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## **The impact of severe mental illness on healthcare use and health outcomes for people with type 2 diabetes: a longitudinal observational study in England**

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# **The impact of severe mental illness on healthcare use and health outcomes for people with type 2 diabetes: a longitudinal observational study in England**

## **Abstract**

### *Background*

People with severe mental illnesses (SMI) have reduced life expectancy compared with the general population. Diabetes is a major contributor to this disparity with higher prevalence and poorer outcomes in people with SMI.

### *Aim*

To determine the impact of SMI on healthcare processes and outcomes for diabetes.

### *Design and setting*

Retrospective observational matched nested case-control study using patient records from the Clinical Practice Research Datalink linked to Hospital Episode Statistics.

### *Methods*

We compared a range of healthcare processes (primary care consultations, physical health checks, metabolic measurements) and outcomes (prevalence and hospitalisation for cardiovascular disease (CVD), and mortality risk) for 2,192 people with SMI and type 2 diabetes (cases) with 7,773 people with diabetes alone (controls). Socio-demographics, comorbidity and medication prescription were covariates in regression models.

### *Results*

SMI was associated with increased risk of all-cause mortality (Hazard Ratio [HR]: 1.92; 95% CI: 1.60 to 2.30) and CVD-specific mortality (HR: 2.24; 1.55 to 3.25); higher physician consultation rates (Incidence Rate Ratio [IRR]: 1.15; 1.11 to 1.19); more frequent checks of blood pressure (IRR: 1.02; 1.00 to 1.05) and cholesterol (IRR: 1.04; 1.02 to 1.06); lower prevalence of angina (Odds Ratio [OR]: 0.67; 0.45 to 1.00); higher emergency admissions for angina (IRR: 1.53; 1.07 to 2.20) and lower elective admissions for ischaemic heart disease (IRR: 0.68; 0.51 to 0.92).

### *Conclusion*

Monitoring of metabolic measurements was comparable for people with diabetes with and without SMI. Increased mortality rates observed in SMI may be attributable to under-diagnosis of CVD and delays in treatment.

### *Keywords*

Severe mental illness; diabetes; cardiovascular disease; mortality; primary care.

## Introduction

The average life expectancy for people with severe mental illnesses (SMI), such as schizophrenia or bipolar disorder, is 15 to 20 years less than the general population.<sup>1</sup> Higher prevalence of non-communicable diseases in people with SMI is a key contributor to this disparity,<sup>2-5</sup> partly driven by socio-economic disadvantage, health risk behaviours<sup>6,7</sup> and side effects of medications.<sup>8-10</sup> Coexisting SMI and comorbid conditions may interact, with poorer outcomes for both while access to healthcare for physical problems may also be more problematic for people with SMI.<sup>11</sup>

In the UK, the prevalence of type 2 diabetes (T2DM) is twice as high in people with SMI compared with the general population,<sup>12</sup> with an increased incidence of acute metabolic emergencies and diabetes complications.<sup>13,14</sup> National guidelines therefore recommend regular screening for diabetes in people with SMI, with the aim of achieving the same standards of care as for the general population.<sup>15-19</sup> The UK's primary care pay-for-performance programme, the Quality and Outcomes Framework (QOF), has included quality targets for both diabetes and SMI since 2004.<sup>20</sup>

Overall recorded quality of care for diabetes has improved substantially following the introduction of national quality improvement initiatives.<sup>21</sup> However, evidence is lacking on the appropriateness and effectiveness of universal quality targets in sub-groups of people with diabetes, including those with SMI, and little is known about how SMI and other risk factors combine to affect diabetes outcomes. We therefore used a linked healthcare dataset to investigate, in people with diabetes, the impact of SMI on healthcare processes and diabetes outcomes including the use of routine primary care services, metabolic monitoring, the diagnosis and hospitalisation for cardiovascular disease (CVD), and the risk of mortality. We aimed to identify the potential elements in the care pathway that might be associated with increased risk of mortality in people with SMI.

## Data and methods

### *Data sources and participants*

The dataset was extracted from Clinical Practice Research Datalink (CPRD) GOLD. Patient information includes symptoms and diagnoses, referrals to specialists and secondary care settings, prescriptions issued in primary care, diagnostic testing, biometric data and other types of care as routinely provided in primary care. Patient characteristics are broadly representative of the general UK population in terms of age, sex and ethnicity.<sup>22</sup> Individual patient data were electronically linked to external data sources including Hospital Episode Statistics (HES) for hospital admissions, Office for National Statistics (ONS) for death records and the Index of Multiple Deprivation (IMD) for area deprivation.<sup>23-25</sup>

We used a matched nested case-control design. Cases were people with comorbid SMI and diabetes; people with diabetes but no SMI were identified as matched controls based on age, sex and primary care practice with a maximum ratio of 4:1. SMI was defined by the presence of at least one diagnostic record entry for schizophrenia, schizoaffective disorder, bipolar disorder, depression or other affective disorder with psychosis in either primary care or hospital admission data. Diabetes was classified by the presence of diagnostic codes for T2DM in primary care or hospital admission data. Cases and controls were included if their health records were up to research standard (UTS), eligible for relevant linkages, and were: i) registered with a participating primary care practice in England in the study period from 1 April 2000 to 31 March 2016; ii) aged 18+ when diagnosed; iii) continuous; and iv) nested within a matched case-control cluster.

