Effects of the COVID-19 pandemic on clinically diagnosed psychiatric disorders in persons with type 2 diabetes

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Abstract
Aims: To examine whether the incidence rates of diagnosed depression, anxiety disorders and stress reactions, as well as prescription rates of antidepressants and anxiolytics were higher during the COVID-19 pandemic than before in persons with type 2 diabetes in Germany. Contrary to earlier studies, clinical diagnoses of psychiatric disorders (ICD classification) were used.

Methods: The German Disease Analyzer (DA) database is an outpatient database containing routine data on patients’ diseases and treatments provided by a representative panel of physician practices selected from across Germany. We assessed incidence rates of depressive disorders (ICD-10: F32, F33), anxiety disorders (F41) and stress reactions (F43) in quarters from January 2019 to March 2021 in 95,765 people with type 2 diabetes included in the DA in 2019 (mean age 68.9 years, 58% men). Prescription rates of antidepressants and anxiolytics in quarters from January 2020 to March 2021 were compared with prescription rates from 1 year earlier.

Results: During the study period, the incidence rate of newly diagnosed depressive disorders in persons with type 2 diabetes declined slightly, while the incidence rates of anxiety and stress disorders remained largely constant. The rates of new prescriptions for antidepressants and anxiolytics were lower in all quarters of 2020 and in the first quarter of 2021 than in the quarters 1 year earlier. Diabetes-related complications were more prevalent in persons with incident psychiatric disorders than in those without.

Conclusions: No increase in the incidence rates of clinically diagnosed psychiatric disorders was observed during the COVID-19 pandemic in Germany in persons with type 2 diabetes.

Keywords
antidepressants, anxiety, COVID-19, depression, diabetes, SARS-CoV-2, stress
1 | INTRODUCTION

Among people with COVID-19, those who also have diabetes have an increased risk of COVID-19-related mortality and severe COVID-19 courses.\(^1\)\(^3\) In a meta-analysis, people with COVID-19 and diabetes were found to have 1.90 (95% confidence interval (CI): 1.37–2.64) times higher odds of death from COVID-19, and 2.75 (95% CI: 2.09–3.62) times higher odds of severe COVID-19 courses than people without diabetes.\(^2\) As a result, persons with diabetes may recognize their increased vulnerability to poor COVID-19 outcomes, and this awareness may impact their mental health. Apart from these health risks for persons with diabetes who contract the virus, concerns about worse diabetes management during the pandemic, for example, difficulties in visiting the doctor, obstacles preventing exercise, may also contribute to poorer mental health.\(^4\)\(^5\) Given these unique pandemic-related burdens for people with diabetes, we hypothesized that they would also experience poorer mental health.

Most studies to date on psychiatric disorders in persons with diabetes during the lockdown were cross-sectional,\(^6\)\(^\text{–}^\text{17}\) and only a small number of studies had a pre-pandemic study period.\(^18\)\(^\text{–}^\text{21}\) Many studies took the form of online surveys.\(^6\)\(^\text{–}^\text{11,14\text{–}17,20}\) Consequently, they are not fully representative and may be affected by selection bias. In addition, diabetes diagnoses in web-based surveys are based on self reports and cannot be validated. Furthermore, self-administered questionnaires were used in the earlier studies on the topic.\(^6\)\(^\text{–}^\text{21}\) Although these questionnaires are validated, they may not be equivalent to a clinical diagnosis by a physician.

The aim of the present study was to compare the incidence of clinically diagnosed depressive disorders, anxiety disorders, and stress reactions in people with type 2 diabetes in Germany during the pandemic with the corresponding incidence 1 year earlier. We also compared people with diabetes and incident psychiatric disorders to those without incident psychiatric disorders with regard to glucose control, features of the metabolic syndrome, and diabetes-related complications. We used routine data from general practices in Germany for this purpose.

