



Contents lists available at ScienceDirect

## Journal of Diabetes and Its Complications

journal homepage: [WWW.JDCJOURNAL.COM](http://WWW.JDCJOURNAL.COM)

## Prevalence of depression in type 2 diabetes patients in German primary care practices

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### ARTICLE INFO

#### Article history:

Received 16 November 2015

Received in revised form 11 December 2015

Accepted 13 December 2015

Available online xxx

#### Keywords:

Diabetes

Psychosocial stressors

Primary care

Prevalence

Macrovascular disease

Microvascular disease

### ABSTRACT

**Aims:** To analyse depression in German type 2 diabetes patients with or without diabetes complications

**Methods:** Longitudinal data from nationwide general practices in Germany (n = 1,202) were analysed. People initially diagnosed with type 2 diabetes (2004–2013) were identified and 90,412 patients were included (age: 65.5 years, SD: 11.7). The main outcome measure was the first diagnosis of depression (ICD 10: F32, F33) within ten years after index date in patients with and without diabetes complications. Cox proportional hazards models were used to adjust for confounders.

**Results:** At baseline, most patients had diabetes complications and 6.4% of them had private insurance. Ten years after type 2 diabetes diagnosis, 30.3% of patients showed symptoms of depression. The prevalence of depression was higher in women than in men (33.7% versus 26.8%), in patients with high HbA1c levels (31.3% when HbA1c ≥ 9 versus 27.5% when HbA1c < 7) and in patients with diabetes complications (37.7% when there were more than two complications versus 29.1% when there were no complications). Women and patients without private health insurance were at a higher risk of developing depression. Retinopathy, neuropathy, nephropathy, coronary heart disease, stroke and HbA1c levels higher than 7 were also positively associated with depression.

**Conclusions:** Diabetes complications and high HbA1c levels had a substantial impact on depression in primary care patients with type 2 diabetes.

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### 1. Introduction

Diabetes and depression are highly prevalent in Europe. There are about 60 million adults with diabetes in this region of the world (10.3% of men and 9.6% of women) and prevalence of the chronic condition is increasing across all age groups, in parallel to an increase in overweight and obesity, unhealthy diet and physical inactivity (WHO, 2015a). Millions of European people, the majority of them women, suffer from serious depression during their lives and 50% of these cases remain untreated (WHO, 2015a,b). As diabetes and depression are common disorders in Europe and as the associated costs for European countries already exceed millions of euros, the relationship between the two warrants careful examination.

A number of works have already shown an association between diabetes and depression (Snoek, Bremmer, & Hermanns, 2015). In 2001, Anderson, Freedland, Clouse, and Lustman (2001) analysed 42

studies aimed at the estimation of depression prevalence in people with type 1 and type 2 diabetes. They showed that the presence of diabetes doubled the odds of comorbid depression and their finding was later confirmed by other studies on the topic (Roy & Lloyd, 2012). They also demonstrated that the prevalence of depression was even higher in people with diabetes when the chronic condition was reported by the patient him/herself rather than by clinicians (Snoek et al., 2015). More recently, another meta-analysis indicated a significant link between treatment non-adherence in diabetes and depression (Gonzalez et al., 2008), underlining the tenuous link between the mental disorder and treatments regulating glycaemia, at least in cases of type 2 diabetes (Zhang et al., 2015). Finally, the association between the two disorders is not unidirectional; depression is also known to predispose individuals to diabetes (Pan et al., 2010), and the association is therefore considered bidirectional.

Despite these works, the relationship between depression and diabetes is still poorly understood (Snoek et al., 2015), with no real consensus as to whether it is causal or merely coincidental. Although depression usually appears before the ages of 25–30, type 1 diabetes and type 2 diabetes often arise in childhood and later in life respectively. Therefore, risk factors related to depression may not be the same for both forms of diabetes. Although depression is more

Funding sources: None.

Conflict of interest: None.

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<http://dx.doi.org/10.1016/j.jdiacomp.2015.12.013>

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prevalent in people with diabetes, it was recently shown that patients newly diagnosed with type 2 diabetes do not display an increased risk of developing depression (Skinner et al., 2010). Another interesting result is that patients exhibit low levels of distress and anxiety during the first years of the chronic condition (Thoolen, de Ridder, Bensing, Gorter, & Rutten, 2006), suggesting that early and intensive treatments can influence the occurrence of depression. Intriguingly, people with diabetes also reported high distress upon diagnosis (85.2% of patients felt shocked, guilty, angry, anxious, depressed, or helpless) (Peyrot et al., 2005). Finally, several authors have shown that complications related to diabetes are additional risk factors for depression (Badawi et al., 2013; Pouwer et al., 2003). The goal of the present study was to analyse depression in German patients with type 2 diabetes, in the presence or absence of diabetes complications.

