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Metabolic disease and cardiovascular risk in people treated with antipsychotics in the community

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Background Prevalence of physical comorbidity in severe mental illness is a significant public health concern, but comparative data in people with diagnoses other than schizophrenia are sparse.

Aims To investigate the prevalence of metabolic disease and cardiovascular risk in people with severe mental illness treated with antipsychotics in the community.

Methods Case–control study of 90 people treated with antipsychotics in the community and 92 age- and gender-matched controls. The prevalence of metabolic syndrome and 10-year cardiovascular risk were calculated.

Results People on antipsychotics had a significantly worse metabolic profile than controls (F=6.583, d.f.=15,161, P<0.0001). Moreover, metabolic syndrome was more prevalent (OR=3.68, 95% CI 1.71–7.93, P=0.001), as was cardiovascular risk across a number of outcomes. These results are consistent across diagnostic groups.

Conclusions People with severe mental illness treated with antipsychotics have excess metabolic dysfunction and heightened risk for cardiovascular disease.

Declaration of Interest P.M., I.N.F. and P.G. have received honoraria for educational meetings from pharmaceutical companies. Funding detailed in Acknowledgements.

Severe mental illness is associated with a significant excess of physical comorbidity and mortality (Brown 1997; Phelan *et al*, 2001; Osborn *et al*, 2007), and as such represents a major public health concern. Although suicide is prevalent in this population, ischaemic heart disease, not suicide, may be the major contributor to excess mortality (Lawrence *et al*, 2003). Recently published UK guidelines on the management of schizophrenia (National Institute for Clinical Excellence, 2002) and bipolar disorder (National Institute for Clinical Excellence, 2006) recognise the impact of physical comorbidity in these disorders, as well as the paucity of high-quality research in this field.

A number of recent studies have quantified the risk of coronary heart disease, based on Framingham risk estimates, in people with severe mental illness (Goff *et al*, 2005; Correll *et al*, 2006; Osborn *et al*, 2006), but these have focused on those with a diagnosis of schizophrenia or non-affective psychoses (Goff *et al*, 2005; Osborn *et al*, 2006) and hospital in-patients (Correll *et al*, 2006). In this study we determined the prevalence of metabolic dysfunction and estimates of cardiovascular risk in a community sample from secondary care of people with severe mental illness from across the diagnostic spectrum, who were taking antipsychotics, and compared the results with those from age- and gender-matched controls.

METHOD

Pariticpants

Patients from all secondary care community mental health services from across the former Newcastle, North Tyneside and Northumberland Mental Health NHS Trust, and the Regional Affective Disorders Tertiary Service were invited to participate in a baseline study of metabolic dysfunction between January 2002 and March 2004. Participants were recruited irrespective of psychiatric diagnosis. Inclusion criteria were a psychiatric diagnosis and the prescription of and adherence to (determined by self-report) antipsychotic medication for a minimum of 6 months. People with a known diagnosis of type 1 or type 2 diabetes mellitus, anorexia nervosa, bulimia nervosa, neoplastic disease or alcohol dependence were excluded. We invited 198 people to participate and 106 (54%) gave their informed consent. Baseline characteristics of this cohort have been described previously (Mackin *et al*, 2005).

All participants with a baseline assessment of metabolic function were invited to participate in a follow-up study between June and December 2005. An age- and gender-matched control group was recruited between January and June 2006 for comparison of metabolic and cardiovascular risk parameters. In an attempt to control for demographic and socio-economic variables, family members and carers were invited to participate as controls, and advertisements for volunteers were placed in local facilities within the geographical environs in which the community mental health teams were based. People with a history of psychiatric disorder and those who had ever taken a prescribed drug for a psychiatric disorder were excluded. All participants gave written informed consent and the study was approved by the Newcastle local research ethics committee.

Procedures

Participants were given written instructions to fast overnight on the day before assessment, and were asked to confirm their fasting status on the morning of study. All assessments were performed in the Department of Psychiatry, University of Newcastle upon Tyne between 08.30 and 10.00 h on the study day. Demographic details of age, gender and ethnic group were obtained. Current and previous tobacco, alcohol and illicit substance use were recorded, as well as any history of cardiovascular disease and diabetes mellitus in first-degree relatives. Information regarding psychiatric diagnosis, duration of illness, number of admissions to psychiatric in-patients facilities, medication (including non-psychotropic drugs) and dosage was recorded and confirmed, where necessary, by reference to case notes and general practitioner records.

Height, weight, and waist and hip circumference were recorded using standardised procedures. Body mass index (BMI) and waist-to-hip ratio were calculated. Conventional BMI categories were used (underweight <18.5; normal 18.5–24.9; overweight 25.0–29.9; obese: >30.0). Blood pressure was recorded using a sphygmomanometer on three occasions during the assessment, and the value expressed as the mean of the three recordings. A 12-lead electrocardiogram (ECG) was recorded at 50 mm/s using a MAC 1200ST portable machine (GE Medical Systems, Slough, Berkshire, UK). For the purposes of cardiovascular risk estimation, ECGs were analysed for Framingham voltage criteria for left ventricular hypertrophy (Levy *et al*, 1990).