2 | METHODS

2.1 | Data source

For the present study, we used data from the German Disease Analyzer (DA), a large outpatient database supplied with data by a representative panel of general and specialist practices selected across Germany. Data from specialists in the field of psychiatry are not included in the DA. Routine data on diseases and treatments are transmitted directly to IQVIA (Frankfurt/Main) by the computers of the physicians’ offices, and are anonymized in accordance with data protection regulations. IQVIA is a healthcare data science company in Germany. The main purpose is to provide data for real-world effectiveness studies, by both academic researchers and pharmaceutical companies. Diagnoses are based on ICD-10 (International Classification of Diseases, 10th revision) codes, and prescription data are based on the European Pharmaceutical Marketing Research Association (EphMRA) Anatomical Therapeutic Chemical (ATC) classification system. Previous studies have shown that the practice panel is representative of general and specialty practices in Germany\(^2^2\)\(^,^2^3\) and that the prevalence and incidence of chronic diseases in the database correspond to national data from the Federal Statistical Office.\(^2^3\)

German law allows the use of anonymous electronic medical records for research purposes under certain conditions. This legislation specifies that it is not necessary to obtain informed consent from patients or approval from a medical ethics committee for this type of observational study, which contains no directly identifiable data. As patients were only queried as aggregates and no protected health information was available for queries, no Institutional Review Board approval was required for the use of this database or the completion of this study.

Novelty statement

- Some survey data suggest that persons with type 2 diabetes are experiencing more depression, anxiety and stress during the SARS-CoV-2 pandemic.
- There is a lack of studies on clinically diagnosed, ICD coded depression, anxiety disorders and stress reactions in persons with type 2 diabetes during the pandemic.
- Our nationwide retrospective study showed that incidence rates of clinically diagnosed psychiatric disorders did not increase during the pandemic compared with pre-pandemic baseline periods.
- In assessing the mental health of persons with type 2 diabetes during the COVID-19 pandemic, it is necessary to distinguish between self-reported data and clinical diagnoses requiring medical treatment.
2.2 Study population and variables

The study included all persons with a diagnosis of type 2 diabetes (ICD-10: E11) in 2018 or earlier with at least one visit to a Disease Analyzer physician practice in 2019 and in 2020, and with no diagnosis of anxiety, depression or stress disorder by 2018. In order to check whether the number of visits to the doctor decreased in 2020, we estimated the median numbers of visits to the doctor in 2019 and 2020 by patients with a diagnosis of type 2 diabetes in 2018 or earlier with no diagnosis of anxiety, depression or stress disorder by 2018.

Psychiatric disorders were identified by ICD-10 codes: anxiety disorders (F41), depression (F32, F33), and severe stress and adjustment disorders (F43). EphMRA ATC codes were N06A for antidepressants, and N05B, N05C for hypnotics, sedatives, and tranquilizers. For comorbidities, diagnoses noted included coronary heart disease (I24, I25), renal disease (E11.2, E14.2, N18, N19), myocardial infarction (I21—I23), stroke or transient ischemic attack (TIA) (I63, I64, G45), and polyneuropathy or diabetic foot (E11.4, E14.4, G63). EphMRA-ATC codes were C03, C07, C08, C09 for anti-hypertensives, C10 for lipid-lowering drugs, and A10C, A10H, A10J, A10K, A10L, A10M, A10N, A10P, A10S for glucose-lowering drugs. BMI, systolic and diastolic blood pressure, HDL and LDL cholesterol, triglycerides, HbA1c, fasting glucose, and creatinine, were recorded in 2019 and 2020, respectively, only for some patients with diabetes.

