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Focusing on Symptom Management for Frail Elders with Diabetes: Assessing the Relationship between Glycemic Control and Urinary Incontinence

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This work is dedicated to my dear friends AB, JP, LCP, LD, MA, MC, ND, NS, SM and ZN with whom I hope to age gracefully.

Introduction

This research project questions the current recommendations for clinical care of frail elders with diabetes. In clinical practice today, diabetes care for frail elders largely follows rules designed for and evaluated with middle-aged adults and non-frail elders. For the past few decades, the focus of the debate over optimal diabetes care has been on the appropriate intensity of glycemic control, as measured with percent glycosylated hemoglobin. I make the case that this approach to diabetic care for frail elders is both illogical and harmful. Using the example of urinary incontinence, I argue that control of diabetic symptoms should have higher priority than maintaining tight glycemic control in management of frail elders' diabetes.

I. Frail Elders

Who are frail elders and what is it about the nature of frailty which necessitates an alternate approach to diabetes care? Frailty is a state of increased vulnerability to stressors that puts an individual at risk for adverse health outcomes such as loss of mobility, increased dependency, and mortality. These changes are caused by the loss of the body's physiologic reserve to withstand challenges due to a combination of impaired neurologic control, decreased mechanical performance, and decreased energy metabolism.[1] Frailty tends to increase with age, but there is significant physiological variation in frailty between people of the same chronological age.[2]

Clinicians who work with frail elders describe aging-related changes that tend to accompany frailty including generalized weakness (such as decreased grip strength), poor endurance, weight loss, low activity, and fear of falling and/or unsteady gait.[1] For practical purposes (such as to assess need for services and risk of harm), frailty is defined as a combination of chronic disease and measurable functional needs such as the level of dependence in ADLs and IADLS.[2] The activities of daily living (ADLs) are the everyday needs of eating, bathing, grooming, dressing, toileting, and transferring from place-to-place. Instrumental activities of daily living (IADLs) are additional activities necessary for independence including preparing meals, managing medications, shopping for groceries, money management, making phone calls, and getting around the community.

For policy purposes, living in a nursing home and having long-term care needs are useful proxy measures for frailty among people over 65.[3] Estimates of the prevalence of frailty depend on the measure used; a population-wide US survey estimated a 10-25% frailty rate among people over 65, and a 40-64% frailty rate among people over 80.[4] In the US, long-term care reimbursement eligibility is typically defined with similar criteria as frailty; assessment of an individual's need for long-term care is determined by a combination of needing personal assistance in ADLs, needing assistance in IADLs, and needing skilled care for chronic conditions.[5, 6] The current estimate is that 17% of all Medicare beneficiaries and 70% of Medicare beneficiaries 85 and older have long-term care needs, based on ADLs and IADL dependence.[3, 7] Even though most frail elders have significant long-term care needs, the majority of frail elders live in the community. Of elders with long-term care needs in the US, one third of elders reside in long-term care facilities while two thirds reside in the community; community-dwelling elders receive assistance with ADLs and IADLs from paid and unpaid caregivers in their homes or as outpatients. [3]

Across all settings for care delivery, there are significant health care implications of frailty. Frailty is characterized by wide fluctuations in health status and risk for complications that interfere with the beneficial effects of treatment. Frail elders are vulnerable to health stressors including hospitalization and medical procedures; even at optimal health, frail elders are at heightened risk for falls, disability, hospitalization, and mortality.[1] Geriatric syndromes are a set of recognized conditions that are common among elders and characterized by their multifactorial causes, low rates of diagnosis and treatment, and association with morbidity and poor outcomes.[8] Elders with frailty often have one or more geriatric syndromes such as delirium, falls, depression, and urinary incontinence. Our understanding of geriatric syndromes and other needs that accompany frailty should be used to tailor health care for frail elders with chronic disease.

II. Frail Elders with Diabetes

Over a few generations, the rate of type 2 diabetes among frail elders has increased rapidly, without a concomitant adjustment in diabetes treatment protocols. In the US today, over a quarter of people over 65 have

diabetes.[9] Although type 2 diabetes is preventable, once acquired type 2 diabetes is a progressive chronic disease that is difficult—though not impossible--, to reverse. As result the combination of increasing diabetes prevalence at every age range and the aging of the population in the US has led to high diabetes rates among elders. Of people over 65 with type 2 diabetes, about 60% acquired diabetes in middle-age and 40% acquired diabetes after 65; every year, the greatest increases in diabetes prevalence in industrialized countries are among elders.[10] Diabetes prevalence rates are even higher in some ethnic groups; compared to non-Hispanic white adults, the risk of diabetes is disproportionately higher among Asian Americans (18% increased risk), non-Hispanic African Americans (77% increased risk), Mexican-Americans (87% increased risk), and Puerto Ricans (94% increased risk).[9]

Among elders admitted to nursing homes, diabetes is increasingly likely to be the primary admission diagnosis.[11] In 2010, there were 453,000 people with diabetes in U.S. nursing homes; which is 30% of the nursing home population.[12, 13] In addition, there are an estimated equal number of frail elders with diabetes and long-term care needs who live in the community. Compounding the problem of caring for increasing number of elders with diabetes; diabetes itself is a major risk factor for frailty; having diabetes significantly increases the likelihood that an elder judged frail in a clinical assessment.[14]

III. Diabetes Mellitus

Among frail elders, type 2 diabetes is predominant, currently 90-95% of elders with diabetes have type 2 diabetes. [9, 15] For elders, the appropriate treatment of diabetes depends on the body's ability to self-regulate glucose levels, regardless of whether the etiology of disease is type 1 or type 2 diabetes. However, the natural history of diabetes including duration and severity, the risks and benefits of glycemic control, and the social perception of diabetes can be very different for people with type 1 and type 2 diabetes.

Type 2 diabetes begins when the body gradually loses its ability to maintain the appropriate balance of glucose levels. Early in type 2 diabetes, the body's tissues become less sensitive to the metabolic effects of the body's insulin (insulin resistance). At first, the body compensates by increasing insulin release from the

pancreas. Over time, if the underlying risk factors are not changed, the pancreatic cells are gradually destroyed, leading to development of diabetic state that is dependent on exogenous insulin to maintain glucose balance. Known underlying risk factors for type 2 diabetes include obesity (particularly excess abdominal fat around organs), a diet high in simple carbohydrates, a family history of type 2 diabetes, sedentary lifestyle, and older age.[16] The American Diabetes Association diagnostic criteria for type 2 diabetes include HbA1c $\geq$ 6.5%, elevated glucose levels after fasting (>126 mg/dl), inability to decrease glucose after drinking a high-glucose solution (>200mg/dl two hours post OGTT), and/or an extremely elevated random blood glucose test accompanied by diabetic symptoms (>200mg/dl)[17, 18].

Type 1 diabetes, which was formerly known as juvenile-onset diabetes, usually starts in childhood or young adulthood when the body's immune system mistakenly attacks the pancreatic beta cells. This attack on the pancreas destroys the body's ability to make insulin. Without insulin, the body cannot regulate blood glucose levels or use available glucose; people with type 1 diabetes must receive exogenous insulin infusions throughout their lives.

Unlike type 1 diabetes, type 2 diabetes can be prevented, delayed, or even reversed by risk factor reduction such as dietary modification, exercise, and weight loss. For people with partially impaired glucose control that is not yet considered type 2 diabetes (known as pre-diabetes), oral anti-diabetic medications can modify the body's secretion of insulin, response to insulin, and/or response to glucose in order to postpone or prevent the development of diabetes. Another crucial difference from type 1 diabetes is that type 2 diabetes is a progressive disease that worsens over time due to increasing insulin resistance; for most people, treatment for type 2 diabetes must be intensified regularly to maintain appropriate glucose homeostasis.

IV. Diabetes Treatment

For people diagnosed with type 2 diabetes, the central goal of medical care is maintaining glucose regulation within a narrow range to prevent hyperglycemia, avoid hypoglycemia, and minimize long-term damage to end-organs and vasculature. Treatment options for diabetes include diet, exercise, weight loss, oral

anti-diabetic medications, and insulin injections.[16] Diabetes is managed using a treatment algorithm with four key features: treatment goal of glycemic control, a tiered treatment system, collaboration between providers and patients, and secondary prevention of diabetes complications. In this review I'll refer to the American Diabetes Association[19], the Kaiser Foundation[20],and the Veteran Affairs/Department of Defense[2120] guidelines for descriptions of the current standard-of-care for diabetes treatment; the glycemic control algorithms are excerpted from these examples and included in the Appendix.

The mainstay of current treatment is a glycemic control goal. A glycemic control-based management program uses a proxy measure of hyperglycemia, the percent glycosylated hemoglobin (known as HbA1C), to determine whether treatment protocols are adequate or should be intensified. HbA1C percent is an approximate measure of the average blood glucose concentration over the previous three months. There are other critical treatment goals for diabetes in addition to glycemic control assessment targeting low % HbA1C. These goals include maintaining fasting glucose within an appropriate range such as 90-130 mg/dL, maintaining postprandial glucose measures within 100-180 mg/dL, and reducing cardiovascular disease risk factors. For most adults, the recommended glycemic control target is HbA1C < 7%. All the diabetes treatment guidelines recommend a less strict HbA1c target of < 8% or < 9% for patients with enhanced risk of hypoglycemia, but most of the guidelines neither describe how to identify high-risk groups nor make clear what level of risk for hypoglycemia is tolerable. Of the three major guidelines discussed here, only the Veterans Affairs/Department of Defense (VA/DoD) guideline has a nuanced recommendation for an individualized glycemic control target. The VA/DoD guideline recommends less strict control for people with a life expectancy of less than 5 years, who require a combination regimen with insulin, with a history of hypoglycemia, with advanced microvascular complications or comorbid illness, and/or with a longer duration of diabetes.

