BJPsych | The British Journal of Psychiatry (2021)
Page 1 of 8. doi: 10.1192/bjp.2021.131

Healthcare resource use and costs for people with type 2 diabetes mellitus with and without severe mental illness in England: longitudinal matched-cohort study using the Clinical Practice Research Datalink

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Background

Approximately 60 000 people in England have coexisting type 2 diabetes mellitus (T2DM) and severe mental illness (SMI). They are more likely to have poorer health outcomes and require more complex care pathways compared with those with T2DM alone. Despite increasing prevalence, little is known about the healthcare resource use and costs for people with both conditions.

Aims

To assess the impact of SMI on healthcare resource use and service costs for adults with T2DM, and explore the predictors of healthcare costs and lifetime costs for people with both conditions.

Method

This was a matched-cohort study using data from the Clinical Practice Research Datalink linked to Hospital Episode Statistics for 1620 people with comorbid SMI and T2DM and 4763 people with T2DM alone. Generalised linear models and the Bang and Tsiatis method were used to explore cost predictors and mean lifetime costs respectively.

Results

There were higher average annual costs for people with T2DM and SMI (£1930 higher) than people with T2DM alone, driven primarily by mental health and non-mental health-related hospital admissions. Key predictors of higher total costs were older age, comorbid hypertension, use of antidepressants, use of first-generation antipsychotics, and increased duration of living with both conditions. Expected lifetime costs were approximately £35 000 per person with both SMI and T2DM. Extrapolating nationally, this would generate total annual costs to the National Health Service of around £250 m per year.

Conclusions

Our estimates of resource use and costs for people with both T2DM and SMI will aid policymakers and commissioners in service planning and resource allocation.

Keywords

Severe mental illness; type 2 diabetes; cost; resource use; matched cohort study.

Background

Severe mental illness (SMI), including bipolar disorder, schizophrenia, and other psychotic disorders, has a dramatic impact on physical health and life expectancy. Studies show that people with SMI die on average 15 to 20 years earlier than the general population,[1,2] incurring over three times more health service expenditure (including primary and secondary care) than those without SMI.[3,4] SMI often co-occurs with chronic physical illnesses, including diabetes.[5–7] In the UK, type 2 diabetes mellitus (T2DM) is twice as common among people with SMI as those without,[8] and each condition influences the severity of the other.[7] Currently, approximately 60 000 people in England live with coexisting diabetes and SMI,[9] and this number is likely to increase.[8,10]

Although the relationship between T2DM and SMI has been previously explored,[7] little is known about the healthcare resource use and costs for people with both conditions. Having SMI may lead to increased resource use in primary care,[11] admissions to hospital[12–14] and all-cause readmission and potentially preventable readmissions,[15–17] but it is unclear how resource consumption and economic costs are split across primary and secondary care settings for people with T2DM and SMI. Also, predictors of healthcare costs for this group remain unknown.

Aims

To address this evidence gap, we aimed to: (a) compare healthcare resource use and costs for people with T2DM and SMI (exposed) with people with T2DM but no SMI (unexposed); (b) investigate the predictors of healthcare costs for people with both T2DM and SMI (exposed); and (c) extrapolate the lifetime costs for people with T2DM and SMI (exposed).

Method

Data source

We used a matched-cohort study design. Data were extracted from the Clinical Practice Research Datalink (CPRD) GOLD, a database of individual patient records from UK primary care practices[18] covering 9% of the population and broadly representative in terms of age and gender.[19] Data include patient demographics, symptoms, diagnoses, prescriptions, tests, and referrals from primary care were further linked to the Hospital Episode Statistics (HES) for secondary care information, the Office for National Statistics data for mortality, and the Index of Multiple Deprivation (IMD) for area deprivation. Since HES is England-

based (not UK-based like the CPRD), our sample only includes practices in England.

Study population

Patients with a first diagnosis of T2DM and SMI between 1 April 2000 and 31 March 2016, and who were aged 18 or over for both conditions were drawn from the CPRD database. T2DM was classified by the presence of diagnostic codes in primary or secondary care data, and SMI was characterised by the presence of at least one diagnosis for schizophrenia, schizoaffective disorder, bipolar disorder, depression with psychosis, or other affective disorder (such as affective psychoses, unspecified affective psychoses and other affective psychoses) in primary or secondary care data.

Diagnoses were based on Read codes[20] in CPRD and ICD-10 codes[21] in HES. Detailed code lists are described in Lister et al.[22] People with SMI and T2DM were matched, with a maximum ratio of 1:4, to people diagnosed with T2DM between 1 April 2000 and 31 March 2016 but without SMI, on age (plus or minus 2 years), gender and primary care practice. Matching methods have been described in more detailed elsewhere.[23] All participants had at least 15 months' continuous health records up to research standard, and at least 1 year of follow-up. All the resource utilisation within the follow-up period was considered for the analysis. The methods for determining the start and end dates of follow-up and the baseline characteristics identification period (15-month window) are presented in Supplementary Appendix 1 available at https://doi.org/10.1192/bjp.2021.131.

