Title
Clinical Inertia in Management of Type 2 Diabetes Among Different Ethnic Groups

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IRVINE

Clinical Inertia in Management of Type 2 Diabetes Among Different Ethnic Groups

THESIS

submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in Biomedical and Translational Science

by

Sophia Yang

Thesis Committee:
Professor John Billimek, PhD, Chair
Professor Sherrie H. Kaplan, PhD
Professor Andrew Reikes, MD

2017
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Clinical Inertia in Management of Type 2 Diabetes Among Different Ethnic Groups

By

Sophia Yang

Master Of Science in Biomedical and Translational Science

University of California, Irvine, 2017

Professor John Billimek, Chair

Clinical inertia is defined as a delay in intensifying medical treatment despite the fact that patients have not met clinical goals for control of their medical conditions. Little is known about clinical inertia among racial/ethnic minority groups with type 2 diabetes mellitus. This analysis uses three constructs—Access, Beliefs/Preferences, Communication—represented by the proxies of insurance status, race/ethnicity minority status, and English language fluency status—to evaluate the effect of race/ethnicity on clinical inertia in diabetes outcomes. This study was an observational retrospective review of a database of outpatient medical visits from January 2012 to December 2014. The database was organized to analyze clinical inertia for these patients, which was defined as the time to medication intensification after having a HbA1C greater than the target HbA1C≥8%. English-fluent patients were found to have greater odds of receiving medication intensification during a given time period, supporting the idea that non-English-fluent patients may be disproportionately affected by clinical inertia.
CHAPTER 1: INTRODUCTION AND BACKGROUND

This introductory chapter will give a brief overview of type 2 diabetes mellitus, the known ethnic/racial disparities in diabetes outcomes, and discuss guidelines for medical management. The chapter begins with a discussion of glycemic control as a key component of management and prevention of complications from diabetes. Then, clinical inertia, or the failure to adequately intensify a medication regimen when indicated, is discussed as a contributor to poor glycemic control. A review of the literature relating to clinical inertia in type 2 diabetes, including its prevalence, importance, and contributing factors, will follow. Finally, a conceptual model discussing how clinical inertia may contribute to ethnic/racial disparities in diabetes management and outcomes will be introduced.

Overview of Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM, or “diabetes”) is a growing national and international problem. According to the 2014 National Diabetes Statistics Report, based on 2012 information, more than 20 million people in the United States (9.3%) have T2DM. Of these, 27.8% are unaware that they even have diabetes. The cost of diabetes is high, accounting for an estimated $245 billion annually in medical cost and lost work and wages in the US.

Minorities, specifically black, Hispanic, American Indian/Alaska Native adults were two times as likely to have diabetes, compared to non-Hispanic whites (see Table 1).¹
Table 1. Age-Adjusted Percentage Of People Aged 20 Years Or Older With Diagnosed Diabetes, By Race/Ethnicity, United States, 2010-2012

<table>
<thead>
<tr>
<th>Race/Ethnic Group</th>
<th>Age-Adjusted Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Hispanic Whites</td>
<td>7.6</td>
</tr>
<tr>
<td>Asian-Americans</td>
<td>9.0</td>
</tr>
<tr>
<td>Hispanics</td>
<td>12.8</td>
</tr>
<tr>
<td>Non-Hispanic Blacks</td>
<td>13.2</td>
</tr>
<tr>
<td>American Indians/Alaska Natives</td>
<td>15.9</td>
</tr>
</tbody>
</table>


To understand how to improve disparities in outcomes, it is necessary to know how to properly treat diabetes.

**Appropriate Medical Management of Type 2 Diabetes**

The American Diabetes Association has long provided guidelines for evidence-based treatment for type 2 diabetes (see Figure 1). The first intervention is always behavioral and lifestyle modifications. Initial pharmacologic therapy is metformin monotherapy, unless the patient has a contraindication. If monotherapy at maximal tolerated dose does not achieve or maintain target HbA1C over 3 months, a second medication should be added from one of the following classes: sulfonylureas, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) agonists, or basal insulin. The specific drug choice depends on patient circumstances. Other choices can include meglitinides, alpha-glucosidase inhibitors, and pramlintide. If the patient has a HbA1C level greater than 9%, initial therapy should be with a dual regimen to more quickly achieve control. Similarly, if after 3 months of dual therapy the goal still has not been reached, a third drug from the above classes should be added. If triple therapy is unsuccessful, injectable insulin is the next step.²
Figure 1. Guidelines from the American Diabetes Association

<table>
<thead>
<tr>
<th>Healthy eating, weight control, increased physical activity, and diabetes education</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy*</td>
<td>High</td>
<td>Low</td>
<td>Neutral/loss</td>
<td>Low</td>
<td>Neutral/loss</td>
<td>Low</td>
</tr>
<tr>
<td>Hypoglycemia risk</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>Neutral/loss</td>
<td>High</td>
</tr>
<tr>
<td>Weight</td>
<td>Gain</td>
<td>Gain</td>
<td>Gain</td>
<td>Gain</td>
<td>Gain</td>
<td>Gain</td>
</tr>
<tr>
<td>Side effects</td>
<td>Edema, HF, and fractures</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Costs*</td>
<td>High</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after about 3 mo of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference; choice dependent on a variety of patient- and disease-specific factors):

<table>
<thead>
<tr>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
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</thead>
<tbody>
<tr>
<td>SU</td>
<td>TZD</td>
<td>DPP-4 inhibitor</td>
<td>SGLT2 inhibitor</td>
<td>GLP-1 receptor agonist</td>
<td>Insulin (basal)</td>
</tr>
<tr>
<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>SGLT2 inhibitor</td>
<td>or</td>
<td>GLP-1 receptor agonist</td>
<td>or</td>
<td>Insulin</td>
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<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>Insulin</td>
<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after about 3 mo of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference; choice dependent on a variety of patient- and disease-specific factors):

<table>
<thead>
<tr>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
<th>Metformin</th>
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</thead>
<tbody>
<tr>
<td>SU +TZD</td>
<td>SU +TZD</td>
<td>SU +TZD</td>
<td>SU +TZD</td>
<td></td>
</tr>
<tr>
<td>or DPP-4 inhibitor</td>
<td>or DPP-4 inhibitor</td>
<td>or DPP-4 inhibitor</td>
<td>or DPP-4 inhibitor</td>
<td></td>
</tr>
<tr>
<td>or SGLT2 inhibitor</td>
<td>or SGLT2 inhibitor</td>
<td>or SGLT2 inhibitor</td>
<td>or SGLT2 inhibitor</td>
<td></td>
</tr>
<tr>
<td>or GLP-1 receptor agonist</td>
<td>or GLP-1 receptor agonist</td>
<td>or GLP-1 receptor agonist</td>
<td>or GLP-1 receptor agonist</td>
<td></td>
</tr>
<tr>
<td>or Insulin</td>
<td>or Insulin</td>
<td>or Insulin</td>
<td>or Insulin</td>
<td></td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after about 3 mo of triple therapy and patient on oral combination therapy, move to injectables; if patient receiving GLP-1 receptor agonist, add basal insulin; if patient receiving optimally titrated basal insulin, add GLP-1 receptor agonist or mealtime insulin. In refractory patients, consider adding TZD or SGLT2 inhibitor:

<table>
<thead>
<tr>
<th>Metformin</th>
<th>Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal insulin + Mealtime insulin</td>
<td>GLP-1 receptor agonist</td>
</tr>
</tbody>
</table>

Figure 1 reproduced from “Diagnosis and Management of Diabetes: Synopsis of the 2016 American Diabetes Association Standards of Medical Care in Diabetes”³

Given the burden of diabetes, it is important to understand what factors influence achievement, or lack thereof, of glycemic goals. Diabetes is a chronic illness that requires a significant amount of patient self-management in concert with physician intervention and management. It is also a progressive disease—as part of the pathophysiology of diabetes, beta-
cells become increasingly dysfunctional, meaning that with time glycemic control becomes harder to achieve. In addition, many of the oral anti-diabetic medication eventually lose their effectiveness and thus it is necessary to add additional oral medications and/or insulin. There are no medications that can address the underlying pathophysiologic defects of diabetes. The very nature of diabetes makes it a difficult disease to manage. However, the key to managing diabetes is maintaining glycemic control.