2.3 Statistical analyses

Incidence rates with 95% confidence intervals (CI) of depressive disorders, anxiety disorders, and stress reactions were estimated for nine successive quarters from January 2019 to March 2021. Rates of new prescriptions with corresponding 95% CIs for antidepressants (ATC: N06A) and hypnotics, sedatives, tranquilizers (ATC: N05B, N05C), respectively, were estimated by quarters (January 2019 to March 2021). For each quarter of the year 2020, incidence rates of psychiatric disorders were compared with incidence rates of the corresponding quarters in 2019, and differences in incidence rates (95% CI) between the 2 years were estimated. Analogously, for each of the four quarters in the year 2020, prescription rates of antidepressants and anxiolytics were compared with the corresponding prescription rates observed in each respective quarter 1 year earlier, and differences in prescription rates with 95% CIs were estimated. Furthermore, differences in incidence rates with 95% CIs, and differences in prescription rates with 95% CIs, respectively, were estimated as part of the comparison of the first quarter 2020 with the first quarter 2021. In addition, the analyses for incidence rates of psychiatric disorders were stratified by baseline age (18–40, 41–60, 61–80, ≥80 years). Furthermore, characteristics of patients with an incident psychiatric disorder (depressive disorder, anxiety disorder and stress reaction) were compared with the characteristics of those without such disorders: age, sex, BMI, systolic and diastolic blood pressure, HbA1c, fasting glucose, serum lipids, drug intake and complications of diabetes. Differences in means and proportions, respectively, were estimated with 95% confidence intervals.

All statistical analyses were performed using SAS Version 9.4 (SAS Institute, Cary, USA).

3 RESULTS

Of the 124,505 persons with a diagnosis of type 2 diabetes in 2018 or earlier who did not have a diagnosis of psychiatric disorder by 2018, 95,765 (76.92%) had at least one visit to the doctor in 2019 and in 2020, and thus fulfilled the inclusion criteria (Table 1; Table S4). Of these 124,505 persons, the median of the number of visits to the doctor was 11 (q1 = 6, q3 = 17) in 2019, compared with 11 (q1 = 6, q3 = 17) in 2020.

The mean age of patients in 2019 was 68.9 years, and 58% were men. The mean HbA1c was 7.0% (53.0 mmol/mol) in both years. Between 2019 and 2020, there were hardly any changes in systolic and diastolic blood pressure, HDL and LDL cholesterol, triglycerides, HbA1c, fasting glucose, and creatinine, were recorded in 2019 and 2020, respectively, only for some patients with diabetes.

The incidence rate of depressive disorders was 26.5 (95% CI: 25.5–27.5) and 23.3 (95% CI: 22.3–24.3) per 1000 person-years in 2019 and 2020, respectively. The corresponding figures were 7.8 (95% CI: 7.3–8.4) and 8.9 (95% CI: 8.3–9.5) per 1000 person-years for anxiety disorders, and 15.0 (95% CI: 14.2–15.8) and 14.1 (95% CI: 13.4–14.9) per 1000 person-years for stress disorders. The incidence rates of newly diagnosed depressive disorders declined steadily between January 2019 and March 2021, whereas the incidence rates of anxiety and stress disorders remained largely constant during this period except for some small fluctuations (Figure 1). For depressive disorders and stress reaction, the incidence rates in all quarters of 2020 and in the first quarter of 2021 were lower than or equally high to those as 1 year before (Table 2; Figure 1). As an example, in the last quarter of 2020 the number of
TABLE 1  Characteristics of persons with type 2 diabetes in primary care practices in 2019 to 2020 (Disease Analyzer, Germany)