Baseline characteristics included age at diagnosis of T2DM, gender, ethnicity, area deprivation, comorbidity and medication use. Details about derivation of variables and resolving disagreements between CRPD and HES have been described elsewhere.[22,23] Area deprivation was categorised in five quintiles based on residential postcodes using IMD 2010 calculated at the Lower layer Super Output Area level.

Cardiovascular comorbidities at baseline were measured by the clinical diagnosis of cardiovascular disease (CVD) and hypertension. Comorbidity was summarised by the number of Charlson comorbidities,[24] excluding diabetes and diabetes with complications. Medication was defined based on prescription of three types of medications (antidiabetes drugs, antidepressants and antipsychotics) at least once within a 15-month window. Identified baseline characteristics were used to adjust analyses for sample heterogeneity or to explore potential cost predictors.

Resource use and cost estimation

Resource use and cost estimation included both primary and secondary care services. Primary care services included general practitioner (GP) or primary care physician consultations, practice nurse consultations, prescriptions and diagnostic tests. Secondary care services comprised in-patient stays in general hospitals. All included resources were costed using a bottom-up costing approach, and calculated costs were expressed in 2018 British pounds. An overview of all the sources of healthcare utilisation data and unit costs (both primary and secondary care) is shown in Supplementary Appendix 2.

Primary care costs

Data relating to primary care utilisation were extracted from CPRD based on Read codes,[20] a clinical coding system that classifies diagnoses, patient characteristics, procedures and tests for primary care in the UK. Our study included costs associated with primary care consultations, prescriptions and diagnostic tests. Following the approach proposed by Ride et al,[25] consultation costs were calculated by the duration multiplied by the costs per minute of staff time. Different members of staff, such as doctors and practice nurses, attracted different unit costs. Data about the latter were extracted from the Unit Costs of Health and Social Care (2018).[26] Multiple visits to the same staff on the same day were considered as duplicates and discarded, whereas visits to different staff on the same day were counted separately.

Prescription data were derived from the Therapy data-set of CPRD. Prescription costs were calculated by the number of prescriptions multiplied by unit costs from the Prescription Cost Analysis 2018.[27] Prescription records were costed at British National Formulary subparagraph level, which provides detailed information about a drug, including chemical substance, strength and formulation. Higher hierarchy levels (paragraph, section, or chapter) were used where subparagraph codes were unavailable.

Diagnostic test data were derived from the test data-set of CPRD and included diagnostic imaging, diagnostic services and pathology services. Following the costing approach proposed in Ride et al,[25] the test records were first grouped into Healthcare Resource Groups (HRGs) that are also used in National Health Service (NHS) Reference Costs 2017/18.[28] HRGs are the NHS equivalent of the diagnosis-related groups in the USA, and the NHS Reference Costs are average unit costs for NHS activities. Costs were estimated using the type of tests multiplied by the unit costs from the NHS Reference Costs. Details of the grouping method, including the Read codes and corresponding HRGs appear in Supplementary Appendix 3.

Secondary care/hospital care costs

The use and cost of secondary care was calculated only for admissions to general hospitals (including non-specialist mental health providers). Admissions to specialist mental health hospitals such as psychiatric hospitals were not included due to data constraint. Both number of admissions and number of in-patient days were reported as secondary care resource use. Hospital activities, such as diagnoses and procedures, were first grouped into HRGs using HRG4 + 2017/18 Reference Costs Grouper[29] and then linked to the national average costs from the NHS Reference Costs 2017/18[28] at spell level. Hospital admissions and associated costs were further split into mental and physical health-related admissions using HRG codes.[30]

Statistical methods

The resource utilisation and costs of both people with T2DM, with and without SMI, were presented at aggregate annual level. A two-phase analysis was conducted. The first phase estimated differences in resource use and costs between groups using a matched-cohort design. Unadjusted comparisons compared simple averages of annual resource utilisation and costs. Adjusted comparisons were performed using a series of generalised linear models (GLMs), appropriate for non-negative and highly skewed cost and resource data.[31] All GLM regressions were adjusted for age at diagnosis of T2DM (continuous variable), gender, ethnic group, time since diagnosis of T2DM (continuous variable) and characteristics at diagnosis of T2DM, including area deprivation, comorbid hypertension, comorbid CVD, number of Charlson comorbidities (continuous variable), medications (antidepressant and antidiabetes drugs) and financial year in order to account for sample heterogeneity. Choices of distributional family and link functions of all GLMs were informed by the Park test[32] and the Pregibon link test.[33] To ensure robustness of GLM results, a sensitivity analysis without extreme values, defined as those over the 99th percentile, was also conducted.