Individual follow-up periods started on the later date of T2DM diagnosis or the beginning of UTS data plus 15 months, to ensure a large window for observing baseline participant characteristics.

Follow-up ended on the earlier date of 31 March 2016 or the end of UTS data (**Supplementary Figure S1**).

### *Variables*

The exposure variable was SMI diagnosis. Outcome variables were primary care consultations, completion of physical health checks, metabolic measurements, diagnosis and hospitalisation for CVD, and risk of all-cause and CVD-specific mortality.

Primary care consultation rates were expressed as the average number of face-to-face consultations per year in the follow-up with practice-based health professionals. The average number of health checks per year was calculated as recorded checks on blood pressure, serum cholesterol, HbA<sub>1c</sub> and body mass index (BMI) as incentivised under QOF for people with T2DM. Metabolic measurements were expressed by the average levels of blood pressure, serum cholesterol and HbA<sub>1c</sub> in the study period.

CVD was identified as the presence of diagnostic codes recorded in primary care data during the follow-up, with separate indicators for angina, myocardial infarction (MI, including acute coronary syndrome), stroke, chronic ischaemic heart disease (IHD), as well as a combined indicator for macrovascular complications (MI, stroke and peripheral vascular disease (PVD)). Hospital admissions for CVD were measured as the average number of admissions per year in the follow-up, separated by emergency and elective admissions, as well as by diagnosis groups including angina, MI, chronic IHD and stroke.

We adjusted for age, ethnicity and area deprivation obtained by linking people's residential postcodes to the 2010 English Indices of Multiple Deprivation (IMD) at the Lower Layer Super Output Area (LSOA) level, and dividing into quintiles. Baseline comorbidities were measured by the diagnosis of CVD, hypertension, dementia, learning disability and the number of Charlson Index comorbidities (excluding diabetes and diabetes complications) prior to follow-up. Baseline medication use was measured by at least one prescription issued in the 15-month window prior to follow-up for antihypertensive, antidiabetes, lipid lowering medications, antidepressants and antipsychotics (first and second generations). Baseline smoking status (as a health risk behaviour) and biometric measures (BMI, blood pressure, serum cholesterol and HbA<sub>1c</sub>) were constructed using the most recent records extracted from the 15-month window.

### *Statistical methods*

A case-control cluster entered the analysis only after the 'case' was diagnosed with SMI. We applied 'within' estimators in our regressions to only examine the variations in outcomes among matched individuals. Conditional logistic regression models, Poisson or negative binomial models and stratified Cox proportional hazard models were applied depending on the type of outcome variables. Status of SMI was treated as time-dependent in survival analyses, and the proportional hazard assumption was tested by the inclusion of interaction effects between explanatory variables and time – interaction terms with significant coefficients were retained in the final models. Goodness of fit was assessed by the C-statistic, the Akaike information criterion (AIC) and Bayesian information criterion (BIC) as appropriate. Due to the extent of missing data, family history of diabetes, smoking status and baseline biometrics were retained in the model only if they improved model fit. Further adjustments were made to account for duration of T2DM, death during follow-up, length of follow-up and financial years. Stata version 15 was used for all analyses.

## Results

### *Participant characteristics*

Baseline characteristics of people with and without SMI are summarised in **Tables 1-2**. A total of 2,192 people with SMI (cases) were matched to 7,773 people without SMI (controls): 88% of cases matched to 3-4 controls, 53% of cases had schizophrenia and 32% bipolar disorder. People with SMI were similar to people without SMI for age, sex, duration of T2DM and follow-up length, but were more likely to live in the most deprived neighbourhoods, have dementia or learning disability, and less likely to have physical comorbidities recorded. People with SMI were also more likely to be prescribed antidepressants and antipsychotics, and less likely to be prescribed antihypertensive and lipid lowering medications.

Proportions of missing values were generally similar between people with and without SMI for smoking status and biometric variables, with BMI and smoking slightly better recorded for people with SMI. On average, people with SMI had higher BMI and levels of serum cholesterol and lower HbA<sub>1c</sub> and blood pressure.

Crude outcomes for these two groups are summarised in **Table 3**. People with SMI had, on average, a higher number of contacts with primary care and received more health checks for BMI compared with those without SMI. The crude consultation rate was 13.7 per year for people with SMI including 9.0 contacts with primary care physicians and 4.7 with practice nurses. Rates were respectively 11.2, 6.9 and 4.3 per year for people without SMI. Frequency of health checks for HbA<sub>1c</sub> and cholesterol were similar in both groups, whereas blood pressure checks were less likely for people with SMI.

For CVD, people with SMI had lower crude risks for MI, PVD, angina, chronic IHD and macrovascular complications. The crude prevalence of stroke was higher in people with SMI than in people without SMI. Hospital admission rates for these conditions were similar between the groups, with emergency admission rate slightly higher in those with SMI. All-cause and CVD-specific crude mortality rates were higher in people with SMI.

Average serum cholesterol and HbA<sub>1c</sub> levels declined between 2000/01 and 2006/7 for both groups, and then remained relatively stable thereafter. Average blood pressure levels declined throughout the study period, and people with SMI had lower levels at all time points (**Figure 1**).

