. A recurring theme in this Thesis is that a comprehensive, personalized CDST is a

viable way forward. The Tool described in this Thesis supports patient autonomy, one of the pillars of Medical Ethics discussed in Section 4.8. The Tool engenders a patient-centered discussion between the patient and clinician about the recommendations the Tool presents and why they are important yet leaves the decision to follow these recommendations to the patient. It is possible, following Wilkinson, that this Tool may engender deeper therapeutic relationship between the patient and Caregiver because of the collaborative, patient-centered, personalized approach to care that the Tool. We now move on to the details of the Tool's design.

Section 4.3: The Details of the Tool's Design

In what follows next, we examine the Tool itself in some detail. We will look at the Tool's functionality, structure, the inference engine and in a long and detailed section, we examine the many facets of the Tool's knowledge base. Following this, the justification for a new type of tool for managing CMD and DM2 is presented in the context of a side-by-side comparison of currently-available web-based tools that address the risk patients with CMD and DM2 face.

Section 4.4: The Tool's Functionality

This CSDT is directed at the care of patients with CMD and DM2 and the Tool's functionality supports four specific aspects of this care.

1. Assess the patient's level of risk with respect to CMD and DM2.
2. Expose existing care gaps in the patient's current clinical management with respect to CMD and DM2.

3. Recommend changes in the patient's care management such as lifestyle improvement, medication regimens, additional laboratory values and consultations with other team caregivers.
4. Create an action plan by working with the recommendations the patient chooses to follow. This page can become a written summary of the next steps in clinical care and further coordination of care as needed. This page can also be copied and pasted into the patient's EHR.

Section 4.5: The Tool's Structure

As envisioned, the tool will consist of sets of pages that flow logically from the input of patient-specific data to the eventual action items that will be taken based on the patient's agreement to follow suggested recommendations. Each of these sets of pages (see figure1 for an overview) is outlined below and covered in detail in Section 2 of Appendix 1. The wireframes of these pages are shown in Appendix 2.

1. The Inputs Page allows patient specific data, (including personal data, medication data and laboratory data), to be entered for computation. The outputs of this computation become the inputs for the subsequent page, i.e., the Assessments Page.

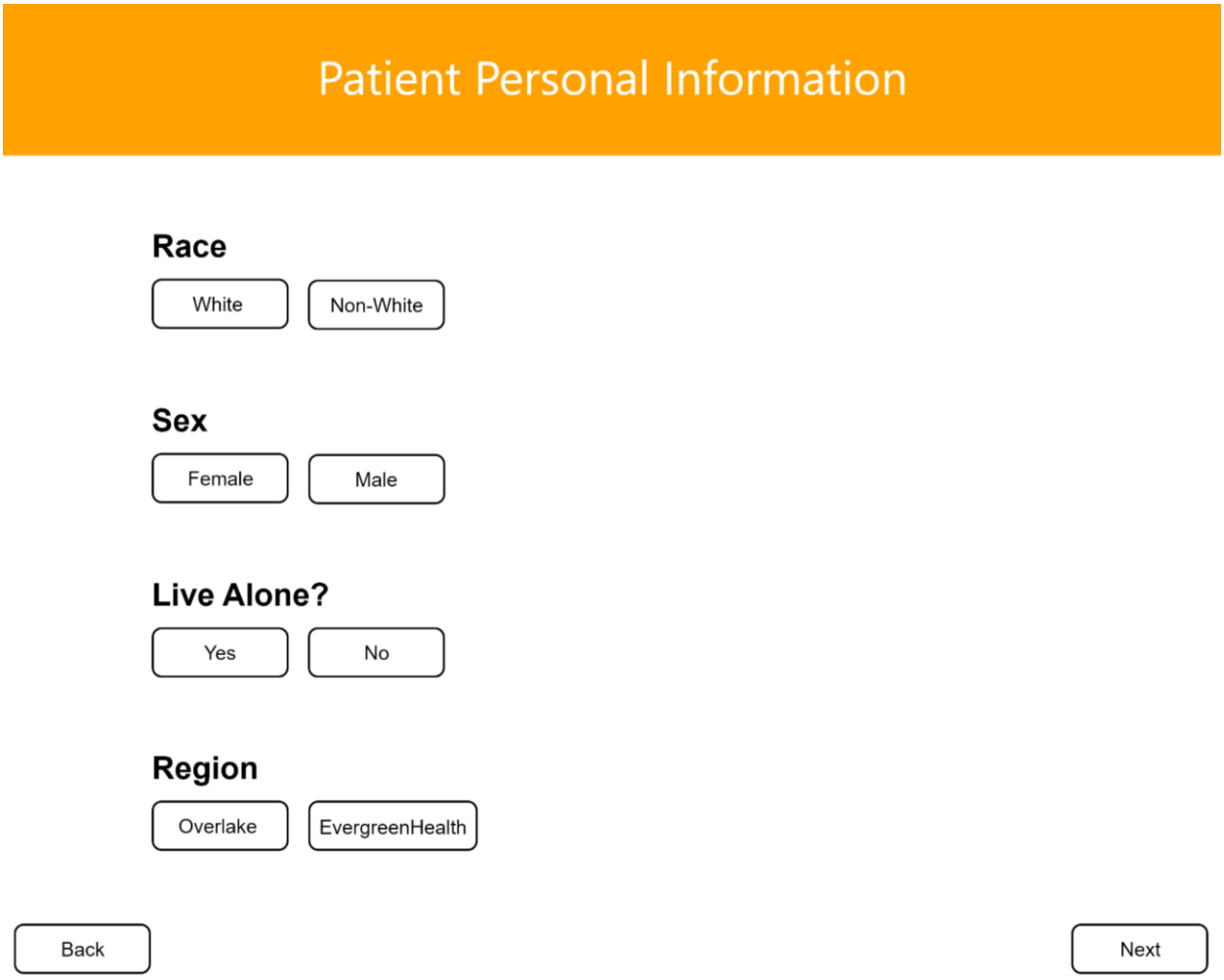

Figure 1 Example Inputs wireframe page for personal information. Please see Appendix 2 for all of the Inputs Pages

2. The Assessments Page presents the patient and clinician with a summary of the patient's health status with respect to CMD or DM 2 as derived from computing on the outputs of the input page. For example, on this page a patient's abnormal BMI, elevated blood pressure or elevated hemoglobin A1c will be presented. These assessments in turn become inputs for the subsequent page, the Recommendations Page.

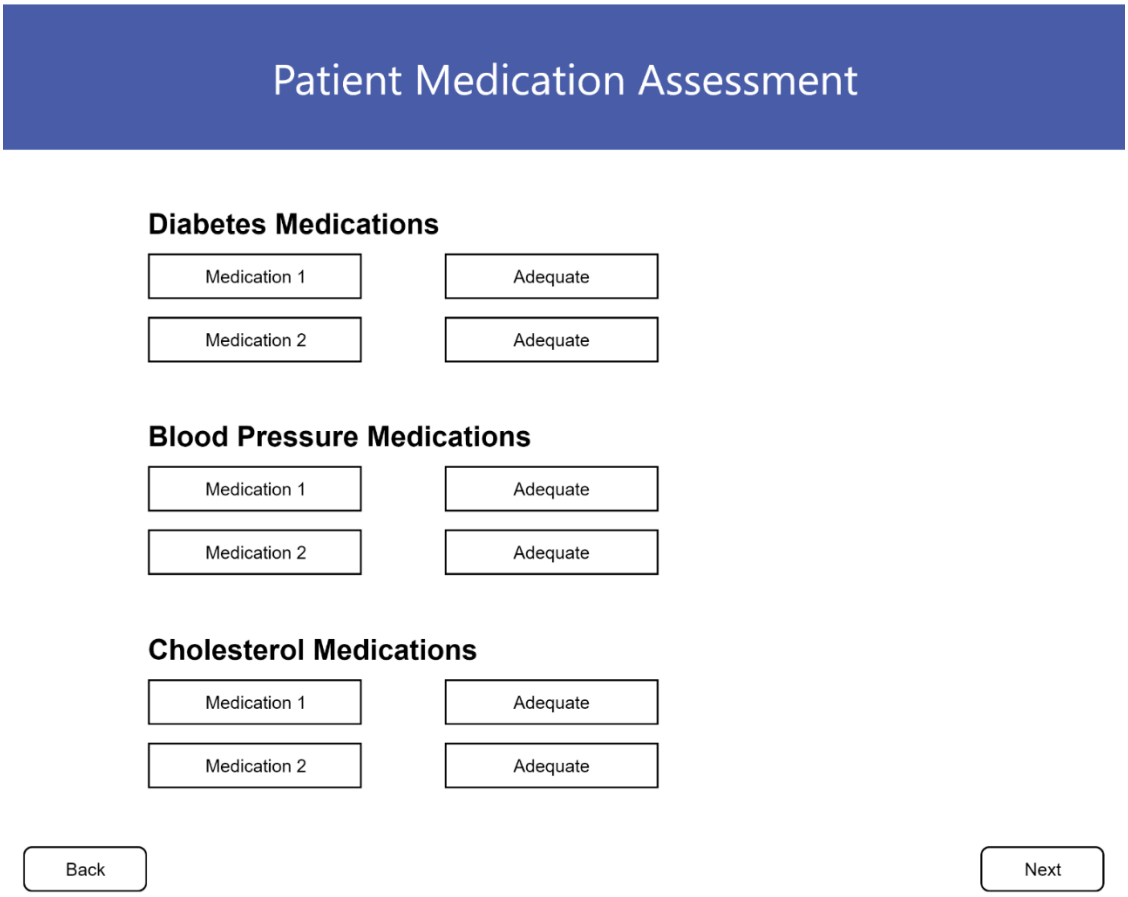

Figure 2 Example Assessment wireframe page for medications. Please see Appendix 2 for all of the Assessments Pages.

3. The Recommendations Page uses the outputs from the Assessments Page to present the patient and clinician with the patient-specific recommendations regarding the management of the patient's CMD or DM 2. Each of these recommendations will be accompanied by a checkbox that allows the patient, after a patient-centered discussion with the clinician, to agree or disagree with the recommendations. The outputs of the Recommendations Page in turn flow to the Actions Page.

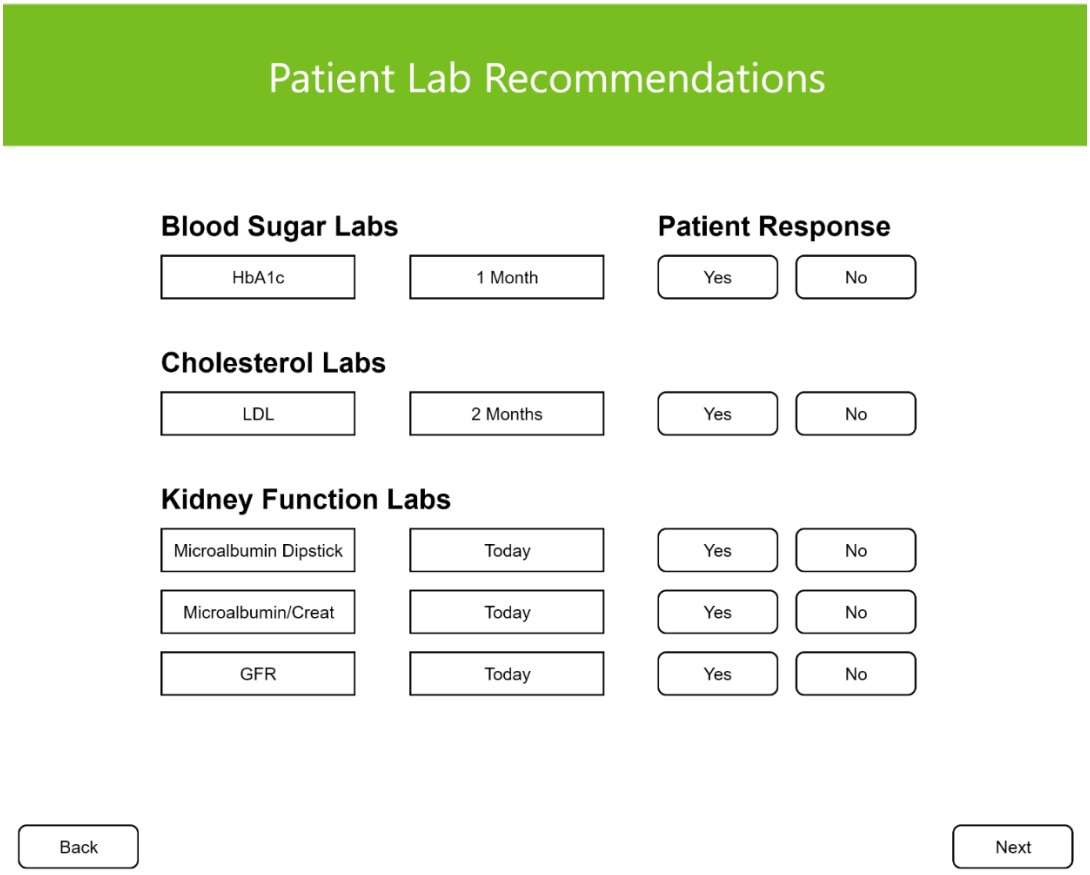

Figure 3 Example Recommendation wireframe page for labs. Please see Appendix 2 for all of the Recommendations Pages.

4. The Actions Page summarizes the next steps in the care of the patient with respect to CMD or DM 2. Examples include specific changes in medication, the need for further laboratory investigations, visits with a diabetic educator or consultation with a clinical pharmacist. Each of these actions will be accompanied by a brief explanation. Once the Actions Page has been reviewed with the patient, a document that summarizes the data and information on each of these pages is created. It can be printed as a handout for the patient or copied and sent to the patient via the EHR's portal. This document can also be copied and pasted into the patient's EHR.

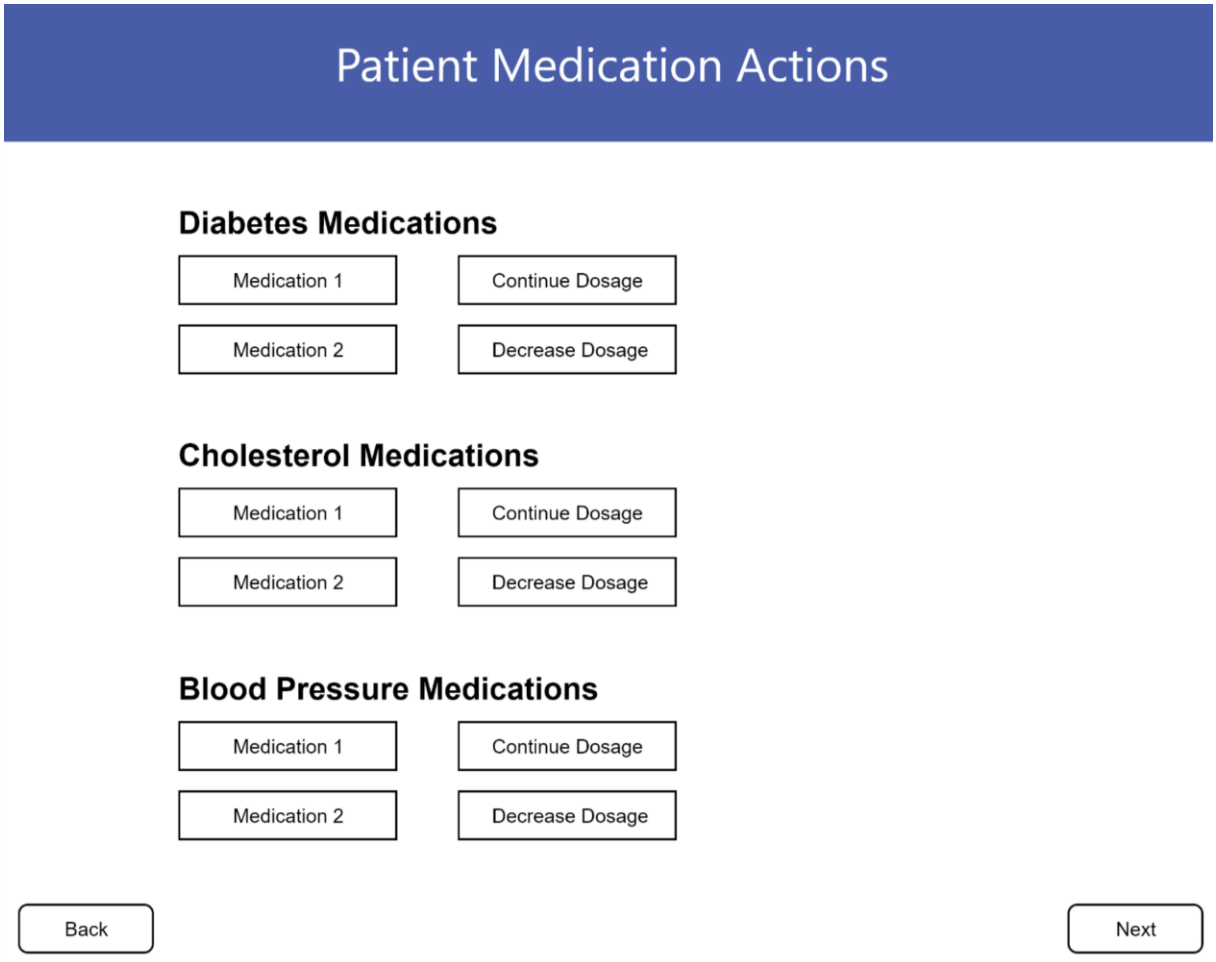

Figure 4 Example Action wireframe page for medication. Please see Appendix 2 for all of the Actions Pages.

Section 4.6: The Tool's Inference Model

This tool's underlying logic is "if-then." The operators include "and," "or," "not" and "else." This is conditional logic fits naturally into the objectives of the tool. The data that are added in the Inputs Page form the base from which logical inferences can be drawn and the results of the logical manipulation of these inputs creates the assessments on the Assessments Page. These assessments in turn become the inputs which are logically operated on to form the Recommendations Page and based on the recommendations to which the patient agrees a simplified form of the logic, ("if yes, then add to action page"). Examples of the logic involved in this Tool's inference is detailed in Sections 3.4-5.1.8 of Appendix 1.

Section 4.7: The Tool's User Interface Design

The user interface design of this tool has three central perspectives. The first is patient safety(235, 236). Data input is simple and each of the pages is uncluttered and has plenty of white space to reduce the possibility of data input errors. Implicit in patient safety is the adoption of accepted standards of care. The computation model's rules are based on published clinical guidelines and carefully curated expert opinion. Second is clarity. The conditional logic used in the rules engine generates clear, understandable endpoints by using explanatory facilities as described by Darlington(224) in Section 3.4.1. The final stage of this logic results in the Actions Page. This page can be printed for further reference at a time of the patient's choosing. Third is ease-of-use(237, 238). Pages are designed to make scrolling unnecessary and as the user moves through the application, progress and next steps are clear.

The user interface design of any application represents a potential constraint on how the user will respond to that application. This tool is designed to unobtrusively fit into the workflow of a busy ambulatory office environment and as such the interface must facilitate the user's workflow. Pages have a large amount of white space the icons on the various pages make use of shape color and varying fonts facilitating "understanding at a glance." Use of a "next" and "previous" choice appear on each page and of the real estate on each page is laid out such that scrolling is unnecessary. Search functionality is present on the input page section dealing with medications to assist with rapidly entering a patient's medications. As discussed in Section 2.1.3 of Appendix 1, the beta version of this tool has a constrained number of medications because most of the medications available for treating hypertension are not commonly used. The vast majority of hypertensive medications include diuretics, ACE, Angiotensin Converting Enzyme Inhibitor, and ARB, Angiotensin Receptor Blocker, inhibitors calcium channel blockers, and beta blockers. A query of our population health application generated a list of the most commonly used medications in the ACO. These medications are part of the Tool's knowledge base which is discussed in the following section.

Section 4.8: The Tool's Knowledge Base

In Section 3.5.1 we covered a model for an Expert System, ES which included the concepts of a data base and a knowledge base. In the launch version of the Tool, there may not be a database per se. Instead, there are likely to be look-up tables that support the search functionality used to rapidly enter the patient's medications. Since no data from any given session using this tool is stored, there is no database of patient medications, lab values or any other PHI.

This Tool's knowledge base has several facets that may not appear directly related to how this Tool's functionality with respect to a comprehensive, personalized approach to the care of patients with Cardiometabolic Disease and Diabetes Mellitus Type 2. An important distinction is made here: A "knowledge base" in the present context is construed as a structure upon which concepts are built. This is distinct from "knowledge representation" in the pure informatics sense where ontologies with detailed logical relationships, capable of machine-to-machine interaction are at the core of an informatics system. Along this line of thinking about a knowledge base, several components are included below. As an example, "Medical Ethics" is in this work is a way of calling out underlying concepts as detailed in Section 4.8.1. This Tool does not search for and call out violations in medical ethics. Instead it stands in relation to other core concepts in this Thesis. For example patient-centered personalized care stands in relationship to autonomy where the caregivers ethical duty is to explain the options of care that are available, listens to and respects the patient choice, patient safety, (as an example giving an elderly patient a diabetic medication that may cause a significant drop in blood sugar), stands in relationship to non-malfeasance, administering a medication that will decrease excess morbidity and mortality, (as an example, lowering the patient's cholesterol level), stands in relation to beneficence, and following the laws and rules that govern the delivery of healthcare, (as an example following the Federal, State, and ACO rules), stands in relation to the legal aspects of medical ethics. By way of emphasis via repetition, this tool will not alert the user to potential legal violations.

This line of thinking is carried forward in all of the components of the Tool's knowledge base as detailed immediately below. To drive home the point about a knowledge base as construed in this Tool vs. a form of knowledge representation as noted above, we can look at Engle's biopsychosocial model detailed below. This model stands in relation to the personal data found

in the lab section, (“bio”), data collected concerning patient habits, (both “psycho” and “social”), the presence or absence of anxiety or depression, (“psycho”), and whether the patient lives alone, (“social”), all of which have a bearing on the outcomes of care in patients with Cardiometabolic Disease or Diabetes Mellitus Type 2.

Given this distinction between a knowledge base and knowledge representation as discussed in the immediately previous paragraphs, we can now turn to the components of this Tool’s knowledge base. These include:

- Medical ethics
- The biopsychosocial model
- The community health mode
- The Quadruple Aim
- Published care guidelines that reference evidence-based healthcare
- Patient demographics
- Vital signs
- Family history
- Past medical history
- Laboratory data
- Patient medications
- Patient labs
- ACO guidelines for referral management

Some of these knowledge base facets are covered below, others are covered in detail in Section 2.1 of Appendix1.

Section 4.8.1: Medical Ethics (239)

1. Patient autonomy(240, 241): The Patient is at the center of healthcare decisions. The system engages the patient by inputting will the various required data elements, demonstrating the patient's risk of further complications of cardio metabolic disease, and shows how these assessments were made. Recommendations are made for changing the medical regimen after this initial assessment and patients are then offered the choice of following up on these recommendations.
2. Non-maleficence(242, 243): Do no harm. Recommendations guard against harm in several different ways. As examples overmedication of hypertension can cause falls and overmedication with hypoglycemic agents can cause severe hypoglycemia. Harms can also include increased body weight which further complicates the treatment of cardio metabolic disease and an economic form of harm. Many of the newer medications being used to treat cardio metabolic disease are extremely expensive and purchasing these medications may prove difficult for the patient as well as the family.
3. Beneficence(244, 245): What we do will help the patient. The recommendations made by this tool are both evidence-based and domain expert gathered from the ACO's quality committee and a multi-disciplinary team that is making recommendations related to the care of patients with DM2 that is severely out of control. Beneficence in this context means positively altering the apparent disease trajectory of the patient's condition. Examples include lipid management that either slows or arrests atherosclerosis managing the blood pressure within parameters that have been shown to decrease mortality and morbidity and optimally managing blood glucose as it is reflected by hemoglobin A1c values.

4. Legal(246, 247): We work within the constraints of the Patient's health plan and existing healthcare law. Beyond this basic tenant, this Tool does not address legal aspects of medical ethics.

Section 4.8.2: The Community Health Model

The community health model has been present in various forms for decades. (248, 249) (250, 251). Broadly speaking its intention is to provide a global set of resources for a given community with the intent of optimizing health of that community(250, 251). In the present context, the community health model is applied in a narrower sense. It is construed as a population health management model that is dealing specifically with the population of patients diagnosed with diabetes mellitus type II.

1. Health Promotion. This tool encourages diet, exercise, ideal body weight and optimal medication management.
2. Disease Prevention. This tool enables a form of secondary prevention. Patient with diabetes are already at risk for cardiovascular disease, stroke, blindness, kidney disease and lower extremity amputations. With optimal care management that utilizes the resources within the ACO, the sequelae of CMD and DM2 can either be prevented or delayed.
3. Early Disease Detection. Given that this tool is being applied within the context of patients who already have diabetes type II early disease detection is not supported as is generally construed in this model.
4. Coordinated Disease Management. This tool acknowledges the need for a team-based system of care. Neither primary care physicians or specialists in cardiology or

endocrinology for example can manage all the aspects of optimizing a patient's diabetic care. Examples include diabetes classes, individual nutrition instruction, lipid management by clinical pharmacists in difficult clinical presentations and the services of care managers.

5. End of Life Care. This tool does not support this aspect of the model.

For the purposes in the present context, primary prevention is health promotion and disease prevention. Care management includes a patient-centric team-based approach, for the management of co-incident comorbidities, including secondary and tertiary prevention. Examples of secondary prevention include preventing the development of vascular disease, myocardial infarction, stroke, peripheral vascular disease and renal failure. Tertiary prevention involves the avoidance of procedures such as carotid embolectomy, coronary revascularization, restoring lower extremity vascular function, amputation, or renal dialysis.

Quaternary prevention(252) involves ensuring that a given institution, (in this case the EHN ACO), does not "over-diagnose" or "over-treat" a given patient. This is also been referred to as "disease-mongering," where patients are subjected to unnecessary testing, treatments or procedures. In medical ethics this concept is represented as non-malfeasance and futility.

Striking a balance between over-treatment and undertreatment in the managed care setting is difficult and imprecise. There is a strong incentive to reduce the cost of care by not providing unnecessary services or performing necessary procedures, which harmonizes the notions of quaternary prevention, non-malfeasance, futility, and high-value healthcare.

Section 4.8.3: The Biopsychosocial Model

Engle's biopsychosocial model(253, 254) encourages the given patient's healthcare to be delivered within a broader construct that includes the following points of view.

1. Biological aspects of care. This tool addresses the biological aspects of care by concentrating on biometrics, laboratory values and medications.
2. Psychological aspects of care. Depression and anxiety, for example impact the patient's health care outcomes in the domain of cardio metabolic disorder. Screening for and attending to the behavioral aspects of a patient's care are accounted for in this tool.
3. Social aspects of care. Similarly, the social aspects of a patient's care are important. This tool addresses this dimension by accounting for the patient's dietary and exercise habits.

Section 4.8.4: The Quadruple Aim

The Quadruple Aim was originally proposed by Bodenheimer and Sinsky(37) and is seen as a method for increasing clinician wellbeing and decreasing burnout(255). The Quadruple Aim is an extension of the Triple Aim. Which first appeared in the publication by the Institute of Medicine (53). This model focuses on 3 aspects of healthcare delivery: the health of the population being cared for(51), as defined by meeting a set of healthcare delivery metrics, the per capita cost of the care of that population (250, 251, 256), and the population's experience of the healthcare delivery process(52).

There are inherent tensions generated by this model: increasing the health of the population can be costly as infrastructure is added, while costs are expected to decrease, and patients may experience upset on experiencing that resources they expect are being denied. It is within this tension that the reason for expanding the Triple Aim to the Quadruple Aim noted above is found.

This tension generates significant clinician stress particularly where the Biopsychosocial model is applied. A comprehensive approach is required and difficult to deliver. It is also within this tension that this project was proposed: CMD and DM2 are costly disorders to care for and clinicians need better tools to deal with the increasing incidence of these disorders, the burden of care they generate and the proliferation of medications available to treat them. This is discussed more fully in what immediately follows.

1. Population Health(257). This tool will account for the diabetes management metrics followed by payers. This includes the following the level of a given patient's hemoglobin A1c, a patient's LDL cholesterol level, screening for microalbuminuria or managing the diabetic patients blood pressure.
2. Per Capita Cost of Care (251). This tool will not directly address the cost of care. In the recommendations section the cost of medication is addressed, and carefully coordinating care is considered cost-effective(66). The tool however does not support a global approach to all of the expenses involved in caring for a diabetic patient.
3. Patient Experience(257). This metric will not be directly supported by the tool. There are no specific measurements of a change in a patient's experience of care is a function of the use of this tool. There is a tacit assumption that sequentially following the flow involved in using this tool will serve to demonstrate to the patient that a careful approach to that individual's care is thoughtful and comprehensive.
4. Caregiver Experience(258). This tool will not directly attend to this aspect of care. Given the marked increase in the number of diabetic medications available, their various indications contraindications and risks and the complex interplay of managing cholesterol blood pressure lipids and treating microalbuminuria when it is found is a source of

caregiver frustration. It is thought that the caregivers experience in delivering care, especially in the case of a complicated diabetic patient, will be enhanced by the use of this tool.

Section 4.8.5: Existing Standards and Expert Opinion

A CDST's logic can be traced back to the opinions and practices of domain experts. (259-263) and evidenced-based standards of care. This Tool's inputs and underlying logic are driven by a combination of acceptable standards of care and the opinions of the caregivers in the ACO's patient quality committee. Additionally, as part of the desire to have a clean and simple user interface the choice was made to have very few subcategories to choose from within and any given category. What follows is a discussion of several of these categorical inputs.

Section 4.8.6: Risk Assessment

The risk of future complications owing to CMD or DM 2 is important to assess (264-266). The intensity with which one these patients are managed varies with their level of risk: as risk increases, it is more likely that increased medications, interventions, specialty consultations and visits with dietitians etc. will occur(265, 267-269) . Said differently level of a patient's risk is fundamental to the comprehensive patient management action plan. This Tool assigns three levels of relative risk, including moderate, high, and very high. An underlying design assumption resident in this tool is that all patients with CMD or DM 2 are at higher risk than the general population. In a future version of this Tool, we may wish to have five levels of risk, thereby creating a more precise and personalized depiction of a given patient's situation.

Creating a risk stratification algorithm for the management of CMD and DM 2 is a complex affair as set forth in this resource, Assessing Cardiovascular Risk(270). As is demonstrated in this resource, evidence is carefully collected and validated. It is important to note that in this resource sex and gender are used interchangeably, and that this distinction is strictly binary. A line of logic from section 8.1 associated with reference (270) noted 2 sentences above reads "AND (subject=("sex factors" or "sex distribution") or sex? or gender? or male? or female? or men or women)." Said differently, this resource does not address the issues associated with the more current approach to gender, for example, M>F Trans, F>M Trans, or born intersex. No reference to this issue was found in this resource by searching for "transgender" or "bisexual."

This binary distinction is found in all of the resources listed in Section 4.5 where the Inputs page is demonstrated, Sections 4.9.1-4.9.3 above and in both Appendix 1 Section 2.1.1.4. here the inputs logic is described and in Appendix 2 where all of the wireframes are set forth. In like manner, race is restricted to White and Black as specifically noted in the same reference (270) above. To quote verbatim, "Most scores had been derived in exclusively or overwhelmingly White samples, without adequate representation of or sufficient events in non-White groups.1,19,23-28 The RAWG judged that it would be important to include data on African Americans and to produce sex- and race-specific equations, given known differences in event rates and possible differences in coefficients for Whites and African Americans. The work group recognizes that data are limited for follow-up of Hispanic and Asian American samples and calls for further research in these and other groups." In this Tool this binary distinction is carried forward as seen in Appendix 1 Section 2.1.1.4. Algorithms are created to independently assess each of the various known risk factors known to play a part in the risk of cardiovascular disease. These include variables like hypertension, lipid control, blood pressure control, age, sex

and ethnicity. Each of these variables is assessed individually and these various risks are then combined to form a global risk assessment algorithm. This process creates an output that is a single aggregated depiction of a given patient's risk(271).

Section 4.8.7: Medication management

Medication management is a fundamental component of caring for patients with diabetes. Managing patients with blood sugars that are difficult to control, blood pressure that may require several medications, optimally managing a patient's lipid levels and addressing microalbuminuria is a complex cognitive task. Addressing these issues in the fast-paced outpatient environment as additional complexity and impacts caregiver experience.

This model divides medication management into several categories. The first is current medication as documented on the input page, the second is appropriate medications as summarized on the assessment page, the third is medication changes as summarized on the recommendations page, (with subcategories for medications that may promote weight gain, medications that may cause hypoglycemia and medications that are costly), and the last are the medications and doses with which the patient's care will go forward, as noted on the actions page.

Since this project encompasses the launch of the beta version of this tool, there are certain constraints that have been agreed to by the group in the interest of a timely launch. These constraints include a limited domain of medications, including those medications that the group believes are most commonly used. There are literally hundreds of medications for high blood pressure management several lipid management medications that while available are now rarely used and some diabetic medications that are essentially never used by the primary care provider.

Ease of use is a central goal of this tool, and if the tool is not easy to use with this limited set of medications, the project long-term success can rightfully be called into question.

An ontology is an attempt to represent Reality by linking various concepts together in a logical manner. From this perspective, it should logically follow the medications in the lipid management class are used to treat dyslipemia, diabetic medications are used to treat blood sugar and antihypertensive medications are used to treat hypertension.

In the treatment of both CMD and DM 2, the above classes of medications are often used to treat a patient who does not have the underlying disorder subsumed by that class. A patient who is at high risk of secondary and tertiary complications based on a cluster of clinical findings may be treated with a lipid management medication while dyslipemia does not exist in that given patient. As an example, a diabetic with a high risk score may have a reasonable cholesterol level is still treated with a lipid management drug because lower lipid levels lower risk and the statin family of drugs is thought to lower the inflammation diabetes causes in the endothelium(272-274). This effect has implications regarding the development of stroke, heart attack and renal damage. Relatedly, a patient without hypertension maybe treated with an ARB because of diabetic nephropathy(275). In the broader sense of CMD, a woman with polycystic ovary syndrome, (PCO)(276), is treated as having CMD even though PCO is a "gynecological disorder." She will often be treated with Metformin, a "blood sugar medication," and spironolactone(277), a "blood pressure medication."

In summary, treating patients with CMD or DM2 involves using medications for disorders that may not be present in these patients. The above paragraphs are included in an attempt to avert potential confusion. The launch of this Tool is directed at is blood sugar management, but the

choice has been made to incorporate notions of risk, and laboratory values that do not necessarily directly bear on the treatment of blood sugar per se. Using this Tool, recommendations for treatment of a diabetic patient may include all of the above categories of medication, even though, from an ontological perspective, it is logical that "diabetic patients are treated with diabetic medications." Dyslipemia medications and antihypertensive medications are often part of a diabetic's treatment even if they have neither dyslipemia nor hypertension.