Table 1 Baseline characteristics of people with severe mental illness (SMI) and type 2 diabetes mellitus (T2DM) (exposed) and matched people with T2DM but no SMI (unexposed)

	Total	Exposed (T2DM with SMI)	Unexposed (T2DM without SMI)
People, *n* (%)	6383	1620	4763
Matched unexposed individuals, *n* (%)			
1 unexposed individual		158 (9.8)	
2 unexposed individuals		332 (20.5)	
3 unexposed individuals		579 (35.7)	
4 unexposed individuals		551 (34.0)	
Age at diagnosis, mean (s.d.)			
T2DM	57.9 (12.6)	57.4 (12.9)	58.0 (12.5)
SMI		47.8 (17.2)	
Gender, *n* (%)			
Male	3080 (48.3)	780 (48.1)	2300 (48.3)
Female	3303 (51.7)	840 (51.9)	2463 (51.7)
SMI diagnosis, *n* (%)			
Schizophrenia		850 (52.5)	
Bipolar disorder		524 (32.3)	
Depression and psychosis		140 (8.6)	
Schizoaffective disorder		83 (5.1)	
Mixed and other		23 (1.4)	
Diagnosis order, *n* (%)			
SMI then T2DM		1269 (78.3)	
T2DM then SMI		351 (21.7)	
Ethnic group, *n* (%)			
White	5264 (82.5)	1375 (84.9)	3889 (81.7)
Asian, Black, other, mixed ethnicity	726 (11.4)	203 (12.5)	523 (11.0)
Unknown	393 (6.2)	42 (2.6)	351 (7.4)
Deprivation, *n* (%)			
1st quintile (least deprived)	972 (15.2)	217 (13.4)	755 (15.9)
2nd quintile	1210 (19.0)	275 (17.0)	935 (19.6)
3rd quintile	1215 (19.0)	281 (17.3)	934 (19.6)
4th quintile	1475 (23.1)	401 (24.8)	1074 (22.5)
5th quintile (most deprived)	1505 (23.6)	445 (27.5)	1060 (22.3)
Unknown	6 (0.1)	1 (0.1)	5 (0.1)
Comorbidities, *n* (%)			
Cardiovascular disease[a]	2141 (33.5)	510 (31.5)	1631 (34.2)
Hypertension[a]	3513 (55.0)	777 (48.0)	2736 (57.4)
Number of Charlson comorbidities, mean (median)	0.51 (0)	0.49 (0)	0.51 (0)
0, *n* (%)	3915 (61.3)	1001 (61.8)	2914 (61.2)
1, *n* (%)	1880 (29.5)	485 (29.9)	1395 (29.3)
2, *n* (%)	440 (6.9)	99 (6.1)	341 (7.2)
≥3, *n* (%)	148 (2.3)	35 (2.2)	113 (2.4)
Medications, *n* (%)			
Antidepressants	1696 (26.6)	792 (48.9)	904 (19.0)
Antipsychotics			
First generation	360 (5.6)	307 (19.0)	53 (1.1)
Second generation	760 (11.9)	733 (45.3)	27 (0.6)
Antidiabetes	893 (14.0)	251 (15.5)	642 (13.5)
Death at the end of follow-up, *n* (%)			
Yes	740 (11.6)	234 (14.4)	506 (10.6)
No	5643 (88.4)	1386 (85.6)	4257 (89.4)
Average follow-up time for matched-cohort analysis (years)[b]			
Mean (s.d.)	6.4 (3.7)	6.1 (3.6)	6.5 (3.7)
Median (minimum–maximum)	5.8 (1–16)	5.4 (1–16)	5.9 (1–16)
Average follow-up time for cost predictor analysis (years)[c]			
Mean (SD)		5.3 (3.5)	
Median (minimum–maximum)		4.5 (0.5–16)	

a. Including those diagnosed by general practitioners.
b. From date of T2DM diagnosis to study end date.
c. From date of diagnosis of both T2DM and SMI to study end date.

The second phase focused on people with both T2DM and SMI only. The cost predictors of total, primary care and secondary care costs were explored using the multivariate GLM method as described above. Lifetime costs (costs from having T2DM and SMI to death) were estimated using the Bang and Tsiatis partition method, which estimates mean costs by adjusting survival when these costs are right censored.[34] Average lifetime cost for those that died within the follow-up period was also calculated for the purposes of comparison. Furthermore, to estimate the economic impact of people with T2DM and SMI to the NHS each year, prevalence-based healthcare costs were calculated based on the prevalence reported in the National Diabetes Audit[9] and the average annual cost estimated in this study. All analyses were performed using SAS software, version 9.4 (SAS Institute, North Carolina, US) and Stata version 15 (StataCorp LP, College Station, TX, USA).