A single venous blood sample was withdrawn and analysed for glucose, glycosylated haemoglobin (HbA_{1c}), insulin and lipid profile (total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, and triglycerides). Insulin was measured by enzyme-linked immunosorbent assay. The Homeostasis Model Assessment (HOMA; Levy *et al*, 1998) was used to assess glucose handling, which is expressed as pancreatic beta-cell function, insulin sensitivity and insulin resistance. Values for these parameters were based on fasting glucose and insulin levels and calculated using the HOMA Calculator, version 2.2 (Diabetes Trial Unit, University of Oxford, UK). The model is calibrated to give beta-cell function and insulin sensitivity of 100% in healthy adults with currently available insulin assays. Impaired fasting glucose was defined as fasting blood glucose between 6.1 and 7.0 mmol/l, and diabetes mellitus as fasting blood glucose $\geqslant 7.0$ mmol/l (National Diabetes Data Group, 1979). The presence of the metabolic syndrome was based on the definition by the International Diabetes Federation (Alberti *et al*, 2006).

Cardiovascular risk estimates were based on established risk factors using the Joint British Societies' (JBS) definition of cardiovascular disease, and the Framingham definition (Anderson *et al*, 1991). The University of Edinburgh Cardiovascular Risk Calculator (http://cvrisk.mvm.ed.ac.uk/calculator.htm) was used to compute percentage risk estimates for a number of outcomes over a 10-year period. Risk estimates using the Framingham equation have important differences from the JBS definition which include the ability to calculate specific risks (for cardiovascular disease, coronary heart disease, myocardial infarction, stroke, death due to cardiovascular disease and death due to coronary heart disease) and the option to vary the time period over which risk is computed. Cardiovascular risk is calculated from the following parameters: age, gender, smoking status, blood pressure, total cholesterol and HDL cholesterol. The Framingham equation also incorporates the presence of left ventricular hypertrophy in the risk estimate.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences, version 11 for Windows. Demographic characteristics were examined by *t*-test or χ^2 test where appropriate. Owing to the number of metabolic parameters measured and the risk of Type 1 error, we first conducted a multivariate analysis of covariance (MANCOVA) to test for a significant overall difference in continuous metabolic parameters between the group with mental illness and controls. Differences in individual measures were then examined by follow-up *t*-tests or Mann–Whitney tests. χ^2 analysis was used to compare the distribution of discrete variables. Analysis of variance (ANOVA) was used to examine the effect of specific factors such as smoking status or antipsychotic drug (i.e. typical or atypical) on metabolic and cardiovascular risk estimates. All reported *P* values are two-tailed. Statistical significance is defined as $P<0.05$.

RESULTS

Characteristics of participants

Of the original 106 participants in the baseline study, 90 (85%) consented to participate in the current study; 6 (5.7%) did not reply to the invitation; 6 (5.7%) refused to consent; 2 (1.9%) were too unwell to participate; and 1 (1%) denied having participated in the original study. Characteristics of the participants with mental illness and the 92 controls are given in Table 1. The groups were well matched in terms of age and gender. Participants with mental illness were recruited from across the diagnostic spectrum: bipolar disorder (n=32, 35.6%); schizophrenia (n=27, 30.0%); schizoaffective disorder (n=9, 10.0%); other (including delusional,

Table 1 Characteristics of participants with severe mental illness and controls

	People with mental illness (n=90)	Controls (n=92)
Age, years: mean (s.d.)	45.7 (11.8)	43.5 (13.6)
Gender, *n* (%)		
Male	44 (48.9)	43 (46.7)
Female	46 (51.1)	49 (53.3)
Ethnicity, *n* (%)		
White	88 (97.8)	90 (97.8)
Asian (Indian)	2 (2.2)	0 (0)
Asian (Oriental)	0 (0)	1 (1.1)
Mixed race	0 (0)	1 (1.1)
Current smoker, *n* (%)		
Yes	36 (40.0)**	13 (14.1)
No	54 (60.0)	79 (85.9)
History of substance misuse, *n* (%)		
Yes	27 (30.0)**	4 (4.3)
No	63 (70.0)	88 (95.7)
Family history of cardiovascular disease, *n* (%)		
Yes	61 (67.8)	50 (54.3)
No	29 (32.2)	42 (45.7)
Family history of diabetes mellitus, *n* (%)		
Yes	31 (34.4)	22 (23.9)
No	59 (65.6)	70 (76.1)

**$P<0.001$.

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Table 2 Medication taken by participants with mental illness

