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Cardio-metabolic risk in individuals prescribed long-acting injectable antipsychotic medication

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ABSTRACT

People living with severe mental illness (SMI) experience significant physical health co-morbidity. Few studies have focused on physical health outcomes for those prescribed long-acting injectable (LAI) antipsychotics. This observational cross-sectional study aimed to assess the prevalence of metabolic syndrome (MetS) and other cardio-metabolic risk factors in a large cohort prescribed LAI and managed by community mental health services. For participants with elevated cardio-metabolic risk factors, the proportion receiving appropriate management was assessed. Of the 301 eligible participants, many met the full criteria for MetS (44%) and its components. Cardio-metabolic risk factors were largely under- or un-treated. Smoking rates were very high (62%) along with reported high rates of physical inactivity and poor dietary intake. The vast majority (89%) reported seeing their general practitioner in the preceding twelve months. Individuals prescribed LAI have a very high prevalence of MetS and potentially modifiable risk factors for cardiovascular disease. Routine monitoring accompanied by evidence-based treatment of cardiometabolic abnormalities which contribute to significant morbidity, disability and premature death should be prioritised. Better collaboration between mental health services and primary care providers should be pursued to optimise the delivery of effective physical health care to individuals living with SMI.

1. Introduction

People experiencing severe mental illness (SMI) are likely to die 12–15 years earlier than the general population, with the primary driver for this premature mortality being cardio-vascular disease (CVD) (Correll et al., 2017; Lawrence et al., 2013). The poor physical health of people with SMI is well recognised, with significantly higher rates of smoking, type 2 diabetes (T2DM), CVD and metabolic syndrome (MetS) (De Hert et al., 2009; Lappin et al., 2018; Rummel-Kluge et al., 2010; Vancampfort et al., 2015b) than their general population peers. MetS is a key measurable predictor for the development of both T2DM and CVD (Lakka et al., 2002). Individuals with MetS have 3–6 times increased risk of mortality due to coronary heart disease and 5–6 times the risk of developing T2DM than people without (Alberti et al., 2009). MetS is identified by the comorbidities of abdominal fat distribution, insulin and lipid irregularities and hypertension (Alberti et al., 2009). There are numerous contributors to these MetS components among people with SMI including disparities in health care provision (Lawrence and Kisely, 2010), positive and negative symptoms associated with SMI, diagnostic overshadowing (Leucht et al., 2007), lifestyle and socio-economic factors (Leucht et al., 2007) and particularly medication that is prescribed to treat SMI such as antipsychotics (Newcomer, 2007).

Long acting injectables (LAI) offer an alternative to oral antipsychotic (AP) medications in the treatment of SMI including schizophrenia. LAI have been argued to have pharmacokinetic benefits compared to oral APs that enable the use of lower doses, and result in greater relapse prevention (Leucht et al., 2011; Spanarello and Ferla, 2014) however evidence of the extent they may impact cardio-metabolic outcomes is limited. A meta-analysis comparing 13 randomised control trials (RCTs) of second-generation LAI and oral APs over a mean timeframe of 39 weeks found no significant differences in weight gain, suggesting that metabolic effects may be independent of the route of administration (Fusar-Poli et al., 2013). Importantly, second-generation LAI were almost three times (RR = 2.75) more likely

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to lead to weight gain than placebo, highlighting that metabolic effects are a crucial issue to consider when prescribing APs (Fusar-Poli et al., 2013). Other metabolic markers, including glucose and lipid levels have been compared in only a small number of studies comparing oral APs to LAI antipsychotic medications, none of which have demonstrated differences according to route of administration in trials of between 24 weeks and two years (Detke et al., 2014; Ishigooka et al., 2015; McDonnell et al., 2011). Important caveats in considering the evidence from meta-analysis of RCTs is that they report on evidence in the early stages of AP treatment, and often exclude individuals with common comorbidities. A more recent cross-sectional analysis found no significant difference in rates of MetS when comparing 151 day clinic patients on oral and LAI APs (Ventriglio et al., 2018) and another small study of 130 outpatients on LAI described the cohorts MetS to be higher when compared to more broad Spanish studies for people with Schizophrenia, Schizoaffective disorders or a severe mental disorder including major depressive disorder (Sanchez-Martinez et al., 2018). To date, to our knowledge, there have been no comprehensive studies of metabolic risk factors associated with LAI treatment in large samples ascertained in routine clinical settings.

