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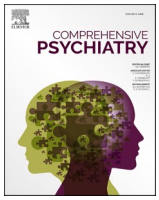

Cardiometabolic screening and monitoring in patients prescribed antipsychotic drugs in primary care: A population-based cohort study

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ABSTRACT

Background: This study aimed to investigate the level of guideline adherence for cardiometabolic health monitoring for patients prescribed antipsychotic medicines in UK primary care.
Methods: In this population-based retrospective open cohort study, we used dataset of patients from the IQVIA Medical Research Data (IMRD) database between 1st January 2003 to 31st December 2018. Clinical Read codes were used to identify a cohort of adult patients with a diagnosis of Schizophrenia and at least four prescriptions of an anti-psychotic medication within 12 months of diagnosis. We then extracted data in relation to monitoring of cardiometabolic parameters (body compositions, lipids, and glucose outcomes) at baseline, then at six weeks, 12 weeks, and then 12 months. The frequency of outcome monitoring was described using descriptive statistics.
Findings: A total of 11,435 patients were eligible and of them (n = 9707; 84·8%) were prescribed second-generation antipsychotics (SGAs). Only a small portion of the cohort (≈2·0%) received complete monitoring (at time points) for certain outcomes. Just over half the patients (n = 6599, 52%) had evidence of any cardiometabolic baseline testing for any of the study outcomes and the high majority had at least one abnormal lab value at baseline (n = 4627, 96·7%).
Interpretation: In UK primary care, cardiometabolic monitoring practices among patients prescribed antipsychotics remain suboptimal. There is a need to promote guideline adherence to prevent adverse outcomes in antipsychotic users.

1. Introduction

Antipsychotics are considered the cornerstone in the management of psychotic disorders along with other non-psychotic conditions such as dementia. Despite their wide use, antipsychotic drugs have the potential to cause cardiovascular risk or accelerate pre-existing conditions [1]. Antipsychotic-induced metabolic side effects are attributed to multiple functional pathways. Among the proposed mechanisms by which antipsychotics induce metabolic disturbances includes blocking of histamine and histamine receptors, dopaminergic receptors (D2 and D3), muscarinic receptors (M2 and M3), and central 5-HT receptors. Blocking these receptors may contribute to disturbances in appetite, eating behaviour and insulin regulation [2].

In 2003, the U.S. Food and Drug Administration (FDA) launched a black box warning regarding the diabetogenic effect of antipsychotics [3,4]. In response to these warnings, a panel of regulatory bodies and professional associations, including the American Diabetes Association (ADA)/American Psychiatric Association (APA), published a consensus statement that recommends early and regular monitoring of metabolic side effects among antipsychotic users [5]. Consequently, cardiometabolic dysregulation management in patients with mental illness has received considerable attention and focus from clinical guidance and healthcare policy perspectives [6]. In July 2014, the National Institute for Health and Care Excellence (NICE) guideline for managing schizophrenia in adults was updated to include monitoring and managing cardiometabolic abnormalities [7]. The NICE/Royal College of Psychiatrists (RCP) guideline recommended measurements of body composition, blood pressure (BP), fasting plasma glucose, and lipid profile measures to be taken at baseline, then at six weeks, 12 weeks, and then annually [7]. Effective monitoring and management of cardiometabolic

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abnormalities in patients taking antipsychotics aim to identify high-risk populations, for example, diabetic patients prescribed clozapine; and track cardiometabolic disturbances among antipsychotic users and assess their association with antipsychotic therapy [8].

Despite the guideline recommendations, it has been suggested that routine cardiometabolic monitoring has remained suboptimal. As a result, undiagnosed and untreated cardiovascular and metabolic diseases among patients prescribed antipsychotics remain high due to suboptimal screening, leading to missed opportunities for using primary preventive measures [9], exacerbating co-existing comorbidities and early mortality. In addition, previous studies also suggest that those with mental health problems face disparities in the level of cardiometabolic screenings and monitoring compared to the general population [10,11].

1.1. Aim and objectives

This study sought to investigate the extent of cardiometabolic monitoring for patients prescribed antipsychotic drugs as per NICE guidelines in primary care [7]. Also, the study aimed to describe and compare the monitoring frequencies among different antipsychotics.

2. Material and methods

2.1. Study design

This was a retrospective longitudinal open cohort study using patients' clinical data from the IQVIA Medical Research Database (IMRD). The study period was set between the 1st of January 2003 and to 31st of December 2018. The study start date (1st of January 2003) was selected as the warnings regarding the increased metabolic risks of second-generation antipsychotics were first introduced by the FDA during this time [3].

The study was reported as per the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) statement for observational studies (see supplementary A) [12]. Studies using the IMRD database gain ethical approval from the UK National Health Service Southeast Multicentre Research Ethics Committee. The Scientific Review Committee (SRC) approved the study protocol (no. SRC 19THIN070). The data was extracted using the DExtER (Data extraction for epidemiological research) software program [13].

2.2. Data source

The IQVIA Medical Research Data (IMRD), (previously the Health Improvement Network [THIN] database), is an extensive electronic database containing routine patient records collected from over 800 general healthcare practices (GPs) around the UK. The IMRD database is considered a representative data source of the UK population and holds data of approximately 11 million (≈ 6.2% of the UK population) patients [14]. Clinical data related to medical diagnoses, disease symptoms, examinations and referrals are coded using the Read code system [15]. This standard clinical terminology system is used by general practices in the UK, allowing the data to be structured to facilitate data entry and extraction [15]. Also, the IMRD database has a hierarchical prescription coding system that mainly classifies drug information using the British National Formulary (BNF) codes.