Ethics approval and consent to participate

A data-use agreement for CPRD records and linked HES and Office for National Statistics mortality data was granted by the Independent Scientific Advisory Committee (ref: 17_161R). Individual patient consent is not required for observational CPRD studies, but patients have the opportunity to opt out of contributing to the database.

Results

Descriptive statistics

A total of 6383 people (1620 exposed and 4763 matched unexposed participants) were included in the analysis with 1 023 257 primary care contacts and 22 253 hospital admission spells. Table 1 shows baseline characteristics for the total sample, and the two groups. The mean age of the sample population was 57.9 years (s.d. = 12.6). Overall, 48.3% were male, 82.5% were White, 55.0% had hypertension, 33.5% had CVDs, 26.6% were prescribed antidepressants and 17.5% received antipsychotics.

People with both T2DM and SMI (exposed) and people with T2DM but no SMI (unexposed) were similar for age, gender and ethnicity. As expected, those with SMI were more likely to have been prescribed psychotropic medications (antidepressants and antipsychotics) (chi-square, $P < 0.001$).

Annual resource utilisation and costs

The annual resource use and costs for the two groups are presented in Table 2. People with SMI used more primary and secondary care services on average every year compared with those without SMI. On average, people with SMI received 20 primary care contacts every year, and the majority were non-prescription or test-related consultations. They spent a mean of 10.2 (s.d. = 29.1) days in hospital per annum, and the majority were non-mental health related (details in Supplementary Appendix 4). The main differences between the two groups were the all-cause annual number of

Table 2 Average resource use per person per year for people with severe mental illness (SMI) and type 2 diabetes mellitus (T2DM) (exposed) and matched people with T2DM alone (unexposed)

	Unadjusted			Adjusted[a]			
	Total	Exposed (T2DM + SMI)	Unexposed (T2DM only)	Total	Exposed (T2DM + SMI)	Unexposed (T2DM only)	P^b
n	6383	1620	4763	6383	1620	4763	
Resource use, mean (s.d.)							
Primary care contacts[c]	16.3 (10.6)	20.1 (12.3)	15.0 (9.7)	16.8 (6.5)	20.9 (7.8)	15.3 (5.3)	<0.001***
Consultation only	9.5 (7.1)	12.1 (8.4)	8.7 (6.4)	9.8 (3.8)	12.7 (4.4)	8.8 (2.9)	<0.001***
Medicine prescription related	5.7 (4.6)	6.9 (5.7)	5.4 (4.1)	5.9 (2.6)	7.2 (3.2)	5.5 (2.2)	0.245
Test related	1.3 (1.5)	1.3 (1.5)	1.2 (1.5)	1.3 (0.5)	1.4 (0.5)	1.3 (0.5)	0.491
In-patient stays							
Annual number of admissions[d]	0.6 (1.7)	0.8 (2.0)	0.6 (1.6)	0.6 (0.6)	0.9 (0.7)	0.6 (0.5)	0.001**
Mental health related[e]	0.2 (0.1)	0.1 (0.3)	0.0 (0.1)	0.0 (0.1)	0.1 (0.2)	0.0 (0.0)	<0.001***
Non-mental health related	0.6 (1.7)	0.7 (2.0)	0.6 (1.6)	0.6 (0.4)	0.7 (0.4)	0.6 (0.4)	0.018*
Annual number of in-patient days	4.7 (17.4)	10.2 (29.1)	2.9 (10.3)	6.0 (14.0)	15.1 (24.3)	2.8 (4.9)	<0.001***
Mental health related	0.9 (8.9)	3.2 (15.6)	0.1 (4.6)	2.3 (10.5)	8.9 (19.3)	0.1 (0.3)	<0.001***
Non-mental health related	3.8 (14.5)	7.0 (24.0)	2.8 (9.1)	4.6 (9.6)	10.1 (16.1)	2.8 (4.7)	<0.001***
Cost, mean (s.d.), £							
Total	2619 (7215)	4059 (12 231)	2129 (4238)	2707 (2705)	4473 (3767)	2109 (1888)	<0.001***
Primary care contacts	618 (614)	804 (786)	555 (529)	637 (331)	849 (411)	565 (263)	<0.001***
In-patient stays	2001 (7100)	3255 (12 181)	1574 (4050)	2171 (3034)	3883 (4544)	1588 (1945)	<0.001***
Mental health related	156 (1672)	511 (2771)	36 (1039)	343 (1475)	1271 (2720)	27 (83)	<0.001***
Non-mental health related	1844 (6834)	2745 (11 771)	1538 (3889)	1982 (2562)	3154 (3578)	1584 (1954)	<0.001***

