Title: Type 2 diabetes mellitus in people with severe mental illnesses; inequalities by ethnicity and age. Cross-sectional analysis from the UK

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Abstract:

Objective: To investigate the association of severe mental illnesses (SMI) with type 2 diabetes mellitus (T2DM) and assess variations by ethnicity and age.

Design: Cross-sectional analysis of primary care records

Setting and participants: In total, 1.06 million individuals registered to 98% of general practices in the London boroughs of Tower Hamlets, Newham, City & Hackney and Lambeth. Ethnic groups included in analyses were: Indian, Pakistani, Bangladeshi, black Caribbean, black African, white British and Irish.

Main outcome measure: Prevalent diagnosed cases of type 2 diabetes mellitus.

Results: Relative risk (RR) of T2DM in people with SMI was greatest in the youngest age groups; in the white British group this was RR: 9.99 (95% CI: 5.34, 18.69) at age 18-34 years, RR: 2.89 (95% CI: 2.43, 3.45) at age 35-54 and RR: 1.16 (95% CI: 1.04, 1.30) at age 55+, with similar trends by age, across all ethnic minority groups.

Assessment of absolute differences in T2DM prevalence suggested that ethnic minorities were more likely to be diagnosed with T2DM if they also had a record of SMI. Estimated prevalence of T2DM was greatest in Bangladeshi people with SMI (vs. without SMI) across all age bands (at age 18-34: 7.6% vs 1.0%, age 35-54: 31.8% vs. 15.7% and age 55+: 63.4% vs. 51.7%), with large risk differences for T2DM (SMI vs. non-SMI) in other ethnic minority groups at age 35-54 (Indian 19.4% vs. 9.2%, Pakistani 21.4% vs. 9.9%, black Caribbean 14.1% vs. 5.9% and black African 13.2% vs. 6.2%).

Conclusions: Compared to people not known to have SMI, the relative risk of T2DM in people living with SMI is elevated in young populations. Some ethnic minority groups are more likely to have T2DM in the presence of SMI, which may indicate a 'double disadvantage' for health. This should be considered in future research and service provision in ethnically diverse areas.

Background

Life expectancy in people with severe mental illnesses (such as schizophrenia, bipolar affective disorder and non-organic psychosis) is reduced by 15-20 years, compared with the general population[1]. A large proportion of these deaths are accounted for through natural causes[2]. At least one third of the reduction in life expectancy may be through cardiovascular mortality[3]. Modifiable risk factors such as type 2 diabetes mellitus[4], are also known to be more prevalent in this population.

The prevalence of type 2 diabetes mellitus has been estimated to be 2-4 times higher in people with severe mental illnesses, compared with the general population[5, 6], with overall prevalence estimated to be between 8-15% in severe mental illnesses[7]. Proposed mechanisms include impact of medications such as anti-psychotics[7], social deprivation; and lifestyle[4]; as well as the direct effect of severe mental illness[4]. However, previous studies of type 2 diabetes mellitus in severe mental illness have been limited by reliance on small convenience samples and secondary care data[6], which may represent populations of individuals with a more severe course of illness.

Despite a growing appreciation that severe mental illness is associated with an increased risk of type 2 diabetes mellitus[7], there is a dearth of epidemiological evidence highlighting how these associations vary by ethnicity[8]. This is a concern as there is considerable evidence indicating that type 2 diabetes mellitus is more prevalent in some ethnic minority groups, for example high rates of type 2 diabetes mellitus have been reported in Bangladeshi, Pakistani, Indian and black Caribbean[9, 10] people. A recent review highlighted the possibility that ethnic minority groups in the US may be more likely to develop type 2 diabetes mellitus if also diagnosed with severe mental illness, relative to white Americans[8]. The possibility that having a severe mental illness *and* being of an ethnic minority background as being worse for physical health outcomes such as type 2 diabetes mellitus (the so called 'double jeopardy'[11] or 'double disadvantage' hypothesis[12]) remains yet to be explored. Mechanisms which may underlie this may relate to potential differences by ethnicity in treatment and impact on health, as well as the dual challenges of living with a stigmatised condition such as schizophrenia, intermeshed with belonging to a marginalised ethnic group[12], and the impact on health and access to treatments[12].