To achieve glucose regulation, diabetes is managed with tiered treatment protocols. For instance in the Kaiser algorithm if treatment targets are not met via lifestyle modifications, a new medication is added every 6 weeks to reach the target HbA1C levels of glucose control. Whereas people with type 1 diabetes require insulin from the start of treatment, people with type 2 diabetes only require insulin if diabetic damage progresses and

destroys the body's ability to make insulin. Since type 2 diabetes tends to progress steadily; over several decades, almost all people with type 2 diabetes require increasing numbers of medications, eventually including insulin, to continue to meet treatment targets.[20]

Working in partnership with patients to choose treatments and monitor therapy is an essential aspect of good diabetes care.[22] Joint patient-provider decision-making and monitoring is important because there is a variation in the body's physiological response to diabetes therapy and a wide range of preferred diabetes treatments amongst individuals. Diabetic monitoring by patients and providers requires regular and detailed assessment of diet, fasting glucose levels, postprandial glucose levels, and long-term glycemic control. Ideally, the results of diabetes monitoring should inform treatment recommendations and help guide patients and providers to appropriate treatment choices from the wide variety of diabetes treatment options. Considering medication options alone, treatment choices include three types of injectable insulin and six classes of oral antidiabetic medications. Comparative effectiveness research has shown that many available treatment options have an equivalent effect on diabetes control. For instance, almost all oral anti-diabetic medication classes have similar efficacy for diabetes control, but the side effects and burdens of classes of medications differ significantly.[23] Most algorithms and guidelines for diabetes control propose multiple feasible treatment combinations and ask providers to choose the best treatment appropriate for their patients' care. Over the last few decades, there has been increasing support for system changes that might enable more patient participation in diabetes care.

V. Complications of Diabetes

In addition to maintaining glucose regulation, diabetes treatment is used to prevent secondary complications of long-term exposure to hyperglycemia. The types of long-term damage due to diabetic hyperglycemia are classified as microvascular and macrovascular complications.[24] The microvascular complications include diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy. If glucose values are unchecked over the long-term, these complications can worsen to serious irreversible damage; retinopathy can

worsen to blindness, kidney damage can progress to end stage renal disease and renal failure requiring dialysis, and neuropathy can cause non-healing leg wounds that may require limb amputations.

Diabetes is a strong independent predictor risk factor for macrovascular disease including stroke, heart attacks, and peripheral artery disease. More than 60% of people with type 2 diabetes die of cardiovascular disease.[25] The macrovascular complications of diabetes are primarily due to increased risk of atherosclerosis. For men, independently of other risk factors, type 2 diabetes increases the risk of cardiovascular disease mortality by 45-80%.[26] In addition to the risks directly attributable due to diabetes, type 2 diabetes often occurs in the setting of metabolic syndrome which includes abdominal obesity, hypertension, dyslipidemia and increased coagulability; all of these factors are independent risk factors for cardiovascular disease.

Glycemic control aims to prevent both micro- and macrovascular complications. Because of the enhanced macrovascular risks of diabetes, blood pressure reduction, cholesterol control, exercise, and smoking cessation are all critical components of clinical diabetes treatment. [24,19] The evidence suggests that these types of non-diabetes-specific cardiovascular risk reduction are more effective at preventing macrovascular mortality than most glycemic control interventions.[27]

VI. Glycemic Control Targets

The current framework for glycemic control is relatively new; over the past few decades there has been an active debate about glycemic control and over the nature of optimal diabetes treatment. In the 1980s, observational studies of people with type 1 diabetes found that lower HbA1C levels were associated with lower rates of long-term diabetes complications. This observation was revelatory because it was an early piece of evidence that microvascular and macrovascular complications of diabetes were potentially avoidable. People without diabetes have HbA1C values of about 3.5-5.5% whereas adults with diabetes have higher HbA1C values; in the 1980s and 1990s, there was a series of controlled research trials designed to test whether diabetic treatment regimens could achieve "near normal" levels of glycemic control. These trials aimed to decrease HbA1C values to test whether intensifying glycemic control could prevent diabetes complications.[28] The first

large study of this kind was the Diabetes Control and Complications Trial (DCCT/EDIC), which found that intensified insulin therapy reduced HbA1C levels significantly and reduced the progression of microvascular complications among people with type 1 diabetes. Even more strikingly, the extent of decreased complication rates among DCCT subjects was correlated with the percent decrease in HbA1C levels.[29, 30] The results from the DCCT/EDIC trial led to a slew of longer term trials, trials examining macrovascular complications, and trials among people with type 2 diabetes.[31]

There are now 30 years of results from controlled trials aiming to intensify glycemic control (reduce HbA1C %) in order to reduce long-term diabetes complications. Among people with type 1 diabetes and among people recently diagnosed with type 2 diabetes, there are clear benefits to early intervention with intensified glycemic control and low glycemic control targets.[32] For the large population of people with diabetes who have had type 2 diabetes for many years, intensive glycemic control has some benefits, but the positive benefit is diminished. Several major trials of intensive glycemic control for type 2 diabetes were published in 2008 and 2009. All of the trial interventions were able to reduce HbA1C levels to a median level of 6.5 to 7% using intensive glycemic control, but the trials did not detect any effect of intensive control on all-cause mortality or on macrovascular disease mortality within the average two-year follow-up period; in the Action in Diabetes and Vascular Disease (ADVANCE) trial intensive glycemic control was associated with a small *increase* in deaths, which was not significant at the $p < 0.05$ level.[33, 34]

In 2011, the Cochrane Collaboration published a meta-analysis using data from all randomized controlled trials that have compared intensive glycemic control for type 2 diabetes with conventional glycemic control; the trials had a combined 30,000 subjects.[33] The Cochrane analysis did not find any significant reduction in death from any cause or in death from heart disease due to intensive glycemic control. Targeting lower HbA1C levels did not change the risk of macrovascular disease overall. However targeting intensive glycemic control was associated with a reduced risk of amputation, a reduced risk of nonfatal myocardial infarction, and a reduced risk of microvascular disease.

The Cochrane researchers found that the net benefit of glycemic control was limited by a serious adverse effect of treatment; intensive glycemic control was associated with higher rates of both mild and severe hypoglycemia, with an overall 30% increase in severe hypoglycemia. The conclusion of this and other recent reviews is that there are only minimal benefits of intensive glycemic control for type 2 diabetes in trials with 2-15 year follow-up periods. The researchers suggest that a significant treatment benefit might accrue over longer follow-up periods, but there is no current evidence of that benefit.[32, 33] Subgroup analyses from glycemic control trials also found extensive variation in the trials' successes at decreasing vascular complications depending on the population studied and details of the intervention, meaning that the results may not be generalizable to populations that have not been studied.[35] The current consensus in reviews of glycemic control implementation is that intensive glycemic control should be implemented for some populations but should be used with caution.[21,28]

Although the current research science is lukewarm in its assessment of the benefit of intensive glycemic control, there is a different picture in clinical practice; focusing on intensifying glycemic control to prevent long-term complications is the current clinical standard of care. Since the publication of the DCCT trial, there have been intense efforts to incorporate intensified glycemic control into clinical practice.[17, 28] For instance, the 2006 American Diabetes Association guideline says that HbA1C of 7% or higher should be "A call to action to initiate or change therapy with the goal of achieving an HbA1C level as close to the non-diabetic range as possible or at a minimum, decreasing the HbA1C to less than 7%."[19] Since HbA1C approximates cumulative levels of blood glucose over the preceding three months, percent HbA1C provides a single number that can approximately reflect the effect of clinical diabetes treatment over time. This has enabled the popularity of reducing HbA1C (intensifying glycemic control) as a target for health care improvement interventions. Partly because HbA1C is easily measurable and reportable, quality indicators such as the percent of patients meeting the HbA1C target have been incorporated into system-wide and nationwide performance measures for assessment of health care quality.[36]

Due to the emphasis on strict glycemic control, the median HbA1C among people with diagnosed diabetes has been decreasing over time. In the 1990s the median HbA1C level among people with diabetes was 9.5%.[37] By the mid 2000s, the median HbA1C in the National Health and Nutrition Examination Survey cohort was 7.2%, meaning that just under half of the surveyed population of diabetics met the target glycemic control level of < 7%.[38] This can be put in other terms; in 2006, about 50% of patients with diabetes did not meet the recommended HbA1C < 7% target. Furthermore, about 20% of the national sample had a glycemic control level above 8% HbA1C and 11% of the sample had an HbA1C measurement above 9%.[38]

Some researchers and policy makers have expressed alarm at the health care system's failure to intensify population glycemic control further,[39, 40] while other researchers have worried that there is an excessive emphasis on glycemic control.[27] Given the guidelines recommending HbA1C < 7% and clinicians' awareness of the co-morbidities associated with untreated diabetes, the larger share of the diabetes treatment literature has focused on the need to increase the intensity of glycemic control. There have been countless interventions to encourage tighter control of diabetes in primary care. Interventions targeting many levels of care delivery have been successful in intensifying control and lowering average HbA1C levels.[41]

An assessment of current levels of glycemic control is useful for thinking about the nature of clinical care for diabetes. Key influences on the level of glycemic control include patient's access to health care, providers' decisions about initiating or intensifying treatment, and the level of patients' participation in treatment. For a particular individual, high HbA1C levels and minimal treatment of severe disease may represent purposeful intention, neglect, or error. In many cases, poor control (higher HbA1C) is a true reflection of poor quality of care. In other cases, the decision not to intensify control may be in accordance with patient's wishes, family's wishes, and clinician's intentions. It can be difficult to disentangle which components are affecting diabetes treatment.

