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Cost-effectiveness of dapagliflozin (Forxiga®) added to metformin compared with sulfonylurea added to metformin in type 2 diabetes in the Nordic countries

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ABSTRACT

Aims: The aim of this study was to assess the long-term cost-effectiveness of dapagliflozin (Forxiga®) added to metformin, compared with sulfonylurea (SU) added to metformin, in Nordic Type 2 diabetes mellitus (T2DM) patients inadequately controlled on metformin.
Methods: Data from a 52-week clinical trial comparing dapagliflozin and SU in combination with metformin was used in a Cardiff simulation model to estimate long term diabetes-related complications in a cohort of T2DM patients. Costs and QALYs were calculated from a healthcare provider perspective and estimated over a patient's lifetime.
Results: Compared with metformin + SU, the cost per QALY gained with dapagliflozin + metformin was €7944 in Denmark, €5424 in Finland, €4769 in Norway, and €6093 in Sweden. Metformin + dapagliflozin was associated with QALY gains ranging from 0.236 in Norway to 0.278 in Sweden and incremental cost ranging from €1125 in Norway to €1962 in Denmark. Results were robust across both one-way and probabilistic sensitivity analyses. Results were driven by weight changes associated with each treatment.
Conclusions: Results indicate that metformin + dapagliflozin is associated with gains in QALY compared with metformin + SU in Nordic T2DM patients inadequately controlled on metformin. Dapagliflozin treatment is a cost-effective treatment alternative for Type 2 diabetes in all four Nordic countries.

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1. Introduction

Rapidly increasing prevalence of Type 2 diabetes mellitus has developed into a major health concern worldwide [1–3]. The treatment goal in T2DM is to achieve blood glucose (HbA1c) control and to avoid diabetes-related complications. Although ensuring adequate long-term blood glucose control is emphasized as one of the key goals of T2DM treatment [4,5], minimizing the risk for hypoglycemia and avoiding weight gain are also important considerations [6]. Yet, hypoglycemia is a commonly observed side effect of diabetes treatments such as sulfonylurea and insulin [6]. Experiencing hypoglycemic events negatively affects patients' Health Related Quality of Life (HRQoL) [7–9].

Another common side effect of some diabetes treatments (e.g. sulfonylurea and insulin) is weight gain [6,10]. Excess weight is directly linked to worsened insulin resistance, high cardiovascular morbidity and mortality risks, and continually increasing economic burden [3,10–14]. However, achieving and maintaining the treatment goals remains challenging as around 80% of T2DM patients suffer from overweight [9]. Optimizing diabetes management therefore requires a multifactorial approach to treatment which goes beyond glycemic control and encompasses other risk factors such as reduction of blood pressure, blood lipid levels, and weight.

Dapagliflozin (Forxiga®) is the first compound of the new class of sodium-glucose co-transporter 2 (SGLT-2) inhibitors for the oral treatment of T2DM. Dapagliflozin reduces HbA1c and body weight significantly and has a positive impact on blood pressure [15]. Compared with sulfonylureas, the most commonly used oral antidiabetics beside metformin, dapagliflozin showed similar HbA1c reduction, but was associated with significant weight loss and significantly fewer hypoglycemic events. Dapagliflozin is thus an alternative to sulfonylureas for T2DM patients inadequately controlled on metformin plus diet/exercise [15].

This study examines the long-term cost-effectiveness of metformin + dapagliflozin compared with metformin + SU in T2DM patients in Denmark, Finland, Norway, and Sweden.

2. Materials and methods

2.1. Model

This analysis uses a simulation model based on a previously developed model designed for evaluating treatment regimens in T2DM [16,17]. Our model uses the UKPDS 68 equations to forecast the occurrence of seven diabetes-related events and death [18]. We simulate a T2DM patient cohort consisting of 10 000 individuals over 40 years (a lifetime horizon as the baseline age is 58 years). The model reports the number of cumulative diabetes-related complications (macro- and microvascular events), hypoglycemia events avoided, diabetes mortality, non-diabetes mortality, and cost-effectiveness results. The costs and QALYs associated with each treatment are calculated from a healthcare provider perspective. Based on country-specific pharmacoeconomic guidelines, future costs and benefits were discounted at the rate of 3% annually in Sweden, Finland and Denmark and 4% in Norway. The discount rate was varied in the one-way sensitivity analysis.

Baseline demographics and modifiable risk factors define a time-dependent risk-factor profile, which determines the patient's risk of developing diabetes-related complications. The baseline demographics are set at the start of the analysis, and are updated with time in the model, while the modifiable risk factors (HbA1c, weight, etc.) are altered by drug treatment over time.

Diabetes-related events have a direct impact on costs and utilities. Utility weights are applied to the event both in the year of occurrence and where relevant also in subsequent years.

The impact of uncertainty around model inputs is assessed both in a one-way sensitivity analysis and a probabilistic sensitivity analysis (PSA) performed as a second order Monte-Carlo simulation. HbA1c lowering effects associated with treatment and control, weight changes, and symptomatic hypoglycemic events are sampled from a normal distribution, the probability of a severe hypoglycemic event and utility decrements from a beta distribution, and costs from a gamma distribution.

2.2. Patient population, treatment strategies, HbA1c threshold, and outcomes

The analyzed patient population is characterized by a demographic and risk factor profile taken from the study of Nauck et al. [15] (Table 1), a randomized controlled trial where 801 individuals received either metformin + dapagliflozin or metformin + SU.

Diabetes is a progressive disease, meaning that HbA1c-levels increase over time also in patients who receive treatment. In our analysis, the HbA1c progression is modeled based on the glucose profile observed in the UKPDS trial [18]. The slopes of the HbA1c curves, which determine the pace at which the blood glucose increases over time, are assumed to be identical for both arms.

When HbA1c reaches a threshold level of 7.5%, treatment intensification is needed and a patient is switched to rescue therapy – NPH insulin [5]. An HbA1c threshold of 8% is tested in one-way sensitivity analyses.

2.3. Weight gain

The utility impact of weight change is modeled linearly, so that each unit change in BMI is associated with an identical utility weight. This linear approach gives a conservative estimate of the utility decrements associated with weight gain, as the disutility of weight gain increases with body weight and has been found to be larger than the positive impact of weight loss [7]. Body weight changes also have an impact on the long-term risk of cardiovascular complications [11].

2.4. Hypoglycemia

We differentiate between symptomatic and severe hypoglycemic events, where a severe event is defined as a major symptomatic episode requiring 3rd party assistance due to severe impairment in consciousness [15]. Each drug therapy is