With this in mind, the aim of this study was to assess the association of severe mental illness with diabetes mellitus, using a large cross-sectional dataset of approximately 1.06 million

patient records from UK primary care. Practices were located in an ethnically diverse urban location where many ethnic minority people reside and where the incidence of severe mental illnesses is elevated[13]. Our primary hypothesis was that prevalence of type 2 diabetes mellitus would be elevated in people with severe mental illnesses. Our secondary hypothesis was the prevalence of type 2 diabetes mellitus in severe mental illnesses would be most elevated in ethnic minority groups already known to be at an increased risk of type 2 diabetes mellitus, specifically Indian, Pakistani, Bangladeshi, black Caribbean and black African people[9], and that the added risk of living with a severe mental illness for these groups would be greater than for white British people.

Methods

Design, setting and population

Data from 1,056,213 individuals registered to (189 of the 192) general practices (98%) in the London boroughs of Tower Hamlets, Newham, City & Hackney and Lambeth, were used for the analyses. Each of these boroughs are resident to some of the largest ethnic minority communities in the United Kingdom, including Bangladeshi, black Caribbean and black African communities; 51% of the population in the study area self-identify as belonging to an ethnic minority group[14]. The areas are also characterised by high population density and high levels of poverty[14]. All patient records for one year prior to the date of extraction were included in the analyses. This was 31st March 2013 for records from East London (Tower Hamlets, Newham, City & Hackney) and 31st October 2013 for records from Lambeth.

Measures

A pay-for-performance scheme, the *Quality and Outcomes Framework* (QOF), was established as part of the general practitioner (family physician) contract introduced in 2004[15] and covers the care of all patients registered to primary care in the England[15]. The QOF provides general practitioners with a financial incentive to keep an up-to-date register of people with a confirmed diagnosis of schizophrenia, bipolar affective disorder and non-organic psychosis[15]. At the time of this study, general practitioners were incentivised to ensure that health checks in people with severe mental illnesses, (including the assessment of HbA1c and glucose measurement), were undertaken annually[15]. Diagnostic Read codes[16] were used to derive main exposure and outcome measures used in the analysis. Read codes are a thesaurus of standardised clinical terms which provide the means through which clinicians record patient health indicators[16].

Exposure

Severe mental illness

Individuals with a diagnosis of schizophrenia, bipolar affective disorder or non-organic psychosis, were identified using Read codes[16] and grouped together to form the main exposure category of ‘severe mental illness’. The use of computer-based electronic records to identify patients with severe mental illness has previously been validated[17]; recent work has shown that this diagnostic grouping remains stable over time[18]. In the UK, almost all of the

population are registered with general practice[19]. Up to one third of people with a severe mental illness may be registered with a general practitioner but not known to secondary care[20].

Outcome

Type 2 Diabetes

Diagnosis in primary care sample

Primary care diagnoses of diabetes mellitus were ascertained by reviewing diagnostic codes[16] entered by general practitioners. A clinician (JD) manually reviewed all diagnostic codes. Criteria for diagnosis of diabetes mellitus were based on approaches used in other primary-care database studies such as The Health Improvement Network (THIN)[21] and the Clinical Practice Research Datalink (CPRD)[22]. We did not re-categorise patients prescribed Metformin without diagnostic codes indicating type 2 diabetes mellitus, since Metformin is also prescribed for other non-diabetic conditions[23]. Figure 1 displays how the sample was derived.

[Figure 1]

Effect modifiers and confounders

Age, gender and area-level deprivation

Age at last birthday and gender were available for all participants. Age was categorised into three groups (18-34, 35-54, 55+). Measures for area-level deprivation were derived by mapping postcodes of participants to Lower Level Super Output Areas (LLSOAs) which were then mapped to national quintiles for the Index of Multiple Deprivation (IMD 2010) by area[24].

