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REVIEW

Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors

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Abstract: At least 45% of patients with type 2 diabetes (T2D) fail to achieve adequate glycemic control (HbA1c <7%). One of the major contributing factors is poor medication adherence. Poor medication adherence in T2D is well documented to be very common and is associated with inadequate glycemic control; increased morbidity and mortality; and increased costs of outpatient care, emergency room visits, hospitalization, and managing complications of diabetes. Poor medication adherence is linked to key nonpatient factors (eg, lack of integrated care in many health care systems and clinical inertia among health care professionals), patient demographic factors (eg, young age, low education level, and low income level), critical patient beliefs about their medications (eg, perceived treatment inefficacy), and perceived patient burden regarding obtaining and taking their medications (eg, treatment complexity, out-of-pocket costs, and hypoglycemia). Specific barriers to medication adherence in T2D, especially those that are potentially modifiable, need to be more clearly identified; strategies that target poor adherence should focus on reducing medication burden and addressing negative medication beliefs of patients. Solutions to these problems would require behavioral innovations as well as new methods and modes of drug delivery.

Keywords: glycemic control, HbA1c, hypoglycemia, medication adherence, psychosocial, type 2 diabetes

Introduction

The prevalence of type 2 diabetes (T2D) is at epidemic proportions worldwide,[1,2] and the incidence and prevalence of T2D continue to increase (Figure 1).[3,4] Indeed, the worldwide prevalence of T2D is expected to increase from 382 million individuals (2013) to 417 million individuals by 2035.[1] This is of critical concern because T2D represents the largest budget item in many health care systems,[5,6] primarily due to the high rates of morbidity and mortality associated with the disease.[7–9] Even worse, it has been well documented that this cost burden has been inexorably growing worldwide.[10]

A key contributor to the remarkably high rates of morbidity and mortality is chronic poor metabolic control, especially poor glycemic control.[7] Although a wide array of options are now available for treating T2D, including several new pharmacological classes of drugs that are included in the current American Diabetes Assocation/European Association for the Study of Diabetes (ADA/EASD) and American Association of Clinical Endocrinologists (AACE) recommendations,[11,12] ~50% of patients with T2D fail to achieve adequate glycemic control (glycated hemoglobin [HbA1c] <7%).[13,14] Using data from the National Health and Nutrition Examination Survey, targets for glycemic

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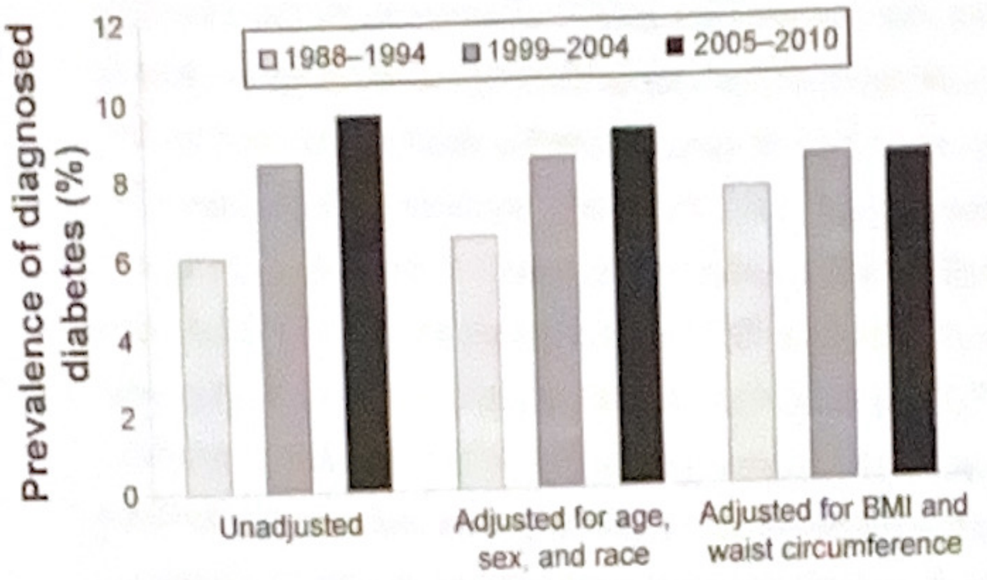

Figure 1 Prevalence of diagnosed diabetes among adults ≥20 years old from the NHANES of 1988–1994 and 1999–2010.
Note: Data from a previous study.[4]
Abbreviations: NHANES, National Health and Nutrition Examination Survey; BMI, body mass index.

