Incidence of Type 2 Diabetes in People With a History of Hospitalization for Major Mental Illness in Scotland, 2001–2015: A Retrospective Cohort Study

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OBJECTIVE

To determine the incidence of type 2 diabetes in people with a history of hospitalization for major mental illness versus no mental illness in Scotland by time period and sociodemographics.

RESEARCH DESIGN AND METHODS

We used national Scottish population-based records to create cohorts with a hospital record of schizophrenia, bipolar disorder, or depression or no mental illness and to ascertain diabetes incidence. We used quasi-Poisson regression models including age, sex, time period, and area-based deprivation to estimate incidence and relative risks (RRs) of diabetes by mental illness status. Estimates are illustrated for people aged 60 years and in the middle deprivation quintile in 2015.

RESULTS

We identified 254,136 diabetes cases during 2001–2015. Diabetes incidence in 2015 was 1.5- to 2.5-fold higher in people with versus without a major mental disorder, with the gap having slightly increased over time. RRs of diabetes incidence were greater among women than men for schizophrenia (RR 2.40 [95% CI 2.01, 2.85] and 1.63 [1.38, 1.94]), respectively) and depression (RR 2.10 [1.86, 2.36] and 1.62 [1.43, 1.82]) but similar for bipolar disorder (RR 1.65 [1.35, 2.02] and 1.50 [1.22, 1.84]). Absolute and relative differences in diabetes incidence associated with mental illness increased with increasing deprivation.

CONCLUSIONS

Disparities in diabetes incidence between people with and without major mental illness appear to be widening. Major mental illness has a greater effect on diabetes risk in women and people living in more deprived areas, which has implications for intervention strategies to reduce diabetes risk in this vulnerable population.

The life expectancy of people with major mental illness, including schizophrenia, bipolar disorder, or major depressive disorder, is reduced by 10–20 years compared with the general population (1–3). This excess mortality is largely due to an increased risk of cardiovascular disease (3–6), for which type 2 diabetes is a major risk factor. Numerous studies have reported the higher prevalence of diabetes among those with a major mental disorder. Recent meta-analyses have demonstrated that,

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although estimates vary substantially across studies, the prevalence of type 2 diabetes is ~10% in those with schizophrenia and bipolar disorder and 8% in those with major depressive disorder (7–10). This relates to about a twofold increased prevalence of diabetes when compared with the general population after adjustment for age and could extend to as much as a three- to fourfold excess risk in some subgroups of the population. However, these estimates are almost entirely derived from cross-sectional studies, with few existing prospective studies on the incidence of diabetes in those with major mental illness. Where prospective studies have been carried out, they focused more on diabetes incidence among people with depression (11–13) than schizophrenia or bipolar disorder (14,15).

The association between major mental illness and diabetes is explained at least in part by key lifestyle factors such as BMI that are known to be associated with mental illness and are also major risk factors for type 2 diabetes. The relationship between major mental illness and diabetes risk factors might vary with age, sex, and socioeconomic status, providing the rationale for examining whether the association between major mental illness and subsequent diabetes might differ by these sociodemographic factors. However, this has been studied little in prospective studies. Meta-analyses have suggested that the association between depression in general and type 2 diabetes may be more marked in younger than in older people (11), but this suggestion is derived from cross-study comparisons rather than investigation of age differences within the same study population. Also, the prevalence of comorbid mental disorder and diabetes prevalence has been proposed to be higher in women than in men (8,16), based on cross-sectional data, with few prospective studies reporting sex-specific associations of comorbid mental disorder and diabetes. To our knowledge, no study has prospectively examined how the association between mental illness and type 2 diabetes differs by socioeconomic status. Similarly, to our knowledge, there have been no studies of time trends in type 2 diabetes incidence by major mental illness status, and so it is also unclear whether the difference in risk has narrowed or widened over time.

Therefore, in the current study we examined incidence of type 2 diabetes in Scotland from 2001 to 2015 among those with a prior hospital record for major mental illness versus those without a history of hospitalization for any mental health disorder, exploring differences by time period, age, sex, and socioeconomic status.

RESEARCH DESIGN AND METHODS

We used the Scottish Morbidity Record General/Acute Inpatient and Day Case (SMR01) data set and the Mental Health Inpatient and Day Case (SMR04) data set to identify hospital admissions where the discharge diagnoses included schizophrenia (ICD-10 F20 and F25 and ICD-9 295.0–295.3 and 295.6–295.9), bipolar disorder (ICD-10 F30 to F31 and ICD-9 296.0–296.1 and 296.4–296.7), or depression (ICD-10 F32-F34 and ICD-9 296.2–296.3, 298.0, and 311). We initially carried out exploratory analyses to investigate whether associations differed for people with an uncomplicated mental illness (i.e., diagnosis of a single mental illness) and complex mental illness (i.e., diagnoses of multiple mental illnesses). The patterns of associations were broadly similar. Hence, we applied a hierarchy of severity to assign people to one group only, ranking disorders as schizophrenia, bipolar disorder, and depression; thus, someone with a record of both bipolar disorder and depression was assigned to the bipolar group only. Individuals entered the cohort from the date of first hospital admission for the most severe of the three disorders. We identified prevalent cases of mental health disorder among those aged 18 years or older between 1 January 1981 and 31 December 2014.