a. Adjusted for age at diagnosis of T2DM, gender, ethnic group, time since diagnosis of T2DM, and characteristics at diagnosis of T2DM, including area deprivation, comorbid hypertension, comorbid cardiovascular disease, number of Charlson comorbidities, medications (antidepressant and antidiabetes drugs) and financial year.
b. For difference between adjusted cases and controls.
c. Including all the consultation records from medical staff with associated Read code.
d. Number of admissions is at the spell level. Hence, if a person transfers to another hospital, it will count as two admissions.
e. Spells contain mental health-related Healthcare Resource Groups codes.
***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

hospital in-patient days (10.2 and 2.9 days for exposed and unexposed individuals, respectively), the annual number of consultations (12.1 contacts for exposed versus 8.7 contacts for unexposed individuals) and the all-cause annual number of admissions (0.8 admissions for people with SMI versus 0.6 for those without SMI). The differences remained significant even after extreme values were removed (Supplementary Appendix 5).

Unadjusted mean annual costs per patient were £4059 (s.d. = 12 231) for people with SMI. This is £1930 higher compared with those without SMI, with £2129 (s.d. = 4238). Admission to hospital was the main contributor to the annual costs, accounting for 80.2% and 73.9% of overall healthcare expenditure for those with and without SMI, respectively.

Table 2 summarises the results of the GLM models adjusting for age at diagnosis of T2DM, gender, ethnic group, time since diagnosis of T2DM and characteristics at diagnosis of T2DM, including area deprivation, comorbid hypertension, comorbid CVD, number of Charlson comorbidities and medications (antidepressant and antidiabetes drugs). Adjusted differences in resource utilisation and costs between those with and without SMI were significant, with the exception of differences in the numbers of prescription-related and test-related consultations (further details in Supplementary Appendix 6).

Cost predictors of total costs for people with T2DM and SMI

The results of the analysis using GLM models for predictors of total, primary and secondary care costs for those with T2DM and SMI can be found in Table 3. Key predictors of higher total costs for those were older age at diagnosis (for the latest of SMI or T2DM), comorbid hypertension, use of antidepressants, use of first-generation antipsychotics, and longer duration of both T2DM and SMI. For example, the average marginal effect of time since having T2DM and SMI is £1666 (95% CI 1160–2172), suggesting that the total cost was increased by £1666 (95% CI 1160–2172) when people lived one additional year of living with both conditions. In addition, younger age, female gender, White ethnicity, diagnosis with bipolar disorder or depression and psychosis, comorbid hypertension, increased number of Charlson comorbidities, and use of antidepressants, antipsychotics or antidiabetes drugs were associated with higher primary care costs. For secondary care costs, the significant cost predictors were age, comorbid hypertension and duration of illness.

Lifetime and prevalence-based costs for people with T2DM and SMI

Of the 1620 people with T2DM and SMI, 234 (14.4%) died within the follow-up period, leaving 85.6% of people with cost data censored. The average lifetime cost for those that died within the follow-up period was estimated at £26 354. The average lifetime cost increased to £34 518 when living participants were included, and censored cost data were considered using the Bang and Tsiatis partition method.[27] The study time period was partitioned into 1-year time intervals, and average costs incurred in each interval were multiplied by the inverse probability of not being censored. Weighted costs were summed across intervals and divided by the sample size to account for censoring. Regarding prevalence-based costs, it was estimated that people with SMI and T2DM cost NHS (England) £268 380 000 per year based on the prevalence reported in the National Diabetes Audit,[9] and the adjusted average annual cost of £4473 (s.d. = 3767) reported in Table 2.

Discussion

Main findings

This study, to the best of our knowledge, is the first to estimate the resource use and costs of people with T2DM and SMI using information from both primary and secondary care sources. The presence of SMI was associated with increased resource use and costs

Table 3 Cost drivers of total cost for people with severe mental illness (SMI) and type 2 diabetes mellitus (T2DM) (exposed)[a]