Drug	*n* (%)
Antipsychotic	
None	7 (7.8)
One antipsychotic	71 (78.8)
Combination antipsychotics	12 (13.3)
Typical or atypical antipsychotic[1]	
Typical	16 (22.5)
Zuclopenthixol	2 (2.8)
Flupenthixol	5 (7.0)
Haloperidol	1 (1.4)
Fluphenazine	1 (1.4)
Pipothiazine	1 (1.4)
Sulpiride	4 (5.6)
Trifluoperazine	2 (2.8)
Atypical	55 (77.5)
Amisulpiride	3 (4.2)
Clozapine	7 (9.9)
Olanzapine	29 (40.8)
Quetiapine	8 (11.3)
Risperidone	8 (11.3)
Other psychotropic drugs	
Antidepressants	
SSRI	29 (32.2)
SNRI	9 (10)
NaSSA	4 (4.4)
TCA	7 (7.8)
MAOI	3 (3.3)
Mood stabilisers	
Valproate	16 (17.8)
Lamotrigine	8 (8.9)
Carbamazepine	1 (1.1)
Lithium	15 (16.7)
Others	
Gabapentin	2 (2.2)
Benzodiazepines	28 (31.1)
Tryptophan	2 (2.2)
Anticholinergic agent	15 (16.7)
Non-psychotropic drugs	
Antihypertensive agent	13 (14.4)
Lipid-lowering therapy	7 (7.8)
Thyroxine	10 (11.1)
Hypoglycaemic agent	4 (4.4)

SSRI, selective serotonin reuptake inhibitor; SNRI, selective noradrenaline reuptake inhibitor; NaSSA, noradrenaline and specific serotonin antagonist; TCA, tricyclic antidepressant; MAOI, monoamine oxidase inhibitor.
1. Includes 71 people on one antipsychotic.

depressive and anxiety disorders, n=22, 24.4%). The mean duration of mental illness was 252.6 months (s.d.=161.1). Significantly more people with mental illness currently smoked tobacco (40.0 *v.* 14.1% of controls χ^2=15.87, $P<0.001$) and had a history of substance misuse (30.0 *v.* 4.3% of controls, χ^2=21.18, $P<0.001$).

Medication

Of the 90 people with mental illness who participated in this study, 83 (92%) were still receiving antipsychotic medication; 71 (86%) were receiving one antipsychotic drug and 12 (14%) were prescribed combination antipsychotic medication. Of those taking just one antipsychotic, 16 (23%) were taking a typical agent and 55 (77%) an atypical. Details of antipsychotic and other medication are given in Table 2.

Metabolic parameters

Metabolic parameters for participants with mental illness and controls are given in Table 3. From the MANCOVA model, age was found to be a highly significant covariate (F=5.873, d.f.=15,161, $P<0.0001$) but those with mental illness had a significantly worse metabolic profile (age-adjusted main effect: F=6.583, d.f.=15,161, $P<0.0001$). Body mass index, waist circumference, waist-to-hip ratio, total cholesterol, LDL cholesterol, serum triglycerides, fasting blood glucose, HbA_{1c} and serum insulin were all significantly higher in those with mental ilness than controls. Moreover, HDL cholesterol (which is cardioprotective) was significantly lower. Estimation of insulin sensitivity and insulin resistance by HOMA revealed differences between the two groups; that is people with mental illness were more insulin resistant, more had disorders of glucose homeostasis compared with controls (14.4 *v.* 1.1%, P=0.003), and there was a higher prevalence of the metabolic syndrome (33.3 *v.* 11.9%, P=0.001). There were no differences in either systolic or diastolic blood pressure between the groups.

Cardiovascular risk

Ten-year risk estimates based on the JBS definition of cardiovascular disease and the Framingham cardiovascular outcome risk estimates are given in Table 4. The risk calculator allows estimation of risk for people between 35 and 75 years of age (participants with mental illness n=72; controls n=65). Figure 1 represents the differences in cardiovascular outcome risks between the two groups.

Participants with mental illness had statistically greater mean 10-year risk estimates than controls for all outcomes with the exception of stroke (but there was a statistical trend towards a greater 10-year risk for stroke). Those people with a 10-year risk of cardiovascular disease according to the JBS definition of greater than or equal to 20% or those with established disease and/or diabetes mellitus should be considered 'high risk'.

Effect of smoking

Significantly more participants with mental illness than controls smoked tobacco. Univariate ANOVA was used to examine the interaction between smoking status, metabolic and cardiovascular risk parameters. Each variable was entered into the model with group and smoking status as factors. With the exception of BMI (F=4.25, d.f.=1,93, P=0.04), there was no group × smoking status interaction.

Effect of diagnosis

The impact of diagnostic group on metabolic and cardiovascular risk was examined. All metabolic and cardiovascular risk parameters were entered into a one-way ANOVA with diagnostic group (bipolar disorder, schizophrenia, schizoaffective disorder, other) as the factor in the model. There were no statistical differences in any of the variables between diagnostic groups.

Effect of antipsychotic treatment

In order to investigate the interaction between the type of antipsychotic treatment (i.e. no treatment, atypical, typical or combination) and metabolic/cardiovascular risk parameters, all variables were entered into a one-way ANOVA with treatment group as the factor in the model. Serum insulin was significantly higher in participants taking atypical agents compared with all other groups (F=2.8, d.f.=3,173, P=0.04). There were no other statistically significant differences between treatment groups.

Treatment of metabolic dysfunction and cardiovascular risk factors

The proportion of patients receiving appropriate pharmacological treatment for cardiovascular risk factors (hypertension and dyslipidaemia) was examined.