Comparison Cohort

Our comparison cohort was derived from the total general population after removal of people who had a hospital record for any mental illness listed in ICD-10 chapter 5 (mental and behavioral disorders) or the corresponding ICD-9 codes, with the exception of organic disorders (F00–F09) and mental retardation (F70–F79). Details of the ICD codes used are provided in Supplementary Table 1.

Type 2 Diabetes

We identified incident cases of type 2 diabetes through a research extract of the Scottish Care Information–Diabetes (SCI-Diabetes) data set. This national diabetes register includes ~99% of all patients diagnosed with diabetes since 2004 (17), collating information from primary and secondary care clinics on clinical care, demographic, and lifestyle factors. It also includes information on people diagnosed with diabetes between 2001 and 2004 and who did not die during that time period. For research purposes, an algorithm is used to differentiate between type 1 and type 2 diabetes, based on clinician-recorded diagnosis, prescription data, and age at diabetes diagnosis. In this study, we included all incident type 2 diabetes cases occurring between 1 January 2001 and 31 December 2015.

Person-Time

We calculated person-time (in fractional years) for the mental health cohort from the date of hospital admission with a mental health disorder until the end date of follow-up. We followed the cohort until the earliest of type 2 diabetes diagnosis date, date of death, or end of follow-up (31 December 2015). We obtained person-time for the comparison population via midyear estimates of the population. Person-time after an event was subtracted from the estimates in each year.

Events and person-time were broken down by calendar year, age in 5-year categories, sex, and area-based deprivation. The latter was defined using quintiles of the Carstairs index, which uses census data at the postcode level on lack of car ownership, low occupational social class, overcrowded households, and male unemployment to create a measure of material deprivation of an area (18).

Statistical Analyses

We summarized baseline characteristics for the complete cohort and calculated age-standardized type 2 diabetes incidence rates, per 1,000 person-years, using the 2013 European Standard Population (see http://www.isdscotland.org/Products-and-Services/GPD-Support/Population/Standard-Populations/ for more details). We fitted quasi-Poisson models with incidence of type 2 diabetes as the outcome, which included main effects for history of a mental illness, age, sex, time period, and area-based deprivation index and all two-way interactions. Age (using the midpoint

of each 5-year block) and time period were modeled as continuous variables using natural cubic splines. Area-based deprivation index was modeled as a categorical variable. The models were used to calculate relative risks (RRs). All analyses were conducted using R software (19).

Ethics Approval

Approval for the linkage of the administrative health data sets used in this study was provided by the NHS Scotland Public Benefit and Privacy Panel for Health and Social Care. Approval for the use of diabetes data was obtained from the Scottish Diabetes Research Network, and ethics approval was obtained from the South East Scotland Research Ethics Committee (reference 16/SS/0152).

This article is written in accordance with the Strengthening Reporting of Observational Studies in Epidemiology (STROBE) (20) and REporting of Studies Conducted using Observational Routinely-collected health Data (RECORD) (21) statements.

RESULTS

Between 2001 and 2015, there were 246,046 incident type 2 diabetes cases in Scotland among people with no prior hospital record of a mental illness and 2,315 among those with a hospital record for schizophrenia, 1,720 among those with bipolar disorder, and 4,055 among those with depression.

Type 2 Diabetes Incidence by Mental Health Status, Age, and Sex

Type 2 diabetes incidence increased with increasing age (until ~60 years) in all groups, peaking at an earlier age among people with a mental disorder compared with those with no history of mental illness. Thus, the average age of type 2 diabetes onset was lower in people with an admission for schizophrenia (mean ± SD 51.4 ± 12.6 years) and depression (57.6 ± 13.1 years) but not bipolar disorder (60.0 ± 12.1 years) compared with the population with no mental illness (60.8 ± 13.2 years) (Table 1). In all comparison groups, age of onset was slightly younger in men than women and in the most versus least deprived in all groups. The age-standardized incidence of type 2 diabetes at all time points was higher among people with a hospital record for each mental disorder than the group without mental illness (Table 2). This concurred with predicted incidence rates obtained from quasi-Poisson models, as illustrated in Fig. 1, which shows type 2 diabetes incidence by age for the middle deprivation quintile in 2001 and 2015. Absolute rates of type 2 diabetes were higher in men than in women in all cohorts, although the difference in incidence was smaller for people with schizophrenia and bipolar disorder (Fig. 1).