## 2. Patients and methods

### 2.1. Database

The Disease Analyzer database (IMS HEALTH) compiles drug prescriptions, diagnoses, basic medical and demographic data obtained directly and in anonymous format from computer systems used in the practices of general practitioners (Becher, Kostev, & Schröder-Bernhardi, 2009). Diagnoses (ICD-10), prescriptions (Anatomical Therapeutic Chemical (ATC) Classification System) and the quality of reported data have been monitored by IMS based on a number of criteria (e.g. completeness of documentation, linkage between diagnoses and prescriptions).

In Germany, the sampling method used for the selection of physicians' practices is appropriate for obtaining a representative database of primary care practices. The sampling is based on summary statistics from all doctors in Germany published yearly by the German Medical Association. IMS uses these statistics to determine the panel design according to the strata including specialist group, German federal state, community size category and age of physician (Becher et al., 2009).

This database was shown to be representative of general practice in Germany from the perspective of regional, gender and age stratification (Becher et al., 2009).

Prescription statistics for several drugs were very similar to data available from pharmaceutical prescription reports (Becher et al., 2009). The age groups for given diagnoses in Disease Analyzer also agreed well with those in corresponding disease registries (Becher et al., 2009).

### 2.2. Study population

Patients initially diagnosed with type 2 diabetes mellitus (ICD 10: E11) between January 2004 and December 2013 (index date) were identified by 1202 general practitioners (GPs) in the IMS Disease Analyzer database. Patients were included in the analysis only if: (i) they did not suffer from depression prior to index date, (ii) their follow-up lasted more than a year, (iii) they were more than 40 years old. Selected patients were observed for up to ten years after the index date, the latest follow-up date for any patient being March 31, 2015. A total of 90,412 patients were available for analysis.

### 2.3. Study outcome

The main outcome measure was the first diagnosis of depression (ICD 10: F32, F33) within ten years after index date. Only confirmed diagnoses were included, meaning that depression was documented by general practitioners after a first diagnosis either performed by a psychiatrist or a general practitioner. The share of patients with depression was estimated in presence and in absence of different diabetes complications.

### 2.4. Independent variables

Demographic data included age, gender and health insurance type (private or statutory). Several complications related to diabetes and co-morbid conditions were determined based on primary care diagnoses (ICD-10 codes): retinopathy (E11.5), neuropathy (E11.4), nephropathy including renal insufficiency (E11.2, N18, N19), coronary heart disease (I20, I24, I25), myocardial infarction (I21, I22, I23), peripheral artery disease (E11.5, I73.9) and stroke (I63, I64, G45). These complications and conditions could occur throughout the entire follow-up period prior to initial diagnosis of depression or, when there was no depression diagnosis, prior to the end of follow-up. In addition, diagnosed hypertension (I10), lipid disorders (E78) and obesity (E66) were assessed for each study individual. Mean HbA1c values for the follow-up time of study patients were calculated and included as an independent variable. Finally, prescriptions of oral antidiabetic drugs and insulin treatments were determined for each patient.

### 2.5. Statistical analyses

Descriptive analyses were obtained for all demographic variables and diagnoses and mean  $\pm$  SD were calculated for normally distributed variables. Depression-free survival analyses were carried out using Kaplan–Meier curves and log-rank tests. Kaplan–Meier curves were stratified by gender, HbA1c levels and presence of diabetes complications. Multivariate Cox proportional hazards models (dependent variable: incident depression) were used to adjust for confounders (gender, private insurance, diabetes complications, co-diagnoses and prescriptions). Diabetes duration is an important factor both in the development of diabetes complications and in the development of depression. Yet according to our study, diabetes duration is automatically considered as the follow-up time, since we start on the day of the first diabetes diagnosis. Since we present Kaplan–Meier curves showing time to development of depression, they also automatically indicate the correlation between diabetes duration and depression incidence.

P-values  $<$  0.05 were considered statistically significant. The analyses were carried out using SAS version 9.3.

## 3. Results

### 3.1. Patient characteristics

A total of 90,412 primary care patients were diagnosed with diabetes in German practices between January 2004 and December 2013. The clinical characteristics of these patients are shown in Table 1. As expected, the mean age was 65.5 years and most of these older patients had diabetes complications or co-diagnoses, most commonly hypertension, lipid metabolism and coronary heart disease (79.7%, 56.0% and 28.8% respectively). 19.7% of them also had high levels of HbA1c, indicating poor glycaemic control. 5786 patients (6.4%) had private insurance. Finally, 75.0%, 5.5% and 12.5% of patients were treated with oral antidiabetic drugs, insulin, and both medications, respectively (7.0% of them did not receive any antihyperglycaemic therapy).

### 3.2. Shares of patients with depression

The Kaplan–Meier curve for time to diagnosis of depression in patients newly diagnosed with type 2 diabetes is shown in Fig. 1. 5.9%, 17.7% and 30.3% of patients displayed depression one, five and ten years after the diabetes diagnosis, respectively. The same analyses were performed for gender, mean HbA1c value and number of complications and co-diagnoses (Figs. 2, 3 and 4 respectively). The prevalence of depression was higher in women (33.7%) than in men (26.8%) ten years after diagnosis of type 2 diabetes. We also showed

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