Insulin Dosing and Outcomes Among Commercially Insured Patients With Type 2 Diabetes in the United States

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ABSTRACT

Purpose: The purpose of this study was to examine costs, resource use, adherence, and hypoglycemic events among patients with type 2 diabetes mellitus (T2DM) treated with increasing doses of 100-U/mL (U-100) insulin regimens.

Methods: Data from Truven's Health Analytics Commercial Claims and Encounters database from January 1, 2008, through January 31, 2011, were used. Regressions were used to examine the associations among costs, resource use, adherence, and receipt of a hypoglycemic event and index dose of insulin. Specifically, general linear models with a γ-distribution and log link were used to examine costs, whereas logistic and negative binomial regressions were used to examine resource use and hypoglycemic events. All analyses controlled for patient characteristics, preindex comorbidities, general health, use of antidiabetic medications, and visits to an endocrinologist.

Findings: The study focused on 101,728 individuals with T2DM who received an outpatient prescription for U-100 insulin. In general, costs and resource use are highest among patients treated with the highest dose of insulin (>300 U/d). For example, all-cause and diabetes-related hospitalizations and office visits were highest in the highest-dose cohort. Costs generally followed the same pattern. Patients who were prescribed the lowest dose of insulin (10-100 U/d) generally had higher all-cause or diabetes-related inpatient and emergency department costs and resource use compared with those patients with an index dose >100 to 150, >150 to 200, and >200 to 300 U/d. There were generally no significant differences in rates of hypoglycemic events based on index dose.

Implications: These results suggest significant differences in patient outcomes based on dosing of insulin. Those patients with T2DM using insulin at the highest and lowest dose ranges have the highest costs and resource use. (*Clin Ther*. 2015;37:2297–2308) © 2015 The Authors. Published by Elsevier HS Journals, Inc.

Key words: adherence, costs, dosing, hypoglycemia, insulin, resource use.

INTRODUCTION

Diabetes mellitus is a highly prevalent, chronic condition that can lead to severe complications, such as kidney failure, lower-limb amputations, blindness, heart disease, stroke, and early death.[1,2] Currently in the United States, 11.3% of the adult (≥20 years of age) population has diabetes,[1] and approximately one-third of Americans are predicted to have this diagnosis by the year 2050.[3] The total cost of the disease in the United States in 2012 was $245 billion, comprising $176 billion in direct medical costs and $69 billion in decreased productivity.[4]

Of all diabetes cases, approximately 5% are type 1 diabetes mellitus (T1DM) and 90% to 95% are type 2 diabetes mellitus (T2DM).[2] Metformin therapy, in combination with lifestyle interventions, is the first line of treatment for T2DM.[5] However, individuals with T2DM often require insulin treatment over time

Accepted for publication August 6, 2015.
http://dx.doi.org/10.1016/j.clinthera.2015.08.004
0149-2918/$ - see front matter

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because of the progressive loss of β-cell function.[6] In 2011, an estimated 24.1% of US adults with T2DM used insulin.[7,8] Insulin therapy is the oldest and most effective glucose-lowering treatment available,[5] and patients with T2DM taking insulin soon after the failure of oral antidiabetic therapy have a greater likelihood of attaining the standard glycemic control (hemoglobin A_{1c} [HbA_{1c}] $<7\%$) relative to those whose insulin treatment is delayed.[9,10]

Given the increasing use of insulin, as well as the increasing prevalence of T2DM among young adults,[11] the present study sought to examine associations between insulin dosing and outcomes among the US working-age adult population with T2DM. To this end, this retrospective study used a medical insurance claims database to examine the records of patients at varying doses of standard strength (100 U/mL [U-100]) insulin. Outcomes of interest included costs, resource use, adherence, and hypoglycemic events.

METHODS

The Truven Health Analytics Marketscan® Commercial Claims and Encounters database provided the data used in this retrospective analysis. Encompassing a geographically diverse population of insured patients in the United States, the database contains demographic characteristics and enrollment information, as well as inpatient, outpatient, and prescription drug claims. All data were fully compliant with the Health Insurance Portability and Accountability Act.

This study examined the associations between a patient's highest mean daily dose of insulin for 90 days and direct medical costs, resource use, adherence, and probability of a hypoglycemic event. The mean daily dose during a 90-day period was calculated based on the quantity of insulin prescribed during a 90-day period and the number of days of insulin covered by the prescription. The use of a 90-day period was chosen because HbA_{1c} measurement generally measures the amount of glucose that binds to hemoglobin during a 3-month period,[12] as well as the fact that the American Diabetes Association states that HbA_{1c} measurement "approximately every 3 months determines whether a patient's glycemic targets have been maintained."[13]

The insulin was from pens or vials that contained U-100 insulin, which is the standard strength of nonconcentrated insulin distributed in the United States,[14–16] and the total daily dose encompassed basal (intermediate or long-acting insulin), bolus (rapid or short-acting insulin), or premixed formulations (of basal and bolus). The highest mean daily dose found in any 90-day timeframe during the study period was defined as the index dose range, and the first day in this 90-day window was identified as the index date. Patients were excluded if their highest mean daily dose was <10 U or >2500 U. Patients were then grouped based on their index dose range of 10 to 100, >100 to 150, >150 to 200, >200 to 300, and >300 to 2500.

Patients identified as having T2DM were included in the analysis based on the following criteria: (1) receipt of at least one diagnosis of T2DM in the 1 year before index date (ie, the preindex period) and no receipt of diagnosis of T1DM in the preindex period; (2) receipt of at least 2 diagnoses of T2DM in the preindex period and no more than 1 receipt of T1DM in the preindex period; or (3) receipt of an oral antidiabetic in the preindex period. Given that research has found differences in patient outcomes, costs, and adherence between U-500 insulin users and high-dose U-100 insulin users,[17,18] patients receiving U-500 insulin were excluded. Females were also excluded if they were pregnant at any time from the start of the preindex period through the end of the postindex period. In addition, patients were required to have had continuous insurance coverage from the start of the preindex period through the end of the postindex period. Finally, given that our database spanned the time horizon from January 1, 2007, through December 31, 2011, our 1-year preindex and 1-year postindex necessitated that the index date be between January 1, 2008, and January 1, 2011. These inclusion and exclusion criteria yielded a sample of 101,728 individuals. **Figure 1** illustrates how each of these criteria affected sample size.

Outcomes of interest were measured during the 1-year postindex date and included costs, resource use, adherence, and hypoglycemic events. Medical costs for these analyses were proxied by total gross payments to all providers who submitted claims for covered services rendered and were inflated to 2011 dollars using the medical component of the Consumer Price Index.[19] Costs were also categorized as all-cause or diabetes related if they had an accompanying diagnosis of 250.xx or were for receipt of antidiabetic medication or diabetic supplies. Within the all-cause