Given the chronic poor physical health experienced by people living with SMI, physical health outcomes for those prescribed LAI need to be better understood. The aim of this study was to comprehensively assess the prevalence of MetS and other cardio-metabolic risk factors in a large cohort of individuals with SMI prescribed LAI antipsychotic medication.

2. Method

2.1. Study design and setting

This cross-sectional study was completed across three hospital sites within the South Eastern Sydney Local Health District (SESLHD), Australia, between October 2016 and December 2017. Assessments were provided as part of routine clinical care, and therefore written consent was not obtained. Assessments were conducted either on-site at the hospitals, community centres or at the participant's home. This study was deemed a quality improvement or quality assurance project by the SESLHD Human Research Ethics Committee HREC (17/298 (LNR/17/POWH/580)) and has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

2.2. Participants

Participants were people prescribed LAI and linked with community mental health services across the three hospital sites in SESLHD for the administration of the LAI.

2.3. Outcome measures

Cardiometabolic risk measures were obtained during a face-to-face interview with participants who were also asked to rate their interest in interventions addressing smoking cessation, poor diet, and low physical activity.

2.4. Socio-demographic and treatment details

Participant's socio-demographic and medication details including sex, age, country of birth, psychiatric diagnosis, whether LAI was prescribed under an involuntary community treatment order (CTO), psychotropic medication prescription, and prescription of medication for glucose, lipid and blood pressure dysregulation, were obtained directly from participants or from their medical file. Defined Daily Dose (McClave et al., 2010) (DDD) of all LAI antipsychotic medications administered was calculated according to WHO standardised guidelines (Leucht et al., 2016). Antipsychotics were classified as first– (typical) (FGA) or second- (atypical) (SGA) generation on the basis of dopamine D-1, D-2 and serotonin2 pKi values (Meltzer et al., 1989).

2.5. Anthropometry

Anthropometric data including height, weight, Body Mass Index (BMI), blood pressure and waist circumference was collected using standardised procedures. Participants were weighed without shoes and wearing light clothing on the OMRON HN-283 digital scale to the nearest 0.1 kg. Height was measured with shoes off, using a wall-mounted stadiometer to the nearest 0.1 cm. BMI was calculated as weight (kg)/height $(m)^2$ with participants characterised as normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (30–39.9 kg/m^2) and morbidly obese ($\geq$40 kg/m^2) according to WHO criteria (World Health Organization, 1995). Blood pressure was measured on the left arm in a seated position using an OMRON automatic sphygmomanometer. Waist circumference was measured horizontally at the navel at the end of expiration to the nearest 0.1 cm. Waist circumference was categorised as 'at risk' according to International Diabetes Federation (IDF) criteria for Europids ($\geq$80 cm for females and $\geq$94 cm for males) (Alberti et al., 2006) with ethnic specific values of $\geq$80 cm for Asian women and $\geq$90 cm for Asian men.

2.6. Biochemistry

Metabolic blood measures were obtained via pathology services within 6 months of the interview and included fasting blood glucose, total cholesterol, triglycerides, LDL cholesterol and HDL cholesterol.