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Table 3 Metabolic parameters in participants with mental illness and controls

	People with mental illness (n=90)	Controls (*n*=92)
BMI, kg/m^2: mean (s.d.)	29.9 (4.9)***	25.6 (4.6)
Underweight, *n* (%)	2 (2.2)	1 (1.1)
Normal, *n* (%)	9 (10)***	42 (45.7)
Overweight, *n* (%)	39 (43.3)	35 (38.0)
Obese, *n* (%)	40 (44.4)	14 (15.2)
Blood pressure, mmHg: mean (s.d.)		113.7 (15.3)
Systolic	116 (19.9)	69.6 (9.9)
Diastolic	70 (11.1)	
Waist circumference, cm: mean (s.d.)	96.6 (13.1)***	84.1 (13.7)
Waist-to-hip ratio: mean (s.d.)	0.89 (0.09)***	0.82 (0.09)
Lipids, mmol/l: mean (s.d.)		
Total cholesterol	5.7 (1.4)**	5.2 (0.9)
HDL cholesterol	1.3 (0.4)***	1.6 (0.4)
LDL cholesterol	3.4 (1.2)**	3.1 (0.9)
Triglycerides	2.1 (1.3)***	1.2 (0.6)
Glucose homeostasis		
Fasting blood glucose, mmol/l: mean (s.d.)	5.5 (1.4)***	4.8 (0.5)
HbA_{1c}, %: mean (s.d.)	5.6 (0.9)**	5.2 (0.4)
Serum insulin, mU/l: mean (s.d.)	11.1 (8.1)***	7.2 (5.1)
HOMA beta-cell function, %: mean (s.d.)	98.8 (38.8)	93.6 (36.9)
HOMA insulin sensitivity, %: mean (s.d.)	98.6 (55.6)***	147.5 (72.0)
HOMA insulin resistance, %: mean (s.d.)	1.47 (1.1)***	0.93 (0.64)
Normoglycaemia, *n* (%)	77 (85.6)	91 (98.9)
Impaired fasting glucose, *n* (%)	8 (8.9)**	1 (1.1)
Diabetes mellitus, *n* (%)	5 (5.5)	0 (0)
Metabolic syndrome, *n* (%)		
Yes	30 (33.3)***	11 (11.9)
No	60 (66.7)	81 (88)

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA_{1c}, glycosylated haemoglobin; HOMA, Homeostatic Model Assessment.
*$P<0.05$, **$P<0.01$, ***$P<0.001$.

Dyslipidaemia

Current recommendations state that treatment of dyslipidaemia should be based on an overall assessment of risk rather than an isolated serum lipid value. However, 'high-risk' patients should be offered prophylactic lipid-lowering therapy. Of the 13 high-risk patients, only 4 (30.8%) were receiving lipid-lowering therapy. One control participant was considered to be 'high risk' and was receiving appropriate therapy.

Hypertension

Hypertension was considered to be present if systolic blood pressure was $\geqslant$135 mmHg and/or diastolic blood pressure was $\geqslant$85 mmHg (Alberti *et al*, 2006). Fifteen participants with mental illness (16.7%) met criteria for hypertension compared with 13 controls (14.1%). Nine participants with mental illness and hypertension (60%) were not receiving an antihypertensive agent, compared with 10 controls with hypertension (77%).

DISCUSSION

Current research is increasingly adding to the weight of evidence that the burden of physical comorbidity is greater in people with severe mental illness. Studies investigating the prevalence of metabolic dysfunction and cardiovascular risk have focused largely on people with schizophrenia, and comparative data in other diagnostic groups are sparse.

Main findings

The current study sought to investigate markers of metabolic dysfunction and cardiovascular risk estimates in a diagnostically heterogeneous sample of people with severe mental illness treated in the community. Compared with controls, people with mental illness, irrespective of diagnosis, had a significantly higher BMI (the mean BMI of 29.9 being within the overweight category and marginally short of the obese), waist circumference and waist-to-hip ratio (reflecting increased visceral adiposity). Dyslipidaemias and disorders of glucose homeostasis were more prevalent, as was the metabolic syndrome diagnosed according to the definition of the International Diabetes Federation (Alberti *et al*, 2006). The mean 10-year risk for cardiovascular disease (estimated according to both British and Framingham definitions) and the risk for a number of cardiovascular outcomes, including myocardial infarction and death due to cardiovascular disease, were consistently higher in participants with mental illness compared with controls. Moreover, a high proportion of people whose level of cardiovascular risk exceeds the threshold for intervention are not receiving appropriate treatment.