The Importance of Glycemic Control

Patients are typically diagnosed with type 2 diabetes when their HbA1C exceeds 6.5%. In terms of management, type 2 diabetes is typically considered “well-controlled” if the A1C remains below 7%, and this is a goal that physicians counsel their patients to achieve. There are also many patients for whom this goal is inappropriate or impractical, such as those with limited life expectancy, advanced complications, or advanced age. For adults who are frail or have limited life expectancy, American Diabetes Association guidelines suggest that a less strict target, such as 8%, may be more appropriate. It is also important to consider that older adults are more likely to be prone to severe hypoglycemia, and this should also be taken into account when deciding glycemic goals.

The main impetus for achieving glycemic control is to prevent the development of microvascular complications, such as neuropathy, nephropathy, and retinopathy. Diabetes is also associated with increased cardiovascular risk and complications like heart disease, amputation, and stroke. There are four major trials that have shaped knowledge about appropriate HbA1C goals in treatment of type 2 diabetes. The United Kingdom Prospective Diabetes Study (UKPDS) compared patients with newly diagnosed T2DM receiving intensive treatment with sulfonylurea or insulin to those receiving conventional treatment—diet with drugs added if necessary—for
over 10 years. The goal of intensive treatment was to achieve a fasting plasma glucose below 6 mmol/L, compared to 15 mmol/L for patients in the conventional treatment group. They found that intensive control significantly decreased the risk of microvascular complications. There was a non-significant trend toward improvement in the rate of myocardial infarction (MI), but otherwise no benefit for macrovascular complications. Intensive treatment increased the risk of hypoglycemia and weight gain. At the time, UKPDS provided proof that intensive glycemic control could contribute to reducing microvascular complications. However, the effect on macrovascular outcomes was unclear. The other trials that followed would further complicate the interpretation of the effect of intensive treatment on glycemic control.

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial was originally designed to determine whether intensive therapy targeting lowering HbA1C levels to “normal” levels of 6% would reduce cardiovascular risk in patients with a history of diabetes and cardiovascular disease. Participants were randomly assigned to either “intensive glucose-lowering therapy” with a target HbA1C<6% or “standard glucose-lowering therapy” with a target HbA1C of 7-7.5%. However, the trial discontinued the intensive therapy arm due to findings of higher mortality, though the exact cause is unclear. The authors concluded that intensive therapy with the goal of achieving a HbA1C<6% for patients with advanced type 2 diabetes and high risk of cardiovascular disease could not be recommended.

The Action in Diabetes and Vascular disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial assigned over 10,000 patients with T2DM to have either standard (defined by local guidelines) or intensive glycemic control with a goal HbA1C<6.5%. This was conducted in an older population (at least 55 years) that had been previously diagnosed with T2DM, with a history of macrovascular/microvascular disease, or a risk factor for vascular
disease. This study found a significant decrease in microvascular events, particularly nephropathy, but not macrovascular events. More intensive patients were hospitalized and had severe hypoglycemia more frequently, but there were no significant increase in mortality, compared to the ACCORD trial.9

The Veterans Affairs Diabetes Trial (VADT) involved 1791 military veterans with poor response to therapy for T2DM, randomly assigned to intensive or standard management. The goal of the intensive therapy was an absolute reduction of 1.5%, compared to standard management. The study found no significant differences in macrovascular or microvascular complications, except for a reduction in the progression of albuminuria.10

The results of the UKPDS, ACCORD, ADVANCE, and VADT trials provided evidence for reduction of microvascular complications with intensive glucose control. The effect on macrovascular events was less clear. However, the 10-year follow-up of the UKPDS patients added some clarifying evidence. After the trial concluded, patients were no longer required to maintain their previously randomized therapies, and between group differences in HbA1c were lost after the first year. The 10-year follow-up of the UKPDS patients found that even though glycemic differences between groups rapidly extinguished, patients from the intensive treatment arm continued to benefit from significant reductions in microvascular disease risk and any diabetes related endpoint (defined as “sudden death, death from hyperglycemia or hypoglycemia, fatal or nonfatal myocardial infarction, angina, heart failure, fatal or nonfatal stroke, renal failure, amputation, vitreous hemorrhage, retinal photocoagulation, blindness in one eye, or cataract extraction”).11

In addition, the post-trial follow-up revealed that over time there were risk reductions for diabetes-related death, myocardial infarction, and death from any cause in the intensive treatment
arm. It is important to note that the UKPDS patients were newly diagnosed and had fewer patients with a history of macrovascular disease—overall, low-risk compared to the ADVANCE and ACCORD patients. Regardless, data from this study provides some evidence suggesting the importance of lowering HbA1C for the purpose of reducing macrovascular complications. This study also supports the importance of early and maintained intensive control of type 2 diabetes, to prevent long-term complications.

Furthermore, a post-hoc analysis of the ADVANCE trial found that baseline patient-specific characteristics could be used to quantify how particular patients would be affected by intensive or standard management in terms of macrovascular events and hypoglycemic episodes. The study model predicted that majority of the patients would have had an estimated net benefit from intensive glycemic control if positive and negative effects were assumed to have equal importance, with the caveat that treatment needs to be tailored to individual patients. This analysis also showed that intensive glycemic control was not associated with increased risk of death. A meta-analysis of randomized control trials found that intensive glycemic control had significant cardiovascular benefit. Overall, the evidence from these landmark trials and further analyses suggests that intensive glycemic control can prevent and/or delay the progression of both micro- and macro-vascular outcomes. For individual patients, the specific glycemic goal may vary, but regardless patients should be receiving appropriate treatment to reach their goal for glycemic control.

**Clinical Inertia**

*Definition and Prevalence*

The primary method for patients to reach glycemic control is via the provision of anti-diabetic medications and/or insulin on an appropriate timeline. Clinical inertia is defined as a
delay in increasing treatment—or “medication intensification”—despite the fact that patients have not met clinical goals for control of their medical conditions (see Figure 2). A patient is typically already on a baseline regimen of diabetic medications to control their disease. However, this regimen may eventually prove to be inadequate for their needs, resulting in an initial elevated HbA1C, when it exceeds a target HbA1C. The target HbA1C is the point below which a patient’s diabetes is considered controlled. According to guidelines, when this target is exceeded, there should be medication intensification. If there is a delay to medication intensification, this is known as clinic inertia. Additionally, there is time to target, or the time that it takes a patient to achieve the goal HbA1C.

**Figure 2. Visual Representation of Clinical Inertia and Time to Target**

A review of electronic health record showed clinical inertia, defined as no medication intervention within 6 months of a baseline elevated A1C (defined as HbA1C >7%, >7.5%, and >8%) in 38%, 31%, 28% of patients, respectively. In a study of 10,000 patients with diabetes already being treated with basal insulin and/or oral anti-hyperglycemics, only 30.9% of patients received intensification when clinically indicated—i.e. had a HbA1C ≥7.5% —and had a median time of 3.7 years until intensification. A retrospective population study of over 100,000 UK patients with newly diagnosed T2DM
found 46% of patients received medication intensification during follow-up, but 26% of patients with HbA1C >7% did not receive intensified treatment within 2 years after diagnosis.\textsuperscript{15} A retrospective UK cohort study of over 80,000 individuals with a history of type 2 diabetes, found that median time from first elevated HbA1C to intensification, defined as an additional oral anti-diabetic medication or insulin, could range from 1.6 to 7.2 years. This range depended on the investigator selected elevated target HbA1C—ranging from HbA1C of 7-8%—and the number of oral anti-diabetic medications at study baseline.\textsuperscript{16} A US retrospective health care claims study found that despite suboptimal glycemic control, only 38% of subjects already on metformin monotherapy had evidence of an additional medication to the primary monotherapy of metformin in their 2.5 years of data collection. Of these individuals, 35.7% received medication intensification within 1 year of evidence of suboptimal glycemic control i.e. HbA1C>7%. Of these, 65.9% of treatment additions occurred within the first month of the index lab result.\textsuperscript{17}

In the treatment of diabetes, clinical inertia is of particular relevance due to the specific benefits of early and intensive glycemic control.