2.7. Metabolic syndrome and risk for type 2 diabetes

All participants were screened for the presence of metabolic syndrome using the IDF definition criteria (Alberti et al., 2006):

Central Obesity, defined according to IDF criteria as outlined above.
Plus two of the following four factors:

1 Serum triglycerides $\geq$1.7 mmol/L or receiving drug treatment for this lipid abnormality
2 Serum high-density lipoprotein (HDL) cholesterol $<$1.03 mmol/L in men and $<$1.29 mmol/L in women, or receiving drug treatment for this lipid abnormality
3 Systolic blood pressure $\geq$130 mmHg, diastolic blood pressure $\geq$85 mmHg, or treatment of previously diagnosed hypertension
4 Fasting plasma glucose (FPG) $\geq$5.6 mmol/L or previously diagnosed type 2 diabetes

Risk for Type 2 Diabetes: The AUSDRISK questionnaire is a validated tool for identification of Australian adults at high risk of developing T2DM in the next five years (Chen et al., 2010). Participants had waist measurement recorded and completed nine questions related to demographic characteristics, family history of diabetes, history of high blood sugar, smoking, diet, high blood pressure, physical activity, ethnicity, and Aboriginal and Torres Strait Islander heritage. Scores were categorised as follows:

- *low risk* (5 or less) [approximately one person in every 100 will develop diabetes]
- *intermediate risk* (6–11) [6–8: approximately one person in every 50 will develop diabetes; 9–11: approximately one person in every 30]
- *high risk* (12+) [12–15: approximately one person in every 14 will develop diabetes; 16–19: approximately one person in every 7; 20 and above: approximately one person in every 3]

2.8. Lifestyle components (smoking, physical activity and dietary intake)

Nicotine dependence was measured using the Fagerström Test for

Nicotine Dependence (Heatherton et al., 1991), a 6-item questionnaire. Scores of 1–2 indicate low dependence; 3–4 low to moderate dependence; 5–7 moderate dependence; and 8+ high dependence. Additionally, clients who smoked were asked to rate out of 10 how important quitting smoking was to them (1 being not important at all; 10 being of utmost importance).

Previous seven-day levels of physical activity were assessed using the International Physical Activity Questionnaire – Short Form (IPAQ) (Craig et al., 2003). The IPAQ asks participants in four questions to recall time spent in 10 or more minutes of vigorous and moderate intensity physical activity, time spent walking and time spent sitting. A continuous indicator of physical activity at each intensity was calculated as a sum of weekly minutes per week. The identification of clients achieving the WHO guidelines (World Health Organization, 2010) of 150 min of moderate to vigorous physical activity (MVPA) per week was included as a categorical variable. The IPAQ has demonstrated reliability as a tool to assess levels of physical activity in people with schizophrenia (Faulkner et al., 2006).

Diet quality was assessed through the use of a targeted 10-question, picture-guided, food intake questionnaire specifically developed to evaluate food consumption patterns in people with mental illness. The questionnaire evaluated the frequency of intake of five core and five non-core food categories. Core food categories were fruit, vegetables, wholegrain foods, unsweetened dairy and alternatives and protein foods. Non-core food categories included unhealthy fats, sugary drinks, sweet foods, savoury discretionary foods and alcoholic beverages. Participants were asked to consider average intake over the last month and select from multiple choice responses; (i) less than once per week, (ii) multiple times per week, (iii) once per day, and (iv) multiple times per day.

2.9. Statistical analysis

For normally-distributed variables, means and standard deviations (SD) were calculated whilst medians and ranges were reported for variables with skewed distributions. The Mann-Whitney U (MWU) test was used for bivariate comparison of non-normally distributed variables. Chi-square tests were calculated for bivariate comparison of MetS rates in those with factors hypothesized *a priori* to predict MetS (age >44 years; gender; DDD >1 mg; antipsychotic polypharmacy; antipsychotic type). Variables found to be associated with MetS at a significance level of $p < 0.2$ were included as independent variables in a binary logistic regression analysis, for which odds ratios (OR) and 95% confidence intervals (CI) were calculated. All analyses were conducted using IBM SPSS Statistics v.24.0 (IBM Corporation, 2016).