Other studies

Osborne *et al* (2006) reported raised 10-year coronary heart disease risk scores (based on Framingham criteria), HDL cholesterol levels, total cholesterol level and an increased prevalence of diabetes mellitus in a sample of people with schizophrenia or non-affective psychoses from primary care. Another study has also reported increased 10-year cardiac risk in people with schizophrenia from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study (Goff *et al*, 2005). Correll *et al* (2006) studied the prevalence of the metabolic syndrome and 10-year risk of coronary heart disease in psychiatric inpatients from across the diagnostic spectrum receiving atypical antipsychotics. Thirty-seven per cent of patients in this sample met National Cholesterol Education Program criteria for metabolic syndrome, and 47% fulfilled International Diabetes Federation criteria (Correll *et al*, 2006). This study lacked a control group, and although the prevalence of defined metabolic syndrome was higher than in our study, differences in participant characteristics (i.e. we studied community out-patients treated with typical and atypical antipsychotics), and a greater overall prevalence of obesity and the metabolic syndrome in

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Table 4 Ten-year cardiovascular risk estimates[1]

	People with mental illness (n=72)	Controls (n=65)
CVD risk (JBS) definition: mean (s.d.)	10.7 (13.2)**	5.7 (5.2)
⩾5%, *n* (%)	43 (59.7)	31 (47.7)
⩾10%, *n* (%)	24 (33.3)	16 (24.6)
⩾20%, *n* (%)	9 (12.5)*	1 (1.5)
CVD risk (Framingham definition): mean (s.d.)	11.3 (12.3)**	6.8 (6.4)
⩾5%, *n* (%)	47 (65.3)*	31 (47.7)
⩾10%, *n* (%)	26 (36.1)	19 (29.2)
⩾20%, *n* (%)	12 (16.7)*	3 (4.6)
CHD risk: mean (s.d.)	9.3 (10.5)**	4.7 (4.3)
⩾5%, *n* (%)	41 (56.9)*	26 (40)
⩾10%, *n* (%)	23 (31.9)*	10 (15.3)
⩾20%, *n* (%)	7 (9.7)**	0 (0)
Myocardial infarction risk: mean (s.d.)	4.1 (5.6)***	1.8 (2.2)
⩾5%, *n* (%)	22 (30.6)**	6 (9.2)
⩾10%, *n* (%)	9 (12.5)*	1 (1.5)
⩾20%, *n* (%)	2 (2.7)	0 (0)
Stroke risk: mean (s.d.)	1.7 (3.2)	1.0 (1.1)
⩾5%, *n* (%)	5 (6.9)	0 (0)
⩾10%, *n* (%)	3 (4.2)	0 (0)
⩾20%, *n* (%)	0 (0)	0 (0)
Risk of death due to CVD: mean (s.d.)	2.2 (4.9)	0.9 (1.2)
⩾5%, *n* (%)	9 (12.5)*	1 (1.5)
⩾10%, *n* (%)	4 (5.6)	0 (0)
⩾20%, *n* (%)	2 (2.8)	0 (0)
Risk of death due to CHD: mean (s.d.)	1.5 (3.3)*	0.6 (0.9)
⩾5%, *n* (%)	5 (6.6)	0 (0)
⩾10%, *n* (%)	2 (2.8)	0 (0)
⩾20%, *n* (%)	0 (0)	0 (0)
High risk[2], *n* (%)	13 (18.1)**	1 (1.5)

CVD, cardiovascular disease; JBS, Joint British Societies; CHD, coronary heart disease.
1. Risk estimate data were skewed and therefore means were compared with parametric and non-parametric statistical tests.
2. High risk is ⩾20% 10-year risk of CVD according to the JBS definition. Patients with established CVD and/or diabetes mellitus are also classified as high risk.
*$P<0.05$, **$P<0.01$, ***$P<0.001$.

the USA compared with the UK (Ford *et al*, 2002), is likely to account for the disparity.

Strengths of our study

Our findings confirm the results of several other studies, and offer further insights into the nature of metabolic disease and cardiovascular disease risk in severe mental illness. The inclusion of a diagnostically heterogeneous sample is important in terms of understanding the effect of diagnosis on the development of metabolic dysfunction and cardiovascular risk. The problem of physical comorbidity and strategies for improving physical health in schizophrenia have been addressed previously (Marder *et al*, 2004). However, research in other psychiatric disorders such as bipolar disorders, lags behind (Clement *et al*, 2003) and there is an urgent need to establish whether there is a similar pattern of physical comorbidity. A high prevalence of metabolic syndrome and cardiovascular risk in psychiatric in-patients from across the diagnostic spectrum has recently been reported (Correll *et al*, 2006), and we confirm these findings in a sample of community out-patients treated with typical and atypical antipsychotics.

Investigating metabolic dysfunction in a community out-patient sample overcomes, to some extent, the confounding impact of physical inactivity on glucose homeostasis (Fulton-Kehoe *et al*, 2001) which is inherent in studies of psychiatric in-patients (Martinsen *et al*, 1989). All our participants were considered to be clinically stable, and thus the confounding influence on metabolic function of acute stress resulting from psychosis (Shiloah *et al*, 2003) or other distressing psychiatric symptoms was avoided.

Unlike previous studies investigating metabolic disease and cardiovascular risk, we also measured serum insulin and calculated insulin sensitivity and beta-cell function using the HOMA. Serum insulin and insulin resistance, both established independent risk factors for cardiovascular disease (Reaven, 2002), were increased in participants with mental illness. However, the mechanism underpinning the pathophysiology of insulin resistance in severe mental illness is poorly understood.