Ethnicity

Self-ascribed ethnicity mapped to the 2011 UK census categories was used[25] and classified using similar approaches as the *Health Surveys for England*[9, 10]. Resultant ethnic groups were: white British, Irish, Indian, Pakistani, Bangladeshi, black Caribbean, and black African.

Statistical Analysis

Analyses were conducted in Stata-13 MP[26]. A generalised linear model with log link and Poisson distribution[27] were used to derive relative risks (RR)[27]. As the variation in binary data may be overestimated using Poisson regression, a robust variance estimator was initially used[27]. 95% confidence intervals derived using this approach against one which used Poisson regression with robust standard errors to account for clustering by general practice were similar to three decimal places. Therefore final models were stratified by age and ethnicity and adjusted for confounders (gender, area-level deprivation), with clustering by general practice accounted for through robust standard errors.

To clarify differences in baseline risk of type 2 diabetes mellitus in ethnic groups and the effect on this of also being diagnosed with severe mental illnesses, (therefore leading to estimates with more direct relevance to clinical practice), absolute measures for risk of type 2 diabetes mellitus were derived. These were derived using generalised linear models with a binomial distribution and an identity link, giving adjusted estimated prevalence and absolute risk difference of type 2 diabetes mellitus in people with severe mental illnesses relative to those without severe mental illness[28], stratified by ethnicity and age. All models were adjusted for gender, area-level deprivation and robust standard errors to account for practice-level clustering. Wald tests were used to assess strength of associations.

Ethical approval

The study was approved by Kings College London Research Ethics Committee. Locally, the South London Primary Care Research Governance Team reviewed the process of anonymised data analysis confirming that research governance assurance was not required. As a secondary analysis of anonymised data this study did not require national ethics approval.

Results

In total there were data from 588408 individuals, registered to 189 practices, included in the study. Data for age, gender and practice location was complete. There were 33656 (6%) individuals without information on area-level deprivation. Table 1 displays key demographic features of the sample.

[Table 1]

Relative risk of Type 2 diabetes

Table 2 displays stratum-specific estimates for relative risk of type 2 diabetes in people with severe mental illnesses, relative to those without severe mental illnesses, stratified by ethnicity and age, and adjusted for confounders. Across all ethnic groups, relative risks for the association of severe mental illnesses with type 2 diabetes mellitus showed a reduction with increasing age. There was strong evidence in support of effect modification (Wald test $p<0.001$) in models in which the three-way interaction of age, ethnicity and severe mental illness, in the association with type 2 diabetes, was assessed.

[Table 2]

Prevalence and risk difference of type 2 diabetes mellitus in severe mental illnesses

Adjusted estimated prevalence of type 2 diabetes mellitus was increased in the presence of severe mental illnesses, across all age and ethnic groups (Figure 2). Although there was a larger magnitude of risk of type 2 diabetes mellitus (in relative terms) in the youngest age group (table 2), absolute estimates of prevalence were most elevated for Bangladeshi people with severe mental illnesses, who had an estimated prevalence of type 2 diabetes mellitus of 7.6% (95% CI: 5.5%-9.6%) in the youngest age band (18-34); this was 1.0% (95% CI: 0.9-1.1) in the Bangladeshi population without severe mental illnesses (figure 2). At age 35-54, estimated prevalence of type 2 diabetes mellitus increased further across all ethnic groups living with severe mental illnesses and was most notable for Indian, Pakistani, Bangladeshi and black Caribbean people with severe mental illnesses (online table 1, figure 2). At later life (age 55+) prevalence estimates for type 2 diabetes mellitus remained elevated in people with severe mental illnesses, across all ethnic groups, however was greatest for Bangladeshi people living with severe mental illnesses (online table 1).

The excess risk of type 2 diabetes mellitus due to the presence of severe mental illness, within each age band and by ethnic group, are displayed in the online supplement (online table 1). Wald tests to assess for statistical interaction in these models indicated strong evidence supporting a departure from additive models in all three age groups (online table 1).