Sadly, some patients have untreated diabetes due to of lack of access to adequate health care. This may be a less significant effect when considering treatment of diabetes among elders, since Medicare provides near universal health care coverage to U.S. citizens over 65. At the cutoff for Medicare eligibility, insurance

coverage for the U.S. population rises from 84% among people 40-64 to 98% among 65-year-olds.[42, 43]

Coverage does not necessarily mean access to health care services; in particular, rural elders with diabetes who technically have health insurance coverage have limited access to adequate diabetes treatment.[44]

Patient factors that limit the intensity of glycemic control include the difficulty of medication regimens, beliefs that treatment is ineffective, perception that injections are dangerous, and concern about more severe complications.[45] There is low patient adherence to the drug regimens. Based on pharmacy records and patient reports, about 10-30% of people with diabetes withdraw from prescribed regimens within a year of diabetes diagnosis.[46] Patient non-adherence to treatment can be intentional or unintentional; for instance, poor adherence to a glycemic control regimen may be due to a patient belief that treatment is ineffective or to a low sense of self-efficacy.[46]

Clinicians' framing of diabetes and treatment can have a powerful effect on patient participation in treatment. For example, if a patient with type 2 diabetes is not aware that treatment regimens usually need to be intensified regularly, she is less likely to agree with future recommendations for treatment intensification. When a patient returns for a 6 month follow-up, she may perceive a need for a treatment increase as a failure of diabetes treatment or of her participation, rather than as a common and expected outcome.[47]

Providers' unwillingness to initiate or intensify treatment for diabetes is a common reason for glycemic control below recommended targets.[46] Physicians who don't recommend an intervention may be overestimating the current quality of care, anticipating patient resistance to intensified therapy, unaware of therapeutic goals, or may be disagreeing with the therapeutic goals. This phenomenon has been described as clinical inertia, defined as "The inappropriate management of at least one medical condition for a given patient because of minimal or lack of appropriate therapeutic interventions.[48]" There is a body of research literature on clinical inertia in the treatment of diabetes.[48] Studies of clinical inertia in diabetes usually define an appropriate response to a high HbA1C as a dose increase, increase in the number of prescribed drug classes, or medication switch to another drug class. Using this definition, the prevalence of clinical inertia for diabetes may be very high. Studies on

treatment decisions for people with poorly-controlled diabetes found that physicians did not "respond appropriately", meaning intensify treatment, for 30-50% of patients who had high HbA1C levels.[49]

A number of clinicians and researchers have spoken out to disagree with the guidelines for glycemic control and have argued for purposeful and valid reasons that glycemic control should not be intensified.[50-52] Others simply disagree with the prioritization of HbA1C targets at the expense of other factors and have attributed clinical inertia to competing demands on clinicians' time. There is evidence that for adults with diabetes, control of hyperglycemia often takes precedence during clinical visits over control of hypertension and treatment for dyslipidemia. [50] This phenomenon persists despite the strong evidence that hypertension control is more important than glycemic control for reducing the rates of cardiovascular disease. In response to an editorial on clinical inertia in hypertension treatment for people with diabetes, two geriatricians, Drs Boyd and Leff, make a strong case against the current treatment paradigm that prioritizes decreasing HbA1C numbers and treating blood pressure; Boyd and Leff argue for the clinician's responsibility to do a global assessment of the patient's condition. [27] They propose that a clinician's failure to intensify glycemic control is only a missed opportunity for prevention of microvascular disease for some patients with diabetes. Perhaps appropriately, the failure to intensify diabetes regimens tends to be more common in situations when diabetes treatment intensity is relatively low priority: clinical inertia is more common when HbA1C values are only slightly above guidelines and when patients have more competing health care demands.[53] A hurried clinician who defers intensification of glycemic control may be aware that due to the significant risks of diabetes treatment, intensifying diabetes with only a hasty discussion is considerably more dangerous than failing to intensify a diabetes regimen.[53]

VII. Benefits and burdens of diabetes and of diabetes therapy for elders

Diabetes *per se* and diabetes treatments both become more dangerous with age, and the treatments should adjust to reflect this reality. As of yet, there are minimal data on the benefits and burdens of diabetes control among elders. For instance, while hypoglycemia is a risk of insulin-dependent diabetes and of diabetes

treatment, the risk of hypoglycemia is higher for elders.[54] Increased harms of diabetes treatment for elders include increasing danger associated with insulin treatment, dangers of dietary restriction, and use of many medications among elders. Both diabetes and diabetes treatment are associated with increased risk for geriatric syndromes including increased risk for cognitive dysfunction, physical functional decline, falls and fractures, incontinence, and depression.[55]

There is universal agreement that avoiding hypoglycemic events should be a priority in management of diabetes for elders. The rates of hypoglycemia increase exponentially with age for both diabetics and non-diabetics, and hypoglycemia is a significant risk for diabetic elders treated with tight glycemic control.[54, 56] Compounding the risk, elders may be less aware of hypoglycemic symptoms because physical autonomic symptoms that indicate low blood sugar levels diminish with age.[56] Even mild hypoglycemia among elders can increase the risk for an injurious fall, and severe hypoglycemia can cause confusion, coma, and death. Among elders with diabetes, episodes of severe hypoglycemia are extremely serious; severe hypoglycemia is associated with increased risk of cardiovascular events, cerebrovascular events, confusion, dementia progression, falls, emergency room visits, and hospitalization.[57] Hypoglycemia is more common among diabetics with tight glycemic control, but can also occur among elders with HbA1C levels greater than 8% and greater than 9%, which would be considered loose diabetes control.[57] In one study, implementation of an intensified glycemic control regimen (HbA1C<8%) was associated with higher rates of hypoglycemia in a community population of frail elders.[58] Elders using simplified diabetes treatment regimens may have lower rates of hypoglycemia,[59] which suggests one possibility for future research into safer treatment regimens.

The risks of diabetic treatment for elders also include risks of dietary limitation, risks of medication interactions and polypharmacy, and particular risks associated with insulin use among elders. Dietary restriction, which is designed to assist with glucose control, can inadvertently cause protein and vitamin deficiencies. For frail elder patients with diabetes, malnutrition can be a more important concern than obesity. A Cleveland Clinic review of appropriate diabetes treatment for the elderly suggests that all patients in danger of

malnutrition should be given unrestricted menus rather than diabetic menus, with the goal of diabetes-related nutrition being consistent levels of carbohydrates at meals and snacks.[56]

Another risk of diabetic treatment is polypharmacy; taking many medications increases the risk of medication interactions and toxicities, increases side effects, and risks confusion about appropriate dosing and times. Elders with diabetes take 10.3 medications a day on average, compared with 8.4 medications for peers without diabetes.[11] The ability to handle oral medication containers and insulin depends on cognition, dexterity, vision, and an ability to read and understand the medication instructions. Hospital admission due to unintentionally missing medication is twice as common among elders as in the general population. Factors that contribute to accidental non-adherence include confusion about the drug regimen (28%), fear of side effects (19%), and forgetfulness (16%).[42]

Insulin therapy can be especially challenging for elders with diabetes. Many older patients have difficulty managing home glucose monitoring and insulin injections.[47, 55] Insulin treatment options include frequent doses of short-acting agents or less frequent doses of long-acting agents. Frequent doses of short-acting agents control hyperglycemia more effectively and are associated with less frequent hypoglycemia, but regimens that require glucose monitoring and appropriate response to high or low glucose levels can be too complex for some elderly patients.

Patient education is a critical component of all diabetic treatment, but especially for insulin therapy. And while patient education is important for diabetes patients of all ages, it is especially important for older patients who are cognitively impaired, and often should include education of family members or caregivers.[56, 60] Whether patients are living in a long-term care facility or in the community, the extent of caregiving and support is essential for determining appropriate treatment plans; more guidelines should echo this Cleveland Clinic note: "patient's support system must be evaluated before recommended [insulin] therapy."[56]

VIII. Geriatric Syndromes and Diabetes

An elder's health status and abilities are likely to shape the benefits and burdens of each diabetes care regimen. As someone with diabetes ages, the assessment, prevention, and treatment of geriatric syndromes become a necessary piece of diabetes care. Geriatric syndromes may not have a direct identifiable cause, they are often due to a combination of clinically identifiable and subclinical disease processes. Diabetes increases geriatric syndromes via direct mechanisms (e.g. diabetes can cause urinary incontinence) and indirect mechanisms (e.g. hypoglycemia can lead to increased fall risk).[61] Increased recognition of geriatric syndromes is needed, the Assessing Care of Vulnerable Elders (ACOVE) study on medical care for elders found that geriatric syndromes were less much likely to be properly addressed than other medical diagnoses.[62]

Possible benefits of glycemic control on geriatric syndromes include improvement in cognition, reduction in symptomatic hyperglycemia, reduction in depression, and decreased incontinence. Yet the associations between diabetes and geriatrics syndromes can be complicated. For instance, there seems to be a bidirectional association between cognitive function and glycemic control. Elders with diabetes have a greater risk of developing dementia, and poorer cognitive function are associated with lower success rates of clinical interventions designed to improve glycemic control. A study conducted by Munshi and colleagues found an association between higher executive function score and decreased HbA1C values. This association did not reach statistical significance of $p < 0.05$ with the small sample size of 95 elders, but this result suggests the possibility that impaired executive function could also interfere with ability to manage diabetes, leading to worse glycemic control.[63]

Researchers and clinicians have also tried to understand which aspects of diabetes and diabetes treatment are commonly distressing for patients. Diabetic elders are depressed more often than other elders, and suffer from diabetes-specific health burdens including burdens of complications, burdens of diabetes treatment and comorbid disease.[64] Looking at the big picture, several studies have found that changes in glycemic control (HbA1C) are not associated with patients reporting change in quality of life.[65] In one study, the predominant health care goal of patients with diabetes was to maintain independence in activities of daily living.[64] In a

qualitative study on elders in Japan, patients reported diabetes burden due to other factors, the most common burdens of diabetes were dietary restriction (89%), social burden (89%), worry about diabetes (85%), treatment dissatisfaction (85%), burden due to medication tablets or insulin (77%). In contrast, only 55% of elders reported less being distressed by the symptom burdens of diabetes.[66]

There is minimal literature focused on understanding the ideal approach to diabetes treatment for frail elders, and there is no clear evidence on the advantage or disadvantage of glycemic control for this population.[51, 52] Current clinical care regimens are based on controlled trials of intensified glycemic control for diabetes, yet these trials mostly excluded adults over 65 or 70 and adults with significant co-morbidities. The Diabetes and Aging Study retrospectively studied the rates of mortality among elders with diabetes and found that both high HbA1C levels (8-9% and 9-10%) and low HbA1C levels (5-6%) are associated with increased mortality among elders relative to 7-8% HbA1C.[67] Diabetes and Aging Study results also suggest that for elders, glycemic control does not affect macrovascular disease rates and that microvascular disease benefit can take as much as 8 years to accrue.[60] Vijan and colleagues developed a model to estimate the magnitude of the reduction in microvascular disease risk in glycemic control trials. They found that glycemic control is most effective at reducing microvascular complications for patients with onset of diabetes at a younger age and for patients with very poor glycemic control (e.g. 11%).