\textit{Clinical Inertia and Time to Achieving Target After Initial Elevated HbA1C}

When clinical inertia is decreased, time to achieving target goal after an initial elevated HbA1C is decreased. A large population study showed that patients who underwent an early intervention (defined as within 6 months of the initial elevated HbA1C) were compared to later intervention (after 6 months, or never), patients who were underwent early intervention were more likely to have their HbA1C at goal.\textsuperscript{5} A simulation using an Archimedes model showed that a cohort of patients that had appropriate medication intensification was able to achieve a below target A1C within a year, whereas the delayed group remained above target.\textsuperscript{18} If medication
intensification occurred within 3 months, there was a 26% higher odds of achieving a HbA1C<7% compared to 10 months.¹⁹

A large retrospective population cohort study found that patients who were able to achieve goal HbA1C<6.5% and/or had a large reduction within 6 months had a lower risk of cardiovascular events and mortality.²⁰ A large retrospective study of electronic medical records with a target value of 7.5% found that earlier medication intensification was associated with better glycemic status compared to those with later medication intensification. A simulation was able to show that early medication intensification resulted in a substantial reduction in the risk of myocardial infarction, stroke, death from coronary heart disease, heart failure, and amputation at both 5 and 20 years.¹⁸ A retrospective cohort study of over 100,000 patients found that a 1-year delay in medication intensification in those with newly diagnosed diabetes and poor glycemic control increased the risks of heart failure, stroke, and overall macrovascular events even in patients without a history of cardiovascular disease.¹⁵ The longer an elevated HbA1C persists, the more glycemic burden—the amount of time with uncontrolled hyperglycemia—a patient accrues.⁴

In addition to the direct patient benefit, there may be economic benefit to early initiation of insulin, in terms of life expectancy and quality-adjusted life expectancy. Also, early insulin initiation could reduce or prevent diabetes complications, reducing associated management costs.²¹ Increased clinical inertia is associated with longer time to reach target HbA1C, putting patients at risk for carrying a higher glycemic burden and increasing their risk of complications.

A study within the Kaiser Permanente Northwest system examined the delay in adding insulin to patients with inadequate control on sulfonylurea and metformin. They found that 18.1% of their study population did not reach the goal of HbA1C 8% while 24.3% reached and
maintained the goal. Patients who never reached the goal were more likely to need to add insulin, but had accrued two times the glycemic burden compared to patients who had reached but failed to maintain the goal. Despite elevated HbA1C, on average, patients remained solely on sulfonylurea and metformin for 3 years, sustaining an equivalent of 32 months of HbA1C levels of 9%. In addition, less than half of these patients were receiving the maximum dose of either medication.22

The literature suggests that clinical inertia is common and at all levels of treatment. Given the accumulating body of literature on the benefits of early initiation of appropriate medications, it is necessary to examine contributors to clinical inertia. Beyond the progressive nature of the disease, there are multiple variables contributing to inadequate management.5

**Clinical Inertia and Minority Groups**

A study of National Health and Nutrition Examination Survey (NHANES) from 2007-2010 found that only 52.5% of people with diabetes were able to achieve an HbA1C of <7.0%. When analyzed by ethnicity, 52.9% white patients, 52.6% black patients, and 47.3% of Hispanic patients were able to achieve an A1C of <7.0%.23 A later study analyzed the same data and found that disparities among these groups worsened when analyzed using individualized glycemic goals for each group.24

Although clinical inertia is relatively prevalent, there is little research on disparities in clinical inertia among minority patients with diabetes. Much of the current literature makes little or no comment about race/ethnicity. If it is mentioned, it is as part of the risk adjustment—acknowledged, but not a major factor of the analysis. A recent study mentions Hispanic patients as part of the study sample characteristics, but actually had no Hispanic patients in their sample.17 Most recent studies do not address disparities.14,16,19,22 Disparities in outcomes for minorities with
type 2 diabetes are well documented,\textsuperscript{25} as is clinical inertia.\textsuperscript{5,14-17,26,16,27} What is not clear is how these two intersect, and what effect, if any, does clinical inertia have on diabetes outcomes for minorities.

**Factors Associated with and Contributing to Clinical Inertia**

Major factors that contribute to clinical inertia can be organized into three constructs—access to care, beliefs/preferences, and communication. Each of these constructs has factors that can further be subdivided into three categories: patient, physician, and system.

*Access to Care*

**Patient Factors**

The construct of access to care is defined as the ability to receive medical care at appropriate times to manage medical conditions. One of the major factors affecting access to care is financial status and insurance status, which are closely intertwined, given that many uninsured individuals have lower incomes.\textsuperscript{28} In addition, uninsured individuals are disproportionately Hispanic or black, such that minority patients are less likely to have access to care.\textsuperscript{28}

**System Factors**

Many system factors contribute to access to care. The current health system does not support smooth information sharing among caregivers and fellow professionals, making coordination and continuity of care challenging. There may be no active outreach to patients and a lack of coordinated follow-up due to insufficient staff support. Rather than a comprehensive, preventative health approach, treatment is more reactive.\textsuperscript{29}

The average outpatient office visit with a primary care provider is about 20 minutes.\textsuperscript{30} In that span of time, there are many demands on the provider’s time, and it may be insufficient for
them to adequately address a patient’s diabetes.\textsuperscript{31} While this may also be categorized as a physician factor, it is considered to be system factor over which the physician may truly have limited control.

While lack of insurance is a patient factor, is also a system factor in a country where 28.5 million people remain uninsured.\textsuperscript{32,33} Patients with low socioeconomic status, no insurance, and/or limited insurance lack access to medical care and may be less likely to seek care, attend medical appointments, and affording prescriptions.\textsuperscript{31,32}

**Insurance Status as a Proxy for Access to Care**

There are many factors that affect an individual’s ability to access care. However, financial status certainly plays a large role. If more specific financial data is unavailable, given the close relationship between financial status, the ability to afford insurance, and access to healthcare, insurance status would be an acceptable proxy for access to care.

**Beliefs/Preferences**

**Physician Factors**

Physicians’ attitudes and beliefs regarding diabetes management can influence patient attitudes. A lack of knowledge about the current guidelines or the importance of intensive glycemic control can prevent a physician from appropriately intensifying therapy when necessary. They may be reluctant to move beyond monotherapy in patients that are asymptomatic, or may not be confident about prescribing newer therapies.\textsuperscript{34} Physicians could overestimate the care given, be hindered by too brief clinic visits for a complicated disease, be reluctant to increase the complexity of the medical regimen, be concerned about side effects, and not want to increase medications for those who are not already adherent. They may not be clear with patients about realistic treatment goals and the steps needed to achieve these goals.\textsuperscript{27,29} In a
physician survey about why their older patients did not receive anti-glycemic medications, there was a desire to try lifestyle modifications, a perception that glycemia was only mildly elevated. The physicians surveyed indicated the mean HbA1C for initiating therapy was 7%, however more than half of the patients already had HbA1C above this level. For these patients, physicians tended to defer to patient concerns, including reluctance to take more medications, concern about side effects, and increased financial burden. Other “soft” reasons may include concerns about whether results can be generalized to individual patients, a concern about side effects and complicated medication regimens, and sensitivity to patients’ concerns. Unsurprisingly, a good patient-provider relationship and effective communication can positively influence diabetes management.

### Patient Factors

Patient perspectives and beliefs affect their perception of the importance of self-management. A qualitative exploratory study (n=60) of adults with hypertension and diabetes found that 48% of participants expected to discontinue diabetes medication in six or fewer years by lifestyle improvement; 85% participants thought they would not need additional diabetes medications in the future; 65% thought that their diabetes could be cured. This discrepancy could be a reason why patients may resist medication intensification.

While certainly not all beliefs are tied to culture, patients’ cultural backgrounds strongly influence their beliefs and attitudes. In Hispanic patients, cultural beliefs may be even stronger than financial barriers. Of particular interest are cultural perspectives on insulin. This may include the ideas that insulin causes diabetes complications, that starting insulin implies failure or is a personal punishment, a fear of injections, and/or insufficient family/social support for beginning insulin. While these perspectives are certainly not unique or true of all Hispanic
patients, these negative culturally-bound beliefs may play a significant role in patients’ reluctance to initiate insulin. Nichols et al, in a population that was eligible for insulin, describes “psychological insulin resistance,” a commonly observed reluctance for patients and providers to begin insulin therapy. However, they also note that many of the patients for whom insulin may have been indicated were also not receiving maximum doses of their oral medication.