[Figure 2]

[link to online supplement table 1 here]

Discussion

Main findings

The study provides confirmatory evidence that the prevalence of type 2 diabetes mellitus is elevated in people with severe mental illnesses, irrespective of age and ethnicity. Relative to people not known to have severe mental illness, the risk of type 2 diabetes mellitus in people with severe mental illnesses was most elevated in young populations (age 18-34). For example white British people with severe mental illnesses were 9.81 times more likely to be diagnosed with type 2 diabetes relative to white British people without severe mental illnesses (95% CI: 5.25, 18.36) , with a similar trend across all other ethnic minority groups. As age increased, this relative risk decreased across all ethnic groups. In models estimating absolute risk, estimated prevalence of type 2 diabetes mellitus in people with severe mental illnesses were most elevated in Bangladeshi people living with severe mental illness (all ages) and in most other ethnic minority groups (Indian, Pakistani, black Caribbean and black African people) diagnosed with severe mental illnesses, at age 35-54 and all ethnic minority groups (including Irish people) with severe mental illnesses at age 55+.

Comparison with other studies and implications

Our findings are in keeping with previous work which has shown a strong association between severe mental illness and type 2 diabetes mellitus[1, 7, 29]. We also found evidence to suggest notable variations in this association by ethnicity and age. Previous studies have suggested the risk of type 2 diabetes mellitus in people with severe mental illness may be 2-4 times higher than in the background population[5, 6]. Although this magnitude of association was confirmed in our study sample for people aged 35-54, in the youngest age band of 18-34, the relative risk of type 2 diabetes mellitus was more elevated than this. By age 75+ the relative risk for association of severe mental illness with type 2 diabetes mellitus was diminished across all ethnic groups. If this finding is considered alongside evidence that the life expectancy of people with severe mental illness is much reduced[1], it is possible that our findings indicate a healthy survivorship effect among those with severe mental illnesses. A similar trend has been demonstrated previously for cardiovascular and stroke mortality in people with severe mental illnesses[5]. A related explanation may be that the findings reflect competing risks[30], in other words, the increased risk of premature death from related causes removes people from the ‘at risk’ (severe mental illness) population, leading to a reduced relative risk of type 2 diabetes in people with severe mental illnesses, in the oldest age

groups. Finally, it is also possible that the diabetogenic effects of treatments for severe mental illnesses show variations by age and ethnicity. Future work potentially using longitudinal data linked to mortality records could be used to understand this further.

The variations in estimated prevalence and risk difference of type 2 diabetes mellitus by ethnicity and presence of severe mental illness also deserves comment. In particular, although the presence of severe mental illness was associated with a greater estimated prevalence of type 2 diabetes mellitus across the sample, this was greatest in Bangladeshi people (all ages) and most other ethnic minority groups at mid-life and older ages. These findings indicate that some ethnic minority groups are more likely to have type 2 diabetes mellitus, in the presence of severe mental illness. In particular, it is possible that the differing prevalence estimates are due to differences in treatment across ethnic groups as well as a possible differential impact of severe mental illness on the physical health and ability to access preventative health-care, in some ethnic minority groups. The findings support the possibility of 'double disadvantage'[12], or the possibility that those who are multiply disadvantaged may have poorer health than those who are singly or not disadvantaged[12]. This require further investigation in order to understand underlying mechanisms.

Limitations

Although a healthy survivor effect could account for the findings, the cross-sectional nature of this dataset means than it is not possible to be certain about this association. It is also possible that the differential association of severe mental illness with type 2 diabetes mellitus by age could have been accentuated by ascertainment biases, as incident type 2 diabetes mellitus may have been less likely to have been ascertained in older people with severe mental illnesses as there may be less attention to medication side-effects in this age group, especially if people had been on a stable regime for long periods of time. It is also possible that older people with chronic mental disorders may be less likely to visit primary care physicians, complain of relevant symptoms, or have family members who can assist and advocate for them, which could have also led to a lower reported prevalence of type 2 diabetes mellitus in this group, relative to older people not living with severe mental illnesses. More work is needed to determine if this could have accounted for the differences observed.