### *Regression analyses*

The adjusted impact of SMI on outcomes is summarised in **Table 4**. People with SMI had higher primary care consultation rates and were more likely to receive checks for blood pressure, cholesterol and BMI. The estimated increase was 10% (Incidence Rate Ratio [IRR]: 1.10; 95% CI: 1.07 to 1.13) for overall consultations, and 15% (IRR: 1.15; 1.11 to 1.19) for contacts with primary care physicians. Checks were increased by 2% (IRR: 1.02; 1.00 to 1.05) for blood pressure, 4% (IRR: 1.04; 1.02 to 1.06) for cholesterol and 7% (IRR: 1.07; 1.04 to 1.09) for BMI for people with SMI compared with those without SMI.

People with SMI were less likely to have a primary care diagnosis of angina (Odds Ratio [OR]: 0.67; 0.45 to 1.00) but more likely to have a diagnosis of stroke (OR: 1.38; 1.04 to 1.84). For emergency admissions, people with SMI had varied risks for different types of CVD, including increased risk for angina (IRR: 1.53; 1.07 to 2.20) and stroke (IRR: 1.44; 1.06 to 1.97) and decreased risk for MI (IRR: 0.68; 0.48 to 0.97). These people were less likely to have an elective admission for CVD (IRR: 0.64; 0.47 to 0.88) and had lower admission rates for chronic IHD (IRR: 0.68; 0.51 to 0.92) compared with People without SMI.

The all-cause mortality rate was 92% higher (Hazard Ratio [HR: 1.92]; 1.60 to 2.30) and CVD-specific mortality rate 124% higher (HR: 2.24; 1.55 to 3.25) in people with SMI compared with people without this condition.

Full results of adjusted models are provided in **Supplementary Tables S1-S6**. Predictors for more frequent consultations were deprivation, longer duration of T2DM, comorbidity, and some medications. Dementia was associated with fewer consultations. Higher frequencies of health checks were associated with less deprived status (for cholesterol and HbA<sub>1c</sub> checks), Charlson comorbidities, use of medications, obesity, family history of diabetes, and higher biometric measures at baseline.

History of CVD and use of lipid lowering medications were the strongest predictors for future CVD events such as hospital admissions. Baseline antihypertensive prescriptions were associated with increased risk of hospital admission for angina and stroke. Longer duration of T2DM was associated with increased risk of CVD admissions, whilst deprivation, history of CVD and the presence of comorbidities were associated with increased risk of all-cause mortality.

## **Discussion**

### *Summary*

After adjusting for confounders, we found no evidence that people with SMI and diabetes experienced reduced access to routine primary care such as consultations and physical health checks than people with diabetes alone. People with SMI were, however, more likely to be socio-economically disadvantaged and to have some recorded conditions (e.g. dementia), and less likely to have others (e.g. physical comorbidity). Despite this, there were complex associations between SMI and the risk of CVD outcomes across diagnosis groups and healthcare settings. Recorded prevalence of angina was lower for people with SMI, as were elective hospital admission rates for CVD and emergency admission rates for MI. In contrast, emergency hospital admission rates for angina and stroke were substantially higher. Finally, people with SMI were more likely to die compared with those without SMI, with more than double the risk of CVD-related mortality.

### *Strengths and limitations*

We analysed a large, linked longitudinal dataset of individual primary care records, allowing study of multiple elements along the care pathway for diabetes and CVD, and our matched nested case-control study design and application of 'within' estimators reduced the impact of unobserved confounders. Our interrogation of multiple diagnosis groups can be considered as sensitivity checks of our key findings, and the adjustment of medication prescriptions has improved the identification of comorbidities, particularly for the physical long-term conditions in people with SMI. Furthermore, patient characteristics in this database have been shown to be broadly representative of the general UK population in terms of age, sex and ethnicity,<sup>22</sup> meaning our findings are likely to have wider generalisability.

As with all studies using routine healthcare records, data accuracy and completeness create limitations. There were high levels of missing data for some variables and we could not adjust for factors such as lifestyle, environmental and social determinants of health. Coding behaviour is likely to vary by individual primary care staff and practices, presenting further potential errors in primary care records. Under QOF, however, primary care providers have been incentivised to maintain registers of various conditions including SMI. We therefore expect diagnosis is less likely to be

affected by this limitation compared with other areas. Data on pathways, including referral and outpatient records, were limited; this restricted our exploration of service use along the full care pathway and potential service gaps. Severity of mental illness or diabetes is not routinely recorded and could not be inferred reliably. Heart failure, which is more common in people with diabetes, has not been analysed. As with all observational studies, it was not possible to control for unobserved confounders and systematic measurement biases which might lead us to over- or under-estimate associations between risk factors and outcomes.

### *Comparison with existing literature*

Our analysis of both primary care and hospital admission records has highlighted two potential inequalities in the identification and subsequent treatment of CVD. First, diagnosis of angina in primary care was lower in people with SMI, but emergency admission rates were higher. This may reflect more rapid and severe onset, presentation and diagnostic delay, and/or greater preference for emergency hospital services as the first contact point for people with SMI experiencing chest pain. The lower admission rate for MI might be related to this and suggest fewer but more fatal admissions for coronary heart disease, rather than an indicator of better outcomes. Second, the lower diagnosis and elective admission rates for IHD in people with SMI suggests that this population was less likely to be referred to cardiovascular specialist care, a finding consistent with an Australian study.<sup>26</sup> Elective admissions for IHD were mainly accessed through referrals by primary care physicians, either for initial clinical investigation (e.g. coronary arteriography) or for carrying out invasive procedures (e.g. CABG and stent insertion) following an emergency admission for MI. These findings agree with an existing literature<sup>5</sup> that people with SMI may under-use both investigations and invasive procedures due to under-diagnosis of coronary heart disease.

