

BMJ Open Assessing cardiometabolic parameter monitoring in inpatients taking a second-generation antipsychotic: The CAMI-SGA study – a cross-sectional study

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ABSTRACT

Objectives This study aims to determine the proportion of initial cardiometabolic assessment and its predicting factors in adults with schizophrenia, bipolar disorder or other related diagnoses for whom a second-generation antipsychotic was prescribed in the hospital setting.

Design Cross-sectional study.

Setting The psychiatry unit of a Canadian tertiary care teaching hospital in Montreal, Canada.

Participants 402 patients with aforementioned disorders who initiated, restarted or switched to one of the following antipsychotics: clozapine, olanzapine, risperidone, paliperidone or quetiapine, between 2013 and 2016.

Primary outcome measures We assessed the proportion of cardiometabolic parameters monitored.

Secondary outcome measures We identified predictors that influence the monitoring of cardiometabolic parameters and we assessed the proportion of adequate interventions following the screening of uncontrolled blood pressure and fasting glucose or glycated haemoglobin (HbA1c) results.

Results Only 37.3% of patients received monitoring for at least three cardiometabolic parameters. Blood pressure was assessed in 99.8% of patients; lipid profile in 24.4%; fasting glucose or HbA1c in 33.3% and weight or body mass index in 97.8% of patients while waist circumference was assessed in 4.5% of patients. For patients with abnormal blood pressure and glycaemic values, 42.3% and 41.2% subsequent interventions were done, respectively. The study highlighted the psychiatric diagnosis (substance induced disorder OR 0.06 95% CI 0.00 to 0.44), the presence of a court-ordered treatment (OR 0.79 95% CI 0.35 to 1.79) and the treating psychiatrist (up to OR 34.0 95% CI 16.2 to 140.7) as predictors of cardiometabolic monitoring.

Conclusions This study reports suboptimal baseline cardiometabolic monitoring of patients taking an antipsychotic in a Canadian hospital. Optimising collaboration within a multidisciplinary team may increase cardiometabolic monitoring.

Strengths and limitations of this study

- We present real-world evidence regarding adherence to guidelines of cardiometabolic parameters monitoring in patients with schizophrenia, bipolar disorder or other related diagnoses.
- We selected five antipsychotics with the highest inherent risk of cardiometabolic adverse events (clozapine, olanzapine, risperidone, paliperidone or quetiapine) for increased clinical relevance.
- We identified predictors of cardiometabolic parameters monitoring in a tertiary centre in Canada.
- The lasso statistical model cannot determine whether some variables are stronger predictors for cardiometabolic parameters monitoring than others, nor does it allow to infer causality.
- Despite clear international guidelines to this effect, there is still a large gap in monitoring of cardiometabolic parameters in patients taking antipsychotics with the highest inherent risk of cardiometabolic adverse events.

INTRODUCTION

Second-generation antipsychotics (SGA) are first-line therapy for various psychiatric disorders, such as schizophrenia spectrum and other psychotic disorders, as well as bipolar affective disorder and related disorders.^{1 2} However, this class of medication is known to contribute to cardiometabolic adverse events (AEs), such as hypertension, weight gain, type 2 diabetes and dyslipidaemia.³ Exposure to antipsychotics may also increase the risk of stroke,⁴ and acute myocardial infarction,^{5 6} mainly in the older population. Patients with schizophrenia and bipolar affective disorder are at a higher baseline cardiometabolic risk⁷⁻¹³ and have higher risk of cardiovascular disease and associated death.¹⁴ Patients

having both diabetes and serious mental illness are at increased mortality by 3–4 fold.¹⁵ Long-term use of SGA in individuals with serious mental illness further increases the risk of cardiovascular events, including an increased risk of developing diabetes by about threefold.^{16–18} Although SGA are known to cause cardiometabolic AE, they have been demonstrated to decrease overall mortality in patients with schizophrenia, including from cardiovascular causes.¹⁹ The use of antipsychotic polypharmacy among patients with schizophrenia²⁰ and bipolar disorder²¹ is common, although the impact of polypharmacy on cardiometabolic AEs remains unclear.²² The increased baseline cardiometabolic risk combined with the cardiometabolic AE of SGA emphasises the importance of cardiometabolic parameter monitoring (CMPM) in these patients.

Although there are specific guidelines that recommend CMPM when initiating a SGA, it is not routinely done in practice.^{23 24} A meta-analysis assessed the guideline adherence for inpatients and outpatients treated with antipsychotics and found that blood pressure, triglycerides, cholesterol, plasma glucose and weight were measured in 69.8%, 59.9%, 41.5%, 44.3% and 47.9%, respectively.²⁵ To our knowledge, no study has been published on the baseline CMPM in a Canadian inpatient setting and this study aims to fill this gap.