| N                           | Proportion of patients with ≥1 measurement in 2019 | 2019 | Proportion of patients with ≥1 measurement in 2020 | 2020 |
|-----------------------------|--------------------------------------------------|------|--------------------------------------------------|------|
|                             | 95,765                                           |      | 95,765                                           |      |
| Age (years)                 | 68.9 (12.8)                                      |      | 69.9 (12.8)                                      |      |
| Sex (n, male (%))           | 55,384 (57.7)                                    |      | 55,264 (57.7)                                    |      |
| BMI (kg/m²)                 | 21.8% (6.1)                                      |      | 13.6% (6.2)                                      |      |
| Systolic blood pressure (mmHg) | 27.8% (19.1)                              |      | 25.8% (19.0)                                     |      |
| Diastolic blood pressure (mmHg) | 27.6% (10.6)                                 |      | 25.7% (10.5)                                     |      |
| HbA1c [%]                   | 56.9% (1.2)                                      |      | 52.1% (1.2)                                      |      |
| HbA1c (mmol/mol)            | 56.9% (12.7)                                     |      | 52.1% (12.8)                                     |      |
| Fasting glucose (mmol/l)    | 45.4% (2.8)                                      |      | 42.0% (2.8)                                      |      |
| HDL cholesterol (mmol/l)    | 42.3% (0.35)                                     |      | 39.6% (0.35)                                     |      |
| LDL cholesterol (mmol/l)    | 46.2% (0.99)                                     |      | 44.3% (1.00)                                     |      |
| Triglycerides (mmol/l)      | 42.4% (1.18)                                     |      | 41.0% (1.17)                                     |      |
| Creatinine (μmol/l)         | 53.2% (31.8)                                     |      | 52.1% (34.5)                                     |      |
| eGFR (ml/min/1,73 m²)⁴      | 53.2% (22.3)                                     |      | 52.1% (22.4)                                     |      |
| Anti-hypertensives (%)      | 72.2                                            |      | 72.0                                             |      |
| Lipid-lowering drugs (%)    | 42.3                                            |      | 42.4                                             |      |
| Glucose-lowering drugs (%)  | 73.2                                            |      | 72.2                                             |      |
| Coronary heart disease (%)  | 14.0                                            |      | 13.9                                             |      |
| Renal disease (%)           | 11.6                                            |      | 12.6                                             |      |
| Myocardial infarction (%)   | 1.5                                             |      | 1.5                                              |      |
| Stroke or transient ischemic attack (%) | 3.1  |      | 3.3                                              |      |
| Polyneuropathy or diabetic foot (%) | 12.9 |      | 14.8                                             |      |

Note: Type 2 diabetes: ≥1 confirmed diagnosis of ICD 10 E11 in 2018 or earlier.
Data are means (standard deviation) or median (interquartile range) [triglycerides, creatinine] or proportions (%).
Abbreviation: eGfR, estimated glomerular filtration rate.
⁴eGFR was estimated using the CKD Epi formula.

FIGURE 1  Incidence of depressive disorders, anxiety disorders and stress reactions (per quarter, per 1000 persons, with 95% confidence intervals) in people with type 2 diabetes from January 2019 to March 2021
incident depressive disorders per 1000 person-years was 0.63 (95% CI: −0.06–1.33) lower than in the last quarter of 2019 (Table S1). One exception was the second quarter of 2020, in which the incidence rate of anxiety disorders was 0.76 (95% CI: 0.36–1.16) incident cases per 1000 person-years higher than 1 year earlier. Likewise, age-stratified analyses showed no increases or at most very small increases in incidences for all three psychiatric disorders. Incidences are presented for the three psychiatric disorders separately for patients with type 2 diabetes aged 18–40, 41–60, 61–80, and ≥80 years in Table S3a–d. Across all age strata, patients showed no worsening of anxiety disorders, stress reactions and depression.

The rates of new prescriptions of antidepressants were lower in all quarters of 2020 and in the first quarter of 2021 than in the respective quarters a year earlier (Table 3; Table S2; Figure 2A). For example, the rate of new prescriptions of antidepressants was 1.11 (95% CI: 0.48–1.75) per 1000 person-years lower in the last quarter of 2020 than in the last quarter of 2019 (Table S2). The same applies for the prescription of hypnotics, sedatives and tranquillizers (Table 3; Table S2; Figure 2B).

People with type 2 diabetes with an incident psychiatric disorder (depressive or anxiety disorder, or stress reaction) were slightly younger (68.0 vs. 70.0 years) and more often female (53.1% vs. 41.3%), but hardly differed from those without incident psychiatric disorders with regard to HbA1c, fasting glucose, BMI, blood pressure and levels of triglycerides and creatinine (Table 4). However, patients with diabetes and newly diagnosed psychiatric disorders more often had diabetes-related complications: 16.2% versus 13.9% for coronary heart disease (difference in prevalence (PD) = 2.3% (95% CI: 1.4–3.2)); 14.6% versus 12.3% for renal disease (PD = 2.3% (1.5–3.2)); 1.9% versus 1.5% for myocardial infarction (PD = 0.4% (0.1–0.7)); 4.5% versus 3.1% for stroke or transient ischemic attack (PD = 1.4% (0.9–1.9)); 16.1% versus 15.0% for polyneuropathy or diabetic foot syndrome (PD = 1.1% (0.2–2.0)).