Section 4.9: Assigning Risk: A Review and a New Approach

It is reasonable to ask why the novel approach to a patient's risk assessment is required in this Tool, given that there are will several web-based risk stratification tools available to assign risk to individuals. The answer is that the risk assessment component of this tool is a necessary component of the algorithm that eventually generates the Actions Page. The intent of this Tool is to guide the clinician and patient to make those changes which will improve the patient's clinical trajectory with respect to the morbidity and mortality associated with CMD and DM2.

The other commonly-used web-based tools either simply assess risk, offer suggestions concerning statin use, or offer generic advice that is not specifically directed at the clinical needs of the patient who is being treated. The aim of this CDST is to create a treatment action plan for those individuals with CMD or DM2, that has been agreed to in a patient-centered discussion with a clinician. This is in keeping with Wilkinson's work(12) discussed in Section 3.6 above. In what follows, several of the web-based resources directed at the assessment of patients with possible CMD or DM 2 are introduced and discussed. The attributes of these various web-based resources are compared and contrasted in a table at the end of this section.

Section 4.9.1: The Framingham Risk Score Calculator

Details concerning the Framingham Risk Score Calculator can be found at: (278)), and(279), where a risk calculator based on Framingham is presented. Of note, this tool does not include risk factors such as sex, or the presence of DM2. The advice which appears at the bottom of the page is generic. It is not patient-specific with respect to interventions for the benefit of the patient being assessed, however, modifiable risk factors such as blood pressure and smoking can be changed, and the risk associated with this new set of parameters can be compared with the previous set of parameters. A similar tool, named The Calculator is found at(280) .

Section 4.9.2: The ACC/AHA Cardiovascular Risk Calculator

This tool represents the work of the American College of Cardiology and the American Heart Association(271). It is found at:(281). The American College of Cardiology has an updated version based on 2016 data(282). The inputs that influence the assessment of a given patient's risk is broader than the Framingham risk calculator referenced above. The outputs are more patient-specific, including suggestions about the use of aspirin, statins, and the control blood pressure. There are no inputs and therefore no statements regarding the control of blood sugar, even though diabetes is an input data element. As with the Framingham risk score calculator above, modifiable risk factors such as blood pressure and smoking can be changed, and the risk associated with this new set of parameters can be compared with the previous set of parameters.

Section 4.9.3: The Mayo Clinic Lipid Decision Aid

This resource can be found at(283). The function of this tool, as expected, is to assess the patient's cardiovascular risk, and guide the clinician and patient as they decide on the implications of using statins, including the choice to use either low or high-dose statins.

Choosing to start statins at either a low or high demonstrates, the commensurate risk changes. This tool also supports other perspectives. Most notably, the presence or absence of diabetes is an input variable that is not found in the above references. Other perspectives include an updated Framingham- based set of inputs, and the Reynolds input set. The output includes a summary of the cost of statins and expected adverse outcomes associated with their use. No comments are made about the control of blood pressure, the control of blood sugar, or lifestyle changes such as tobacco use cessation.

By way of commentary, the output compares the initial 10-year risk percentage of the patient and compared the changes in risk associated with changes in the use of statins. For example, a patient may be assigned a risk of 9%, placing them at high risk, and statin treatment this risk drops to 7%. Based on the trainee's personal experience with the use of this tool in clinical practice, it is not unusual for a patient to react that there is "only a 2% change." In reality a patient's risk reduction associated with the use of statins approximates 20%, speaking to the need for a careful patient centered(64, 284, 285) interaction between the clinician and patient. Expanding this concept to a population of 10,000 patients with diabetes are being cared for in an ACO, about 2,000 patients who start statins based on the tool's output can be expected to experience decreased morbidity or mortality.

In summary, the tools mentioned above do not address the needs of individuals who already have complications related to their CMD or DM 2, and are of limited utility in managing all of the treatment possibilities associated with the care of these patients. In some cases, the advice is very limited and generic, in other cases a more comprehensive approach to managing some of the input variables is offered.

Section 4.10: A More Comprehensive Approach

A consistent theme this Thesis is the comprehensive management of patients with CMD and DM2. The ultimate version of this tool will include comprehensive advice concerning treatment resistant treatment resistant hypertension, the management of complex dyslipemias, the selection of a set of medications for managing blood sugar, renal function, and the advice and management of lifestyle risk factors. This comprehensive advice extends well beyond what is available in the above-captioned web-based tools. The tools above do not support this goal. That said, there is one other tool worth mentioning, however. It is the Mayo Clinic Heart Disease Risk Calculator. This resource is found at(286).

Of interest, this resource was never mentioned in any of the meetings concerning the development of the Tool being developed. It was discovered by the trainee while doing further research, and after the ACO team had completed its collaborative discussions concerning the inputs required for this Tool. Interestingly, there is a high degree of concordance concerning the inputs chosen by the ACO team, and those that appear in this Mayo Clinic tool. These inputs are compared in the table below.

Also of note, if personal risk factors, such as the history of myocardial infarction are selected as inputs, no further inputs can be selected: the tool's output immediately goes to the recommendation that a collaborative conversation with a clinician concerning next steps in management be undertaken. No specific advice concerning this management is included on this output page. In the absence of these personal risk factors, the tool's output presents a generic set of recommendations. It is important to note that this tool is web-based and available to the

general public, whereas the Tool that is being developed in the present context will be used during a clinical interaction in a medical office where trained medical personnel are involved in both the inputs as well as reviewing the assessments, recommendations and creating an action plan.

Section 4.10.1: Modifiable and Non-Modifiable Risk Factors

There are some inherent challenges associated with assigning risk. Broadly speaking, risk factors are either modifiable(287-291) or non-modifiable(292-294). Non-modifiable risk factors include such concepts as age, gender, sex, family history, and personal past medical history such as past history of stroke myocardial infarction, diabetic retinopathy, or diabetic nephropathy. These variables are extant, and while medical interventions can optimize the treatment of the consequences of CMD or DM2, these risk factors remain non-modifiable. Modifiable risk factors include such concepts as maintaining a healthy body weight, exercising regularly, making wise dietary choices, and managing laboratory values such as blood sugar, lipid levels and renal function.

Assigning risk can become a complex matter. Several non-modifiable risk factors, in and amongst themselves, when combined together, create a risk corridor that suggests further treatment is indicated before even considering modifiable risk factors. Said differently, non-modifiable risk factors like age, gender and race in and of themselves create the possibility for assigning a patient high risk even if other clinical parameters appear well-controlled.

As an example of how non-modifiable risk factors influence the overall assignment of risk, some clinical vignettes are presented. In the day-to-day outpatient clinical environment, it is not unusual to see a patient who roughly fits the following profile: male, white, age 66, no diabetes,

no hypertension, total cholesterol of 200, HDL cholesterol 40, and a blood pressure of 120/80. The modifiable risk factors appear well-controlled: blood pressure and cholesterol are at ideal levels without treatment. Using the ACC/AHA risk calculator a 10-year risk of 13.9% is returned. This is well above the threshold of 7.5% which is set to suggest the initiation of statin therapy. This raises the clinical question, "does this mean that all white males age 65 and older with ideal parameters should be treated with statins?" To further emphasize the inherent difficulties involved in assessing the impact of non-modifiable risk factors, the same set of parameters above when applied to an African-American male yields a 10-year risk of 9.8%, and a black female a 10-year risk of 7.8%, and in a white female a 10-year risk of 6.2%. All patients except the white female, using the above analysis, are candidates for statin therapy.

Using the same above low risk nonmodifiable parameters, and changing the truth value of diabetes to yes, the white male' s 10-year risk becomes 25.1%, the black male' s 10-year risk is 17.9%, the black female's risk is 17.8%, and the white female' s 10-year risk is 11.6%. In other words, treatment with a statin is suggested in all of the above patients. A precise first-decimal-place risk value appears to be of minimal pragmatic in the daily care of patients. Age and sex are leading drivers in the risk of developing cardiovascular sequelae(295), explaining 63-80% of risk in this study. Diabetes is associated with stroke risk(296) and myocardial infarction risk(23). Said differently, the risk of serious sequelae owing to DM2 are already increased. Adding the male gender and an age over 55 markedly increases risk above the 7.5% threshold(297), and it is not clear how helpful it is to know in the clinical setting if a patient's risk is 25.1%, 17.9% or 11.6%.

Table 4.10.1a. Comparison of Input Variables in other commonly-used web-based risk-assessment tools

	Risk Score				
Clinical Variables	Framingham	MayoRisk	MayoLipid	ThisTool	ACC/AHA
Age	Yes	Yes	Yes	Yes	Yes
Height		Yes		Yes	
Weight		Yes		Yes	
Systolic BP	Yes	Yes	Yes	Yes	Yes
Diastolic BP		Yes			Yes
Sex	Yes	Yes	Yes	Yes	Yes
Race		Yes	Yes	Yes	Yes
Smoking	Yes	Yes	Yes	Yes	Yes
Alcohol Use				Yes	
Total Cholesterol	Yes	Yes	Yes		Yes
LDL Cholesterol				Yes	
HDL Cholesterol	Yes	Yes	Yes		Yes
HgbA1c				Yes	
Renal Function				Yes	
BP Treatment	Yes	Yes	Yes	Yes	Yes
Diabetes		Yes	Yes	Yes	Yes
Diabetic Medications				Yes	
Hypertension Medications				Yes	
Lipid Medications				Yes	
Physical Fitness		Yes		Yes	
Diet, Fat Intake		Yes		Yes	
Diet, Carbohydrate Intake				Yes	
Diet, Fruit and Veg Intake		Yes		Yes	
Emotional Wellbeing				Yes	
Live Alone				Yes	
Past CMD History		Yes		Yes	
Family CMD History		Yes		Yes	

Table 4.10.1b. Risk score results across models for two test cases

	Risk Score				
Case	Framingham	MayoRisk	MayoLipid	ThisTool	ACC/AHA
1	8.2% 10-	67% **30-Year**	14% 10-Year	High	14.4% 10-Year
2	2% 10-Year	60% **30-Year**	5% 10-Year	Moderately-	5.4% 10-Year

Case 1 input variables: 53-year-old, African-American, Male, Height 6 feet, Weight 220 Pounds, No BP Meds, Diabetic, BP 142/85, No BP Meds, Total Cholesterol 220, HDL 44, LDL 136, Physically Activity Intermediate, Diet Low Fat and High Fruit, Non-Smoker, No Past CMD History, No Family CMD History.

Case 2 input variables:53-year-old, White female, Height 5 feet, 6 inches, Weight 160 Pounds, No BP Meds, Diabetic, BP 142/85, No BP Meds, Total Cholesterol 220, HDL 44, LDL 136, Physically Activity Intermediate, Diet Low Fat and High Fruit, Non-Smoker, No Past CMD History, No Family CMD History

Section 4.10.2: The Value of Assigning a Precise Value to Risk

As mentioned above a 10-year risk of 7.5% is considered the threshold for treating patients with statins. This leads to the question of why a granular output to the first decimal point is required as part of risk assessment, once the risk exceeds 7.5%. Overall the logic involved in the current process for assigning risk is straightforward: if risk is greater than 7.5% then start either low or high-dose statins. In other words, there are two inputs, (yes/no, risk equal to or greater than 7.5%), and three outputs, (do not start statins, start low-dose statins, or start high-dose statins). This Tool takes a different approach. Risk is assigned to one of three categories, including moderate risk, high risk and very high risk. It is assumed that patients with diabetes are all at moderate risk of complications. The basis for this assertion is illustrated by the above clinical vignettes.

As noted above, the Tool ingests a broad array of inputs and generates a broad array of assessment outputs, extending well beyond the three assessment outputs concerning lipid management mentioned above. The Tool's logic uses this array of assessment outputs to eventually create a personalized action plan for the patient. As an example, a moderate-risk patient with relatively well-controlled clinical parameters, (excellent lifestyle choices, normal blood pressure, low hemoglobin A1c and low LDL cholesterol), will have a different action plan than a patient at very-high-risk with poorly-controlled clinical parameters.

Section 4.10.3: Section Summary and Discussion

Sections 4.3.6-4.5.2 addressed various mechanisms for assessing a patient who may be, or who is already at risk concerning CMD or DM2. Several commonly used web-based resources were identified and compared. Two central concepts emerged. First is the number of available inputs in these tools is variable. Second, the number of resultant outputs is also varied. These outputs vary not only in quantity but also in quality: the granularity of the recommendations is different. In all cases, the web-based resources do not create a highly personalized action plan that details the next steps involved in caring for a patient with CMD or DM2. The table comparing these various resources also included in a risk assessment of two patient exemplars. The Tool's risk assessment performed within the parameters of the other web-based tools.

It is expected that when using this Tool that is under development, an individual patient's risk is inferred by accounting for an expanded set of the various well-known risk factors that are that are needed to comprehensively care for patients with CMD or DM 2. These include variables such as BMI, uncontrolled blood pressure, uncontrolled blood sugar, elevated LDL levels, diabetic nephropathy, diabetic retinopathy, peripheral vascular disease, functional status, and

various psychosocial determinants of health. Accounting for this expanded set of well-known risk factors facilitates a more complex approach to risk assessment in patients with CMD and DM2, and goes well beyond what is available in the above-captioned web-based tools.

Tools such as the ADA, Framingham risk assessment and the Mayo Clinic lipid decision guide all have similar inputs some of which are continuous variables and some of which are categorical. These tools however are meant to be used for screening purposes only and are therefore not applicable in patients with known cardiovascular disease. Additionally, these tools do not include family history or the types of medications that may change the ultimate recommendations that this tool will make. The decision was made not to link one of these tools into the systems logic because of the additional complexity involved in doing so, copyright issues that need to be attended to, and the fact that many patients with diabetes already have a form of cardiovascular disease that disqualifies them from using these particular tools. This tool includes several of the data elements required for the above-mentioned tools but with several notable differences.

The lipid inputs in this tool are restricted to the LDL cholesterol since this component of the lipid panel is most predictive of future risk and is also one of the data elements the various pavers follow as part of defining the quality of care within the context of population health. Again instead of a continuous variable LDL inputs are categorical. This reflects a combination of the desire for a clean simple user interface and the reality that some controversy remains concerning how best to approach lipid management in diabetics based on their lipid level. On one hand the above-mentioned tools suggest either moderate or high intensity statin use, (atorvastatin 40 or 80 mg daily, or rosuvastatin 20 or 40 mg daily), while others recommend treating sufficiently aggressively to lower the LDL either below 100 mg/mL or 75 mg/mL. An extension of this

concept of treating to the measured level of LDL includes observations that apparently there is no clear LDL level below which treatment becomes unsafe. Recent literature mentions and LDL of 10 mg/mL being acceptable and demonstrates that the risk of cardio metabolic disease sequelae follows a linear relationship (298-300). This tool therefore has selections for LDL cholesterol less than 75, from 76 to 100, from 101 to 130, from 131 to 150 and greater the 151. Furthermore, it is generally accepted that all diabetics should be treated with a statin sense diabetes can be seen as representing accelerated cardio metabolic disease. As such even those patients with an LDL less than or equal to 75 will have a statin recommended. The tools logic will suggest that those patients on maximal oral therapy for lipid control whose values are greater than 100 will be referred to a clinical pharmacist for possible treatment with PCSK-9 inhibitors. The management of LDL cholesterol as just discussed, is part of a larger topic, the various medications used in the treatment of patients with CMD and DM2.

Section 4.11: Current Design Constraints

The scope of this Thesis involves the development of a wireframe of a CDST directed at the care of patients with CMD and DM2 that will lead to the launch of the beta version of this Tool. There are several anticipated constraints expected in this beta version.

First, every instance of the Tool's use is new; there is no capability to incorporate previous data elements in order to compare recommendations once therapies have been changed. An important aspect of this restriction is the lack of data integration with the patient's electronic health record. The user is required to look at the patient's record to find the most recent data used on the input page. In other words, all required data needed for the Tool to execute its logic must be entered every time the Tool is used. This design choice was made for two reasons. First as a beta version

to test the viability of this kind of tool simplicity of design was considered important. Incorporating all PHI into this tool raises important and complex HIPAA issues. Additionally, there are approximately 70 electronic health records in the ACO and integrating this tool individually into each of these records is not plausible. If this beta version proves useful the tool will likely be integrated into a population health application at the ACO level. Many of the data elements required to populate the input page are present in this application.

Second, the choice was made to restrict this Tool's inputs to categorical and ordinal data. These data may not allow for the same level of precision obtainable using continuous variables with respect to a more comprehensive lipid profile. However, it is not clear from a pragmatic point of view how much the use of continuous variables will impact the recommendations with respect to lipid management using medications. As mentioned above there are two lines of thought concerning lipid management one that selects for moderate and the other for intensive statin use. In the above-mentioned tools available on the web it is possible to discover how much risk is impacted by proposing high intensity statin use even when moderate intensity statin use is recommended. In these cases, despite moderate intensity statin's being recommended, the tools suggest that using a high intensity statin further decreases the patient's long-term risk by approximately 25%. Also, as mentioned above there is discussion concerning treat-to-value. Driving the LDL below 75 is recommended by several sources and driving the LDL to values as low as 10 mg/mL is apparently safe and salubrious.

Categorical/ordinal data are also used for age. This decision was made once again for simplicity of design but also because of real-world experience. Below the age of 50, the 10-year risk of cardiovascular disease is generally fairly low and there are not good data to support the use of certain therapies like statins above the age of 75. Further complicating this issue is that the

above-mentioned tools do not screen for risk above the age of 65. The use of a continuous variable for a 35-year-old patient with diabetes type II was thought by the group not to confer substantial excess risk beyond that of a 45-year-old so 45 was chosen as the lowest age the system would except for computing excess risk. Additionally, it is known that there is a non-linear relationship between age and cardiovascular risk. For this reason, shorter intervals were chosen in the categorical variables for age as age increases. That said, the remains some pragmatic difficulty involved in assigning excess risk that is dependent upon a non-modifiable risk factor. Using the above-mentioned tools, a diabetic with hypertension will be a signed substantially increased risk despite being on statins and having their hypertension well-controlled.

Blood pressure is also represented in the system as a categorical variable. Again, this represents a pragmatic point of view. Current recommendations suggest that in office blood pressure management is optimal when the patient's blood pressure is below 130/80. Any value above that, when verified with home monitoring, should be addressed with a combination of lifestyle changes and medication. If a patient's blood pressure is above 150/90 and the patient is on no medications the system will recommend beginning to medication simultaneously. A blood pressure above 160/90 will prompt frequent follow-up to address blood pressure management given the excess risk associated with an elevated blood pressure in diabetics.

Glucose control is represented in this tool by the measurement of hemoglobin A1c as a categorical variable. There are several aspects to the management of hemoglobin A1c that are well handled using categorical variables. Studies suggest in general that maintain a hemoglobin A1c below seven is optimal. The first choice on the input page is less than or equal to seven. From a health plan contracting point of view quality is currently defined as a value below eight.

The group felt that this level was too high and decided on an initial goal of well-controlled being defined as less than 7.5 with the expectation that this threshold may be lowered in the future. Health plans consider poor control to be greater than nine and clinically speaking patients with a hemoglobin A1c greater than 10 are likely to need insulin therapy if they are not currently taking insulin. Other categorical variables include dietary choices tobacco and alcohol choices and functional status.

Section 4.12: The Tool's Development Roadmap

The ultimate objective of this Tool is to assist caregivers with the management of patients with CMD and DM2. This Thesis is the first step towards the objective: the wireframe of the Tool is presented. The next step is to launch a beta version of the Tool, the focus of which will be limited to managing the diabetic medications in keeping with evidence-based guidelines, while also responding to patient preferences such as oral vs. injectable medication, price and potential side effects. Future versions of this Tool will address DM2 more comprehensively, since as we have seen, blood pressure and lipid medications are an important part of a diabetic's care. These future versions will be developed iteratively, based on user experience, changes in standards of care and the availability of new medications. Future versions will address CMD more comprehensively, given the diseases that are often sequelae to both CMD and DM2.

As these diseases progresses complications like stroke, myocardial infarction, congestive heart failure, treatment resistant hypertension, and chronic kidney disease are likely to develop. Creating a comprehensive rule set that anticipates the primary, secondary, and tertiary prevention of these disorders is a complex undertaking. Since many of the attributes of CMD are also present in DM2, the launch version of this Tool will address the needs of patients with DMs.

Future versions will incrementally address the nuances and complexities involved in caring for patients with CMD and the clinical sequelae of both CMD and DM2.

One of the desiderata noted in section 3.5.4 is interoperability. Given that this Tool with be used in an ACO with approximately 70 different EHR's, it is likely that this Tool will remain web-based. To further facilitate speed, (speed is everything as noted in Section 3.5.6) a likely next step will involve integrating the Tool with the ACO's population health tool in order to prefill as much of the data required on the Input Page as possible.

Another desired feature in a future version will empower consumers: using the Tool's same interface via a secure log in, patients receiving care in the ACO will access the Tool for their own use, either filling in data on the Input Page themselves, (unless these data are automatically entered via integration with the population health tool), and proceed through the subsequent pages to arrive at their own action plan, since the various caregivers available for care will be available in Tool. This approach may lighten the care burden on PCP's who can act on the patient's preferred action plan.

At a different level, any consumer with web access could anonymously use the Tool the same way the other tools presented in Section 3.5. Speculatively speaking from a public health perspective, this use case may increase the public's awareness of the potential impact of CMD and DM2 in general and may help them identify gaps in their own care.

On the informatics side the single greatest improvement that can be made to this Tool in the future is to pre-populate the Inputs Page with as much data as possible from by either extracting the data from the EMR at a given location via API's or extracting the data from a web-based centralized data repository. This will speed up data entry.

Another enhancement is for the Tool to integrate PHI in the HIPAA-compliant manner using a secure web-based repository in which data will persist to track progress. Each instance of the Tool's assessments and recommendations will be readily available for comparison. This also enables consumer health informatics: patients can sign via a secure log in or perhaps from a link within an EHR's patient portal to review their past data, assessments and recommendations, and perhaps invoke another instance of the Tool to update personal data such as home blood pressure metrics, a change in body weight, or a change in exercise status and see how their assessments and recommendations change. Following the theme of consumer health informatics, an instance of this Tool could be made available to the general public. This would follow the model of other web-based tools we covered in Section 3.5. If these consumers "know their numbers" and their medications, they can run the tool to assess their risk, see an assessment of their status, and generate the resulting recommendations which they may wish to share with their Caregiver. In this scenario, none of the data entered by the consumer will persist.

Continuing the informatics theme, other forms of inference are possible. This wireframe uses categorical data and a deterministic if/then rule system. Machine learning may have a role to play early in the versioning process of this Tool. If continuous data from a repository noted above were mapped to the existing discrete categorical data in this wireframe a training set could be generated. Perhaps 200 qualified Caregivers could be given 100 input scenarios and asked to consider the hypothetical patient's assessment and recommendation. Based on these domain expert's opinions a training set would be generated and the system further tuned by "shadowing" the Tool as it continues in its present mode. At some point the rule set could be abandoned in favor of an algorithm.

Section 4.12: The Launch Version

As is typical of the development of any digital tool, design and implementation is an iterative process. The goal of this Thesis is to produce a wireframe of a CDST that aids Caregivers as the care for patients with CMD and DM2. This wireframe will guide the development of the beta or launch version of the Tool, the scope of which will be limited to the management of patients with the diagnosis of DM2. The users will be limited to physicians, advanced care providers, clinical pharmacists, care managers and medical assistants.

The launch version will have no PHI and will not store past instances of interactions for comparison. There will be no integration with existing sources of patient data. As seen in Section 3.1, the launch version will have a set of manually-entered data inputs. The scope of these data inputs, while still more comprehensive than those found in other tools addressing DM2, is restricted to facilitate speed of use. The data categories and the input data set presented in detail in Section 2.1 of the Appendix was derived from feedback gained at the first user-centered design session. The pages of the Tool can be printed or copy/pasted into another digital healthcare application if desired as a method for comparing serial interactions over time. It is important to emphasize that the launch version of this Tool will only be used in a clinical setting by trained medical personnel. With use, user feedback will guide future versions of the Tool and will likely incorporate new features as noted in the immediately preceding section.

Section 4.13: Chapter Summary

In this Chapter we built upon the concepts covered in Chapter 3 which included what an ideal CSDT's attributes include, several of which were reiterated and commented on at the beginning of this chapter. We then examined how this Tool's design follows many of these attributes in its

general structure and function, including the Tools knowledge base, inference engine, and user interface. We then compared several of the web-based tools currently available for treating CMD and DM2, and how they lack a comprehensive, personalized approach to a patient's risk assessment and individualized treatment and defended the proposition that a tool such as the presented in this Thesis is required. We also examined risk assessment using a more simplified model, given that it is not clear why risk should be calculated precisely when a designation of moderate, high and very high risk should suffice when managing these patients. We then identified several design constraints associated with this Tool, the Tool's development roadmap and expected launch version.

CHAPTER 5: Reflections and Personal Learnings

5.1: Reflections

5.1.1: Gratitude

First off, reflecting on this project generates a deep sense of gratitude: I can't imagine where my life would be without the outstanding instructors I studied under at the University of Washington, both in medical school and during my BIME coursework. This not a simple case of Husky Fever. Over my nearly 40-year career as a family physician, I have interacted is some form or fashion with hundreds of physicians. I know I am blessed to call the U Dub my Alma Mater.

5.1.2: My Medical School Education

I graduated from Medical School in 1997 and still feel the gravitational influence of several core concepts that were taught, some of which include that illness is a family system issue, and by counterweight, all individual care is patient-centered and should follow Engel's Biopsychosocial Model. A Family Doctor who is continuously learning and improving her craft can deliver 90% of the care needed by her panel; a primary care physician provides comprehensive care. (Translated to the present context, by using the Clinical Decision Support Tool presented in this Thesis, only 10% of her patients with CMD and DM2 will need to see an endocrinologist, despite the fact that there are so many new ways to treat these disorders). When referrals are needed, follow your intuition and whenever possible and select the specialist who will most likely be a fit, based on your knowledge of your patient. When making a referral, be clear about what you do not understand about your patient's condition and why you need your colleague's

help. Expresses your confidence in your colleague's clinical abilities: a primary physician provides coordinated care. Follow the Primary Care Model of health promotion, disease prevention, early disease detection, disease management (by delivering primary, secondary and tertiary care, including co-management with other colleagues), and when death occurs, work with the family members left behind; a primary care physician provides longitudinal continuity of care. I think that these gravitational waves undulate throughout this Thesis; it is likely that even a casual reader will sense them.

5.1.3: Creating Healthcare Value

I often despair about the state of healthcare in the US. We are number ten of ten with respect to the quality of care we deliver when compared with the other industrialized nations. Our healthcare costs per capita are double those of the next most expensive country. Healthcare costs in the US continue to rise faster than the CPI, and healthcare is the fastest-growing segment of the economy. This is obviously unsustainable.

I think the ACO model provides a possible way forward as we address the value of the care we deliver. I serve on both the Contracting and Patient Quality committees in our ACO and I think there is an opportunity for Caregivers to lead as the principles of the Quadruple Aim take hold. Many of the themes in the paragraph about my medial education have generative potential as we work to increase the value of the care we deliver to our patients, enabled by informatics.

The business language used by Payors perhaps mirrors the Primary Care and the Community health models. "Population health" mirrors Community Health. Patients considered to be at increased risk for expensive consequences of their disease are considered to be in the "rising risk" category. In the Primary Care Model, these are patients who need secondary and tertiary

prevention. “Providing care across the continuum” means the coordination of a given patient’s care within the ACO. Primary care clinicians, specialty clinicians and other colleagues with focused skills, (perhaps a care manager or a diabetic nurse educator) thoughtfully and purposefully suggest additional resources that match the needs of the patient. Managing care across the continuum mirrors primary and community-based personalized, comprehensive, longitudinally-based coordinated care. Given business-based language and market pressures, “healthcare reform” need not be about the nickels and dimes of the healthcare dollar, but instead can be about the heart and soul of medicine, which is delivering high-value patient-centered care in the context of the primary and community-care based models.

In the ACO model it is possible to be well-compensated for delivering high-value care. It is also possible to lose your shirt. Only time will tell if Caregivers can lead how healthcare delivery is transformed by leveraging the ACO model, in the end providing our communities with high-value care and increase our international standing regarding the value of the healthcare being delivered in the US. Relatedly, I know that Caregivers can only influence about 10% of the cost of care. DNA makes messes, and many of the psychosocial aspects of a given patient’s situation cannot be directly addressed by healthcare alone. Political will is required.

5.2: Learnings

5.2.1: The EMR

I find my daily work burdened by the myriad of clicks I must endure to document my patient care in our EHR. I came to graduate school to learn more about why EHR’s are such archaic, bloated, cumbersome applications, and what can be done to change this. As my time in graduate school comes to an end, I have developed the somewhat cynical view that there is no substantive

incentive for the major EHR vendors to truly modernize their applications. By contrast, I leave with the hope that a group of well-trained clinical informaticians will find a transformative way forward by building an interoperable web-based system that makes use meaningful.

5.2.2: Clinical Informatics is Work Hard

I was surprised by how difficult and time-consuming a clinician informatician's job is a I worked to understand what Caregivers needed in a CDST and what a CDST can realistically deliver. Helping focus a group of Caregivers is an exercise in patience. We all have our opinions about how best to care for certain conditions and a group of Caregivers can become hung up for the better part of a meeting deciding on a detail. As an example of this in a different domain than CMD and DM2, a question arose concerning the management of a patient with an ovarian cyst that was incidentally found the Emergency Department. The question was whether an ED clinician should refer this patient back to primary care or to a gyn specialist, based on the size of the cyst. The debate lasted for over 15 minutes, and the decision was tabled while more research was planned in order to decide whether the cyst size of 5,6 or 7 centimeters should be the point of departure.

Arriving at a care management standard is difficult when an evidence-guided standard is not available.

5.2.3: Evidence-Guided Care is Difficult to Adopt

I was surprised by the apparent resistance Caregivers might demonstrate when evidence-guided standards are presented with the expectation that they will become the ACO's standard of care. Two examples show up in this Thesis. The current evidence-based guideline for HbgA1c

management suggests the ideal value of 7.0 or less in most cases. The care gap metric for diabetes control expected by the Payor community is 8.0. Many providers suggested we use 8.0 as our standard because "that is what we get paid for." The endocrinologist in the group was at pains to emphasize that there will be more harm done to patients if we adopt the Payor standard. Eventually the threshold of 7.5 was decided upon, along with the commitment to revisit the decision in the future. This 7.5 metric is present on the Inputs Page.

In another example, microalbuminuria is a prognostic sign of other complications of diabetes, such as a heart attack or stroke. It is important to follow this data element and Payors include it in their care gap analysis. There are 2 ways to test for microalbuminuria. One is qualitative and involves simply doing a dipstick exam of the patient's urine. The test will either be positive or negative for the presence of microalbumin. Since the level of microalbumin can fluctuate perhaps creating a false negative result, a quantitative test, the microalbumin/creatinine ratio is now available. This test is positive when the ratio exceeds 30, and as the value of this ratio increases, the risk of complications also increases. The ratio is the preferred test, and most of the clinicians on the committee use it. Others do not and saw no need add the additional work of sending a far more expensive test to the lab. A compromise was made and either test was deemed acceptable. Both of these tests are on the Inputs Page.

Arriving at a care management standard is difficult when an evidence-guided standard is available.

5.2.4: Collaboration is Key

I learned new levels and types of professional collaboration as this project unfolded. In addition to working in the large group, mainly comprised of physicians in our Patient Quality Committee,

I worked with closely with a clinical pharmacist who runs our hyperlipidemia clinic on the hospital campus and spearhead the imbedding of 2 clinical pharmacists in our clinic to whom we could refer patients with DM2 that is not well-controlled. I also closely with our Quality Program Manager. She has an MPH and serves in several other administrative capacities in our ACO. The three of us met, sometimes weekly as a subcommittee to collate input from the larger group and create lists and categories of medications that will become part of the launch product of this wireframe. We also worked on our success measures for managing DM2.

We formed a cross functional group to address the care of actual patients who fell out of our population management tool as high or rising-risk. This group includes the three of us above, a hospitalist, an endocrinologist, care managers and diabetic nurse educators. We meet via phone and video, often weekly and discuss how to improve the care of the given patient under discussion. This approach has been fruitful. So far, all of the high-risk patients we have collaborated on have seen their HbgA1c drop back to single digits. We have also created and iterated a form that captures information gleaned from the EHR that is distributed before our conferences. Some of the ideas represented in these forms are part of this wireframe.

5.2.5: Writing Well is Difficult

I learned how difficult it is to write a well-formed science-based document. Under Peter's tutelage I was held to account to create topic sentences, a consistent, a logically progressing theme in a paragraph and a concluding paragraph sentence that summarizes that paragraph and introduces the subsequent paragraph's topic sentence. I learned that in long documents it important to support the reader who may be new to the document's content by repeating certain concepts in multiple places and carefully linking these repetitions to the other places they exist in

the document, enabling the reader to consume these concepts more fully. I am also aware that this document would benefit from the skills of a trained editor, but I reached a point where rewrites had to stop and the Enter key had to be tapped for the last time.

5.2.6: Rules are Difficult to Write

I learned how hard it is to create a rules-based system. It is still not clear to me how many rules there can be in a project like this, nor how many that should exist that have not been or will not be written. It is clear to me that existing rules will need to change as new evidence-guided suggestions are accepted. This will spill over into new assessments and recommendations. As we add resources to our ACO, there will be new action items to create. These resources will likely need new rules.

I also discovered the need for "intermediate targets" in the rule system used in this Thesis. As a simplified toy example, in the case of a patient whose DM2 is very poorly controlled and has a HbA1c of 10, one can write a simple rule "if (HbA1c is 10) then (add insulin)." Using intermediate targets such as "(control of diabetes not adequate)" and "(is taking diabetic medicine)," was found helpful. A more complex, clinically accurate rule set along the lines of "if (control of diabetes not adequate) and (is taking diabetes medication glimepiride) and (is taking diabetes medication metformin) and (is taking diabetes medication sitagliptin) then (stop diabetes medication glimepiride) and (stop diabetes medication sitagliptin) and (add diabetes medication insulin) " Said differently, applying the simple rule "if (HbA1c is 10) then (add insulin)" could have harmed the patient who was already taking 3 diabetic medicines.