2.3. General practice eligibility

To maximise data quality, the general practice was considered eligible one year after 1) reporting an acceptable mortality rate reporting (AMR) (the year at which the level of recording of all-cause mortality by each practice is deemed acceptable; based on a comparison with the predicted numbers of deaths derived from the National statistics given the individual practice's demographics [16]. and 2) the installation of electronic health records.

2.4. Participants and cohort identification

The study cohort comprised patients prescribed long-term antipsychotic treatment for mental illnesses, primarily schizophrenia-related disorders, affective mood disorders, and depression. To ensure data quality, particularly for those transferring practices, patients were considered eligible if they were actively registered with an eligible practice for a minimum of one year.

Within the IMRD database, a cohort of adults (aged ≥18 years) diagnosed with mental illness and prescribed antipsychotic therapy was identified. The participants were considered eligible if they; a) were aged 18 and above and had a clinical diagnosis of mental illness (defined as the presence of clinical Read Code [Supplementary B] for diagnosing schizophrenia and other mental illness within their medical records); and b) had a prescription code for antipsychotics [Supplementary C] on at least 4 occasions during a single year. To ensure patients' eligibility for treatment chronicity, a testing window was set up where records were screened one year after diagnosis of Schizophrenia to ensure patients had at least four repeated antipsychotic prescriptions (trial period). The process of cohort identification is detailed in Fig. 1.

2.5. Follow up

The index date was assigned as the date of the first antipsychotic prescription that was directly issued after the patient was diagnosed with mental illness. Participants were followed until the earliest of the following dates: death, patient leaving practice, the practice stopped contributing to the database, and study end date (Dec 31, 2018); thus, the cohort follow-up varied across patients as patients left the study at different times. The records of outcome measurement were extracted for one year in the database. This allows investigation of cardiometabolic monitoring patterns for the first year of initiating the antipsychotic treatment.

2.6. Study outcomes and measurements

The outcomes of interest were the frequency (presented as proportion in %) of cardiometabolic monitoring at predefined time points. This was defined as the presence of patients with at least one monitoring record for any components of the cardiometabolic profile [7]. The term 'cardiometabolic profile' refers to the measurements of body compositions and biochemical parameters, including:

I. Parameters for body weight: body mass index (BMI) and waist circumference (WC)
II. Blood pressure (BP)
III. Parameters for blood glucose: random blood glucose (RBG), fasting blood glucose (FBG) and glycosylated haemoglobin (HbA1c).
IV. Lipid profile: high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TGs).

2.7. Outcomes definition

2.7.1. Baseline monitoring

Baseline monitoring was defined as the recorded measurement of cardiometabolic profile components closest to the index date, up to 180 days prior to the index date and up to seven days after the index date (to allow for the lag period owing to delayed appointments).

2.7.2. Subsequent follow-up monitoring

We only included measurements for one year. Follow-up monitoring for each time point (at six weeks, 12 weeks, or annually) was determined if monitoring records for a specific outcome existed around that time point. Such practice allows flexibility to capture the outcome at each time point and helps minimise unintentional skipping. For instance, for

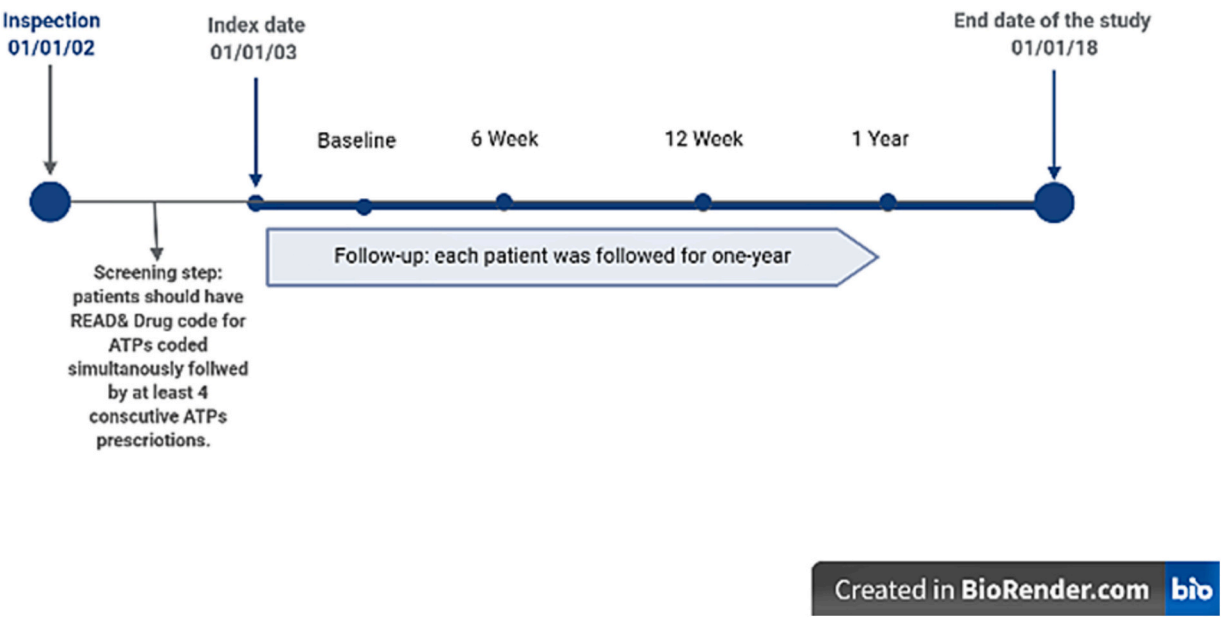

Fig. 1. Flow diagram of the data extraction process and selection. ATPs: antipsychotics. Data were extracted for 15 years and 11 months (≈16 months), but each patient was followed for only one year. Created using BioRender.com [17].

patients to be monitored at week-6, relevant records available closest to week-6, 8–42 days from the prior time point check (baseline), were considered. The same concept was applied to the remaining time points. A period of 43–84 days from the baseline was selected for the 12-weeks checkpoint. Similarly, 85–365 days from baseline was applied for the one-year checkpoint.