> For example, in patients who develop diabetes at 45 years of age, improving glycemic control from a hemoglobin A_{1c} level of 9% to a level of 7% results in an estimated 2.3-percentage point decrease in lifetime risk for blindness caused by diabetic retinopathy (from 2.6% to 0.3%). In contrast, the same change in hemoglobin A_{1c} level in patients with diabetes onset at 65 years of age would decrease the lifetime risk for blindness by only 0.5 percentage points.[68]

So how do we put this information together? The uncertainty about glycemic control for elders is partly due to the heterogeneity of elders' physiological status and partly due to lack of information. There are divergent recommendations for caring for elders with diabetes. The current evidence suggests that glycemic levels that could cause cognitive impairment and other geriatric syndromes are much higher than the glycemic levels associated with long-term risk for macrovascular and microvascular complication[51, 60] If further research

bears that out, these data suggest that a higher HbA1C target (for instance HbA1C <9%) rather than intensive glycemic control (such as HbA1C <7%) would be concordant with optimal glycemic control for frail elders.

To address this, the California Healthcare Foundation/American Geriatrics Society (AGS) Joint Panel on Improving Care for Elders with Diabetes wrote a 2003 report recommending individualized diabetes treatment goals for older patients. The AGS report recommendations include individualizing HbA1C treatment targets, and monitoring macrovascular complications, microvascular complications, and geriatric syndromes (including incontinence). The AGS panel also recommends prioritizing direct cardiovascular risk factor reduction over glycemic control and aiming to avoid complicated, costly, and uncomfortable treatment regimens. The AGS starting recommendation is HbA1C <7% for relatively healthy older adults and HbA1C <8% for frail elders with a life expectancy of less than 5 years.[9, 60] The panel also recommended regular assessment of treatment goals and diabetes management skills because functional and cognitive status may change quickly over time among elders.

IX. Current diabetic care for elders

Many elders with diabetes have considerable functional impairment and dependency; thus, providing adequate care for elders with diabetes is often labor-intensive and costly. Due to the burden of diabetes treatment and treatment for co-morbidities, medical expenses for people with diabetes are twice as high as expenses for people without diabetes.[9] The appropriate treatment depends on the level of care surrounding an elder with diabetes. The settings for diabetes care for U.S. elders are varied; care regimens may be prescribed and managed by primary care clinics, home health care, nursing homes and/or hospital teams. To give one example, treatment such as insulin administration or glucose monitoring may not be burdensome in a well-funded long-term care setting, but can be very burdensome in a home environment with a patchwork network of several caregivers without formal medical training.

For frail elders who live in the community, diabetes is managed on an outpatient basis. Assistance with care may be limited or extensive; diabetic elders receive a range of support. Sinclair and colleagues surveyed 100

diabetic British elders living at home and found considerable unmet need in both domestic activities and diabetes care.[69] In this population, the majority of care work was undertaken by family and friends. Although family and friends assisted with many diabetes-related activities including assisting with medication administration, insulin injection, glucose measurement, and meal preparation, the informal caregivers in the study had limited diabetes education and information. More research is needed to understand diabetes care for elders who live in the community.

In long-term care settings there has been more extensive research, but there is disagreement about whether diabetes tends to be over-treated, under-treated, or perhaps both. A 2010 Center for Medicare and Medicaid Services (CMS) on unnecessary hospitalizations described over-treatment of diabetes as the biggest current problem: "Diabetes is often over-treated in long-term care patients. Patients should be monitored at appropriate frequencies, and hypoglycemic medications adjusted to keep blood sugar in a broad range in most patients. Over-aggressive treatment results in frequent and unnecessary episodes of hypoglycemia."[5] On the other hand, according to guidelines recommending HbA1C <7% or <8% for people with diabetes, diabetes among frail elders is under-treated, which has led to concern about ways to improve treatment in long-term care settings.

Certainly, in many long-term settings there is a lack of appropriate attention to diabetes. A 2008 survey of diabetes treatment by Feldman and colleagues found that only 2 of the 13 surveyed nursing home facilities had a diabetes treatment algorithm in place and only one had a policy for testing HbA1C level; the researchers found that "knowledge of diabetes tends to be relatively poor among staff of these facilities."[70, 71] Feldman and colleagues conducted medical record review of 372 nursing home patients with diabetes selected from several of the surveyed facilities. The average age of diabetic residents was 79 years old, 90% had type 2 diabetes and 10% had type 1 diabetes. The most recent HbA1C value was obtained for each surveyed resident and HbA1C values were quite low: 19% of residents had HbA1C less than 6%, 34% had a recent HbA1C between 6-6.9%, 35% between 7-7.9, 7% between 8 and 9, 3% between 9 and 10, and less than 1% had a most recent HbA1C>10 (see Figure 1). The high rates of low HbA1c values, low rates of HbA1C values >8%, and lack of staff knowledge of diabetes care suggests that low HbA1C values are prioritized over safety.

Problems with diabetes treatment related to reporting, such as lack of accurate monitoring, and inadequate reporting of hypoglycemia, can make it difficult for researchers or physicians to detect problems with diabetes care. In the Feldman survey, although HbA1C levels were very low, there were few nursing home-generated reports of hypoglycemia. Pharmacists and nursing home managers at 6 of the 13 facilities reported that there were no episodes of hypoglycemia in their facilities in the preceding 6 months. Yet based on chart review by the research team, 1% of residents with diabetes were sent to the hospital for symptoms of hypoglycemia and 6% of residents had hypoglycemic symptoms of diabetes recorded in their charts. Overall, it seems likely that there is significant over-treatment of diabetes in nursing homes and under-monitoring of disease. It is more difficult to tell what the nature of diabetic care is for frail elders outside of nursing homes. The underlying problem may that a mismatch between guidelines and appropriate treatment makes it harder to provide good care and easier to provide poor care by neglecting diabetes and avoiding treatment.

X. Framework for decision-making

Care for elders requires considering prognosis and life expectancy, the potential harms and benefits of treatment, and patients' preferences. The calculus of the benefits and burdens are not the same for all elders.

For some elders, clinicians and patients need to find a balance between the advantages of reducing vascular complications and the short-term harms of hypoglycemia and burden of diabetes treatment. A recent clinical case in the Journal of the American Medical Association sparked a debate about when it is appropriate for physicians to push for treatment intensification when the patient has strong objections. Writing in 2007, Martin Abrahamson described a patient in his primary care practice, a 74 year old woman with diabetes referred to as "Ms. M", who had worsening glycemic control with an A1C of 7.4%. Ms. M was reluctant to comply with Dr. Abrahamson's suggestion that she add insulin to her treatment regimen. Dr. Abrahamson's assessment was that Ms. M would reap significant benefit from improved glycemic control to below 7% and that she should be encouraged to start insulin treatment, given her good health and life expectancy.[45] Other clinicians wrote in to the journal, arguing that there is only evidence of a minimal benefit of glycemic control for a patient like Ms. M, and in fact that close examination of the microvascular disease data indicates that most patients like Ms. M are unlikely to have a reduction in vascular complications due to glycemic control. Since in this case

Ms. M's personal preference was to avoid insulin treatment at all costs, and the potential benefit of insulin treatment was small, several letter-writers felt that her preference should prevail in this case.[52, 72]

At the time the article was printed, Ms. M had an estimated life expectancy of about 15 years. When making decisions about diabetes care for frail elders with more limited life expectancy, the terms of the debate should change. The best current evidence on the effect of glycemic control suggests that it takes 8 or more years for intensified glycemic control to have a significant effect in reducing vascular complications of diabetes.[33] Without the possibility of intensifying glycemic treatment to reduce macrovascular and microvascular disease, the main safety priority of diabetes treatment is to reduce hypoglycemia. Furthermore, for elders with limited life expectancy, one of the most important treatment considerations should be to understand what about diabetes and diabetes treatment is distressing and uncomfortable for each individual, and whether any of these aspects can be changed. The most likely domains that diabetes or diabetes treatment could affect have been identified by the AGS panel and other researchers; there is clear evidence that long-term diabetes and/or diabetes treatment cause symptomatic hypoglycemia, symptomatic hyperglycemia, altered cognition, heightened risk of infection, and urinary incontinence. Further research is needed to understand whether treatment has a short-term effect on these domains.[51]

A useful theoretical framework for these considerations is the idea of patient-centered care. In their critique of the focus on meeting health care quality standards for diabetes treatment, Drs Boyd and Leff emphasize a patient-centered model of care.

