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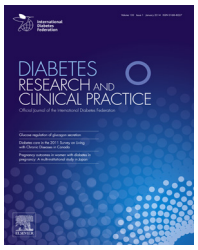

Patterns and determinants of new first-line antihyperglycaemic drug use in patients with type 2 diabetes mellitus

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ABSTRACT

Aims: We evaluated the patterns and determinants that influence the selection, timing and duration of first-line antihyperglycaemic drug (AHD) treatment in patients with type 2 diabetes in Germany, focusing specifically on treatment-naive AHD initiators.

Methods: Pharmacy dispensing claims data were linked with a cohort of patients newly enrolled in a German Disease Management Program for type 2 diabetes (DMP-DM2) between 2003 and 2009. We examined uptake of first-line pharmacotherapy in previously unmedicated patients and identified predictors of receiving AHD therapy in general and metformin in particular using multivariable regression analyses.

Results: There were 27,138 unmedicated patients with type 2 diabetes and 47.0% of them were started on AHD treatment within 5 years after enrollment. Initial severity of diabetes was the major predictor of receiving first-line pharmacotherapy. Metformin accounted for 63% of newly prescribed AHD in 2003 and more than 80% in 2009 while sulfonylureas accounted for only 10%. Initiating metformin as first-line AHD was associated with younger age, higher BMI, lower HbA1c, and shorter diabetes duration (multivariate $p < 0.001$ for all). Therapy switch or step-up was less frequent among metformin initiators than sulfonylurea initiators.

Conclusions: The majority of patients were not started on AHD therapy within 5 years after enrollment. In line with recent therapy guidelines, current first-line antihyperglycaemic treatment was increasingly based on metformin. AHD initiators started on sulfonylurea were generally more advanced in their disease and were started later on primary pharmacotherapy.

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Abbreviations: ADA, American Diabetes Association; AHD, antihyperglycaemic drugs; ATC, Anatomical Therapeutic Chemical Classification System; DDG, Deutsche Diabetes Gesellschaft; DMP-DM2, disease management program for type 2 diabetes mellitus; EASD, European Association for the Study of Diabetes.

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1. Introduction

Germany is one of the European countries with the highest numbers of patients with type 2 diabetes [1]. The prevalence of type 2 diabetes was recently estimated at 7.2% among the 18- to 79-year-old resident population, posing substantial challenges for the health care system [2,3]. In 2003, statutory health insurance funds in Germany introduced Disease Management Programs for type 2 diabetes (DMP-DM2) to better address the growing diabetes epidemic and to improve the quality of diabetes care [4]. A major objective of the DMP-DM2 is the provision of antihyperglycaemic drug (AHD) treatment in accordance with evidence-based guidelines [5]. It is well established that an optimized antihyperglycaemic therapy is essential for reducing elevated blood glucose levels and preventing short and long-term complications of type 2 diabetes [6].

The most widely prescribed oral first-line AHD is metformin which has been recommended for previously untreated patients with type 2 diabetes [6]. The ADA/EASD guideline of 2006 highlighted beneficial effects of metformin for all patients independent of body weight and endorsed its use as the main first-line pharmacotherapy [7] giving it clear precedence over first-line alternatives, such as sulfonylureas or other AHD.

Detailed utilization studies focusing on antihyperglycaemic drugs in Germany are rare and often based on reports of physicians or patients rather than on prescription data sources [8–10]. At the international level, various drug utilization studies, differing in research aims and extent, examined anti-diabetic treatment patterns [11–18]. However, only a limited number of studies focused on initial pharmacotherapy selection and changes from initial to subsequent therapy [19,20]. Thus, little is known in detail about how the utilization parameters of antihyperglycaemic pharmacotherapy, that is, drug selection, timing and continuity, actually evolved over recent years following the ADA/EASD guidelines.

The first objective of this study was, therefore, to determine predictors of receiving first-line AHD therapy in a cohort of patients with type 2 diabetes who were treatment-naive at DMP enrollment and evaluate in detail the AHD utilization patterns by use of detailed pharmacy dispensing claims data. The second aim was to compare the two largest groups of AHD initiators in order to obtain further insights into AHD prescribing patterns and their determinants.

2. Materials and methods

We conducted a cohort study within a DMP-DM2 organized by AOK NordWest, a statutory health insurance fund in the Northwest of Germany. The DMP-DM2 was implemented in 2003 and is open to all AOK members with type 2 diabetes; however, participation is self-selective on a voluntary basis. Major elements of the DMP-DM2 are regular physician–patient consultations, regular determination of laboratory values, patient education, a standardized documentation of the course of the disease and evidence-based antihyperglycaemic treatment. The study cohort consisted of patients who were between 40 and 79 years old when they enrolled in the DMP between June 2003 and December 2009 and who were resident in the region of Westphalia-Lippe. Patient characteristics age, body mass index (BMI), HbA1c, smoking status, and year of diabetes diagnosis were recorded at the time of DMP-DM2 enrollment. In addition, AOK NordWest provided the complete and detailed individual pharmacy dispensing records of each DMP patient for the entire time of DMP involvement, including ATC codes for each dispensed anti-diabetic drug, the date of each dispensing, the package size and the defined daily doses (DDD) contained in each package. These data were linked with the DMP data of the above defined cohort. Due to local data confidentiality regulations, record linkage was executed with encrypted personal identifiers. Details of data encryption and the stochastic record linkage procedures, and their performance, have been reported before [21]. The study was approved by the ethics committee of the responsible medical council.

To determine predictors and patterns of first-line pharmacotherapy use among patients who had not been treated with AHD before, we assembled a study cohort of AHD treatment-naive patients. Patients were considered as initially untreated when they had not been treated with any AHD in the six months prior to each patient's individual day of DMP-DM2 enrollment. In a first analysis step, patients were followed until they were started on anti-diabetic drug therapy, death or study end date (31st of December 2010), whichever came first. We determined baseline characteristics of the treatment-naive cohort at DMP enrollment and identified predictors of receiving pharmacotherapy during study duration by conducting a Cox proportional hazards model including information on sex, age, BMI, HbA1c, smoking status, diabetes duration and concurrent treatment with lipid-lowering medication or anti-hypertensive medication at enrollment.

Among the drug initiator group, patients were then assigned to groups of first-line treatment based on the first dispensing for any AHD after enrollment, and the dispensing date was defined as the first-line treatment index date. We distinguished the following classes of antihyperglycaemic drugs (AHD): metformin, sulfonylureas (including sulfonylurea analogs), insulin therapies (including human insulin, short acting insulin analogs, insulin glargine, insulin detemir) and other medications (including glitazones, DPP-4 inhibitors, GLP-1 analogs, alpha-glucosidase inhibitors). Patients who received a fixed-dose combination therapy or filled two prescriptions for any AHD on this index date were categorized as initiators of a first-line combination therapy. Cumulative incidence functions that accounted for competing risks were drawn for therapy start with the different AHD medication classes [22]. To depict temporal trends of first-line pharmacotherapy initiation, we determined the proportion of each AHD class among all new AHD users per calendar year.

In a second analysis step, we focused on the two largest groups of AHD initiators. The crude values for the characteristics of incident users of metformin were compared with those of incident users of the second most common drug class, the sulfonylureas. We further computed the adjusted odds ratios for starting on metformin, as compared to sulfonylureas, based on a logistic regression model which included year