2.7.3. Monitoring consistency

The monitoring consistency was assessed from the baseline until the 12-month follow-up to reflect the NICE recommendation of cardiometabolic monitoring for antipsychotics [7]. Regular monitoring for each of the cardiometabolic profile components was defined as patients who had the outcome measure of interest at all recommended time points, regardless of the presence of any abnormalities within one year (e.g., having records for BMI at baseline, 6-weeks, 3-months, and 1-year). The NICE guidance summary of the recommended monitoring times for each of the cardiometabolic profile components is provided in the supplementary materials [7]. [see Supplementary D].

2.7.4. Analysis strategies and statistical plan

Baseline demographics and clinical characteristics were reported using descriptive statistics as numbers and proportions. Continuous variables were reported as mean ± standard deviation (SD) or median (interquartile range: IQR).

Monitoring frequency was calculated for each cardiometabolic parameter within the 1st year of starting antipsychotic therapy. For each time point, patients with complete follow-up until that time point were included in the numerator, while the denominator represented the overall number of patients who received monitoring. This was reported as proportions (%) and corresponding 95% confidence intervals (CI). The statistical analysis was undertaken using Statistical Package for STATA Version 17.1.

3. Results

3.1. Cohort characteristics

Between 2003 and 2018, 11,435 adult patients diagnosed with mental illness and treated with antipsychotics were eligible for the study. The demographic characteristics and comorbidities of the selected cohorts are described in Table 1

The majority of the cohort was diagnosed with mood disorders (n = 9988, 87.3%), while the remaining were presented with schizophrenia and its related disorders (n = 1447, 12.6%). Most patients were initiated on second-generation antipsychotics (SGAs) at the study index (n = 9707; 84·8%), and 1728 (15·1%) were prescribed first-generation antipsychotics (FGAs). Antipsychotics with known high cardiometabolic risk i.e. quetiapine (37·0%), olanzapine (27·0%) and risperidone (15.3%) were the most commonly prescribed medications.

Regarding cardiometabolic profiles, a total of 6599 (52·0%) patients had evidence of at least one of the cardiometabolic profiles (i.e., BMI, BP, HDL—C, LDL-C) recorded at baseline. Among these groups, only 3·0% of the patients were free of any biochemical abnormalities, while the majority (n = 4627, 96·7%) had at least one abnormal lab value at baseline. Over half of the patients had BMI >25 kg/m^2 (57%), while a small proportion (n = 73, 0·6%) presented with central obesity (male >102 cm and female >88 cm). Around 28% (n = 445) of the patients had diabetes at baseline (HbA1c >6·5% and FBG ≥7·0 mmol/L). Data is provided in supplementary materials [Supplementary E].

Most of the cohort (80·0%, n = 9148) had at least one cardiometabolic risk factor at baseline. Over half of the patients (52·4%, n = 4795) were aged >50 years old and were males (56·5%, n = 5175). A small proportion of patients presented other CV risk factors such as dyslipidaemias (7·3%, n = 672) and central obesity (0·4%, n = 40) [Supplementary E].

3.2. The persistence of cardiometabolic monitoring during follow-up

Overall, the majority of the cohort failed to receive complete monitoring for any outcome (99·0%). Furthermore, metrics related to central obesity (e.g. WC) and some biochemical parameters, mainly TGs were not recorded among the minority of patients, who received regular monitoring. Data on patients who received complete cardiometabolic monitoring over the study period for each component of the cardiometabolic profile is presented in the supplementary materials [Supplementary F].

Table 1
Baseline demographic and clinical characteristics of the study cohort.