The primary aim of this study was to measure adherence to practice guidelines for CMPM in adult inpatients with schizophrenia or bipolar disorder who are initiating, restarting, or switching to a SGA during their hospitalisation in a tertiary psychiatric care centre. The secondary objectives were to identify predictors of CMPM and to assess the frequency of adequate interventions following the screening of an abnormal value.

METHODS

Patient and public involvement

No patient nor public were involved in the design, conduct, choice of outcome or recruitment to the study.

Population

This study was conducted at the Jewish General Hospital, a Canadian tertiary care teaching hospital that serves a multiethnic community in Montreal, Canada. To be included, patients had to be 18 years and older; hospitalised in the psychiatry unit; with a diagnosis of schizophrenia spectrum and other psychotic disorders or bipolar affective disorder and related disorders. The included diagnoses were selected due to greater inherent cardiometabolic risk in this population^{7–13} (online supplemental table S1).

At the time of inclusion, patients needed to be initiating, restarting or switching to one of the following SGA: clozapine, olanzapine, quetiapine, risperidone or paliperidone, with a follow-up period within the time frame of 9 March 2013 to 1 January 2017. A schematic representation of the study period is shown in online supplemental

figure S1. The five SGA mentioned above will be referred to as study SGA.

Design

In an observational cross-sectional design, we used the pharmacy dispensing software (GesPharx 8, CGSI TI, Quebec City, Quebec, Canada) to identify patients hospitalised in the psychiatry unit of the Jewish General Hospital, and who received a study SGA during the predefined time frame. Patients were randomly selected in blocks throughout the study period. If a patient was hospitalised more than once during the study time frame, a single randomly selected admissible hospitalisation was included.

Studies show that there is generally a greater cardiometabolic risk associated to some SGA compared with most first-generation antipsychotics. In particular, almost all studies put clozapine and olanzapine as the highest cardiometabolic AE, followed by quetiapine.^{26–30} Indeed, metabolic syndrome is considered one of the potentially most life threatening common AE of clozapine.³¹ Depending of the studies, risperidone and paliperidone are next in line for cardiometabolic risk,^{26–28} while current data suggest minimal increased risk for cholesterol and glucose disturbances for the newer generation, including aripiprazole, lurasidone, ziprasidone, brexpiprazole and cariprazine. However, there are some signal that even those new antipsychotics could cause weight gain and triglycerides increase.³² Therefore, even though the guidelines recommend to measure baseline CMPM with all antipsychotics, to increase external validity and clinical relevance, first generation antipsychotics, aripiprazole, lurasidone, ziprasidone, brexpiprazole and cariprazine were excluded as they were deemed at less metabolic risk as per national guidelines²⁴ and recent network meta-analysis,³² and the two latter were unavailable on the Canadian market during the study time frame. We can also note some emerging data seem to put some doubts on strength of this broad affirmation.³³ However, in clinical practice, it is recommended to adhere to these guidelines for all antipsychotics.

All doses of study SGA were included in the study because cardiometabolic AE do not appear to be dose-dependent.³⁴ The study SGA had to be prescribed for chronic use, defined as a duration of at least 7 days. Risperidone and paliperidone were considered to be equivalent, not requiring new baseline CMPM, as paliperidone is the active metabolite of risperidone.³⁵

Outcomes

The primary objective of this study was to assess the proportion at which the recommended cardiometabolic parameters were monitored. Monitoring parameters of blood pressure, lipid profile, fasting glucose or glycated haemoglobin (HbA1c), weight or body mass index (BMI), and waist circumference had to be ordered, measured or charted within the follow-up period of 4 weeks prior to or

4 weeks following the index date (online supplemental figure S1).

Secondary objectives consisted of identifying predictors that influence the monitoring proportion of cardiometabolic parameters and assessing the proportion of adequate intervention following the screening of uncontrolled blood pressure and fasting glucose or HbA1c results. Blood pressure and fasting glucose or HbA1c results were considered abnormal as per the definitions published in Canadian Hypertension guidelines (three values of blood pressure $\geq 140/90$ mm Hg or one value of $\geq 180/110$ mm Hg over the follow-up period) and Canadian Diabetes guidelines (fasting glucose ≥ 7.0 mmol/L or HbA1c $\geq 6.5\%$), respectively.^{24 36} An adequate intervention following an abnormal result was considered to be any of the following: an initiation of treatment or a change in treatment for hypertension and/or diabetes, a consultation, or a referral for a subsequent follow-up in any outpatient clinic regarding the issue.

Sample size

Based on the results from a meta-analysis and a previous study, we hypothesised the following CMPM adherence levels: blood pressure $\geq 60\%$, lipid profile $\geq 50\%$, fasting glucose or HbA1c $\geq 40\%$, weight or BMI $\geq 40\%$ and waist circumference $\geq 10\%$.^{25 37} A sample size calculation was necessary due to limited time and budget. Thus, a sample size of 402 patients was calculated to obtain a precision of $\pm 5\%$ of the expected proportion with a 95% CI (Sample Size Calculators, Clinical and Translational Science Institute, University of California, San Francisco, San Francisco, California, USA).

