Cost-Effectiveness of Switching Patients with Type 2 Diabetes from Insulin Glargine to Insulin Detemir in Chinese Setting: A Health Economic Model Based on the PREDICTIVE Study

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A B S T R A C T

Objectives: To evaluate the long-term cost-effectiveness of switching from insulin glargine (IGla) to insulin detemir (IDet) in patients with type 2 diabetes in the setting of Chinese secondary and tertiary hospitals. **Methods:** A published and validated computer simulation model of diabetes (the Center for Outcomes Research model) was used to make the long-term (30 years) projection of health economic outcomes. Patient demographic information and clinical end points were derived from a subgroup analysis of the Predictable Results and Experience in Diabetes through Intensification and Control to Target: an International Variability Evaluation (PREDICTIVE) study. Baseline risk factors and racial characteristic data were obtained from Chinese cohort studies. The diabetes management and complications costs were obtained from Chinese published data and adjusted to 2010 values by using the Chinese consumer price index. An annual discounting rate of 3% was used for both health and cost outcomes, and one-way sensitivities analysis was performed, which illustrated that the results were

robust. **Results:** Conversion to IDet from IGla was projected to improve patient life expectancy by 0.06 year and 0.48 quality-adjusted life-years. Drug costs and management costs of diabetes mellitus were increased by US$368 (US$17,466 vs. US$17,097) and US$31 (US$5464 vs. US$5433), respectively. However, the costs of complications, including cerebrovascular disease, renal complications, ulcer/amputation/neuropathy, eye complications, and hypoglycemia events, were reduced by US$819 (US$21,294 vs. US$22,114), resulting in a total direct medical cost saving of US$420 when converting to IDet. **Conclusions:** Conversion to IDet from an IGla regimen improved life expectancy and was a cost-saving treatment approach in a Chinese setting.

Keywords: Chinese setting, cost-effectiveness, cost-utility, insulin detemir.

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Introduction

The effective prevention and management of diabetes mellitus (DM) is an increasing serious challenge to China. The China National Diabetes and Metabolic Disorders Study estimated that the age-standardized prevalence of diabetes and prediabetes was 9.7% and 15.5%, respectively, accounting for 92.4 million adults with diabetes and 148.2 million adults with prediabetes in China [1]. According to another survey conducted by the Ministry of Health [2], type 2 DM (T2DM) constitutes about 95% of all patients and the total costs of DM in China were estimated to be $20.5 billion for 2007, which accounted for 14.2% of national health-care expenditures [3].

In China, DM-related complications are the key driver of medical costs. The results of the first national DM-related complications survey based on a sample of 24,496 patients with diabetes in China showed that 73.2% of patients with diabetes had one or more complications [4]. The research conducted by Chen et al. [5] revealed that the annual direct medical cost of patients with complications was increased by 3.71 times compared with that of those without complications.

In the treatment of DM, insulin plays an important role. Earlier use of insulin in patients with T2DM will help to better control the glucose level and reduce the risk of complications. Detemir and glargine are both long-acting human insulin analogues used for maintaining the basal level of insulin. They have been proved to more closely reflect physiological basal insulin and are associated with a significantly less risk of hypoglycemia and weight gain [6,7]. Two pharmacoeconomic studies conducted in Germany [8] and the United States [9] evaluated the cost-effectiveness of detemir based on the clinical results of the German PREDICTIVE study. Moreover, other researches from the United Kingdom [10], Canada [11], and Europe [12] also systematically evaluated the long-term health benefits of detemir caused by the reduction in the hemoglobin A_{1c} (Hb A_{1c}) level.

Insulin detemir came to the Chinese market in 2010 and is being used in secondary and tertiary hospitals in China. To better inform the insurance coverage decision makers and the doctors whether it is value for money in the long run, it is necessary to assess the long-term cost-effectiveness of insulin detemir com-

pared with that of the existing long-acting human insulin analogues such as insulin glargine.

This study was conducted to quantify the long-term cost-effectiveness of insulin detemir compared with that of insulin glargine for the treatment of T2DM in China from a societal perspective, and to assess the sensitivity of results to disutility values.

Methods

Model

We used a validated computer simulation model of diabetes (the Center for Outcomes Research [CORE] model) specifically for diabetes to convert the short-term clinical effects to long-term economic outcomes [13]. The model is based on a series of submodels that simulate the important complications of DM. Each submodel is a Markov model using Monte Carlo simulation. The CORE model takes into account baseline cohort characteristics, history of complications, current and future diabetes management and concomitant medications, screening strategies, and changes in physiological parameters over time. The development of complications, life expectancy, quality-adjusted life-year (QALY), and total costs within populations can be calculated. Furthermore, the reliability of simulated outcomes has been tested [13,14].