Characteristics	Proportion of patients n (%)	Mean (S·D) or median (IQR)
Total number of the cohort	11,435	
Deceased cases	1302 (11.0%)	
Gender		
Male	5175 (45.3%)	
Female	6260 (54.7%)	
Age band (years) at index		46 (IQR 33–62)
17–30	2072 (18.1%)	
31–40	2159 (18.9%)	
41–50	2409 (21.1%)	
51–60	1652 (14.5%)	
61–70	1038 (9.1%)	
71–80	1105 (9.7%)	
≥81	1000 (8.8%)	
Diagnosed mental illness		
Schizophrenia, schizotypal and delusion	1447 (12.6%)	
Mood [affective] disorders	9988 (87.3%)	
Treatment duration with antipsychotic (years)		3.3 (IQR1.3–6.2)
Prescribed antipsychotic during initiation		
First-generation	Total: 1728 (15.1%)	
Amisulpride	232 (2.0%)	
Benperidol	4 (0.03%)	
Chlorpromazine	531 (4.6%)	
Flupentixol	286 (2.5%)	
Fluphenazine	9 (0.08%)	
Haloperidol	314 (2.8%)	
Levomepromazine	55 (0.5%)	
Pericyazine	76 (0.7%)	
Pimozide	1 (0.01%)	
Sulpiride	66 (0.6%)	
Thioridazine	2 (0.02%)	
Trifluoperazine	142 (1.2%)	
Zuclopenthixol	14 (0.1%)	
Second-generation	Total: 9707 (84.9%)	
Aripiprazole	618 (5.4%)	
Clozapine	3 (0.03%)	
Lurasidone	3 (0.03%)	
Olanzapine	3090 (27.0%)	
Paliperidone	5 (0.04%)	
Quetiapine	4230 (37.0%)	
Risperidone	1754 (15.3%)	
Baseline clinical profile		
Blood pressure (mmHg)	Total: 4959 (43.3%)	SBP 128.9 (18) DBP 77.2 (10.6)
Low BP (Systolic:60–90 or Diastolic: <60)	22 (0.4%)	
Normal BP (Systolic: 90–120 or Diastolic: 60–80)	1113 (22.4%)	
Pre-HTN (Systolic: 120–140 or Diastolic: 80–90)	2287 (46.1%)	
HTN (Systolic >140 or Diastolic >100)	1537 (31.0%)	
Unrecorded†	6476 (57.0%)	
Body compositions		
Body mass index (BMI); (kg/m2)	Total: 2915 (26.0%)	27.4 (7.7)
Underweight (<18.5)	154 (5.28%)	
Normal (18.5–24.9)	1089 (37.4%)	
Overweight (25.0–29.9)	800 (27.4%)	
Obese 1 (30.0–34.9)	397 (13.6%)	
Obese 2 (35.0–39.9 and above)	475 (16.3%)	
Unrecorded	8476 (74.1%)	
Waist circumference (cm)	Total: 73 (0.6%)	96.59 (15.8)
Low risk for CVD		
Male (< 102 cm or 40 in.) or Female (< 88 cm or 35 in.)	33 (45.2%)	
High risk for CVD		
Male (>102 cm or 40 in.) or Female (>88 cm or 35 in.)	40 (54.7%)	
Unrecorded	11,362 (99.3%)	
Glycaemic profile		
Fasting blood glucose (mmol/L)	Total: 540 (4.7%)	5.5 (1.7)
Normal (< 5.6 mmol/L) or (<100 mg/dL)	364 (67.3%)	
Pre-diabetic (5.6 to 7.0 mmol/L) or (100 to 125 mg/dl)	107 (19.7%)	
Diabetic (≥7.0 mmol/L) or (≥125 mg/dL)	70 (12.9%)	
Unrecorded	10,895 (95.2%)	
HbA1c (mmol/mol)	1029 (9.0%)	42.5 (19.7)
(Normal <47 mmol/mol or < 5.7%)	761 (74.0%)	
(Pre-diabetic >5.7% but ≤48 mmol/L or < 6.4%)	12 (1.1%)	
(Diabetic >48 mmol/mol or > 6.5%)	256 (24.8%)	
Unrecorded	10,406 (91.0%)	
Lipid profile		
LDL (mmol/L)	Total: 1499 (13.1%)	2.9 (1.1)
(Normal lipid profile ≤3 mmol/L)	1086 (72.2%)	
(Dyslipidaemia >3 mmol/L)	416 (27.7%)	
Unrecorded	9936 (86.8%)	
HDL (mmol/L)	Total: 1831 (16.0%)	1.4 (0.54)
(Normal lipid profile ≥1 mmol/L)	1831	
Unrecorded	9604 (83.9%)	
TGs (mmol/L)	Total: 1650 (14.4%)	1.7 (1.1)
(Normal lipid profile ≤2.3 mmol/L)	1394 (84.4%)	
(Dyslipidaemia >2.3 mmol/L)	256 (15.5%)	
Unrecorded	9785 (85.5%)	

†This corresponds to the non-recorded patients; CVDs: cardiovascular diseases; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; HbA1c: glycosylated haemoglobin, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TGs: triglycerides; IQR: interquartile range; SD: standard deviation; n: the absolute number of patients.

3.3. Cardiometabolic monitoring frequencies across antipsychotic drug classes at different time points

Infrequent cardiometabolic monitoring was also observed across individual antipsychotic drugs. Generally, no clear pattern emerged when comparing monitoring prevalence between different antipsychotic drug classes. Tables 2-4 shows the monitoring prevalence at different time points for each cardiometabolic outcome for the most commonly prescribed antipsychotic drugs.

Among different antipsychotics, the monitoring pattern for most measurements (BMI, BP, and blood glucose) was similar. However, patients prescribed certain antipsychotic drugs were monitored more often for certain parameters. For example, patients receiving aripiprazole tend to receive the yearly HbA1c monitoring more frequently at 22·0% than patients taking olanzapine, quetiapine, and risperidone, at 11·0%, 14·0% and 15·0%, respectively. Additionally, the subsequent yearly follow-up for biochemical measures (HDL) was slightly higher among quetiapine and risperidone users than among other antipsychotics. Conversely, for antipsychotics with higher metabolic risks (olanzapine, quetiapine, and risperidone), the baseline data for LDL monitoring were not recorded for over 80.0% of the cases (86·0%, 83·0% and 83·0% respectively). Similarly, the prevalence of baseline TGs monitoring was less frequently recorded (<20·0%) among all subjects receiving prescribed antipsychotics.

Table 2
Descriptive data of the differences in body weight and blood pressure monitoring at baseline, 6,12 weeks and one year by different index antipsychotic drugs (only the ten top prescribed antipsychotics were included in the table).