Statistical analysis

Clopper-Pearson CI was used to calculate 95% CI as some parameters contained few data points. For the first secondary objective, a lasso logistic regression model was used to identify predictors of CMPM.^{38 39} The monitoring of at least three cardiometabolic parameters was chosen as it was thought to be practically feasible while still assessing at least one indicator of metabolic dysfunction. A prespecified sensitivity analysis was planned to set the threshold of monitoring to 4/5 parameters. Given a large number of predictors, a lasso model was used as it permits to identify a smaller subset of predictors that exhibit the strongest effects. These predictors can be interpreted with confidence to exert an effect on CMPM. Coefficients and OR are presented for descriptive purposes. The parameters analysed by the LASSO model as potential predictors of CMPM are presented in online supplemental table S2. This list is comprised of parameters that have been previously analysed in the literature, including some exploratory parameters judged to be pertinent by the investigators.^{37 40–42} Statistical analyses were performed using the R statistical software, V.3.5.1.

RESULTS

Levels of adherence to practice guidelines for CMPM

A total of 402 patients were included in the study. The main diagnosis was Schizophrenia spectrum disorder (69.7%) and almost half (49.1%) were prescribed risperidone or paliperidone. More than half of patients had legal confinement during their hospitalisation. Their demographic and clinical characteristics are presented in table 1.

Figure 1 shows the proportion of patients in whom cardiometabolic parameters were assessed and the expected rates from the literature. While blood pressure monitoring was almost always carried out, screening for lipid and glycaemic parameters was done in approximately a quarter to a third of patients. Weight or BMI were reported in almost all patients' charts; however, waist circumference was seldom measured. One third of the patients had the majority of baseline cardiometabolic assessment. A complete baseline CMPM profile was found in less than 2% of patient charts. Of the five cardiometabolic parameters, blood pressure and weight or BMI were ordered, measured or charted more often than expected.

Predictive variables

Of the predefined parameters in online supplemental table S2), risk of aggressivity was excluded from the lasso model due to a high number of missing data. Four patients were excluded from the lasso regression model due to missing data or because a variable was unique and could not be included. Finally, route of administration for risperidone and paliperidone, including PO or intramuscularly, were combined.

As shown in table 2, CMPM was influenced by the underlying psychiatric condition, whether the patient underwent court-ordered treatment, and the treating psychiatrist. Patients with a substance-induced disorder diagnosis were the least likely to have the majority of CMPM (OR=0.06), followed by bipolar and related disorders (OR=0.93) and other diagnosis (OR=3.09) as compared with the category of schizophrenia and other psychotic disorders. The presence of a court-ordered treatment (OR=0.79) negatively influenced cardiometabolic monitoring. Each treating psychiatrist was compared with an arbitrarily chosen psychiatrist in order to preserve prescriber anonymity; the treating psychiatrist was a key determinant of CMPM, as the smallest OR of 0.80 and the largest OR of 34.

A sensitivity analysis was performed using a threshold score of $\geq 4/5$ cardiometabolic parameters for monitoring. Three variables were shown to be predictors of cardiometabolic monitoring: number of concomitant antipsychotic medications, presence of a court-ordered treatment and treating psychiatrist.

Intervention following abnormal blood pressure or glycaemic control

Blood pressure and glycaemic values were deemed abnormal in 104 patients and in 17 patients, respectively.

Table 1 Study population

Variable	N (%) or mean ($\pm$ SD)
Age	45.4 ($\pm$ 18.5)
Male sex	225 (56%)
Diagnosis	
Schizophrenia spectrum and other psychotic disorders	280 (69.7%)
Bipolar and related disorders	107 (26.6%)
Substance induced	11 (2.7%)
Other diagnosis*	4 (1.0%)
Study SGA†	
Clozapine	24 (6.0%)
Olanzapine	99 (24.6%)
Risperidone/paliperidone (PO/IM)	198 (49.3%)
Quetiapine	81 (20.1%)
No of patients with at least two antipsychotics‡	181 (45.0%)
No of concomitant chronic cardiometabolic medication§	2.68 ($\pm$ 1.56)
Presence of psychiatry resident	349 (86.8%)
Psychiatric closed unit stay	305 (76.1%)
Doctor ordered urgent confinement, up to 72 hours	254 (63.2%)
Hospital confinement	234 (58.2%)
Court-ordered treatment	56 (13.9%)
Aggressivity¶	
None	3 (0.7%)
Low	187 (46.5%)
Medium	132 (32.8%)
High	52 (12.9%)
Missing data	28 (7.0%)
Duration of hospital stay in days	56.7 ($\pm$ 176.1)
Hospital-affiliated outpatient clinic referral at discharge	
No	241 (60.0%)
Yes	158 (39.3%)
Missing data	3 (0.7%)

*Other diagnosis includes schizotypal (personality) disorder, psychotic disorders or bipolar and related disorders due to another medical condition (see online supplemental table S1). Data for the full classification of the psychiatric diagnoses used in this study.