There are several inter-related potential explanations. Reasons for systematic under-diagnosis of CVD could include symptom underreporting by people with SMI, diagnostic overshadowing and a lack of confidence by mental health professionals to diagnose and manage physical comorbidities.<sup>27</sup> Primary care providers might be reluctant to prescribe medications for long-term conditions and refer people with SMI for standard surgical procedures,<sup>28,29</sup> perhaps due to perceived psychological stress, capacity for post-operative care and a higher risk of developing complications after surgical interventions. A lack of integration among primary care, specialist physical healthcare and psychiatric services may have made navigation of the care pathway more difficult for people with SMI.<sup>30,31</sup>

### *Implications for research and practice*

Our analysis shows that the greatest challenge is no longer general monitoring of metabolic risk factors as incentivised by national guidelines, as these now appear to be equally delivered to people with and without SMI. Rather, people with SMI appear to be under-diagnosed for cardiovascular disease in primary care and consequently have poorer access to specialist and elective hospital care, leading to an elevated risk of cardiovascular mortality in this population. Policies to reduce excess deaths should therefore focus on activities earlier along the care pathway to facilitate early diagnosis and timely treatment for CVD. Furthermore, current QOF targets do not consider the implications of antipsychotic medication and other unique challenges people with SMI face in managing their diabetes. Living in more deprived circumstances, as seen in this study, can also increase the likelihood of developing chronic health problems, and reduce capacity to successfully manage them. Policies should be designed to encourage primary care providers to initiate effective conversations with patients and carers on both mental and physical health needs; improve coordination between primary care and specialist physical healthcare services; and develop strategies for tackling the particular challenges faced by people with SMI dealing with multimorbidity.

### **How this fits in**

People with severe mental illnesses (SMI) have poorer physical health and a lower life expectancy by around 20 years than the general population, mostly due to comorbid non-communicable diseases. Diabetes contributes significantly to this health inequality through multiple mechanisms including a 2-3 times higher prevalence, increased incidence of diabetes complications, and its interaction with SMI in aspects of health behaviours, access to health services and effectiveness of treatments. National guidelines have recommended regular screening for diabetes in people with SMI and monitoring of metabolic risk factors in people with diabetes. This study has provided new evidence that monitoring of diabetes and metabolic control is no worse for people with SMI and diabetes compared to people with diabetes alone. However, people with SMI are under-diagnosed for cardiovascular disease in primary care and consequently have poorer access to specialist and elective hospital care, which might explain the elevated risk of mortality due to cardiovascular disease in this population.

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## References

1. Chesney E, Goodwin GM, Fazel S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World Psychiatry* 2014;**13**:153-60. <https://doi.org/10.1002/wps.20128>
2. National Mental Health Intelligence Network. *Severe mental illness (SMI) and physical health inequalities: briefing*; Public Health England; 2018.
3. Firth J, Siddiqi N, Koyanagi A, et al. The Lancet Psychiatry Commission: a blueprint for protecting physical health in people with mental illness. *Lancet Psychiatry* 2019;**6**:675-712.
4. 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**:166-74. <https://doi.org/10.1002/wps.20309>
5. Smith DJ, Langan J, McLean G, Guthrie B, Mercer SW. Schizophrenia is associated with excess multiple physical-health comorbidities but low levels of recorded cardiovascular disease in primary care: cross-sectional study. *BMJ open* 2013; **3**(4), e002808. <https://doi.org/10.1136/bmjopen-2013-002808>
6. McCreddie RG, Scottish Schizophrenia Lifestyle Group. Diet, smoking and cardiovascular risk in people with schizophrenia: descriptive study. *Br J Psychiatry* 2003;**183**:534-9.
7. Holt RI, Gossage-Worrall R, Hind D, et al. Structured lifestyle education for people with schizophrenia, schizoaffective disorder and first-episode psychosis (STEPWISE): randomised controlled trial. *Br J Psychiatry* 2019;**214**:63-73.
8. Citrome L, Kalsekar I, Baker RA, Hebden T. A review of real-world data on the effects of aripiprazole on weight and metabolic outcomes in adults. *Curr Med Res Opin* 2014;**30**:1629-41.
9. Yood MU, delorenze G, Quesenberry Jr CP, et al. The incidence of diabetes in atypical antipsychotic users differs according to agent—results from a multisite epidemiologic study. *Pharmacoepidemiol Drug Saf* 2009;**18**:791-9.
10. Yood MU, DeLorenze GN, Quesenberry CP, et al. Association between second-generation antipsychotics and newly diagnosed treated diabetes mellitus: does the effect differ by dose? *BMC Psychiatry* 2011;**11**:197.
11. Mitchell AJ, Malone D, & Doebbeling CC. (2009). Quality of medical care for people with and without comorbid mental illness and substance misuse: systematic review of comparative studies. *Br J Psychiatry* 2009 Jun;**194**(6):491-9. doi: 10.1192/bjp.bp.107.045732. PMID: 19478286.
12. Reilly S, Olier I, Planner C, et al. Inequalities in physical comorbidity: a longitudinal comparative cohort study of people with severe mental illness in the UK. *BMJ Open* 2015;**5**:e009010. <https://doi.org/10.1136/bmjopen-2015-009010>
13. Brown S, Kim M, Mitchell C, Inskip H. Twenty-five year mortality of a community cohort with schizophrenia. *Br J Psychiatry* 2010;**196**:116-21. <https://doi.org/10.1192/bjp.bp.109.067512>
14. Jones LE, Clarke W, Carney CP. Receipt of diabetes services by insured adults with and without claims for mental disorders. *Med Care* 2004;**42**:1167-75.
15. De Hert M, Dekker JM, Wood D, et al. Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European