Prescribed antipsychotic	Presence of a test within these time points n (%); [95% CI]									
	BMI				WC			BP		
FGAs (n = 1505)	Baseline	6-weeks	3-months	12-months	Baseline	3-months	12-months	Baseline	3-months	12-months
Amisulpride (232)	74 (31%); [25%–38%]	16 (6%); [3%–10%]	19 (8%); [5%–12%]	96 (41%); [34%–48%]	4 (1%); [0%–4%]*	1 (0%)*; [0%–2%]	4 (0%)*; [0%–4%]*	130 (55%); [49%–62%]	46 (19%); [14%–25%]	146 (62%); [56%–69%]
Chlorpromazine (531)	139 (26%); [22%–30%]	37 (6%); [4%–9%]	48 (9%); [6%–11%]	189 (35%); [31%–39%]	1 (0%)*; [0%–1%]*	NR	2 (0%)*; [0%–1%]*	197 (37%); [32%–41%]	64 (12%); [9%–15%]	250 (47%); [42%–51%]
Flupentixol (286)	73 (25%); [20%–30%]	26 (9%); [6%–13%]	19 (6%); [4%–10%]	97 (33%); [28%–39%]	NR	1 (0%)*; [0%–1%]*	2 (0%)*; [0%–2%]*	139 (48%); [42%–54%]	42 (14%); [10%–19%]	152 (53%); [47%–59%]
Haloperidol (314)	88 (28%); [23%–33%]	24 (8%); [4%–11%]	29 (9%); [6%–12%]	107 (34%); [28%–39%]	2 (0%)*; [0%–2%]*	NR	2 (0%)*; [0%–2%]*	182 (57%); [52%–63%]	55 (17%); [13%–22%]	203 (64%); [59%–69%]
Trifluoperazine (142)	38 (26%); [19%–34%]	7 (4%); [2%–9%]	9 (6%); [2%–11%]	46 (32%); [24%–40%]	3 (2%); [0%–6%]*	NR	NR	72 (50%); [42%–59%]	19 (13%); [8%–20%]	75 (52%); [44%–61%]
SGAs (n = 9692)	Baseline	6-weeks	3-months	12-months	Baseline	3-months	12-months	Baseline	3-months	12-months
Aripiprazole (618)	195 (31%); [27%–35%]	56 (9%); [6%–11%]	64 (10%); [8%–13%]	278 (45%); [41%–49%]	8 (1%); [0%–2%]*	NR	14 (2%); [1%–3%]	280 (45%); [41%–49%]	87 (14%); [11%–17%]	358 (57%); [53%–61%]
Olanzapine (3090)	746 (24%); [22%–25%]	240 (7%); [6%–8%]	284 (9%); [8%–10%]	1179 (38%); [36%–39%]	18 (0%)*; [0%]*	3 (0%)*; [0%]*	35 (1%); [0%–1%]*	1256 (40%); [38%–42%]	385 (12%); [11%–13%]	1625 (52%); [50%–54%]
Quetiapine (4230)	1082 (25%); [24%–26%]	266 (6%); [5%–7%]	327 (7%); [6%–8%]	1585 (37%); [36%–38%]	26 (0%)*; [0%]*	13 (0%)*; [0%]*	52 (1%); [0%–1%]*	1808 (42%); [41%–44%]	506 (12%); [10%–12%]	2209 (52%); [50%–53%]
Risperidone (1754)	453 (25%); [23%–27%]	150 (8%); [7%–9%]	150 (8%); [7%–9%]	683 (39%); [36%–41%]	11 (0%)*; [0%–1%]*	3 (0%)*; [0%]*	25 (1%); [0%–2%]*	781 (44%); [42%–46%]	224 (13%); [11%–14%]	970 (55%); [52%–57%]

* Value <0.00. Abbreviations: SGAs: second-generation antipsychotics, FGAs: first-generation antipsychotics, BMI: body mass index, WC: waist circumference, NR: observation not recorded, n: absolute number of patients.

4. Discussion

4.1. Main findings

The NICE guidelines for psychosis and schizophrenia recommend appropriate physical health checks, including yearly checks for the cardiometabolic variables [7]. However, considering the NICE guidelines, none of the recommended parameters was regularly monitored as per the definition adopted in this study.

This work examined the extent of adherence to cardiometabolic monitoring guidelines for patients treated with antipsychotic medicines in primary care settings. The findings of this work revealed a trend showing a considerable variation in the overall cardiometabolic monitoring prevalence for different outcomes. A key finding in this study was the extremely low prevalence of waist circumference measurement. Similar findings were reported in a previous study that suggested that waist circumference is often poorly recorded in antipsychotic users despite efforts such as quality improvement audits [18].

The current study also detected a noticeably low frequency of glucose monitoring compared to other biochemical parameters (e.g., plasma lipids). These findings contradict similar studies reporting a considerably high prevalence of glucose testing in patients prescribed antipsychotics in the US. For example, two US studies investigated the impact of educational audits on cardiometabolic screening state in a community mental health system [19,20] and the metabolic testing for adults newly prescribed antipsychotics in a state Medicaid program. Compared to our findings, both studies showed high proportions of patients receiving yearly blood glucose testing ranging from 40·0% [21] and 70·0% [22], while lipid testing reached up to 40·0% [21,22]. It is important to note that the relatively high prevalence of blood glucose and lipid checks observed in these works was likely to be a responsive action to the interventions applied (e.g., reimbursed testing). Nonetheless, maintaining long-term performance is crucial.

4.2. Antipsychotic and cardiometabolic monitoring

Due to their low risk of neurological side effects, namely motor symptoms, SGAs have been widely used to treat both psychotic and nonpsychotic psychiatric disorders in the past two decades. [19] However, SGA use was linked to significant weight gain and other metabolic complications, leading to significant cardiovascular and metabolic health concerns among SGA users [19,20].

Considering the effect of antipsychotics prescribed at index on the monitoring profile, the baseline and short-term monitoring frequency

Table 3
Descriptive data of the differences in glucose, monitoring at baseline, 12 weeks and one year by different index antipsychotic drugs (only the ten top prescribed antipsychotics were included in the table).