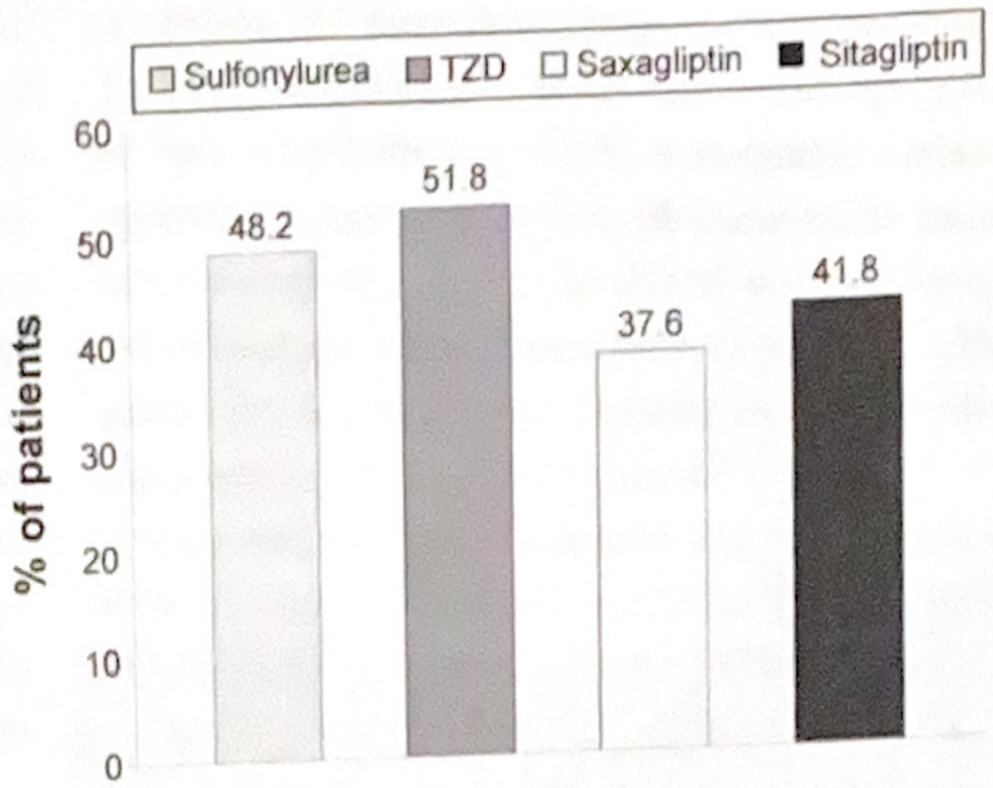

Figure 2 Percentage of patients discontinuing therapy (>60 days without drug) with oral hypoglycemic drugs during a 1-year follow-up of patients initiating therapy.
Note: Data from a previous study.[18]
Abbreviation: TZD, thiazolidinedione.

control (HbA1c) were achieved by only 55.5% of participants during 2009–2010.[15] A number of factors contribute to poor glycemic control, including lack of integrated care in many health care systems, clinical inertia among health care providers, and poor patient adherence to self-care recommendations. Among them, it is evident that poor medication adherence looms large.[16] This article reviewed the magnitude of the problem of poor medication adherence, the impact of poor adherence on long-term outcomes and health care costs, and the key contributors to poor medication adherence. In addition, the barriers and challenges that patients with T2D and their health care providers face regarding medication adherence are reviewed and the potential future approaches for enhancing long-term adherence and persistence are highlighted.

Scope of the problem

Much of the evidence regarding poor medication adherence in diabetes is based on retrospective or observational studies that collect data from claim databases using a broad range of definitions. Consequently, the reported incidence of poor medication adherence in patients with T2D ranged widely from 38% to 93% owing to widely different methodological approaches.[17–19] For the purposes of this article, we focused on one of the more common metrics and definitions of acceptable medication adherence, eg, a medication possession ratio (MPR) of ≥80% over the period of observation.[20] A review of studies found that among patients with diabetes, hypertension, and dyslipidemia, only 59% had MPR ≥80%.[17] An analysis of 238,000 patients with T2D from the MarketScan database reported adherence rates (MPR ≥80%) of 47.3% with dipeptidyl peptidase-4 inhibitors, 41.2% with sulfonylureas, and 36.7% with thiazolidinediones (Figure 2).[18] Similarly, a recent meta-analysis of 40 studies in which patients taking oral antidiabetic drugs found that medication adherence rates were suboptimal, with only 67.9% of patients having an MPR ≥80%.[21]

Another commonly used metric is medication persistence. Unfortunately, definitions vary even more widely here. Persistence is often defined as no gap in prescription drug supply for at least 30 days, although in some studies the definition is extended to ≥60–90 days. Other researchers have defined persistence on the basis of the proportion of patients who discontinue treatment, which may include discontinuation for lack of efficacy, side effects, patient preferences, and other causes. In total, the body of current findings can be difficult to interpret. In one recent meta-analysis that included randomized clinical trials of patients with T2D, persistence rates ranged from 41% to 81% and discontinuation rates ranged from 10% to 61% over a 12-month follow-up.[21] According to the MarketScan database, 47% of 238,000 patients discontinued therapy (last day of drug prior to a 60-day gap) over a 1-year follow-up.[18] A retrospective study of 1,321 patients with T2D treated with liraglutide (Novo Nordisk A/S, Bagsværd, Denmark) reported that 60% were persistent with therapy (no 90-day gap) over a 12-month period, but only 34% were adherent (MPR ≥80%).[22] Among 40,000 patients with T2D, persistence (no ≥30-day gap) over a 12-month follow-up ranged from 27% to 32%.[23] A retrospective analysis of persistence (time to discontinuation prior to ≥60-day gap) with different oral or noninsulin injectable agents for T2D reported an overall discontinuation rate of 52.2% over 12 months.[24]

In total, despite the wide range of definitions, there is relatively broad agreement across studies that problematic medication adherence and/or persistence is far from uncommon in T2D and may affect at least half of the population, if not more.