Society of Cardiology (ESC). *Eur Psychiatry* 2009;24:412-24.  
<https://doi.org/10.1016/j.eurpsy.2009.01.005>

16. Cooper SJ, Reynolds GP, Barnes T, et al. BAP guidelines on the management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment. *J Psychopharmacol* 2016;30:717-48.
17. Citrome L, Yeomans D. Do guidelines for severe mental illness promote physical health and well-being? *J Psychopharmacol* 2005;19:102-9.
18. National Institute for Health and Care Excellence (NICE). *Psychosis and schizophrenia in adults: treatment and management. NICE clinical guideline 178*. 2014. URL: <http://www.nice.org.uk/guidance/cg178/chapter/key-priorities-for-implementation> (accessed November, 2019).
19. Holt RI. Association Between Antipsychotic Medication Use and Diabetes. *Curr Diab Rep* 2019;19:96.
20. Health and Social Care Information Centre (HSCIC). *Quality and Outcomes Framework (QOF) - 2014-15*. Leeds: NHS Digital; 2015. URL: <http://www.hscic.gov.uk/catalogue/PUB15751> (accessed May, 2016).
21. Kontopantelis E, Reeves D, Valderas JM, Campbell S, Doran T. Recorded quality of primary care for patients with diabetes in England before and after the introduction of a financial incentive scheme: a longitudinal observational study. *BMJ Qual Saf*. 2013;22(1):53-64. doi:10.1136/bmjqs-2012-001033
22. Herrett E, Gallagher AM, Bhaskaran K, et al. Data Resource Profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol* 2015;44:827-36. <https://doi.org/10.1093/ije/dyv098>
23. NHS Digital. *Hospital Episode Statistics (HES)*. Leeds: NHS Digital; 2019. URL: <https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/hospital-episode-statistics> (accessed September, 2019).
24. NHS Digital. *Linked HES-ONS mortality data*. Leeds: NHS Digital; 2018. URL: <https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/linked-hes-ons-mortality-data> (accessed November, 2019).
25. Lad M. *The English indices of deprivation 2010*. London: Department for Communities and Local Government; 2011.
26. Lawrence D, Coghlan R. Health inequalities and the health needs of people with mental illness. *N S W Public Health Bull* 2002; 13, 155-158.
27. Blythe J, White J. Role of the mental health nurse towards physical health care in serious mental illness: an integrative review of 10 years of UK literature. *Int J Ment Health Nurs* 2012; 21(3), 193–201. <https://doi.org/10.1111/j.1447-0349.2011.00792.x>
28. Kisely S, Campbell LA, Wang Y. Treatment of ischaemic heart disease and stroke in individuals with psychosis under universal healthcare. *Br J Psychiatry* 2009; 195(6), 545–550. <https://doi.org/10.1192/bjp.bp.109.067082>
29. Baxter AJ, Harris MG, Khatib Y, et al. Reducing excess mortality due to chronic disease in people with severe mental illness: meta-review of health interventions. *Br J Psychiatry* 2016; 208(4), 322–329. <https://doi.org/10.1192/bjp.bp.115.163170>
30. Goodwin N, Lawton-Smith S. Integrating care for people with mental illness: the Care Programme Approach in England and its implications for long-term conditions management. *Int J Integr Care* 2010; 10, e040. <https://doi.org/10.5334/ijic.516>

31. Reilly S, Planner C, Gask L, et al. Collaborative care approaches for people with severe mental illness. *Cochrane Database Syst Rev* 2013, Issue 11. Art. No.: CD009531. DOI: 10.1002/14651858.CD009531.pub2

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**Table 1. Baseline characteristics of participants.**