3. Results

Eligible participants ($n = 517$) were identified from medical records at each of the community health centres. Of these, 301 (57.4%) completed a survey administered by mental health clinicians to elicit the physical health parameters.

3.1. Demographic characteristics

Participants in the survey were mostly male ($n = 197$, 65.4%), with a mean age of 44.4 years (SD ± 12.3 years) (Table 1). Sixty-two percent ($n = 185$) were born in Australia. Ninety-two percent ($n = 277$) had a diagnosis of schizophrenia or schizoaffective disorder and 8% ($n = 23$) bipolar affective disorder. Just over half were currently on a CTO ($n = 156$, 51.8%). The majority received their LAI at the community centre or hospital ($n = 238$, 79.6%) whilst the remainder were administered their LAI during a home visit ($n = 38$, 12.7%) or by a general practitioner (GP) ($n = 23$, 7.7%).

Individuals who did not complete the survey ($n = 216$) had similar demographic and clinical characteristics to those who did complete the survey. There were no significant differences in age ($p = 0.39$), gender ($p = 0.40$) or diagnosis ($p = 0.70$). Proportionately more received their LAI from a GP ($n = 53$, 25.1%) or at a home visit ($n = 31$, 14.7%) ($p < 0.0001$) among non-completers. There was no significant difference in the proportion of individuals on a CTO in both groups ($p = 0.29$).

Table 1
Demographic and cardio-metabolic risk characteristics of the survey participants.

Characteristic	N[a]	%[a]
Male Gender ($n = 301$)	197	65.4
Age ($n = 301$)		
<35 years	70	23.3
35–44 years	87	28.9
45–54 years	77	25.6
55–64 years	49	16.3
65+ years	18	6.0
Country of Birth[b] ($n = 298$)		
Australia	185	62.1
Asia, Middle East, N. Africa, Southern Europe	44	14.8
Other	69	23.2
Diagnosis ($n = 300$)		
Schizophrenia	214	71.3
Schizoaffective disorder	63	21.0
Bipolar affective disorder	23	7.7
Community Treatment Order ($n = 301$)	156	51.8
Injection administration venue ($n = 299$)		
Community clinic/Hospital	238	79.6
Home visit	38	12.7
General Practitioner	23	7.7
Body Mass Index ($n = 273$)		
Underweight (<18.5)	3	1.1
Desired (18.5–24.9)	66	24.2
Overweight (25.0–29.9)	76	27.8
Obese (30.0–39.9)	103	37.7
Morbidly Obese (>40.0)	25	9.2
Smoker ($n = 301$)	187	62.1
Nicotine Dependence ($n = 175$)		
Moderate	78	44.6
High	33	18.9
AUS-D Risk category[c] ($n = 256$)		
Low	22	8.6
Intermediate	68	26.6
High	166	64.8
Physical Activity ($n = 289$)		
Moderate-Vigorous (minutes per week)	0[d]	0–1,970[d]
MVPA of 150 (minutes per week)	31	10.7
Walking (minutes per day)	21[d]	0–420[d]
Sitting (minutes per day)	450[d]	0–1,110[d]
Last visit to General Practitioner ($n = 293$)		
<3 months ago	176	60.1
3–6 months	45	15.4
6–12 months	40	13.7
>12 months ago	32	10.9

[a] unless otherwise stated.
[b] categories as per AUSDrisk.
[c] In those not prescribed treatment for glucose dysregulation.
[d] median (range).

3.2. Treatment prescription and service use

Participants had been prescribed an LAI for a median of 3.0 years with a median DDD of 1.0 mg. Most LAI prescribed were SGAs (59.8%) and a large proportion (36.2%) of participants were prescribed one or more additional oral antipsychotic medications. This antipsychotic polypharmacy comprised either a combination of SGAs (52.3%) or a combination of FGA and SGAs (47.7%). More than a quarter ($n = 81$, 26.9%) were additionally prescribed a mood stabiliser and/or an antidepressant. The majority ($n = 176$, 60.1%) reported seeing their GP within the prior three months and 89% ($n = 261$) within the prior twelve months.