Although much of the current literature focuses on the risk of metabolic dysregulation in people taking atypical antipsychotics, significant numbers of people continue to take first-generation agents. Our study was designed to gather data on metabolic dysfunction and cardiovascular risk in a typical clinical setting. Although the study was not designed or powered to investigate the contribution of specific antipsychotic drugs, or classes of drugs, to metabolic or cardiovascular disease, with the exception of serum insulin levels, which were significantly higher in people taking atypical antipsychotics, the metabolic and cardiovascular risk profiles were similar in those taking typical, atypical or no antipsychotic medication. However, the small sample who were not receiving antipsychotic medication at the time of investigation had previously been prescribed an antipsychotic drug; any impact of this drug on metabolic function might have continued after the drug was no longer prescribed.

A further unique contribution of this study is the estimation of a number of cardiovascular outcomes. There is a striking and consistent difference in cardiovascular risk across a number of domains between people with mental illness and controls. Cardiovascular risk estimates were based on robust models derived from the JBS and the Framingham risk charts. These are frequently used by physicians to guide management of high-risk patients and to assist in decisions regarding intervention. Our data suggest that a high proportion of people with mental illness who are at high risk for adverse cardiovascular

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events are not offered appropriate prophylactic intervention. This is in keeping with another recent study that has reported low rates of treatment for hypertension, dyslipidaemia and diabetes in people with schizophrenia from the CATIE trial (Nasrallah *et al*, 2006).

Limitations of the study

Although we did not detect differences in the prevalence of metabolic disease or estimates of cardiovascular risk across the diagnostic groups, the study might not have been sufficiently powered to detect such differences.

Selecting an appropriate control group for studies of this nature is complex. We attempted to control for demographic characteristics by specifically targeting carers and family members, and by recruiting controls from the geographical locale of participants with mental illness. This methodology might be considered somewhat crude, and as our analysis did not control for socio-economic variables we cannot exclude the possibility that the disparity in rates of metabolic disease and increased cardiovascular risk estimates are attributable to differing levels of deprivation.

People who volunteer to participate in medical research may take a more active interest in their physical health, and thus the prevalence of metabolic dysfunction and cardiovascular risk in the general population without severe mental illness might have been underestimated in our control group. The existence of such a potential bias is supported by the observed low prevalence of tobacco smoking in the control group (14%) compared with the reported prevalence in the general population. We cannot exclude the possibility, however, that a similar selection bias occurred in the recruitment of participants with mental illness: only 40% of this group smoked, which is lower than the prevalence (51%) reported in a recent large retrospective cohort study of people with severe mental illness (Osborn *et al*, 2007). These potential sources of bias may have resulted in an underestimate of the true prevalence of risk in both groups.

Although most of our participants with mental illness were taking antipsychotic medication at the time of investigation, the direction of causality cannot be established. There is accumulating evidence that antipsychotic drugs add to the metabolic burden in people with severe mental illness, but physical inactivity and diet are probably also influential. Tobacco smoking is also a well-established risk factor for cardiovascular disease (Unal *et al*, 2005), and although significantly more people with mental illness smoked compared with controls, differences in smoking behaviour did not account for the excess metabolic and cardiovascular risk. A genetic contribution to the increased metabolic and cardiovascular risk in people with severe mental illness should also be considered, as an increased prevalence of type 2 diabetes mellitus has been reported in unaffected first-degree relatives of people with schizophrenia (Mukherjee *et al*, 1989). This may suggest shared loci of genetic susceptibility for severe mental illness and diabetes, but shared environmental factors may also be important.