	Overall	Cases (T2DM + SMI)	Controls (T2DM)
<b>No. of participants, N (%)</b>	<b>9,965 (100%)</b>	2,192 (22.0%)	7,773 (78.0%)
<b>No. of controls per case, n (%)</b>			
4 controls		1,599 (73.0%)	
3 controls		323 (14.7%)	
2 controls		138 (6.3%)	
1 control		132 (6.0%)	
<b>Diagnosis age, mean (SD)</b>			
SMI		47.98 (17.40)	
T2DM	57.83 (12.97)	56.81 (13.19)	58.12 (12.89)
<b>SMI type, n (%)</b>			
Schizophrenia		1,161 (53.0%)	
Schizoaffective disorder		113 (5.2%)	
Bipolar disorder		701 (32.0%)	
Depression and psychosis		184 (8.4%)	
Other affective disorder		26 (1.2%)	
Mixed		7 (0.3%)	
<b>Age at follow-up start, mean (SD)</b>	58.63 (12.83)	57.67 (13.11)	58.90 (12.74)
<b>Duration of T2DM (years), mean (SD)</b>	0.82 (2.85)	0.89 (3.02)	0.80 (2.80)
<b>Follow-up length (years), mean (SD)</b>	6.19 (4.43)	6.02 (4.45)	6.23 (4.43)
<b>Family history of diabetes, n (%)</b>	1,766 (17.7%)	324 (14.8%)	1,442 (18.6%)
<b>Sex, n (%)</b>			
Male	4,758 (47.8%)	1,051 (48.0%)	3,707(47.7%)
Female	5,207 (52.3%)	1,141 (52.1%)	4,066 (52.3%)
<b>Ethnicity, n (%)</b>			
White	8,095 (81.2%)	1,826 (83.3%)	6,269 (80.7%)
Asian	638 (6.4%)	139 (6.3%)	499 (6.4%)
Black	363 (3.6%)	106 (4.8%)	257 (3.3%)
Mixed, other and unknown	869 (8.7%)	121 (5.5%)	748 (9.6%)
<b>Deprivation (IMD 2010), n (%)</b>			
1st quintile (least deprived)	1,490 (15.0%)	279 (12.7%)	1,211 (15.6%)
2nd quintile	1,860 (18.7%)	358 (16.3%)	1,502 (19.3%)
3rd quintile	1,984 (19.9%)	415 (18.9%)	1,569 (20.2%)
4th quintile	2,287 (23.0%)	542 (24.7%)	1,745 (22.5%)
5th quintile	2,334 (23.4%)	595 (27.1%)	1,739 (22.4%)
Missing	10 (0.1%)	3 (0.1%)	7 (0.1%)

Table 2. Baseline characteristics of participants (continued).

	Overall	Cases (T2DM + SMI)	Controls (T2DM)
<b>Comorbidities, n (%)</b>			
Cardiovascular disease	1,591 (16.0%)	285 (13.0%)	1,306 (16.8%)
Hypertension	4,318 (43.3%)	734 (33.5%)	3,584 (46.1%)
Dementia	64 (0.6%)	32 (1.5%)	32 (0.4%)
Learning disability	40 (0.4%)	19 (0.9%)	21 (0.3%)
Charlson, mean (SD)	0.53 (0.78)	0.49 (0.73)	0.54 (0.79)
<b>Medications, n (%)</b>			
Antidepressants	2,585 (25.9%)	1,062 (48.5%)	1,523 (19.6%)
Antipsychotics			
1 <sup>st</sup> generation	524 (5.3%)	434 (19.8%)	90 (1.2%)
2 <sup>nd</sup> generation	1,009 (10.1%)	957 (43.7%)	52 (0.7%)
Antidiabetics	2,164 (21.7%)	521 (23.8%)	1,643 (21.1%)
Antihypertensives	5,349 (53.7%)	1,000 (45.6%)	4,349 (56.0%)
Lipid lowering drugs	3,361 (33.7%)	684 (31.2%)	2,677 (34.4%)
<b>Smoking, n (%)</b>			
Non-smoker	2,775 (27.9%)	544 (24.8%)	2,231 (28.7%)
Ex-smoker	2,049 (20.6%)	390 (17.8%)	1,659 (21.3%)
Current smoker	1,873 (18.8%)	650 (29.7%)	1,223 (15.7%)
Missing	3,268 (32.8%)	608 (27.7%)	2,660 (34.2%)
<b>Biometric measures, n (%)</b>			
BMI, mean (SD)	32.66 (6.95)	32.97 (6.99)	32.56 (6.94)
< 20 kg/m <sup>2</sup>	62 (0.6%)	12 (0.6%)	50 (0.6%)
20 – 24 kg/m <sup>2</sup>	617 (6.2%)	145 (6.6%)	472 (6.1%)
25 – 29 kg/m <sup>2</sup>	1,752 (17.6%)	401 (18.3%)	1,351 (17.4%)
30+ kg/m <sup>2</sup>	3,004 (30.2%)	733 (33.4%)	2,271 (29.2%)
40+ kg/m <sup>2</sup>	871 (8.7%)	221 (10.1%)	650 (8.4%)
Missing	3,659 (36.7%)	680 (31.0%)	2,979 (38.3%)
HbA <sub>1c</sub> (%), mean (SD)	7.88 (1.95)	7.82 (1.99)	7.90 (1.95)
≤ 7.5% (58 mmol/mol)	2,998 (30.1%)	672 (30.7%)	2,326 (29.9%)
> 7.5% (58 mmol/mol)	2,188 (22.0%)	460 (21.0%)	1,728 (22.2%)
Missing	4,779 (48.0%)	1,060 (48.4%)	3,719 (47.9%)
Total Cholesterol (mmol/L), mean (SD)	5.30 (1.31)	5.36 (1.42)	5.28 (1.28)
≤ 5 mmol/L	3,477 (34.9%)	722 (32.9%)	2,755 (35.4%)
> 5 mmol/L	4,105 (41.2%)	892 (40.7%)	3,213 (41.3%)
Missing	2,383 (23.9%)	578 (26.4%)	1,805 (23.2%)
BP systolic (mmHg), mean (SD)	139.17 (18.28)	135.82 (18.16)	140.13 (18.21)
≤ 140 mmHg	5,154 (51.7%)	1,280 (58.4%)	3,874 (49.8%)
> 140 mmHg	3,306 (33.2%)	605 (27.6%)	2,701 (34.8%)
Missing	1,505 (15.1%)	307 (14.0%)	1,198 (15.4%)
BP diastolic (mmHg), mean (SD)	81.87 (10.72)	81.47 (10.72)	81.99 (10.71)
≤ 80 mmHg	4,391 (44.1%)	1,011 (46.1%)	3,380 (43.5%)
> 80 mmHg	4,069 (40.8%)	874 (39.9%)	3,195 (41.1%)
Missing	1,505 (15.1%)	307 (14.0%)	1,198 (15.4%)

