Effect of lifestyle, medication and ethnicity on cardiometabolic risk in the year following the first episode of psychosis: prospective cohort study

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Background
The first episode of psychosis is a critical period in the emergence of cardiometabolic risk.

Aims
We set out to explore the influence of individual and lifestyle factors on cardiometabolic outcomes in early psychosis.

Method
This was a prospective cohort study of 293 UK adults presenting with first-episode psychosis investigating the influence of sociodemographics, lifestyle (physical activity, sedentary behaviour, nutrition, smoking, alcohol, substance use) and medication on cardiometabolic outcomes over the following 12 months.

Results
Rates of obesity and glucose dysregulation rose from 17.8% and 12%, respectively, at baseline to 23.7% and 23.7% at 1 year. Little change was seen over time in the 76.8% tobacco smoking rate or the quarter who were sedentary for over 10 h/day. We found no association between lifestyle at baseline or type of antipsychotic medication prescribed with either baseline or 1-year cardiometabolic outcomes. Median haemoglobin A1c (HbA1c) rose by 3.3 mmol/mol in participants from Black and minority ethnic (BME) groups, with little change observed in their White counterparts. At 12 months, one-third of those with BME heritage exceeded the threshold for prediabetes (HbA1c >39 mmol/mol).

Conclusions
Unhealthy lifestyle choices are prevalent in early psychosis and cardiometabolic risk worsens over the next year, creating an important window for prevention. We found no evidence, however, that preventative strategies should be preferentially directed based on lifestyle habits. Further work is needed to determine whether clinical strategies should allow for differential patterns of emergence of cardiometabolic risk in people of different ethnicities.

Declaration of interest
F.G. has received honoraria for advisory work and lectures or CME activity support from Roche, BMS, Lundbeck, Otsuka, Janssen and Sunovion, is a collaborator on an NHLS innovations project co-funded by Janssen and has a family member with professional links to Lilly and CSdK, including share. R.M.M. has received honoraria for lectures from Lundbeck, Otsuka, Janssen and Sunovian. M.D.F. has received honoraria for lectures from Janssen and Sunovian. Z.A. has received honoraria for advisory work and lectures from Roche, Sanofi, Lilly and Otsuka. O.H. has received investigator-initiated research funding from and/or participated in advisory/speaker meetings organised by AstraZeneca, Actifony, Biogen, BMS, Eli Lilly, Heptares, Jansenn, Lundbeck, Lyden-Delta, Otsuka, Servier, Sunovion, Rand and Roche. D.T. has received funding for lectures and research from Janssen, Otsuka, Servier, Lundbeck, Sunovion.

Keywords
First episode psychosis; cardiometabolic risk; weight; glucose dysregulation; ethnicity.

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People with psychotic illnesses die prematurely, mostly from natural causes, with markedly raised standardised mortality ratios for cardiovascular disease (CVD, 3.6, 95% CI 3.5–3.6), with young adults (4.5, 95% CI 4.1–4.8), women (4.6, 95% CI, 4.5–4.7) and people of White ethnicity (4.9, 95% CI, 4.8–5.0) especially at risk.1 Cardiometabolic dysregulation is evident even from the early stages of psychosis2 and increases in the months after first presentation, with olanzapine having the most marked effect.3 Clozapine also affects metabolism, with 55% exhibiting glucose dysregulation within 3 months of starting.4 A recent meta-analysis reported that antipsychotics were associated with greater weight gain in Asian as opposed to Western studies, although very few studies looked directly at the effects of ethnicity.5 Evidence is needed to determine whether or not interventions to modify cardiometabolic risk can be targeted in first-episode psychosis (FEP). Few studies have investigated whether health behaviours at presentation including diet, physical activity and substance use predict subsequent deterioration in cardiometabolic status. An exception is a recent prospective study of 101 people with FEP6 that found that low aerobic fitness was a significant risk factor for metabolic syndrome. Overall, however, insufficient prospective observational studies have attempted to disentangle the impact of lifestyle on the emergence of cardiometabolic risk to reliably inform the development and targeting of effective preventative strategies.