Time Trends in Diabetes Incidence by Mental Disorder

Between 2001 and 2015, age-standardized type 2 diabetes incidence decreased overall in the group with no history of mental illness in both men and women. Among those with schizophrenia and bipolar disorder, type 2 diabetes incidence increased between 2001 and 2008 and then started to decrease up to 2015. In contrast, incidence of type 2 diabetes increased between 2001 and 2015 among people with a hospital record for depression. These findings are illustrated in Supplementary Fig. 1 with use of data from men and women aged 60 years and in the middle deprivation quintile. We observed similar patterns of type 2 diabetes incidence among those aged 40 and 50 years (especially for depression), although there was less of a decline in incidence in the cohort without mental illness compared with the 60 year olds and diabetes incidence tended to plateau from 2008 onward in people with schizophrenia and bipolar disorder (Supplementary Fig. 2). In general, having a hospital record for each mental disorder was associated with increased incidence of type 2 diabetes compared with the group without mental illness. For example, in 2015, among men aged 60 years and in the middle deprivation quintile, type 2 diabetes incidence was higher in those with schizophrenia (RR 1.63 [95% CI 1.38, 1.94]), in men with bipolar disorder (RR 1.50 [95% CI 1.22, 1.84]), and in men with depression (RR 1.62 [95% CI 1.43, 1.82]) compared with the group with no mental illness (Table 3). RRs were greater among women than men, with incidence of type 2 diabetes in 2015 almost 2.5-fold higher in women with schizophrenia (RR 2.40 [95% CI 2.01, 2.85]), 65% higher in those with bipolar disorder (RR 1.65 [95% CI 1.35, 2.02]), and 2.0-fold higher in those with depression (RR 2.10 [95% CI 1.86, 2.36]) compared with the group with no mental illness (Table 3). Among both men and women, RRs compared with the group without mental illness among those aged 60 years increased over time for the schizophrenia, depression, and, to a lesser extent, bipolar disorder cohorts (Table 3 and Supplementary Fig. 3). RR estimates over time followed similar patterns for ages 40 and 50 years (Supplementary Fig. 4).

Type 2 Diabetes Incidence by Mental Disorder, Sex, and Deprivation Level

The proportion of people in the most deprived quintile was much higher in the cohorts with schizophrenia (32.8%), bipolar disorder (27.0%), and depression (27.0%) than the comparison group (21.7%) (Table 1). Type 2 diabetes incidence was positively associated with deprivation among women in all cohorts and men with a mental disorder (Table 4 and Supplementary Fig. 5). We did not observe a deprivation gradient in type 2 diabetes incidence among men without mental illness at 60 years of age. For all disorders, the RR of type 2 diabetes incidence was greatest among people in the most deprived quintiles (Table 4). For instance, in 2015 the RR for type 2 diabetes incidence in 60-year-old men with versus without schizophrenia in the most deprived quintile was 1.69 (95% CI 1.45–1.98), whereas the association for men with versus without schizophrenia in the least deprived quintile was not statistically significant (RR 1.09 [95% CI 0.88, 1.36]). A similar pattern was observed among men with bipolar disorder and depression. RRs for women were larger than for men for all mental disorder groups. As with men, RRs were positively associated with deprivation, but in contrast to men, the association was statistically significant in the least deprived group. For example, schizophrenia was associated with 2.5-fold (RR 2.48 [95% CI 2.12, 2.91]) and 60% (RR 1.60 [95% CI 1.28, 2.01]) increased risk of type 2 diabetes incidence in the most and least deprived quintiles, respectively (Table 4). We observed similar deprivation gradients in type 2 diabetes among men and women aged 40 and 60 years with mental illness, with the deprivation pattern also evident among men without mental illness at age 40 years (but not 60) (Supplementary Fig. 6).

Table 1—Characteristics of people with incident type 2 diabetes by mental health disorder in Scotland, 2000–2015

	No mental illness	Schizophrenia	Bipolar disorder	Depression
N	246,046	2,315	1,720	4,055
Male, *n* (%)	136,753 (55.6)	1,361 (58.8)	683 (39.7)	1,664 (41.0)
Age at type 2 diabetes onset (years)				
All	60.8 ± 13.2	51.4 ± 12.6	60.0 ± 12.1	57.6 ± 13.1
Men	59.6 ± 13.7	49.1 ± 11.8	59.5 ± 11.9	56.8 ± 12.3
Women	62.3 ± 13.7	54.7 ± 12.9	60.3 ± 12.2	58.1 ± 60.3
Area-based deprivation quintile, *n* (%)*				
1 (most deprived)	53,350 (21.7)	759 (32.8)	464 (27.0)	1,094 (27.0)
2	51,519 (20.9)	496 (21.4)	335 (19.5)	927 (22.9)
3	50,702 (20.6)	445 (19.2)	326 (19.0)	822 (20.3)
4	47,275 (19.2)	358 (15.5)	318 (18.5)	679 (16.7)
5 (least deprived)	43,200 (17.6)	257 (11.1)	277 (16.1)	533 (13.1)

Data are means ± SD unless otherwise indicated. *Carstairs index.