Even when patients do recognize the need for medication, they may be concerned about adverse medication side effects and complex regimens, particular if they have other chronic conditions and medications. Patients with diabetes often have other co-morbid conditions and medications, which has been shown to reduce medication adherence. A lack of adherence to a medication regimen is detrimental for management of conditions such as diabetes. While medication adherence is a multifactorial, complex issue with significant dedicated research, and a barrier to reaching target goals, it is separate from clinical inertia. Clinical inertia is specifically referring to the failure of the provider to act and prescribe appropriate medications, rather than the patient’s lack of compliance with said medications. Medication adherence can certainly lengthen the time to reach the target goal, but it is a separate entity from clinical inertia.

However, Schmittdiel and colleagues conducted a cross-sectional assessment comparing the relative contributions of patient lack of adherence and clinician clinical inertia to patient difficulty achieving target HbA1C values. They found that of those patients with HbA1C above goal (>7%), 23% had poor medication adherence. Of the remaining individuals, there was no evidence of difficulty with medication adherence, but 47% had still not received appropriate treatment intensification, while the remaining 32% did receive appropriate intensification. The authors were unable to distinguish whether any patients who had received intensification were
also poorly adherent to previous medication regimens. They do note that when deciding whether or not to intensify treatment, it is important to identify whether patients have difficulty with medication adherence so as to counsel them appropriately.\textsuperscript{26} Grant and colleagues found that patients with the highest level of adherence to previously prescribed medications were more likely to have subsequent medication intensification, indicating that patient behavior could potentially influence physician actions.\textsuperscript{27} Thus, if a physician believes that a patient already has difficulty with medication adherence, the physician may be less likely to intensify medications, leading to greater clinical inertia.

\textbf{Race/Ethnicity as a Proxy for Belief/Preferences}

Physician and patient beliefs/preferences likely play a role in clinical inertia. There is a broad range of factors that could be associated with belief/preferences. However, these may not be easily recorded in a medical record. While it is imprecise, race/ethnicity may be an acceptable proxy for patient preferences, especially in the context of culturally bound beliefs regarding diabetes and insulin, as a potential source of significant opposition to medication intensification and thus, greater clinical inertia.

\textbf{Communication}

\textbf{Patient and Provider Factors}

Poor patient-provider communication has been linked to poor outcomes, such as decreased medication adherence and worsened glycemic control.\textsuperscript{40} While there are certainly many different components to communication, a major component is language concordance. Patients with limited English proficiency (LEP)/non-English speaking patients have decreased access to medical care, receive poorer care, and have difficulty communicating with their physician.\textsuperscript{41} Poor health literacy and/or lack of English proficiency may hinder their
understanding of disease, or the importance of medication and lifestyle modifications. Patients may not be concerned about delays in intensification, perhaps due to the belief that medications would worsen, rather than prevent, complications. They may not even be concerned about developing complications, especially if currently asymptomatic.\textsuperscript{34,36,42}

Especially given the incorrect nature of some of the beliefs some patients have about diabetes and medication, it is important for providers to have realistic conversations with patients about the natural history of their disease, the rarity of remission, and to otherwise manage their expectations.\textsuperscript{37} This challenging conversation would only be more difficult if patients speak little to no English, or if there is no interpreter available.

\textbf{System}

Ideally, trained, professional interpreters should provide medical interpretation. However, in many situations informal interpreters such as friends and family or bilingual medical personnel are used. Informal interpreters are not ideal, as they are prone to error, unlikely to know proper terminology, and/or may inhibit discussion of sensitive subjects. While telephone or video interpretation is often available, providers typically prefer to have an in-person interpreter.\textsuperscript{43} In addition to preference, there are often issues with telephone or video such as difficulty hearing, the need to set up equipment, technical issues, or loss of eye contact.\textsuperscript{44}

\textbf{Language as a Proxy for Communication}

While communication is very broad and can involve many factors, language and communication are closely intertwined. For this study, patients who can speak English serves as a proxy to indicate that the patient is able to communicate fluently with the provider. In the extreme case, a patient who does not speak English at all would result in a situation where little to no communication can occur. In addition, language is a quantifiable factor. Of course, this is a
very rough correlation, since miscommunications can still occur among native speakers, and communication skills require more than just language fluency. However, inability to understand each other certainly would not improve communication.

**Conceptual Model**

Patient, provider, and system variables are hypothesized to map roughly to the three constructs of communication, access, and beliefs/preferences, which are further represented by their respective proxies of preferred language, insurance status, and race/ethnicity (see Figure 3). Disparities in these factors may cluster in minorities, who are less likely to speak English, have access to insurance, and are more likely to have culturally-bound beliefs. These constructs—patients who do not speak English, are uninsured, and are racial/ethnic minorities—are hypothesized to correlate with greater clinical inertia and longer time to achieve goals. As previously discussed, greater clinical inertia and longer time to achieve goals are both associated with worse long-term outcomes.
Hypotheses

The specific aim of this project is to determine whether there is a difference in clinical inertia and time to target among racial/ethnic groups. The study will test the following hypotheses:

1. Negative, culturally-bound beliefs about medications, communication barriers, and poor access to care are associated with greater clinical inertia.

1a. Racial/ethnic minority status, as a proxy for negative, culturally-bound beliefs about medications, is associated with greater clinical inertia.

1b. Non-English-fluent status, as a proxy for communication barriers, is associated with greater clinical inertia.
1c. Uninsured status, as a proxy for poor access to care, is associated with greater clinical inertia.

2. Negative, culturally-bound beliefs about medications, communication barriers, and poor access to care are associated with greater time to target.

2a. Racial/ethnic minority status, as a proxy for negative, culturally-bound beliefs about medications, is associated with greater time to target.

2b. Non-English-fluent status, as a proxy for communication barriers, is associated with greater time to target.

2c. Uninsured status, as a proxy for poor access to care, is associated with greater time to target.

In the subsequent chapters, these hypotheses will be analyzed using methods that will be discussed in Chapter 2. The results will be presented in Chapter 3, and interpreted and discussed in Chapter 4.
CHAPTER 2: METHODS

This chapter will include discussion of the data source and provenance, definitions of the study measures, and description of the statistical methods employed in the study.

Data Source

This was an observational retrospective review of a database of 5282 patients who had at least two medical visits from January 1, 2012 to December 31, 2014 at six outpatient clinics affiliated with an academic medical center. The de-identified dataset was received from Health Informatics and Research Computing through the Honest Broker process. The Honest Broker process allows for preparation of de-identified data so IRB approval was not required; instead, written determination of non-human subject research was obtained. Originally, there were three de-identified datasets, linked by an arbitrary study identifier. The datasets were organized and merged using SPSS version 21 (IBM Corporation, Armonk, NY).

Because the merged dataset included all medication orders and lab results any given patient had received, the dataset was reviewed and all lab results and medications unrelated to diabetes were excluded resulting in 4735 patients. This database was then linked to demographics and HbA1C lab data by a study identifier. Demographic information included age, gender, marital status, preferred language, ethnicity, and insurance status. Next, an additional 1033 patients without established baseline diabetes medication therapy was excluded. Finally, 1990 patients who never had a HbA1C lab result ≥ 8, the selected target value, were also excluded, resulting in a final population of 1712 patients (see Figure 4).
Figure 4. Consort Diagram

n=4735

Excluded those who had never received baseline diabetes medication order (n=1033)

n=1712

Excluded those who had never had a HbA1C lab result above 8 (n=1990)

n=5282

Excluded those who did not have diabetes medication order or HbA1C lab result (n=547)
Study Measures

Sociodemographic Factors

Sociodemographic factors, including gender, race/ethnicity, preferred language, and insurance status, were obtained from patients’ medical records. Gender was dichotomized into male and female. Race/ethnicity was coded and categorized into 3 groups—white, Hispanic, and other. Preferred language, which was abstracted from the medical record as the patient’s primary language, was dichotomized into whether a patient was fluent in English or not. To determine those who were uninsured, patients that were listed as purely “self-pay” were coded as uninsured, and patients with any form of insurance were coded as insured.