The main aims of this study were therefore to (a) to determine the prevalence of cardiometabolic risk factors in an ethnically diverse population at first presentation with psychosis; (b) to describe the emergence of additional cardiometabolic risk over
the year following first presentation with psychosis and (c) to determine the relationship between lifestyle factors (diet, sedentary behaviour, smoking, substance use) and antipsychotic medication, in particular olanzapine and clozapine use, on cardiometabolic risk both at baseline and at 12-month follow-up. We hypothesised that there would be an association between baseline lifestyle choices and (a) cardiometabolic risk at baseline and (b) prospectively in change in cardiometabolic risk over a 1-year follow-up period. We also hypothesised that the emergence of glucose and lipid dysregulation would be greater in those prescribed the dibenzodiazepines, clozapine or olanzapine, compared with other antipsychotics.

Method

Setting and design
A prospective observational cohort of people was followed up for 12 months after their first presentation with psychosis. The study took place in in-patient and early intervention in psychosis community mental health teams in three English mental health National Health Service (NHS) services.

Eligibility criteria
Inclusion criteria were as follows: (a) aged between 16 and 65 years; (b) within 6 months of first presentation with psychosis (ICD-10 codes F20–29 and F30–33); (c) proficient in English with no requirement for an interpreter. Patients were excluded if they were pregnant or had a major medical illness or neurological disease; had been diagnosed with a severe intellectual disability; had an organic cause for their psychosis; or had previous contact with health services for the presence of psychosis. All participants were included in the study only after giving written, confirmed consent. The study protocol was approved by the Joint South London and Maudsley and the Institute of Psychiatry NHS Research Ethics Committee (08/H0807/53).

Assessments
Patients were assessed at baseline and after 12 months. Sociodemographic data were recorded at baseline, namely age, gender, ethnicity (self-report) and years of education. The operational criteria checklist for psychotic and affective illness (OPCRIT) was used to assess type of mental health state over the lifetime. All other measures were recorded at both time points. Selected clinical measures unaffected by fasting state (weight, blood pressure, haemoglobin $A_{1c}$ ($HbA_{1c}$), cholesterol, high-density lipoprotein (HDL), triglycerides) were recorded where available and utilised in analyses at baseline if the relevant measure post-dated the onset of psychosis and preceded the research measures, being thus less likely to have been affected by the introduction of psychotropic medication. Follow-up clinical measures were utilised if research measures for that period were missing.

Psychopathology
Mental health status was measured using the Positive and Negative Symptom Scale, Global Assessment of Functioning, Clinical Global Impression Scale, Calgary Depression score, and the Young Mania Rating Scale.

Pharmacological history
Type(s) (British National Formulary definitions) of psychotropic medication and duration of antipsychotic (in days) were retrospectively extracted from electronic medical records.

Cardiometabolic measures
Metabolic measures comprised anthropometric measures of weight, height, body mass index (BMI), waist circumference and blood pressure, as well as fasting blood samples for glucose, glycated haemoglobin ($HbA_{1c}$), lipids and C-reactive protein (CRP). Standardised techniques were used to measure height, blood pressure and weight. Where available, the blood pressure values are the second blood pressure measurements (first reading presented in 75/219 participants at baseline; and 39/147 at 12 months). Waist circumference was measured at the umbilicus with the patient standing.

Obesity was defined by the World Health Organization (WHO) reference standard (BMI ≥30 kg/m²) and overweight as BMI ≥25 kg/m². Diabetes was diagnosed based on a $HbA_{1c}$ of ≥48 mmol/mol (≥6.5%), or a fasting glucose ≥7.0 mmol/L or a prior diagnosis of diabetes. In keeping with recent guidance from the American Diabetes Association, an $HbA_{1c}$ of 39–47 mmol/mol (5.7–6.4%) was taken to indicate glucose dysregulation or a high risk of diabetes. The International Diabetes Federation definitions of other cardiometabolic risk factors were used. Insulin resistance was presented using the homeostasis model assessment – insulin resistance (HOMA-IR), calculated from fasting glucose and insulin levels. Inflammation was estimated using high-sensitivity CRP as a marker.