Prescribed antipsychotic	Presence of a test within these time points n (%); [95% CI]								
	BG			FBG			HbA1c		
Total FGAs (1505)	Baseline	3-months	12-months	Baseline	3-months	12-months	Baseline	3-months	12-months
Amisulpride (232)	60 (25%); [20%–31%]	19 (8%); [5%–12%]	52 (22%); [17%–28%]	20 (8%); [5%–12%]	4 (2%); [0%–4%]*	23 (9%); [6%–14%]	30 (12%); [8%–17%]	7 (3%); [1%–6%]	27 (11%); [7%–16%]
Chlorpromazine (531)	100 (18%); [15%–22%]	29 (5%); [3%–7%]	135 (25%); [21%–29%]	9 (1%); [0%–3%]*	3 (0%)*; [0%–1%]*	19 (3%); [2%–5%]	28 (5%); [3%–7%]	12 (2%); [1%–3%]	38 (7%); [5%–9%]
Flupentixol (286)	60 (20%); [16%–26%]	11 (3%); [1%–6%]	59 (21%); [16%–25%]	13 (4%); [2%–7%]	2 (0%)*; [0%–2%]*	12 (4%); [2%–7%]	23 (8%); [5%–11%]	4 (1%); [0%–3%]*	22 (8%); [4%–11%]
Haloperidol (314)	88 (28%); [23%–33%]	21 (7%); [4%–10%]	89 (28%); [23%–33%]	14 (4%); [2%–7%]	1 (0%)*; [0%–1%]*	18 (6%); [3%–8%]	40 (12%); [9%–16%]	9 (3%); [1%–5%]	40 (13%); [9%–16%]
Trifluoperazine (142)	26 (18%); [12%–25%]	4 (3%); [0%–7%]*	38 (27%); [19%–34%]	5 (2%); [1%–8%]	NR	8 (5%); [2%–10%]	7 (5%); [2%–9%]	3 (2%); [0%–6%]*	16 (11%); [6%–17%]
Total SGAs (9692)	Baseline	3-months	12-months	Baseline	3-months	12-months	Baseline	3-months	12-months
Aripiprazole (618)	115 (18%); [15%–21%]	18 (3%); [1%–4%]	157 (25%); [22%–29%]	29 (5%); [3%–6%]	9 (1%); [0%–2%]*	32 (5%); [3%–7%]	91 (16%); [12%–17%]	28 (4%); [3%–6%]	133 (22%); [18%–24%]
Olanzapine (3090)	597 (19%); [17%–20%]	145 (4%); [3%–5%]	724 (23%); [21%–24%]	149 (5%); [4%–5%]	32 (1%); [0%–1%]*	239 (8%); [6%–8%]	215 (7%); [6%–7%]	57 (2%); [1%–3%]	336 (11%); [9%–12%]
Quetiapine (4230)	883 (21%); [19%–22%]	163 (3%); [3%–4%]	960 (23%); [21%–23%]	208 (5%); [4%–5%]	52 (1%); [0%–1%]*	294 (7%); [6%–8%]	403 (10%); [8%–10%]	103 (2%); [1%–2%]	575 (14%); [12%–14%]
Risperidone (1754)	361 (20%); [18%–22%]	87 (4%); [3%–6%]	420 (24%); [21%–26%]	88 (5%); [4%–6%]	17 (0%)*; [0%–1%]*	118 (7%); [5%–8%]	175 (10%); [8%–11%]	39 (2%); [1%–3%]	269 (15%); [13%–17%]

* Value <0.00. Abbreviations: SGAs: second-generation antipsychotics, FGAs: first-generation antipsychotics, BG: blood glucose, FBG: fasting blood glucose, HbA1c: glycosylated haemoglobin, NR: observation not recorded, n: absolute number of patients.

Table 4
Descriptive data of the differences in lipid profile monitoring at baseline, 12 weeks and one year by different index antipsychotic drugs (only the ten top prescribed antipsychotics were included in the table).

Prescribed antipsychotic	Presence of a test within these time points n (%); [95% CI]								
	HDL			LDL			TG		
Total FGAs (1505)	Baseline	3-months	12-months	Baseline	3-months	12-months	Baseline	3-months	12-months
Amisulpride (232)	51 (22%); [16%–27%]	21 (10%); [5%–13%]	27 (12%); [7%–16%]	41 (18%); [12%–23%]	17 (7%); [4%–11%]	54 (23%); [17%–29%]	53 (10%); [17%–28%]	22 (9%); [6%–14%]	64 (28%); [21%–33%]
Chlorpromazine (531)	52 (10%); [7%–12%]	18 (3%); [2%–5%]	38 (7%); [5%–9%]	50 (10%); [7%–15%]	16 (3%); [1%–4%]	90 (17%); [13%–20%]	53 (10%); [7%–12%]	22 (4%); [2%–6%]	98 (18%); [15%–22%]
Flupentixol (286)	42 (15%); [10%–19%]	12 (4%); [2%–7%]	22 (8%); [4%–11%]	33 (12%); [8%–15%]	9 (3%); [1%–5%]	38 (13%); [9%–17%]	36 (13%); [8%–16%]	10 (3%); [1%–6%]	44 (15%); [11%–20%]
Haloperidol (314)	65 (21%); [16%–25%]	9 (3%); [1%–5%]	40 (13%); [9%–16%]	47 (15%); [11%–19%]	5 (2%); [0%–3%]*	62 (20%); [15%–24%]	55 (18%); [13%–22%]	5 (2%); [0%–3%]*	71 (23%); [18%–27%]
Trifluoperazine (142)	18 (13%); [7%–19%]	6 (4%); [1%–8%]	16 (11%); [6%–17%]	15 (11%); [6%–16%]	5 (4%); [1%–8%]	19 (13%); [8%–20%]	16 (11%); [6%–17%]	5 (4%); [1%–8%]	23 (16%); [10%–23%]
Total SGAs (9692)	Baseline	3-months	12-months	Baseline	3-months	12-months	Baseline	3-months	12-months
Aripiprazole (618)	121 (20%); [16%–22%]	30 (5%); [3%–6%]	133 (22%); [18%–24%]	102 (17%); [13%–19%]	26 (4%); [2%–6%]	172 (28%); [24%–31%]	107 (17%); [14%–20%]	30 (5%); [3%–6%]	179 (29%); [25%–32%]
Olanzapine (3090)	434 (14%); [12%–15%]	138 (4%); [3%–5%]	336 (11%); [9%–12%]	50 (2%); [1%–2%]	105 (3%); [2%–4%]	659 (21%); [19%–22%]	408 (13%); [11%–14%]	115 (4%); [3%–4%]	723 (23%); [21%–24%]
Quetiapine (4230)	725 (17%); [16%–18%]	191 (5%); [3%–5%]	575 (14%); [12%–14%]	33 (1%); [0%–1%]*	163 (4%); [3%–4%]	849 (20%); [18%–21%]	645 (15%); [14%–16%]	171 (4%); [3%–4%]	919 (22%); [20%–22%]
Risperidone (1754)	292 (17%); [14%–18%]	75 (4%); [3%–5%]	269 (15%); [13%–17%]	47 (3%); [1%–3%]	61 (3%); [2%–4%]	378 (22%); [19%–23%]	257 (15%); [13%–16%]	65 (3%); [2%–4%]	416 (24%); [21%–25%]