Beliefs/Preferences

Beliefs/preferences was operationalized as race/ethnicity. Race/ethnicity categories were “American Indian/Eskimo,” “Asian,” “Asian/Pacific,” “Black,” “Other,” “Pacific/Hawaiian”, Unknown, and “White.” There was a separate variable for “Hispanic,” “Not Hispanic,” and unknown. Patients who were identified as White and Non-Hispanic were designated as white. Patients who were identified as White and Hispanic were designated as Hispanic. All other patients were grouped into “other ethnicity.”

Communication

Communication was operationalized as English fluency. Patient’s primary language was part of the dataset abstracted from the medical record. Those whose primary language was English were coded as “English-fluent.” All other languages were coded as “Non-English-fluent.” The most common other language was Spanish.
Access

Access was operationalized as insurance status. Primary and secondary insurance were abstracted from the medical record. If insurance was noted to be self-pay, with no other insurance, were identified as uninsured. All others were grouped as insured.

Target Values

The appropriate “target” laboratory value that requires increased medication was established. In the literature, typical target goals for diabetes have been chosen as 7, 7.5, and/or 8%. Given that the average age of this study population is 60 years old, a less stringent target point of 8% was chosen in order to capture a wider sample. This would also capture those who may have had a more relaxed glycemic goal, yet are still not receiving appropriate intensification. By design, all patients in the sample had a HbA1C ≥8% at some point and so would be considered eligible for medication intensification.

Initial Elevated HbA1C

The first HbA1C result above the target value, i.e. ≥8%, after a baseline regimen was established.

Clinical Inertia

Clinical inertia was operationalized as a failure to intensify the diabetes medication regimen following the occurrence of the initial elevated HbA1C. For the statistical analysis, clinical inertia was defined as time to medication intensification. This was the number of days from when a patient exceeds the target value with an initial elevated HbA1C to when they receive medication intensification.

Appropriate medication intensification was defined as 1) an increase in the dosage or frequency of an oral diabetic medication or 2) the addition of a new diabetes medication class
after an initial elevated HbA1C. Table 2 lists common classes of diabetes medication that could be prescribed for a patient. If a patient was prescribed basal or prandial insulin, this was considered to be a permanent addition to their medical record, even if no further prescriptions were documented. If a patient was receiving prandial insulin prior to initial elevated HbA1C, these patients were excluded from the analyses.

To evaluate medication intensification, a baseline medication regimen needs to be established first. To account for this, if an elevated HbA1C lab value was recorded, but with no preceding diabetic medication orders, this was discarded until at least one diabetic medication order was captured—“the baseline regimen.”

**Table 2: Common Classes of Diabetes Medication**

<table>
<thead>
<tr>
<th>Class</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td></td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td></td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td></td>
</tr>
<tr>
<td>Dipeptidyl peptidase 4 inhibitors</td>
<td></td>
</tr>
<tr>
<td>Meglitinides</td>
<td></td>
</tr>
<tr>
<td>SGLT-2 inhibitors</td>
<td></td>
</tr>
<tr>
<td>Amylin analogs</td>
<td></td>
</tr>
<tr>
<td>Bromocriptine*</td>
<td></td>
</tr>
<tr>
<td>Bile Acid Sequestrants*</td>
<td></td>
</tr>
<tr>
<td>GLP1 receptor agonist</td>
<td></td>
</tr>
<tr>
<td>Basal Insulin</td>
<td></td>
</tr>
<tr>
<td>Prandial Insulin</td>
<td></td>
</tr>
<tr>
<td>Combination medication</td>
<td></td>
</tr>
</tbody>
</table>

*Bile acid sequestrants and bromocriptine were excluded from the analysis since it was difficult to evaluate whether these medications were used for the purpose of diabetes management or to manage other conditions.

**Time to Target**

Time to target was the number of days between the initial elevated HbA1C and the next HbA1C result that was $\leq 8\%$, the target HbA1C.
Some patients reached target “spontaneously” e.g. they did not receive any intensification of their baseline medications, yet their next HbA1C was lower than 8%; others reached target after receiving medication intensification. Though there may have been fluctuations and multiple points at which a patient had a lab result that exceeded the target of 8%, only the first of these events were considered for this analysis. Once a patient reached target after an initial elevated HbA1C, no further medication intensifications or elevated HbA1C were included in the analysis.

**Statistical Analysis**

Patient characteristics were compared using the Chi-squared test for dichotomous variables. One-way ANOVA, or Welch test when appropriate, was used to compare continuous variables.

Hypothesis testing for time to medication intensification and time to target was performed using survival analyses. Kaplan-Meier curves were generated to show the cumulative probability of each outcome (medication intensification and target) within the three racial/ethnic groups and compared using the Log-Rank test.

For survival analysis of time to medication intensification, the event was defined as medication intensification. Patients were censored if they achieved target goal or if they had neither achieved the target nor had received medication intensification by their last observed contact with the study clinic—either the date of the last lab order or the date of the last medication order, whichever was later. This calculation took into account all lab and medication orders, not just those related to diabetes to provide the most accurate picture of the last recorded patient contact.

For time to target, the event was defined as the date of the next target HbA1C after initial elevated HbA1C. Patients were considered to be censored on either the date of the last lab order
or the date of the last medication order, whichever was later. This calculation took into account all lab and medication orders, not just those related to diabetes to provide the most accurate picture of the last recorded patient contact.

Multivariable Cox regression models were generated to compare the three groups, adjusting for the covariates gender, age, ethnicity, insurance status, English-fluent, and initial elevated HbA1C. The following chapter will describe the results obtained from these analyses.
CHAPTER 3: RESULTS

After excluding patients that did not fit the criteria, the final dataset included a sample of 1712 patients. Table 3 presents the overall demographics of this sample. The majority of these patients were female (57.2%), older (mean age (SD)=60 years (12.5)), Hispanic (57.9%), insured (85.4%), Spanish-fluent (51%), and their average initial elevated HbA1C was 9.6%. Of the 1712 patients, 1301 (76%) received some form of medication intensification after initial elevated HbA1C (see Table 3) and 43.2% were able to achieve target goal after initial elevated HbA1C.

Table 3. Overall Patient Demographics

<table>
<thead>
<tr>
<th>Total</th>
<th>N=1712</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong>a</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>978 (57.2%)</td>
</tr>
<tr>
<td>Male</td>
<td>733 (42.8%)</td>
</tr>
<tr>
<td><strong>Age</strong>b</td>
<td>60 (12.5)</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong>a</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>457 (26.7%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>990 (57.8%)</td>
</tr>
<tr>
<td>Asianc</td>
<td>41 (2.4%)</td>
</tr>
<tr>
<td>Blackc</td>
<td>45 (2.6%)</td>
</tr>
<tr>
<td>Other ethnicitiesc</td>
<td>179 (10.5%)</td>
</tr>
<tr>
<td><strong>Insurance Status</strong>a</td>
<td></td>
</tr>
<tr>
<td>Insured</td>
<td>1463 (85.5%)</td>
</tr>
<tr>
<td>Uninsured</td>
<td>249 (14.5%)</td>
</tr>
<tr>
<td><strong>Primary Language</strong>a</td>
<td></td>
</tr>
<tr>
<td>English</td>
<td>800 (47%)</td>
</tr>
<tr>
<td>Spanish</td>
<td>878 (51%)</td>
</tr>
<tr>
<td>Vietnamesed</td>
<td>15 (0.9%)</td>
</tr>
<tr>
<td>Othersd</td>
<td>19 (1.1%)</td>
</tr>
<tr>
<td><strong>Initial Elevated HbA1C</strong>b</td>
<td>9.6 (1.6)</td>
</tr>
</tbody>
</table>

a. Table entries - dichotomous variables - reported as n, %  
b. Table entries - continuous variables - reported as mean (SD)  
c. For the purpose of analysis, these 3 groups were consolidated into 1 group and will be henceforth be referred to collectively as “other ethnicities”  
d. For the purpose of analysis, Vietnamese and other languages were small enough samples that they were combined with Spanish and referred to as “other languages.”

Demographics among racial/ethnic groups were compared, and shown to be significantly different among the three groups. Hispanic patients were predominantly female, younger,
uninsured, and non-English-fluent. Patients of other ethnicities had a significantly lower initial elevated HbA1C. Because these covariates were significantly different among groups, they were all included in the Cox Regression analyses.