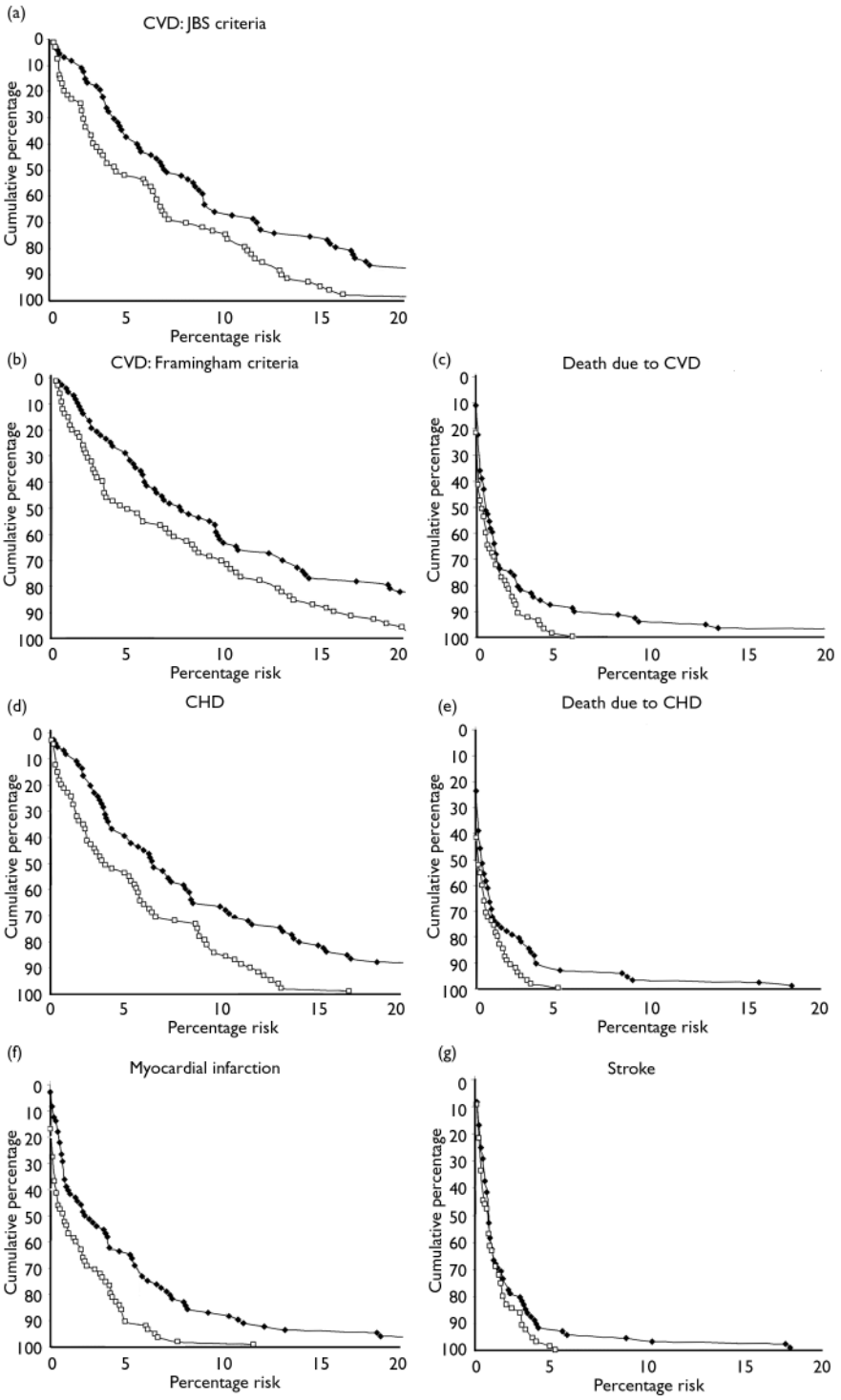

Fig. 1 Ten-year estimates for risk of adverse cardiovascular outcomes in people with mental illness (—•—) and controls (—□—). CVD, cardiovascular disease; CHD, coronary heart disease; JBS, Joint British Societies.

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Implications

Current models of care appear to be failing a large proportion of people with severe mental illness. The reasons for this are likely to be manifold. Use of physical healthcare services often decreases after the onset of a psychiatric disorder (Jeste *et al*, 1996), and even when patients are engaged with healthcare services, rates of undiagnosed physical illnesses are often high (Mackin *et al*, 2005). Other factors may also contribute to poor detection and diagnosis of physical illness, including impaired ability to verbalise concerns (Lieberman & Coburn, 1986; Massad *et al*, 1990), poor insight into illness (Massad *et al*, 1990), denial of illness (Goldman, 1999), or an unwillingness to consult a doctor other than their psychiatrist. When people are cared for by psychiatrists, primary care physicians and physicians from other disciplines, there may be a shared assumption that a colleague is taking responsibility for managing a particular medical problem, when in fact the problem is not being attended to at all.

There are few studies specifically examining the impact of differing models of care on physical well-being and comorbidity in severe mental illness. One randomised trial from the USA evaluated an integrated model of primary medical care for a cohort of people with serious mental disorders, and the authors concluded that on-site, integrated primary care was associated with improved quality and outcomes of medical care (Druss *et al*, 2001). Interventions such as improving provider competencies through education and profiling, and organisational interventions such as computerised reminders to prompt mental health professionals to refer to primary care for appropriate screening, require further investigation.

There is a need for greater communication and collaboration between primary and secondary care, and for the establishment of clear guidelines outlining responsibilities and protocols for screening and managing physical health and disease in people with severe mental illness. Integrated models of care, including mental and physical health professionals, may be more appropriate for delivering care to this group.

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REFERENCES

Alberti, K. G., Zimmet, P. & Shaw, J. (2006) Metabolic syndrome – a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabetic Medicine*, **23**, 469–80.

Anderson, K. M., Odell, P. M., Wilson, P. W., *et al* (1991) Cardiovascular disease risk profiles. *American Heart Journal*, **121**, 293–298.

Brown, S. (1997) Excess mortality of schizophrenia. A meta-analysis. *British Journal of Psychiatry*, **171**, 502–508.

Clement, S., Singh, S. P., Burns, T., *et al* (2003) Status of bipolar disorder research: bibliometric study. *British Journal of Psychiatry*, **182**, 148–152.

Correll, C. U., Frederickson, A. M., Kane, J. M., *et al* (2006) Metabolic syndrome and the risk of coronary heart disease in 367 patients treated with second-generation antipsychotic drugs. *Journal of Clinical Psychiatry*, **67**, 575–583.