Physical activity and dietary intake
Physical activity was assessed by the International Physical Activity Questionnaire, which has been validated in psychosis. The self-report Dietary Instrument for Nutrition Education (DINE) was used to assess dietary patterns over the previous week. Additional questions were included to account for sugar intake, the consumption of take-away food, carbonated drinks and adding either salt or sugar to food/drinks.

Substance use
Cigarette and tobacco consumption were measured using the Nicotine Dependence Questionnaire and alcohol use with the Alcohol Use Disorders Identification Test (AUDIT), where scores of eight or more indicate hazardous and harmful alcohol use. A modified Cannabis Experience Questionnaire (CEQ-4) was used to enquire about lifetime and current use of substances and a urine drug screen requested.

Statistical analysis
Descriptive data are presented in tabular form. Pairwise comparisons were done using t-tests for continuous and $\chi^2$ tests for categorical outcomes. Baseline associations between continuous scores for lifestyle and cardiometabolic factors were investigated using unadjusted and adjusted linear regression models. To account for different patterns of missingness, we used multiple imputation by chained equations prior to these analyses, using the lifestyle factors (DINE saturated fat score, AUDIT hazardous drinking score, number of h sitting per day and whether taking olanzapine), cardiometabolic factors (cholesterol, diastolic blood pressure, $HbA_{1c}$, waist circumference, BMI, HDL and triglycerides), age, gender, ethnicity and pre-baseline number of days on antipsychotic medication in the multiple imputation model. We used the ‘mi impute chained’ command in Stata version 15.1, with 50 imputed data-sets for each multiple imputation model. Binary variables were imputed using logistic regression, using augmented logistic regression where perfect prediction was detected. Continuous variables were imputed using linear regression unless they appeared...
non-normal, in which case the predictive mean matching imputation method, drawing from five nearest neighbours, was used.25

Imputed data-sets were then used to examine cross-sectional associations between each lifestyle factor and cardiometabolic factor separately using linear regression, unadjusted and adjusted for prespecified potential confounders of CVD risk, namely age, gender, ethnicity and pre-baseline number of days on antipsychotic medication. We further explored the cross-sectional associations between use of dibenzodiazepine medications (yes/no) prior to baseline and cardiometabolic factors at baseline using the same model and potential confounders.

For each outcome (change in cardiometabolic factor) at 12 months we employed separate multiple imputation models (using the same method as above) using the outcome and the same variables at baseline. We then explored for each baseline lifestyle factor, separately, whether they were associated with change in cardiometabolic factors over the 12-month follow-up period, unadjusted, and then adjusted for the above potential confounders, investigating associations between use of dibenzodiazepine medications between baseline and 12 months (yes/no) and cardiometabolic factors in the same way.

We separately assessed whether cardiometabolic factors at baseline differed between (a) participants taking medication with less than or greater than 14 days of antipsychotic medication prior to baseline and (b) participants who were taking medication and those who were unmedicated prior to baseline.

To account for multiple testing a stricter alpha of 0.01 was pre-specified as the significance level.26 Tests with a P-value between 0.01 and 0.05 were discussed as a trend and conclusions should be treated as explorative. Sensitivity analyses were carried out for all the analyses using complete cases from the full data-set, and also using a reduced data-set (with only participants with <5 variables of interest missing) prior to using multiple imputation to check the extent to which the original multiple imputation was plausible.

Results

We screened 11 705 people for eligibility; 971 were eligible of whom 321 (33.1%) consented to participate (263 declined, 50 transferred, 337 uncontactable). Twenty-eight were excluded after consent when further information became available, leaving 293 eligible people, (mean age 30.6 years (s.d. = 10.5)) in the study at baseline, 46.4% of whom were of White ethnicity; 36.9% Black and 7.8% Asian.