Table 4. Demographics by Race/Ethnicity

<table>
<thead>
<tr>
<th></th>
<th>White n=457</th>
<th>Hispanic n=990</th>
<th>Other n=265</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>218 (48%)</td>
<td>621 (63%)</td>
<td>140 (53%)</td>
<td>&lt;0.001&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Male</td>
<td>239 (52%)</td>
<td>369 (37%)</td>
<td>125 (47%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>60.3 (12.8)</td>
<td>58.7 (11.7)</td>
<td>63.9 (14.0)</td>
<td>&lt;0.001&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Insurance status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insured</td>
<td>405 (89%)</td>
<td>815 (82%)</td>
<td>240 (91%)</td>
<td>&lt;0.001&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Uninsured</td>
<td>51 (11%)</td>
<td>175 (18%)</td>
<td>23 (9%)</td>
<td></td>
</tr>
<tr>
<td><strong>English-fluent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>359 (79%)</td>
<td>226 (23%)</td>
<td>215 (81%)</td>
<td>&lt;0.001&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>No</td>
<td>96 (21%)</td>
<td>764 (77%)</td>
<td>50 (19%)</td>
<td></td>
</tr>
<tr>
<td><strong>Initial Elevated HbA1C</strong></td>
<td>9.6 (1.6)</td>
<td>9.7 (1.6)</td>
<td>9.2 (1.4)</td>
<td>&lt;0.001&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>e</sup> Table entries - dichotomous variables - reported as n, %; p-value calculated with Chi-square test

<sup>f</sup> Table entries - continuous variables - reported as mean (SD); p-value calculated with Welch test in lieu of one-way ANOVA due to statistically significant difference in homogeneity of variance among the three groups

Figure 5 presents the Kaplan-Meier curve that illustrates that the racial/ethnic groups did not differ in time to medication intensification.
Figure 5. Survival Analysis For Time To Medication Intensification Among Different Racial/Ethnic Groups (N=1712)

![Kaplan-Meier curves for measuring time until medication intensification](image)

*Race/Ethnicity*
- White
- Hispanic
- Other
- White-censored
- Hispanic-censored
- Other-censored

The curves are not significantly different as calculated by the log-rank test ($p=0.299$).

Table 5 presents the median time to medication intensification for each racial/ethnic group, as well as overall.
Table 5. Unadjusted Median Time to Medication Intensification (N=1712)

<table>
<thead>
<tr>
<th></th>
<th>White n=457</th>
<th>Hispanic n=990</th>
<th>Other n=265</th>
<th>Overall N=1712</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unadjusted Median Time to Medication Intensification, days</strong>a</td>
<td>89.0 (66.7-111.2)</td>
<td>109.0 (96.2-121.8)</td>
<td>130.0 (98.0-162.0)</td>
<td>106.0 (96.0-116.0)</td>
</tr>
</tbody>
</table>

h. Table entries reported as median (95% CI)

Table 6 presents the percentage of each ethnic group that had received medication intensification by the 6 month and 12 month mark.

Table 6. Medication Intensification by 6 and 12 months (N=1712)

<table>
<thead>
<tr>
<th></th>
<th>White n=457</th>
<th>Hispanic n=990</th>
<th>Other n=265</th>
<th>Overall N=1712</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% Intensified at 6 months</strong></td>
<td>64.7%</td>
<td>61.3%</td>
<td>61.7%</td>
<td>62.3%</td>
</tr>
<tr>
<td><strong>% Intensified at 12 months</strong></td>
<td>77.8%</td>
<td>78.5%</td>
<td>74.9%</td>
<td>77.7%</td>
</tr>
</tbody>
</table>

The unadjusted Cox Regression Model showed no significant differences among the three racial/ethnic groups with regards to time to medication intensification. When adjusting for covariates, non-English-fluent and initial elevated HbA1C were significant. The odds of intensification occurring for a non-English-fluent patient, compared to an English-fluent patient, within a given time interval are 15.2% lower [HR (95% CI) = 0.84 (0.73-0.98)]. For every additional unit increase in initial elevated HbA1C, the odds of intensification within a given time interval are 6.2% higher [HR (95% CI) = 1.06 (1.03-1.10)].
Table 7. Unadjusted and Adjusted Hazard Ratios for Time to Intensification (N=1712)

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted HR (95% CI)</th>
<th>p-value (unadjusted)</th>
<th>Adjusted HR (95% CI)</th>
<th>p-value (adjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>Ref.</td>
<td></td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.91 (0.80-1.04)</td>
<td>0.146</td>
<td>0.97 (0.83-1.14)</td>
<td>0.706</td>
</tr>
<tr>
<td>Other</td>
<td>0.89 (0.74-1.08)</td>
<td>0.236</td>
<td>0.90 (0.74-1.09)</td>
<td>0.276</td>
</tr>
<tr>
<td><strong>English-fluent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>-</td>
<td></td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td>0.84 (0.73-0.98)</td>
<td>0.021</td>
</tr>
<tr>
<td><strong>Initial elevated HbA1C</strong></td>
<td></td>
<td></td>
<td>1.06 (1.03-1.10)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>-</td>
<td></td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td>1.10 (0.97-1.22)</td>
<td>0.129</td>
</tr>
<tr>
<td><strong>Insurance Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insured</td>
<td>-</td>
<td></td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>-</td>
<td></td>
<td>1.00 (0.85-1.18)</td>
<td>0.977</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td>1.00 (0.99-1.00)</td>
<td>0.677</td>
</tr>
</tbody>
</table>

1. Ref. refers to the reference group.

Figure 6 presents the Kaplan-Meier curve that illustrates that racial/ethic groups differed significantly in the time to target, with patients of other racial/ethnic groups achieving targets fastest, and Hispanic patients reaching targets slowest.
Figure 6. Survival Analysis For Time To Target Among Different Racial/Ethnic Groups (N=1712)

Table 8 presents the median time to target for each racial/ethnic group, as well as overall.

Table 8. Unadjusted Median Time to Target by Race/Ethnicity (N=1712)

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Unadjusted Median Time to Target, days&lt;sup&gt;k&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>591.0 (461.6-720.4)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>695.0 (615.6-774.4)</td>
</tr>
<tr>
<td>Other</td>
<td>410.0 (288.5-531.5)</td>
</tr>
<tr>
<td>Overall</td>
<td>644.0 (577.7-710.3)</td>
</tr>
</tbody>
</table>

k. Table entries reported as median (95% CI)

Table 9 presents the percentage of each ethnic group that had reached achieved target by
the 6 month and 12 month mark.

Table 9. Achieved Target HbA1C ≤8% by 6 and 12 Months (N=1712)

<table>
<thead>
<tr>
<th></th>
<th>White n=457</th>
<th>Hispanic n=990</th>
<th>Other n=265</th>
<th>Overall N=1712</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Achieved Target at 6 months</td>
<td>23.9%</td>
<td>21.3%</td>
<td>28.5%</td>
<td>23.1%</td>
</tr>
<tr>
<td>% Achieved Target at 12 months</td>
<td>38.5%</td>
<td>35.9%</td>
<td>47.2%</td>
<td>38.3%</td>
</tr>
</tbody>
</table>

The unadjusted Cox Regression Model showed a non-significant trend for patients of other ethnicities to recover faster than white patients. Age and initial elevated HbA1C were significant covariates. For every additional unit increase in HbA1C, the odds of achieving target within a given interval of time are 31.9% lower. [HR (95% CI) = 0.68 (0.64-0.73)]. With each additional year of age, the expected odds of achieving target within a given interval of time increase by 1.8% [HR (95% CI) = 1.02 (1.01-1.02)]. The odds of reaching target within a given interval of time were 16.1% lower for non-English-fluent patients compared to English-fluent patients [HR (95% CI) = 0.84 (0.70-1.01)]—however, this was a non-significant trend.
Access, Beliefs/Preferences, and Communication and their proxies as contributors to clinical inertia and time to target were examined in a sample of adult patients with type 2 diabetes. These patients were predominantly female, older, Hispanic, insured, and Spanish fluent. In general, it did not appear that Access and Beliefs/Preferences were associated with clinical inertia, however, Communication, represented by language, was a significant factor, as was initial elevated HbA1C. Access, Beliefs/Preferences, and Communication were also not found to be associated with time to target, though initial elevated HbA1C and age were significant. These results will be discussed in the context of the conceptual model and extant literature in the final chapter.
CHAPTER 4: DISCUSSION

This final chapter will include a summary and discussion of the study findings in the context of the previously introduced conceptual model. The proposed conceptual model describes the potential links between three constructs associated with race/ethnicity (Access, Beliefs/Preferences, Communication) and clinical inertia and time to target. The purpose is to examine clinical inertia as a potential contributor to disparities in minority outcomes in diabetes. Evidence for an association between these racial/ethnicity-linked constructs and clinical inertia may inform future areas of study of clinical inertia as a contributor to racial disparities. The strengths and limitations of this study will be discussed in order to put the results in context. The implications of the findings and conclusions will be presented.