†When no medication route is specified, it is by mouth.

‡Any antipsychotics (AHFS 28:16.08) at study inclusion, includes cross-tapering regimen.

§Number of cardiometabolic medications used prior to hospitalisation (antiplatelet therapy or medication approved in Canada for the treatment of arterial hypertension, dyslipidaemia, diabetes or obesity) except if explicitly used for another indication.

¶Risk of aggressivity or violence was determined by the treating psychiatrist at admission.

AHFS, American Hospital Formulary Service; IM, intramuscularly; PO, by mouth; SGA, second-generation antipsychotic.

Of the 104 patients with uncontrolled blood pressure, 42.3% (95% CI 32.7% to 52.4%) received a subsequent intervention. Similarly, 41.2% (95% CI 18.4% to 67.1%) of the 17 patients with uncontrolled glycaemic indices received a subsequent intervention.

DISCUSSION

While the non-adherence to guidelines was already suspected by clinicians, this is the first study, to our knowledge, to rigorously assess adherence to practice guidelines of cardiometabolic monitoring in inpatients receiving an SGA in a Canadian tertiary hospital setting. We have found that (1) while some parameters were almost always monitored (eg, blood pressure and weight or BMI), others were less often assessed (eg, lipid profile, fasting glucose or HbA1c, and waist circumference); (2) in the context of a global baseline cardiometabolic assessment, approximately one-third of patients had at least three cardiometabolic parameters measured, and less than 2% received a complete baseline cardiometabolic assessment and (3) the quality of cardiometabolic screening was strongly influenced by the treating psychiatrist, the presence of a court-ordered treatment and the psychiatric diagnosis.

The high proportion of blood pressure and weight or BMI measurement was expected, as it is routine nursing practice in the psychiatry unit of the Jewish General Hospital to obtain these values without requiring a psychiatrist's intervention. It was also expected that the proportion of patients receiving a complete monitoring would be very low, as it has been reported that a cultural barrier limits the frequency at which waist circumference measurement is performed.³⁷ However, abdominal obesity, which can be measured by waist circumference, is a better predictor of cardiovascular risk than BMI.⁴³ Therefore, waist circumference measurement should be reinforced in addition to weight measurement. Moreover, it is concerning that lipid profile and fasting glucose or HbA1c, major predictors of cardiovascular events, were not monitored more consistently.⁴⁴

The hospital setting is an important environment to obtain baseline CMPM, as psychiatric patients are often subject to lost to follow-up in an outpatient setting.⁴⁵ It has been demonstrated that this population receives suboptimal medical screening for other diseases as well.⁴⁶ The inpatient setting should be considered an opportune timeframe for appropriate CMPM, however, this study highlights that the majority of patients do not get full CMPM.

Predictors and their impact

A court-order treatment and the treating psychiatrist were deemed predictors by the LASSO model for both the primary analysis and the sensitivity analysis.

A court-order treatment was negatively associated to CMPM, suggesting an inverse correlation between