Sixteen withdrew at baseline, and 251 completed baseline measures of whom were of White ethnicity; 36.9% Black and 7.8% Asian. Further information became available, leaving 293 eligible people, 321 (33.1%) consented to participate (263 declined, 50 transferred, 50 transferred, 251 completed baseline measures.

We separately assessed whether cardiometabolic factors at baseline differed between (a) participants taking medication with less than or greater than 14 days of antipsychotic medication prior to baseline and (b) participants who were taking medication and those who were unmedicated prior to baseline.

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Cardiometabolic and lifestyle factors in the year following onset of psychosis

Rates of obesity, hypertriglyceridaemia, diabetes, raised CRP and low HDL cholesterol all rose over the first year of illness, and the proportion of people with HbA1c in the glucose dysregulation range almost doubled (Tables 1 and 2, supplementary Tables 2 and 7 and Fig. 1). Rates of tobacco smoking were high (Tables 2 and 3); smokers consumed a median of ten cigarettes per day, with little change over time. Combining both self-report and urinary drug screen data, 49.5% (102/206) of participants were current users of cannabis at baseline, and 23/183 (12.6%) reported current usage of ‘other recreational drugs’. The corresponding figures at 12 months were 38.1% (40/105) and 12/102 (11.8%), respectively. From baseline to 12 months, 12 (11.3%) participants initiated cannabis use while 16 (15.5%) stopped using cannabis.

Data were available on antipsychotic prescriptions prior to baseline for 242 (82.6%) participants. In total 22% (54/242) were antipsychotic-free before baseline, and a further 65 (26.9%) had received antipsychotics for less than 2 weeks. The median duration of antipsychotic treatment for those prescribed antipsychotics pre-baseline was 21 days (interquartile range (IQR) = 9.0–55.5 days) (mean 43.3 days (s.d. = 53.3), with most (94.7%; n = 178/188) prescribed second-generation antipsychotics. Overall, 128 people were prescribed olanzapine across the year, 102 as their first antipsychotic. Of those on olanzapine at baseline (n = 89; median dose 10 mg (IQR = 10–75; range 2.5–25)), 71% (52/73) remained on olanzapine at follow-up.

At follow-up, 66 people were prescribed olanzapine (we had dose data of 45 people), at a median dose of 12.5 mg (n = 45, IQR = 10–17.5; range 2.5–30). All bar 15 had been prescribed antipsychotic medication over the course of the study, for a median of 378 (IQR = 302–434) days (mean of 354.6 (s.d. = 138.9) days), with those receiving olanzapine prescribed it for a median of 236 (IQR = 61–388) days (mean of 239.6 (s.d. = 169.8) days). No patients were prescribed clozapine. We did not have data on somatic medications prescribed over the course of the follow-up.

Participants taking medication prior to baseline had higher baseline average waist circumferences (+7.7 cm, 95% CI 2.0–13.4; P = 0.009) compared with those unmedicated. Those who had received over 2 weeks antipsychotic medication prior to baseline had higher total cholesterol (+0.5 mmol/L, 95% CI 0.1–0.8; P = 0.007) than those prescribed antipsychotics for less than 2 weeks (excluding those prescribed no antipsychotic) (supplementary Table 3).

At baseline, 57% consumed a carbonated drink daily, half (50%) drinking more than one 500 mL bottle per day and 24.4% of the total sample drank diet carbonated drinks daily. Three-quarters (75.7%) consumed tea on a daily basis, most (90.8%) drinking more than one cup, with 44% of the sample adding 2 teaspoons or more of sugar to each cup of tea. Salt was added to food during cooking by 66.5% of participants. A total of 78.5% consumed take-away meals, three-quarters of whom (75.8%) did so more than once weekly.

Relationship between lifestyle/medication and cardiometabolic outcomes at baseline and 12-month follow-up.