Clinical Inertia

The median time to intensification was 106 days, or approximately 3 months. The recommendation is to intensify medication regimen if goals are not met after 3 months, though some will relax this to 6 months. Overall, nearly 77% of patients received some type of medication intensification by 12 months. While this is promising, 23% of patients were not receiving appropriate treatment at that time and were experiencing clinical inertia. To further investigate clinical inertia and its potential contribution to disparities, three constructs associated with race/ethnicity—Access, Beliefs/Preferences, and Communication—were examined.

In the analysis comparing clinical inertia, or time to medication intensification, across race/ethnicity (a proxy for Beliefs/Preferences) there were no statistically significant differences among the three groups. This was an unexpected result, given that there are well-documented disparities in diabetes among minority groups. Admittedly, race/ethnicity is a very crude proxy
for beliefs and preferences, as each group in this study is very heterogeneous and there was no mechanism to assess patient perspectives.

There may have also been an element missing in the way race/ethnicity is coded into the electronic medical record. Patients are asked about their race/ethnicity and preferred language on check-in, but perhaps intake workers make assumptions or mistakes as they enter the data. Given that there are 96 non-Hispanic white patients whose primary language is Spanish, this does indicate there may be some mistakes in the coding. It is possible that Spanish-fluent patients are more likely to be coded correctly as Hispanic, compared to a English-fluent Hispanic patient who may be incorrectly coded as white based on their language skills and presentation. In addition there may be patients with Hispanic appearing last names who identify as a different race/ethnicity. Race/ethnicity is broad, imprecise, and more prone to error and incorrect assumptions. The imprecise coding may obscure a potential race/ethnicity effect on clinical inertia. A more precise study would focus on direct assessment of beliefs and preferences with regards to medication intensification.

English-fluent status, a proxy for communication barriers, was significantly associated with greater clinical inertia. This is unsurprising as poor communication would inhibit the patient-physician relationship, and poor patient-provider communication has been linked to worse outcomes, such as decreased medication adherence and poor glycemic control. Poor communication would make it difficult to achieve medication intensification and would contribute to clinical inertia. This is a novel finding, as there is no previous discussion comparing clinical inertia between English-fluent and non-English-fluent patients. Poor communication, as it contributes to clinical inertia, may be a significant factor in diabetes disparities in minority groups, who are more likely to have difficulty communicating with providers.
Measuring communication with English fluency may also capture the influence of other factors that are associated with language proficiency, like acculturation. There is evidence that language fluency represents acculturation such that an individual’s fluency is directly correlated to the degree of acculturation.\textsuperscript{45} Acculturation is the psychosocial integration, culturally and socially, into a new group—in this case, it would be the minority groups into the dominant white group.\textsuperscript{45} Individuals who are less fluent in English and thus less acculturated may hold stronger culturally-bound beliefs about medication. Patients with these beliefs may be reluctant or refuse to intensify medication regimen.\textsuperscript{31,38} They may also be non-adherent to medications, and non-adherence is a factor that influences providers to be less likely to intensify medication regimens.\textsuperscript{31} As a result, their physicians would not order a more intensive regimen, so this would appear to be clinical inertia driven by culturally-bound beliefs. Previously, race/ethnicity was chosen as the proxy for Beliefs/Preferences. However, given the association of language with acculturation, beliefs, and their effect on clinical inertia, language may actually be a more suitable proxy to capture the influence of Beliefs/Preferences on clinical inertia. Compared to race/ethnicity, which has room for ambiguity, language may be less ambiguous when witnessed—that is, a Spanish-fluent patient is more likely to be Hispanic, whereas an English-fluent patient could be Hispanic, white, or of another ethnicity. As a result, the language effect on clinical inertia as related to Beliefs/Preferences and acculturation may be more easily detected than the race/ethnicity effect.

Access was the third major construct and was assessed with insurance status as the proxy. There was no association between Access (insurance status) and clinical inertia. A possible reason for this finding is that even though it was possible to identify those who are insured versus uninsured, not all insurances are equal. Even though 89\% of the patients were insured, a
number of patients may have Medi-Cal, and it is unclear what effect this may have had. Further investigation after stratification of the insurance would be warranted to determine if the type of insurance has an effect on clinical inertia.

Another significant factor was having a higher initial elevated HbA1C. Patients who presented with a higher initial elevated HbA1C had greater odds of receiving medication intensification in a given period of time, compared to those with a lower initial elevated HbA1C. This is consistent with the literature where those with higher initial elevated HbA1C and thus, poorer glycemic control, had greater odds of medication intensification.\textsuperscript{5,14,17} Physicians may feel that treatment is clearly indicated for patients with higher initial elevated HbA1C and may treat these patients more aggressively.

In this analysis, barriers to Communication, captured by the proxy of non-English-fluency, were found to be associated with greater clinical inertia. Access and Beliefs/Preferences were found to be non-significant, possibly due to imprecise coding issues. English-fluency may be better able to capture Beliefs/Preferences, where those who speak English less fluently are less acculturated and thus hold to culturally-bound beliefs. These culturally-bound bound beliefs may be associated with greater clinical inertia. Therefore, the effect of English-fluency on clinical inertia may be explained by a combination of factors, including language barriers impeding patient-provider communication, and negative beliefs about medications that are widely held in Hispanic patients with low acculturation.

**Time to Target**

To further investigate time to target and its potential contribution to disparities, three constructs associated with race/ethnicity were examined. Insurance status, a proxy for Access, Race/Ethnicity, a proxy for Belief/Preferences, and English fluency, a proxy for Communication,
were not significantly associated with time to target. Potential explanations for this will be discussed.

Access was assessed with insurance status as the proxy. As discussed previously, one possibility for why this construct was not significant may be due to the heterogeneity of the insurance pool. The potential effect of separating out the different types of insurance is unclear. It is possible that those patients who are uninsured, yet still come to the medical center for treatment, may be more motivated to take care of their health and thus are able to achieve the target after initial elevation of HbA1C within a similar time frame compared to their insured peers. To further clarify this, it would be best to further stratify insurance status in future studies.

Beliefs/Preferences, via the proxy of race/ethnicity, was not significantly associated with time to target. As discussed previously, there is a possibility for imprecise coding, obscuring potential race/ethnicity effects on time to target. In addition, race/ethnicity is a rough construct for a heterogeneous group, and may have had difficulty capturing the effects of Beliefs/Preferences on time to target.

English-fluent status, a proxy for communication barriers, was not significantly associated with time to target. There was a non-significant trend, which may indicate some evidence for the idea of language barriers contributing to disparities. As discussed, poor communication can inhibit a productive patient-physician relationship, which can impact both clinical inertia and adherence to medication regimen. Both of these can lengthen the time to achieve target.

In the time to target analysis, initial elevated HbA1C was a significant factor. For patients who presented with higher initial elevated HbA1C, the odds of achieving the target HbA1C were lower compared to those who presented with a lower initial elevated HbA1C. This is
unsurprising, as patients who present with a higher initial elevated HbA1C already have more difficulty with glycemic control, resulting in the higher elevation of HbA1C, and may not have been under appropriate care. Even after receiving appropriate care, it may take more time for their HbA1C to return to an appropriate level. A higher elevated HbA1C may also be an indicator for patients who are less adherent to medication regimen, and thus may continue to be less adherent even after medication intensification. This would explain a slower achievement of the target.

There was also a significant association between age and time to achieving target. In the literature, older patients were less likely to receive medication intensification.\textsuperscript{14,15,17} In this model, age was not a significant factor in time to intensification, though it was associated with greater odds of intensification in a given period of time. However, there was a modest but significant effect of age, such that older individuals have greater odds of attaining HbA1C goals in a given period of time.\textsuperscript{23} Perhaps younger patients have a more severe case. Perhaps older patients were better able to manage their medication or may be more motivated to achieve goals. In addition, age was significantly different across the three groups, so there may be another factor modifying the age effect. Further studies will be needed on the effect of age on attaining HbA1C goals.