3.3. Cardio-metabolic risk factors

The mean waist circumference was 105 ± 17 cm for males and 102 ± 19 cm for females with 79.6% (n = 230) meeting the at-risk criteria for cardio-metabolic complications based on their gender and ethnicity. Mean BMI of participants was 30.3 (SD ± 7.9). Seventy-five percent (n = 204) were overweight/obese whilst 9% (n = 25) were morbidly obese. Of those not on medication for T2DM, 64.8% (n = 166) were at a high risk of T2DM within the next five years and 26.5% (n = 68) were at an intermediate risk according to the AUSDRISK tool.

Participants reported high rates of smoking (62.1%), with moderate to high nicotine dependence reported among 63.5% of smokers. Only 10.7% (n = 31) undertook 150 min or more moderate to vigorous physical activity (MVPA) weekly and median reported time spent walking was 21 (range = 0–420) minutes per day. Seventy-four percent (n = 213) reported sitting for a minimum of 6 h per day with a median of 7.5 h daily sedentary behaviour. Fruit, vegetables and wholegrains were not consumed on a daily basis by the majority of participants - 61.9% (n = 172), 60.0% (n = 167) and 57.4% (n = 158) respectively. Forty-three percent (n = 117) reported at least daily intake of sugary drinks such as soft drinks and 33.5% (n = 92) reported consuming sweet or savoury discretionary foods at least once per day. Less than 6% (n = 15) of participants reported alcohol consumption at least once per day.

Only a minority had received physical activity (n = 36, 12.6%), dietetic or weight management (n = 33, 11.4%) support in the prior 12 months while 44.4% (122) indicated they were interested in taking part in a lifestyle intervention, and an additional 13.5% (n = 37) indicated potential interest. Most of those who smoked were interested in quitting smoking (n = 99, 66.9%).

3.4. Metabolic syndrome prevalence

Sufficient data to determine MetS were available for 198 participants, of whom 43.7% (n = 86) met IDF criteria (Table 2). In reference to the specific criteria, a large majority (79.6%) met the criteria for waist circumference, while 48.0% (n = 131) of participants met criteria for blood pressure; 40.5% (n = 70) met criteria for triglycerides; 29.7% (n = 43) for HDL; and 31.7% (n = 46) for fasting blood glucose. The majority of those with at-risk levels of elevated triglycerides (58/70) received no treatment for this. Of those prescribed medication for lipid dysregulation (n = 24), 50% (n = 12) continued to have at-risk levels of triglycerides, suggesting treatment was sub-optimal. Likewise, for those with at-risk level fasting blood glucose, most (35/46) received no treatment for this, and of those on treatment 52.4% (n = 11) continued to have at-risk levels.

3.5. Variables associated with metabolic syndrome

Variables entered into a logistic regression analysis were (Table 3): age >44years (χ^2 = 6.42, p = 0.01), DDD >1 mg (χ^2 = 2.15, p = 0.14), first or second generation LAI antipsychotic (χ^2 = 2.67, p = 0.10), antipsychotic polypharmacy (χ^2 = 1.71, p = 0.19) and prescription of a mood stabiliser and/or antidepressant (χ^2 = 3.90, p = 0.05). Only greater age was found to be a significant predictor of MetS (Exp(B) = 2.04, 95%CI 1.12–3.71, p = 0.02).

4. Discussion

Metabolic syndrome and multiple cardio-metabolic risk factors, including smoking, poor diet and a predominantly sedentary lifestyle, were highly prevalent in this large cohort of community-based individuals' prescribed LAI antipsychotic medications. These findings are deeply concerning: the physical health of people with SMI in the care of mental health services is very poor and predisposes them to premature death. Only a minority of individuals received treatment for identified

Table 2
Treatments prescribed and proportion of the population meeting metabolic syndrome criteria.