	Total (n = 1620)		Primary care (n = 1620)		Secondary care (n = 1620)	
	Average marginal effect (£)	95% CI	Average marginal effect (£)	95% CI	Average marginal effect (£)	95% CI
Age at diagnosis of having both T2DM and SMI	140**	(34 to 245)	−22**	(−39 to −6)	202***	(101 to 304)
Gender						
Male	Reference		Reference		Reference	
Female	1362	(−1103 to 33 826)	917***	(537 to 1297)	728	(−1531 to 2988)
Ethnic group						
White	Reference		Reference		Reference	
Asian, Black, other, mixed ethnicity	560	(−3425 to 4544)	−251*	(−500 to −2)	2172	(−2661 to 7005)
Unknown	−13 699***	(−15 930 to −11 468)	−1860***	(−2580 to −1140)	−12 198***	(−13 852 to −10 544)
Type of SMI						
Schizophrenia	Reference		Reference		Reference	
Schizoaffective disorder	−262	(−5464 to 4940)	557	(−354 to 1468)	−874	(−5564 to 3815)
Bipolar disorder	2605	(−191 to 5400)	515*	(79 to 952)	1961	(−740 to 4663)
Depression and psychosis	26	(−4285 to 4336)	839*	(56 to 1621)	−2144	(−5443 to 1155)
Other[b]	3363	(−8021 to 14 746)	1979	(−207 to 4164)	2003	(−6193 to 10 198)
Deprivation						
1st quintile (least deprived)	Reference		Reference		Reference	
2nd quintile	374	(−3886 to 4633)	52	(−608 to 713)	−163	(−4741 to 4413)
3rd quintile	861	(−3456 to 5179)	203	(−467 to 875)	192	(−3989 to 4737)
4th quintile	−289	(−4235 to 3657)	6	(−617 to 629)	−770	(−4884 to 3344)
5th quintile (most deprived)	931	(−3093 to 4954)	409	(−223 to 1042)	236	(−3871 to 4343)
Unknown	−16 728***	(−20 129 to −13 326)	−2877*	(−5171 to −583)	−13 397***	(−16 945 to −9849)
Comorbidities						
Cardiovascular disease	−547	(−3398 to 2304)	377	(−62 to 815)	−1235	(−3804 to 1335)
Hypertension	2820*	(190 to 5451)	639**	(234 to 1043)	2137*	(87 to 4187)
Number of Charlson Comorbidities	1660	(−111 to 3431)	603***	(321 to 885)	1150	(−287 to 2587)
Medication						
Antidepressants	2836*	(241 to 5431)	1056***	(645 to 1467)	1932	(−595 to 4458)
Antipsychotics						
First generation	3394*	(195 to 6592)	1332***	(826 to 1839)	1993	(−1013 to 4998)
Second generation	2308	(−224 to 4841)	649**	(247 to 1051)	2214	(−274 to 4702)
Antidiabetes	1206	(−2274 to 4686)	708*	(163 to 1252)	410	(−2571 to 3490)
Time since having T2DM and SMI (years)	1666***	(1160 to 2172)	875***	(752 to 963)	947***	(524 to 1370)
Family[c]	Gamma		Gamma		Gamma	
Link[c]	Log		Log		Log	

a. The financial year at T2DM or SMI diagnosis (whichever was the latest) was adjusted in all the analyses.
b. Other included other affective disorder and mixed conditions.
c. Both family and link functions are the model specifications of corresponding generalised linear model. Also please add some extra spacing between "Time since having T2DM and SMI (years)" and "Family"
***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

for people with diabetes. The significant cost differences were mainly driven by secondary care services, and were related to higher numbers of admissions and days in hospital. As expected, people with SMI had higher numbers of mental health-related admissions and in-patient days compared with those without. However, people with T2DM and SMI also had, on average, more non-mental health admissions and in-patient days. One possible explanation for this is 'diagnostic overshadowing'; previous studies have shown that having a SMI diagnosis can overshadow diabetes care[35,36] leading to later presentations of physical illnesses that are then more likely to require a non-mental health hospital admission. Regular physical health checks, appropriate treatment for diabetes and greater support for diabetes self-management have been proposed for people with T2DM and SMI, in order to improve health outcomes and reduce healthcare costs.[37] Similarly, as the majority (78.3%) of individuals with T2DM and SMI developed diabetes after SMI, such health checks and treatments may also delay or prevent the onset of diabetes and provide clinical and economic benefits.[38] Importantly, some non-mental health admissions and in-patient days are unrelated to diabetes and may benefit from further investigation.

Another possible explanation for the long average non-mental health-related in-patient days is that managing a greater number of comorbidities (SMI) is associated with lengthier admissions.[39,40] For our study group, this could be exacerbated because of lack of continuity of care, poor coordination with secondary care or lack of person-centred care. Further investigation of the underlying mechanisms behind this finding is needed.

For people with T2DM and SMI, older age, White ethnicity, female gender, more comorbidities (including hypertension), use of antidepressants or antipsychotics and increased duration of living with both T2DM and SMI were associated with higher healthcare costs. Among these cost predictors, ethnicity, gender, use of antidepressants or antipsychotics, and number of Charlson comorbidities only had a significant impact on costs in primary care. This finding complements previous findings showing that people with T2DM

and SMI had higher average annual costs than those with T2DM alone, and indicates that more attention should be given to coordination of care for people with these characteristics, in order to reduce healthcare costs and improve outcomes. These cost predictors may also help policymakers to project future costs and to manage costs.