It is also possible that prevalence estimates are residually confounded by social deprivation over and above what we were able to capture with the area-level deprivation measures. We did not adjust for Body Mass Index or anti-psychotic medication prescriptions as this was

beyond the scope of the current analyses which sought to describe the prevalence of type 2 diabetes mellitus in this population. Future research could explore the role of these variables and others as potential mediators for observed associations.

Conclusions

These findings suggest that type 2 diabetes mellitus, an important predictor of premature mortality[31] in people with severe mental illnesses, shows marked variation by age and ethnicity. This is an important finding from the perspective of service provision as efforts to concentrate case-finding and management may need to include type 2 diabetes mellitus screening in younger populations with severe mental illnesses.

These findings also suggest that some ethnic minority groups may be more likely to have type 2 diabetes mellitus in the presence of a severe mental illness diagnosis. This has been largely overlooked in previous research and policy[8] and will need to be considered in future research as well as in considering service provision in areas which are ethnically diverse.

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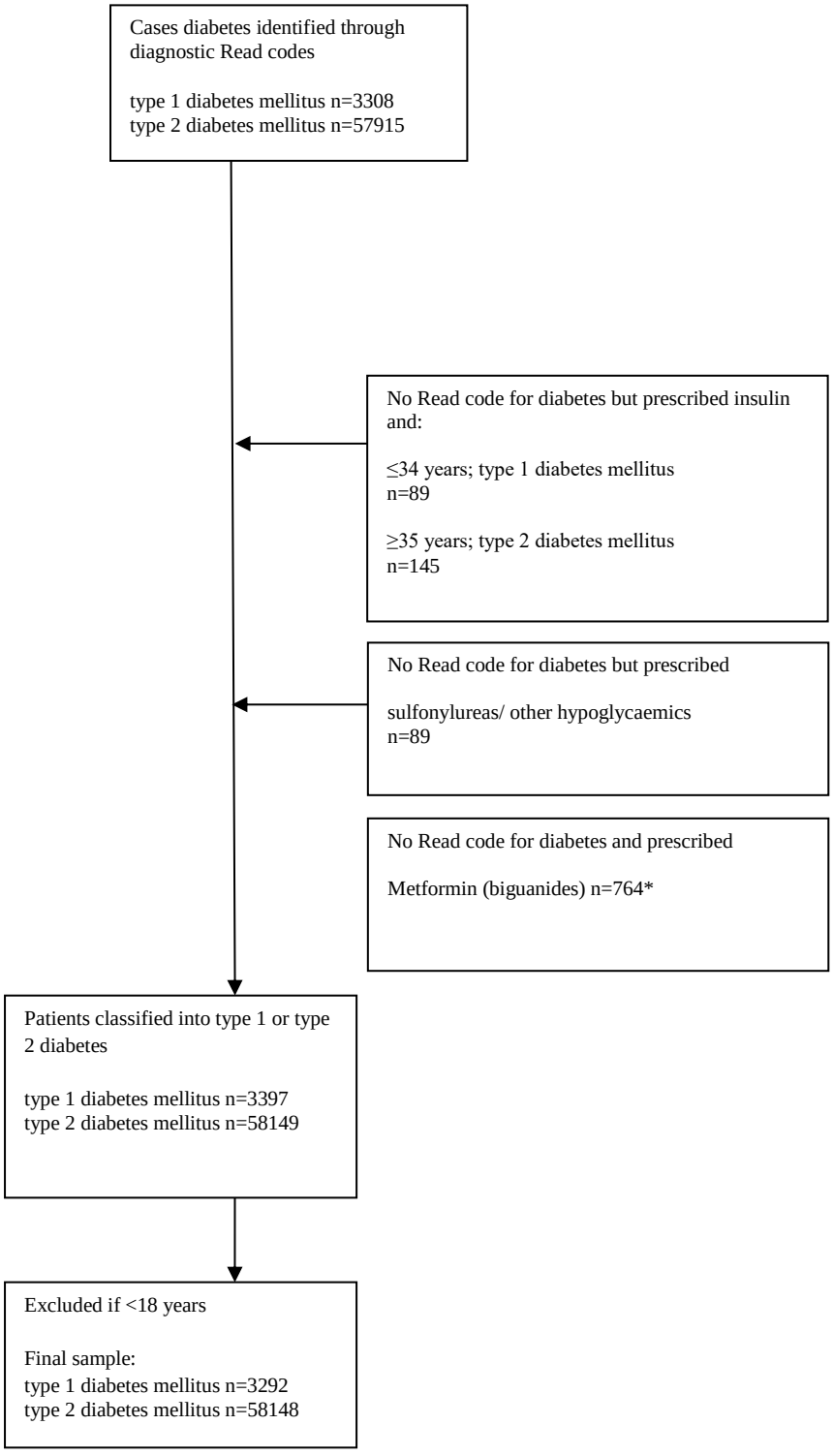
All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf. All authors except FG declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. FG has received honoraria for advisory work and lectures from Roche, Lundbeck, and Sunovion and has a family member with professional links to Lilly and GSK.