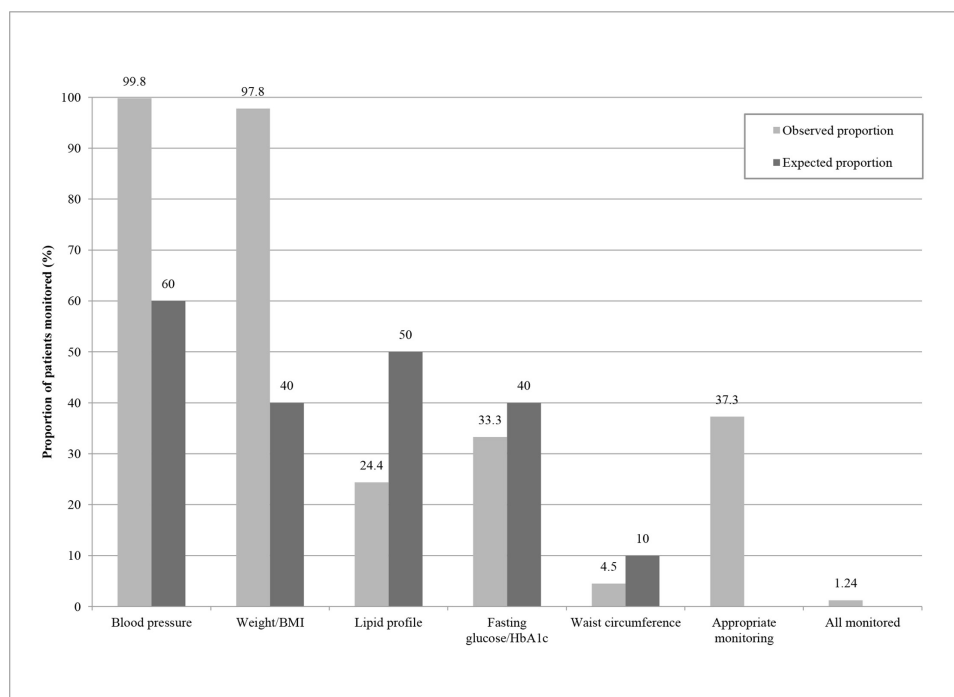


Figure 1 Proportion of cardiometabolic parameter monitoring. n=402. Appropriate monitoring=3/5 parameters monitored. The dark grey bar represents expected monitoring proportion compared with the proportion observed in light grey. BMI, body mass index; HbA1c, glycated haemoglobin.

a difficult patient-treating team collaboration and an adequate CMPM.

This predictor was evaluated as a surrogate marker for disease severity and patient collaboration. Appropriate biopsychosocial treatment could help to minimise the impact of the severity of the illness, and decrease hostility while increasing collaboration. Baseline CMPM can be obtained later in the admission when patient-treating team collaboration is more optimal.

The treating psychiatrist was a predictor of adequate CMPM, with a wide range of OR between psychiatrists,

indicating that different practices could greatly influence the level of monitoring. It also suggests that the published recommendations can be adhered to in practice.

A few variables put in the model were not statistically significant, including some that were more surprising to us. The prevalent use of cardiometabolic medication, which would indicate a more physically impaired population, did not play a role in the assessment. Moreover, the use of SGA with the highest risk of AE (clozapine and olanzapine), as well as polypharmacy, noted in almost half of the patients, were not associated to higher monitoring.

Table 2 Predictors of 3/5 cardiometabolic parameters monitored*, obtained from lasso regression model

Parameter	Coefficient	OR	95% CI†
Court-ordered treatment (ref=No)	-0.24	0.79	(0.35 to 1.79)
Diagnosis (ref=Schizophrenia spectrum and other psychotic disorders)			
Bipolar and related disorders	-0.07	0.93	(0.52 to 1.62)
Substance induced	-2.78	0.06	(0.00002 to 0.44)
Other‡	1.13	3.09	(0.27 to 129 545.5)
Treating psychiatrist (ref=C)			
A	-0.23	0.80	(0.40 to 1.54)
B	3.53	34.0	(16.2 to 140.7)
D	0.51	1.67	(0.85 to 3.35)
E	-0.10	0.90	(0.35 to 1.99)

*All predictors of CMPM were compared with the mode, which served as the reference for each category.

†95% CIs were calculated using bootstrap method for informational purposes. The 95% CI serves as a measure of the range and instability of the OR.

‡Refer to online supplemental table S1. Data for details on the classification of 'other' psychiatric diagnoses.

Patient care is a shared responsibility that often involves the expertise of a highly trained multidisciplinary team. While baseline assessment generally falls under the responsibility of the treating psychiatrist who initiates SGA treatment, the lack of resources and time may be a limiting factor. The involvement of medical hospitalists or general practitioners in this type of monitoring has shown promise in improving CMPM.⁴⁷ In-hospital multidisciplinary collaboration, has become common practice and has been associated with positive patient outcomes.⁴⁸ In particular, the presence of a nurse practitioner in an acute psychiatric unit has been shown to significantly increase the number of patients with cardiometabolic screening.⁴⁹

Furthermore, it has been demonstrated that pharmacists favour adherence to prescribing guidelines or CMPM in both hospital and outpatient settings.^{50–53} One study shows that pharmacists play a key role in the multidisciplinary team in an outpatient metabolic risk screening programme, specifically in patients to whom antipsychotics are prescribed.⁵⁴ Currently, pharmacists are permitted to prescribe laboratory testing in the context of pharmacotherapy surveillance in some jurisdictions.⁵⁵ Prescribing lipid levels and fasting glucose and/or HbA1c may significantly help improve adherence rates to guidelines.⁵⁶

Considering the potential impact pharmacists and nurses can have on CMPM, the implementation of an internal procedure consisting of sharing and/or delegating the monitoring of SGA cardiometabolic parameters to the multidisciplinary team could be a solution to this lingering issue and could increase the quality of patient care.

Moreover, less than half of patients with abnormal blood pressure or glycaemic values had a subsequent intervention done. This highlights the importance of the multidisciplinary approach for patient treatment, in addition to baseline monitoring.

Strengths and limitations

The population chosen was clinically oriented, leading to relevant results. Indeed, a more strenuous follow-up in this population would be expected considering that these patients have an elevated inherent cardiometabolic risk due to their underlying disease state in addition to their treatment with higher risk antipsychotics.^{7–13 26 27} Rigorous data done over a prolonged period of almost 4 years reflects the real-world clinical practice.