* Value <0.00. Abbreviations: SGAs: second-generation antipsychotics, FGAs: first-generation antipsychotics, BMI: body mass index, WC: waist circumference, n: absolute number of patients.

were below 50·0% in the current study. Nevertheless, it was even lower among patients prescribed second-generation antipsychotic medications than those who used FGAs. Although the included cohorts in this study comprised vast numbers of patients prescribed SGAs with high metabolic risks, the findings of this work demonstrate apparent deficiencies in cardiometabolic monitoring in such patients despite the FDA warnings [3] and NICE recommendations [7]. Indeed, it could be speculated that clinicians would automatically monitor metabolic abnormalities in those SGAs. The association between the type of prescribed antipsychotic and the probabilities of cardiometabolic monitoring were highlighted in previous work. Few studies explored the use of antipsychotics as an indicator for cardiometabolic monitoring; [23,24] however, the findings were inconclusive. Notably, a study [25] assessing the quality of monitoring for metabolic effects associated with SGA use showed that patients prescribed clozapine were more likely to be monitored for metabolic syndrome in the presence of dyslipidaemia or diabetes. Furthermore, general practitioners are likely to be unfamiliar with side effects of antipsychotic drugs. A systematic review of qualitative evidence suggested that infrequent physical health monitoring among patients prescribed SGAs can be attributed to a lack of knowledge

among healthcare professionals in primary care regarding the cardiometabolic side effects associated with SGAs [26]. Furthermore, the observed low blood glucose monitoring in this study could also be linked to the fear associated with needles as patients may often be reluctant to give blood samples [27]. These findings suggest that reasons other than initiating SGA can be more important determinants of cardiometabolic monitoring among antipsychotic users. Nevertheless, it is necessary to conduct additional research to support these claims and undertake qualitative research with healthcare providers in primary care regarding barriers to monitoring practices.

Continuity of care is essential to improve monitoring practices. Our previous systematic review highlights the lack of clarity on the roles and responsibilities among service providers as an important barrier to routine monitoring of side effects [26]. Ensuring that one clinical setting or practice remains primarily responsible for treatment initiation, monitoring and follow up for an individual patient is likely to minimise adverse events and improve monitoring practices.

4.3. Limitations

Some patients using antipsychotics may be solely managed in secondary care, which may not be reflected in IMRD data; however, we anticipate this group to be small. The present study is subjected to misclassification bias or under-recording of patients who may be eligible for the study. In addition, evaluation of a direct link between specific antipsychotic exposure and the target outcome was challenging because of the potential antipsychotic switching during the study period (trial period) and the possibility of drug selection bias. For example, drugs with a greater propensity for weight gain may be used less often in patients who are already overweight. Additionally, other psychotropic medications might be prescribed to our cohort patients, including antidepressants and mood stabilizers, which can also contribute to metabolic side effects and the monitoring pattern; however, such an assumption needs further investigation. Finally, data for established modifiable cardiovascular risk factors were extracted except for data related to smoking history and alcohol drinking habits as they were not available for extraction.

5. Conclusions

This study demonstrates suboptimal monitoring of cardiometabolic risk factors in patients prescribed antipsychotics in primary care with a vast majority of patients failing to receive monitoring for all risk factors at all time points. There is an urgent need to improve routine screening and appropriate follow-up care of cardiometabolic risk factors among this population to improve safe and effective use of these drugs, promote patient outcomes and prevent adverse events.

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Contributors

This work contributed to the PhD thesis of the first author RAA. VP and ZJ were the supervisors of the study. JSC, KN, KG, AS and NA extracted the data and provided advice regarding the data analysis and presentation. RAA led the write up to which all authors contributed through editing and recommendations. All authors agreed to the final version of the manuscript.

Declaration of Competing Interest

We declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.comppsych.2023.152419.