4 | DISCUSSION

The present study including a large unselected sample of people with type 2 diabetes from primary care practices found no increase in the incidences rates of psychiatric disorders during the COVID-19 pandemic in Germany until March 2021. Likewise, there was no increase in the rates of new prescriptions of antidepressants, hypnotics, sedatives and tranquillizers. The proportion of persons with diabetes-related complications was larger in people with type 2 diabetes with incident psychiatric disorders.
4.1 | Comparison with other studies

High prevalences of psychiatric disorders were reported for 2020 in summary reviews and meta-analyses in the general population. For example, in one meta-analysis based on 16 studies, which were all cross-sectional but one, the mean prevalence of anxiety, depression and psychological stress was 38.1%, 34.3% and 37.5%, respectively. However, there is a lack of prospective, longitudinal studies comparing pre-pandemic prevalences to prevalences during the pandemic. Survey data on depression symptoms in US adults from spring 2020 were compared with data from the National Health and Nutrition Examination Survey (NHANES) from 2017 to 2018. Depression was measured using the Public Health Questionnaire 9 (PHQ-9), and the results of this study suggest that there were more persons with mild, moderate (14.8 vs. 5.7%) and severe (5.1 vs. 0.7%) depression during than before the pandemic.

Few studies have been completed to date on COVID-19 related depression, anxiety and stress in persons with diabetes. Many of these studies have significant limitations, for example, a cross-sectional study design and limited generalizability because they are web-based. Some studies have a very small sample size with less than 120 participants, whereas one study was based solely on the observations of nurses regarding patients with diabetes. The cross-sectional studies produced inconclusive results: in persons with diabetes, higher psychiatric disorders were reported in some studies but not in all.

There are currently only a small number of longitudinal studies on depression, anxiety and stress in persons with diabetes which also include a pre-pandemic baseline period. These studies also yielded inconsistent results. In the Look AHEAD (Action for Health in Diabetes) cohort study, data from 2829 adults (mean age 75.6 years) from two pre-pandemic visits were compared with data from a visit during the pandemic in July–December 2020. Patient Health Questionnaire-8 was used to assess depressive symptoms. Although differences in the prevalences of depressive symptoms in the two pre-pandemic visits were small, larger differences were observed between the second pre-pandemic visit and the visit during the pandemic: there was an increase from 19.3% to 30.4% for mild or greater depressive symptoms, and from 4.6% to 8.5% for moderate or greater depressive symptoms.

In a Danish study of two user panels consisting of people with diabetes who volunteered to share personal information, 1,366 people with diabetes filled in questionnaires at six points in time during the first 3 months of the pandemic. Levels of psychological distress and of anxiety were lower in June 2020 than in March 2020. In the Australian PREDICT Study with 489 participants, grades
of anxiety and depressive symptoms in mid-2020 were compared with pre-pandemic levels. The study found no deterioration in anxiety and depressive symptoms but did reveal a reduction in diabetes distress. For the GAD-7, 8.4% of the study participants showed moderate to severe anxiety before and during the pandemic (22.4% and 16.4%, respectively, showed mild anxiety symptoms). On the PHQ-8 questionnaire, 5.3 and 5.6%, respectively, showed major symptoms of depression before and during the pandemic.

The main difference between these earlier studies and the present study is that in the earlier studies survey data were used to assess depressive symptoms, anxiety symptoms and stress, whereas in the present study clinical diagnoses based on ICD 10 codes were used. Increased levels of self-reported symptoms found in some studies may be appropriate reactions to the additional burden faced by patients with diabetes during the pandemic. However, such self-reported mental health problems may require little or no treatment contrary to severe psychological disorders documented by clinical diagnoses. Thus, COVID-19 may have a negative impact on the mental health of people with diabetes, as shown in some of the online surveys mentioned above, but hardly cause severe clinically relevant psychiatric disorders, as shown in the present study.