The lasso statistical model is useful to identify predictors among a large array of variables, but it cannot determine whether some variables are stronger predictors for CMPM than others, nor does it allow to infer causality.

Furthermore, some patients leaving the psychiatry unit without medical consent may have prevented the planning of appropriate follow-ups and posed an obstacle to baseline CMPM. These patients could have been excluded from this study to limit confusion bias. Moreover, the study design could not take into account the

psychiatrist's clinical judgement in cases where it was justified not to treat an abnormal value on the basis of specific patient characteristics or clinical context. Therefore, the study may overestimate the lack of intervention following abnormal values, which was noted to be less than 50% of the time. In addition, interventions were not evaluated for lipid profile as multiple clinical approaches could be justified for this heterogeneous patient population.

Future directions

The care of patients with serious mental disorder is complex, especially in the treatment integration of multiple comorbidities. Future research addressing the advantages of a multidisciplinary approach to the cardiometabolic follow-up is warranted, with the exploration of automated monitoring. A consideration of an 'opt-out' admission prescription for cardiometabolic monitoring rather than an 'opt-in' might increase the compliance to guidelines, with the caveat of possible over-prescription of those tests. Furthermore, there should be an assessment of the clinical outcomes of patients having regular monitoring and the treatment of SGA-induced cardiometabolic disorders.

CONCLUSIONS

This study highlights that despite access to patients in a controlled environment amenable to cardiometabolic screening, global baseline assessment of key cardiometabolic parameters remains a clinical challenge. This is a shared responsibility between the inpatient and outpatient setting, which might benefit from multidisciplinary approaches involving the collaboration of general practitioners, nurses, pharmacists and other healthcare professionals, as well as automation and baseline admission protocols.

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Contributors All authors had contributed to the conception of the study, analysis and interpretation of data for the work. JF, EC, J-FP and AR did the acquisition of the data and first draft of the manuscript. DW, CR, SR, ML and VD-B revised it critically. All authors approved the final version of the work and are in agreement to be accountable for all aspects of the work. VD-B accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish

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Competing interests ML has received speaker fees from Bayer; has participated in industry-funded trials from Idorsia and Phase3Bio; has served on advisory boards for Servier and Orimed Pharma; and has received in-kind and financial support for investigator-initiated grants from Leo Pharma, Roche Diagnostics, Aggreedyne and Fujimori Kogyo, for unrelated work. VD-B has received fees for consulting by HLS therapeutics and Otsuka for unrelated work, and speaker fees by HLS therapeutics, Otsuka and Jansen for unrelated work. SR has received an investigator-initiated research grant from Satellite Healthcare. The remaining authors declare that there is no conflict of interest.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the Research Ethics Committee at the Jewish General Hospital (CR17-061). To ensure confidentiality, data were denormalised and coded.