The larger RRs in women than men are only partly due to lower absolute rates of diabetes in women than men, since we observed a greater difference in type 2 diabetes incidence among those with versus without schizophrenia (and, to a lesser degree, depression) in women compared with men (Supplementary Fig. 7). Therefore, having a hospital record for schizophrenia or depression is more strongly associated with incidence of type 2 diabetes in women than in men in all deprivation groups, but particularly the most deprived groups.

CONCLUSIONS

Main Findings

In Scotland, having a hospital admission for major mental illness is associated with a 1.5- to 2.5-fold higher risk of type 2 diabetes incidence, with RRs for those with compared with those without mental illness appearing to have increased over the last 15 years. In people with a hospital admission for schizophrenia or depression, type 2 diabetes incidence occurs at a younger age compared with people without a hospital admission for any mental illness. We found important sociodemographic differences, with the absolute and relative effects of mental illness being stronger in women than men and in deprived subgroups, indicating a greater impact of mental illness on type 2 diabetes risk in women and in people living in more deprived areas.

Strengths and Limitations

To our knowledge, this is the first study to examine time trends in type 2 diabetes incidence by mental health disorder status, the first to examine differences in incidence by socioeconomic status, and one of the first to investigate whether the prospective association differs by age and sex. Other strengths include the objective ascertainment of a diagnosis of type 2 diabetes, which was >99% complete from 2004 onward, being based on a national diabetes register that collates information from primary care and secondary care clinics. The national scale and long-term running of the diabetes register also led to the inclusion of large numbers of diabetes cases, thus facilitating the investigation of interaction by time, age, sex, and socioeconomic status.

Our study does, however, have some shortcomings. The main limitation is that, in the absence of national primary care data for research purposes, our definitions of major mental disorders were based on hospital records only. Therefore, our findings may not be generalizable to those with a mental disorder who have never had their disorder recorded in hospital. This limitation is mitigated by the fact that hospital records extend as far back as 1981. Since we used both psychiatric and general hospital admission records to identify people with depression, there may have been selection bias in that people with less severe depression may have been included purely because they were admitted to a general hospital for an unrelated disease/episode. It is difficult to speculate how the definition of depression might have affected the results, since it could have overestimated the association between depression and diabetes (if a dose-response relationship exists between depression and diabetes risk) or underestimated the association, since people with depression that has not been recorded in hospital would not have been identified. Also, it is possible that those with a major mental disorder and admitted to hospital would be more likely to have their diabetes diagnosed, purely through having more contact with the health service. Also, we were not able to identify whether the associations differed depending on whether the mental illness diagnosis was recorded from psychiatric or acute hospital medical records; it would be of interest to explore this in

Table 2—Age-standardized* incidence of type 2 diabetes by mental illness cohort, sex, and time period

	Age-standardized type 2 diabetes incidence rate per 1,000 person-years (95% CI)*			
Time period	No mental illness	Schizophrenia	Bipolar disorder	Depression
Men				
2001–2005	4.92 (4.88, 4.97)	6.56 (5.86, 7.27)	6.52 (5.65, 7.38)	5.24 (4.69, 5.79)
2006–2010	4.94 (4.90, 4.99)	8.26 (7.50, 9.01)	6.72 (5.85, 7.59)	5.78 (5.29, 6.26)
2011–2015	4.49 (4.45, 4.53)	8.61 (7.90, 9.31)	7.12 (6.21, 8.03)	6.46 (6.00, 6.91)
Women				
2001–2005	3.64 (3.61, 3.68)	6.95 (6.13, 7.78)	5.17 (4.63, 5.70)	5.17 (4.74, 5.60)
2006–2010	3.42 (3.38, 3.45)	7.89 (7.03, 8.75)	5.37 (4.80, 5.94)	5.10 (4.74, 5.46)
2011–2015	3.02 (2.99, 3.05)	8.60 (7.71, 9.50)	5.17 (4.61, 5.73)	5.74 (5.40, 6.09)

*Standardized to the European Standard Population.