> "We suggest that this [focus on clinical inertia] is the wrong way to frame the issue because it does not adequately acknowledge a patient-centered perspective of chronic illness care, in which all of the patient's conditions are considered in terms of the relative benefit of treating each condition in the presence of the other conditions, the cumulative effect of all the recommended treatments, and the individual's treatment priorities."[27]

Along these lines, Victor Montori and colleagues propose a theory of minimally invasive medicine for diabetes care that includes avoiding treatments that aren't beneficial, making individualized treatment decisions with joint patient-clinical team decision making, and recognizing that patients with diabetes are likely to have many different personal priorities. This concept has been applied to the idea of diabetes care for elders, In a 2011 commentary, Drs. Sei Lee and Cathy Eng propose that the two most important factors for determining diabetes treatment should be the degree of frailty the patient experiences and prioritizing the health outcomes that the patient values most.[51]

XI. Elders with urinary incontinence and diabetes

Urinary incontinence is a geriatric syndrome that is twice as common among people with diabetes. Urinary incontinence is a prototypical geriatric syndrome since it is common among elders, has a multifactorial etiology, has high potential for contributing to functional decline and is underdiagnosed and undertreated.[73] Among people over 60, about a fifth of women and a tenth of men have some degree of urinary incontinence and the prevalence of urinary incontinence increases in each subsequent decade. At each age, dependency and chronic disease increase the risk of urinary incontinence.[73] Based on nursing home mandatory data reporting in 2010, 34% of nursing home residents were completely incontinent in the preceding 14 days, 36% had some incontinence, and only 30% of residents were completely continent. Of residents with some incontinence, two-thirds wore pads or briefs and 7% of residents used an indwelling catheter.[12] As with other geriatric syndromes, there is a paucity of attention to urinary incontinence; in a study off vulnerable elders in the community only 29% had documentation of the presence or absence of urinary incontinence in their medical records which is much lower than the population prevalence in other studies.[62]

Urinary incontinence has important effects on elders' lives. Some elders find incontinence personally distressing or deeply embarrassing and as a result urinary incontinence can lead to a contraction in social activities. Other elders may be unaware of incontinence, or unconcerned with the results of incontinence, yet may still be indirectly impacted by urinary incontinence when it leads to increased dependency on others, movement into a higher level of care, or sequelae such as a urinary tract infection or decubitus ulcers (bedsores). For instance, having urinary incontinence is the biggest single risk for nursing home admission.[73] As a result of these sequelae, urinary incontinence is associated with significant care costs for patients, families and the health care system.[74] Increased care costs due to incontinence costs the US health care system an estimated 32 billion dollars a year.[75]

The causes of urinary incontinence for frail elders are incompletely understood. The current understanding is that many factors contribute to incontinence, contributing factors include age-related decline in

bladder function, medical and surgical conditions (such as diabetes and history of stroke), and medication use. Urinary incontinence among both men and women is usually due to a combination of stress incontinence and urge incontinence. Persistent, or established urinary incontinence is usually due to neurological processes and gynecological (for women) or urological processes (for men). Transient or periodic incontinence is often due to infectious causes or medication.[73] Risk factors for urinary incontinence include female sex, older age, impaired cognitive function, impaired mobility, and diabetes. In one study, 22% of women who were continent at nursing home admission became incontinent within the first year of nursing home stay.[73] Women with recent cognitive and physical decline are more likely to report greater frequency of incontinence, which may be due to a combination of physiological changes and inability to cope with incontinence symptoms.[76]

Diabetes increases the risk of urinary incontinence through both fixed effects and transient effects.[77] For women, diabetes causes about a 50% increase in the rate of mild incontinence and almost a 100% increase in the rate of severe incontinence.[78] Among older men, diabetes is associated with a 25-100% increase in urinary incontinence rates.[79] Stroke-related damage, neurogenic bladder, and involuntary bladder contractions are fixed effects that may cause urinary incontinence.[77, 78] Over the short-term, hyperglycemia causes glycosuria which can lead to increased urination and increased risk of urinary tract infection; both increased urine volume and infection risk can cause new incontinence or exacerbate prior urinary incontinence.[77] Frail elders with diabetes have a heightened risk of many medical conditions and treatments that are independently associated with urinary incontinence including obesity, cognitive impairment, history of strokes, and diuretic use.[80] Urinary incontinence can have an incredible physical, emotional and economic cost. Due to the relationship between urinary incontinence and diabetes, urinary incontinence may be an important symptomatic target for diabetes treatment, but little is known about how variation in glycemic control among people with diabetes may or may not affect urinary incontinence. [60]

XII. Analysis of Glycemic Control and Urinary Incontinence in a population of frail elders

As outlined above, there is a large and growing population of frail elderly patients with diabetes and limited life expectancy. In 2010, there were 453,000 people with diabetes living in U.S. nursing homes and an estimated equal number of nursing-home eligible people with diabetes living in the community.[9,12] Urinary incontinence is also very common and increases with age; in fact the rates of urinary incontinence in US nursing homes are as much as 35-60%. Urinary incontinence, the inability to control urine flow, is associated with lower self-reported quality of life, risk of pressure sores and other sequelae, and need for higher levels of care.[74]

Diabetes itself means "to pass through" and for centuries polyuria has been recognized as a hallmark of uncontrolled diabetes. Several types of research suggest that diabetes may worsen urinary incontinence. For instance the risk of incontinence is approximately doubled among diabetic patients compared to people without diabetes[51]. Plausible mechanisms for the relationship between diabetes and incontinence include short-term osmotic glycosuria and long-term peripheral neuropathy leading to impaired control of micturition[79].

Although tighter glycemic control may be associated with reduced rates of urinary incontinence, studies examining this relationship have had conflicting results. Especially when treating elderly patients, clinicians must weigh the benefits of tighter glycemic control against the increased risk of hypoglycemia; improved information about the level of glycemic control associated with worsening urinary incontinence could aid clinician decision-making.

XIII. Analytic Methods

Participants

This is a cross-sectional cohort study using data collected during routine clinical care at On Lok Lifeways. The participants are all On Lok enrollees with diabetes mellitus enrolled between October 2002 (when an electronic medical record system was implemented) and December 2011. On Lok is a Program for

All-inclusive Care for the Elderly; to enroll in On Lok or another PACE program, participants must be nursing home-eligible and currently reside in the community. PACE centers provide or coordinate all healthcare services with the aim of helping participants to continue living in their homes; participants typically spend 1-5 days per week at the affiliated adult day health center where they have health appointments, meals, and recreational activities. Each On Lok enrollee receives a comprehensive health assessment upon enrollment and every 6 months afterwards; this includes medical evaluation, functional assessment, and geriatric syndrome assessment (including assessment of urinary incontinence) conducted by a coordinated team including physicians, nurses, physical therapists and social workers. Patients with diabetes mellitus are also routinely monitored at three-month intervals with an assessment of glucose measurement, HgbA1c values and diabetic complications.

Measures: Outcomes

The primary outcome variable is the prevalence of moderate or severe urinary incontinence, assessed every 6 months. This variable was coded as positive if the subject was "often" incontinent or used a catheter.

Measures: Predictors and Confounders

The primary predictor was HgbA1c level divided into four categories (<7.0%, 7.0–7.9%, 8.0–8.9%, and ≥9.0%). HgbA1c was assessed categorically because previous studies suggest that the relationship between HgbA1c and outcomes may be nonlinear.[83] Factors that may confound the relationship between HgbA1c and urinary incontinence were accounted for including age, sex, and race. We also controlled for depression, cognitive impairment, dependence in transferring and ambulating, use of thiazide diuretics, use of oral anti-hyperglycemic medications or insulin, and diabetic complications. Because individuals on catheters may differ from other individuals who have severe urinary incontinence. Analyses were also performed stratified according to diabetes treatment to determine whether the relationship between HgbA1c and urinary incontinence varied

according to treatment. Co-morbid conditions were captured through ICD-9 codes associated with hospitalizations, emergency department visits, and outpatient physician visits.

Statistical Analysis

The unit of analysis was contemporaneous pairs of HgbA1c measure (predictor) and urinary incontinence (outcome), where contemporaneous is defined as less than 3 months apart. Multiple pairs of HgbA1c measures/urinary incontinence were used from each individual. If there were measurements of HgbA1c 3 months before and 3 months after a 6 month visit but not at the time of the visit, the closest HgbA1c measurement was used. Observations were excluded from the analysis if participants were on dialysis, receiving end-of-life care, or if participants had a HgbA1c<6.5 without receiving any anti-hyperglycemic medications. HgbA1c/incontinence pairs were also excluded if they were within 6 months of another pair of measures from the same individual.

Mixed effects logistic regression was used to assess the relationship between HgbA1c and incontinence while accounting for clustering of HgbA1c by participant. ANOVA was used to assess the relative rates of incontinence for participants with each secondary predictor. An HgbA1c level of 7.0% to 7.9% was chosen as the reference because the AGS guideline recommends HgbA1c of 8.0% or less as the appropriate glycemic target for "frail elders with limited life expectancy."[60] All analyses were performed using Stata MP (version 10.1, StataCorp, College Station, TX) and SAS (version 9.2, SAS System for Windows, SAS Institute Inc, Cary, NC). The data for this analysis were de-identified at On Lok and, as such, this study does not qualify as human subjects research under the UC Berkeley Committee on Human Research guidelines.

XIV. Results

Characteristics of the Population

Figure 1 shows the inclusions and exclusions in selection of the HgbA1c/incontinence pairs used for the analysis. There were 799 On Lok participants with diabetes enrolled from 2002-2011. 228 participants were

excluded due to one or more of the following criteria: no HgbA1c/incontinence pairs prior to receipt of treatment for end-stage renal disease or prior to receiving end-of-life care, or if throughout the study period HgbA1c measures were < 6.5% without use of any anti-hyperglycemic medication. Data from 571 participants were included in the analysis; the analysis was done comparing a total of 2745 pairs of contemporaneous HgbA1c/incontinence measures.

Table 1 shows baseline characteristics of subjects at time of HgbA1c measurements. Participants were elderly, with a mean age of 81, and most were female (67%) and Asian (65%). The mean HgbA1c value was 7.4. Almost one third of participants were taking only oral anti-hyperglycemic medications at baseline, and 11% were taking insulin. Many participants had diagnoses of diabetic complications; renal complications of diabetes were most common (62%), followed by ophthalmic (35%), neurologic (24%), and peripheral circulatory complications (13%). Over a third of participants had moderate or severe cognitive impairment (37%), and many were partially or fully dependent in mobility-related activities of daily living such as transferring (20%) and ambulating (24%).

Relationship Between HgbA1c and Urinary Incontinence

Overall, 18% of the incontinence observations described subjects as "often" incontinent or with a catheter. Many of the secondary predictors were individually associated with risk of incontinence including older age, race or ethnicity, dependence in transferring, dependence in ambulating, cognitive impairment, depression, use of diuretics, and the presence of renal or ophthalmological diabetic complications (all p < 0.001). In contrast, neither female gender (p = 0.28) nor obesity (p = 0.12) was associated with incontinence .