**Table 3. Crude healthcare use and health outcomes of participants.**

	Overall	Cases (T2DM + SMI)	Controls (T2DM)
<b>Primary care consultations (per year)</b>			
Overall			
Mean (SD)	11.72 (10.05)	13.65 (10.07)	11.18 (9.97)
Median (min, max)	9.60 (0, 365.30 <sup>a</sup> )	11.10 (0, 113.00)	9.20 (0, 365.30 <sup>a</sup> )
Primary care physicians			
Mean (SD)	7.32 (7.77)	8.98 (7.83)	6.85 (7.69)
Median (min, max)	5.70 (0, 365.30 <sup>a</sup> )	7.10 (0, 91.30)	5.30 (0, 365.30 <sup>a</sup> )
Practice Nurses			
Mean (SD)	4.40 (5.29)	4.67 (5.26)	4.32 (5.30)
Median (min, max)	3.30 (0, 143.40)	3.40 (0, 68.30)	3.20 (0, 143.40)
<b>Health checks (per year)</b>			
HbA <sub>1c</sub>			
Mean (SD)	1.80 (1.16)	1.78 (1.27)	1.81 (1.13)
Median (min, max)	1.70 (0 - 45.70)	1.70 (0 - 28.10)	1.70 (0 - 45.70)
Blood pressure			
Mean (SD)	3.01 (4.27)	2.93 (2.49)	3.03 (4.66)
Median (min, max)	2.60 (0 - 365.30 <sup>a</sup> )	2.50 (0 - 52.20)	2.60 (0 - 365.30 <sup>a</sup> )
Total Cholesterol			
Mean (SD)	1.35 (0.86)	1.38 (0.97)	1.35 (0.82)
Median (min, max)	1.30 (0 - 26.10)	1.30 (0 - 26.10)	1.30 (0 - 13.50)
BMI			
Mean (SD)	1.98 (4.07)	2.08 (1.95)	1.95 (4.49)
Median (min, max)	1.60 (0 - 365.30 <sup>a</sup> )	1.70 (0 - 30.40)	1.60 (0 - 365.30 <sup>a</sup> )
<b>Macrovascular complications (combined), n (%)</b>			
MI	344 (3.5%)	70 (3.2%)	274 (3.5%)
PVD	305 (3.1%)	58 (2.7%)	247 (3.2%)
Stroke	293 (2.9%)	72 (3.3%)	221 (2.8%)
<b>Angina</b>	324 (3.3%)	55 (2.5%)	269 (3.5%)
<b>Chronic IHD</b>	101 (1.0%)	17 (0.8%)	84 (1.1%)
<b>Hospital admissions for cardiovascular disease (per year), mean (SD)</b>			
Emergency	0.03 (1.20)	0.03 (0.25)	0.02 (0.18)
Elective	0.01 (0.15)	0.01 (0.05)	0.01 (0.16)
Angina (I20 <sup>b</sup> )	0.01 (0.06)	0.01 (0.06)	0.01 (0.07)
MI (I21&I22 <sup>b</sup> )	0.01 (0.17)	0.01 (0.24)	0.01 (0.15)
Chronic IHD (I25 <sup>b</sup> )	0.01 (0.15)	0.01 (0.05)	0.01 (0.17)
Stroke (I60 - I64 <sup>b</sup> )	0.01 (0.07)	0.01 (0.08)	0.01 (0.07)
<b>Mortality - all causes, n (%)</b>	1,384 (13.9%)	364 (16.6%)	1,020 (13.1%)
<b>Mortality - CVD, n (%)</b>	511 (5.1%)	132 (6.0%)	379 (4.9%)

a. High consultation and health check rates reflected few consultations recorded over a short follow-up. b. ICD-10 codes used to classify admissions in parentheses.

Figure 1. Average levels of serum total cholesterol, HbA<sub>1c</sub> and blood pressure (health outcomes), 2000-2016.