Findings related to cost predictors also reveal some probable interacting drivers of inequalities. Complementing previously found inequalities in prevalence and health outcomes for people with T2DM and SMI,[9,41] our study indicates that inequality in healthcare costs also exists in relation to ethnicity, gender and age. For example, female gender and White ethnicity were associated with higher primary care costs, suggesting that males and those from a minority ethnic background may have less access to primary care or may be less engaged. This aligns with findings for individuals with SMI alone.[25]

Our results also show that older age is associated with higher costs (lower costs in primary care, but higher costs in secondary care), suggesting that older people may have less access to essential primary care, resulting in increased risk of complications, and require more secondary care resources. Similar findings have been observed for individuals with T2DM alone,[42] whereas Ride et al[25] presented a reverse directional effect of age in people with SMI alone. Data limitations prevented us exploring whether inequalities were because of the severity of illness, complications of T2DM, problems navigating the healthcare system or synergies between these circumstances. Future studies might untangle these observations to map the relationship between disadvantage, discrimination and health outcomes in order to create an environment that can more fairly meet the health needs of individuals with T2DM and SMI.

Finally, the study demonstrated the substantial economic costs associated with people with both T2DM and SMI in England. In terms of incidence-based healthcare costs, the average total cost from diagnosis to death was around £35 000. Regarding prevalence-based healthcare costs, SMI and diabetes multimorbidity costs the NHS approximately a quarter of a billion pounds per year. Moreover, the prevalence of both conditions is rising.[8] Thus, the annual economic impact is likely to increase, which should make management of this comorbidity an NHS priority. Interventions aimed at minimising the impact of SMI (for example, integrated care and supporting patient empowerment[43]) or improving T2DM care (for example, weight reduction[44] and non-pharmacologic interventions[45]) may help to reduce healthcare costs and improve patient outcomes.

Comparison with findings from other studies

Several studies found that individuals with T2DM and SMI were more likely to experience in-patient admissions compared with people with just T2DM.[12–14] Both Kurdyak et al[14] and Guerrero Fernández de Alba et al[12] used data from single-payer health insurance systems to study resource use in the population, but their findings were subject to limitations, such as short-term resource-use data (1-year admission to hospital data in Kurdyak et al and 2-year admission to hospital data in Guerrero Fernández de Alba et al), geographic area (Ontario in Kurdyak et al and Aragón in Guerrero Fernández de Alba et al) and specific type of SMI (such as schizophrenia). By contrast, Krein et al examined 1-year all-cause hospital admissions in people with T2DM and all types of SMI in the USA.[13] However, the use of data from the US Department of Veterans Affairs healthcare system may limit its generalisability to health services outside the Department of Veterans Affairs system. Nonetheless, our study findings are in line with these three studies. As with Krein et al's study,[13] our study focused on all types of SMI. Furthermore, the use of cohort data from CPRD and HES ensured all the resource use was captured, and the long-term effects were examined (mean follow-up time: 6.4 years, Table 1).

Limitations

Our study was subject to certain limitations in terms of representativeness. Although patients in CPRD broadly represent the general population,[18] we cannot ascertain the representativeness of people with T2DM and SMI. This is because our inclusion criteria required individuals to be registered with the practice for at least 15 months, whereas some people with SMI may have transient care relationships with general practice. Also, the representativeness of our study sample can be affected by undetected T2DM or SMI; previous analyses have shown that SMI is often unrecognised among individuals treated for diabetes.[46] Furthermore, people with SMI often have undiagnosed diabetes because of difficulties accessing the healthcare system.[47] Additionally, the data linkage of UK-based CPRD and England-based HES data may have restricted our sampling to individuals registered to CPRD general practices in England that participated in HES data linkage, potentially differing from the average practice. Finally, although people with missing ethnicity data accounted for a small proportion of the study population (Table 1), they played an important role in the matched-cohort analysis. As shown in Table 2 and Supplementary Appendix 6, people with missing ethnicity were associated with low resource use and costs. Although it is possible that care providers are less likely to record ethnicity for individuals not attending services, the missing ethnicity value is likely to cause an underestimation of the difference between those with and without SMI. Notwithstanding these limitations, the generalisability of our findings was supported by the UK National Diabetes Audit[9] that reported a similar distribution to our study group for characteristics such as age at T2DM diagnosis, gender, deprivation and ethnicity.