Similarly, managing blood pressure will have an intermediate set of targets like "(blood pressure is controlled)," and "(is not taking blood pressure medications)." If a patient with normal blood

pressure is found to have microhematuria this patient still needs a blood pressure medication in the ARB family because “if (has microalbuminuria)” is true. Intermediate targets are required for the Tool to suggest “(start blood pressure medication)” in a patient with normal blood pressure. From a “rational point of view”, the rule “if (patient has normal blood pressure) then (start blood pressure medicine)” makes no sense.

5.2.7: More Respect

I have gained a new respect for those who write academic articles. While not a new idea, every important assertion must be sited and considering the number of academic articles that exist, it is hard to imagine the total amount of toil that is represented by all of the papers that have increased and will continue to increase our knowledge base. Our academic community works very hard.

I learned how vast and valuable the PubMed resource is, how helpful the University of Washington Library’s search function is, and how much more quickly I can find resources using Google Scholar. I was introduced to EndNote, a citation manager, and wonder how differently my studies over the last few years would have been had I begun using EndNote from day one. Perhaps I would have created a “treasure trove document” where notes of new learnings from publications could be entered and cited, creating a valuable journal and an accompanying index to my library.

Appendix 1

INTRODUCTION

The purpose of this Thesis is to provide a wireframe representation of a comprehensive Clinical Decision Support Tool that is directed at the care of patients with Cardiometabolic Disease (CMD) and Diabetes Mellitus Type 2 (DM 2). As such, the wireframe presented in this Thesis is not simply a beginning point in the Tool's development process. It also enables a framework for describing the Tool in greater detail than is found in the body of the Thesis.

As presented and cited in Sections 1.1 and 1.3.1-1.5 of the body of this Thesis, CMD and DM2 are becoming progressively more prevalent, and contribute significantly to the disease burden that the healthcare system must address. The diseases themselves are expensive to manage, and the sequelae such as heart attacks, strokes, blindness, kidney disease and amputations add to these expenses. The total cost burden to society of caring for patients with these diseases and their sequelae is remarkable and projected to become progressively costlier. The functionality of Tool that is depicted by the wireframe in this Thesis is intended to support caregivers who manage patients with CMD and DM2 by providing a platform the enables a comprehensive, patient-centered, evidence-based approach to how a caregiver manages the healthcare of patients with these disorders.

The purpose of this Appendix is to provide further detail concerning the structure, machinery and function of the Tool, using the pages of the wireframe as a guide. The Pages of this Tool are described here in greater detail than is present in the body of this Thesis, and the machinery of the inference engine, a work in progress, that ties the pages together is also presented in detail.

A noted, this Appendix presents a comprehensive depiction of the Tool that goes beyond what is presented in the body of this Thesis. It can perhaps be consumed as a separate document. Some of the verbiage in this Appendix is also found in the body of this Thesis. It has been repeated to provide better flow and readability as each section is consumed. This Appendix has 6 sections, 5 of which follow the logical flow of the Pages in the wireframe. These sections are identified in what immediately follows.

Section 1 introduces the types of pages found in the wireframe and provides an overview of these pages. These include the Inputs, Assessment, Recommendations, and Action Pages that form the structure of the Tool.

Section 2 focuses on the Inputs Page and comprehensively presents the input data required to create a comprehensive, personalized CDST that aids Caregivers who are treating patients with CMD or DM2. As we will see, this Tool requires far more data than other web-based tools, the detail of which will be found in section 3. There are three major categories of input data, including the patient's personal data, medication data and laboratory data. Each of these categories have subcategories of the required input data.

Section 3 focuses on the Assessments Page where first the patient's risk is assessed, followed by an assessment of the patient' laboratory and medication data. To set the context for the risk assessment the concept of risk is presented, various types of available web-based risk-assessment tools are discussed and compared, and an argument is presented for a different approach to the risk stratification of patients with CMD and DM2. The patient's risk is inferred from the Input Page data and work in progress concerning the associated algorithms is demonstrated.

Section 4 focuses on the Recommendations Page. The recommendations are inferred from the data on the Assessments Page. Recommendations are organized into several categories, including personal recommendations, medication recommendations which included diabetic medications, lipid medications and hypertension medications. It bears emphasizing that the recommendations from this page do not automatically flow to the Actions Page. In keeping with the principles of patient-centered care, the patient will select those recommendations that he or she chooses to adopt. Details concerning medication side effects, route of administration and cost are provided to support the patient's decision making. The work in progress concerning the associated algorithms is demonstrated.

Section 5 focuses on the Action Page. The actions or next steps in care are inferred from Recommendations Page, including only those the patient decides to adopt. The intent of the Actions Page is to provide the patient with a written summary of the encounter, clearly laying out next steps. The work in progress concerning the associated algorithms is demonstrated.

Section 6 touches on the development trajectory of the project. The alpha version of the planned CSDT will be a form of "dry lab" where the patient scenarios presented in this section will be used to test the algorithms that are demonstrated throughout this Appendix. Said differently, the alpha version of this Tool will not involve direct patient care. The results of this testing will be reported on a form with a 5-point Likert scale that provides feedback concerning the Tool's performance in each of the test scenarios.

Section 1: The Pages of This Wireframe

The intent of the content in Sections 1.1-1.4 immediately below is to provide synopsis and initial orientation to the pages in this wireframe. Some of what was mentioned in the Introduction

above will be touched on again, and some of the content in Sections 1.1-1.4 will be recapitulated Sections 2-5. To see the wireframe in its entirety, please see Appendix2. We begin with the Inputs Page.

Section 1.1: The Inputs Page

The Inputs Page allows patient-specific data, (including personal data, medication data and laboratory data), to be entered for computation. The outputs of this computation become the inputs for the subsequent page, i.e., the Assessments Page. Please see Appendix 2 for all of the Input Page wireframes.

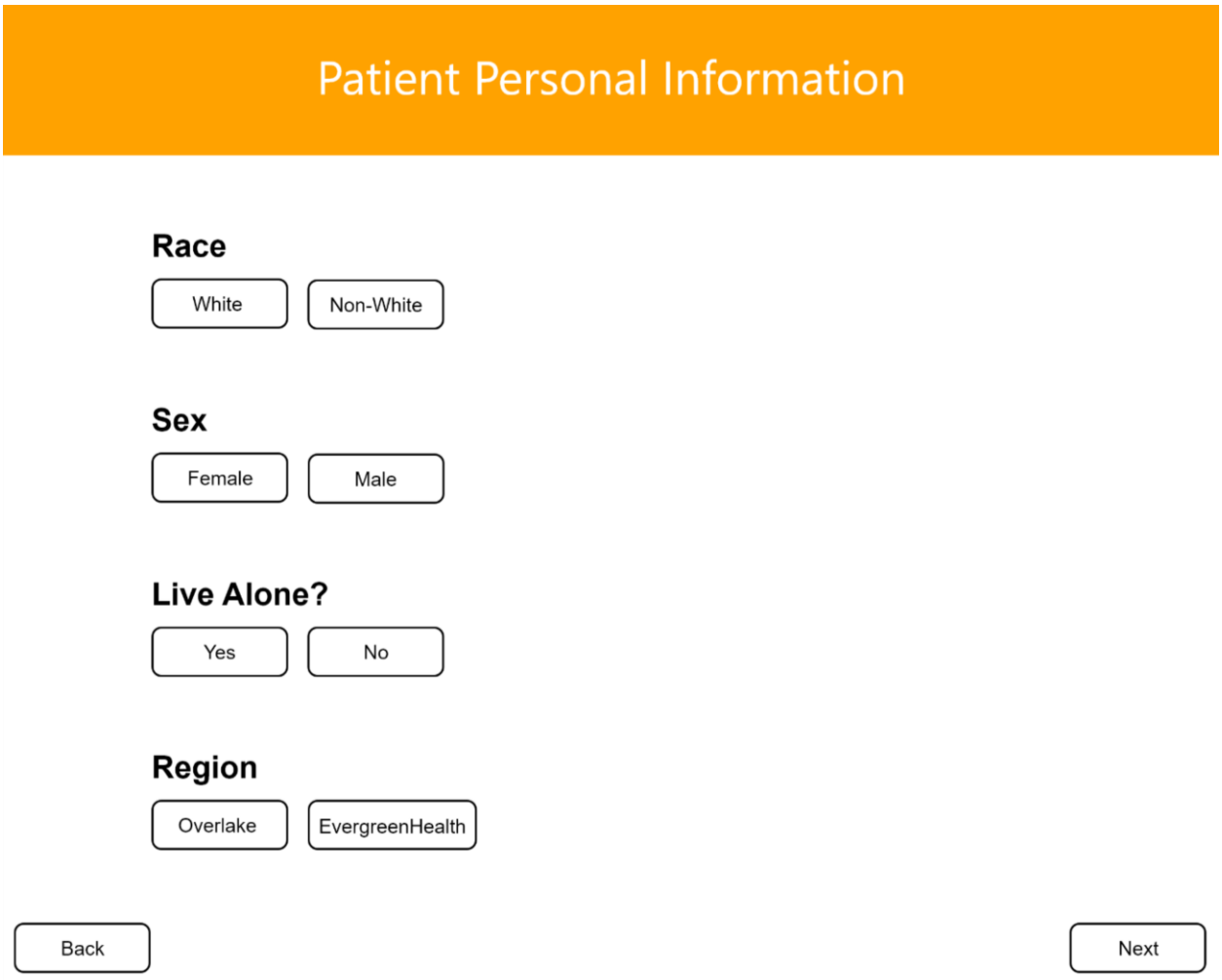

Figure 5 Example Input wireframe page for personal information

Section 1.2: The Assessments Page

The Assessments Page presents the patient and clinician with a summary of the patient's health status with respect to CMD or DM 2 as derived from computing on the outputs of the Inputs Page. For example, on this page a patient's abnormal BMI, elevated blood pressure or elevated hemoglobin A1c will be presented. These assessments in turn become inputs for the subsequent page, the Recommendations Page. Please see Appendix 2 for all of the Assessment Page wireframes.

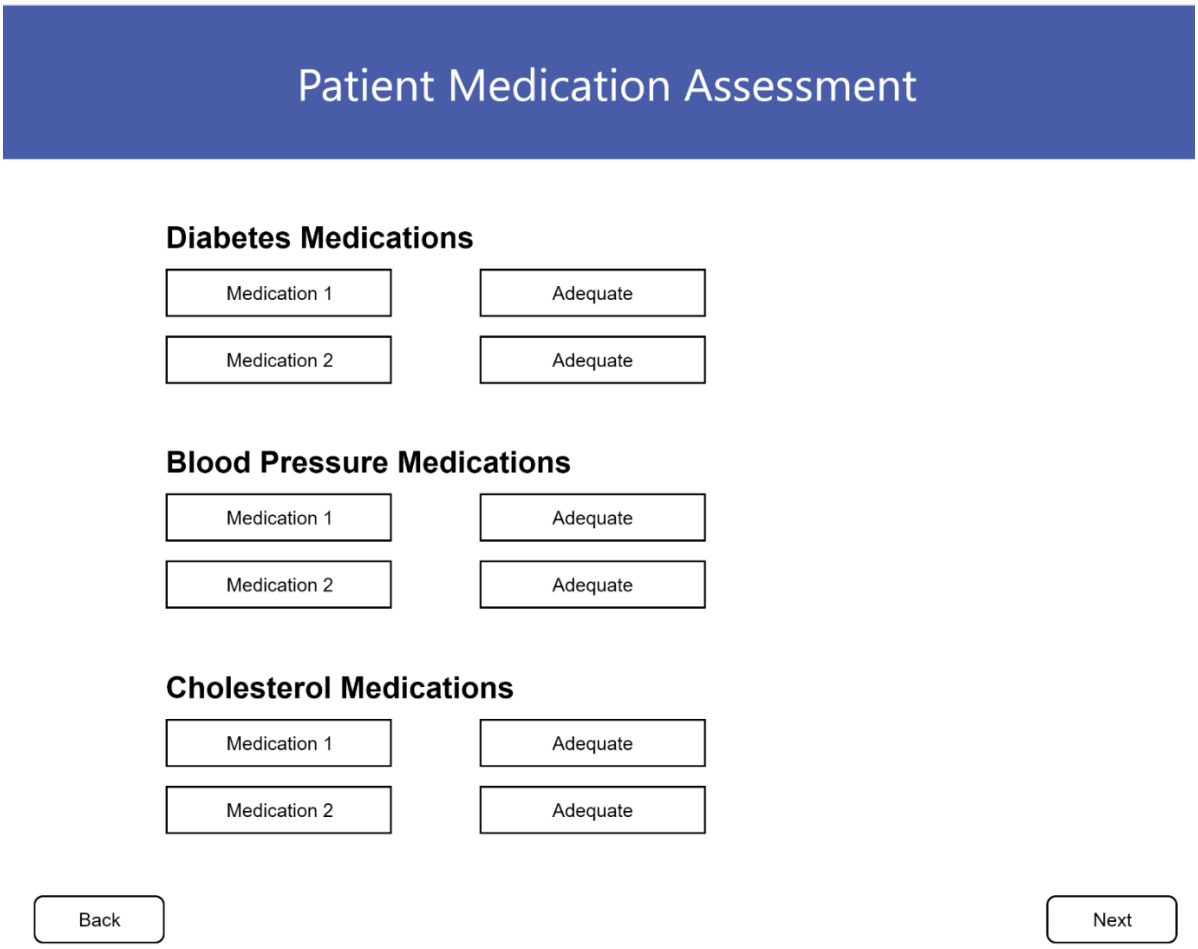

Figure 6 Example assessment wireframe page for medications

Section 1.3: The Recommendations Page

The Recommendations Page uses the outputs from the Assessments Page to present the patient and clinician with the patient-specific, evidence-based recommendations regarding the management of the patient's CMD or DM 2. Each of these recommendations will be accompanied by a checkbox that allows the patient, after a patient-centered discussion with the clinician, to agree or disagree with the recommendations. The outputs of the Recommendations Page in turn flow to the Actions Page. Please see Appendix 2 for all of the Recommendation Page wireframes.

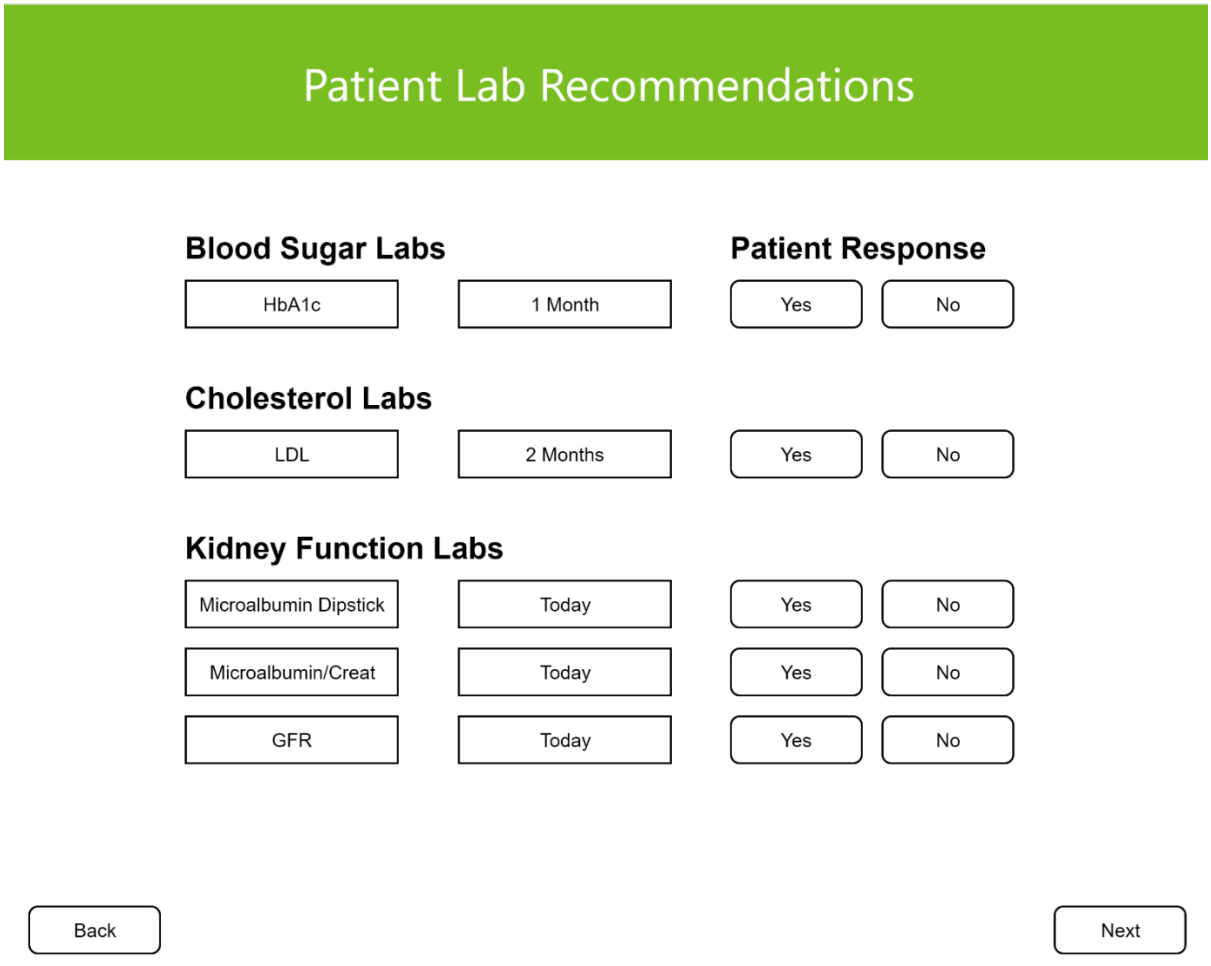

Figure 7 Example recommendation wireframe page for labs

Section 1.4: The Action Page

The Actions Page summarizes the next steps in the care of the patient with respect to CMD or DM 2. Examples include specific changes in medication, the need for further laboratory investigations, visits with a diabetic educator or consultation with a clinical pharmacist. Each of these actions will be accompanied by a brief explanation. Once the Actions Page has been reviewed with the patient, a document that summarizes the data and information on each of these pages is created. It can be printed as a handout for the patient or copied and sent to the patient via the EHR's portal. This document can also be copied and pasted into the patient's EHR. Please see Appendix 2 for all of the Action Page wireframes.

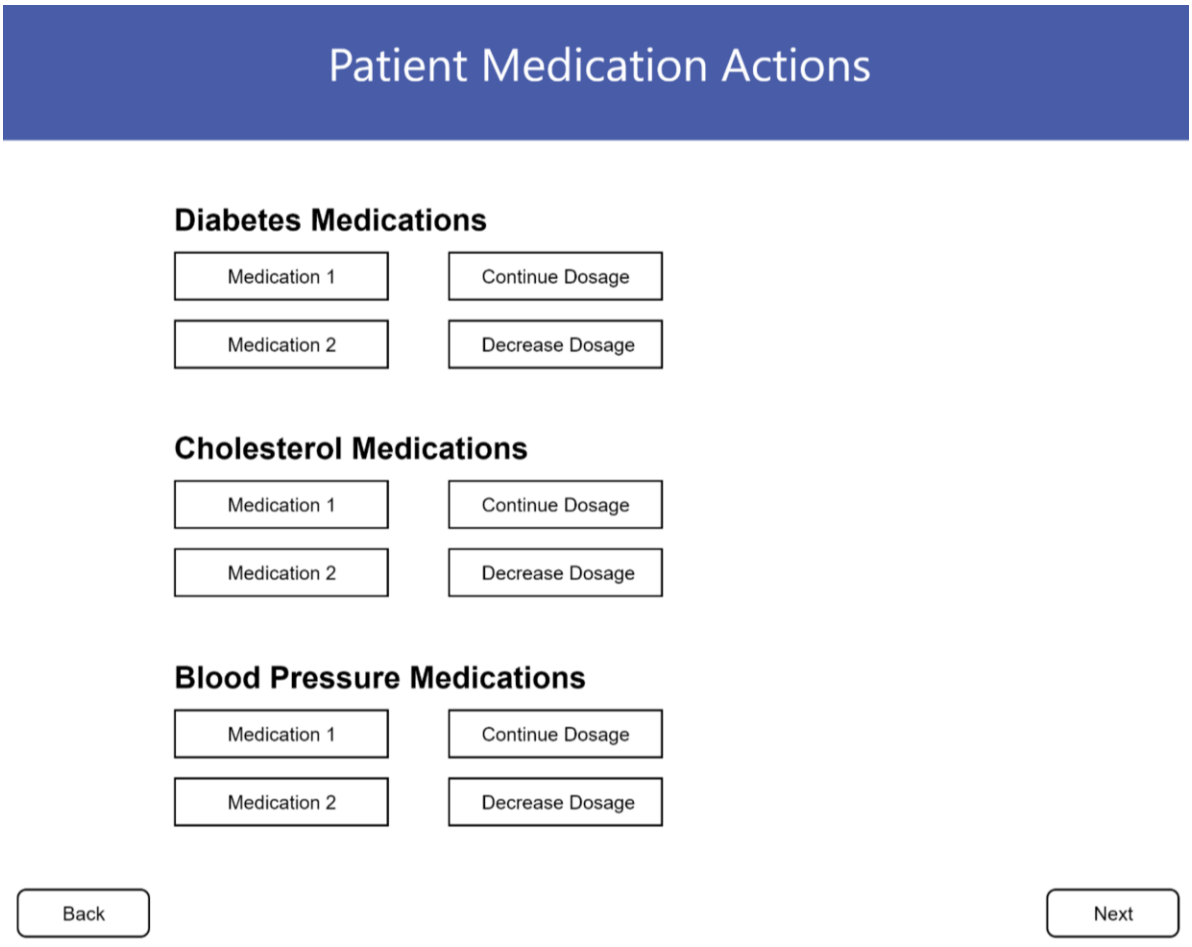

Figure 8 Example action wireframe page for medication

Section 1.5: Summary

The structure of this wireframe is constituted by 4 types of pages, the Actions Page, the Assessments Page, the Recommendations Page and the Action Page. The inference algorithms use the output of the previous Page as input into the next Page. There however, a nuance in this data flow. It is possible to have a recommendation generated not only from the Assessments Page. A recommendation can be generated recursively via an inference involving data from both the Assessments Page and the Inputs Page. For example, it an assessment is that the blood pressure is moderately elevated and data from the Input Page shows that the patient's BMI is elevated, and the patient is not physically active, a recommendation might be to engage in exercise and lose weight, instead of logically linking the assessment of high blood pressure directly to the recommendation to start a blood pressure medication. We now move on to a detailed examination of the Pages in this wireframe.

Section 2: The Pages Detailed

As noted in the previous Section, there are four pages (figures 1-4) that constitute the structure of the Tool, and inference algorithms that constitute the machinery of the Tool as it functions to guide the clinical decisions that represent the best next step in the care of the patient being treated. In what follows, each of these pages is described in detail. Where applicable, the Tool's inference machinery is demonstrated.

There are several points to be made before proceeding. First, the logic in what follows is a work in progress. More rules will be necessary before the actual Tool can be launched, and it is likely that there are errors and the need to refine the rules. Said differently, these rules are not production ready. As such, it is not possible to use resources like the "System Usability Scale" or NASA TLX to evaluate the present work in progress.

Second, since this work is a wireframe prototype of the Tool, the boxes noted in the wireframes are in a sense, placeholders for future content. For example, in an assessment page concerning medications, the word "adequate" refers to the concept that there is no need, based on inputs and the application of logic to change the blood pressure medication. The logic would be along the lines of "if hypertension and taking blood pressure medication, and blood pressure is normal, then current medication is adequate." This in turn will fire a rule in the Recommendations Page content that says something along the lines of "your blood pressure is controlled with your medications, please continue your regimen."

Section 2.1: The Inputs Page

The discussion of the Inputs Page begins with concepts involved in, and the reasoning behind the attendant design decisions. It then moves on to detail the various types of inputs, all of which are

categorical and ordinal data. These are arranged as subcategories under patient personal data, patient laboratory data, and patient medication data. The data will be entered by trained clinical staff in a clinical setting and in the presence of the patient.

The inputs chosen for this Tool were agreed to by both the Patient Quality Committee in our ACO and subgroups of the Committee. In this Tool, inputs are generated by clicking a box that represents the categorical data included in a given interval of context-specific numbers or words. It is important to emphasize that these inputs are done by trained medical personnel such as medical assistants, nurses and other caregivers. In a future version of this Tool, it will be possible for patients, with the assistance of help screens, to enter their own data and use the tool to arrive at actions they may wish to take based on the Tools computation. Again, in the present context, trained medical personnel will be entering the data on this inputs page.

Categorical and ordinal data elements (301, 302) were chosen as inputs based on user group requirements: it was felt that using the mouse, (and perhaps soon the voice), as opposed to typing in continuous variables will speed the process of inputting data. It was understood and accepted that categorical data are less granular than continuous data with the result that certain aspects of a patient's assessment may be slightly inaccurate. That said, most data used in day-to-day clinical work are categorical in the sense that the interval between values matches the discrete increments of the natural number line, some laboratory values are reported to the third decimal, not the tenths, and medications are dispensed categorically in most cases: a given molecule at a given quantity via a tablet or capsule. The trade-offs involved in the Tool's use of categorical data were accepted by the group.

The inputs selected for use in this Tool are based on what is known in the literature about treating patients with CMD and DM 2, as well as the expert opinions of members of the Quality Committee. These inputs represent various clinical concepts. There are non-modifiable risk factors such as age, sex and family history(292-294). There are personal, patient-specific modifiable risk factors such as following a healthy lifestyle, including dietary choices, a regular exercise program, maintaining an optimal BMI, avoiding tobacco use and managing stress(287-291). Clinically-based modifiable risk factors are represented by laboratory values such as the HbA1c(303), LDL cholesterol levels(153), and renal function as represented by the presence of microalbuminuria(304-306) or decreased GFR, all of which may need to be addressed clinically.

As noted above, arriving at the inputs required for this Tool required several rounds of consensus building by members of the patient quality committee and the input of subgroups in our ACO(307). Important care concepts and workflows were identified by the multidisciplinary team that meets frequently to review the management of patients whose DM2 is severely out of control.(67-71) The consensus building included various perspectives included those of primary care physicians, diabetic case managers, clinical pharmacologists and endocrinologist. There is a great deal known about the team-based approach to caring for patients with CMD and DM 2, and what all needs to be attended to in order to care for these patients. There are literally pages of information that can be made available as inputs to a given Clinical Decision Support Tools. A pragmatic decision was made to include as few inputs as possible, in order to make this tool as efficient as possible in a busy clinic's day-to-day work.

To summarize, the Inputs Page represents the categorical and ordinal data that was deemed pragmatically sufficient and was arrived at by a consensus. There are three divisions within the inputs page, these include patient personal information, patient medication information that

relates directly to the care of CMD and DM 2, and patient laboratory information. Each of these divisions and the inputs associated with these divisions, is addressed in what follows.

Section 2.1.1 Patient Personal Information

Section 2.1.1.1 Age

The age categories roughly match clinical experience. In relative terms risk is relatively low below the age of 40 and relatively high after age 60 in diabetics(308, 309). Additionally, age-related hemoglobin A1c must be accounted for in the older population: there is increased risk associated with tighter control in the older population. At age 60, with long-standing DM2, tight glucose control does not change outcomes(289, 310) and may cause harm.

The age categories include:

Age of:

1. less than 40
2. 40-49
3. 50-60
4. 61-65
5. 66-70
6. 71 or greater

Section 2.1.1.2 Body Weight and Height

The patient's body mass Index is a modifiable risk factor(311). Weight and height will have drop-down boxes with values to select. The system will calculate an approximate BMI based on these inputs: they will not be precise since categorical data are being used.

Weight of:

1. 130-150
2. 151-180

3. 181-220
4. 221-239
5. 240 or greater

Height of:

1. 5 feet to 5 feet 6 inches
2. 5 feet 7 inches to 6 feet
3. 6 feet 1 inch to 6 feet 3 inches
4. 6 feet 4 inches or greater

Section 2.1.1.3 Blood Pressure

Blood pressure control is important in diabetic patients. For simplicity, the input will only include systolic blood pressure(312). Keeping blood pressure below 130 in the office and 120 at home is the current standard of care for diabetics. As blood pressure increases, risk increases dramatically. The algorithm will identify those who are treated for hypertension and will assign a higher risk to those patients who are treated and are out of control. Systolic blood pressure categories as measured in the office will include:

Systolic Blood Pressure of:

1. less than 120
2. 120-130
3. 131-140
4. greater than 140

Section 2.1.1.4 Demographics

1. Sex
   a. Female
   b. Male
2. Race
   a. White
   b. African American
3. Do you live alone?
   a. No
   b. Yes

Section 2.1.1.5 Diet

1. Carbohydrate intake
    a. High
    b. Average
    c. Low
2. Fat intake
    c. High
    d. Average
    e. Low
3. Fruit and vegetable intake
    a. High
    b. Average
    c. Low

Section 2.1.1.6 Habits

1. Tobacco Use
    a. Yes
    b. No
2. Alcohol Use
    a. No
    b. Yes
        i. Less than 1 serving a day
        ii. 1-2 servings a day
        iii. 2 or more servings a day

Section 2.1.1.7 Functional status

1. Do you exercise vigorously 3 or more times a week?
    1. Yes
    2. No
2. Can you walk more than 200 feet without stopping?
    1. Yes
    2. No
3. Can you walk up 3 flights of stairs without stopping?
    1. Yes
    2. No

Section 2.1.1.8 Past Medical History and Family History

1. Have you had a heart attack?
    1. Yes
    2. No

2. Have you had a stroke?
    1. Yes
    2. No
3. Have you had a procedure for a blocked artery in your heart, neck or legs?
    1. Yes
    2. No
4. Do you have diabetic-related eye disease?
    1. Yes
    2. No
5. Has a first-degree relative (father, mother, brother, sister) had a heart attack or stroke before the age of 65?
    1. Yes
    2. No

Section 2.1.1.9 Psychological Issues

1. During the past month, have you often been bothered by feeling down and depressed or hopeless?
    1. Yes
    2. No
2. During the past month have you ever been bothered by little interest or pleasure in doing things?
    1. Yes
    2. No
3. What is your current stress level?
    1. Very high
    2. High
    3. Normal
4. How anxious are you on a daily basis?
    1. Very
    2. Somewhat
    3. Not particularly

Section 2.1.2: Patient Medication Information

Medication management is central to the treatment of patients with CMD or DM 2, and there are hundreds of medication combinations available to treat hypertension alone, not counting the various medications for diabetes and dyslipidemia. Choosing which medications to use when treating these patients is often a complex cognitive task.

The beta version of this application will constrain the universe of medications to those frequently used by our EH and, our ACO. This constrained universe was generated by a query of Wellcentive, our population health management tool. Inputting medications will be accomplished by trained medical personnel using a smart search functionality to speed the input process. As the medication is being typed in, potential selections will be displayed. After the first medication is entered, the patient is asked whether they are taking another medicine in this category. If the answer is "yes," a new search box will appear. For example, a patient may be on an ARB and a calcium channel blocker to treat hypertension and maybe taking three different medications to treat diabetes.

As noted above, medication management can be a complex cognitive involving two concepts. There may be instances where a patient may be taking 4 medications to manage their hypertension, 2 medications to manage their dyslipemia, and 3 medications to manage their DM 2, a clinical state called "polypharmacy"(313). There is also complexity involved in the choice of which class of medication to use when treating patients with CMD or DM(183). Addressing the choice of which class or classes of medication to use in the context of polypharmacy is covered in what immediately follows.

Section 2.1.2.1 Medications by Class

As mentioned above, there is a vast array of medications from which to choose when treating patients with CMD or DM. Additionally, the choice of the selected medication for treating patients with CMD or DM 2 may seem irrational, since the use of a given medications may involve treating clinical conditions that are different than one would expect given the class of medications chosen. It seems intuitive that the reasoning involved in medication selection is

based on medication class: hypertension medications could reasonably be expected to use to treat patients with hypertension, lipid medications used for dyslipidemia and diabetes medicine is used for hyperglycemia, but this is not necessarily the case. For example, in a diabetic patient with diabetic nephropathy, as evidenced by microalbuminuria present on dipstick, or by an elevated microalbumin creatinine ratio, an ACE or an ARB, (hypertension medications), is indicated to prevent further degradation of renal function whether or not the patient may have hypertension, i.e., a medication from the hypertension category is used to treat a patient who may not have hypertension. Similarly, a patient who is at high or extremely high risk as assigned by the risk assessment algorithm is outlined in detail below, should be treated with a statin even if their lipid values are close to normal. Patients who have diabetes and known cardiovascular disease should preferentially be treated with a GLP-1 agonist or an SGLT2 inhibitor. Diabetic patients with diabetic nephropathy should be treated with a GLP-1 agonist.

In summary, medication management can be a complex task for a clinician who is caring for a patient with CMD or DM 2. Patients may be taking multiple medications from several different classes of medication. For the purposes of this Tool, there are three groups of medications. These include antihypertensive medications, dyslipemia medications, and diabetic medications. A recommendation may be made to treat a patient with a class of medication that does not correspond directly to the type of clinical disorder the patient has. The categories of medications, antihypertensive medications, dyslipemia medications and diabetic medications used in this tool are outlined below.

Section 2.1.2.1.1 Anti-Hypertensive Medications

Frequently-used anti-hypertensive medication categories:

1. ACE inhibitors and combinations
2. ARB's and combinations
3. Calcium channel blockers and combinations
4. Beta blockers
5. Diuretics

Section 2.1.2.1.2 Dyslipemia Medications

Frequently used dyslipidemia medications for controlling LDL cholesterol:

1. Statins
    a. Lovastatin
    b. Simvastatin
    c. Atorvastatin
    d. Rosuvastatin
2. Absorption blockers
    a. Ezetimibe
    b. Cholestyramine

Section 2.1.2.1.3 Diabetic Medications

Frequently used diabetic medications:

1. Biguanide
    a. Metformin
2. Sulfonylureas
    a. Glimepiride (Amaryl)
    b. Glyburide (DiaBeta, Glynase, Micronase)
    c. Glipizide (Glucotrol)
3. Thiazolidinediones (TZD
    a. Pioglitazone (Actos)
4. DPP-4 inhibitors
    a. Sitagliptin (Januvia)
    b. Saxagliptin (Onglyza)
    c. Linagliptin (Tradjenta)
5. GLP-1 receptor agonists
    a. Dulaglutide (Trulicity)
    b. Exenatide (Byetta)
    c. Exenatide extended release (Bydureon)
    d. Liraglutide (Victoza)
    e. Semaglutide (Ozempic)

6. SGLT2 inhibitors
    a. Dapagliflozin (Farxiga)
    b. Canagliflozin (Invokana)
    c. Empagliflozin (Jardiance)
7. Insulin preparations
    a. Long-acting preparations
        i. Insulin detemir (Levemir)
        ii. Insulin glargine (Lantus, Basaglar)
        iii. Insulin degludec (Tresiba)
    b. Short-acting preparations
        i. Insulin lispro (Humalog)
        ii. Insulin aspart (Novolog)

Section 2.1.3 Patient Medication Inputs

The Inputs Page of this Tool was covered in detail above in Section 2.1. Data entered into the Tool are categorical and are required for the Tool's machinery. In this section, the medication inputs required for the system to generate outputs are specified. For the beta version of this Tool, trained medical personnel will be inputting these categorical data into the system. This is because the inputs require familiarity with the categories outlined above. In a future version of the Tool, it is anticipated that patients will enter their own data. In order to do so accurately a different user interface will be designed to assist the patient as decisions about medication classes are made.