Baseline DINE fat scores, sedentary behaviour, AUDIT scores and pre-baseline olanzapine use were not significantly associated with any of the baseline cardiometabolic outcomes either unadjusted or after adjusting for potential confounders (supplementary Table 6). Nor did the linear regression models show any association between use of dibenzodiazepine medications (yes/no) prior to baseline and cardiometabolic outcomes at baseline and 12-month follow-up.

Twelve-month follow-up was completed for 125 patients with additional selected anthropometric and blood measures taken from clinical records where available and required. There were no differences in baseline demographics or cardiometabolic measures between those who had 12-month follow-up assessments (n = 125) and those who did not (n = 168) (supplementary Table 4).
Sensitivity analyses using complete cases only gave similar results with no evidence of any associations. Sensitivity analyses using a reduced data-set prior to imputing also gave similar results.

**Effects of gender and ethnicity**

Rates of central obesity at baseline were higher in women (62.7%, \( n = 37/59 \)) than in men (35.3%, \( n = 36/102 \), \( \chi^2 = 11.34, P = 0.001 \)), with a trend towards women from Black and minority ethnic (BME) groups having larger waists than their White counterparts (t = 2.37, \( P = 0.02 \)), this gap increasing over time in the paired sample subgroup (supplementary Table 5). White men overall gained a mean of 4.9 cm in waist circumference over the year, whereas men from BME groups gained 1.6 cm (Table 3), with a trend towards women from Black and minority ethnic (BME) groups having larger waists than their White counterparts (t = 36/102), (\( n \chi^2 = 0.001 \), \( P = 0.02 \)).

Although HbA1c levels were baseline comparable, BME patients exhibited a significant increase in median HbA1c levels over 12 months (P<0.01), rising by 3.3 mmol/mol. In contrast, no change was evident in White patients (t = 3.10, \( P = 0.04 \)) in BMI patients. There was no significant difference in ethnicity between those prescribed olanzapine and those not prescribed it (\( \chi^2(3) = -3.10, P = 0.376 \)).

**Discussion**

This comprehensive large-scale cohort study of patients with FEP prospectively considers the relationship between lifestyle factors, medication and cardiometabolic trajectories. Weight gain is the most obvious problem for many patients both cosmetically and for their health – here 17.8% were obese at onset, rising to 23.7% within 1 year. A case has recently been made for obesity to be recognised as a chronic disease\(^2\) to allow the preventative strategies within 1 year. A case has recently been made for obesity to be recognised as a chronic disease\(^2\) to allow the preventative strategies needed at a population level; in psychosis, the rapidity of weight gain over the first year offers an unrivalled opportunity for prevention, with diet, exercise and medication being key targets. We noted high consumption of saturated fat, carbonated, high-sugar drinks, sweetened beverages and added salt. Calorie intake was further augmented by alcohol use (Table 2). Although neither fat intake nor alcohol use in the early weeks of psychosis predicted longer-term outcomes in our population, the Keeping the Body in Mind programme has successfully worked with dieticians and exercise physiologists to prevent weight gain using lifestyle interventions for all early in the disease process.\(^3\)

We also found early emergence of glucose dysregulation; by 1 year twice as many people had HbA1c levels at or above the American Diabetes Association glucose dysregulation range (Tables 1 and 2). Diabetes is highly predictive of cardiometabolic disease and can have an especially significant impact on health in...
people with psychosis, given the other practical challenges they may face.

There was a remarkably high baseline prevalence of tobacco smoking of 76.8%. Smoking confers an almost fivefold risk of mortality in people with schizophrenia. Further, nicotine dependence after psychosis onset predicts both poor medication adherence and non-remission of psychosis. It is therefore worrisome that we saw little reduction in smoking rates over time. Since this work was completed, many UK mental health hospitals have become smoke-free environments and although a recent trial has demonstrated that smoking cessation can be achieved in the community, work remains to be done to sustain quitting. Rates of current cannabis use and lifetime use of other substances were high, in keeping with previous work.