Our study was also subject to limitations for our cost and resource-use analyses. We are likely to have underestimated some costs because of data constraints preventing us including costs for out-patient services, emergency department and community mental healthcare, the latter being one of the main components of total annual costs for individuals with SMI.[25] In the current matched-cohort analysis, only the resource use and costs of secondary care have been stratified by mental-health/non-mental health. As important differences of resource use could also occur in primary care, the stratification of primary care resource use should be considered in future studies. Finally, averaging costs over multiple years for the matched cohort analysis can limit appreciation of cost trajectories (i.e. costs peak around the time of diagnosis and then tail off). Nevertheless, annual cost results and relevant information can provide valuable information for decision modelling, especially for Markov model construction.

Implications

Our findings indicate that the healthcare costs for people with both T2DM and SMI are substantial. Costs were influenced by age, ethnicity, number of comorbidities and the length of time living with both T2DM and SMI. The results also confirmed that the presence of SMI is associated with increased resource use and costs among people with T2DM. Such differences were primarily driven by secondary care and were related not only to mental health-related but also non-mental health-related hospital admissions, highlighting the need for better coordination of care. The findings can support policymakers and commissioners in service planning and resource allocation. Furthermore, the mechanisms leading to more frequent hospital admissions should be investigated. Finally, strategies to

delay the onset of T2DM should be adopted by policymakers, in order to reduce healthcare costs and improve patient outcomes.

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First received 19 Mar 2021, final revision 4 Aug 2021, accepted 08 Aug 2021

Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1192/bjp.2021.131

Funding

This publication presents independent research funded by the National Institute for Health Research (NIHR) Health Services and Delivery Research (HS&DR) programme (ref 15/70/26). S.G., N.S., S.L.P. and R.J. were also funded by the NIHR Yorkshire and Humber Applied Research Collaboration (NIHR YH-ARC), https://www.arc-yh.nihr.ac.uk/. The views expressed are those of the authors and not necessarily those of the HS&DR programme, the NHS, the NIHR or the Department of Health and Social Care.

Acknowledgements

We would like to express our appreciation to John Radford and DIAMONDS Voice Patient and Public Involvement group for providing advice and insights to support this research. We would also like to extend our special thanks to Jennie Lister for her contribution in project management and Dr Jemimah Ride, Centre for Health Policy, School of Population and Global Health, University of Melbourne, Australia for her valuable advice on methodology.

Data availability

Researchers can apply to access Clinical Practice Research Datalink (CPRD) data with linkage to Hospital Episode Statistics (HES) through https://www.cprd.com/. Data sharing agreements with CPRD do not permit data sharing with third parties. All formulae and additional sources of information are presented in the paper and Supplementary materials. The SAS and stata code for cleaning and analysing the data can be provided upon reasonable request.

Author contributions

N.S., R.I.G.H., D.S., S.G., R.J., T.D., C.H., S.L.P., J.T. and S.A. designed and directed the project. S.B. and C.E.W.K. contributed to project management. H.-I.W. and L.H. processed the data, designed and performed the data analyses. R.J. verified the analytical methods. H.-I.W. took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript.

Declaration of interest

S.A. has received funding from the Wellcome Institutional Strategic Support Fund and a National Institute of Health Research (NIHR) Clinical Trials Fellowship. S.A. is a member of the Health Services & Delivery Research funding committee. S.G. is deputy chair of the NIHR Health Technology Assessment (HTA) Commissioning Board, and a member of the HTA Commissioning Committee, the HTA Funding Committee Policy Group, and the HTA Post-Funding Committee teleconference. C.H. is a member of the NIHR HTA Commissioning Board (2015-current). R.I.G.H. has received honoraria for speaker engagement, conference attendance or advisory boards from: AstraZeneca, Boehringer-Ingelheim, European Association for the Study of Diabetes, Eli Lilly, Janssen, Menarini, Mylan, Novo Nordisk and Omniamed, Otsuka. R.I.G.H. was a member of the HTA Prioritisation Committee C (Mental Health, Women and Children's Health) until July 2019. D.S. is an expert advisor to the National Institute for Health and Care Excellence (NICE) centre for guidelines; a Board member of the National Collaborating Centre for Mental Health (NCCMH); a Clinical Advisor (paid consultancy basis) to the National Clinical Audit of Psychosis (NCAP); these are the personal views of D.S. and not those of NICE, NCCMH or NCAP. D.S. has received personal fees from Wiley Blackwell publication 'Promoting Recovery in Early Psychosis' 2010, ISBN 978-1-4051-4894-8, joint editor in receipt of royalties, outside the submitted work; personal fees received as member of the current NICE guideline development group for Rehabilitation in adults with complex psychosis and related severe mental health conditions. N.S. is a member of the *British Journal of Psychiatry* editorial board but did not take part in the review or decision-making process of this paper. H.-I.W., L.H., R.J., S.L.P., T.D., J.T., C.E.W.K. and S.B. declare no conflicts of interest.

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