Of note, however, most of the studies cited above are limited, given the nature of claim databases, to those patients who had at least an initial prescription filled for the new medication. The risk of poor medication adherence may be higher once consideration is given to those who fail to fill a first prescription. In one study that tracked new prescriptions written electronically over a 12-month period for >75,000 patients, 31.4% of new prescriptions for diabetes drugs were never filled.[25] This problem, often referred to as primary nonadherence, may be particularly relevant among patients who are refusing to initiate insulin or other injectable hypoglycemic therapy, typically due to injection phobia, inconvenience, poor patient–physician communication, and/or negative patient perceptions.[26]

Consequences of poor medication adherence

Poor adherence is associated with inadequate glycemic control, increased use of health care resources, higher medical costs, and markedly higher mortality rates.[16,27,28] Among >11,000 veterans with T2D who were followed up for at least 5 years, poor medication adherence (MPR <80%) was significantly ($P<0.001$) associated with poor glycemic control (HbA1c >8%).[16] The National Health and Wellness Survey of 1,198 patients with T2D found that each 1-point drop in self-reported medication adherence (using the Morisky Medication Adherence Scale) was associated with 0.21% increase in HbA1c, as well as 4.6%, 20.4%, and 20.9% increase in physician, emergency room (ER), and hospital visits, respectively.[28]

Most importantly, poor medication adherence in T2D has also been linked to increased mortality. For example, among 15,984 patients from general practices in the UK who were treated with an oral antidiabetic agent, poor medication adherence and missed clinical appointments were each independently associated with a significant ($P<0.001$) 1.6-fold increase in all-cause mortality.[7] Similarly, Ho et al[8] reported a significant association between poor medication adherence in T2D and all-cause mortality over time (odds ratio 1.8; $P<0.001$).

Finally, poor medication adherence results in increased costs of T2D outpatient care, ER visits, hospitalization, and managing T2D complications.[6,29] An analysis of adherence to medications used to treat diabetes, dyslipidemia, and hypertension estimated that the direct cost of poor adherence was $105.8 billion in 2010 across 230 million patients, which represented $453 per adult.[6] The pharmacy and administrative claim databases of CVS Caremark were used to assess the impact of medication adherence on hospital days, ER visits, and outpatient visits.[29] The annual medical spending per patient with diabetes was projected to decrease by $4,413 for all adults and by $5,170 for those at the age of 65 years or older when MPR was ≥80%. A systematic review of the economic impact of medication adherence and/or persistence on the overall cost of T2D care found that the average total annual cost per patient ranged from $4,570 to $17,338, and medication adherence was inversely associated with total health care and hospitalization costs.[30]

Improved medication adherence has the potential to significantly impact T2D health care costs. Patients with T2D who evidenced an improvement in medication adherence had a 13% reduction in the risk of hospitalization or ER visits, while a 15% increase in hospitalization and ER visits was associated with worsening adherence over time.[31] Based on this analysis, improved adherence was projected to save $4.7 billion annually, while reduced incidence of poor adherence was projected to save $3.6 billion annually. Egede et al[27] compared a large group of poorly adherent Veterans Administration (VA) patients (5-year MPR of 58%) with a similar large group of adherent VA patients (5-year MPR of 93%) and found that the poorly adherent group had a 37% lower pharmacy cost and a 7% lower outpatient cost over the 5-year period (likely associated with a decreased use of health care resources), but the inpatient cost was 41% higher. Annual cost savings in the range of $661 million–$1.16 billion were projected in the VA system by improving adherence in the poorly adherent group.

In total, it is apparent that addressing problematic medication adherence in the T2D population offers the potential for dramatically reducing costs and improving care and outcomes for patients.

Key contributors to poor medication adherence

Studies based on large claim databases have identified key demographic factors, such as younger age, lower education level, and lower income, that are associated with poor medication adherence in T2D,[24,32] but it may be of greater importance to identify those critical factors that are potentially modifiable. In total, the available body of data points to six key factors: perceived treatment efficacy, hypoglycemia, treatment complexity and convenience, cost of treatment, medication beliefs, and physician trust. It should be noted that many additional factors have been described in the extant literature (eg, depression, forgetfulness, and limited diabetes knowledge), but we suggest that it is these six factors that may be the most critical as well as the most amenable to change:

1. Perceived treatment efficacy: Patients are more likely to be adherent to medication regimens when they have