Characteristic	Median	Range
Duration of treatment on LAI (years) (n = 181)	3.0	0–36
Defined daily dose LAI (mg) (n = 301)	1.0	0.2–2.9
	n	**%**
Class of LAI antipsychotic (n = 301)		
First-generation (FGA)	121	40.2
Second-generation (SGA)	180	59.8
Antipsychotic polypharmacy (n = 301)		
LAI only	192	63.8
One or more additional antipsychotics to LAI	109	36.2
Polypharmacy: antipsychotic type (n = 109)		
First-generation (FGA)	0	0
Second-generation (SGA)	57	52.3
FGA and SGA	52	47.7
On Antidepressant and/or Mood Stabiliser (n = 301)	81	26.9
Antidepressant	29	9.6
Mood Stabiliser	56	18.6
Benzodiazepine (n = 301)	22	7.3
Medication for lipid dysregulation (n = 301)	29	9.6
Statin	28	9.3
Medication other than/additional to statin	3	1.0
Antihypertensive medication (n = 301)	17	5.6
Medication for glucose dysregulation (n = 301)	39	12.9
Metformin	39	12.9
Medication other than/additional to metformin	11	3.6
Meet metabolic syndrome IDF diagnostic criteria (n = 198)	86	43.7
Under 35 years	16	30.2
35 – 44 years	27	43.5
45 −54 years	21	43.8
55 – 64 years	14	60.9
Over 65 years	8	72.7
Waist Circumference at or above metabolic syndrome risk level (n = 289)	230	79.6
Blood Pressure at metabolic syndrome risk level (n = 273)	131	48.0
High diastolic	29	10.6
High systolic	28	10.3
High systolic and diastolic	67	24.5
Normotensive and on antihypertensive treatment	7	2.6
Triglyceride level at metabolic syndrome risk level (n = 173)	70	40.5
In those not prescribed treatment for lipid dysregulation (n = 149)	58	38.9
In those prescribed treatment for lipid dysregulation (n = 24)	12	50.0
HDL level at metabolic syndrome risk level (n = 145)	43	29.7
In those not prescribed treatment for lipid dysregulation (n = 131)	37	28.2
In those prescribed treatment for lipid dysregulation (n = 14)	6	42.9
Blood glucose at metabolic syndrome risk level (n = 145)	46	31.7
In those not prescribed treatment for glucose dysregulation (n = 124)	35	28.2
In those prescribed treatment for glucose dysregulation (n = 21)	11	52.4

Table 3
Logistic regression model of metabolic syndrome on a priori variables of interest.

Independent variable	Odds ratio 95% ± CI[a]	P
Age > 44 years	2.04 (1.12–3.71)	**0.02**
DDD[b] > 1mg	1.59 (0.87–2.91)	0.13
LAI antipsychotic generation	1.42 (0.77–2.60)	0.26
Antipsychotic polypharmacy	0.65 (0.35–1.20)	0.17
Mood stabiliser and/or antidepressant prescription	1.62 (0.85–3.09)	0.14

Bold indicates significance at $P < 0.05$.

[a] Odds ratios and 95% Confidence Intervals for each variable as an independent predictor of metabolic syndrome.

[b] Defined daily dose.

metabolic risk factors despite the majority having been seen by the mental health service and/or their GP in the prior three months. Finally, metabolic outcomes were equally poor among individuals prescribed first- or second-generation LAI, consistent with previous evidence comparing metabolic side effects of oral typical and atypical APs (Falissard et al., 2011).