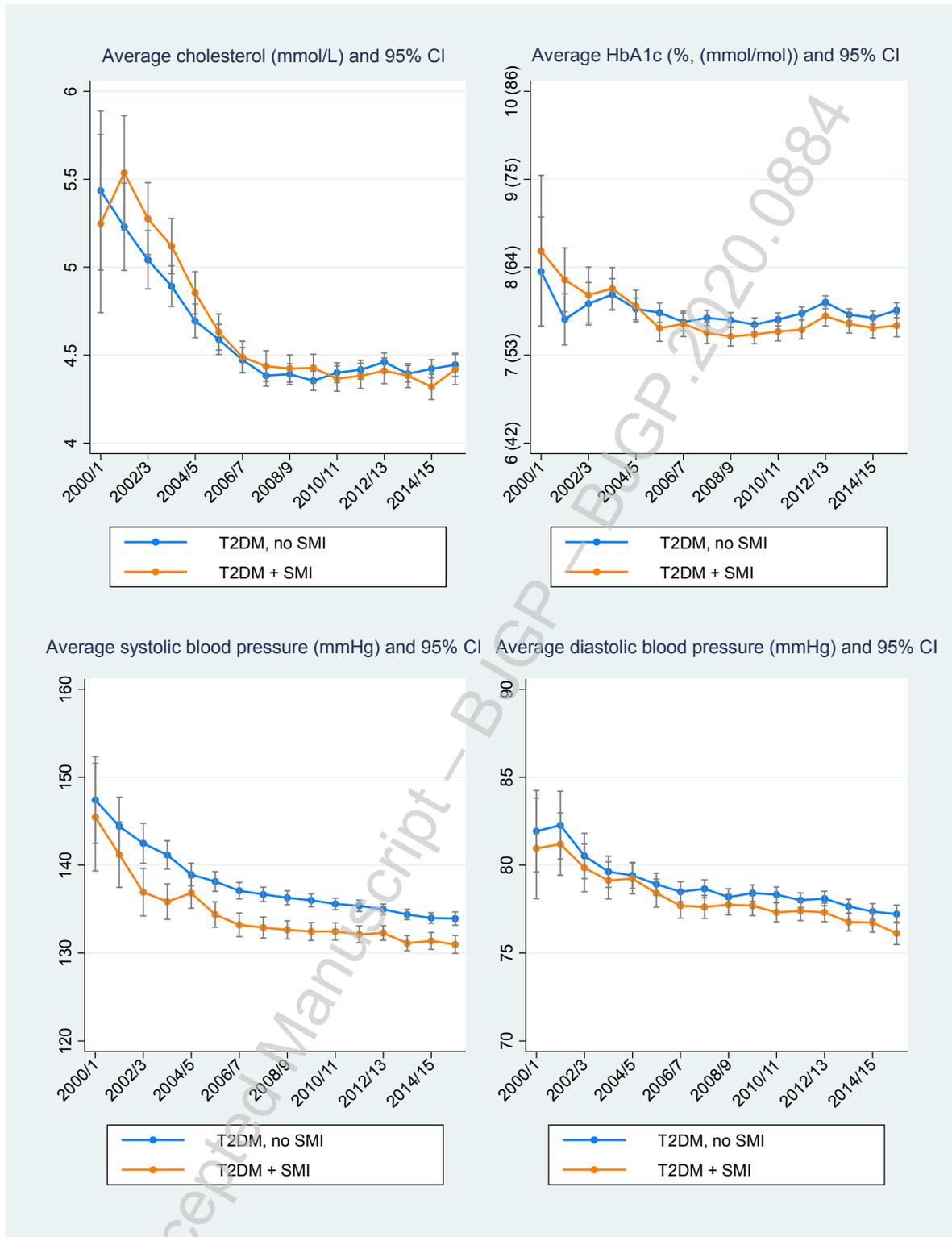


Table 4. Adjusted impact of SMI on healthcare use and health outcomes.

<b>Diagnosis of SMI</b>			
	<b>Adjusted IRR<sup>a</sup></b>	<b>95% CI</b>	<b>p value</b>
<b>Primary care consultations</b>			
Overall	1.101	[1.069 - 1.134]	< 0.001
Primary care physicians	1.149	[1.111 - 1.188]	< 0.001
Practice Nurses	1.020	[0.982 - 1.060]	0.297
<b>Physical health checks</b>			
Blood pressure	1.024	[1.003 - 1.046]	0.028
Cholesterol	1.038	[1.019 - 1.058]	< 0.001
HbA <sub>1c</sub>	0.989	[0.970 - 1.009]	0.297
BMI	1.068	[1.044 - 1.093]	< 0.001
<b>Hospital admissions for cardiovascular disease (I20-25&amp;I60-69)</b>			
<b>Emergency</b>			
Angina (I20)	1.149	[0.959 - 1.378]	0.132
MI (I21&I22)	1.532	[1.069 - 2.195]	0.020
Stroke (I60-I64)	0.683	[0.482 - 0.967]	0.032
<b>Elective</b>			
Chronic IHD (I25)	1.440	[1.055 - 1.965]	0.022
	0.644	[0.470 - 0.882]	0.006
	0.682	[0.508 - 0.915]	0.011
<b>Primary care diagnosis of cardiovascular disease</b>			
Macrovascular complications (MI, stroke and PVD)	0.970	[0.794 - 1.185]	0.765
Angina	0.671	[0.450 - 1.001]	0.050
MI	0.929	[0.698 - 1.236]	0.613
Stroke	1.381	[1.036 - 1.841]	0.028
Chronic IHD	0.742	[0.394 - 1.399]	0.356
<b>Mortality</b>			
All-cause	1.919	[1.602 - 2.300]	< 0.001
Cardiovascular disease	2.242	[1.547 - 3.250]	< 0.001

Robust 95% CI in brackets. a. Incidence rate ratio (IRR); b. Odds ratio (OR); c. Hazard ratio (HR). Models were adjusted for age, ethnicity, deprivation, financial years and statistically significant confounders in comorbidities, medications use, duration and family history of T2DM, death in follow-up, smoking and biometric measures.