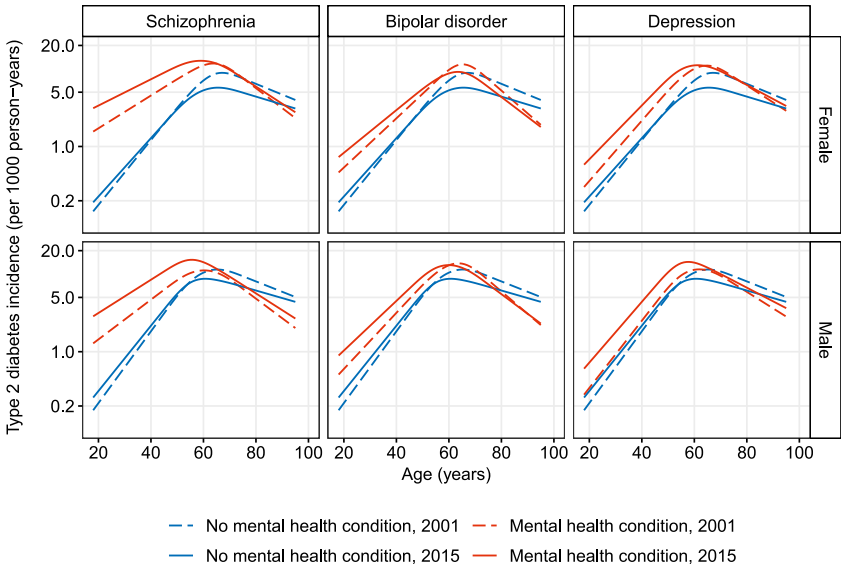

Figure 1—Type 2 diabetes incidence among people in the middle deprivation quintile, for 2001 and 2015, by age and type or absence of mental disorder and sex. Predicted incidence rates obtained from quasi-Poisson regression models including mental health status, age, sex, deprivation, and time period, plus all mental health status and age interactions.

future research. Finally, we were unable to adjust for factors known to be associated with mental illness and to be major risk factors for type 2 diabetes, such as use of psychotropic medications, sleep disruption, low physical activity, and poor dietary choices that influence BMI, the key risk factor for type 2 diabetes. However, given that BMI may lie on the causal pathway between mental illness and type 2 diabetes, one could argue that minimally adjusted estimates more accurately convey the associated risk of diabetes. Data on BMI were not available for the cohort, so it was not possible to investigate potential mediation.

Interpretation in Context of Previous Studies

Despite the limitations of our study, our findings are consistent with previous prospective studies on the association between major mental disorders and type 2 diabetes incidence. In general, cohort studies have found that depression is associated with a 30–100% increased risk of type 2 diabetes prior to adjustment for lifestyle factors (11–13) and schizophrenia and bipolar disorder are associated with a 70–80% increased risk of type 2 diabetes (14).

The slight decline in type 2 diabetes incidence observed among those with no hospital record for mental illness in our study is in line with overall trends in diabetes incidence in the general Scottish population (22). Since 2004, type 2 diabetes incidence in Scotland has declined or stabilized, depending on sex, age, and socioeconomic status, which is thought to be attributed to stabilizing obesity prevalence and intensified diagnosis of type 2 diabetes leading to a smaller number and proportion of undiagnosed type 2 diabetes cases (22). However, our study demonstrates that this stabilization or decline in type 2 diabetes incidence has not been observed among people with major mental illness. The reasons for the excess risk of type 2 diabetes in people with a major mental disorder are multifactorial and complex, including environmental, genetic, and lifestyle factors. Potential side effects of drug treatments for mental illness are also important, with antipsychotic and antidepressant medication having been linked to type 2 diabetes via weight gain and other metabolic abnormalities (23,24). Furthermore, mental illness itself may have a direct physiological effect. For instance, there is evidence of glucose homeostasis disruption among antipsychotic-naive individuals presenting with a first episode of schizophrenia (25). Many mechanisms ultimately increase risk of obesity, the key risk factor for type 2 diabetes. The apparent increase in diabetes incidence over time among those with a major mental illness in our study could be due to a number of factors, including improved diabetes diagnosis in this group over time. Primary care screening for cardiometabolic disease in general and among people with mental illness was incentivized through the Quality and Outcomes Framework, a pay-for-performance scheme for general practitioners, which was in place in Scotland between 2004 and April 2017 (26). This offered a financial reward to promote good practice against a set of evidence-based indicators, including monitoring of cardiometabolic risk in people with mental illness. The increase in type 2 diabetes incidence among those with schizophrenia might also reflect the introduction, and more widespread use, of second-generation antipsychotics, which, compared with first-generation antipsychotics, are thought to be associated with a slightly higher increased risk of type 2 diabetes via weight gain or effects on insulin

Table 3—RRs (95% CI)* for type 2 diabetes at 5-yearly intervals among people aged 60 years and in the middle deprivation quintile