People with psychosis engage in low levels of physical activity. Although physical activity at baseline did not predict cardiometabolic outcome in our study, by 12 months 40% of the participants were engaging in the 150 min of physical activity per week recommended by the WHO (2014). Worryingly however, sedentary behaviour changed little and CRP levels increased over time. Sedentary behaviour is associated with inflammation in psychosis, and inflammation is in turn linked to cardiometabolic disease. Both exercise and sedentary behaviour are important targets for health promotion with studies underway to examine ways of changing patterns of behaviour in clinical settings.

Our regression analyses revealed no relationship between cardiometabolic outcomes and lifestyle, nor any effect of dibenzodiazepine medication, despite the high risk of weight gain demonstrated with olanzapine in other settings. A high proportion were prescribed olanzapine as a first antipsychotic, a practice now not recommended. Of note, no participants were prescribed clozapine in the first year of their illness, in keeping with the reported mean lag time to starting clozapine of 47.7 months (s.d. = 49.7). The omission of clozapine is noteworthy as 23% of people presenting with their first episode of psychosis are treatment resistant from illness onset.

Our sensitivity analyses illustrated the rapidity of cardiometabolic change in early psychosis; those exposed to antipsychotic medication for more than 14 days before baseline had higher cholesterol levels than those on antipsychotics for less than a fortnight, and those exposed to any antipsychotic medication had a larger waist circumference at baseline than did individuals who were antipsychotic naive.

Effects of ethnicity and gender

Men of White ethnicity appeared to have a particular vulnerability to emergence of central obesity, increasing their mean waist size by 4.9 cm, whereas men of other ethnicities gained a more modest 1.6 cm. These changes are clinically significant and the variation between ethnic groups was in keeping with findings in established psychosis. Central obesity is a better predictor of CVD risk than is general obesity, so this may relate to the lower hazard ratios seen for all-cause mortality in Black African, Black Caribbean and South Asian patients with severe mental illness compared with their White British counterparts.

Women were at risk of central obesity throughout, with 72.7% in that category by 1 year, again consistent with the local feature of 95% seen in women with established psychosis. Central adiposity in women is predictive of all-cause mortality in White, but not Black women.

Minority ethnic groups appeared vulnerable to emergent glucose dysregulation, with highly clinically relevant increases in median HbA1c of 3.3 mmol/mol (Table 3 and supplementary Table 5), but no change seen in White patients. Within the non-diabetic range, this reflects a highly clinically significant shift in glycaemia in the BME group, with one-third exceeding the American Diabetes Association HbA1c threshold for pre-diabetes (>39 mmol/mol (5.7%)), although it is useful to note that some would not have been identified as at risk by current National Institute for Health and Care Excellence guidelines. This change in glucose regulation in a relatively young population over just 1 year highlights the risk of accelerated emergence of diabetes in people of ethnicities other than White, and is in keeping with a recent large cross-sectional analysis of London primary care data that showed a three- to tenfold relative risk of type 2 diabetes in young people with severe mental illness.

Strengths and limitations

This is to our knowledge the most comprehensive study to date examining the effects of lifestyle choice on emergent cardiometabolic risk. In conducting this study, we recruited an incident sample of people presenting to both in-patient and community services for the first time with psychosis and we followed them up for 1 year, thereby capturing the period with the greatest change in physical