Table 2 shows the unadjusted and adjusted results of the relationship between HgbA1c and urinary Incontinence. In the unadjusted analysis, we found that higher HgbA1c levels were associated with less urinary incontinence. For example HgbA1c values <7% were associated with a 19.2 % incidence of urinary incontinence while HgbA1c values >9% had 16.9% risk of urinary incontinence. However, when we adjusted for confounding variables, there was no significant association between HgbA1c and incontinence. For

example, compared to patients with an HgbA1c <7%, patients with a HgbA1c >9% had an odds ratio of 0.98 (CI 0.5, 1.9) for having urinary incontinence.

XV. Discussion

After controlling for secondary predictors, we found no evidence that HgbA1c levels were associated with urinary incontinence in nursing home-eligible older adults, even at HgbA1c>9%. We found fairly high rates of frequent urinary incontinence among the women in this population; this matches the trends reported in other studies. Notably, the rates of moderate/severe urinary incontinence among men were as high as among women in this older cohort; these rates are comparable to rates in men over 75 from national survey data.[73]

Only a few studies have explored the relationship between urinary incontinence and glycemic control among postmenopausal women, and these studies have had conflicting results. Phelan and colleagues studied 2994 women with diabetes and obesity and found no association between glycemic control and incontinence; however, Phelan's cohort had very low rates of diabetes complications.[75] Jackson and colleagues found no relationship between glycemic control and incontinence among postmenopausal women with diabetes, although only 73 women exceeded the recommended HgbA1c > 7.5%.[82] On the other hand, Lee and colleagues looking at a much larger cohort found a positive association between poor glycemic control and incontinence (unpublished data). No prior studies have analyzed urinary incontinence and diabetes specifically among frail elders to examine the relationship between poor glycemic control and urinary incontinence.

Strengths, Limitations, and Next Steps

A challenge of this analysis is the heterogeneity of the population of frail elders. We can be certain that there are a multitude of factors contributing to the etiology of urinary incontinence in this population, some are captured in the secondary predictors. Future analyses could assess changes in urinary incontinence over time, investigating whether patients with long-term hyperglycemia are at higher risk for worsening urinary incontinence than their peers with lower glycosylated hemoglobin levels.

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XVI. Conclusions

This study provides a rare analysis of the effects of diabetes care in a real practice setting, among a cohort of nursing-home eligible elders with a number of co-morbidities and a wide range of HgbA1c levels. It is increasingly well established that benefits and harms of diabetes treatment are different for frail elderly people than for their younger counterparts.[51,79] In particular, frail elders with diabetes are at higher risk for hypoglycemic events and less likely to benefit from reductions in microvascular and macrovascular complications. As a result, recent guidelines recommend less aggressive glycemic control targets for elders with limited life expectancy (for instance HgbA1c target < 8%) and individualized glycemic control goals for elder with consideration of each person's risks and potential benefits. Our results suggest that for the vast majority of patients, improving glycemic control is unlikely to reduce the incidence of urinary incontinence. Further work should be done to explore other causes of incontinence more likely to contribute.

Tables and Figures

Figure 1. HbA1C measurements from elders with diabetes in surveyed nursing homes[70]

HbA1C Values
- Most recent, for those residents with results
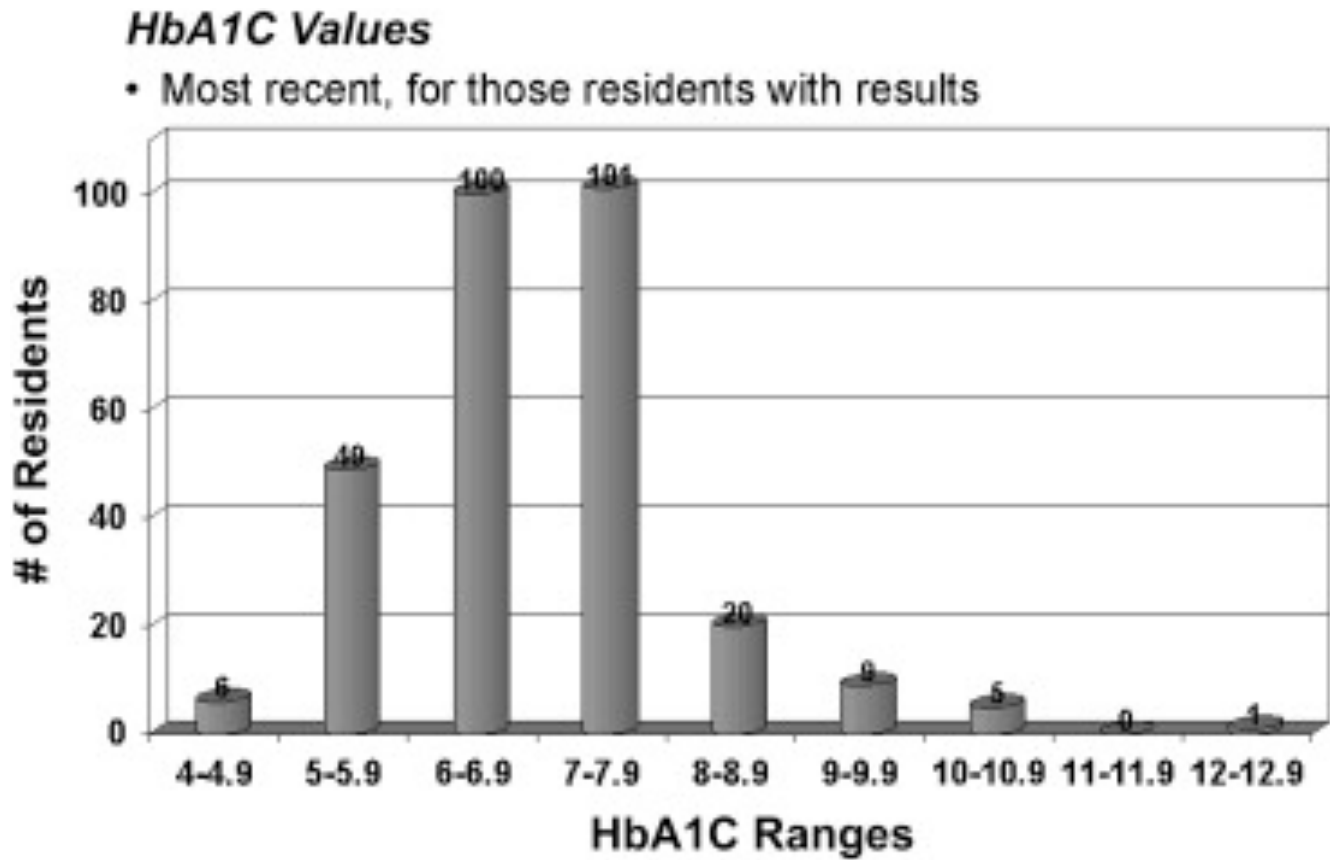
Table 1. Demographic characteristics of subjects with and without incontinence.

Table 1. Demographic characteristics of subjects with and without incontinence					
			No Incontinence N=2242 (82%)	Incontinence N=503 (18%)	
Characteristic	N(observations) (observations(obs	%	%	%	p-value
Demographics					
Age	80.5 ± 8.2	55-101	80.2 ± 8.3	81.9 ± 7.6	<0.001
Female	1835	66.8%	67.3%	64.8%	0.28
Race/Ethnicity					
White	347	12.6%	11.7%	16.9%	
African-American/ Other	248	9.0%	7.4%	16.3%	<0.001
Hispanic	362	13.2%	13.8%	10.5%	
Asian	1788	65.1%	67.1%	56.3%	
Activities of Daily Living					
Partially or fully dependent in Transferring	546	20.0%	14.0%	46.6%	<0.001
Partially or fully dependent in Ambulating	655	24.0%	17.8%	51.8%	<0.001
Chronic Conditions					
Depression	720	26.2%	28.1%	18.1%	<0.001
Cognitive impairment or dementia	1003	36.5%	32.4%	54.9%	<0.001
UTI within 30 days	252	9.2%	7.5%	16.5%	<0.001
Obesity	129	4.7%	5.0%	3.4%	0.12
BPH or prostate cancer	177	6.4%	6.6%	6.0%	0.62
Medications					
Thiazide Diuretic	619	22.6%	23.6%	17.7%	0.00
Urinary Antispasmodic	162	5.9%	5.5%	7.6%	0.08
DM Meds					
No DM Meds	1636	59.6%	58.5%	64.4%	0.05
Metformin, Sulfonylureas, TZD, other	810	29.5%	30.4%	25.4%	

Table 2. Adjusted and unadjusted models of the relationship between glycemic control and urinary incontinence.

Table 2. Adjusted and Unadjusted						
A1C Category	**N**	**Outcome Rate**	**Unadjusted OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**
<7	1259	19.2%	1		1	
7-7.9	784	17.9%	0.87 (0.58,1.3)	0.487	0.88 (0.57,1.36)	0.566
8-8.9	389	17.5%	0.86 (0.52,1.43)	0.569	1.06 (0.62,1.82)	0.826
≥9	313	16.9%	0.68 (0.37,1.25)	0.214	0.98 (0.5,1.9)	0.951
p for trend				0.233		0.978

*Adjusted for age, gender, Asian race, depression, cognitive impairment, use of thiazide diuretics, diabetic medication use, diabetic complications (neurological, renal, ophthalmologic, peripheral circulation, other), and dependence in transferring and/or ambulating.

Figure 2. Study population inclusions and exclusions.