The workflow on the medications input page is accomplished via an intelligent search. As mentioned above, for the beta version of this Tool we decided to constrain the universe of medication choices based on what our population health tool suggests are the most common medications used by our group. The inputs are made based on categories which include diabetic medications, high blood pressure medications and cholesterol medications. It will be the responsibility of trained medical personnel to assist patients with these answers since as noted above a patient may not realize that he or she is taking a cholesterol medication since he or she

may not have hyperlipidemia. If the answer is “yes” to trained medical personnel will be presented with a search box to enter a medication. The search box will rapidly reduce the number of choices which to select. For example, a diabetes medication beginning with D will return to choices; either Dulaglutide or Dapagliflozin.

Beginning this section with asking the yes or no question concerning this class of medications is important. There may be cases where a patient with evidence for renal dysfunction is taking me there a blood pressure medication or a diabetic medication. And algorithm will pick up this fact and make a recommendation for these medications based on renal dysfunction. Additionally, if a patient answer is yes to diabetic medications and is taking two of them, the algorithm will suggest either an adjustment in medication dose or the addition of another medication if the control of diabetes as categorized by the level of hemoglobin A1c is considered inadequate.

1. Diabetes Medications
    a. Are you taking any diabetes medications?
        i. Input:
            1. Yes (Proceed with entering medication(s))
            2. No (Go to next page. In this case, the patient may be a “new diabetic.”)
2. High blood pressure Medications
    a. Are you taking any high blood pressure medications?
        i. Input:
            1. Yes (Proceed with entering medication(s))
            2. No (Go to next page)
3. Cholesterol medications
    a. Are you taking any cholesterol medications?
        i. Input:
            1. Yes (Proceed with entering medication(s))
            2. No (Go to next page)

Section 2.1.4: Patient Laboratory Inputs

This section addresses the laboratory data inputs entered via the Inputs Page. Managing the laboratory values of patients with CMD or DM 2 is a central component of the care delivery

process, and there are significant number of laboratory values that can be followed, depending upon the level of detail desired. Generally, three categories of laboratory values are followed when treating patients with CMD or DM 2. These categories represent blood glucose metabolism, lipid metabolism and renal function. There is an expanded set of laboratory values that fall under these broad categories and depending on clinical judgment, very specific testing is available.

Section 2.1.4.1 Glucose

Glucose metabolism can be represented by several different laboratory values. These include hemoglobin A1c, fasting blood sugar, nighttime blood sugar, postprandial blood sugar or the results of an oral glucose tolerance test. In the world of ambulatory care that involves managing DM 2 patients, (as opposed to DM 1 patients), managing to the hemoglobin A1c level is generally considered adequate(303). An exception may be a DM 2 will patient on basal insulin whose hemoglobin A1c levels remain high and postprandial glucose measurements are extremely high. In this case, a short acting preparation of insulin may be required, and following fasting glucose and other glucose values throughout the day may be necessary in order to better manage the hemoglobin A1c. Thus, hemoglobin A1c remains a central data element representing glucose metabolism.

In general, keeping hemoglobin A1c at or below 7 it is ideal(303). While health plans consider the hemoglobin A1c below 8 as good control, our group has settled on 7.5 as the value that represents the optimal management of blood sugar at present, with the plan to revisit the decision in a year. This choice followed a collaborative discussion amongst primary care doctors an endocrinologist, a clinical pharmacist, a podiatrist and an urgent care physician at a patient

quality meeting of our ACO. It was strongly felt by the endocrinologists that the standard of care should be a hemoglobin A1c of 7 should be our standard of care. Some primary care clinicians thought that in general a value of 8.0 was more realistic in their clinics and noted that this value reflected the standard of care required by the various contracted payers involved with the ACO. As part of this discussion it was agreed that the standards adopted by our ACO may change in the future, and that perhaps at some point a hemoglobin A1c of 7.0 will be considered the standard of care. The group also decided that when the patient's hemoglobin A1c exceeds 10, it is likely that the patient will either be referred for specialty care or started on insulin, making this input variable important in algorithmic calculations. The bins of categorical data that represent the outcomes of this group discussion are reflected in the hemoglobin A1c inputs section below

Section 2.1.4.2 Lipids

In this Tool, lipid metabolism is represented by LDL cholesterol. This is because there is a clear correlation between morbidity, mortality and LDL levels. Lipid metabolism can be represented by the level of the HDL cholesterol, the LDL cholesterol level, the VLDL level and the triglyceride level. Testing is also available to assess the patient's LDL and HDL particle size or lipoprotein (a) levels. HDL appears to have a protective effect with respect to morbidity and mortality; as it increases patient risk decreases. So far, medications directed at increasing HDL have not been successful in improving clinical outcomes, so in a sense, HDL is not a modifiable risk factor from a medication administration perspective. Since LDL appears to be a modifiable risk factor, it has been chosen to represent lipid metabolism. As LDL is lowered in patients with CMD and DM 2, clinical outcomes improve(314).

Current guidelines suggest treating patients with either moderate or high-dose statins as a function of that patient's overall risk. This concept can be referred to as "treating to risk,"(315) and this concept is covered in more detail below under the section of risk stratification. There is also debate about treating based on the absolute value of LDL cholesterol. This concept can be referred to as "treating to target," and has merit from the standpoint that there appears to be a continuous relationship between LDL and the associated mortality and morbidity in patients with CMD or DM2: the lower the LDL, the lower the risk(314). As mentioned above, other lipid values can also be followed. HDL cholesterol is salubrious: as HDL values rise, the risk of morbidity and mortality decreases. The value of triglyceride as an independent risk factor is debatable. Triglycerides tend to rise when blood glucose is elevated, thus hypertriglyceridemia may be correlated with poor diabetic control rather than being an independent risk factor(153). There are also suggestions that following non-HDL, (total cholesterol minus HDL cholesterol), is an important metric.

In summary, all lipid values play an important part in managing patients with CMD and DM2. Since elevated LDL cholesterol is a well-correlated independent risk factor for excess morbidity and mortality in patients with CMD or DM 2, and given the desire to limit the number of inputs required, this variable has been chosen to represent lipid metabolism in the Tool. This is done with the realization that a patient with an elevated HDL and an elevated LDL is at less risk than a patient with normal HDL and elevated LDL: there is a chance that some patients may be assigned a higher risk category than is warranted.

Section 2.1.4.3 Renal Function

Renal function can be represented by the presence of microalbuminuria, (either positive finding on a random dipstick or by an elevated microalbumin creatinine ratio), GFR, serum BUN, serum creatinine, and the amount of albumin excretion as measured by a 24- hour urine collection. For this tool, microalbuminuria and GFR have been chosen to represent renal function.

Following renal function in a diabetic patient is crucial for several reasons. Declining renal function, (as signified by a decreasing GFR, the presence of microalbuminuria, or in increasing ratio of microalbumin to creatinine), is a harbinger of progressively worsening systemic microvascular pathology(304, 305). Said differently, diminished renal function owing to decreased microcirculation also suggests decreased heart and brain microcirculation, (increasing the risk of myocardial infarction and stroke), as well as decreased circulation in the feet, (increasing the risk of amputation). This risk appears even greater in patients with both high microalbumin to creatinine ratios and markedly diminished GFR (316). Worsening renal function, based on these metrics, algorithmically prompts the clinician start these patients on an ARB or ACE inhibitor, whether or not they have hypertension, per the discussion above in the medication section. Renal function also has implications when dosing other medications that are renally excreted. In summary, following renal function in patients with CMD or DM 2 is important. As noted above, there are several ways to assess renal function. This tool will use GFR and the presence of microalbuminuria to assess renal function. Microalbuminuria will be represented either as dipstick positive yes or no, or by the microalbumin creatinine ratio. The GFR inputs will mirror the accepted divisions associated with the clinical stages of chronic kidney disease.

In summary, representing and following renal function is important in the care of patients with CMD and DM 2. Correcting abnormal renal function decreases morbidity and mortality in these patients. Tighter control of lipid and, blood pressure are key in the context of decreasing renal function is required. In patients without hypertension adding an ACE or ARB who exhibit decreasing renal function is indicated as discussed in Section 2.1.2.1.

Section 2.1.5 Laboratory Inputs Summarized

In summary, following certain laboratory values in patients with CMD or DM 2 is of crucial importance. They are both indicators of a patient's status, and they are modifiable risk factors: managing them correctly decreases a patient's morbidity and mortality. In this Tool, there are 3 categories of laboratory values: blood sugar, lipid levels and renal function. The laboratory values representing these categories include HbA1c, LDL level, microalbuminuria and GFR respectively. Not only are these categories important: the measured values within these categories are also important. As the values change, the patient's risk of morbidity and mortality changes proportionally. As mentioned above, this Tool uses categorical data representing intervals of values. These categories of laboratory values, along with their intervals follows below. In summary, there are several laboratory values in the blood sugar, and lipid domains, as well as the assessment of renal function that can be followed when managing a patient with CMD or DM 2. When building a clinical decision support tool, decisions must be made about which categories of inputs to choose, and number of inputs to be included in these categories. A balance must be struck between the practicality of a functional tool that can be used in a busy clinical setting and the desire for a complete and comprehensive set of inputs available to the decision support tools inference system.

A mentioned above this Tool will employ a narrow set of valid, widely-used laboratory values as patient laboratory inputs. Blood sugar is represented by hemoglobin A1c, cholesterol is represented by LDL, cholesterol and renal function is represented by microalbuminuria, whether it is a positive or negative dipstick in the office, or the microalbumin creatinine ratio that is returned from the reference laboratory. Each of these categories is addressed in further detail below. It bears repeating that all of these laboratory values are categorical variables as opposed to continuous variables, and they will be entered by trained medical personnel. In what follows, the various patient laboratory inputs are summarized.

Section 2.1.6 Patient Laboratory Input Values

1. Patient hemoglobin A1c input values:
    a. less than 7
    b. 7.1-7.5
    c. 7.6-8.0
    d. 8.1-9.0
    e. 9.1-10
    f. greater than 10.
2. Patient LDL input values:
    a. less than 75
    b. 76-100
    c. 101-129
    d. 130-145
    e. 146-179
    f. 180 or greater
3. Patient kidney function input values:
    a. Microalbumin
        i. Dipstick
            1. Positive
            2. Negative
        ii. Microalbumin/Creatinine
            1. less than 30
            2. 31-60
            3. 61-100
            4. 101-300
            5. greater than 300
    b. GFR

i. less than 15
ii. 16-29
iii. 30-44
iv. 45-59
v. greater than 59

Section 2.1.7 Inputs Page Summary and Discussion

This section discussed the reasoning behind how the Tool's inputs were decided upon and then presented the actual inputs that are needed for the Tool to compute the required outputs for the Assessment, Recommendation and Action Pages. Three categories, (personal, laboratory, and medication information), represent the structure of the Inputs Page, and the intervals of the categorical data elements in each of these categories was set forth. The choice to use categorical data as inputs was chosen in order to speed up the input process in a busy clinical setting. In the medication section, the logical paradox of using medications in one category to treat a condition which is apparently in a different category was discussed.

The inputs are entered by trained medical personnel in a clinical setting and are required for the Assessments Page. The structure of the Inputs Page is reflected in the Assessments Page by leveraging the same personal, medication and laboratory categories described above. The Assessments provide feedback to the patient, again in a clinical setting, concerning such things as the status of their lifestyle choices, the adequacy of their medications and whether their laboratory values require more attention. In addition to these categories, a new category is added in the Assessments Page, the level of risk of future complications of CMD or DM 2 the patient may be facing. We now turn to the structure and machinery of the Assessments Page.

Section 3: Assessments

The Assessments Page provides the clinician and the patient with an evaluation of the patient's status with respect to CMD and DM 2. The categorical variables from the inputs page are processed via the Tool's machinery to generate the outputs that appear on the Assessments Page. There is a broad array of output assessments, including patient risk, patient BMI, patient BP, patient well-being, patient functional fitness, patient diet, patient habits, patient labs, patient medications and patient family history. Attending to all of these categories is fundamental to treating CMD and DM 2.

The overall assessment of the patient's status is fundamental to the comprehensive management of that patient. As mentioned above, the assessments page outputs are in turn processed algorithmically as inputs to arrive at recommendations concerning the treatment of the patient in question. Similarly, the recommendations that were generated as outputs become the inputs for the Action Page. Following the principles of patient-centered medicine(161-163), these recommendations are reviewed by the clinician in the presence of the patient. Once the patient has been shown the recommendations, the patient decides which of these recommendations to follow and which of them to ignore at that point. In summary, the overall assessment of the patient is a crucial step in necessary for making recommendations and forming a plan of action.

As noted above, there is a broad array of output assessments planned for the beta version of this Tool. A detailed example of how the system will work is depicted by the risk assessment logic in the next section. Similar methodology will be employed for the other outputs needed for recommendations and action plan, and this will be summarized in the future work section that follows this section.

Perhaps the most important assessment made by this Tool is the assessment of the patient's risk. If the patient's overall risk is elevated, more aggressive treatment is warranted. In the section immediately following, the approach to the patient's risk is comprehensively addressed. These risk rules are considered completed work for launching the beta version of the Tool. The other rules should be construed as work in progress.

Section 3.1: Risk Assessment

This section begins with a discussion that links how the data elements from the Inputs Page are algorithmically-linked with the function of the Assessments Page. This page will be used by the clinician and the patient in the same clinical setting that began with trained medical staff entering the data on the Inputs Page. The function of the Assessments Page is to summarize the patient's healthcare status with respect to CMD and DM 2, and serve as a resource that engenders a discussion between the patient and clinician regarding the patient's healthcare status. The first section in the treatment of the attributes of the Assessments Page deals with patient risk analysis. This is an important concept. Interventions that are found on the Recommendations Page are driven by the level of risk of excess mortality and morbidity that the patient in question may be facing, based on what is entered on the Inputs Page. Said differently, as the risk profile of a patient with DM 2 increases, the intensity of the therapy, increases in a commensurate fashion, as directed at blood pressure control, lipid control, blood sugar control and, if applicable, renal function improvement. The Tool's risk assessment has 3 outputs, including moderately high risk, high risk, and very high risk.

This risk section includes a high level of detail. Other commonly-available web-based risk tools are identified, analyzed and compared in tabular form. Additionally, the algorithm for risk

assessment that will be used in the beta version of this Tool is presented in detail to demonstrate both completed work and to demonstrate the underlying form of inference used in the Tool. This form of inference is present throughout the various pages of the application, so this section also serves to broadly illustrate the Tool's machinery. Other sections in this Appendix include logic that is less detailed, but of the same form. The reader can extrapolate and generalize this less-detailed logic to the Tool's machinery.

After the patient's risk has been assessed, assessments are made of the patient's personal information, including notions such as Body Mass Index, BMI, lifestyle choices concerning diet and exercise, and the level of personal well-being. Next, an assessment is made of the patient's medical regimen, followed by an assessment of the patient's laboratory values. These various assessments are in effect the outputs of the Assessment Page, which in turn become the inputs of the Recommendation Page as is summarized at the end of Assessment Page section.

In summary, the Assessments Page section demonstrates how the categorical data elements from the Inputs Page are computed to arrive at an assessments of the patient's overall risk, along with an analysis of their personal, laboratory, and medication data from the Inputs Page.

The risk of future complications owing to CMD or DM 2 is important to assess. The intensity with which one these patients are managed varies with their level of risk: as risk increases, it is more likely that increased medications, interventions, specialty consultations, visits with dietitians etc. will occur. Said differently level of a patient's risk is fundamental to the comprehensive patient management action plan. This Tool assigns three levels of relative risk, including moderate, high, and very high. An underlying design assumption resident in this tool is that all patients with CMD or DM 2 are at higher risk than the general population. In a future

version of this Tool, we may wish to have five levels of risk, thereby creating a more precise and personalized depiction of a given patient's situation.

Creating a risk stratification algorithm for the management of CMD and DM 2 is a complex affair as set forth in this resource, Assessing Cardiovascular Risk(270). As is demonstrated in this resource, evidence is carefully collected and validated. Algorithms are created to independently assess each of the various known risk factors known to play a part in the risk of cardiovascular disease. These include variables like hypertension, lipid control, blood pressure control, age, sex and ethnicity. Each of these variables is assessed individually and then combined to form a global risk assessment algorithm. This process creates an output that is a single aggregated depiction of a given patient's risk.

Section 3.1.1 Why a New Tool?

It is reasonable to ask why a novel approach to a patient's risk assessment is required in this Tool, given that there are will several web-based risk stratification tools available to assign risk to individuals. The answer is that the risk assessment component of this tool is a necessary component of the algorithm that eventually generates the actions page. The intent of this Tool is to guide the clinician and patient to make those changes which will improve the patient's clinical trajectory with respect to the morbidity and mortality associated with CMD and DM2.

The other commonly-used web-based tools either simply assess risk, offer suggestions concerning statin use, or offer generic advice that is not specifically directed at the clinical needs of the patient who is being treated. The aim of this clinical decision support tool is to create a treatment action plan for those individuals with CMD or DM2, that has been agreed to in a patient-centered discussion with a clinician. In what follows, several of the web-based resources

directed at the assessment of patients with possible CMD or DM 2 are introduced and discussed. The attributes of these various web-based resources are compared and contrasted in a table at the end of this section.

Section 3.1.1.1 The Framingham Risk Score Calculator

Details concerning the Framingham Risk Score Calculator can be found at: (278) and(280), where a risk calculator based on Framingham is presented. Of note, this tool does not include risk factors such as sex, or the presence of DM2. The advice which appears at the bottom of the page is generic. It is not patient-specific with respect to interventions for the benefit of the patient being assessed, however, modifiable risk factors such as blood pressure and smoking can be changed, and the risk associated with this new set of parameters can be compared with the previous set of parameters.

Section 3.1.1.2 The ACC/AHA Cardiovascular Risk Calculator

This tool represents the work of the American College of Cardiology and the American Heart Association(271, 281). The American College of Cardiology has an updated version based on 2016 data(282). The inputs that influence the assessment of a given patient's risk is broader than the Framingham risk calculator referenced above. The outputs are more patient-specific, including suggestions about the use of aspirin, statins, and the control blood pressure. There are no inputs and therefore no statements regarding the control of blood sugar, even though diabetes is an input data element. As with the Framingham risk score calculator above, modifiable risk factors such as blood pressure and smoking can be changed, and the risk associated with this new set of parameters can be compared with the previous set of parameters. The ACC/AHA also has a graphic analyzer available for assigning risk based on a subset of inputs(317).

Section 3.1.1.3 The Mayo Clinic Lipid Decision Aid

This resource can be found at(283). The function of this tool, as expected, is to assess the patient's cardiovascular risk, and guide the clinician and patient as they decide on the implications of using statins, including the choice to use either low or high-dose statins. Choosing to start statins at either a low or high demonstrates, the commensurate risk changes. This tool also supports other perspectives. These include an updated Framingham- based set of inputs, and the Reynolds input set. The output includes a summary of the cost of statins and expected adverse outcomes associated with their use. No comments are made about the control of blood pressure, the control of blood sugar, or lifestyle changes such as tobacco use cessation.

By way of commentary, the output compares the initial 10-year risk percentage of the patient, and compared the changes in risk associated with changes in the use of statins. For example, a patient may be assigned a risk of 9%, placing them at high risk, and statin treatment this risk drops to 7%. Based on the trainee's personal experience with the use of this tool in clinical practice, it is not unusual for a patient to react that there is "only a 2% change." In reality, a patient's risk reduction associated with the use of statins approximates 20%, speaking to the need for a careful patient centered interaction between the clinician and patient. Expanding this concept to a population of 10,000 patients with diabetes are being cared for in an ACO, about 2,000 patients who start statins based on the tool's output can be expected to experience decreased morbidity or mortality.

In summary, the tools mentioned above do not address the needs of individuals who already have complications related to their CMD or DM 2, and are of limited utility in managing all of the treatment possibilities associated with the care of these patients. In some cases, the advice is very

limited and generic, in other cases a more comprehensive approach to managing some of the input variables is offered.

Section 3.2 A More Comprehensive Approach

A consistent theme this Thesis is the comprehensive management of patients with CMD and DM2. The ultimate version of this Tool will include comprehensive advice concerning treatment resistant treatment resistant hypertension, the management of complex dyslipemias, and perhaps the management of congestive heart failure in the context of hypertension and renal failure. The beta version of the Tool will focus on the selection of the medications required for managing blood sugar in DM 2. renal function, and the advice and management of lifestyle risk factors.

The comprehensive advice envisioned with the use of this Tool extends well beyond what is available in the above-captioned web-based tools. These tools present limited, relatively generic advice. That said, there is one other tool worth mentioning. It is the Mayo Clinic Heart Disease Risk Calculator.

This resource is found at (286). Of interest, this resource was never mentioned in any of the meetings concerning the development of the Tool being developed. It was discovered by the trainee while doing further research, and after the ACO team had completed its collaborative discussions concerning the inputs required for this Tool. Interestingly, there is a high degree of concordance concerning the inputs chosen by the ACO team, and those that appear in this Mayo Clinic tool. These inputs are compared in the table below.

Of note, when using this tool, if personal risk factors, such as the history of myocardial infarction are selected as inputs, no further inputs can be selected: the tool's output immediately goes to the recommendation that a collaborative conversation with a clinician concerning next steps in

management be undertaken. No specific advice concerning this management is included on this output page. In the absence of these personal risk factors, the inputs can be completed, and the tool's output presents a generic set of recommendations. It is important to note that this tool is web-based and available to the general public, whereas the Tool that is being developed in the present context will be used during a clinical interaction in a medical office where trained medical personnel are involved in both the inputs as well as reviewing the assessments, recommendations and creating an action plan. It is also important to note that a modifiable risk factor, renal function, is not included in any of the tools mentioned above. Nor is psychosocial well-being. Also of note, this tool reports a 30-year risk profile, and there is evidence that this approach is likely to increase the number of patients for whom statins are recommended(318).

Section 3.2.1 Modifiable and Non-Modifiable Risk Factors

There are some inherent challenges associated with assigning risk. Broadly speaking, risk factors are either modifiable(18, 114, 287-289) or not modifiable(292-294). Non-modifiable risk factors include such concepts as age, sex, family history, and personal past medical history such as past history of stroke myocardial infarction, diabetic retinopathy, or diabetic nephropathy. These variables are extant, and while medical interventions can optimize the treatment of the consequences of CMD or DM2, these risk factors remain non-modifiable. Modifiable risk factors include such concepts as maintaining a healthy body weight, exercising regularly, making wise dietary choices, and managing laboratory values such as blood sugar, lipid levels and renal function. Citations for these modifiable risk factors are noted above in Section 2.2.

Assigning risk can become a complex matter. Several non-modifiable risk factors, in and amongst themselves, when combined together, create a risk corridor that suggests further

treatment is indicated before even considering modifiable risk factors. Said differently, non-modifiable risk factors like age, gender and race in and of themselves create the possibility for assigning a patient high risk even if other clinical parameters appear well-controlled.

As an example of how non-modifiable risk factors influence the overall assignment of risk, some clinical vignettes are presented. In the day-to-day outpatient clinical environment, it is not unusual to see a patient who roughly fits the following profile: male, white, age 66, no diabetes, no hypertension, total cholesterol of 200, HDL cholesterol 40, and a blood pressure of 120/80. The modifiable risk factors appear well-controlled: blood pressure and cholesterol are at ideal levels without treatment. Using the ACC/AHA risk calculator a 10-year risk of 13.9% is returned. This is well above the threshold of 7.5% which is set to suggest the initiation of statin therapy. This raises the clinical question, “does this mean that all white males age 65 and older with ideal parameters should be treated with statins?” To further emphasize the inherent difficulties involved in assessing the impact of non-modifiable risk factors, the same set of parameters above when applied to an African-American male yields a 10-year risk of 9.8%, and a black female a 10-year risk of 7.8%, and in a white female a 10-year risk of 6.2%. All patients except the white female, using the above analysis, are candidates for statin therapy.

Using the same above low risk nonmodifiable parameters, and changing the truth value of diabetes to yes, the white male’ s 10-year risk becomes 25.1%, the black male’ s 10-year risk is 17.9%, the black female’s risk is 17.8%, and the white female’ s 10-year risk is 11.6%. In other words, treatment with a statin is suggested in all of the above patients.

Section 3.2.2 The Value of Assigning a Precise Value to Risk

As mentioned above, a 10-year risk of 7.5% is considered the threshold for treating patients with statins. This leads to the question of why a granular output to the first decimal point is required as part of risk assessment, once the risk exceeds 7.5%. Overall the logic involved in the current process for assigning risk is straightforward: if risk is greater than 7.5% then start either low or high-dose statins. In other words, there are two inputs, (yes/no, risk equal to or greater than 7.5%), and three outputs, (do not start statins, start low-dose statins, or start high-dose statins). This Tool takes a different approach. Risk is assigned to one of three categories, including moderate risk, high risk and very high risk. It is assumed that patients with diabetes are all at moderate risk of complications. The basis for this assertion is illustrated by the above clinical vignettes.

As noted above, the Tool ingests a broad array of inputs and generates a broad array of assessment outputs, extending well beyond the three assessment outputs concerning lipid management mentioned above. The Tool's logic uses this array of assessment outputs to eventually create a personalized action plan for the patient. As an example, a moderate-risk patient with relatively well-controlled clinical parameters, (excellent lifestyle choices, normal blood pressure, low hemoglobin A1c and low LDL cholesterol), will have a different action plan than a patient at very-high-risk with poorly-controlled clinical parameters.

Section 3.3 Section Summary and Discussion

This section addresses various mechanisms for assessing a patient who may be, or who is already at risk concerning CMD or DM2. Several commonly-used web-based resources were identified and compared. Two central concepts emerged. First is the number of available inputs in these

tools is variable. Second, the number of resultant outputs is also varied. These outputs vary not only in quantity but also in quality: the granularity of the recommendations is different. In all cases, the web-based resources do not create a highly personalized action plan that details the next steps involved in caring for a patient with CMD or DM2. The table comparing these various resources also included in a risk assessment of two patient exemplars. The Tool's risk assessment performed within the parameters of the other web-based tools.

Is expected that when using this Tool that is under development, an individual patient's risk is inferred by accounting for an expanded set of the various well-known risk factors that go beyond what is available in currently-available web-based tools. This expanded set is needed to comprehensively care for patients with CMD or DM 2. These include variables such as BMI, uncontrolled blood pressure, uncontrolled blood sugar, elevated LDL levels, diabetic nephropathy, diabetic retinopathy, peripheral vascular disease, functional status, and various psychosocial determinants of health. Accounting for this expanded set of well-known risk factors facilitates a more complex approach to risk assessment in patients with CMD and DM2 and goes well beyond what is available in the above-captioned web-based tools.

In summary, risk is important to assess. The details of this Tool's machinery demonstrated in the next section where we will focus on how a given patient's risk is assessed. The same type of machinery will be used in the Recommendations and Action Pages of the Tool. This will not be demonstrated below. It is part of future work and is summarized in a separate section below.

Section 3.4 The Risk Stratification Algorithm

What follows are the inference rules for assigning the boundary cases of moderate risk and very-high risk levels to patients. The intermediate high-risk classification is arrived at logically: if a

patient is neither at moderate risk or very-high risk, that patient is assigned the high-risk category. In other words, the high-risk category is the complement of the union of the moderate-risk and very high-risk categories.

It is likely that a large number of rules can be written for inferring moderate risk. Relatedly, it is possible that while all the statements implicit within a written rule set are true, it is not the case that all possible true statements are represented in a rule set. As the number of rules increases, the granularity of the rule set increases, allowing the output to become more granular. In the present context, given that only three strata of risk are being accounted for in this Tool, the rule set associated with moderate risk does not have to be extensive. If, in the future a more granular scale of risk assessment is desired, more rules will be required. That said, there does not appear to be much value to increasing the granularity of the risk assessment as outlined in the section concerning this topic above.

The rules for assessing an individual patient's risk are organized around several concepts. In the case of very high-risk patients the rule set is relatively straightforward. Patients with DM 2 who smoke, have had a cardiovascular incident, have a significant family history of a cardiovascular incident, or who have abnormal renal function are assigned to the very high-risk category.

In the moderate risk rule set a broader array of inputs is attended to. This set includes age, sex, race, blood pressure, LDL cholesterol level, hemoglobin A1c level, and renal function. As noted above, these rules were arrived at by group consensus.

In summary the outputs for Risk Stratification are as follows:

1. Moderate
    a. All diabetics are at moderate risk of complications during their lifetime
2. High

   a. This category is assigned as the complement of the union of the moderate and very-high-risk categories.
3. Very high
   a. Diabetics who have had a stroke, myocardial infarction or significant vascular disease are at very high levels of risk.

Section 3.4.1 The Risk Stratification in Natural Language

The purpose of this section is to explain in some detail how the inference engine in this Tool operates by illustrating, using natural language, how the risk assessment algorithm works. There are many forms of inference engine available for computation in tools like the one under discussion in this document. Examples include truth tables, fuzzy logic, conditional logic, and various forms of machine learning.

This tool uses conditional logic. It is of the form "if-then," meaning that if a given input condition exists, then it can then be inferred that a given output exists. Logical operators, including "and," "or," and "not" are included. Parentheses are used to carefully isolate the various components involved in the computation.

Section 3.4.2 Illustrating the Very High-Risk Category Algorithm

The Patient Risk Very High algorithm that follows immediately below his interpreted line-by-line using the English Language.

The first word, "if" is taken to mean:
"if what follows immediately after the word "if" it is true."

The "(" in the second line delineates:
"all that is being considered to be true up and until when all of the following parentheses, both open and closed, have occurred throughout the algorithm in equal number."

The "((age less than 40) or (age 40 to 49) or (age 50 to 60) or (age 61 to 65) or (age 66 to 70) or (age greater than 70))" means:

"the age of the patient is either less than age 40, or in the categorical group age 40 to 49, or in the categorical group age 50 to 60, or in the categorical group age 61 to 65, or in the categorical age group 66 to 70, or in the categorical age group greater than 70." In practical terms, this means "patients of any age."

"And" means:
"what immediately proceeded and what immediately follows must be included together in this portion of the argument."

The "((male) or (female))" means:
"the patient is either male or female," meaning that the algorithm applies to both sexes.

"((tobacco use) or (history of stroke) or (myocardial infarction) or (peripheral vascular disease) or (retinal disease) or (first-degree relative with cardiovascular disease at age 65 or less))" means:
"if the patient uses tobacco, or has a history of stroke, or has a history of a heart attack, or has poor circulation, or has eye disease related to diabetes, or has a family history of cardiovascular disease." Practically speaking, this means "if the patient has any of the risk factors that are clearly associated with a will high risk of future cardiovascular complications."

The ")" that immediately follows means:
"this is the end of the portion of the argument being considered which began with the first "(" and after all of the other parentheses between the beginning and end have been accounted for."

"Then" means:
"it follows that."

"Patient Risk Very High" means:
"the patient's risk of future cardiovascular complications is very high."

The interpreted meaning of this algorithm in natural language is:
"patients of all ages, both men and women, who have even one of the risk factors clearly associated with a higher risk of future cardiovascular complications have been assigned to the Patient Risk Very High category."

Section 3.4.3 Illustrating the Patient Risk Moderate Category Algorithm

Here the Patient Risk Moderate Category algorithm, which follows immediately after the Patient Risk Very High algorithm, is interpreted using natural language directly; a line by line analysis as above will not be used, since the concepts involved throughout the algorithm are the same.

Section 3.4.3.1: African American Males

"African-American males less than 40 years of age do not have hypertension and have relatively low blood pressure a relatively low cholesterol level and well-controlled blood sugar and no evidence of kidney disease are at moderate risk for developing the complications of cardiovascular disease."

Section 3.4.3.2: White Males

"White males less than age 40 who did not have hypertension and yet have relatively uncontrolled blood pressure, and high cholesterol whose blood sugar and kidney function tests are normal are at moderate risk."

Section 3.5 The Actual Algorithms

As noted above, the more the granularity of inputs increases, the more likely a given output is accurate. In what follows these algorithms are not necessarily complete. More study is needed to be certain that the credit granularity of inputs has been achieved in order to be confident in the outputs. This is part of future work. It should be emphasized that the data is entered manually by trained clinical personnel in the clinical setting by trained medical personnel, and when the session is complete, there will be no record of this session. This is because the first versions of the Tool's implementation will have not PHI as per HIPAA requirements. In future versions, it is hoped that the Tool can be integrated with EHR's or a population health application in order to prepopulate many of the input data fields.

It should also be noted that in keeping with changes in best practices, it may be, for example, that a parameter for HbA1c will change. The tables or data base in the Tool will be designed so that changes in these tables or database can be easily updated and the associated logic changed.

Section 3.5.1 Patient Risk Very High:

Algorithm:

If:
((age less than 40) or (age 40 to 49) or (age 50 to 60) or (age 61 to 65) or (age 66 to 70) or (age greater than 70))
And
((male) or (female))
And
((tobacco use) or (history of stroke) or (myocardial infarction) or (peripheral vascular disease) or (retinal disease) or (first-degree relative with cardiovascular disease at age 65 or less))

Then
(patient risk is very high)

Section 3.5.2 Patient Moderate Risk Algorithm

In Section 3.5 the issues involved in assigning moderate risk were discussed. In this Tool risk is assigned using boundary cases. Stratifying patients into the very high-risk category as seen in Section 3.6.1 is relatively straight forward since these patients already have evidence of secondary disease: they have had a myocardial infarction, a stroke, or have worrisome laboratory values.

Patients with DM 2 are generally at moderate risk of secondary illness within the next decade of their lives, but it is not necessarily true of all of these individuals. Categories of sex, gender and age are major drivers in assigning risk, and these categories are demonstrated below. As also covered in Section 3.2.2, and Section 3.5 assigning risk and the value of multiple categories of

risk is a complex matter. In what follows below the current algorithm for Moderate Risk is demonstrated. In a future version, more rules may be added to more precisely stratify these patients.