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Rates of identified cardiometabolic and lifestyle risk factors at each time point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Body mass index (BMI, kg/m²)</td>
<td>90</td>
</tr>
<tr>
<td>BMI ≤25</td>
<td>58</td>
</tr>
<tr>
<td>BMI &gt;25 and ≤30</td>
<td>32</td>
</tr>
<tr>
<td>BMI &gt;30</td>
<td>76</td>
</tr>
<tr>
<td>High total cholesterol (&gt;5 mmol/L)</td>
<td>110</td>
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<tr>
<td>Yes</td>
<td>47</td>
</tr>
<tr>
<td>No</td>
<td>128</td>
</tr>
<tr>
<td>Raised triglycerides (&gt;1.7 mmol/L)</td>
<td>46</td>
</tr>
<tr>
<td>Yes</td>
<td>133</td>
</tr>
<tr>
<td>No</td>
<td>172</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>6</td>
</tr>
<tr>
<td>No</td>
<td>176</td>
</tr>
<tr>
<td>HbA1c ≥39 mmol/mol</td>
<td>20</td>
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<tr>
<td>Yes</td>
<td>147</td>
</tr>
<tr>
<td>No</td>
<td>37</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>131</td>
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<tr>
<td>&gt;3 mg/L</td>
<td>49</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33</td>
</tr>
<tr>
<td>Yes</td>
<td>186</td>
</tr>
<tr>
<td>No</td>
<td>76</td>
</tr>
<tr>
<td>IPAQ sitting hours</td>
<td>3</td>
</tr>
<tr>
<td>≤6 h per day</td>
<td>53</td>
</tr>
<tr>
<td>&gt;6 and ≤10 h per day</td>
<td>49</td>
</tr>
<tr>
<td>≥10 h per day</td>
<td>144</td>
</tr>
<tr>
<td>≤10 h per day</td>
<td>144</td>
</tr>
<tr>
<td>DINE score (saturated fat)</td>
<td>137</td>
</tr>
<tr>
<td>≤40</td>
<td>49</td>
</tr>
<tr>
<td>&gt;40</td>
<td>137</td>
</tr>
<tr>
<td>AUDIT hazardous drinking score</td>
<td>96</td>
</tr>
<tr>
<td>&gt;7</td>
<td>102</td>
</tr>
<tr>
<td>≤7</td>
<td>139</td>
</tr>
</tbody>
</table>

HbA1c, haemoglobin A1c; IPAQ, International Physical Activity Questionnaire; DINE, Dietary Instruments for Nutrition Education; AUDIT, Alcohol Use Disorders Identification Test.

a. Men: ≤1.03 mmol/L; women: ≤1.29 mmol/L.
Table 3  Effects of gender and ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>Difference by gender</th>
<th>White</th>
<th>Other ethnicity</th>
<th>Difference by ethnicity</th>
<th>s.d., standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (kg/m²), mean (s.d.)</td>
<td>25.5 (4.6)</td>
<td>26.0 (6.3)</td>
<td>−0.5</td>
<td>25.7 (5.4)</td>
<td>25.7 (5.1)</td>
<td>0.0</td>
<td>4.6</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L), mean (s.d.)</td>
<td>4.81 (1.05)</td>
<td>4.80 (0.83)</td>
<td>0.01</td>
<td>4.93 (1.12)</td>
<td>4.70 (0.82)</td>
<td>0.23</td>
<td>0.43</td>
</tr>
<tr>
<td>HbA1c (mmol/mol), median (upper and lower quartiles)</td>
<td>34.4 (32.2–37.7)</td>
<td>33.3 (32.2–35.5)</td>
<td>1.1</td>
<td>34.4 (32.2–36.6)</td>
<td>34.4 (32.8–37.7)</td>
<td>0.0</td>
<td>5.3</td>
</tr>
<tr>
<td>Current smoking (%) (at least once a week)</td>
<td>79.8</td>
<td>70.2</td>
<td>9.6</td>
<td>79.2</td>
<td>74.1</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>Mean waist circumference (cm), mean (s.d.)</td>
<td>76.8</td>
<td>67.7</td>
<td>9.1</td>
<td>75.5</td>
<td>70.7</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td>s.d., standard deviation; HbA1c, haemoglobin A1c.</td>
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</table>

Table 4  Association between lifestyle factors at baseline and 12-month change in cardiometabolic risk factors (adjusted for age, gender, ethnicity and pre-baseline number of days on antipsychotic medication)