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┌──────────────────────────────────────────┐
│  On Lok participants with diabetes from   │
│          2002-2010, N = 799                │
└──────────────────────────────────────────┘
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            │        ┌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌┐
            │        ╎ Participant exclusions, N = 228  ╎
            ├───────▶╎   after ESRD diagnosis           ╎
            │        ╎   after receiving EOL care        ╎
            │        ╎   if HgbA1c < 6.5 without DM meds ╎
            │        └╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌╌┘
            ▼
┌──────────────────────────────────────────┐
│  Participants included in analysis, N = 571 │
│   Unique pairs of HgbA1c/incontinence      │
│   measures < 3 months apart, n = 2745      │
└──────────────────────────────────────────┘
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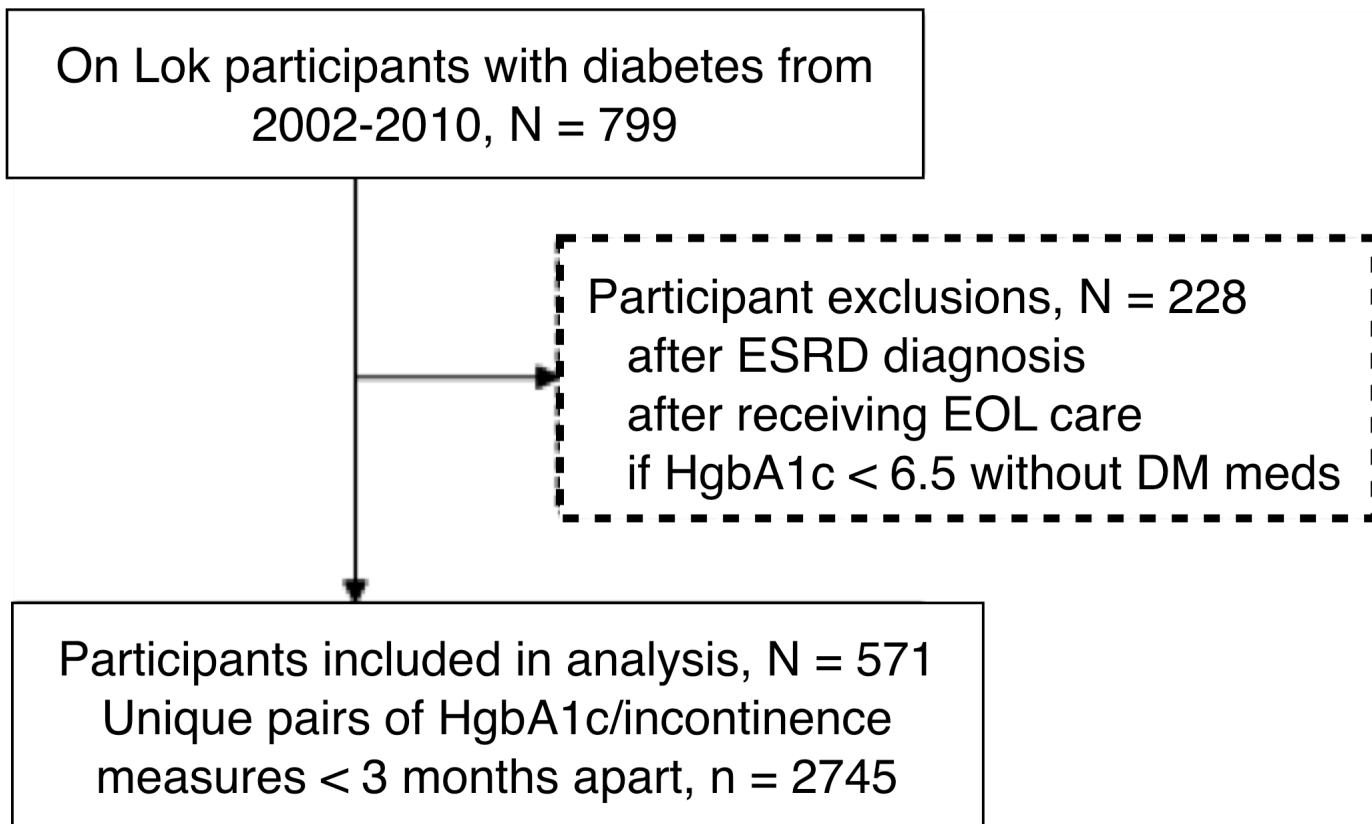
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Appendix: Glycemic Control Guidelines

Figure 1. American Diabetes Association Glycemic Control Algorithm[19]. Algorithm for the metabolic management of type 2 diabetes; Reinforce lifestyle interventions at every visit and check A1C every 3 months until A1C is >7%.
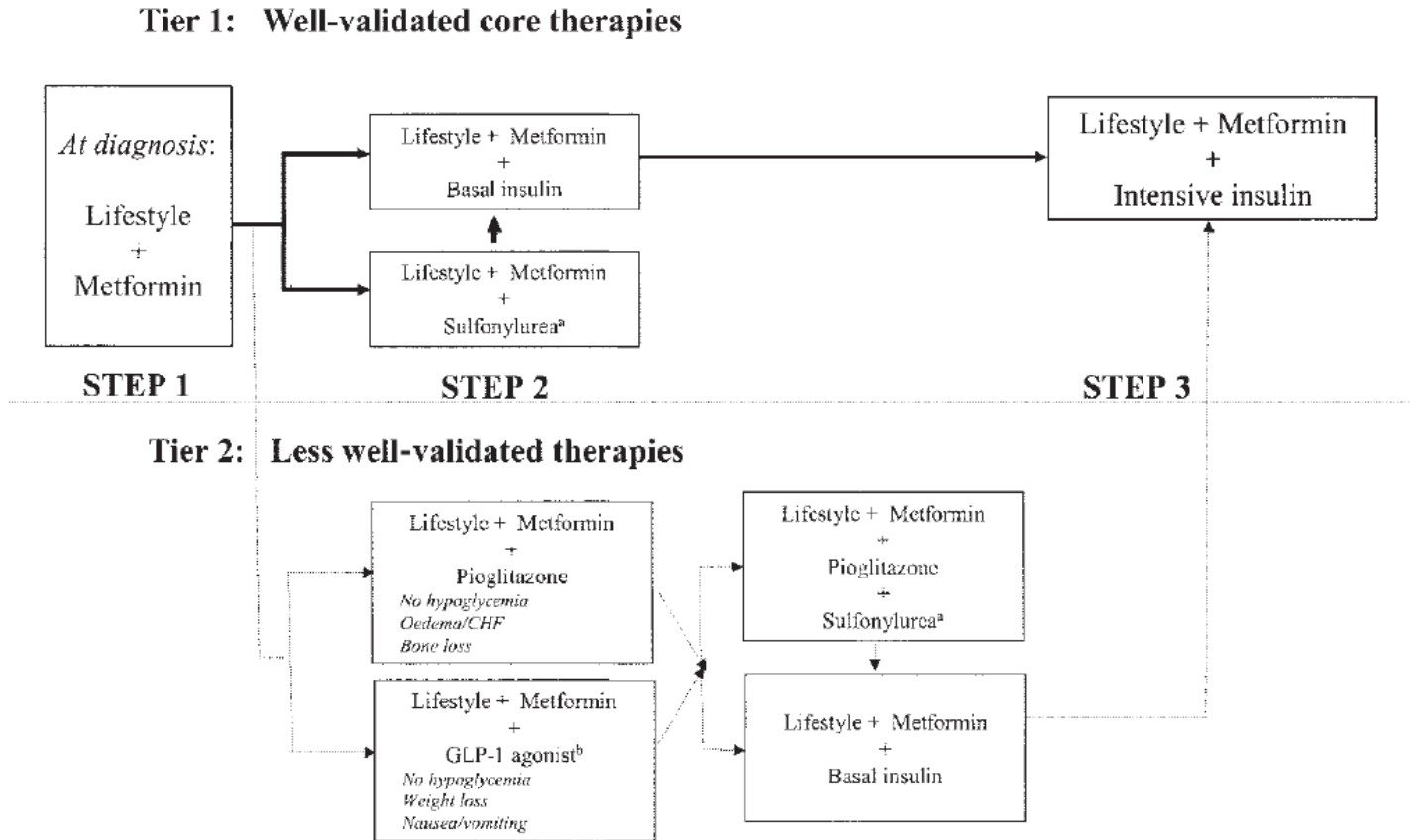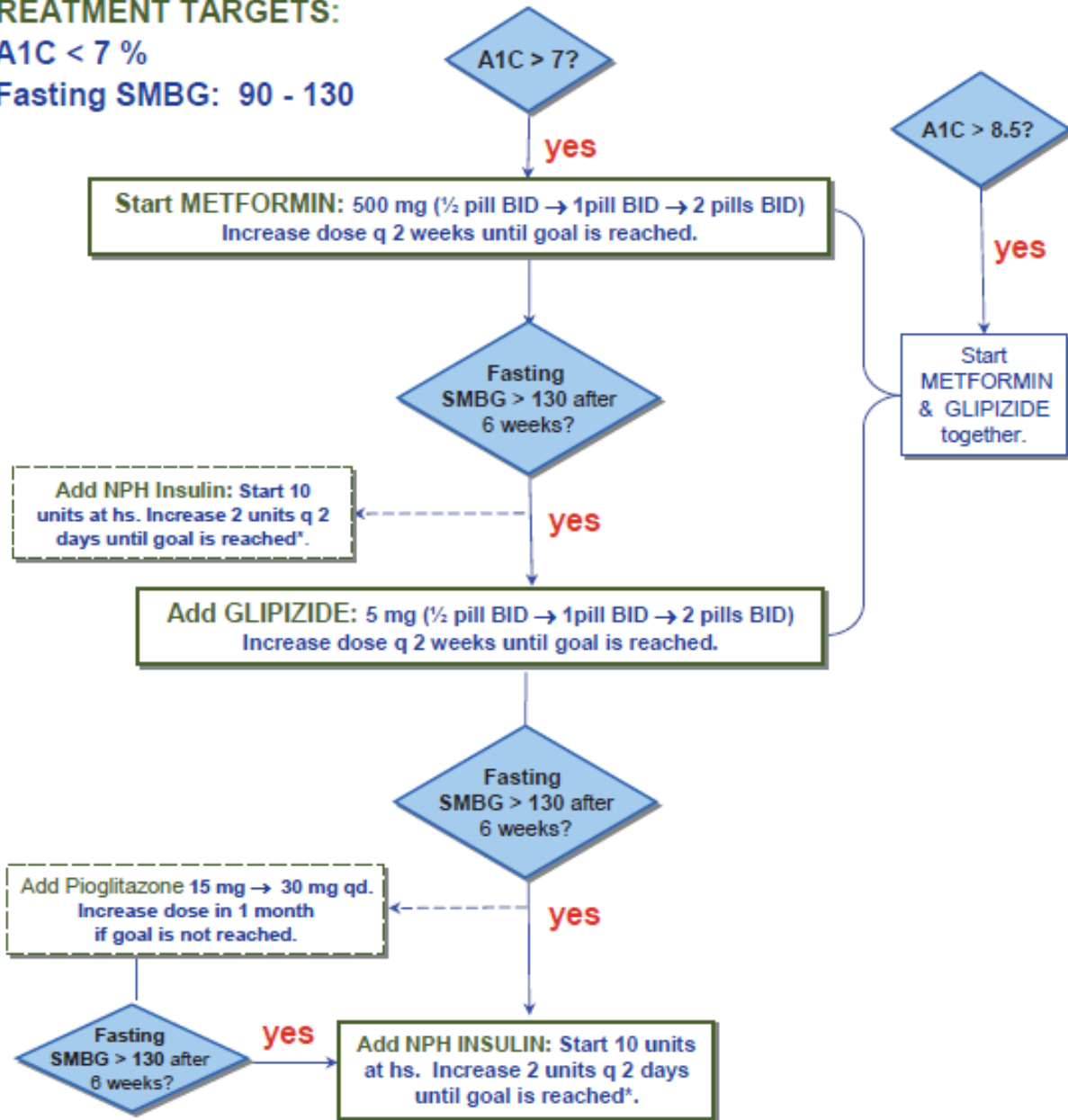
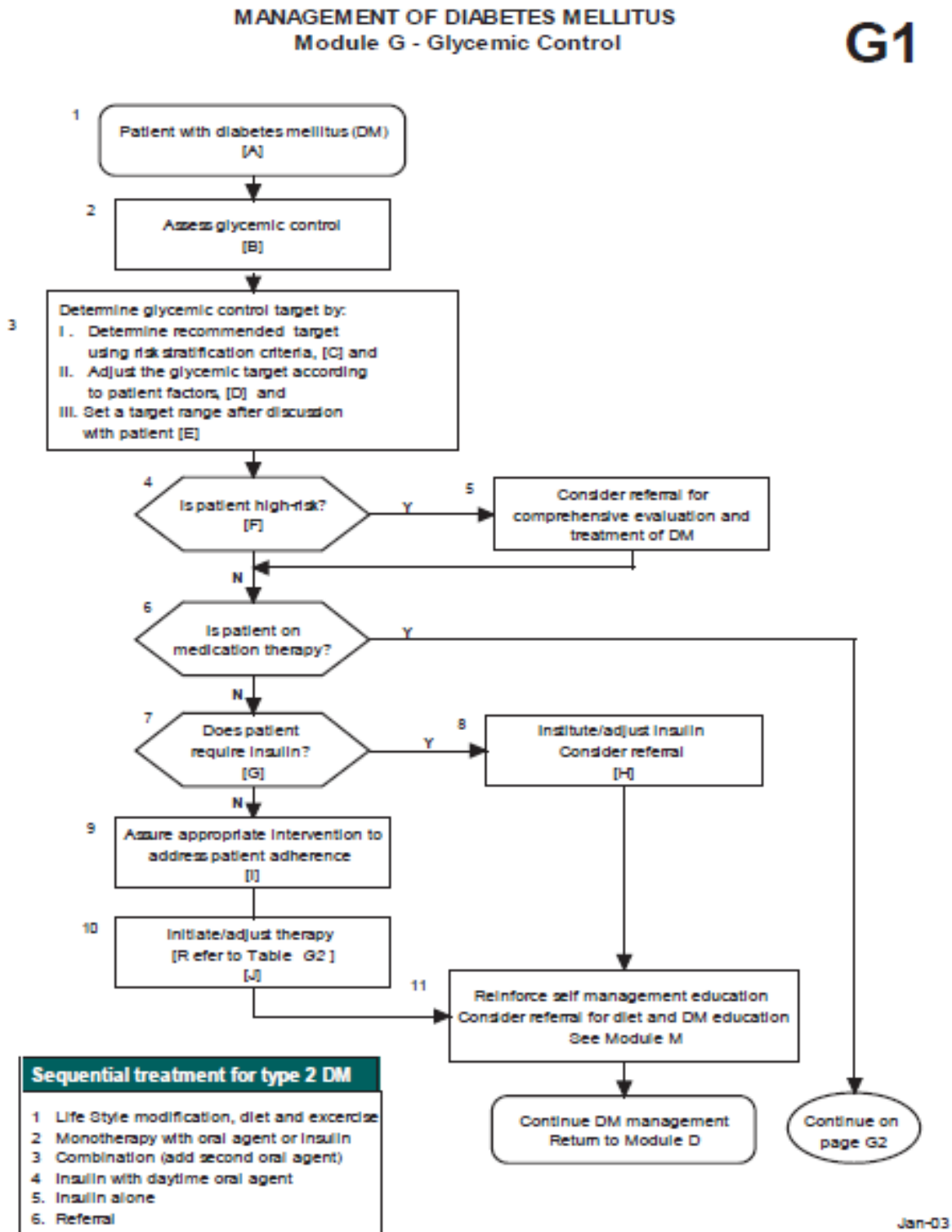**Figure 2.** Kaiser Permanente Glycemic Control Algorithm