Figure 1



Key

**not added to sample as this class of medications is also prescribed for non-diabetic conditions*

Table 1: Demographic features of the sample

	N	(%)
Total sample	588408	100%
Age		
18-34	250883	43%
35-54	213428	36%
55+	124097	21%
Gender		
Male	299796	51%
Female	288612	49%
Ethnicity		
white British	242614	41%
Irish	13745	2%
Indian	63999	11%
Pakistani	35596	6%
Bangladeshi	94643	16%
black Caribbean	54939	9%
black African	82872	14%
Area level deprivation*		
most deprived quintile	370313	67%
	147890	27%
	28657	5%
	5532	1%
least deprived quintile	2360	<0.1%
Severe mental illness		
No severe mental illnesses	577638	98%
Severe mental illnesses	10770	2%
Type 2 diabetes		
No diabetes	541541	92%
Type 2 diabetes	44622	8%

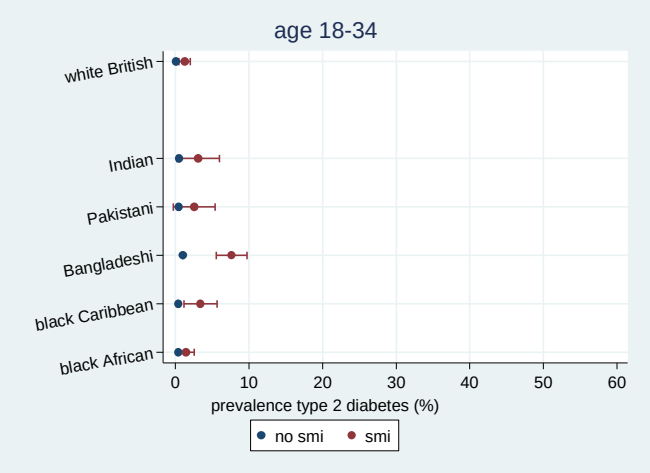
**Index of Multiple Deprivation at Lower-level Super Output Area*