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REFERENCES

- Remington G, Addington D, Honer W, *et al.* Guidelines for the pharmacotherapy of schizophrenia in adults. *Can J Psychiatry* 2017;62:604–16.
- Yatham LN, Kennedy SH, Parikh SV, *et al.* Canadian network for mood and anxiety treatments (CANMAT) and International Society for bipolar disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar Disord* 2018;20:97–170.
- Hirsch L, Yang J, Bresee L, *et al.* Second-Generation antipsychotics and metabolic side effects: a systematic review of population-based studies. *Drug Saf* 2017;40:771–81.
- Douglas IJ, Smeeth L. Exposure to antipsychotics and risk of stroke: self controlled case series study. *BMJ* 2008;337:a1227.
- Lin S-T, Chen C-C, Tsang H-Y, *et al.* Association between antipsychotic use and risk of acute myocardial infarction: a nationwide case-crossover study. *Circulation* 2014;130:235–43.
- Pariente A, Fourrier-Réglat A, Ducruet T, *et al.* Antipsychotic use and myocardial infarction in older patients with treated dementia. *Arch Intern Med* 2012;172:648–53. discussion 54–5.
- Haupt DW, Newcomer JW. Hyperglycemia and antipsychotic medications. *J Clin Psychiatry* 2001;62 Suppl 27:15–26.
- Saddichha S, Manjunatha N, Ameen S, *et al.* Diabetes and schizophrenia – effect of disease or drug? Results from a randomized, double-blind, controlled prospective study in first-episode schizophrenia. *Acta Psychiatr Scand* 2008;117:342–7.
- Fleischhacker WW, Siu CO, Bodén R, *et al.* Metabolic risk factors in first-episode schizophrenia: baseline prevalence and course analysed from the European First-Episode schizophrenia trial. *Int J Neuropsychopharmacol* 2013;16:987–95.
- Fagiolini A, Frank E, Scott JA, *et al.* Metabolic syndrome in bipolar disorder: findings from the bipolar disorder center for Pennsylvanians. *Bipolar Disord* 2005;7:424–30.
- Taylor V, MacQueen G. Associations between bipolar disorder and metabolic syndrome: a review. *J Clin Psychiatry* 2006;67:1034–41.
- van Winkel R, De Hert M, Van Eyck D, *et al.* Prevalence of diabetes and the metabolic syndrome in a sample of patients with bipolar disorder. *Bipolar Disord* 2008;10:342–8.
- Vancampfort D, Mitchell AJ, De Hert M, *et al.* Prevalence and predictors of type 2 diabetes mellitus in people with bipolar disorder: a systematic review and meta-analysis. *J Clin Psychiatry* 2015;76:1490–9.
- Correll CU, Solmi M, Veronese N, *et al.* Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. *World Psychiatry* 2017;16:163–80.
- Ribe AR, Laursen TM, Sandbaek A, *et al.* Long-Term mortality of persons with severe mental illness and diabetes: a population-based cohort study in Denmark. *Psychol Med* 2014;44:3097–107.
- Szmulewicz AG, Angriman F, Pedroso FE, *et al.* Long-Term antipsychotic use and major cardiovascular events: a retrospective cohort study. *J Clin Psychiatry* 2017;78:e905–12.
- Rajkumar AP, Horsdal HT, Wimberley T, *et al.* Endogenous and Antipsychotic-Related risks for diabetes mellitus in young people with schizophrenia: a Danish population-based cohort study. *Am J Psychiatry* 2017;174:686–94.
- Guo JJ, Keck PE, Corey-Lisle PK, *et al.* Risk of diabetes mellitus associated with atypical antipsychotic use among patients with bipolar disorder: a retrospective, population-based, case-control study. *J Clin Psychiatry* 2006;67:1055–61.
- Taipale H, Tanskanen A, Mehtälä J, *et al.* 20-Year follow-up study of physical morbidity and mortality in relationship to antipsychotic treatment in a nationwide cohort of 62,250 patients with schizophrenia (FIN20). *World Psychiatry* 2020;19:61–8.
- Ijaz S, Bolea B, Davies S, *et al.* Antipsychotic polypharmacy and metabolic syndrome in schizophrenia: a review of systematic reviews. *BMC Psychiatry* 2018;18:275.
- Fornaro M, De Berardis D, Koshy AS, *et al.* Prevalence and clinical features associated with bipolar disorder polypharmacy: a systematic review. *Neuropsychiatr Dis Treat* 2016;12:719–35.
- Gallego JA, Bonetti J, Zhang J, *et al.* Prevalence and correlates of antipsychotic polypharmacy: a systematic review and meta-regression of global and regional trends from the 1970s to 2009. *Schizophr Res* 2012;138:18–28.
- American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, *et al.* Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care* 2004;27:596–601.
- Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, Cheng AYY. Canadian diabetes association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. Introduction. *Can J Diabetes* 2013;37 Suppl 1:S1–212.
- Mitchell AJ, Delafon V, Vancampfort D, *et al.* 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.
- Lieberman JA, Stroup TS, McEvoy JP, *et al.* Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005;353:1209–23.
- Nasrallah HA, Newcomer JW. Atypical antipsychotics and metabolic dysregulation: evaluating the risk/benefit equation and improving the standard of care. *J Clin Psychopharmacol* 2004;24:S7–14.
- Loebel A, Citrome L. Lurasidone: a novel antipsychotic agent for the treatment of schizophrenia and bipolar depression. *BJPsych Bull* 2015;39:237–41.
- Solmi M, Murru A, Pacchiarotti I, *et al.* Safety, tolerability, and risks associated with first- and second-generation antipsychotics: a state-of-the-art clinical review. *Ther Clin Risk Manag* 2017;13:757–77.
- Dagenais-Beaulé V, Rafizadeh R, Zhou T. Antipsychotics. In: Procyshyn R, Jeffries JJ, eds. *Clinical Handbook of psychotropic drugs*. 24th ed. Boston: Hogrefe, 2021.
- De Berardis D, Rapini G, Olivieri L, *et al.* Safety of antipsychotics for the treatment of schizophrenia: a focus on the adverse effects of clozapine. *Ther Adv Drug Saf* 2018;9:237–56.
- Pillinger T, McCutcheon RA, Vano L, *et al.* Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia,

- predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. *Lancet Psychiatry* 2020;7:64–77.
- 33 Rogroni C, Bertolani A, Jommi C. Second-Generation antipsychotic drugs for patients with schizophrenia: systematic literature review and meta-analysis of metabolic and cardiovascular side effects. *Clin Drug Investig* 2021;41:303–19.
 - 34 Simon V, van Winkel R, De Hert M. Are weight gain and metabolic side effects of atypical antipsychotics dose dependent? A literature review. *J Clin Psychiatry* 2009;70:1041–50.
 - 35 Corena-McLeod M. Comparative pharmacology of risperidone and paliperidone. *Drugs R D* 2015;15:163–74.
 - 36 Hackam DG, Quinn RR, Ravani P, et al. The 2013 Canadian hypertension education program recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. *Can J Cardiol* 2013;29:528–42.
 - 37 Hor ES, Subramaniam S, Koay JM, et al. Improving metabolic monitoring in patients maintained on antipsychotics in Penang, Malaysia. *Australas Psychiatry* 2016;24:67–71.
 - 38 Tibshirani R. Regression shrinkage and selection via the LASSO. *Journal of the Royal Statistical Society* 1996;58:267–88.
 - 39 Friedman J, Hastie T, Tibshirani R. Regularization paths for generalized linear models via coordinate descent. *J Stat Softw* 2010;33:1–22.
 - 40 Ghate SR, Porucznik CA, Said Q, et al. Predictors of metabolic parameter monitoring in adolescents on antipsychotics in a primary care setting. *Ment Health Fam Med* 2012;9:137–48.
 - 41 Shi L, Ascher-Svanum H, Chiang Y-J, et al. 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.
 - 42 Mangurian C, Giwa F, Shumway M, et al. Primary care providers' views on metabolic monitoring of outpatients taking antipsychotic medication. *Psychiatr Serv* 2013;64:597–9.
 - 43 Lee CMY, Huxley RR, Wildman RP, et al. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *J Clin Epidemiol* 2008;61:646–53.
 - 44 Lind M, Tuomilehto J, Uusitupa M, et al. The association between HbA1c, fasting glucose, 1-hour glucose and 2-hour glucose during an oral glucose tolerance test and cardiovascular disease in individuals with elevated risk for diabetes. *PLoS One* 2014;9:e109506.
 - 45 Agyapong VIO, Rogers C, Machale S, et al. Factors predicting adherence with psychiatric follow-up appointments for patients assessed by the liaison psychiatric team in the emergency department. *Int J Psychiatry Med* 2010;40:217–28.
 - 46 Solmi M, Firth J, Miola A, et al. Disparities in cancer screening in people with mental illness across the world versus the general population: prevalence and comparative meta-analysis including 4 717 839 people. *Lancet Psychiatry* 2020;7:52–63.
 - 47 Tatreau JR, Harris S, Sheitman B, et al. Cardiometabolic assessment, diagnosis, and treatment of chronic medical illnesses during an inpatient psychiatric hospitalization: colocated medical care versus treatment as usual. *Prim Care Companion CNS Disord* 2016;18. doi:10.4088/PCC.16m02017. [Epub ahead of print: 22 Dec 2016].
 - 48 Epstein NE. Multidisciplinary in-hospital teams improve patient outcomes: a review. *Surg Neurol Int* 2014;5:S295–303.
 - 49 Brown T, McKenna B, Furness T. Impact of a nurse practitioner role on metabolic monitoring completion and referrals for consumers admitted to the intensive care area of an acute inpatient psychiatric unit. *Int J Ment Health Nurs* 2018;27:341–8.
 - 50 Axtell SS, Ludwig E, Lope-Candales P. Intervention to improve adherence to ACC/AHA recommended adjunctive medications for the management of patients with an acute myocardial infarction. *Clin Cardiol* 2001;24:114–8.
 - 51 Chapman NRM, Fotis MA, Yarnold PR, et al. Pharmacist interventions to improve the management of coronary artery disease. *Am J Health Syst Pharm* 2004;61:2672–8.
 - 52 Bailey TC, Noirot LA, Blickensderfer A, et al. An intervention to improve secondary prevention of coronary heart disease. *Arch Intern Med* 2007;167:586–90.
 - 53 Locke A, Kamo N. Utilizing clinical pharmacists to improve delivery of evidence-based care for depression and anxiety in primary care. *BMJ Qual Improv Rep* 2016;5. doi:10.1136/bmjquality.u211816.w4748. [Epub ahead of print: 08 07 2016].
 - 54 Schneiderhan ME, Batscha CL, Rosen C. Assessment of a point-of-care metabolic risk screening program in outpatients receiving antipsychotic agents. *Pharmacotherapy* 2009;29:975–87.
 - 55 Canadian Pharmacist Association. Pharmacists' expanded scope of practice in Canada 2019, 2019. Available: <https://www.pharmacists.ca/pharmacy-in-canada/scope-of-practice-canada/> [Accessed cited 2019 June 15].
 - 56 Centers for Disease Control and Prevention. Collaborative Practice Agreements and Pharmacists' Patient Care Services - A Resource for Pharmacists Atlanta: US Dept. of Health and Human Services, Centers for Disease Control and Prevention, 2013. Available: https://www.cdc.gov/dhds/pubs/docs/translational_tools_pharmacists.pdf