4.1. Metabolic syndrome, smoking and polypharmacy

Metabolic syndrome was present in 44% of those who had sufficient measures to determine this, a rate almost double that of the general population (Cameron et al., 2007). A recent prevalence study conducted in Spain of 130 outpatients prescribed LAI found that 46% of the sample met the criteria for MetS (Sanchez-Martinez et al., 2018). These high rates are comparable to those observed in individuals with SMI prescribed clozapine (Lappin et al., 2018) and in other SMI populations (Galletly et al., 2012; Vancampfort et al., 2015a). Individuals younger than 35 years were approximately 2.5 times more likely to have MetS than their age matched peers, as suggested by prevalence estimates in the general population (Cameron et al., 2007). This is consistent with findings (Foley et al., 2013) that at-risk thresholds for cardio-metabolic disease are met very early in people with psychosis, again highlighting the need for early screening and intervention to prevent the onset and progression of CVD. A previous study comparing oral and LAI APs found AP dose and "high risk" AP to be factors preliminarily associated with MetS (Ventriglio et al., 2018) however, aside from older age (>44years), results did not indicate any other significant predictors for MetS. Recent evidence among people with SMI shows that those with MetS are three times more likely to relapse within one year independently of potential cofounders (Godin et al., 2018) indicating the impact on both physical and mental health outcomes of untreated metabolic issues.

Over 60% of participants smoked, in line with many previous studies showing the very high rates of smoking in SMI populations (Cooper et al., 2012; Curtis et al., 2018; Galletly et al., 2012). Polypharmacy was very common in the sample (36.2%), falling within prevalence rates that vary between 10% and 50% internationally (Correll et al., 2008) and comparable to rates within Australians with psychosis (Morgan et al., 2012). Many international guidelines (APA(Lehman et al., 2004), NICE(National Institute for Health and Care Excellence, 2014)), though not all (RANZCP(Galletly et al., 2016)), do not recommend simultaneous prescription of more than one antipsychotic due to insufficient evidence to suggest it safely provides superior treatment outcomes (Correll et al., 2008). In addition, and of crucial importance, is the unknown impact polypharmacy has on metabolic outcomes (Ijaz et al., 2018).

Physical inactivity (both low MVPA and high sedentary behaviour) and a poor diet, characteristic of a high intake of energy dense, nutrient poor processed foods, displacing core nutritious foods, were common in this population. Both are modifiable risk factors for cardio-metabolic risk, and should be key targets for the prevention and management of MetS, CVD and T2DM in people with SMI prescribed antipsychotic medication (Teasdale et al., 2017).

4.2. Metabolic monitoring and treatment

International (American Diabetes Association, 2004; De Hert et al., 2011; Shiers et al., 2014) and Australian (Curtis et al., 2012; Galletly et al., 2016) guidelines recommend routine monitoring for metabolic dysfunction for individuals prescribed APs with schizophrenia and SMI more broadly. Monitoring of waist circumference in this sample was completed for all patients as part of a lifestyle intervention, the Keeping Body in Mind program (Curtis et al., 2016), which is offered to them as part of routine clinical care. Less than half of individuals, however, had pathology blood tests conducted by the mental health service in the prior 12 months, reflecting both a failure of clinicians to request testing and difficulties in completing testing by individuals experiencing SMI. Given the high GP attendance rates (90% within prior 12 months) it is possible that participants may have had pathology tests performed by the GP but these results were unavailable to the mental health service and therefore this study. Those who refused or did not participate in blood testing may have other markers making MetS more likely (e.g. less engagement with health services or poor health literacy) which could mean the study underestimated the true prevalence of MetS.

Among those with comprehensive metabolic monitoring completed, only a minority received any treatment for those metabolic abnormalities that were identified. Less than 15% of those with glucose levels raised to MetS at-risk levels received any treatment. Of those who received glucose regulation treatment (predominantly metformin), over half were inadequately treated as evidenced by glucose levels which remained above the at-risk threshold. Many (39%) of those with at-risk levels of triglycerides were on no prescribed treatment and 50% of those on medication met at-risk thresholds even with the prescription of relevant medication. Similar deficiencies in treatment were found for irregularities in lipid profile and hypertension. Previous studies have found similarly common under-treatment for each of these metabolic abnormalities (Galletly et al., 2012). For the physical healthcare of individuals with SMI to be prioritised it is imperative to move beyond monitoring to provide evidence-based interventions.