Table 2: Association of severe mental illness with type 2 diabetes

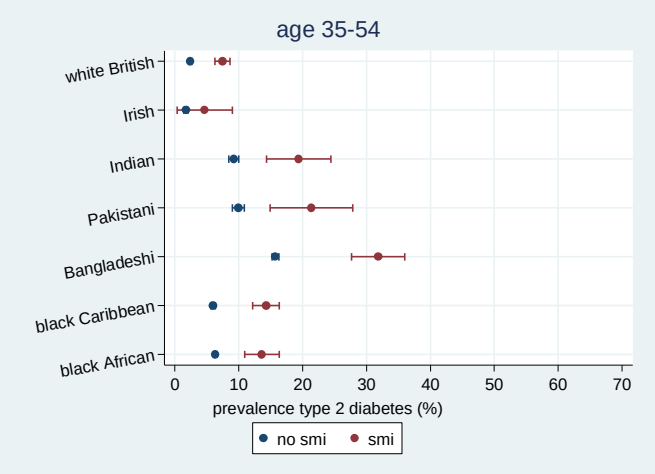
	No Severe Mental Illness	Severe Mental Illness	Age group		
			18-34	35-54	55
Ethnicity	**N with/without type 2 diabetes**	**N with/without type 2 diabetes**	**RR (95% CI)**	**RR (95% CI)**	**RR (95% CI)**
white British	10775/226175	433/3951	9.81 (5.25, 18.36)	2.88 (2.42, 3.44)	1.17 (1.04, 1.31)
Irish	562/12845	34/249	-	2.84 (1.04, 7.79)	1.60 (1.16, 2.20)
Indian	5433/57824	134/482	6.01 (2.32, 15.59)	2.08 (1.59, 2.72)	1.13 (0.96, 1.32)
Pakistani	3071/32073	79/300	5.26 (1.70, 16.26)	2.14 (1.59, 2.89)	1.23 (0.99, 1.53)
Bangladeshi	10965/82056	419/1076	7.28 (5.51, 9.63)	2.02 (1.77, 2.31)	1.25 (1.14, 1.37)
black Caribbean	6427/46204	406/1596	8.31 (4.16, 16.60)	2.36(2.01 2.77)	1.13 (1.02, 1.26)
black African	5688/75350	196/1360	3.45 (1.54, 7.76)	2.13 (1.73, 2.62)	1.11 (0.90, 1.35)

Key: *-too few observations; Estimates are Relative Risks (95% CI) for type 2 diabetes in people with severe mental illness vs. no severe mental illness, stratified by age and ethnicity. All models take into account practice-level clustering using robust standard errors and are adjusted for gender and area-level deprivation. p<0.001(Wald test) for three-way statistical interaction (age, ethnicity and severe mental illness)*

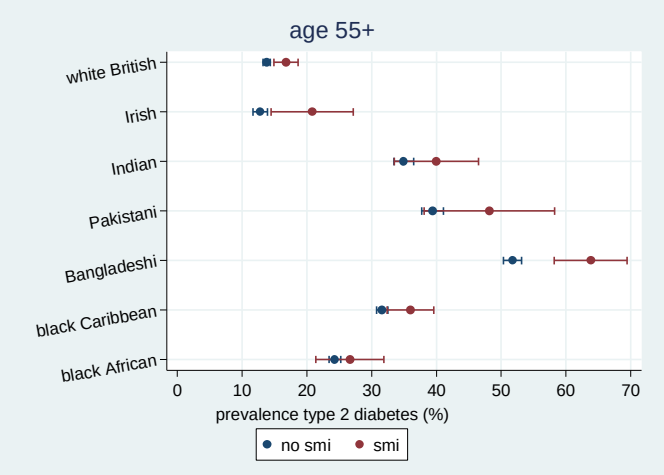
Fig 2: Estimated prevalence of type 2 diabetes mellitus by ethnicity, presence of severe mental illness & age



	Prevalence (%)	(95% CI)
white British no SMI	0.1	(0.1, 0.2)
white British SMI	**1.3**	**(0.5, 2.0)**
Indian no SMI	0.5	(0.4, 0.6)
Indian SMI	**3.1**	**(0.2, 6.0)**
Pakistani no SMI	0.5	(0.4, 0.6)
Pakistani SMI	**2.6**	**(-0.3, 5.4)**
Bangladeshi no SMI	1.0	(0.9, 1.1)
Bangladeshi SMI	**7.7**	**(5.5, 9.8)**
black Caribbean no SMI	0.4	(0.3, 0.5)
black Caribbean SMI	**3.4**	**(1.2, 5.7)**
black African no SMI	0.4	(0.3, 0.5)
Black African SMI	**1.5**	**(0.3, 2.6)**