Treatment effects

The treatment effects were derived from the Korean cohort of the PREDICTIVE study [15]. In the research, subjects who required changing treatment, as assessed by their treating physicians, were transferred to insulin detemir ± oral antidiabetic drugs (OADs) from insulin glargine ± OADs. The major reasons why the treating physicians transferred a patient to insulin detemir included the following: 1) improve glycemic control (89%); 2) reduce plasma variability (53%); 3) patient's dissatisfaction with current therapy (33%); and 4) improve weight control (29%). Because PREDICTIVE is an observational study based on everyday clinical practice, the treating physicians could adjust the patient's OADs and insulin detemir dose and frequency for the duration of the study according to the patient's situation.

The subgroup research of the Korean cohort of the PREDICTIVE study included 875 patients with T2DM who transferred to insulin detemir ± OADs from insulin glargine ± OADs. Reported changes in the Hb A_{1c} level, body mass index (BMI), and hypoglycemic event rate were applied in the simulation as shown. After 3 months of treatment, subjects were associated with a reduction of 0.20% and 0.12 kg/m^2 in the Hb A_{1c} level and BMI, respectively. The hypoglycemic event rates were lower in patients using insulin detemir.

Simulation cohort

A hypothetical simulation cohort was generated on the basis of patient demographics, risk factors, and preexisting complications. The patient demographics corresponded with the values from the Korean arm of the PREDICTIVE study [15]. Other data were extracted from published country-specific articles [16–20] (see Table 1 [Inputs for Chinese simulation cohort with T2DM] in Supplemental Materials found at doi:10.1016/j.jval.2011.11.018). We defined this cohort including 1000 persons.

Costs and perspective

Direct medical costs were accounted from a society perspective in 2010 US dollars. Direct costs were taken to be the sum of patients' management costs and DM-related complications costs. The costs of lost productivity due to illness and death were excluded.

The management costs and DM-related complications costs were referred to the results of the survey conducted by the IMS Health in six tertiary and three secondary hospitals in China [21]. Complication costs refer to medical expenditure that resulted from diabetes-related complications. Management costs refer to administration devices and blood glucose monitoring and took into account OAD usage and variations in insulin dosage as noted in the PREDICTIVE study. The outpatient visit services and others including screening services were included. All the costs were inflated to 2010 values by using the consumer price index of health care, which was 3.2% in 2009, 2.9% in 2008, and 2.1% in 2007, respectively [22]. The annual medication costs were calculated and are shown in Table 2 (Cost data for management and diabetes-related complications in China for 2010) in Supplemental Materials found at doi:10.1016/j.jval.2011.11.018.

Quality of life and utilities

Quality-adjusted life expectancy was incorporated into the analysis by using diabetes-related health state utility and event disutility values published by Palmer et al. [13]. A disutility value of −0.0035 was applied for each minor hypoglycemic event (an event not requiring hospitalization) recorded in the simulation. To capture the reduced utility associated with major hypoglycemic events, a disutility value of −0.0118 was applied. Hypoglycemia disutility values were derived from a published source [23].

Discounting and time horizon

All costs and clinical benefits were discounted at an annual rate of 3.0% in accordance with recommendations by the World Health Organization [24]. Furthermore, to reflect the chronic nature of T2DM and capture both mortality and the incidence of DM-related complications over patient lifetime, the clinical and economic impact of treatment with insulin detemir was prolonged to 30 years.

Sensitivity analysis

Several one-way sensitivity analyses were performed to examine the influence of key input parameters on the outcomes projected by the model. The varying parameters included time horizon (10, 20, or 30 years), discounting rate (0% or 10%), hypoglycemic event rate (assume same), BMI (assume same), and the reduction in the Hb A_{1c} level (assume Hb A_{1c} benefits reduced by 50%).

Statistical methodology

A simulated cohort of 1000 patients was run through the model 1000 times for each simulation (base-case and sensitivity analysis). The mean and standard deviation values were generated by using a nonparametric bootstrapping approach. One thousand mean values of incremental costs and incremental effectiveness in terms of quality-adjusted life expectancy were plotted on a cost-effectiveness plan. For treatment that was not dominant, it was planned to generate an acceptability curve by calculating the proportion of points below a range of willingness-to-pay threshold.

Willingness to pay

There is no specific threshold to judge the cost-effectiveness of an intervention in China. According to World Health Organization recommendations [24], if the incremental costs per effectiveness are not more than three times the gross domestic product per capital, the intervention could be regarded as cost-effective. With gross domestic product per capital for China in 2010 at US$3750, we used a willingness-to-pay threshold of US$11,250 in this analysis to determine the likelihood of insulin detemir being considered cost-effective in China.