1	**Test Twice**	• **3 Months**: A1C measures glycemic control over the previous 3 months. Measure A1C at least every 6 months.
	✓ Measure A1C at least twice a year.	• **2x / Day**: Encourage patients to self monitor their blood glucose (SMBG) twice a day — fasting and 2 hour post prandial.
	✓ Encourage blood glucose testing twice daily.	

2	**Treatment Targets**		
	✓ Excellent glycemic control is the ideal goal for all patients.	A1C ➡	< 7 % is an ideal A1C goal with no severe hypoglycemic reactions < 9 % is a minimum goal for all patients
	✓ A1C < 7 % is an ideal goal for patients.	Fasting SMBG ➡	90 – 130
	✓ Hypoglycemia risk significantly increases for those trying for tight control.	2 hour post prandial SMBG ➡	100 - 180

3	**Tiered Treatment**	• **Add Meds**: When treatment targets are not met with lifestyle changes, add another medication every 6 weeks to reach targets.
	✓ Diet, exercise, patient education and self glucose monitoring remain the foundation of diabetes management.	• **Add Insulin**: Insulin is an important tool of treatment. Nearly all patients will require insulin to achieve long-term glycemic control.
	✓ Most patients will require multiple medications, including insulin.	• **2 or More**: Most patients will require 2 or more medications to achieve glycemic control targets.

4	**Titrate to Targets**	• **SMBG**: Use patient's SMBG results to adjust doses.
	✓ Provide advice and recommendations allowing patients to advance medications.	• **Education**: Educate and encourage patients to advance their medication dosages, including insulin, based on their SMBG results while avoiding severe hypoglycemia.

5	**Treatment Today & Tomorrow**	• **Advance over 6-8 Weeks**: Advance and maximize oral medication doses over 6 weeks to achieve targets.
	✓ Sustained glycemic control is recommended for all patients.	• **Add Medication**: Add a medication if targets are not met within 6 wks after starting and maximizing an oral medication.
	✓ Poor glycemic control is a macro-vascular disease risk factor.	• **Insulin**: A single bedtime dose of NPH insulin will help most patients attain an A1C < 7%. Patients with hypoglycemic reactions may need to switch to insulin glargine. Some patients may require NPH or insulin glargine combined with Regular or insulin aspart achieve targets.
	✓ Remember PHASE.	• **Prevent Heart Attacks and Strokes Everyday (PHASE)**: Smoking cessation, Aspirin, Statin and ACE inhibitor use, plus blood pressure, glycemic and LDL control, provides the most effective macro-vascular disease prevention.

Figure 3. Veteran Affairs/Department of Defense Glycemic Control Algorithm[34]

MANAGEMENT OF DIABETES MELLITUS
Module G - Glycemic Control

G1

1. Patient with diabetes mellitus (DM) [A]

2. Assess glycemic control [B]

3. Determine glycemic control target by:
   I. Determine recommended target using risk stratification criteria, [C] and
   II. Adjust the glycemic target according to patient factors, [D] and
   III. Set a target range after discussion with patient [E]

4. Is patient high-risk? [F]
   Y → 5. Consider referral for comprehensive evaluation and treatment of DM
   N ↓

6. Is patient on medication therapy?
   Y →
   N ↓

7. Does patient require insulin? [G]
   Y → 8. Institute/adjust insulin Consider referral [H]
   N ↓

9. Assure appropriate intervention to address patient adherence [I]

10. Initiate/adjust therapy [Refer to Table G2] [J]

11. Reinforce self management education Consider referral for diet and DM education See Module M

Continue DM management Return to Module D

Continue on page G2

Sequential treatment for type 2 DM
1. Life Style modification, diet and excercise
2. Monotherapy with oral agent or insulin
3. Combination (add second oral agent)
4. Insulin with daytime oral agent
5. Insulin alone
6. Referral

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Continue from page G1

12 Determine if there are side effects or contraindications to current treatment
[K]

13 Is HbA$_1$c level above target range?

14 Are there problems with patient adherence?
[L]

Y

15 Provide appropriate intervention to address patient adherence
[I]

N

20 Continue current treatment
or
Adjust therapy if there are side effects or contraindications to current therapy
[J]

16 Should glycemic control target be adjusted?
[M]

Y

17 Adjust target level

N

18 Adjust medication therapy as indicated; consider side effects and contraindications
[J]

19 Reinforce self management and education Follow-up
[N]

Continue DM management Return to Module D