Clinical and Economic Outcomes Associated With the Timing of Initiation of Basal Insulin in Patients With Type 2 Diabetes Mellitus Previously Treated With Oral Antidiabetes Drugs

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ABSTRACT

Purpose: In patients with type 2 diabetes mellitus (T2DM) not achieving glycemic targets using oral antidiabetes drugs (OADs), studies suggest that timely insulin initiation has clinical benefits. Insulin initiation at the early versus late stage of disease progression has not been explored in detail. This retrospective database analysis investigated clinical and economic outcomes associated with the timing of insulin initiation in patients with T2DM treated with ≥1 OAD in a real-world US setting.

Methods: This study linked data from the Truven Health MarketScan® Commercial database, Medicare Supplemental database, and Quintiles Electronic Medical Records database. A total of 1830 patients with T2DM were included. Patients were grouped according to their OAD use before basal insulin initiation (1, 2, or ≥3 OADs) as a proxy for the timing of insulin initiation. Clinical and economic outcomes were evaluated over 1 year of follow-up.

Findings: During follow-up the 1 OAD group, compared with the 2 and ≥3 OADs groups, had a greater reduction in glycosylated hemoglobin A_{1c} (−1.7% vs −1.0% vs −0.9%, respectively; $P < 0.0001$), greater achievement of glycemic target (38.2% vs 26.7% vs 19.6%, respectively; $P < 0.0001$), and a lower incidence of hypoglycemia (2.7% vs 6.6% vs 5.0%, respectively; $P = 0.0002$), with no difference in total health care costs ($21,167 vs $21,060 vs $20,133, respectively).

Implications: This study shows that early insulin initiation (represented by the 1 OAD group) may be clinically beneficial to patients with T2DM not controlled with OADs, without adding to costs. This supports the call for timely initiation of individualized insulin therapy in this population.

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Key words: early insulinization, economic outcomes, insulin initiation, type 2 diabetes.

INTRODUCTION

After diagnosis of type 2 diabetes mellitus (T2DM), lifestyle changes and oral antidiabetes drugs (OADs) are recommended.[1] If blood glucose targets are not achieved with first-line therapy after approximately 3 months, guidelines from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) advocate the addition of another OAD or insulin to the treatment regimen.[1] Importantly, the treatment regimen should be tailored to each patient's needs. However, because of the progressive nature of diabetes, most patients will eventually need insulin therapy to maintain or achieve glycemic targets (generally glycosylated hemoglobin A_{1c} [A1C] <7.0%).[1,2]

Several clinical studies suggest that timely initiation of insulin therapy is beneficial for patients with diabetes.[3–5] However, the differences between initiating insulin when a patient is unable to control hyperglycemia on an OAD or at a later stage of a patient's disease progression when taking multiple OADs have not been examined fully. This is important because many patients with T2DM with inadequate glycemic control using OADs endure

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a prolonged glycemic burden before they begin insulin therapy.[6,7] Clinical inertia, the failure to intensify treatment despite a patient not meeting glycemic targets, may be a contributing factor.[8,9] Both patients and physicians are responsible for clinical inertia: concerns about hypoglycemia, weight gain, and injectable agents contribute to resistance to the initiation of insulin therapy.[10] However, the association between the timing of insulin initiation and health care outcomes in real-world settings, including the economic impact, remains to be explored.

This analysis assessed the clinical and economic outcomes associated with the timing of basal insulin initiation in US patients with T2DM previously treated with ≥1 OAD.

METHODS

Study Design and Patients

This was a retrospective database analysis of combined data from 3 databases: 2 Truven Health MarketScan databases (Claims and Encounters [Commercial] and Medicare Supplemental and Coordination of Benefits [Medicare]) and the linked Quintiles Electronic Medical Records (EMR) database. These 3 sources provided data for patients insured commercially or through Medicare and information from their EMR. The MarketScan Commercial database contains the health care experience of ~39.5 million employees and their dependents, covered under a variety of fee-for-service and managed-care health plans. The MarketScan Medicare database contains the health care experience of ~3.4 million retirees with Medicare supplemental insurance paid for by employers. Both the MarketScan Commercial and Medicare databases provide detailed cost, use, and outcomes data for health care services performed in the inpatient and outpatient settings. The Quintiles EMR database contains ambulatory clinical data from >9000 providers and covers >13.5 million unique patient lives.

A hybrid deterministic-probabilistic approach was used to link a subset of patients in the MarketScan databases to the Quintiles EMR database at the patient level. The deterministic match required an exact match on several variables from both sources, including the 3-digit ZIP code of residence, sex, and month and year of birth. The probabilistic match involved finding exact matches for ≥3 physician visits. Physician visits were selected as the attribute for matching due to likely agreement between medical records and claims data. In total, 1,348,279 patients were included in the linked MarketScan and Quintiles database.

Patients included in the study were 18 years of age or older and received a diagnosis of T2DM between July 1, 2004 and December 31, 2011. Eligible patients were defined as having had ≥1 inpatient visit or ≥2 non-inpatient visits (≥30 days apart) with a primary or secondary diagnosis of T2DM (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnosis code 250.x0 or 250.x2).[11] Patients initiated on a basal insulin (neutral protamine Hagedorn [NPH] insulin, insulin glargine, or insulin detemir) between July 1, 2004 and December 31, 2010 (index date) and who were also receiving ≥1 class of OADs (metformin, sulfonylureas, thiazolidinediones, α-glucosidase inhibitors, meglitinides, dipeptidyl peptidase-4 inhibitors) at baseline were included. Patients were required to have had continuous health care coverage for 6 months before (baseline) and 12 months after (follow-up) initiation of insulin. Baseline A1C values and weight measurements were available for all patients.

Patients were excluded from the study if they had filled any prescription claims for insulin during the baseline period other than rapid-acting insulin claims within 15 days before insulin initiation, which could be initiated in addition to basal insulin as part of a basal bolus insulin treatment regimen.

The study population was stratified by the number of baseline OADs (1, 2, or ≥3) as a proxy for the timing of insulin initiation relative to diabetes disease progression. This was based on previous[12] and current[1] ADA guidelines on pharmacological therapy for hyperglycemia in T2DM in which the recommendation is to start with OAD monotherapy (metformin or a sulfonylurea), and insulin may be added to either an OAD or subsequently to a combination of OADs.

Baseline Measures

Patient demographic and clinical variables comprised sex, age, weight, body mass index (BMI), duration of diabetes, comorbidities, Deyo-modified Charlson Comorbidity Index,[13] hypoglycemic events, and A1C values for the 6-month baseline period or 15 days after the index date. If there were multiple measurements during the baseline period, the value from the test closest to the index date was used.