Type 2 Diabetes Mellitus Treatment Patterns Across Europe: A Population-based Multi-database Study

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ABSTRACT

Purpose: The aim of this study was to determine the similarities and differences of type 2 diabetes mellitus (T2DM) treatment patterns in daily practice in 5 European countries and whether these reflect differences in guidelines.

Methods: Prescriptions for drugs used in diabetes treatment during a 5-year study period were obtained from electronic databases. Patients initiating T2DM treatment during the study period were included. An SAS analysis tool was developed to create episodes of use of drug classes, which resulted in treatment patterns.

Findings: A total of 253,530 patients initiating T2DM treatment during the study period were included; 52% to 55% were male, and the mean age ranged from 62 to 67 years. Metformin was the most common initial treatment in all countries. After initial therapy, most patients in the Netherlands, Spain, and the United Kingdom switched to a combination of metformin + a sulfonylurea derivative (SU). In Italy, metformin in combination with an SU was outnumbered by "other treatment," mainly because of repaglinide use. In France, treatments including dipeptidyl peptidase-4 inhibitors were most frequent as second- and fourth-line treatment. Metformin monotherapy was again most commonly observed as the third line of treatment in all countries. Fourth treatment was a combination of metformin + an SU in the Netherlands and Spain; in the United Kingdom and France, dipeptidyl peptidase-4 inhibitors were the most frequently used fourth line of treatment.

Implications: This study provides a comprehensive overview of T2DM treatment patterns among patients initiating T2DM treatment in 5 European countries. There were differences, especially regarding the uptake of newer incretin-based treatments, which are usually prescribed as a second and/or third treatment in agreement with local guidelines. These variations reflect the differences between the national guidelines of these countries. (*Clin Ther.* 2017;39:759–770)

Key words: diabetes mellitus, type 2, guidelines, Europe, hypoglycemic agents, treatment pattern.

INTRODUCTION

Changes in lifestyle and ageing of the population have led to an increasing prevalence of type 2 diabetes mellitus (T2DM) worldwide.[1–3] Hyperglycemia is a

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risk factor for excess microvascular and macrovascular complications and mortality.[4] Although initial glycemic control may be achieved through diet and exercise,[5] pharmacologic intervention is necessary at some stage in most patients.

Most European countries have a national guideline on T2DM, and the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) have developed a consensus approach to the management of hyperglycemia to help guide health care providers in choosing the most appropriate interventions for their patients with T2DM.[6] At the time of conducting this study, 8 different blood glucose–lowering drug classes were approved for the treatment of T2DM in Europe: metformin, sulfonylurea derivatives (SUs), α-glucosidase inhibitors (AGIs), thiazolidinediones (TZDs), dipeptidyl peptidase-4 inhibitors (DPP-4i), meglitinides, glucagon-like peptide-1 receptor agonists (GLP-1RAs), and insulin.

The international guidelines for use of these therapies share the common goal of preventing and treating symptoms and microvascular and macrovascular complications by achieving/sustaining glycemic control.[6–11] In general, these guidelines recommend starting pharmacologic treatment with metformin and intensifying treatment as the disease progresses or treatment fails to achieve or sustain the glycemic goals (Table). However, the guidelines differ in recommendations regarding the type of intensification. Disparities in guideline recommendations can differ for several reasons, such as the influence of professional bodies and characteristics of health care systems.[12] Intensification of treatment by adding an SU is well established in the ADA/EASD consensus[6] and the Netherlands,[8] Spain,[9] and the United Kingdom.[7] The guidelines from Italy[10] and France,[11] however, are less strict and offer multiple treatment options as early as the second line of treatment. Guidance for third-line treatment also differs, with strict approaches recommended by the ADA/EASD consensus, the Netherlands, and the United Kingdom (eg, by adding insulin), compared with the addition of a third oral drug, GLP-1RA, or insulin in Spain.

Furthermore, the newer incretin-based classes of DPP-4i and GLP-1RAs, which were introduced in the last decade, have different places in the various guidelines,[6–11] partly due to limited safety information and the higher cost of these classes. With these variations in mind, the present study analyzed the similarities and differences of T2DM treatment patterns in actual practice in 5 European countries and whether these reflected differences in the international guidelines.

MATERIALS AND METHODS

Setting

All data for this observational cohort study were obtained from population-based electronic health care databases from 5 European countries: the PHARMO Database Network[13] in the Netherlands, the Health Search Longitudinal Patient Database[14,15] in Italy, the Sistema d' Informació per al Desenvolupament de la Investigació en Atenció Primària[16,17] in Catalonia, Spain, the Echantillon Généraliste de Bénéficiaires[18] in France, and The Health Improvement Network[19,20] (THIN) in the United Kingdom. The PHARMO Database Network is a population-based, patient-centric data tracking system that currently comprises demographic and health care databases, including patient demographic characteristics, mortality, drug dispensing, hospital morbidity, clinical laboratory, pathology findings, and general practitioner information. The Health Search Longitudinal Patient Database contains patient demographic details that are linked by using an encrypted patient code with medical records, drug prescription information, prevention records, hospital admission, and date of death. The Sistema d' Informació per al Desenvolupament de la Investigació en Atenció Primària database includes common clinical variables (eg, smoking, alcohol drinking, body mass index, blood pressure), primary care laboratory results (eg, glycosylated hemoglobin [HbA_{1c}], glucose), pharmacy invoice data, and hospital discharge information.

THIN is an observational database of electronic health care records from primary care practices throughout the United Kingdom. Demographic and administrative data, primary and secondary care diagnoses, and prescription treatments are routinely recorded against date in individual patient records. The Echantillon Généraliste de Bénéficiaires is a permanent random sample with a 1/97 representation of the nationwide claims and hospitalization database. (Système National d'Information InterRégimes de l'Assurance Maladie SNIIRAM), which covers >98% of the French population from birth (or immigration) to death (or emigration), even if a subject changes occupations or retires. It includes general characteristics, outpatient reimbursed health