<table>
<thead>
<tr>
<th>Dependent (response) variable/independent variable</th>
<th>Baseline DINE fat score</th>
<th>Baseline AUDIT hazardous drinking score</th>
<th>Baseline number of h sitting per day</th>
<th>OLZ versus not OLZ between baseline and 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-month change in cholesterol (mmol/mol)</td>
<td>0.008 (−0.088 to 0.025)</td>
<td>0.009 (−0.018 to 0.036)</td>
<td>0.023 (−0.032 to 0.077)</td>
<td>−0.247 (−0.738 to 0.245)</td>
</tr>
<tr>
<td>12-month change in diastolic blood pressure (mmHg)</td>
<td>−0.029 (−0.192 to 0.134)</td>
<td>0.045 (−0.252 to 0.341)</td>
<td>0.039 (−0.385 to 0.592)</td>
<td>−0.425 (−5.085 to 4.233)</td>
</tr>
<tr>
<td>12-month change in HbA1c (mol/mol)</td>
<td>−0.005 (−0.145 to 0.155)</td>
<td>0.137 (−0.049 to 0.324)</td>
<td>−0.141 (−0.613 to 0.330)</td>
<td>−0.552 (−3.408 to 2.328)</td>
</tr>
<tr>
<td>12-month change in waist circumference (cm)</td>
<td>0.034 (−0.167 to 0.235)</td>
<td>0.042 (−0.329 to 0.412)</td>
<td>−0.233 (−1.172 to 0.707)</td>
<td>0.326 (−4.712 to 5.364)</td>
</tr>
<tr>
<td>12-month change in body mass index (kg/m²)</td>
<td>−0.003 (−0.108 to 0.103)</td>
<td>0.019 (−0.143 to 0.181)</td>
<td>−0.058 (−0.415 to 0.299)</td>
<td>0.437 (−2.094 to 2.968)</td>
</tr>
<tr>
<td>12-month change in high-density lipoproteins (mmol/L)</td>
<td>−0.001 (−0.008 to 0.007)</td>
<td>0.001 (−0.009 to 0.011)</td>
<td>0.002 (−0.021 to 0.024)</td>
<td>−0.084 (−0.259 to 0.090)</td>
</tr>
<tr>
<td>12-month change in triglycerides (mmol/L)</td>
<td>0.005 (−0.010 to 0.021)</td>
<td>0.006 (−0.020 to 0.032)</td>
<td>0.010 (−0.053 to 0.072)</td>
<td>0.051 (−0.389 to 0.491)</td>
</tr>
</tbody>
</table>

CI, confidence interval; DINE, Dietary Instrument for Nutrition Education; AUDIT, Alcohol Use Disorders Identification Test; OLZ, olanzapine; HbA1c, haemoglobin A1c.

a. Separate models used for each association.
The diverse nature of the population studied allows exploration of the effect of ethnicity on emergence of cardiometabolic risk. The use of multiple imputation on a reduced data-set allowed confidence in the results while retaining generalisability.67

The study must be interpreted taking into account a number of methodological aspects. Over half our patients required acute in-patient care at the time of recruitment and many had received treatment for some weeks before being well enough to consent to inclusion. To minimise this effect and minimise missing data, we therefore sought permission to use clinical data, where available and comparable, as well as adjusting for the number of days prescribed antipsychotics before baseline in our analyses. Also, in follow-up studies there is a risk that attrition may not be random. Therefore, considerable efforts were made to minimise loss to follow-up with contact made with 81% (217/268) of the then eligible participants at 12 months, although 73 participants declined 12-month follow-up. There was recompense for time but no financial incentivisation to remain in the study. Analysis showed no differences in baseline demographic or clinical attributes between completers and non-completers. The supplementary tables include a descriptive table of complete paired measures. We also note that although 89 people were prescribed olanzapine at baseline, some did not sustain that prescription throughout the study period, possibly because of emergent metabolic effects. Finally, the number of statistical tests carried out was reasonably large and although we took a more conservative threshold of statistical significance, we cannot completely discount the possibility of type I errors.

In conclusion, our results identify that cardiometabolic risk factors are already pronounced in those presenting to FEP services and worsen over the first year under standard care. No baseline behaviour predicted risk of worsening cardiometabolic parameters, but a greater degree of emergent glucose dysregulation was observed in those from BME groups.

**References**