Section 3.5.2.1 African-American Males

Algorithm:

If:
((African-American) and (male))
and
(age less than 40)
and
((does not have hypertension) and (blood pressure less than 120) or (blood pressure 121-130))
and
((LDL less than 75) or (LDL 76 to 100) or (LDL 101-129))
and
((hemoglobin A1c less than 7) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)

Section 3.5.2.2 White Males

Algorithm:

If:
((white) and (male))
and
(age less than 40)
and
((does not have hypertension) and (blood pressure less than 120) or (blood pressure 121-130) or (131-140) or (blood pressure greater than 140)
and
((LDL less than 75) or (LDL 76-100) or (LDL 101-129) or (130 – 145 or LDL 146 – 179) or (LDL greater than 179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))

and
(GFR greater than 59)
Or
If:
((white) and (male))
and
(age less than 40)
and
((has hypertension) and (blood pressure less than 120) or (blood pressure 121-130) or (131-140) or (blood pressure greater than 140))
and
((LDL less than 75) or (LDL 76 to 100) or (LDL 101-129) or (130 – 145 or LDL 146 – 179) or (LDL greater than 179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)
Or
if:
((white) and (male))
and
(age 40-49)
and
((does not have hypertension) and (blood pressure less than 120)) or (blood pressure 121-130) or (131-140) or (blood pressure greater than 140)
and
((LDL less than 75) or (LDL 76- 100) or (LDL 101-129) or (130 – 145 or LDL 146 – 179) or (LDL greater than 179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)}

Section 3.6.2.3 African-American Females

Algorithm:

If:
((African-American) and (female))
and
(age less than 40)

and
((does not have hypertension) and (blood pressure less than 120) or (blood pressure 121-130) or (131-140))
and
((LDL less than 75) or (LDL 76 -100) or (LDL 101-129) or (130-145) or (146-179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)

Or

If:
((African-American) and (female))
and
(age less than 40)
and
((has hypertension) and (blood pressure less than 120))
and
((LDL less than 75) or (LDL 76 to 100) or (LDL 101-129) or (130-145) or (146-179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)

if:
((African-American) and (female))
and
(age 40-49)
and
((does not have hypertension) and (blood pressure less than 120))
and
((LDL less than 75) or (LDL 76- 100) or (LDL 101-129) or (130-145) or (146-179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)

Section 3.5.2.4 White females

Algorithm:

If:
((white) and (female))
and
(age less than 40)
and
((does not have hypertension) and (blood pressure less than 120) or (blood pressure 121 to 130) or (131 to 140) or (greater than 140))
and
((LDL less than 75) or (LDL 76 to 100) or (LDL 101-129) or (130-145) or (146-179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)
or
if:
((white) and (female))
and
(age less than 40)
and
((has hypertension) and (blood pressure less than 120) or (blood pressure 121 to 130) or (131 to 140) or (greater than 140))
and
((LDL less than 75) or (LDL 76 to 100) or (LDL 101-129) or (130-145) or (146-179))
and
((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)
or
If:
((white) and (female))
and
(age 40-49)
and
((has hypertension) and (blood pressure greater than 140)
and
((LDL (130-145))
and

((hemoglobin A1c less than 7.0) or (hemoglobin A1c 7.1-7.5))
and
((negative dipstick microalbumin area) or (microalbumin creatinine ratio less than 30))
and
(GFR greater than 59)

Section 3.5.3 Patient Risk High

Algorithm:

If:
Not (Patient Risk Very High)
Or
Not (Patient Risk Moderately High)
Then
(Patient Risk High)

Section 3.6 Risk: Section Summary and Discussion

This section demonstrates how rules within a conditional logic framework stratified the risk of a given patient. The risk stratification algorithm assesses age, sex, race, blood pressure, lipid levels, past medical history, family history, and renal function.

Since three strata of risk are contemplated in the beta version of this Tool, the underlying logic determined the boundary cases of very high risk and moderate risk. If a given patient fell into neither of these categories, then by logical deduction, that patient was assigned to the high-risk category.

As we have seen, this tool uses categorical data and this approach introduces more risk of inaccuracies than if continuous variables were used. As an example, a patient with a blood pressure of 131 versus a blood pressure of 129 could be construed as having higher risk than if a

continuous variable were used. That said, chronic kidney disease is classified using categorical data as noted above: a GFR 59 versus 60 places a patient in a higher risk category.

Given this tools use of categorical data, it is possible that some patients will be categorized as high risk if the parameters of the moderate risk calculation are insufficiently granular: if a patient is clearly not in the very high-risk category and is on the borderline of being at moderate risk, it is possible that this patient will be misclassified as high risk. From a clinical perspective, the consequence might be over treatment with a statin drug. The other medically-addressable modifiable risk factors include blood pressure management, (which would not change if blood pressure were normal despite the higher risk category that was assigned), and treatment of renal dysfunction which also would not occur if renal function were normal.

As noted above, the assessment section of this tool has a rich set of outputs that were generated from the Inputs Page. As of the time of this writing, there is ongoing and future work. The status of this work is referenced and summarized in Appendix 2.

As noted above, this tool will generate a rich set of assessments and enable a conversation between the clinician and patient regarding possible next steps. These assessments will be reviewed with the clinician at the time of the patient encounter, and these assessments will serve as inputs to the recommendations page. The model followed in the risk assessment section above will be applied to each of these variables.

Section 3.7 Patient Personal Issues

A core objective of this Tool is the personalization of a given patient's care, based on what inputs, and therefore, composite patterns of inputs are unique to them. In the last section we covered the personal assignment of risk. This section, following the Biopsychosocial Model of

Engle, identifies personal data such as BMI, blood pressure and functional fitness, among others, that Tool requires.

Section 3.7.1 Patient BMI

Outputs:

1. Patient BMI normal
2. Patient BMI high
3. Patient BMI very high

Algorithm:

if:
(height 5 feet to 5’6”) and ((weight (151 to 180) or (182- 220) or (221- 239) or (greater than 239))
Or
if:
(height 5’7” to 6 feet) and (weight (221-239) or (greater than 239))
Or
if:
((height 6 feet to 6’3”) or (height greater than 6’3”) and (weigh greater than 239 pounds))
then
(Patient BMI very high)
else
if:
((height 5 feet to 5’6”) and (weight 130 to 150))
Or
if:
(height 5 feet 7 to 6 feet) and ((weight 151 to 180) or (181 to 220))
Or
if:
(height 6’1” to 6’3”) and (weight 181 to 220)
Or
if:
(height greater than 6’3”) and (weight 221 to 239)
then
(high BMI)
Else
if:
not (Patient BMI very high)
Or
If:

not (Patient BMI high)
Then
(Patient BMI normal)

Section 3.7.2 Patient Blood Pressure

Blood Pressure outputs:

1) Normal
2) mildly elevated
3) moderately elevated
4) severely elevated

Algorithm:

if: (blood pressure less than 120) then (blood pressure normal) else if: (blood pressure 120-130) then (blood pressure mildly elevated) else if: (blood pressure 131-140) then (blood pressure moderately elevated) else if: (blood pressure greater than 140) then (blood pressure severely elevated)

Section 3.7.3 Patient Psychosocial

Psychosocial outputs:

1) you appear to be doing well
2) there is some concern
3) there is marked concern

Algorithm:

if: (no feeling down or no loss of interest or stress level normal or not particularly anxious) then (you appear to be doing well) else if: (feeling down) or (loss of interest) or (stress level high) or (somewhat anxious on a daily basis) then (there is some concern) else if: (feeling down or loss of interest) or (stress level high or very high) or (very anxious on a daily basis) then (there is marked concern)

Section 3.7.4 Patient Functional Fitness

Functional Fitness outputs:

1) very good
2) some concern
3) marked concern

Algorithm:

if: (exercise three times a week) and (yes can walk 200 feet without stopping) and (yes can climb three flights of stairs) then (functional fitness very good) else if: (no exercise three times a week) and (yes can walk 300 feet without stopping) and (yes can climb three flights of stairs) then (some concern) else if: (no exercise three times a week) and (no can walk 200 feet without stopping) and (no can climb three flights of stairs) then (marked concern)

Section 3.7.5 Patient Diet

Diet outputs:

1) very good
2) some concern
3) marked concern

Algorithm:

if: (if carbohydrate intake low) and (fat intake low) and (fruit and vegetable intake high) then (very good) else if: (carbohydrate intake average and fat intake average and vegetable intake average) then (some concern) else if: (carbohydrate intake high) or (fat intake high) or (fruit and vegetable intake low) then (marked concern)

Section 3.7.6 Patient Habits

Habits outputs:

1) No Concern
2) Mild Concern
3) Moderate Concern
4) High Concern

Algorithm:

if: (no tobacco) and (less than one serving of alcohol a day) then (no concern)
if: (no tobacco) and (1 to 2 servings of alcohol a day) then (mild concern)
if: (no tobacco) and (greater than two servings of alcohol a day) then (moderate concern)
if: (yes tobacco) then (high concern)

Section 3.7.7 Patient Family and Past Medical History

Family and Past Medical History outputs:

1) no concern
2) moderate concern
3) marked concern

Algorithm:

if: (have had heart attack) or (have had stroke) or (have had procedure on heart, neck or extremity arteries) or (have a family history of stroke or heart attack in first-degree relative at less than age 65) or (have diabetic eye disease) then (marked concern) else if: (no have had a heart attack) and (no have had stroke) and (no have had procedure on heart or neck or extremity arteries) and (yes have a family history of stroke or heart attack in first-degree relative at less than age 65) then (moderate concern) else if: (no have had heart attack) or (no stroke) or (no have had procedure or heart neck or extremity arteries) and (no have family history of stroke or heart attack in first-degree relative at less than age 65) then (no concern)

Section 3.7.8 Assessments Section Summary

The Assessments Page is formed by computing the categorical variables from the Inputs Page. The Assessments Page adds a new category, risk, to the existing categories of personal, medications and labs. These computed assessments are shared with the patient in a clinical setting by a clinician, providing a broad array of issues to consider. As the Tool is developed the Assessments Page will be fully fleshed out. Future work will include medication assessment, and lab assessment by computing on the categorical variables that were entered on the Inputs Page.

The Assessments Page outputs become the inputs for the Recommendations Page where a patient is guided along the pathway of improving their health status with respect to CMD or DM 2. These recommendations are presented in a patient-centered, shared-decision making context.

Each recommendation will be individually considered by the patient who will choose to either follow the recommendation or not. We now turn to the Recommendations Page.

There is considerable work to be done before the launch of the beta version of this tool. With regard to the Assessments Page, the assessment of the patient's laboratory values and medication regimen is near-term future work. It is anticipated that the assessment outputs for the laboratory values will stratify as adequate, of some concern and of marked concern. The medication assessment outputs will be either adequate or inadequate.

Section 4: Recommendations Page

Here, the advice given to the patient based on the results of the logic in algorithms that process data elements from both the Inputs Page and the Assessments Page is presented. This is a point that bears repeating: The Tool's logic is not constrained only to the outputs generated by the previous Page. As an example, if the patient's blood pressure is elevated, as entered on the Inputs Page, when computed along with the assessment of both an elevated hemoglobin A1c and the presence of renal dysfunction, it is likely that a GLP-1 agonist will be recommended. Along the same lines, if the assessment of and 71-year-old patient's hemoglobin A1c reveals good control, and the patient is on 2 medications for blood sugar management as found on the Inputs Page, the recommendation may be to stop one of the diabetic medications. As another example, a recommendation to see a clinical pharmacist or endocrinologist is likely to be made when a patient is taking 3 diabetic medications per the Inputs Page and has a hemoglobin A1c that is assessed as uncontrolled.

This Tool supports patient-centered, collaborative, team-based care. Each of the recommendations presented on the Recommendations Page occurs alongside an input that signifies whether the patient wishes to follow or not follow the recommendations. After the Recommendations Page is summarized, the Action Page is presented.

In summary, the Recommendations Page generates patient-specific suggestions for next steps in the care of that patient, based on computations involving the Inputs Page and outputs from the Assessments Page. The tool is patient-centered and team-focused. Only those recommendations that are agreed to by the patient move forward to the Actions Page. These recommendations mirror the above categories of personal patient concerns, (for example, lifestyle and well-being),

medication management concerns and new laboratory investigation orders. A new category appears: recommendations may include consultations with other team members including perhaps a clinical pharmacist, a diabetic nurse educator, an endocrinologist or a nephrologist. The Action Page is generated by those recommendations to which the patient has agreed.

Following the same workflow that has been noted elsewhere, the Recommendations Page is generated by the outputs of the Assessment Page. Conditional logic is used to create recommendations based on the patient's risk, and the fundamental categories that were generated by the structure of the inputs page and flowed through to the assessments page. These categories include patient information patient medications and patient laboratory values.

Following the widely-accepted tenets of patient centered care, these recommendations will be reviewed by the clinician during the office encounter with the patient. Each recommendation will have metadata to assist with the decision-making process. For example, the section below diabetic medications and their commonly-associated attributes are listed. As part of the participatory decision-making process, patients can make an informed decision with respect to a potential change in medication management. There are patients who may wish to avoid injectable medicines, there are patients who may wish to avoid the side effect of weight gain or hypoglycemia and there are patients who may have significant financial constraints concerning the acquisition of newer medications that carry a higher cost. The metadata associated with the recommended medications provides the patient with additional information regarding the choice to be made.

The Recommendations Page will also have some additional nuance provided by the Tool's machinery regarding the decision to use a GLP-1 agonist or an SGLT2 inhibitor. These

medications have been shown to decrease the cardiovascular mortality and morbidity associated with DM 2. In patients with a history of myocardial infarction either of these medications is indicated, and both will be recommended. In patients with renal dysfunction a GLP-1 agonist is indicated and will be recommended. In patients with both the history of myocardial infarction and renal dysfunction a GLP-1 agonist will be recommended.

Section 4.1 Patient Personal Issues Recommendations

Following the same of theme noted in Section 3.7, this Tool focuses on the personalized care of patients with CMD or DM 2. The same pattern of personal data, laboratory data and medication data as set forth in Section 1.1 continues. We now focus on Recommendations concerning Patient Personal Issues.

Section 4.1.1 BMI

Algorithm:

if: (BMI is normal) then (congratulations, keep up the good work) else: if (BMI is high) then ((we recommend that you work on your body weight using the Mediterranean diet)) or (we recommend working with one of our dietitians) else: (BMI very high) then (we recommend working with one of our dietitians)

Section 4.1.2 Blood Pressure

Algorithm:

if: (blood pressure normal) then (no changes are needed, keep up the good work) else if: (((((blood pressure mildly elevated) and (functional fitness some concern) or (functional fitness marked concern) or (diet some concern) or (diet marked concern))))) then ((((we recommend the DASH diet) or (we recommend working with a dietitian) or (we recommend a change blood pressure medication)))) else if: (((((blood pressure moderately elevated) and (functional fitness some concern) or (functional fitness marked concern) or (diet some concern) or (diet marked concern))))) then ((we recommend working with a dietitian) and (change blood pressure medication)) else if: (((blood pressure severely elevated) then (we recommend change in blood pressure medication) and (working with a case manager)))

Section 4.1.3 Psychosocial

Algorithm:

if: (you appear to be doing well) then (keep up the good work) else if: (there is some concern) then (we recommend working with a counselor) else if: (there is marked concern) then ((we recommend medication management for this problem) or (referral to a psychiatrist for this problem))

Section 4.1.4 Functional Fitness

Algorithm:

if: (functional fitness very good) then (keep up the good work) else if: (some concern) then (we recommend joining a gym and working with a trainer) else if: (marked concern) then (we recommend working with a case manager)

Section 4.1.5 Diet

Algorithm:

if: (very good) then (keep up the good work) else if: (some concern) then (we recommend following the Mediterranean diet or the DASH diet) else if: (marked concern) then (we recommend working with a dietitian)

Section 4.1.6 Habits

Algorithm:

if: (marked concern) and (((we recommend working with a smoking cessation specialist) or (working on smoking cessation medication management with your physician) or (working with a counselor concerning alcohol use))) else if: (moderate concern) then (we recommend working with your physician or a counselor concerning alcohol use) else if: (no concern) then (keep up the good work)

Section 4.1.7 Family and Past Medical History

Algorithm:

if: (marked concern) then (((take high-dose statins) and (keep blood pressure less than 130) and (work with a case manager))) else if: ((moderate concern) and (risk is moderate)) then ((take moderate-dose statins) and (keep blood pressure less than 130)) else if: ((no concern) and (risk is moderate)) then ((keep blood pressure less than 130) and (consider taking moderate-dose statins))

Section 4.2 Patient Medication Recommendations

This section focuses on the personal needs of the patient being considered with respect to their medication management. The Assessment Page may have uncovered medication deficiencies that need to be addressed. This section follows the pattern introduced in Section 2.1.2.1: there are diabetes medications, hypertensive medications and lipid medications. The outputs associated with these categories are as follows:

1. Continue existing medication
    a. At present dose
    b. At a changed dose
        i. Increase existing medication dose
        ii. Decrease existing medication dose
2. Stop existing medication
    a. Discontinue existing medication
    b. Taper then discontinue existing medication
3. Add new medication
    a. Start at this dose

Section 4.3 Patient Diabetes Medications

These medications focus on the control of the patient's blood sugar as represented by the input HbA1c. As future work continues a given patient's DM 2 control will either be adequate or inadequate. If adequate, no change is recommended. If inadequate the outputs immediately above in Section 4.2 are followed.

Section 4.3.1 Diabetes Medication Logic

As noted immediately above, diabetic medication management is either adequate or inadequate. Recommending which diabetic medication to use next can be further stratified based on medication attributes. In general, using effective generic medications is preferable because they are generally less expensive. From convenience or necessity perspectives, more expensive,

proprietary medications may be needed. Side-effects like weight gain, (which may further complicate disease management), or hypoglycemia are considered.

Logic on the Assessments Page that references current medications will compute an output that allows the patient to see the array of associated attributes associated with each of the diabetic medications they are taking. As an example, "glimepiride is a medication that risks hypoglycemia, is inexpensive, is oral and may cause weight gain."

Logic in the Recommendations page includes patient choices concerning these categories. As an example, a patient may wish, if possible, to avoid injectable medications, or is willing to accept the potential side effects of an inexpensive medication, owing to financial constraints.

Section 4.3.2 Commonly-Associated Diabetic Medication Attributes

1. Medications that risk significant hypoglycemia
2. Medications that do not risk significant hypoglycemia
3. Medications that risk increased body weight
4. Medications that may decrease body weight
5. Medications that may cause GI upset
6. Inexpensive medications
7. Expensive medications
8. Medications for use with coronary vascular disease comorbidity
9. Medications that may reduce myocardial infarction risk
10. Oral medications
11. Injectable medications

Section 4.3.2.1 Diabetic Medications and Their Commonly-Associated Attributes

Frequently used diabetic medications:

1) Biguanide
    a) Metformin
        i) May cause GI upset
        ii) Inexpensive medications
        iii) Oral medications
        iv) Does not risk significant hypoglycemia
2) Sulfonylureas

a) Glimepiride (Amaryl)
    i) Risks significant hypoglycemia
    ii) Risks increased body weight
    iii) Inexpensive medications
    iv) Oral medications
b) Glyburide (DiaBeta, Glynase, Micronase)
    i) Risks significant hypoglycemia
    ii) Risks increased body weight
    iii) Inexpensive medications
    iv) Oral medications
c) Glipizide (Glucotrol)
    i) Risks significant hypoglycemia
    ii) Risks increased body weight
    iii) Inexpensive medications
    iv) Oral medications

3) Thiazolidinediones (TZD
    a) Pioglitazone (Actos)
        i) Does not risk significant hypoglycemia
        ii) Risks increased body weight
        iii) Inexpensive medications
        iv) May reduce myocardial infarction risk
        v) Oral medications
4) DPP-4 inhibitors
    a) Sitagliptin (Januvia)
        i) Does not risk significant hypoglycemia
        ii) Expensive medications
        iii) Oral medications
    b) Saxagliptin (Onglyza)
        i) Does not risk significant hypoglycemia
        ii) Expensive medications
        iii) Oral medications
    c) Linagliptin (Tradjenta)
        i) Does not risk significant hypoglycemia
        ii) Expensive medications
        iii) Oral medications
5) GLP-1 receptor agonists
    a) Dulaglutide (Trulicity)
        i) May decrease body weight
        ii) May cause GI upset
        iii) Expensive medications
        iv) Use with coronary vascular disease comorbidity
        v) May reduce myocardial infarction risk
        vi) Injectable medications
    b) Exenatide (Byetta)
        i) May decrease body weight
        ii) May cause GI upset

iii) Inexpensive medications
iv) Use with coronary vascular disease comorbidity
v) May reduce myocardial infarction risk
vi) Injectable medications

c) Exenatide extended release (Bydureon)
i) May decrease body weight
ii) May cause GI upset
iii) Expensive medications
iv) Use with coronary vascular disease comorbidity
v) May reduce myocardial infarction risk
vi) Injectable medications

d) Liraglutide (Victoza)
i) May decrease body weight
ii) May cause GI upset
iii) Expensive medications
iv) Use with coronary vascular disease comorbidity
v) May reduce myocardial infarction risk
vi) Injectable medications

e) Semaglutide (Ozempic)
i) May decrease body weight
ii) May cause GI upset
iii) Expensive medications
iv) Use with coronary vascular disease comorbidity
v) May reduce myocardial infarction risk
vi) Injectable medications

6) SGLT2 inhibitors

a) Dapagliflozin (Farxiga)
i) May decrease body weight
ii) Expensive medications
iii) Use with coronary vascular disease comorbidity
iv) May reduce myocardial infarction risk
v) Oral medications

b) Canagliflozin (Invokana)
i) May decrease body weight
ii) Expensive medications
iii) Use with coronary vascular disease comorbidity
iv) May reduce myocardial infarction risk
v) Oral medications

c) Empagliflozin (Jardiance)
i) May decrease body weight
ii) Expensive medications
iii) Use with coronary vascular disease comorbidity
iv) May reduce myocardial infarction risk
v) Oral medications

7) Insulin preparations

a) Long-acting preparations

i) Insulin detemir (Levemir)
    (a) Risks significant hypoglycemia
    (b) Risks increased body weight
    (c) Expensive medications
    (d) Injectable medications
ii) Insulin glargine (Lantus)
    (a) Risks significant hypoglycemia
    (b) Risks increased body weight
    (c) Expensive medications
    (d) Injectable medications
iii) Insulin glargine (Basaglar)
    (a) Risks significant hypoglycemia
    (b) Risks increased body weight
    (c) Inexpensive medications
    (d) Injectable medications
iv) Insulin degludec (Tresiba)
    (a) Risks significant hypoglycemia
    (b) Risks increased body weight
    (c) Expensive medications
    (d) Injectable medications

b) Short-acting preparations
i) Insulin lispro (Humalog)
    (a) Risks significant hypoglycemia
    (b) Risks increased body weight
    (c) Expensive medications
    (d) Injectable medications
ii) Insulin aspart (Novolog)
    (a) Risks significant hypoglycemia
    (b) Risks increased body weight
    (c) Expensive medications
    (d) Injectable medications

Section 4.4 Rules Concerning Patient Diabetic Medication Recommendations

Recommending diabetic medications is driven by the Tool's machinery with a goal to adequately control the HbA1c and suggesting medications that may be context-specific. As noted above when discussing cardiovascular risk GLP-1 agonists or SGLT 2 inhibitors are indicated with a history of cardiovascular disease. There are rules concerning age-appropriate blood sugar control: there is little utility to tight control of blood sugar in the elderly. Indeed, there is additional risk of harm from hypoglycemia in this population. There is also a bias in the

machinery towards avoiding medications that promote weight gain and/or risk hypoglycemia in general. As examples, insulin causes weight gain and risks hypoglycemia, but may be the best choice in a given clinical context. Metformin and pioglitazone have a low risk of hypoglycemia, but pioglitazone may cause an increase in body fat while decreasing visceral fat. Glimepiride stimulates the pancreas to secrete insulin, (it is a secretagogue), risking hypoglycemia, weight gain, and future pancreatic insulin secretion failure. It is also a common medication in the community and is relatively inexpensive.

Section 4.4.1 Adequate Regimen Rules:

Section 4.4.1.1: Younger age group

if: (age (less than 40) or (40 to 49) or (50 to 60) or (61 to 65)) and (hemoglobin A1c (less than 7) or (7.1-7.5) then (regimen adequate)

Section 4.4.1.2: Somewhat older age group

if: (age (61 to 65) or (66 to 70)) and (hemoglobin A1c 7.6-8.0) then (regimen adequate)

Section 4.4.1.3: Older age group

if: (age (71 or greater) and (hemoglobin A1c 8.1-9.0) then (regimen adequate)

Section 4.4.2: Inadequate Regimen Rules

Section 4.4.2.1: Global rules

if: (history of heart attack) and (not taking GLP-1 medication) or (not taking SGLT 2 medication) then (diabetes medication severely inadequate)

if: (dipstick microalbumin) or (microalbumin creatinine ratio (61 to 100) or (101 to 300) or (greater than 300) or (GFR less than 15) or (16 to 29) or (30 to 44) then (significant renal dysfunction)

if: (significant renal dysfunction) and (not taking GLP-1 medication) then (diabetes medication severely inadequate)

Section 4.4.2.2: Younger age group

if: (age (less than 40) or (40 to 49) or (50 to 60) or (61 to 65)) and (hemoglobin A1c 7.5-8 .0) then (diabetes medication somewhat inadequate)

if: (age (less than 40) or (40 to 49) or (50 to 60) or (61 to 65)) and (hemoglobin A1c 8.1-9.0) then (diabetes medication mildly inadequate)

if: (age (less than 40) or (40 to 49) or (50 to 60) or (61 to 65)) and (hemoglobin A1c 9.1-10.0) then (diabetes medication moderately inadequate)

if: (age (less than 40) or (40 to 49) or (50 to 60) or (61 to 65)) and (hemoglobin A1c greater than 10.0) then (diabetes medication severely inadequate)

Section 4.4.2.3: Somewhat older age group

if: (age (61 to 65) or (66 to 70)) and (hemoglobin A1c 8.1-9.0) then (diabetes medication somewhat inadequate)

if: (age (61 to 65) or (66 to 70)) and (hemoglobin A1c 9.1-10.0) then (diabetes medication mildly inadequate)

if: (age (61 to 65) or (66 to 70)) and (hemoglobin A1c greater than 10) then (diabetes medication moderately inadequate)

Section 4.4.2.4: Older age group

if: (age (71 or greater) and (hemoglobin A1c 9.1 to 10.0) then (diabetes medication somewhat inadequate) medication

if: (age (71 or greater) and (hemoglobin A1c greater than 10.0) then (diabetes medication or moderately inadequate all)

If: (diabetes medicine adequate) then (continue medication regimen)

if: (diabetes medication (somewhat inadequate) or (mildly inadequate) or (moderately inadequate) or (severely inadequate) then (change medication regimen)
and
if: (history of heart attack) and (diabetes medication severely inadequate all) then (change medication regimen) and (start GLP-1 medication) or (start SGLT 2 medication)

if: (significant renal dysfunction) and (diabetes medication severely inadequate) then (change medication regimen) and (start GLP-1 medication)

if: (hemoglobin A-1 C) less than (7.5) and (greater than 6.5)) and (age less than 71) and (not taking diabetes medications) then (begin Metformin and titrate the dose to 1000 mg b.i.d.) or (begin pioglitazone 15 mg)
if: (change medication regimen) and (hemoglobin A1c low) then (decrease medication dose) or (taper medication and stop) or (stop medication)

if: (change medication) and (hemoglobin A1c high) and (medication not at maximum dose) then (increase medication dose) else if: (change medication) and hemoglobin A1c high) and (medication at maximum dose) then (add new medication)

if: (hemoglobin A1c less than 7.5), and (taking diabetes medicine), then (continue existing medications)

if: (hemoglobin A1c greater than 10.0), and (not taking insulin therapy), then (begin insulin therapy)

if: (GFR less than 30), and (taking diabetes medicine (Metformin)), then (stop diabetes medication (Metformin))

if: (age less than 71 or greater) and (hemoglobin A1c greater than 8.0) and (taking insulin therapy), then (increase insulin dosage)

if: (age 71 or greater) and (hemoglobin A1c less than 8.1) and (taking diabetes medicine) then (no diabetic medication change)

if: (age less than 71 or greater), and (hemoglobin A1c greater than 8.0), and (taking metformin), then (add pioglitazone)

if: (age less than 71 or greater), and (hemoglobin A1c greater than 8.0), and (taking 1000 mg metformin), and (taking pioglitazone 45 mg), or (taking sulfonylurea) then (add GLP-1 agonist) or (add SGLT2 inhibitor)
if: (age less than 71 or greater) and (taking metformin 1000 mg a day) and (hemoglobin A-1 C greater than 8) and (high-risk) then (add SGLT2 inhibitor)

if: (age 71 or greater) and (taking metformin 1000 mg a day) and (and taking sulfonylurea) and (hemoglobin A1c less than 8.0) then (taper sulfonylurea) and (add pioglitazone)

Section 4.5 Patient Hypertensive Medication Recommendations

Managing the blood pressure in a given patient is important. The risk of adverse cardiovascular outcomes increases dramatically as blood pressure increases. This is particularly true in patients

who have CMD or DM 2. The Tool will recommend adequate BP control in patients with DM 2. Consensus suggests a blood pressure of 130/80 or less, as measured in a clinical setting for those with DM 2. As noted elsewhere, the use of hypertensive medications, (an ACE or an ARB), can be used in patients in patients without hypertension who have renal dysfunction. In patients with hypertension and renal dysfunction, one of these medications will be recommended.

Section 4.5.1 Hypertension Management Rules

if: (less than 120) and (no blood pressure medications) then (no added hypertension medications)

if: (blood pressure greater than 130) and (no blood pressure medications) and (dipstick microalbumin negative or microalbumin creatinine ratio less than 30) then add (blood pressure medication, chlorthalidone)

if: (blood pressure greater than 130) and (no blood pressure medications) and ((dipstick microalbumin positive) or (microalbumin creatinine ratio greater than 30) then (add blood pressure medication ARB telmisartan)

if: (blood pressure greater than 130) and (taking blood pressure medication) and (blood pressure medication is thiazide) (and thiazide dose 25 mg) then (add ARB, telmisartan)

if: (blood pressure greater than 130) and ((((taking blood pressure medication) and (blood pressure medication is thiazide) and (dose of thiazide is 25 mg) and (ARB or ACE dose at maximum) then (add calcium channel blocker amlodipine))))

if: (blood pressure greater than 130) and (taking thiazide) and (dose less than 25 mg) then (increase dose to 25 mg)

if: (blood pressure greater than 130) and (((taking blood pressure medication) and (blood pressure medication is a beta blocker) and (not taking thiazide diuretic))) then (add chlorthalidone 25 mg and taper beta blocker)

if: (blood pressure greater than 140) and (not taking blood pressure medication) then ((add chlorthalidone 25 mg) and (telmisartan 20 mg))

if: (blood pressure greater than 130) and ((((taking blood pressure medication) and (taking thiazide) and (thiazide dose 25 mg) and (taking ACE or ARB) and (dose of ACE or ARB not maximal)))) then (increase dose of ACE or ARB)

if: (blood pressure greater than 130) and (((((taking a beta blocker atenolol) and (not taking thiazide diuretic) or (ACE) or (ARB) or (calcium channel blocker))))) then ((taper atenolol) and (add chlorthalidone 25 mg)

if: (blood pressure greater than 130) and (((((taking beta blocker metoprolol) and (not taking diuretic) or (ACE) or (ARB) or (calcium channel blocker))))) then ((taper metoprolol) and (add chlorthalidone 25 mg))

if: (blood pressure greater than 140) and (((((taking beta blocker atenolol)or (metoprolol) and (not taking thiazide) or (ACE) or(ARB))))) then (((add ((chlorthalidone 25 mg) and(telmisartan 20 mg)) and (taper beta blocker)))

if: (blood pressure greater than 130) and (((((taking blood pressure medication) and (hydrochlorothiazide dose is 25 mg) and ((ACE) or (ARB dose is maximal)) and (amlodipine dose is 10 mg) and GFR greater than 60))))) then (add spironolactone 25 mg)

if: (blood pressure greater than 130) and ((((((taking blood pressure medication) and (hydrochlorothiazide dose is 25 mg) and (ACE or ARB dose is maximal) and (amlodipine dose is 10 mg) and (spironolactone dose is 25 mg)))))) then (refer to nephrologist)

if: (blood pressure is greater than 130) and ((((taking beta blocker) and (taking thiazide 25 mg) and (taking submaximal dose of ACE or ARB)))) then ((increase dose of ACE or ARB) and (taper beta blocker))

Section 4.6 Lipid Medication

Cardiometabolic Disease and DM 2 can be construed as a form of accelerated cardiovascular disease. In this light, managing this risk is similar to managing the risk of patients who have cardiovascular disease. Statins are central to this management for two apparent reasons. First, they lower LDL cholesterol, which, as discussed above, is strongly correlated with cardiovascular disease. Second, this class of medications decreases the inflammation associated with LDL's interaction with the vascular endothelium. Adding statins at a moderate dose when a patient is at high risk and adding statins at a high dose when patients are at very high risk is a standard of care. This is termed "treating to risk." There is also a line of thought that, since LDL levels corollate with cardiovascular disease risk, "treating to target," meaning driving the LDL as low as is practically possible is indicated. There are recent references documenting LDL

levels around 10, with no apparent adverse consequences, that are associated with continuously decreased risk when compared with any other higher LDL level. The machinery of this Tool is currently oriented towards the "treat to risk" methodology.

Section 4.6.1 Lipid Management Rules

if: (very high risk) and (not taking statins) then (begin a atorvastatin 80 mg or rosuvastatin 40 mg) else if: (taking lovastatin or simvastatin) then (stop lovastatin or simvastatin) and (start a atorvastatin 80 mg or rosuvastatin 40 mg) else if: (taking atorvastatin less than 80 mg) or (taking rosuvastatin less than 40 mg) then (increase dose to atorvastatin 80 mg or rosuvastatin 40 mg)

if: (high risk) and (not taking statins) then (begin a atorvastatin 40 mg or rosuvastatin 20 mg) else if: (taking lovastatin or simvastatin) then (stop lovastatin or simvastatin) and (begin atorvastatin 40 mg or rosuvastatin 20 mg) else if: (taking atorvastatin less than 40 mg or rosuvastatin less than 20 mg) then (begin a atorvastatin 40 mg or rosuvastatin 20 mg)

if: (moderate risk) then (consider beginning atorvastatin 40 mg or rosuvastatin 20 mg)

Section 5: The Action Page

This Page lists the next steps to be taken in the care of the patient. These next steps are generated by the Tool's logic and incorporate only those recommendations to which the patient has agreed. The actions fall into several subcategories, including personal actions like lifestyle changes, medication changes and follow-up plans with those team members that have been agreed to.