In view of the particular health risks facing people with diabetes who contract COVID-19, and the potential difficulties in managing diabetes during the pandemic, the results of the present study warrant some explanations. The participants of this study had a mean age of 69 years in 2019, and most of them therefore were not affected by home office regulations, fear of job loss and home schooling, which is also a burden for the parents of school-age children. Accordingly, a study in the general population in Germany found an increase in self-reported depressive symptoms and anxiety disorders only in people under 60 years of age. However, in the present study, no worsening in depression, anxiety disorders or stress reactions was observed in the age groups 41 to 60 years or 18 to 40 years. One reason why the stress of the pandemic...
did not lead to an increase in psychiatric disorders in patients with diabetes may be that the pandemic was seen as a societal crisis to be managed collectively, meaning that pandemic-related stress differed from the other stresses from daily life and did not cause psychiatric disorders. It is also conceivable that some patients did not see their GP or diabetologist because of the lockdown or because of fear of contracting the virus, and their psychiatric disorders went unnoticed as a result. However, the median number of visits to the doctor among all patients with a diagnosis of diabetes by 2018 who did not have a psychiatric disorder by 2018 was 11 in both 2019 and 2020. This may be an indication that there was no strong selection bias due to the number of persons who stayed at home and did not see their doctor in 2020.

In line with previous studies, in the present analysis, persons with type 2 diabetes with incident psychiatric disorders were more often female, more often took anti-hypertensives and more often had diabetes-related complications than patients without psychiatric disorders. However, no differences were observed in HbA1c, glucose and lipid levels. A study from the Arabian Gulf region identified other risk factors for depression and anxiety in persons with diabetes during the pandemic, that is, cancellation of visits to the doctor, lack of telecommunication contact with the diabetes clinic, and HbA1c ≥ 10%. A Dutch study found that difficulties in glycaemic control were associated with stress, but not with anxiety.

Our study has several strengths. First, our study was, to the best of our knowledge, the first to use clinically coded diagnoses for anxiety, depression and stress, whereas earlier studies used self-reported data. This made it possible to investigate severe psychiatric disorders requiring treatment. Second, our study was longitudinal in design, contrary to most other studies on the topic which were cross-sectional. Third, the sample size was much larger.
than that of all earlier studies on the same topic. Fourth, we used anonymized routine data collected by general practitioners so that recall bias and selection bias could not occur. Our study is also subject to several limitations, however. First, the data for the description of the study population are incomplete because the Disease Analyser database only includes data assessed by medical doctors in their clinical practices. If a general practitioner does not measure a patient’s BMI or HbA1c in routine practice, these values are not included. Second, incidence rates of depression or anxiety disorders may be underreported because there may be still a stigma attached to these psychiatric disorders and because depression or anxiety disorders may have been diagnosed in some patients by a specialist in psychiatry without informing the family doctor. Third, we did not provide comparisons with persons without diabetes. To give an example, it is possible that the burden of stress is constant in persons with diabetes, whereas it could decline in persons without diabetes. In such a scenario, the psychiatric state of persons with diabetes would not deteriorate, but diabetes would nevertheless appear to have a negative impact on it. Fourth, our results may not be generalizable to other countries with different health care systems.

5 | CONCLUSION

Our study adds to earlier survey studies, some of which found that persons with diabetes exhibited more worries and more symptoms of depression and anxiety. The latter studies were based on self reports regarding mental health and showed that psychosocial health may have been affected during the pandemic. These results have to be taken seriously. Our study adds that there was no deterioration regarding clinical diagnoses of depression, anxiety and stress. Thus, it is important to distinguish between self-reported mental health problems, which may be influenced to a greater extent by the new burdens caused by the pandemic, and clinical diagnoses of psychiatric disorders, which often require pharmacological treatments.

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CONFLICTS OF INTEREST

There are no conflicts of interest to be disclosed.

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**SUPPORTING INFORMATION**

Additional supporting information may be found in the online version of the article at the publisher’s website.

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