	Men			Women		
Year	Schizophrenia	Bipolar disorder	Depression	Schizophrenia	Bipolar disorder	Depression
2001	1.07 (0.89, 1.29)	1.24 (1.02, 1.52)	1.09 (0.94, 1.26)	1.57 (1.30, 1.89)	1.37 (1.13, 1.66)	1.41 (1.22, 1.63)
2005	1.29 (1.12, 1.49)	1.37 (1.17, 1.61)	1.18 (1.06, 1.31)	1.89 (1.64, 2.18)	1.51 (1.30, 1.76)	1.53 (1.38, 1.69)
2010	1.53 (1.33, 1.77)	1.49 (1.27, 1.75)	1.34 (1.21, 1.49)	2.25 (1.94, 2.60)	1.64 (1.40, 1.92)	1.74 (1.57, 1.93)
2015	1.63 (1.38, 1.94)	1.50 (1.22, 1.84)	1.62 (1.43, 1.82)	2.40 (2.01, 2.85)	1.65 (1.35, 2.02)	2.10 (1.86, 2.36)

*Comparing people with hospitalization for each mental disorder versus no mental illness, by sex and year, based on predictive values from quasi-Poisson regression models.

Table 4—RRs (95% CI)* for type 2 diabetes in people aged 60 years in Scotland in 2010 and 2015

		Men			Women		
Year	Deprivation quintile	Schizophrenia	Bipolar disorder	Depression	Schizophrenia	Bipolar disorder	Depression
2010	1 (most deprived)	1.59 (1.40, 1.80)	1.88 (1.61, 2.18)	1.39 (1.26, 1.54)	2.33 (2.05, 2.64)	2.06 (1.79, 2.37)	1.81 (1.65, 1.98)
	2	1.64 (1.44, 1.88)	1.71 (1.46, 2.00)	1.48 (1.34, 1.64)	2.41 (2.10, 2.76)	1.88 (1.62, 2.18)	1.92 (1.74, 2.11)
	3	1.53 (1.33, 1.77)	1.49 (1.27, 1.75)	1.34 (1.21, 1.49)	2.25 (1.94, 2.60)	1.64 (1.40, 1.92)	1.74 (1.57, 1.93)
	4	1.17 (0.99, 1.39)	1.35 (1.14, 1.60)	1.10 (0.98, 1.23)	1.72 (1.45, 2.04)	1.49 (1.26, 1.76)	1.42 (1.27, 1.60)
	5 (least deprived)	1.03 (0.84, 1.25)	1.12 (0.93, 1.35)	0.96 (0.83, 1.10)	1.50 (1.23, 1.84)	1.23 (1.02, 1.48)	1.25 (1.08, 1.43)
2015	1 (most deprived)	1.69 (1.45, 1.98)	1.89 (1.55, 2.29)	1.68 (1.50, 1.88)	2.48 (2.12, 2.91)	2.08 (1.72, 2.50)	2.18 (1.96, 2.43)
	2	1.75 (1.49, 2.06)	1.72 (1.41, 2.10)	1.78 (1.59, 2.00)	2.57 (2.18, 3.03)	1.89 (1.56, 2.30)	2.31 (2.07, 2.59)
	3	1.63 (1.38, 1.94)	1.50 (1.22, 1.84)	1.62 (1.43, 1.82)	2.40 (2.01, 2.85)	1.65 (1.35, 2.02)	2.10 (1.86, 2.36)
	4	1.25 (1.03, 1.52)	1.36 (1.10, 1.68)	1.32 (1.16, 1.51)	1.83 (1.51, 2.23)	1.50 (1.22, 1.85)	1.72 (1.51, 1.96)
	5 (least deprived)	1.09 (0.88, 1.36)	1.13 (0.90, 1.41)	1.16 (0.99, 1.35)	1.60 (1.28, 2.01)	1.24 (0.99, 1.55)	1.50 (1.29, 1.75)

*Comparing people with a hospitalization record for each mental disorder versus no mental illness by sex and area-based deprivation quintile.

resistance (27). However, it has been shown that all antipsychotics are associated with weight gain, albeit to varying degrees (28).

The observed sex differences in our study are interesting. A systematic review of studies found no sex difference in type 2 diabetes prevalence in people with and without bipolar disorder, which is in line with our findings on incidence (9). A later review by the same authors pooled together studies of patients with schizophrenia, bipolar disorder, and major depression and found that prevalence of diabetes was ~40% higher in women than in men (8), but since the analyses combined all mental disorders, it is unclear how sex differences might have differed by mental disorder. Consistent with our findings on depression, a recent prospective study reported greater effects of depression on type 2 diabetes risk in women than in men (29). One explanation for our findings could be the higher prevalence of obesity in women with these mental health disorders compared with men and the larger relative gap in obesity between those with and without mental illness in women compared with men (30). It is intriguing that we did not observe similarly pronounced sex differences in the bipolar disorder group, given similar patterns of obesity by sex in this group.