The actions to be taken as next steps in managing a patient with CMD or DM 2 follow logically from the Recommendations Page: those recommendations to which the patient, in a patient-centered discussion with the clinician decides to follow (as represented by "yes" in the logic below), become action items. In what follows work in progress is demonstrated.

Future work will focus on laboratory actions, medication actions and various types of follow-up evaluations with the treating clinician or another member of the care management team. In what follows, examples of work in progress are presented. Future work requires precise logic to address actions such as exact doses of medications to be changed, new medications to be added, and those to be tapered or discontinued, perhaps simultaneously in the domains of blood pressure management, lipid management, blood sugar management and renal function abnormalities. In the same vein, there are laboratory values to be acted upon to track progress in the domains of lipid management, blood sugar management and, if applicable, renal function management.

Section 5.1 Personal Issues

This section deals with the actions on personal issues such as weight management or diet and exercise that have been agreed to by the patient in consultation with the clinician when

interacting with the Recommendations Page. Given that our ACO involves two hospitals, Overlake and EvergreenHealth, a new concept of location preference is for care is added.

Section 5.1.1 Care Location Preferences

In general, where on the Eastside do you prefer to go for further support services?

1. Overlake area
2. EvergreenHealth area

Section 5.1.2 BMI

if: yes (we recommend that you work on your body weight using the Mediterranean diet) then (print Mediterranean diet) and if: yes (we recommend working with one of our dietitians) then (add resources for Overlake area) else (add resources for Evergreen health area)

Section 5.1.3 Blood Pressure

if: yes (we recommend the DASH diet) then (print DASH diet)
and
if: yes (we recommend working with a dietitian) then (add resources for Overlake area) else (add resources for EvergreenHealth area)
and
if: yes (we recommend a change blood pressure medication) then (change blood pressure medication)
or
if: (blood pressure severely elevated) and yes (we recommend change in blood pressure medication) then change pressure medication)
and
if: yes (working with a case manager) then (add resources for Overlake area) else (add resources for EvergreenHealth area)

Section 5.1.4 Psychosocial

if: (there is some concern) and yes (we recommend working with a counselor) then (add resources for Overlake area) else (add resources for EvergreenHealth area) or else if: (there is marked concern) and yes (we recommend medication management for this problem) then (work with caregiver on medication management) else if: yes (referral to a psychiatrist for this problem) then then (add resources for Overlake area) else (add resources for EvergreenHealth area)

Section 5.1.4 Psychosocial

if: (functional fitness very good) then (keep up the good work) else if: (some concern) then (we recommend joining a gym and working with a trainer) else if: (marked concern) then (we recommend working with a case manager)

Section 5.1.6 Diet

if: (very good) then (keep up the good work) else if: (some concern) then (we recommend following the Mediterranean diet or the DASH diet) else if: (marked concern) then (we recommend working with a dietitian)

Section 5.1.7 Habits

if: (marked concern) and (we recommend working with a smoking cessation specialist) or (working on smoking cessation medication management with your physician) or (working with a counselor concerning alcohol use) else if: (moderate concern) then (we recommend working with your physician or a counselor concerning alcohol use) else if: (no concern) then (keep up the good work)

Section 5.1.8 Family and Past Medical History

if: (marked concern) then (take high-dose statins) and (keep blood pressure less than 130) and (work with a case manager) else if: (moderate concern) and (risk is moderate) then (take moderate-dose statins) and (keep blood pressure less than 130) else if: (no concern) and (risk is moderate) then (keep blood pressure less than 130) and (consider taking moderate-dose statins)

Section 6: Project Trajectory and Testing

The central aim of this Thesis is the delivery of a wireframe depiction of a Web-based Clinical Decision Support Tool that aids the clinicians who are caring for patients with CMD or DM 2. The wireframe is not simply a design template. It creates context for the Tool's functionality. It also provides an indexing function that facilitates the understanding of the Tool and provides a structure that references completed work, work in progress and future work.

Section 6.1 The Tool's Core Functionality

The core functionality envisioned with the launch of the beta version of this Tool is the management of those medications required to maintain a patient's HbA1c within an age and risk-adjusted corridor. Given the importance of lipid, blood pressure and renal function control, there is likely to be some functionality directed at these targets. Before a beta version of the Tool is launched, testing is carried out, followed by the release of the alpha version.

In order to provide sufficient emphasis, it is again stated here that, for the purpose of the Thesis, only the wireframe is created. There will be no testing, nor will there be either an alpha or beta test version of the Tool as part of this Thesis. This is part of future work along the trajectory of the Tool's development.

Section 6.2 Testing and the Alpha Version

As planned, the alpha version will be tested by the clinical pharmacists who care for patients in the diabetes and lipid clinics, the Trainee, and several recruited primary care providers. All of these individuals work in clinical settings with patients, assessing risks, making recommendations, prescribing medications and ordering labs.

The first will include a “dry lab” step where 10 fictional patient scenarios are presented to the testers in written form. The testers will transfer the inputs from the written page to the Inputs Page and move to the Assessment Page and then the Recommendations Page. On the Recommendations Page, the tester will be asked to select “Agree” to each recommendation and proceed to the Actions Page.

As these steps are followed, the tester will compete a step-wise form of the assessment of each page involved, using a 5-point Likert scale ranging from 1-5. The tester will be looking for ease of use, clarity of the interface and a clinical opinion of the content of each page. These recorded assessments will be studied by a core group that includes pharmacists, primary care providers and endocrinologists. Based on consensus, changes to the Tool may be made, followed by another round of dry lab testing and core group analysis. When consensus been reached that the Tool’s functionality is acceptable, testing enters the alpha release and is tested in the clinic settings as noted at the beginning of this section. The same form used in the dry lab will be used again to test the Tool’s functionality in a clinical setting. The content of the tester’s step-wise assessment of the Tool follows next.

Section 6.2.1 Test Scenarios

The purpose of the test scenarios in the alpha version of this Tool is to measure how consonant the recommendations generated by the Tool are with what clinician-users expect. As noted in Section 6.2 the clinician will analyze each scenario by recording their responses on a form as in Table 2 below. Theoretically, the number of test scenarios is the multiplicative of all of the input data elements collected on the Inputs Page, a number that is pragmatically unrealistic for this project. Instead, 6 scenarios designed to test the Tool in situations where intervention is likely to

be required. Two scenarios will include African American individuals and four will include White individuals. Individual ages will include those over 40 years of age, and there will be at least one issue regarding abnormal blood pressure, lipid profile or HbA1c. Each of these scenarios is presented below in Sections 6.2.1.1 through 6.2.1.6

Table 6.2.1. User Feedback assessment of tool during testing

Circle the correct numeric response per row

Test case #_____	Strongly Disagree	Disagree =2	Neutral =3	Agree =4	Strongly Agree =5
Inputs Page					
The layout is clear	1	2	3	4	5
The page is easy to use	1	2	3	4	5
Content is clinically relevant	1	2	3	4	5
Content is clinically accurate	1	2	3	4	5
Comments & observations*					
Assessments Page					
The layout is clear	1	2	3	4	5
The page is easy to use	1	2	3	4	5
Content is clinically relevant	1	2	3	4	5
Content is clinically accurate	1	2	3	4	5
Comments & observations*					
Recommendations Page					
The layout is clear	1	2	3	4	5
The page is easy to use	1	2	3	4	5
Content is clinically relevant	1	2	3	4	5
Content is clinically accurate	1	2	3	4	5

Comments & observations*					
Action Page					
The layout is clear	1	2	3	4	5
The page is easy to use	1	2	3	4	5
Content is clinically relevant	1	2	3	4	5
Content is clinically accurate	1	2	3	4	5
Comments & observations*					

*User feedback assessment of Tool during testing

Section 6.2.1.1: Case #1

Ms. Peterson is a 57-year-old White female who was recently found to have high blood sugar at an employer-sponsored health screening event. She contacted the office for an appointment. Fasting labs were drawn 2 days ago, and she presents for evaluation. She has not been to the office for an exam in the last 3 years and has no history of high blood sugar.

Her height is 5 feet and 6 inches, her weight is 160 pounds, and her blood pressure is 142/92. She is recently divorced and lives alone. She notes feeling fatigued, anxious, depressed and stressed possible lay-offs announced by her employer. She is not eating very many vegetables, consumes a lot of sweets and eats at a fast food restaurant 10 times a week. She is not exercising, gets short of breath after climbing 2 flights of stairs, but not when walking on level ground. She does not use tobacco or alcohol.

Her past medical history is essentially negative. She is taking no medications. She has no surgeries or cardiovascular problems. Her mother and sister have DM2, her father had a fatal myocardial infarction at age 62.

Her laboratory values include a HbA1c of 8.2, and LDL cholesterol of 172, a GFR of 100 and a microalbumin/creatinine ratio of less than 30.

Section 6.2.1.2: Case #2

Ms. Jones is a 57-year-old African-American female with a 5-year history of DM 2 and hypertension. Fasting labs were drawn 2 days ago, and she presents for follow-up. She has not been to the office for an exam in the last 9 months since losing her insurance coverage. She is due for medication renewals and was told she needed an appointment.

Her height is 5 feet and 5 inches, her weight is 170 pounds, and her blood pressure is 156/102. She lives with her spouse and one of their adult children. She notes feeling fatigued and is anxious about finances and insurance coverage. She says her diet is "terrible." She orders take out most nights and finds herself constantly snacking on "junk food." She is not exercising, in an organized fashion, but walks the dog for 15 minutes every morning without getting sort of breath. She continues to smoke about a pack a day and has 2 drinks a day.

Her past medical history is essentially negative. She is taking lisinopril 10 mg a day, and metformin 1000 mg BID. She has no surgeries or cardiovascular problems. Her mother, a sister and her brother have DM2 and hypertension, and her brother had a coronary bypass at age 60.

Her laboratory values include a HbA1c of 8.2, and LDL cholesterol of 180, a GFR of 55 and a microalbumin/creatinine ratio of less than 30.

Section 6.2.1.3 Case #3

Mr. Tucker is a 77-year-old White male with a 10-year history of DM 2 and hypertension. Fasting labs were drawn 2 days ago, and he presents for follow-up. He follows a routine schedule of being seen for follow-up every 3 months or so, given his clinical issues.

His height is 5 feet and 9 inches, her weight is 190 pounds, and his blood pressure is 126/82. He lives with his spouse. He says his life continues to go well. The couple travels a lot and have a comfortable lifestyle since retirement. They enjoy their grandchildren. He reads a lot, goes to yoga and does high-intensity interval aerobic workouts in the gym regularly. He is careful to follow the Mediterranean diet as suggested. He does not use tobacco and consumes 2 glasses of red wine daily.

His past medical history is remarkable for coronary stent placements on 2 occasions and a TIA at age 66. His ophthalmologist recently found early diabetic retinopathy. His family history is positive for multiple siblings with hypertension, DM2, a stroke and a heart attack.

He is taking telmisartan 20 mg a day, chlorthalidone 25 mg a day, and amlodipine 10 mg a day for his blood pressure, metformin 1000 mg BID and dulaglutide 0.75 mg weekly for his diabetes, and rosuvastatin 20 mg daily for his hyperlipidemia.

His laboratory values include a HbA1c of 7.6, and LDL cholesterol of 97, a GFR of 25 and a microalbumin/creatinine ratio of 320.

Section 6.2.1.4 Case #4

Mr. Bolt is a 67-year-old African American male with a 15-year history of DM 2 and hypertension. Fasting labs were drawn 2 days ago, and he presents for follow-up. He follows a routine schedule of being seen for follow-up every 3 months or so, given his clinical issues.

His height is 5 feet and 11 inches, his weight is 220 pounds, and his blood pressure is 144/88. He lives with his spouse. He says he plans to retire sometime in the next year and move to Arizona where the cost of living is lower. His job is stressful, he is anxious that they may not have saved enough for retirement, but he is getting tired more easily and does not want to keep up the pace required by his work for much longer. He occasionally finds himself feeling a little blue, perhaps because he will see his grandchildren less when they move. He gets to the gym twice a week and works out for 40 minutes. He has no trouble climbing stairs. He struggles to get all his fruits and vegetables in on a daily basis and has a “wicked sweet tooth.” He has cut down to 5 cigarettes a day. He has 2 cans of beer every night after work and a six pack on the weekend.

His past medical history is remarkable for coronary stent placement in his LAD 8 months ago. A recent carotid ultrasound demonstrated a 60% blockage bilaterally. His ophthalmologist recently said there is no evidence of retinopathy. His family history is positive for multiple siblings with hypertension, DM2, a stroke and a heart attack.

He is taking lisinopril 20 mg a day, and amlodipine 10 mg a day for his blood pressure, metformin 1000 mg BID and glimepiride 4mg BID for his diabetes, and simvastatin 40 mg daily for his hyperlipidemia.

His laboratory values include a HbA1c of 8.7, and LDL cholesterol of 136, a GFR of 55 and a microalbumin/creatinine ratio of 32.

Section 6.2.1.5 Case #5

Mr. Kline is a 47-year-old White male with a 4-year history of DM 2 and hypertension. Fasting labs were drawn 2 days ago, and he presents for follow-up. He follows a routine schedule of being seen for follow-up every 3-6 months.

His height is 5 feet and 11 inches, his weight is 190 pounds, and his blood pressure is 140/92. He lives alone but has an active social life. His job as a project lead in a software company is stressful. His sleep is often interrupted by thinking about his work. He is anxious most of the time during the week, but less so on weekends. He wonders how he will keep up the pace of his work 20 years from now and sometimes gets philosophical about what kind of value his work actually adds to society. He gets to the gym and works out hard for an hour 3 times a week. He does not smoke, drinks a bottle of wine over the weekend and follows the Mediterranean diet closely.

His past medical history is unremarkable for interventional procedures, and his ophthalmologist recently said there is no evidence of retinopathy. His family history is positive for maternal diabetes and paternal hypertension and hyperlipidemia. His paternal grandfather died of a stroke at age 75. He has a sibling with hypertension.

He is taking hydrochlorothiazide/lisinopril 20 mg a day, for his blood pressure, and metformin 1000 mg BID and sitagliptin 100 mg daily for his diabetes.

His laboratory values include a HbA1c of 7.6, and LDL cholesterol of 136, a GFR of 95 and a microalbumin/creatinine ratio of less than 30.

Section 6.2.1.6 Case #6

Ms. Abbot is a 67-year-old White female with a history of DM2, and hypertension. Fasting labs were drawn 2 days ago, and she presents for follow-up. She has not been to the office for an exam in the last 12 months. She is past due for medication renewals and was told she needed an appointment.

Her height is 5 feet and 3 inches, her weight is 157 pounds, and her blood pressure is 148/92. She lives with her spouse. She notes feeling fatigued and has a headache several times a week. Her spouse was recently disabled by a stroke and she is now the sole breadwinner. She is working on his Social Security benefits and is anxious about finances and her ability to retire anytime soon. She says she has “fallen off the wagon” with respect to her eating and has gained 10 pounds since her spouse’s stroke. She has to work a lot of overtime and is her spouse’s sole caregiver. She orders take out most nights. She is not exercising in an organized fashion. She walks the dog for 15 minutes on weekends and becomes a little sort of breath by the end of the

walk. She does not climb stairs. She has started smoking a pack a day again and drinks a bottle of wine each night.

Her past medical history is essentially negative except for her DM2 and hypertension. She is taking losartan 50 mg a day, and metformin 1000 mg BID. She has no surgeries or cardiovascular problems. Her mother, a sister and her brother have DM2 and hypertension, and her brother had a coronary bypass at age 60.

Her laboratory values include a HbA1c of 9.2, and LDL cholesterol of 172, a GFR of 48 and a microalbumin/creatinine ratio of 67.

Section 6.3 Section Summary

This section's addresses the methodology involved in testing the Alpha version of the Tool as part of the Tool's development trajectory using a "dry lab" approach. No clinical management decisions will be made based on the Recommendations and Actions generated by the Alpha version of the Tool. Clinicians will be presented with each of the 6 clinical scenarios outlined in Sections 6.2.1.1 through 6.2.1.6 and will provide feedback on the user interface and the reasonableness of the Recommendations and Actions generated by the Tool via the form presented in Table 2.

CHAPTER 7: References

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Appendix 2

This Appendix contains the screenshots of the entire wireframe created for the prototype of the Tool described in this Thesis. The figures are presented in the sequential order they are designed to be displayed in production.