References

[1] Wu C-S, Tsai Y-T, Tsai H-J. Antipsychotic drugs and the risk of ventricular arrhythmia and/or sudden cardiac death: a nation-wide case-crossover study. J Am Heart Assoc 2015;4:e001568. http://www.ncbi.nlm.nih.gov/pubmed/25713294 [accessed 11 Jul 2018].
[2] Ho CSH, Zhang MWB, Mak A, Ho RCM. Metabolic syndrome in psychiatry: advances in understanding and management. Adv Psychiatr Treat 2014;20(2):101–12.
[3] Morrato EH, Druss B, Hartung DM, Valuck RJ, Allen R, Campagna E, et al. Metabolic testing rates in 3 state Medicaid programs after FDA warnings and ADA/APA recommendations for second-generation antipsychotic drugs. Arch Gen Psychiatry 2010;67:17–24.
[4] Newcomer J. FDA to Require Diabetes Warning On Antipsychotics. Interviewed by Rosack J for Psychiatric News. 2003.
[5] Clark NG. Consensus development conference on antipsychotic drugs and obesity and diabetes. In: Diabetes Care American Diabetes Association; 2004. p. 596–601. https://care.diabetesjournals.org/content/27/2/596 [accessed 19 Mar 2021].
[6] Citrome L, Yeomans D. Do guidelines for severe mental illness promote physical health and well-being? J Psychopharmacol 2005;19(6_suppl):102–9. https://doi.org/10.1177/0269881105059505 [accessed 14 Mar 2018].
[7] National Institute for Health and Care Excellence. Overview: Psychosis and schizophrenia in adults: prevention and management Guidance. In: NICE Guidelines CG187. London, UK: National Institute for Health and Care Excellence; 2014. https://www.nice.org.uk/guidance/cg178 [accessed 19 Mar 2021].
[8] Cohn TA, Sernyak MJ. Metabolic monitoring for patients treated with antipsychotic medications. Can J Psychiatry 2006;51:492–501. https://doi.org/10.1177/070674370605100804 [accessed 12 Jun 2019].
[9] Newcomer JW, Nasrallah HA, Loebel AD. The atypical antipsychotic therapy and metabolic issues National Survey: practice patterns and knowledge of psychiatrists. J Clin Psychopharmacol 2004;24:1–6.
[10] Mitchell AJ, Delaffon V, Vancampfort D, Correll CU, De Hert M. Guideline concordant monitoring of metabolic risk in people treated with antipsychotic medication: systematic review and meta-analysis of screening practices. Psychol Med 2012;42:125–47.
[11] Solmi M, Fiedorowicz J, Poddighe L, Delogu M, Miola A, Høye A, et al. Disparities in screening and treatment of cardiovascular diseases in patients with mental disorders across the world: systematic review and Meta-analysis of 47 observational studies. Am J Psychiatry 2021;178:793–803.
[12] Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Bull World Health Organ 2007;4:296–1623.
[13] Gokhale KM, Chandan JS, Toulis K, Gkoutos G, Tino P, Nirantharakumar K. Data extraction for epidemiological research (DExtER): a novel tool for automated clinical epidemiology studies. Eur J Epidemiol 2021;36:165–78. https://pubmed.ncbi.nlm.nih.gov/32856160/ [accessed 6 Dec 2022].
[14] Blak BT, Thompson M, Dattani H, Bourke A. Generalisability of the health improvement network (THIN) database: demographics, chronic disease prevalence and mortality rates. Inform Prim Care 2011;19:251–5. https://pubmed.ncbi.nlm.nih.gov/22828580/ [accessed 14 Dec 2022].
[15] THIN Database. University Colege London. https://www.ucl.ac.uk/iehc/research/primary-care-and-population-health/research/thin-database/database; 2019 [accessed 12 Jun 2019].
[16] CHOP Institutional Review Board. Criteria for IRB Approval. Childern Hospital of Philadelphia; 2019. https://irb.research.chop.edu/criteria-irb-approval (accessed 12 Jun 2019).
[17] BioRender. https://app.biorender.com/; 2023 [accessed 16 May 2022].
[18] Barnes TRE, Bhatti SF, Adroer R, Paton C. Screening for the metabolic side effects of antipsychotic medication: findings of a 6-year quality improvement programme in the UK. BMJ Open 2015;5:e007633.
[19] Alves RS, Souza AS. In: Taylor D, Barnes T, Young A, editors. The Maudsley prescribing guidelines in psychiatry. 13th ed.In. John Wiley & Sons; 2021.
[20] Chisholm-Burns MA, Schwinghammer TL, Malone PM, Kolesar JM, Brandon P. Bookstaver LK, et al. In: Chisholm-Burns Marie A, Schwinghammer Terry L, Malone Patrick M, et al., editors. Chapter37. Pharmacotherapy principles and practice. New York: Mcgraw-Hill Education; 2019.
[21] Cotes RO, de Nesnera A, Kelly M, Orsini K, Xie H, McHugo G, et al. Antipsychotic cardiometabolic side effect monitoring in a state community mental health system. Community Ment Health J 2015;51:685–94.

[22] Morrato EH, Campagna EJ, Brewer SE, Dickinson LM, Thomas DSK, Miller BF, et al. Metabolic testing for adults in a state Medicaid program receiving antipsychotics remaining barriers to achieving population health prevention goals. JAMA Psychiatry 2016;73:721–30.
[23] Haupt DW, Rosenblatt LC, Kim E, Baker RA, Whitehead R, Newcomer JW. Prevalence and predictors of lipid and glucose monitoring in commercially insured patients treated with second-generation antipsychotic agents. Am J Psychiatry 2009;166:345–53. https://www.scinapse.io/papers/1989361442 [accessed 19 May 2022].
[24] Shi L, Ascher-Svanum H, Chiang Y-J, Zhao Y, Fonseca V, Winstead D. Predictors of metabolic monitoring among schizophrenia patients with a new episode of second-generation antipsychotic use in the veterans health administration. BMC Psychiatry 2009;9:80.
[25] Moeller KE, Rigler SK, Mayorga A, Nazir N, Shireman TI. Quality of monitoring for metabolic effects associated with second generation antipsychotics in patients with schizophrenia on public insurance. Schizophr Res 2011;126:117–23.
[26] Ali RA, Jalal Z, Paudyal V. Barriers to monitoring and management of cardiovascular and metabolic health of patients prescribed antipsychotic drugs: a systematic review. BMC Psychiatry 2020;20:581.
[27] McLenon J, MAM Rogers. The fear of needles: A systematic review and meta-analysis. J Adv Nurs 2019:30–42.