As with sex, previous studies have tended to adjust for socioeconomic status rather than investigate potential interactions between mental disorders and socioeconomic status. Our findings indicate that, for all mental health disorders, the absolute and relative differences in diabetes rates are exacerbated by increasing level of deprivation, highlighting the additional vulnerability of people with a mental illness who live in deprived areas. Previous Scottish studies have found that the excess mortality associated with severe mental illness is most marked in the most deprived population groups (31) and that multimorbidity, including mental-physical health comorbidity, is more prevalent among more deprived groups (32). By demonstrating that the association between mental disorder and type 2 diabetes varies markedly by deprivation level, our study suggests that this increased diabetes risk is due largely to modifiable factors rather than intrinsic physiological effects of the mental illness itself.

Implications

The temporal and sociodemographic variations in the association between major mental disorders and diabetes have important implications for both clinical care and intervention strategies aimed at equitable improvement of physical health in people with mental illness. Sex and socioeconomic differences highlight the particularly high increased risk of type 2 diabetes among women and people living in more deprived areas with a mental illness. Reasons for these variations are likely multifactorial and should be investigated further in future studies. Higher prevalence of obesity in women compared with men with mental illness could account for some of the observed sex differences in the association between mental illness and type 2 diabetes incidence. The importance of monitoring and attempting to improve the cardiometabolic health of people with major mental illness (and, in particular, women and people with a low socioeconomic status) should continue to be emphasized to psychiatrists and primary care physicians. Novel intervention approaches aimed at reducing type 2 diabetes risk in people with mental illness should be tailored accordingly and involve targeted as well as universal strategies. Factors related to both socioeconomic status and mental illness, and amenable to intervention, include provision of care (33), health literacy (34), engagement with health services (35), and lifestyle behavior. While improvement of each of these is undoubtedly challenging, they must all be tackled if we are to reduce the risk of type 2 diabetes in people with mental illness, particularly in more deprived areas. Furthermore, more pharmacoepidemiological studies are urgently needed to improve our understanding of the potential adverse metabolic consequences of antipsychotics, mood stabilizers, and antidepressants. In an era of precision medicine, advances in the refined tailoring of psychotropic drug prescribing practices to optimize control of mental health symptoms and minimize side effects on physical health may be possible in the future.

Conclusion

In Scotland, major mental illness is associated with a marked increased risk of incidence of type 2 diabetes, with evidence of increasing disparities in the last 15 years. The absolute and relative effects of mental illness are stronger in women than men and in more deprived subgroups. These findings provide important insights into temporal and sociodemographic differences in type 2 diabetes risk across multiple mental health disorders,

which have implications for clinical care and intervention strategies.