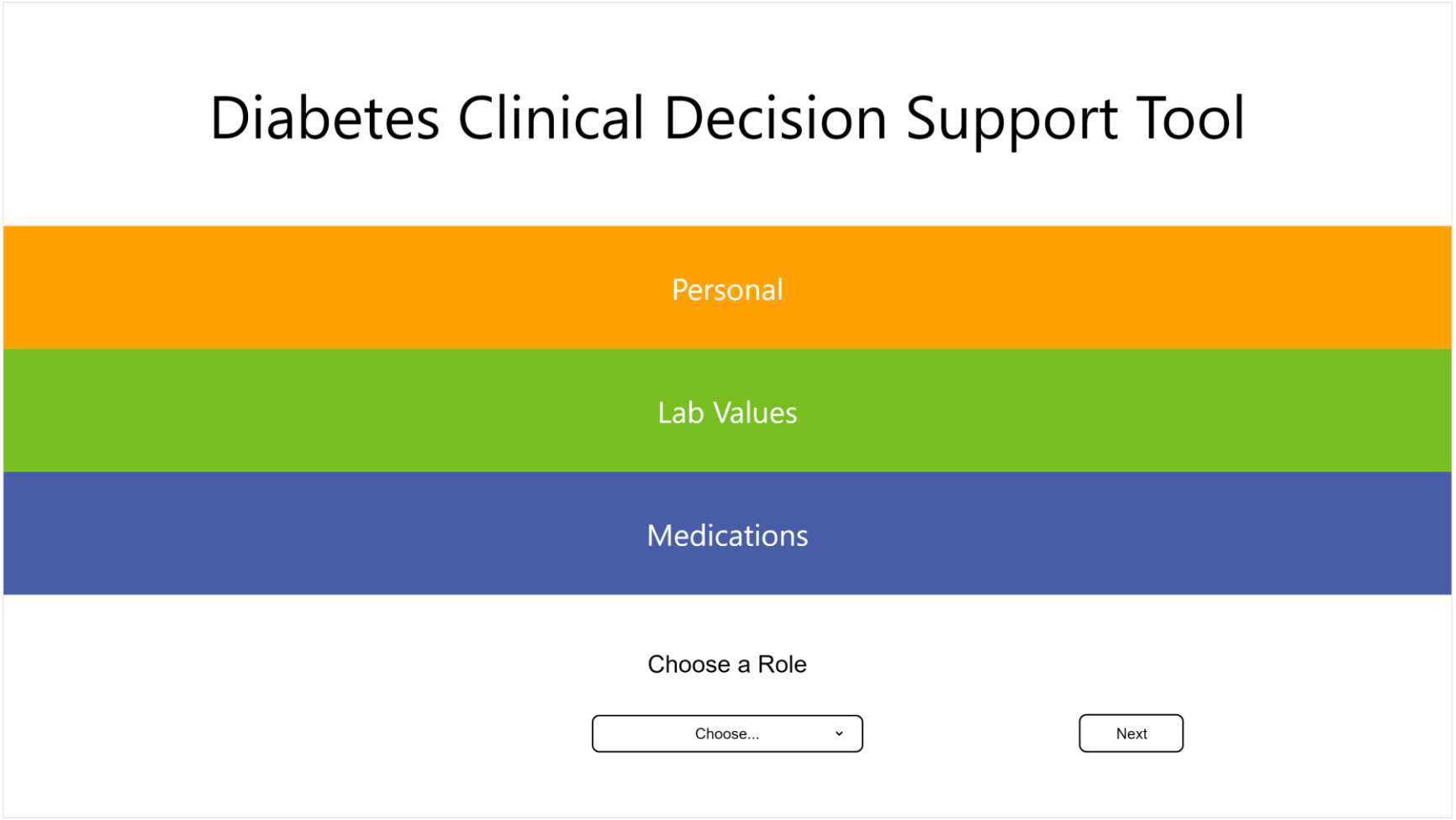

Figure 9 Tool landing page

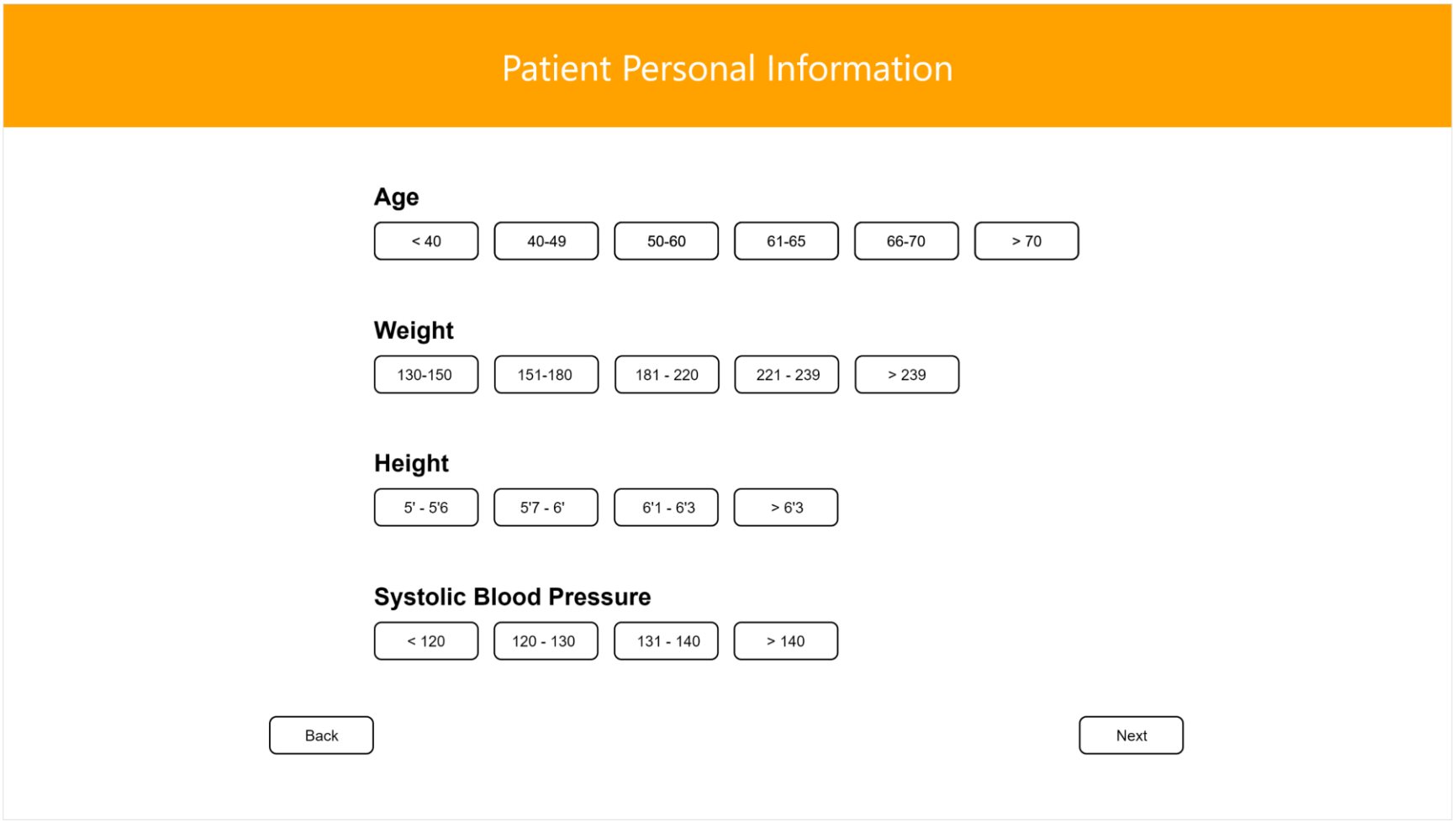

Figure 10 Patient personal information input page

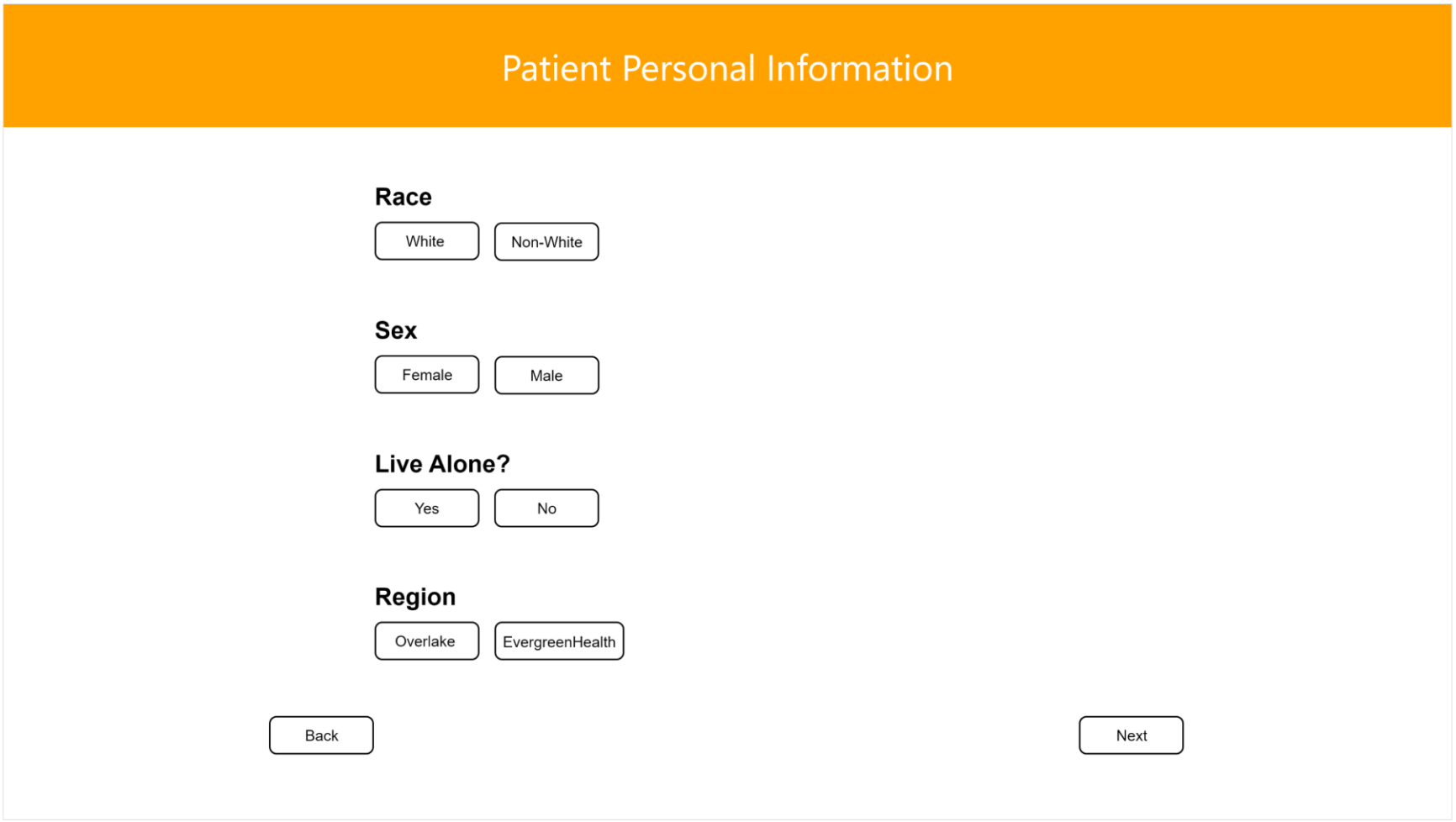

Figure 11 Patient personal information input page continued

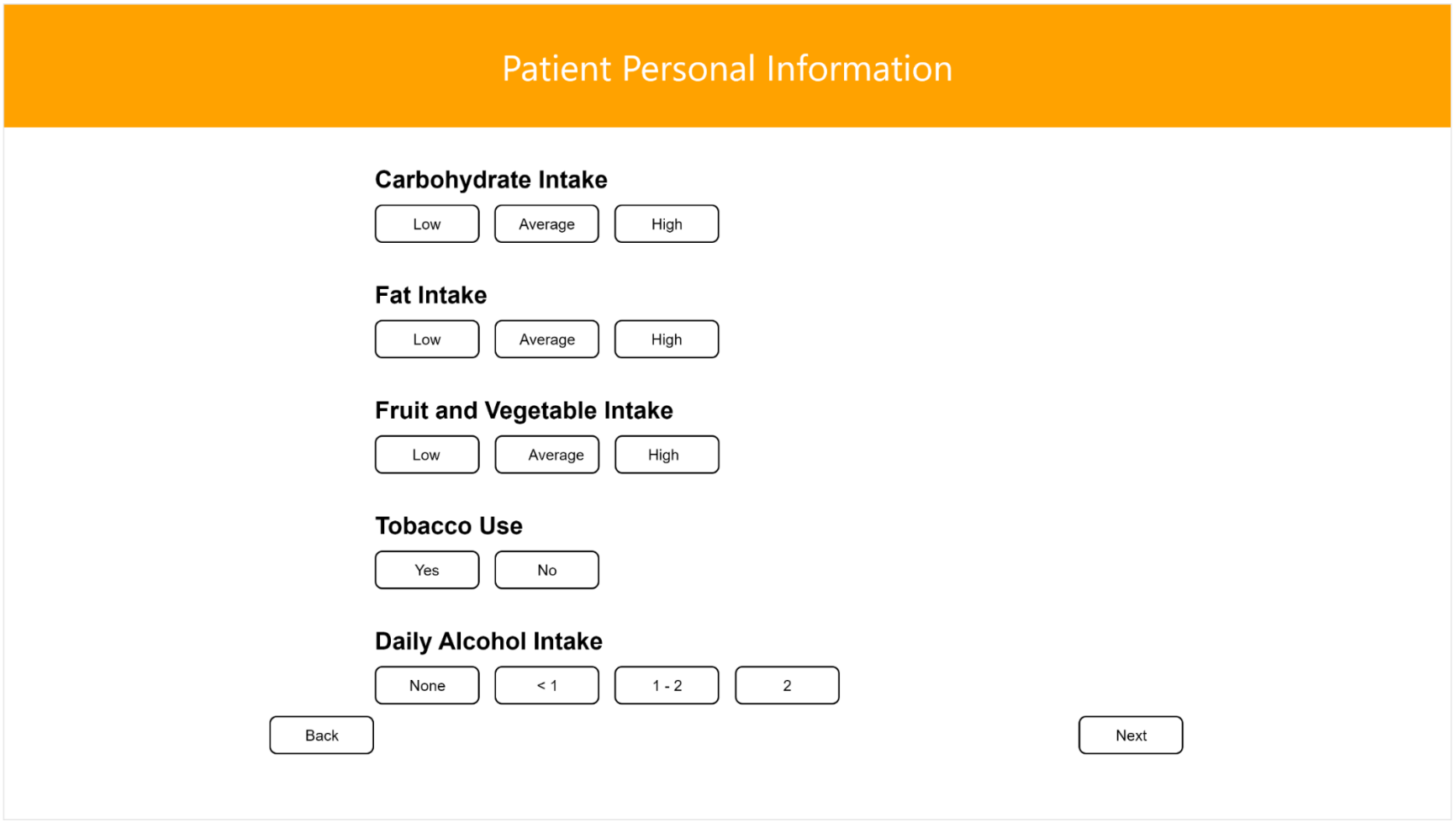

Figure 12 Patient personal information input page continued

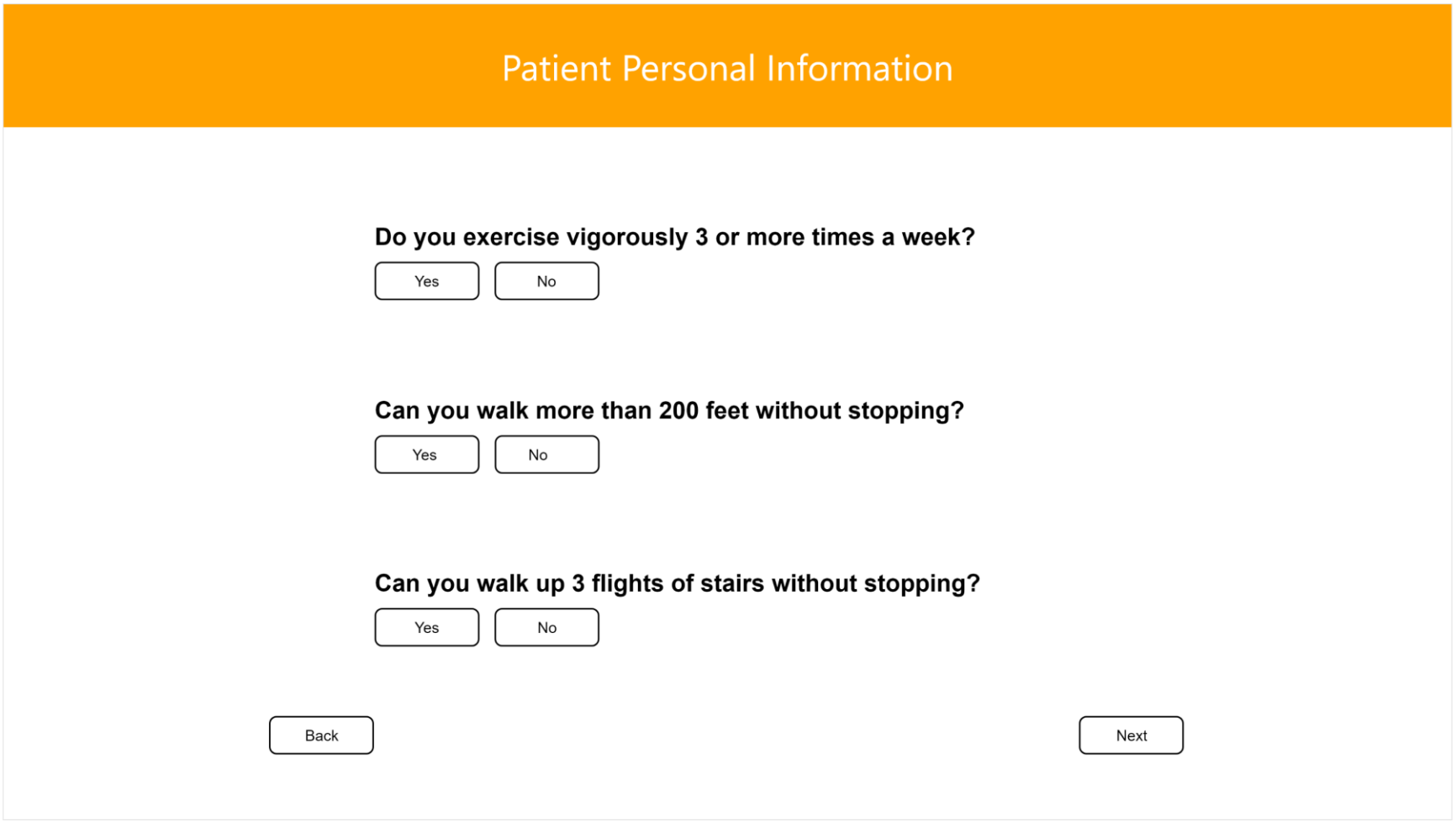

Figure 13 Patient personal information input page continued

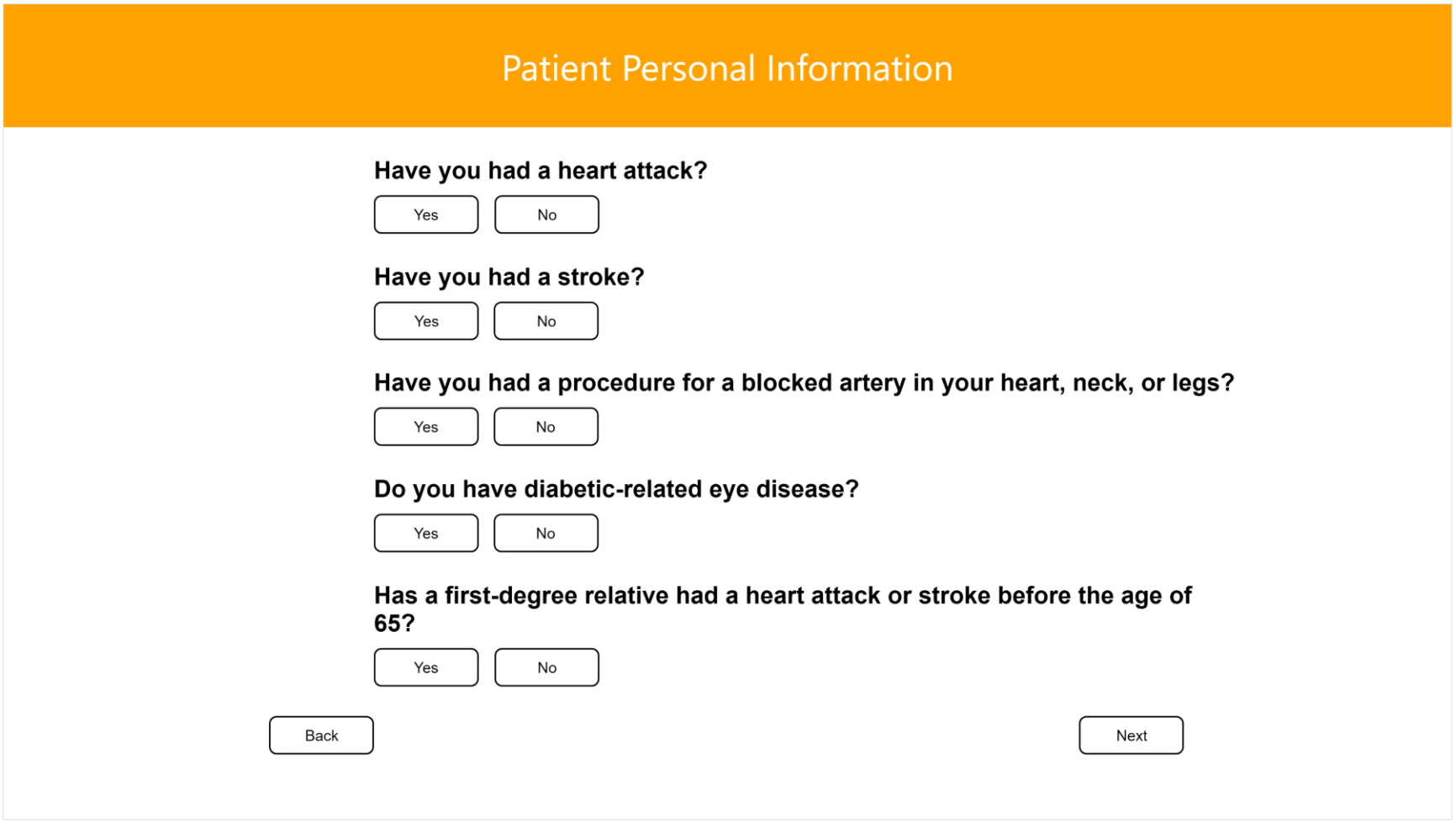

Figure 14 Patient personal information input page continued

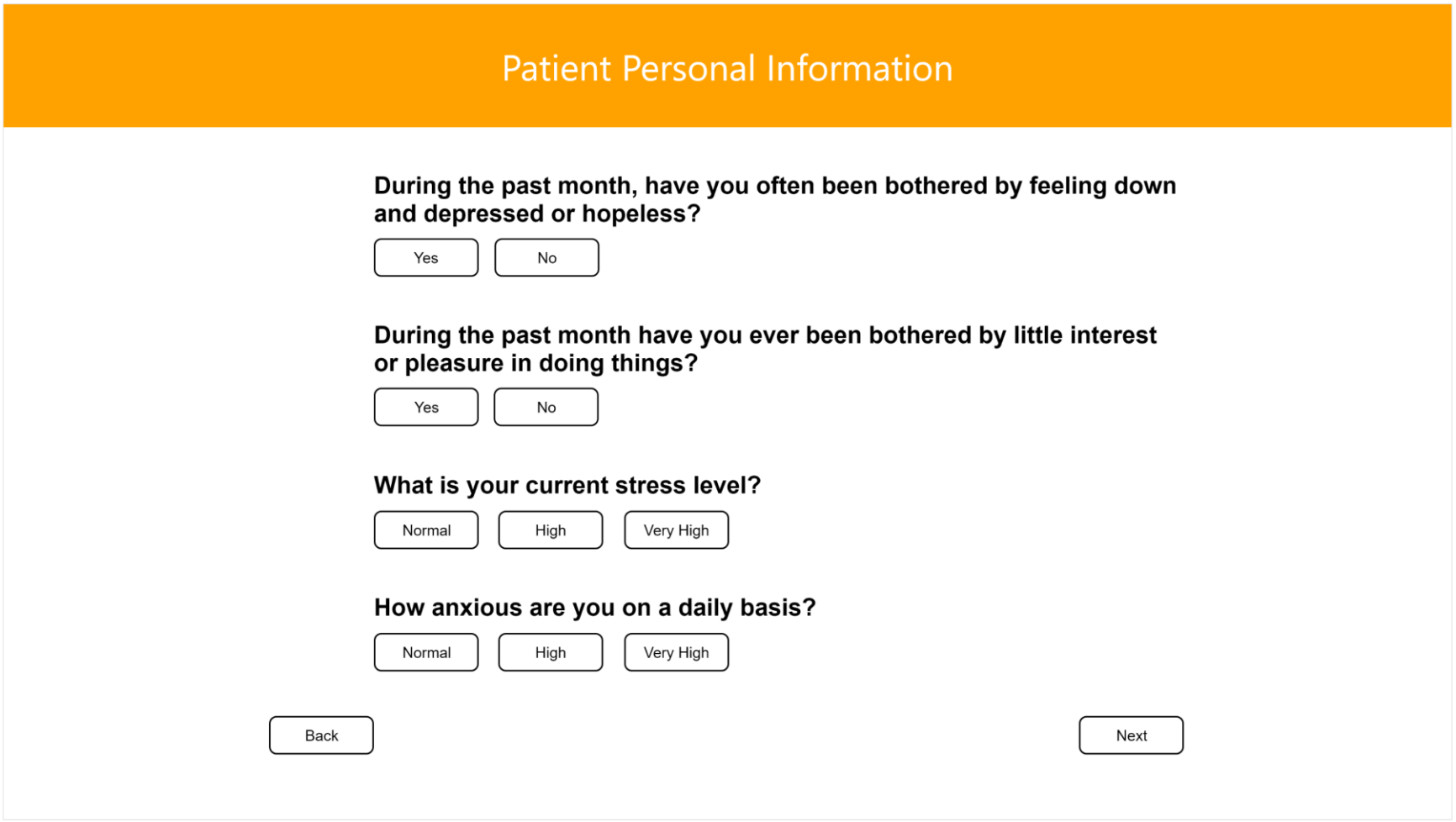

Figure 15 Patient personal information input page continued

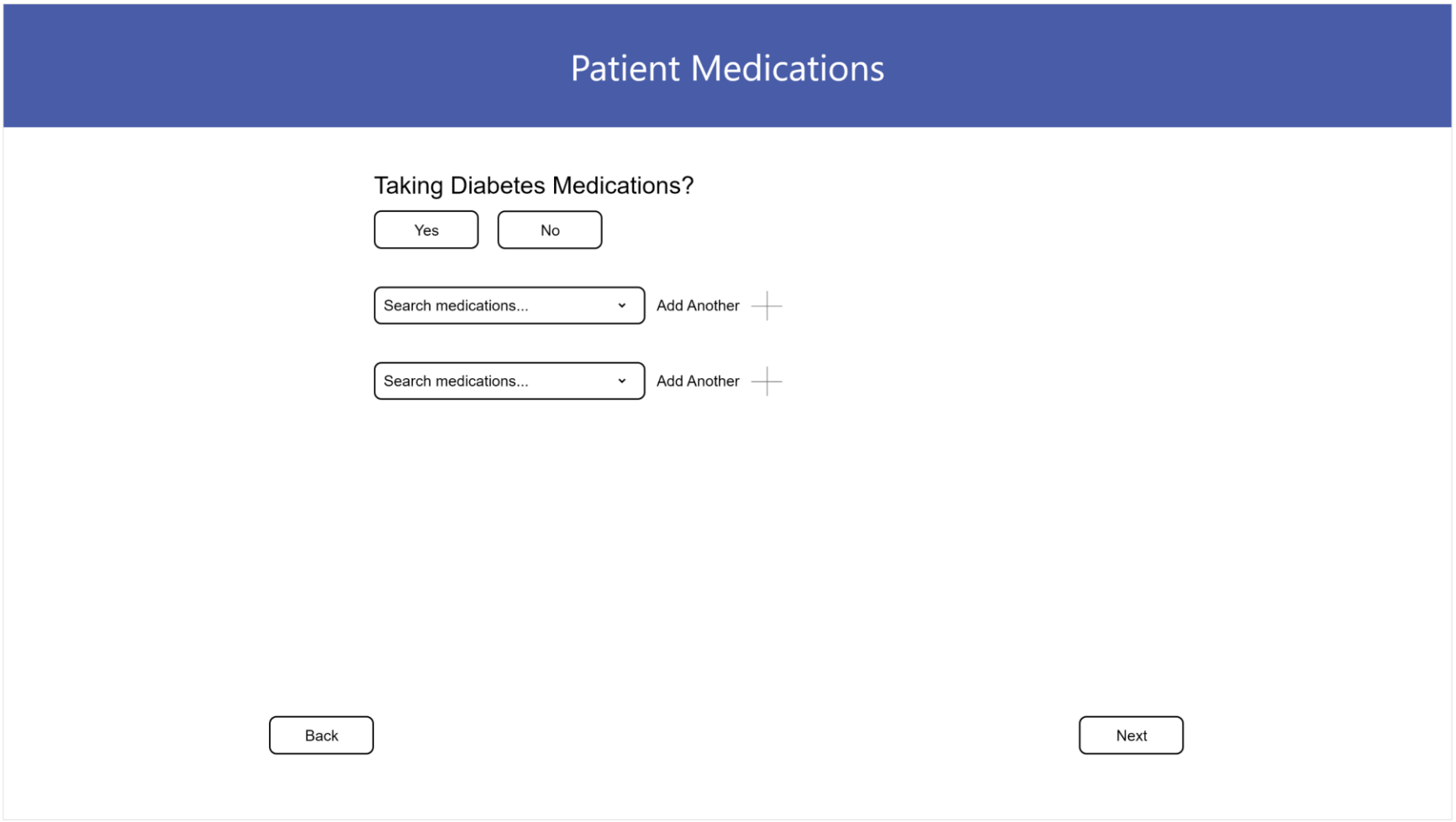

Figure 16 Patient medication input page

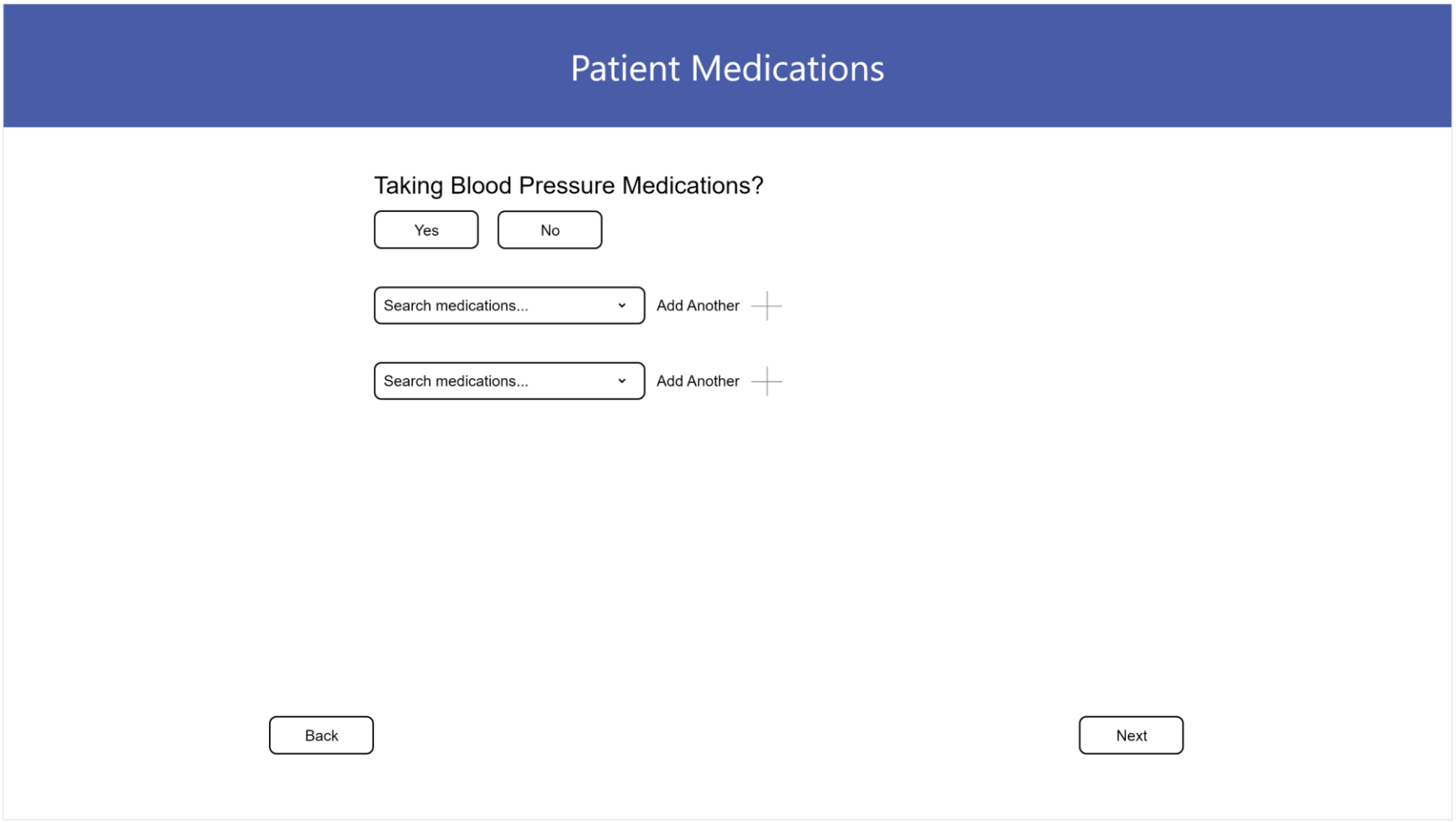

Figure 17 Patient medication input page continued

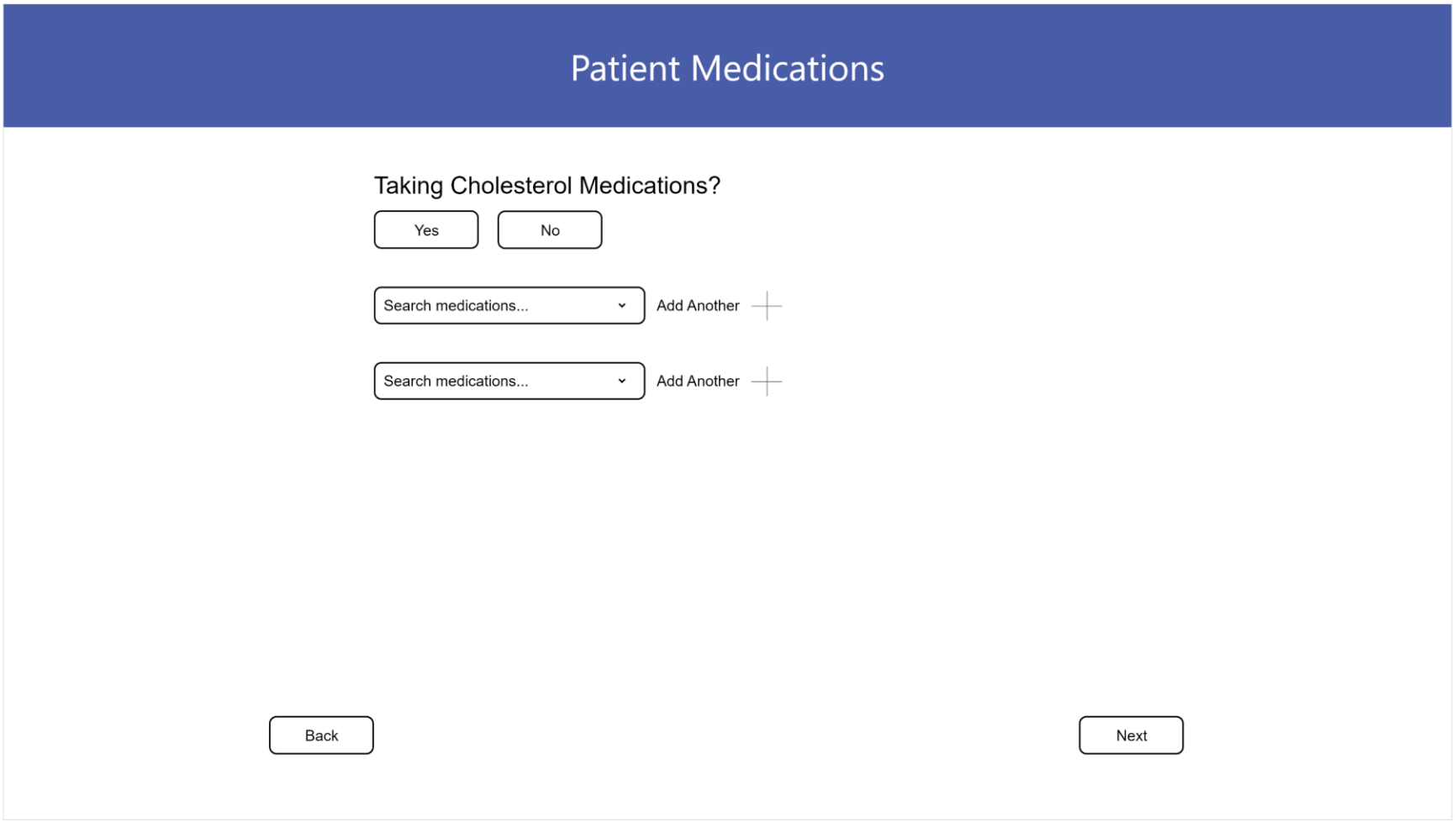

Figure 18 Patient medication input page continued

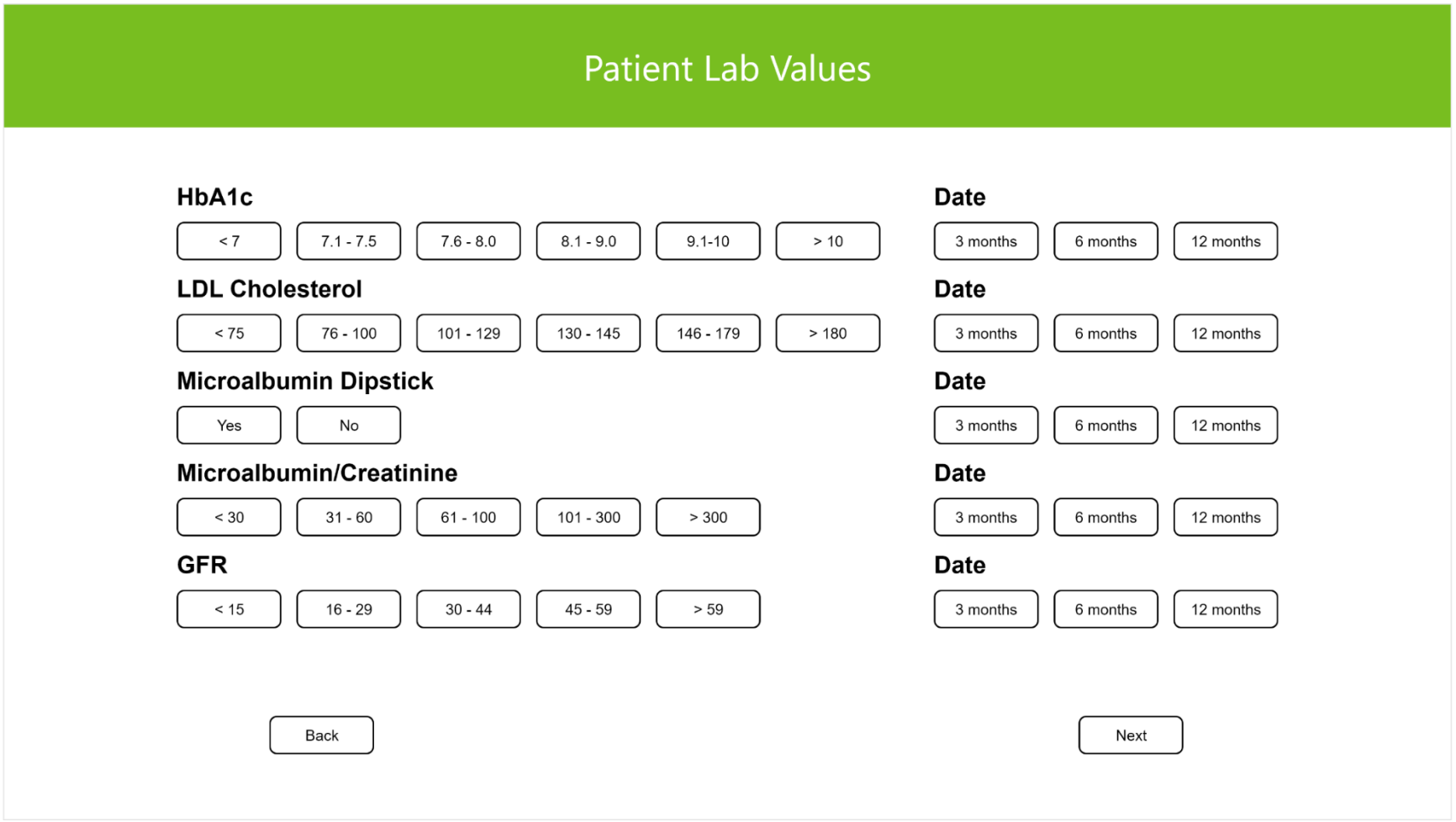

Figure 19 Patient lab values input page