Finally, the overall median time to target is 644 days, or almost 2 years. This is concerning given that medication intensification occurs relatively early. It is true that even though a patient receives a medication intensification order, it does not necessarily follow that the patient will fill the prescription—non-adherence is a known concern that can contribute to lengthened time to achieving HbA1C targets.\textsuperscript{29,31} It is also possible that the medication was insufficient, and a more aggressive dose should have been given, in order to better control and
reach HbA1C. Studies have also shown that earlier intensification can contribute to increased odds of attaining the target HbA1C, however this was not included in the analysis.\textsuperscript{5,18,19}

The significant factors associated with clinical inertia and time to target have been discussed. However, to guide the interpretation of the findings, it is important to be able to evaluate the quality of the evidence gathered and the data analyzed. Both strengths and weaknesses will be discussed.

**Strengths**

Discussing the strengths of this study will provide an idea of the reliability and generalizability of the results. One of the strengths of this study is the ability to examine physician prescription orders, which can be treated as a proxy for behavior. It is a more direct measure of clinical inertia, which refers specifically to the provider’s inaction—lack of a medication order—when a patient has not met their target goals.

In addition, it is a diverse sample, with patients of Hispanic ethnicity, many non-English speakers, and varied insurance types, which is appropriate as this study was attempting to investigate the effect of racial/ethnic minority status and clinical inertia, a topic that is largely unexplored in the literature. Given that this is a relatively small sample, it would be appropriate to repeat this study with a much larger and more diverse patient population. The Asian and black populations are both groups that were represented in this sample, however the numbers were too small for adequate comparison. This is unfortunate as both are also large minority groups that are significantly affected by type 2 diabetes, and are underrepresented in research.

A generous HbA1C target goal $\leq 8\%$ was deliberately chosen to try to encompass the appropriate target goals of most patients with type 2 diabetes, even those that have more permissive goals due to health, age, or other reasons. An appropriate next step would be to
conduct a sensitivity analysis to determine whether adjusting the target value has any effect on these results. As mentioned earlier, it is common to repeat analyses for different HbA1C target goals. These analyses should be repeated for the more stringent HbA1C target goals of 7% and 7.5%, to ascertain whether race/ethnicity has any effect at stricter targets.

The strengths of this study include the examination of physician behavior by prescription order, a diverse sample of patients, and a generous HbA1C target goal. Clinical inertia is a reflection of physician behavior. A diverse sample of patients is appropriate to attempt to address the effects of race/ethnicity on clinical inertia. A generous HbA1C target goal is best to capture the widest population. However, along with strengths, it is also appropriate to consider the limitations of this study.

Limitations

There were several limitations in the database that may have affected the detection of significant associations in the results. For example, the proxies selected for the constructs are rough and imprecise. Race/ethnicity in particular is a loose factor with significant overlap with other factors and constructs. They are not easily separated into neat boxes.

There are other factors that may have affected the analyses that were not included, whether because they were difficult to measure or were not included in the medical record abstraction. For instance, there is no record of the duration of diabetes, patient’s financial/socioeconomic status, education levels, or BMI. While Charlson Comorbidity Index data was abstracted, it was not included in the analysis, where it may have an effect on clinical inertia and time to target—patient co-morbidities have also been associated with a longer delay in time to medication. The current analysis did not allow us to finely parse the insurance to
stratify between private insurance, Medicare, and Medi-Cal. This will be one of the next steps to pursue.

The database does not include any data on whether a patient filled their prescription order nor does it provide any information to assess whether patients were adherent to their medication regimen. In addition, it is difficult to assess the true length of time that patients actually took medication. The method used to estimate the amount of medication a patient receives and presumably takes is imperfect, as it relies on the assumption that every medication order and refill is filled. It is not uncommon for physicians to write for multiple refills, but for those refills to never be used. As a result, it is possible that the true amount of medication a patient is taking may be underestimated. In addition, it is assumed that once a patient begins basal or prandial insulin, they continue the regimen without gaps, which may not be the case.

This study is unable to distinguish degrees of fluency among patients who speak English. In addition, English fluency does not automatically result in strong communication between patient and provider. This also does not account for patients who understand English well but chose to indicate a different preferred language. In addition, there was no data collected on the Spanish ability of the physicians in the study to determine if language concordance between physician and patient alleviates some of the disparities in clinical inertia.

In the case of a patient who typically has a well-controlled HbA1C but has a one-time unusually high lab value, this is accounted for in the analysis in that if the next HbA1C lab value was below target, they would be considered to have achieved the target and been censored from the analysis. We were unable to assess whether patients were able to maintain their HbA1C at or below the target after the first HbA1C at target.
The limitations outline areas that were difficult to account for in the analyses, as either the data was unavailable or required some extrapolation. This may account for one of the non-findings of Race/Ethnicity, in particular, as not significant. Future researchers may be able to better account for some of these limitations in their studies.

**Implications**

Clinical inertia remains a problem. Even 12 months after an initial elevated HbA1C ≥8%, as many as 25% of the sample population had not received appropriate medication intensification. In addition, at the 12-month mark, 38.3% of patients whose HbA1C had risen above 8 had returned to a target HbA1C ≤8%. Given that the recommended goal for most patients is a HbA1C ≤ 7%; it is likely that even fewer patients achieved that goal.

This study showed an association between English-fluent status and clinical inertia, such that patients who do not speak English have lower odds of receiving medication intensification within a given period of time. Non-English-fluent status, leading to worse clinical inertia, could be one explanation for disparities in diabetes outcomes among minority patients, as minority patients are more likely to speak a language other than English. Language could also be a marker for culturally bound beliefs/preferences, where patients who are less fluent in English may be more strongly tied to culturally bound beliefs about medication. Patients with such beliefs may be more reluctant to intensify medication, leading to clinical inertia.

English language fluency was framed as a proxy for the construct of Communication. Difficulty in communication can introduce many issues, at the very least making basic conversation difficult. It can set up a barrier to the patient-physician relationship, making it difficult to communicate the importance of medication intensification and making it more difficult for patients to share their concerns and physicians to address fears.
One implication of this finding is that it is possible that non-English fluent patients are more likely to engage effectively with a language-concordant physician. The difficulty of language discordance between patients and physicians has been a persistent problem with no easy solution. One possible situation is matching non-English fluent patients with language-concordant physicians. One study found that when Spanish-fluent patients switched from English-fluent physicians to Spanish-fluent patients, there was a 10% increase in the prevalence of HbA1C ≤8%. An adjuvant to this would be promoting Spanish fluency in interested medical personnel and recruiting more bilingual physicians. Though interpretation with the aid of technology is often promoted, this comes with its own pitfalls. Perhaps technology will continue to improve so that it may be a better substitute in the future.

Conclusions

This study examines the intersection of clinical inertia with minority health outcomes, with a focus on Hispanic patients. Three constructs—Access, Beliefs/Preferences, and Communication, represented by the proxies of insurance status, racial/ethnic status, and English-fluent status—were hypothesized to be contributing factors to clinical inertia, also defined as time to medication intensification, and time to reach a HbA1C target of 8%. Overall, time to intensification was not associated with Access or Beliefs/Preferences. However, patients who did not speak English had lower odds of medication intensification, implying that it may be Communication or English language ability, not so much minority status per se, that may be a contributing factor to clinical inertia. There was a non-significant association between Communication and time to target, which provides some support for the role of Communication and English-fluent status in poor diabetes outcomes for minority patients.
Clinical inertia is a concern in many patients, but is understudied in racial/ethnic minorities. While this analysis provides a potential avenue of explanation for the disparities in diabetes outcomes faced by minorities, this is a difficult problem to solve. Further study will be needed to further elucidate the association. A potential avenue of exploration would be a comparison of clinical inertia between Spanish-fluent and English-fluent Hispanic patients, to see if the connection remains when race/ethnicity is controlled. It would also be interesting to see how this may be translated in larger groups that speak a language other than English or Spanish. In the meantime, this further underlines the need for culturally competent care to adequately serve all of our patients.
REFERENCES