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References

1. Erlangsen A, Andersen PK, Toender A, Laursen TM, Nordentoft M, Canudas-Romo V. Cause-specific life-years lost in people with mental disorders: a nationwide, register-based cohort study. Lancet Psychiatry 2017;4:937–945
2. Laursen TM, Wahlbeck K, Hällgren J, et al. Life expectancy and death by diseases of the circulatory system in patients with bipolar disorder or schizophrenia in the Nordic countries. PLoS One 2013;8:e67133
3. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatry 2015;72:334–341
4. Crump C, Sundquist K, Winkleby MA, Sundquist J. Comorbidities and mortality in bipolar disorder: a Swedish national cohort study. JAMA Psychiatry 2013;70:931–939
5. Gatov E, Rosella L, Chiu M, Kurdyak PA. Trends in standardized mortality among individuals with schizophrenia, 1993-2012: a population-based, repeated cross-sectional study. CMAJ 2017;189:E1177–E1187
6. Nordentoft M, Wahlbeck K, Hällgren J, et al. Excess mortality, causes of death and life expectancy in 270,770 patients with recent onset of mental disorders in Denmark, Finland and Sweden. PLoS One 2013;8:e55176
7. Stubbs B, Vancampfort D, De Hert M, Mitchell AJ. The prevalence and predictors of type two diabetes mellitus in people with schizophrenia: a systematic review and comparative meta-analysis. Acta Psychiatr Scand 2015;132:144–157
8. Vancampfort D, Correll CU, Galling B, et al. Diabetes mellitus in people with schizophrenia, bipolar disorder and major depressive disorder: a systematic review and large scale meta-analysis. World Psychiatry 2016;15:166–174
9. Vancampfort D, Mitchell AJ, De Hert M, et al. Prevalence and predictors of type 2 diabetes mellitus in people with bipolar disorder: a systematic review and meta-analysis. J Clin Psychiatry 2015;76:1490–1499
10. Vancampfort D, Mitchell AJ, De Hert M, et al. Type 2 diabetes in patients with major depressive disorder: a meta-analysis of prevalence estimates and predictors. Depress Anxiety 2015;32:763–773
11. Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care 2008;31:2383–2390
12. Rotella F, Mannucci E. Diabetes mellitus as a risk factor for depression. A meta-analysis of longitudinal studies. Diabetes Res Clin Pract 2013;99:98–104
13. Yu M, Zhang X, Lu F, Fang L. Depression and risk for diabetes: a meta-analysis. Can J Diabetes 2015;39:266–272
14. Bai YM, Su TP, Chen MH, Chen TJ, Chang WH. Risk of developing diabetes mellitus and hyperlipidemia among patients with bipolar disorder, major depressive disorder, and schizophrenia: a 10-year nationwide population-based prospective cohort study. J Affect Disord 2013;150:57–62
15. Rajkumar AP, Horsdal HT, Wimberley T, et al. Endogenous and antipsychotic-related risks for diabetes mellitus in young people with schizophrenia: a Danish population-based cohort study. Am J Psychiatry 2017;174:686–694
16. Roy T, Lloyd CE. Epidemiology of depression and diabetes: a systematic review. J Affect Disord 2012;142(Suppl.):S8–S21
17. Anwar H, Fischbacher CM, Leese GP, Lindsay RS, McKnight JA, Wild SH; Scottish Diabetes Research Network Epidemiology Group. Assessment of the under-reporting of diabetes in hospital admission data: a study from the Scottish Diabetes Research Network Epidemiology Group. Diabet Med 2011;28:1514–1519
18. Brown D, Allik M, Dundas R, Leyland AH. Carstairs Scores for Scottish Postcode Sectors, Datazones & Output Areas From the 2011 Census. Glasgow, U.K., MRC /CSO Social and Public Health Sciences Unit, University of Glasgow, 2014
19. R Core Team. *R: A Language and Environment for Statistical Computing. R version 3.3.3*. Vienna, Austria, R Foundation for Statistical Computing, 2017
20. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med 2007;4:e296
21. Benchimol EI, Smeeth L, Guttmann A, et al.; RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med 2015;12:e1001885
22. Read SH, McAllister DA, Colhoun HM, et al.; Scottish Diabetes Research Network Epidemiology Group. Incident ischaemic stroke and type 2 diabetes: trends in incidence and case fatality in Scotland 2004-2013. Diabet Med 2018;35:99–106
23. Barnard K, Peveler RC, Holt RI. Antidepressant medication as a risk factor for type 2 diabetes and impaired glucose regulation: systematic review. Diabetes Care 2013;36:3337–3345
24. Holt RI, Mitchell AJ. Diabetes mellitus and severe mental illness: mechanisms and clinical implications. Nat Rev Endocrinol 2015;11:79–89
25. Pillinger T, Beck K, Gobjila C, Donocik JG, Jauhar S, Howes OD. Impaired glucose homeostasis in first-episode schizophrenia: a systematic review and meta-analysis. JAMA Psychiatry 2017;74:261–269
26. Roland M. Linking physicians' pay to the quality of care–a major experiment in the United Kingdom. N Engl J Med 2004;351:1448–1454
27. Smith M, Hopkins D, Peveler RC, Holt RI, Woodward M, Ismail K. First- v. second-generation antipsychotics and risk for diabetes in schizophrenia: systematic review and meta-analysis. Br J Psychiatry 2008;192:406–411
28. Bak M, Fransen A, Janssen J, van Os J, Drukker M. Almost all antipsychotics result in weight gain: a meta-analysis. PLoS One 2014;9:e94112
29. Demmer RT, Gelb S, Suglia SF, et al. Sex differences in the association between depression, anxiety, and type 2 diabetes mellitus. Psychosom Med 2015;77:467–477
30. Jonikas JA, Cook JA, Razzano LA, et al. Associations between gender and obesity among adults with mental illnesses in a community health screening study. Community Ment Health J 2016;52:406–415
31. Martin JL, McLean G, Park J, et al. Impact of socioeconomic deprivation on rate and cause of death in severe mental illness. BMC Psychiatry 2014;14:261
32. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012;380:37–43
33. Lawrence D, Kisely S. Inequalities in healthcare provision for people with severe mental illness. J Psychopharmacol 2010;24(Suppl.):61–68
34. Friis K, Lasgaard M, Osborne RH, Maindal HT. Gaps in understanding health and engagement with healthcare providers across common long-term conditions: a population survey of health literacy in 29,473 Danish citizens. BMJ Open 2016;6:e009627
35. Dixon LB, Holoshitz Y, Nossel I. Treatment engagement of individuals experiencing mental illness: review and update. World Psychiatry 2016;15:13–20