	Prevalence (%)	(95% CI)
white British no SMI	2.4	(2.2, 2.6)
white British SMI	**7.4**	**(6.2, 8.7)**
Irish no SMI	1.8	(1.4, 2.1)
Irish SMI	4.7	(0.4, 9.0)
Indian no SMI	9.2	(8.5, 10.0)
Indian SMI	**19.4**	**(14.4, 24.4)**
Pakistani no SMI	9.9	(9.0, 10.9)
Pakistani SMI	**21.4**	**(14.9, 27.8)**
Bangladeshi no SMI	15.7	(15.2, 16.3)
Bangladeshi SMI	**31.8**	**(27.7, 36.0)**
black Caribbean no SMI	6.0	(5.6, 6.4)
black Caribbean SMI	**14.3**	**(12.2, 16.4)**
black African no SMI	6.3	(6.1, 6.6)
Black African SMI	**13.6**	**(10.9, 16.3)**



	Prevalence (%)	(95% CI)
white British no SMI	13.8	(13.2, 14.4)
white British SMI	**16.8**	**(14.9, 18.6)**
Irish no SMI	12.8	(11.7, 13.9)
Irish SMI	**20.8**	**(14.5, 27.1)**
Indian no SMI	34.9	(33.4, 36.5)
Indian SMI	**40.0**	**(33.5, 46.5)**
Pakistani no SMI	39.4	(37.7, 41.1)
Pakistani SMI	**48.2**	**(38.1, 58.2)**
Bangladeshi no SMI	51.7	(50.3, 53.1)
Bangladeshi SMI	**63.8**	**(58.2, 69.4)**
black Caribbean no SMI	31.6	(30.7, 32.5)
black Caribbean SMI	**36.0**	**(32.4, 39.6)**
black African no SMI	24.3	(23.4, 25.2)
Black African SMI	**26.6**	**(21.4, 31.9)**

Key: *Prevalence estimates adjusted for gender, area-level deprivation and clustering by practice; 'SMI' Severe Mental Illness*

Appendix/ online supplement:

Table 1: Risk difference (RD) with 95% Confidence Intervals in estimated prevalence of type 2 diabetes in people with severe mental illnesses compared to people without severe mental illnesses, by ethnicity and age

	No Severe Mental Illness	**Severe Mental Illness**	**Age 18-34** n= 228561	**Age 35-54** n=200874	**Age 55+** n=118332
	N with/without type 2 diabetes	**N with/without type 2 diabetes**	**RD (95% CI)**	**RD (95% CI)**	**RD (95% CI)**
white British	10775/226175	433/3951	1.13 (0.36, 1.91)	4.71 (3.51, 5.91)	2.57 (0.75, 4.39)
Irish	562/12845	34/249	-	2.61 (-1.71, 6.92)	8.08 (1.69, 14.47)
Indian	5433/57824	134/482	2.59 (-0.31, 5.50)	10.06 (5.00, 15.12)	4.97 (-1.34, 11.28)
Pakistani	3071/32073	79/300	2.08 (-0.75, 4.92)	11.40 (5.08, 17.73)	8.94(-1.49, 19.38)
Bangladeshi	10965/82056	419/1076	6.62 (4.52, 8.72)	16.08 (11.94, 20.22)	12.38 (6.92, 17.84)
black Caribbean	6427/46204	406/1596	3.02 (0.78, 5.26)	8.18 (6.06, 10.30)	4.30 (0.63, 7.97)
black African	5688/75350	196/1360	1.04 (-0.08, 2.16)	7.26 (4.54, 9.99)	2.64 (-2.67, 7.95)
Wald test for interaction of ethnicity and SMI within age group			*p<0.001*	*p<0.001*	*p=0.02*

All risk difference estimates adjusted for gender, area-level deprivation and practice-level clustering.