Druss, B. G., Rohrbaugh, R. M., Levinson, C. M., *et al* (2001) Integrated medical care for patients with serious psychiatric illness: a randomized trial. *Archives of General Psychiatry*, **58**, 861–868.

Ford, E. S., Giles, W. H. Dietz, W. H., *et al* (2002) Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*, **287**, 356–359.

Fulton-Kehoe, D., Hamman, R. F., Baxter, J. *et al* (2001) A case-control study of physical activity and non-insulin dependent diabetes mellitus (NIDDM). The San Luis Valley Diabetes Study. *Annals of Epidemiology*, **11**, 320–327.

Goff, D. C., Sullivan, L. M., McEvoy, J. P., *et al* (2005) A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. *Schizophrenia Research*, **80**, 45–53.

Goldman, L. S. (1999) Medical illness in patients with schizophrenia. *Journal of Clinical Psychiatry*, **60(suppl. 21)**, 10–15.

Jeste, D. V., Gladsjo, J. A., Lindamer, L. A., *et al* (1996) Medical comorbidity in schizophrenia. *Schizophrenia Bulletin*, **22**, 413–430.

Lawrence, D. M., Holman, C. D. J., Jablensky, A. V., *et al* (2003) Death rate from ischaemic heart disease in Western Australian psychiatric patients 1980–1998. *British Journal of Psychiatry*, **182**, 31–36.

Levy, D., Labib, S. B., Anderson, K. M., *et al* (1990) Determinants of sensitivity and specificity of electrocardiographic criteria for left ventricular hypertrophy. *Circulation*, **81**, 815–820.

Levy, J. C., Matthews, D. R., Hermans, M. P., *et al* (1998) Correct homeostasis model assessment (HOMA) evaluation uses the computer program. *Diabetes Care*, **21**, 2191–2192.

Lieberman, A. A. & A. F. Coburn (1986) The health of the chronically mentally ill: a review of the literature. *Community Mental Health Journal*, **22**, 104–116.

Mackin, P., Watkinson, H. M., Young, A. H., *et al* (2005) Prevalence of obesity, glucose homeostasis disorders and metabolic syndrome in psychiatric patients taking typical or atypical antipsychotic drugs: a cross-sectional study. *Diabetologia*, **48**, 215-221.

Marder, S. R., Essock, S. M., Miller, A. L., *et al* (2004) Physical health monitoring of patients with schizophrenia. *American Journal of Psychiatry*, **161**, 1334–1349.

Martinsen, E. W., Strand, J., Paulsson, G., *et al* (1989) Physical fitness level in patients with anxiety and depressive disorders. *International Journal of Sports Medicine*, **10**, 58–61.

Massad, P. M., West, A. N., Friedman, M. J., *et al* (1990) Relationship between utilization of mental health and medical services in a VA hospital. *American Journal of Psychiatry*, **147**, 465–469.

Mukherjee, S., Schnur, D.B & Reddy, R. (1989) Family history of type 2 diabetes in schizophrenic patients. *Lancet*, **i**, 495.

Nasrallah, H. A., Meyer, J. M., Goff, D. C. *et al* (2006) Low rates of treatment for hypertension, dyslipidemia and diabetes in schizophrenia: data from the CATIE schizophrenia trial sample at baseline. *Schizophrenia Research*, **86**, 15–22.

National Diabetes Data Group (1979) Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes*, **28**, 1039–1057.

National Institute for Clinical Excellence (2002) *Schizophrenia: Core Interventions in the Treatment and Management of Schizophrenia in Primary and Secondary Care*. NICE.

National Institute for Clinical Excellence (2006) *Bipolar Disorder: The Management of Bipolar Disorder in Adults, Children and Adolescents, in Primary and Secondary Care*. NICE.

Osborn, D. P. J., Nazareth, I. & King, M. B. (2006) Risk for coronary heart disease in people with severe mental illness: cross-sectional comparative study in primary care. *British Journal of Psychiatry*, **188**, 271–277.

Osborn, D.P., Levy, G., Nazareth, I., *et al* (2007) Relative risk of cardiovascular and cancer mortality in people with severe mental illness from the United Kingdom's general practice research database. *Archives of General Psychiatry*, **64**, 242–249.

Phelan, M., Stradins, L. & Morrison, S. (2001) Physical health of people with severe mental illness. *BMJ*, **322**, 443–444.

Reaven, G. (2002) Metabolic syndrome: pathophysiology and implications for management of cardiovascular disease. *Circulation*, **106**, 286–288.

Shiloah, E., Witz, S., Abramovitch, Y. *et al* (2003) Effect of acute psychotic stress in nondiabetic subjects on beta-cell function and insulin sensitivity. *Diabetes Care*, **26**, 1462–1467.

Unal, B., Critchley, J. A., Capewell, S., *et al* (2005) Modelling the decline in coronary heart disease deaths in England and Wales, 1981–2000: comparing contributions from primary prevention and secondary prevention. *BMJ*, **331**, 614.

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