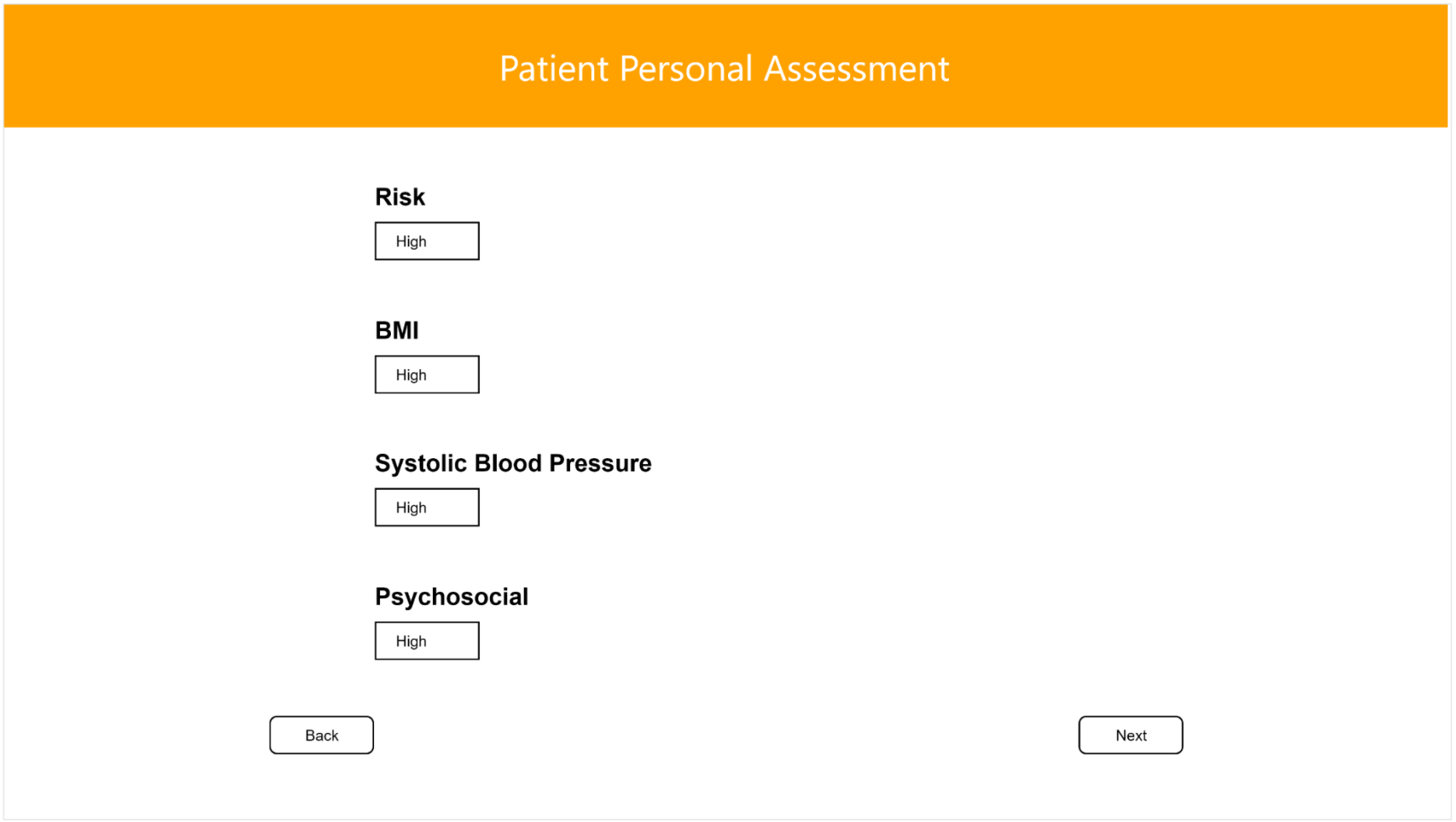

Figure 20 Patient personal assessment page

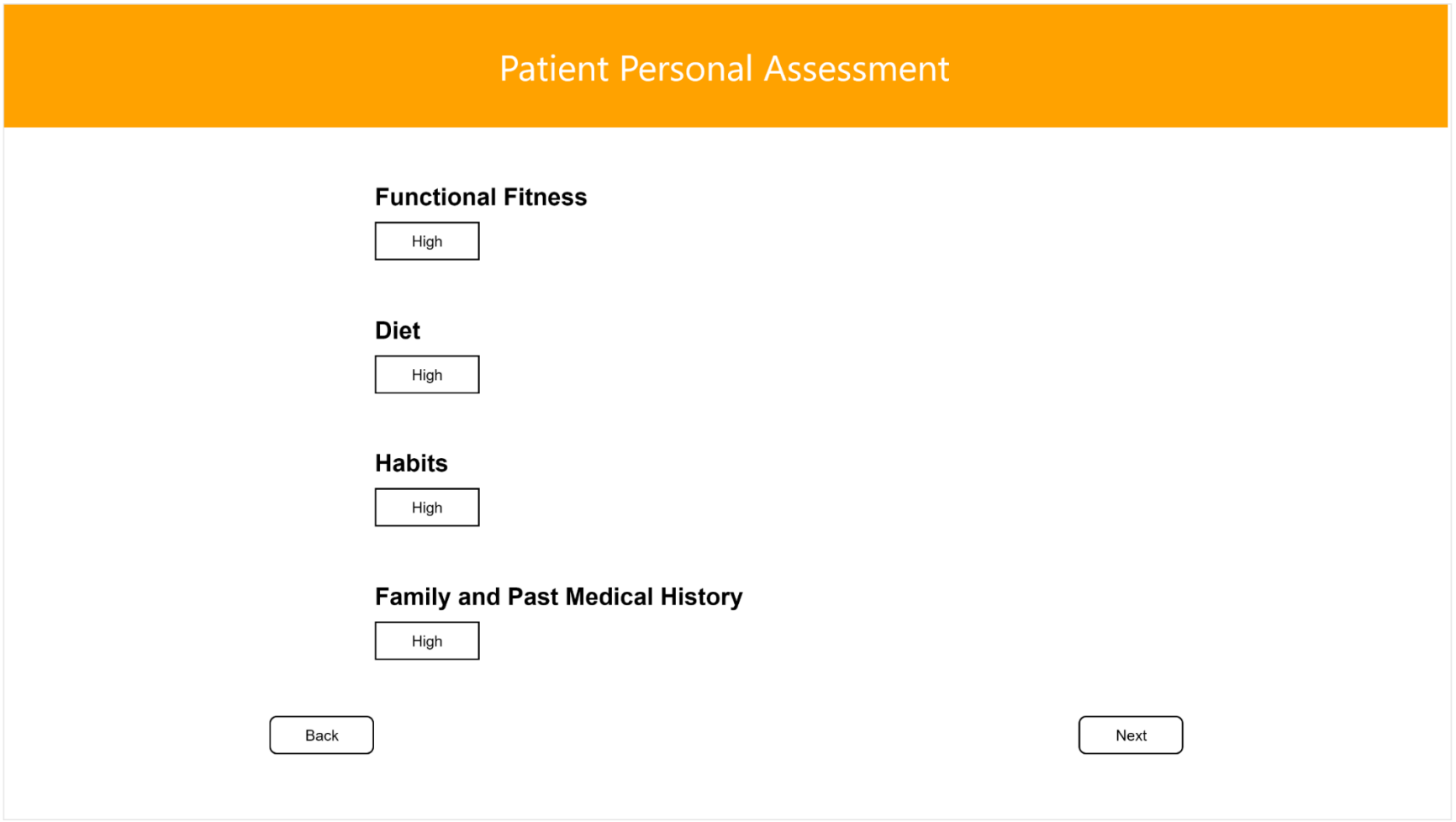

Figure 21 Patient personal assessment page continued

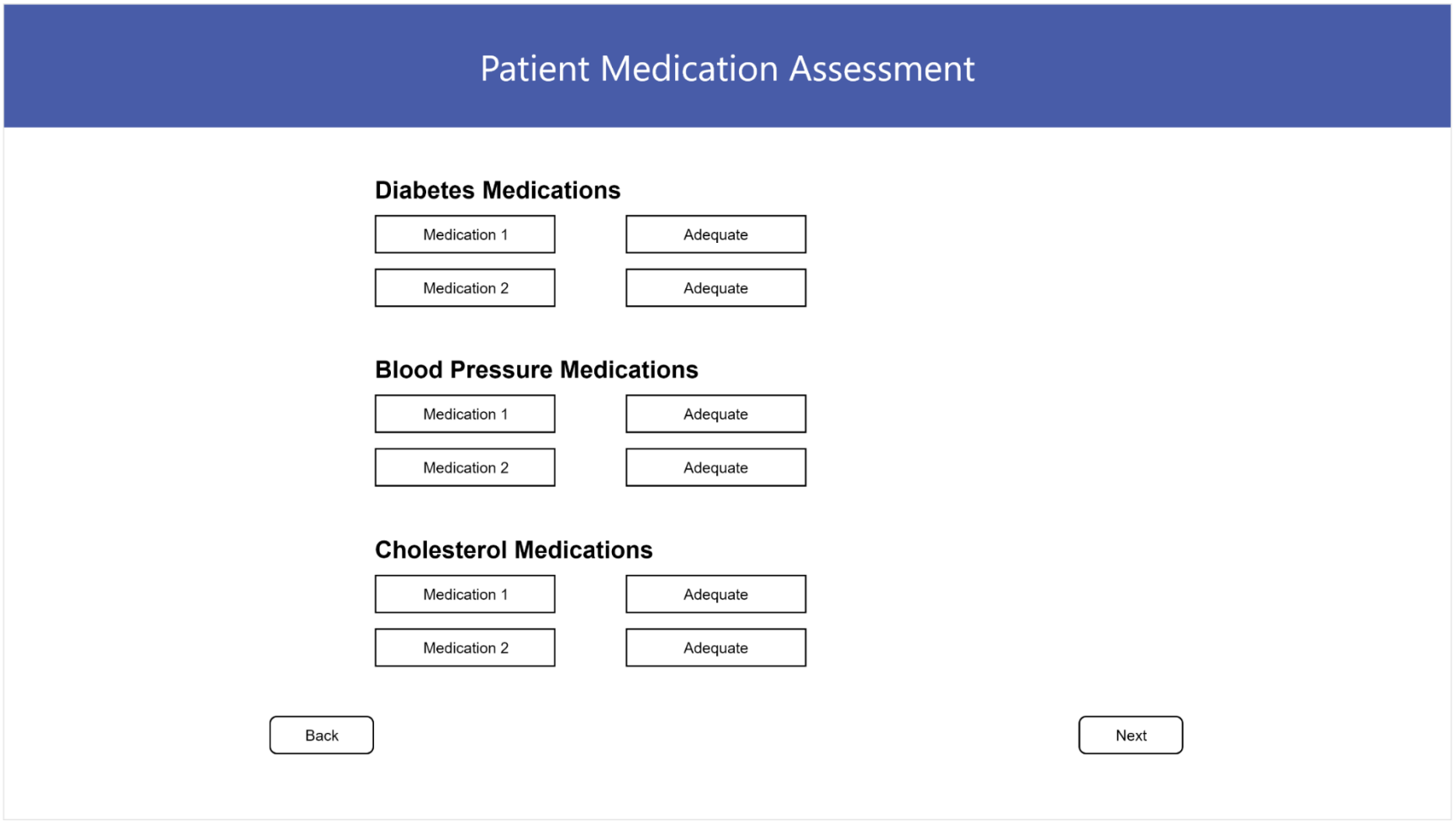

Figure 22 Patient medication assessment page

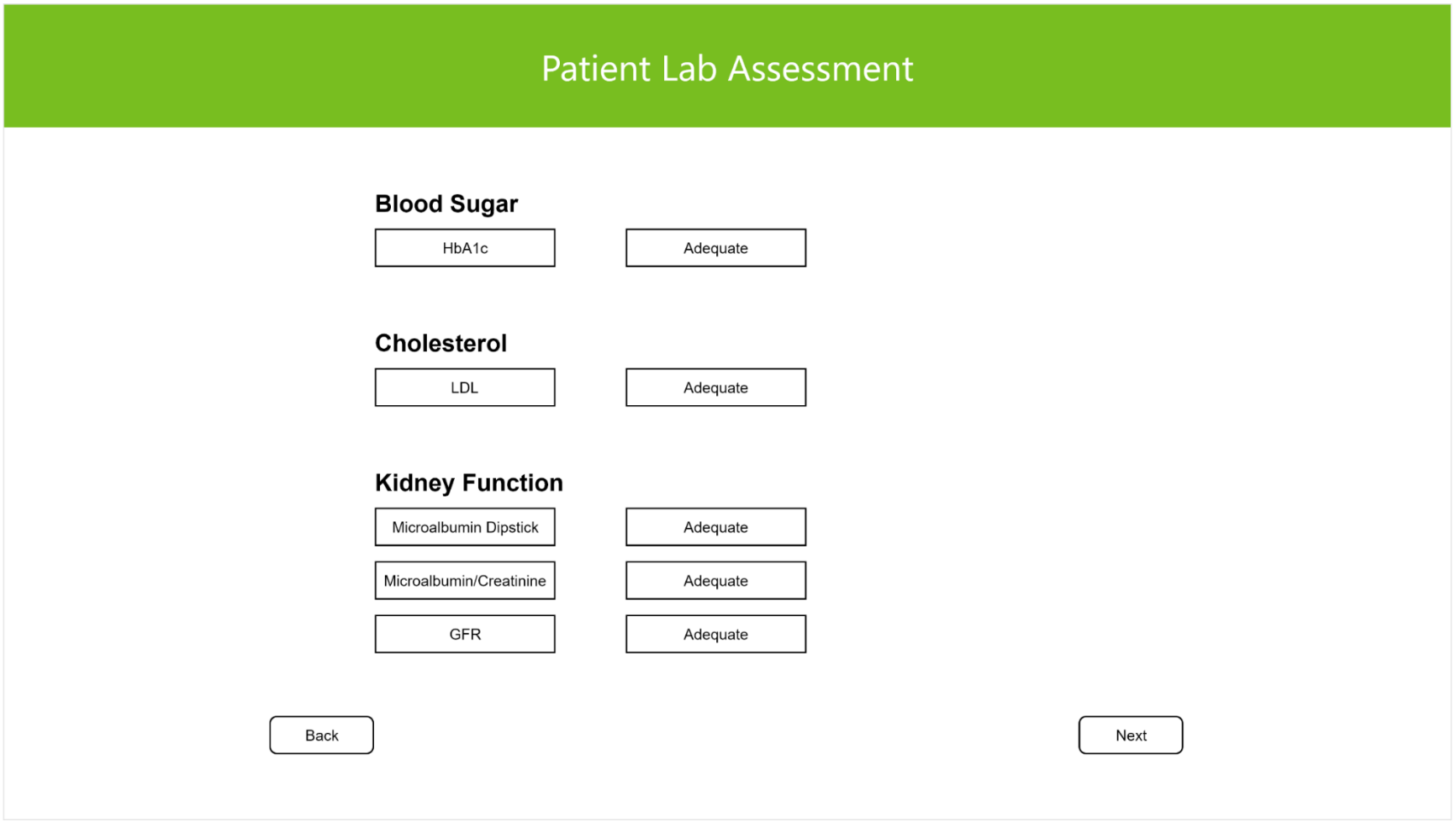

Figure 23 Patient lab assessment page

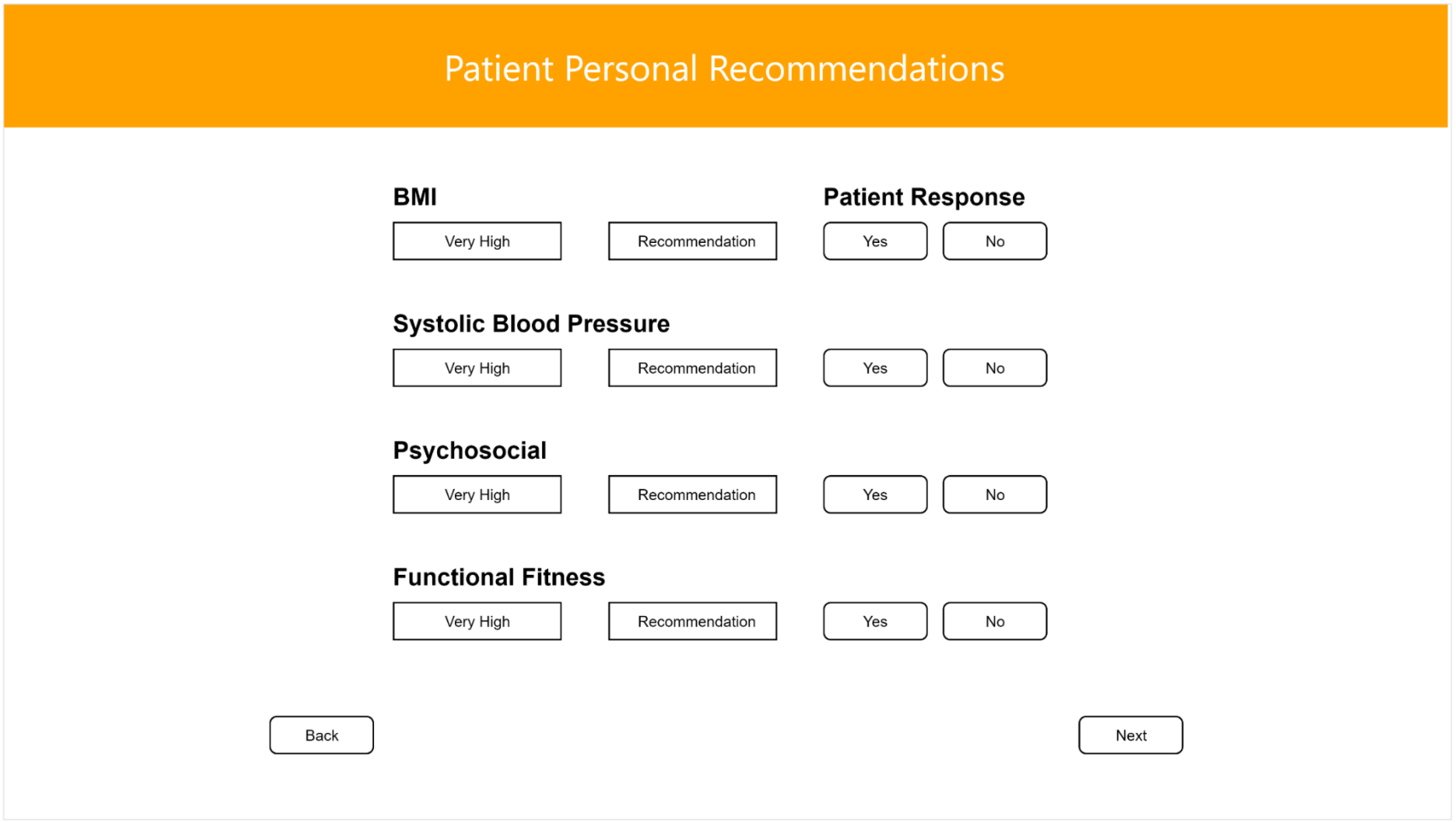

Figure 24 Patient personal recommendations page

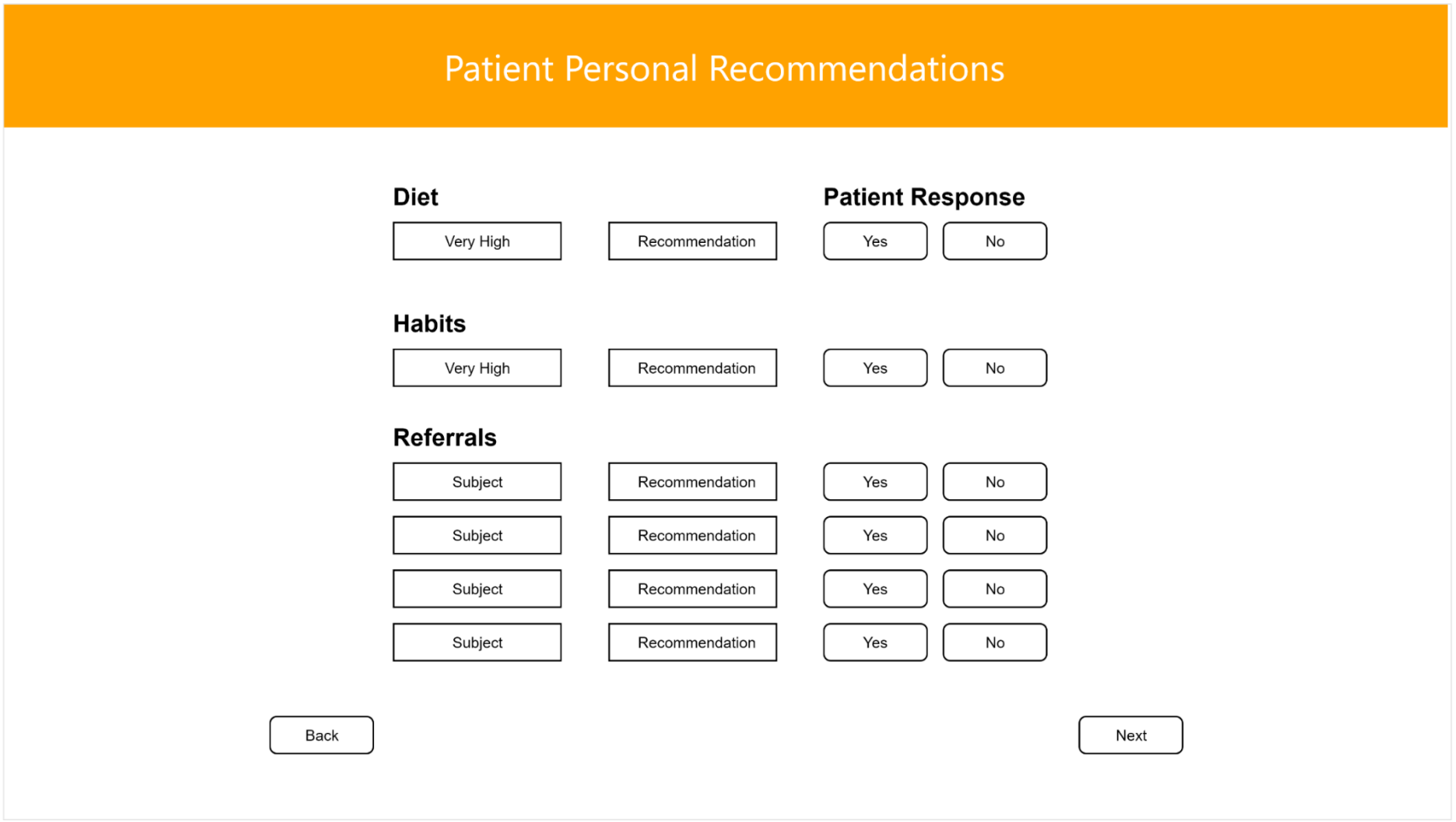

Figure 25 Patient personal recommendations page continued

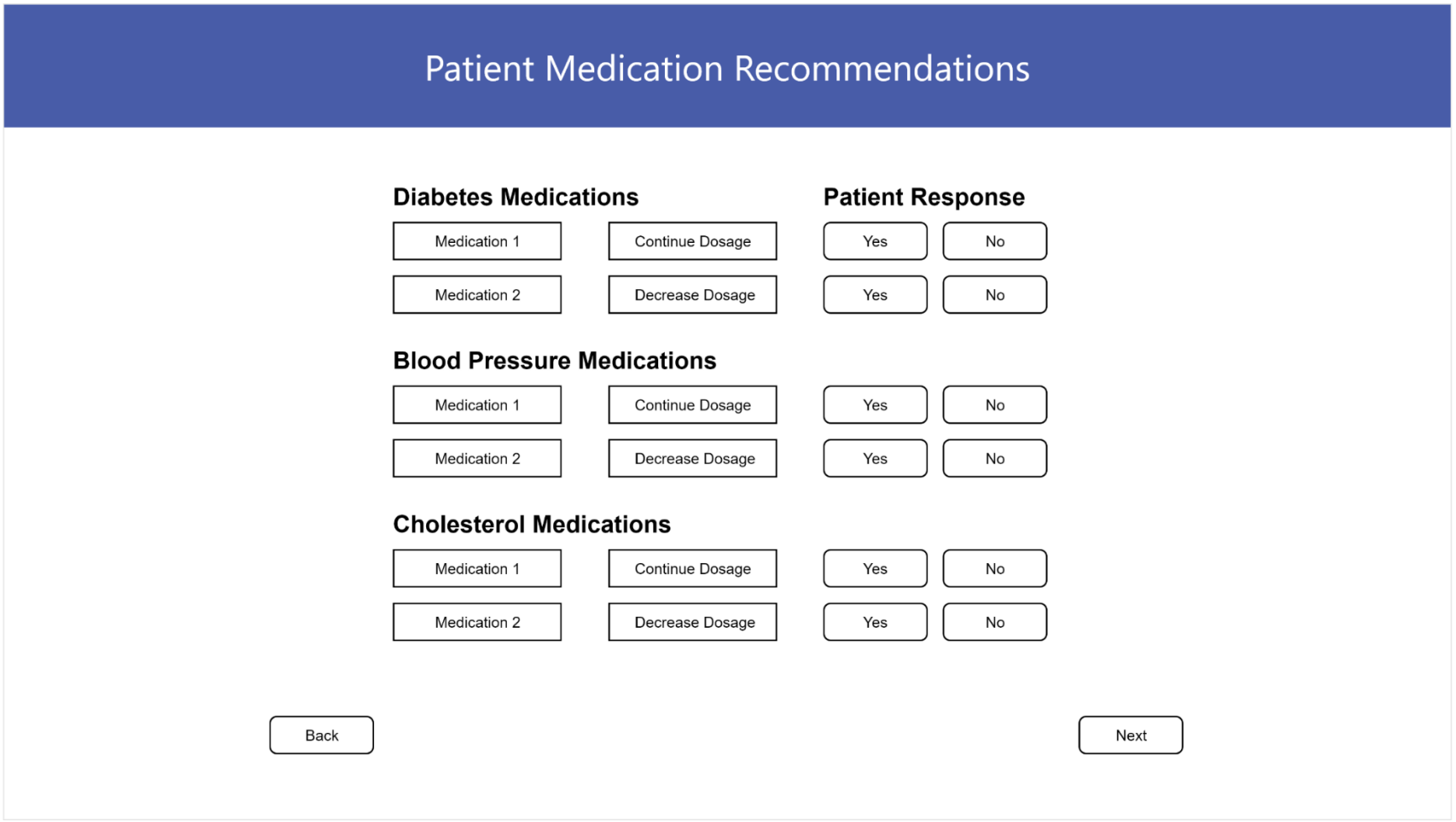

Figure 26 Patient medication recommendations page

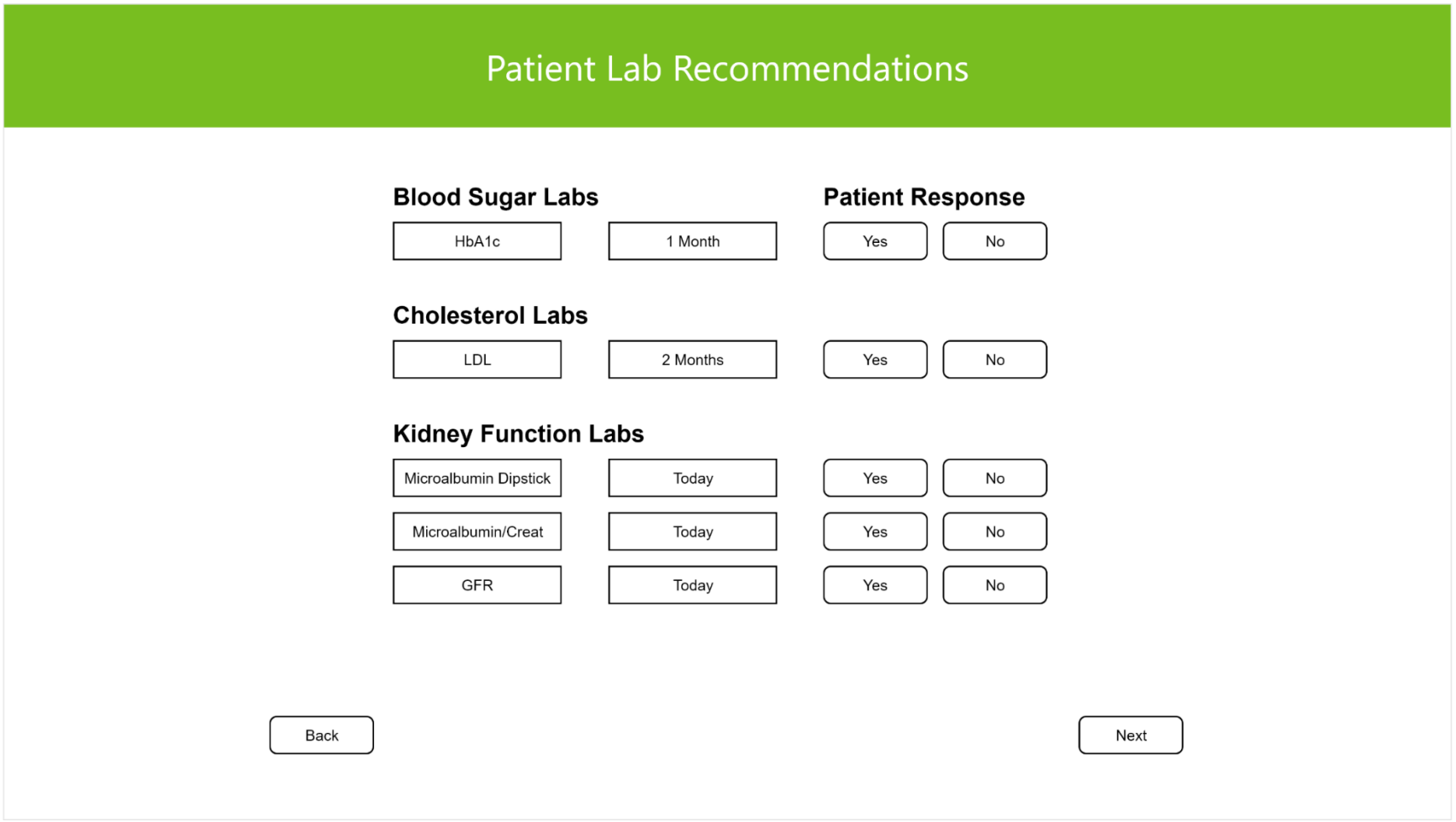

Figure 27 Patient lab recommendations page

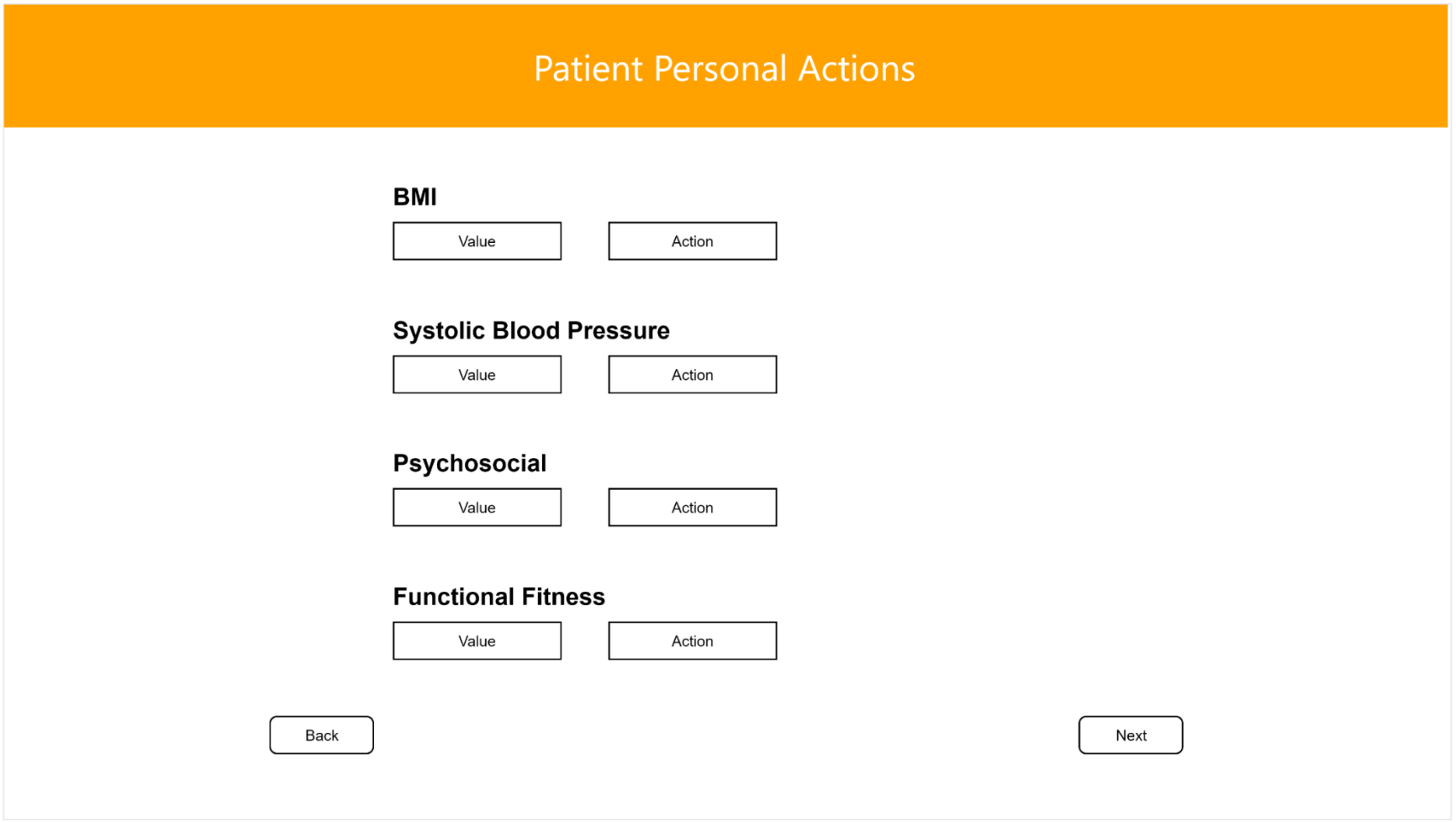

Figure 28 Patient personal actions page

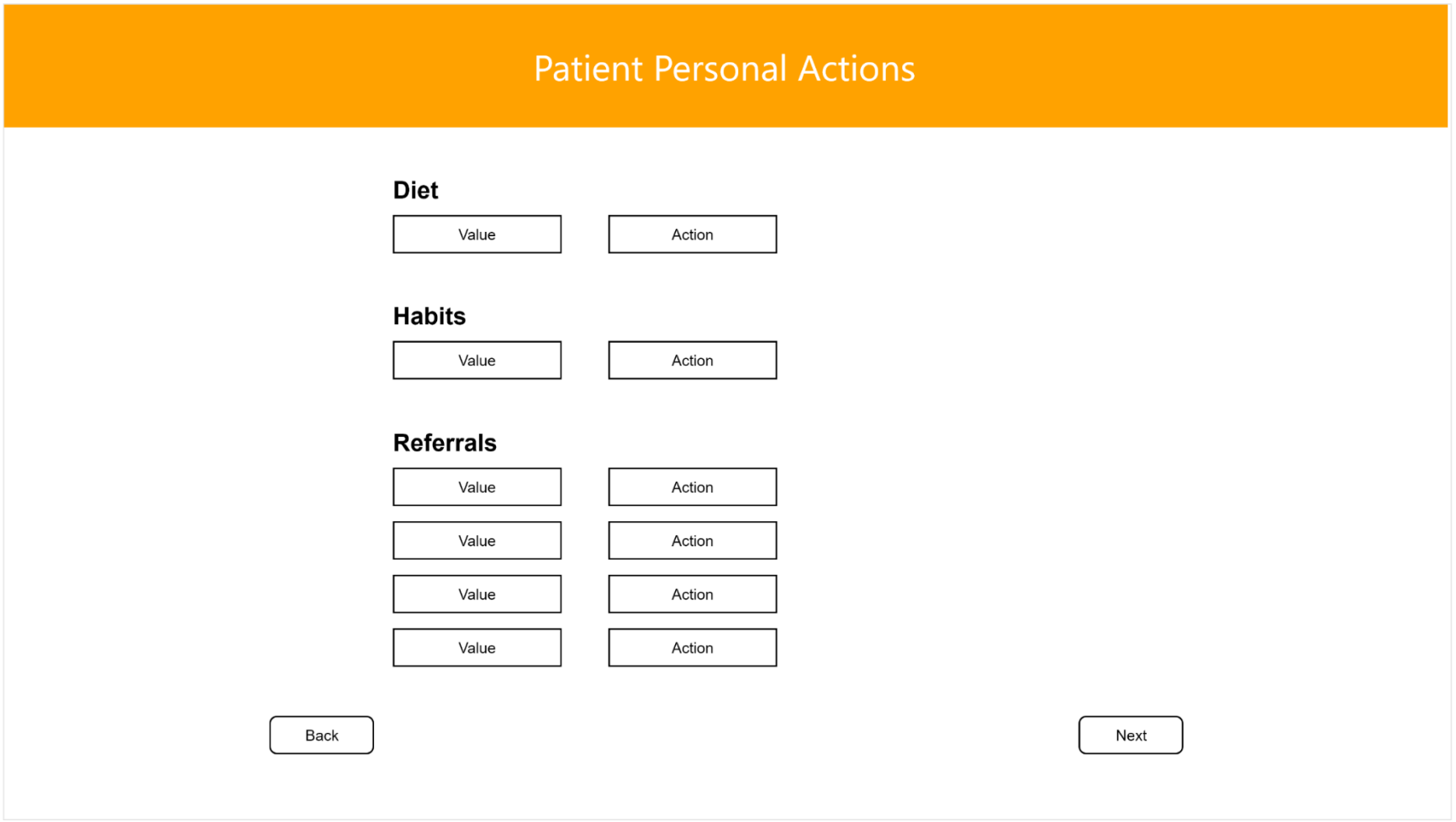

Figure 29 Patient personal actions page continued

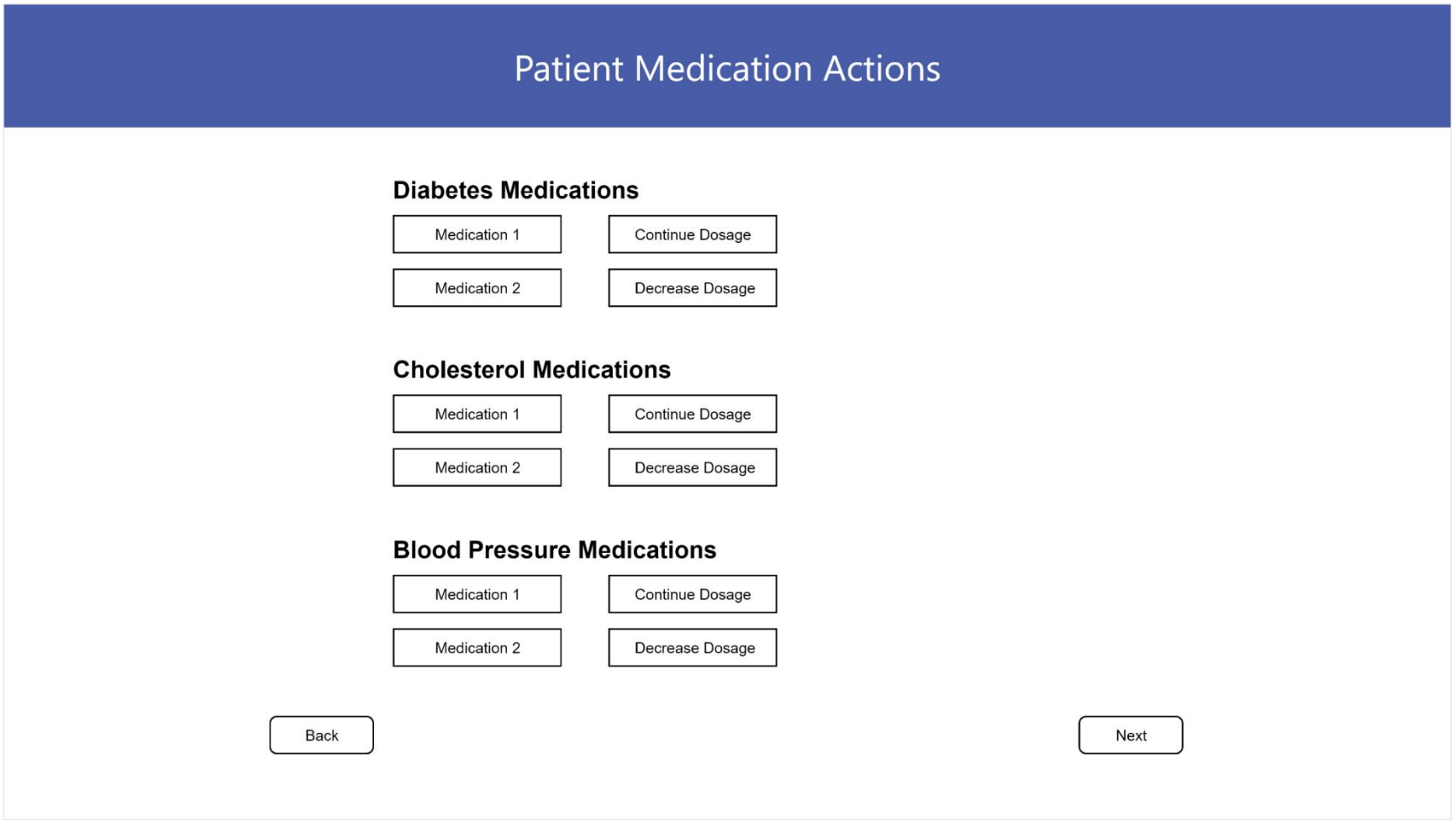

Figure 30 Patient medication actions page

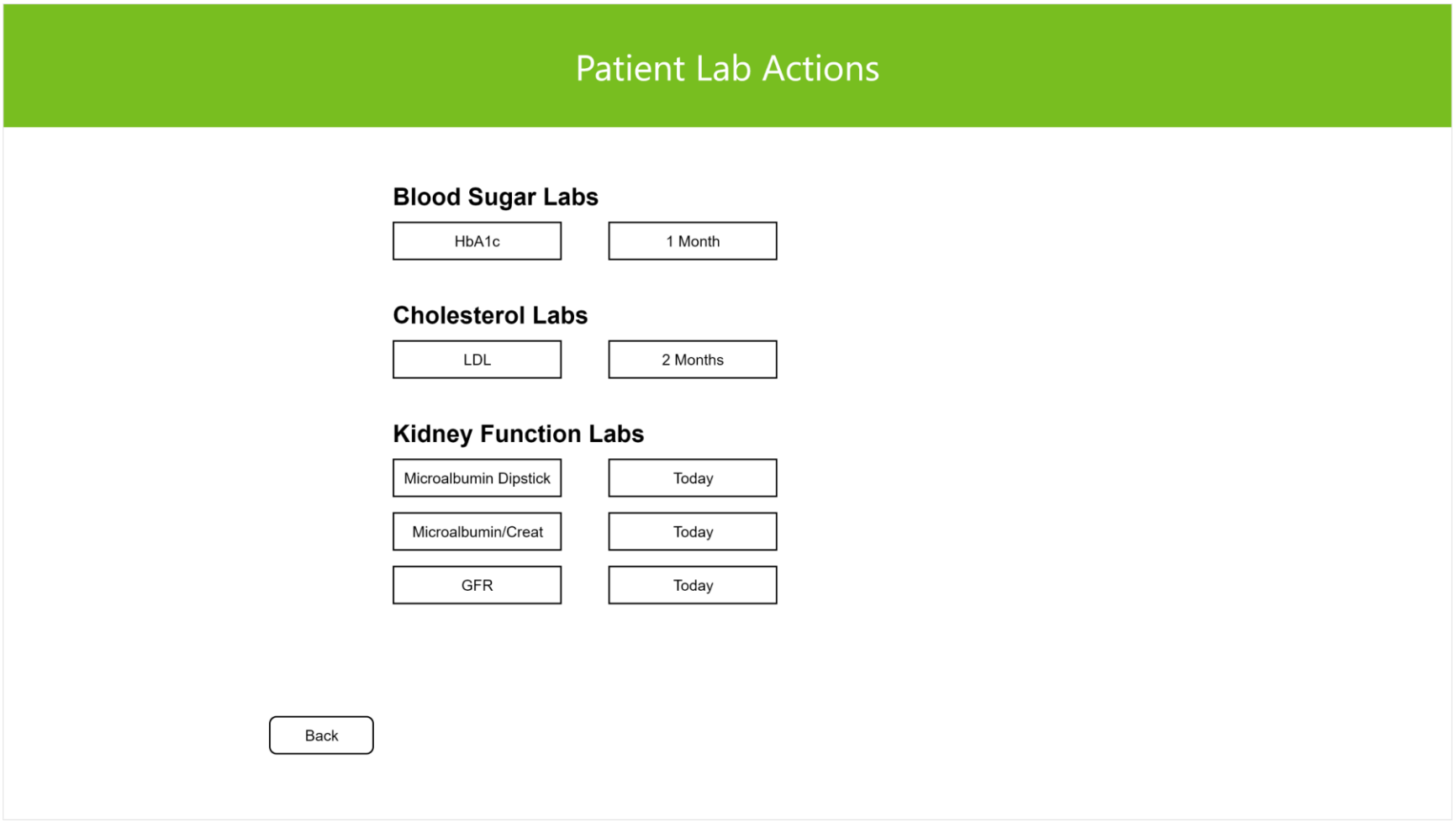

Figure 31 Patient lab actions page