Over 60% of clients had been in contact with their GP in the three months prior to this cross-sectional assessment and 90% had contact within the prior 12 months which is similar to attendance rates reported in national samples (Morgan et al., 2012) which also found that 76% of GP visits were related to physical health. It is possible that those receiving LAIs from their GP may have physical health issues addressed more frequently and diligently. As this cohort under represents clients that receive LAI from their GP, future studies could explore this idea. Regardless, multiple factors are likely to contribute to the finding of under-treatment of identified metabolic abnormalities, just as it has been identified that multiple explanations contribute to the persistently high rates of smoking among people with SMI. For example, evidence shows that people with SMI are less successful in their quit attempts (despite having comparable motivation to quit as smokers without mental health issues) (McClave et al., 2010). This under-treatment may be linked to cognitive deficits, self-efficacy and wider support networks: the same issues are likely to be relevant to the ability of people with SMI to seek, accept and or follow through on advice offered to improve their physical health, including but not limited to adherence to pharmacological treatments for metabolic irregularities. Despite the significant challenges, there is good evidence that people with SMI can make valuable improvements to their physical health through the uptake of lifestyle improvements such as increased physical activity and a balanced diet (Daumit et al., 2013; Deenik et al., 2018).

There is longstanding debate about where responsibility for the care of physical health conditions in people with SMI should lie. Lester (2006) argued that a collaborative approach is needed if there is to be adequate development of high-quality healthcare for individuals with SMI (Lester and Gask, 2006). Suboptimal communication between primary care and mental health services is likely to contribute to insufficient treatment and management of metabolic dysfunction (Morgan et al., 2012). A large Australian study of recipients of rehabilitation services found that despite high rates of metabolic monitoring being completed there was inadequate sharing of results, and their implications, with recipients and/or with their primary health care provider (Benson et al., 2018). The frequent attendance with both primary health care and mental health services as identified in this cohort present valuable opportunities for regular review and treatment of physical health issues holistically. LAI in particular provide this opportunity for physical health monitoring and treatment as they are administered at regular intervals in a clinical setting, whether in primary care or a mental health service.

4.3. Limitations

A number of limitations need to be considered in this study. First, being a cross-sectional study it is limited to an assessment at a point in time, and so temporal effects cannot be observed. Second, 41.7% of eligible participants did not complete the survey. While their demographic characteristics did not significantly differ, those receiving their LAI via GP or Home Visit were under-represented. Third, while much data was collected in face-to-face interview, where this was not possible electronic medical records were reviewed, which may not always have been complete. Lastly, data on physical activity, diet and smoking status were assessed by self-report and may not be wholly reliable. In addition, the dietary questionnaire employed has not been validated in people with mental illness. Nonetheless, the measures employed have all been used previously in populations with SMI.

4.4. Conclusions

Individuals living with SMI treated on LAI have very high prevalence of MetS and potentially modifiable risk factors for CVD. Prevalence was equally high among those treated with typical and atypical APs, highlighting the need for diligent monitoring but also treatment of these abnormalities which contribute to significant morbidity, disability and premature death. Cardiometabolic risk for individuals prescribed antipsychotic LAIs is comparable to the wider cohort of people living with SMI. Better collaboration between mental health services and primary care should be pursued in order to optimise the delivery of effective care to individuals with SMI.

Contributors

J.Curtis, A.Watkins and S.Teasdale were responsible for the study concept and design. J.Poole, H.Fibbins, E.Rossimel, M.Gerrard and A.White were responsible for data collection. R. Morell was responsible for data extraction. R.Morell, S.Teasdale, A.Watkins, P.B.Ward and J.Lappin were responsible for statistical analysis. R.Morell, P.B.Ward and J.Lappin were responsible for drafting the manuscript. All other authors were responsible for critical revision of the manuscript and have accepted the final version.

Declaration of Competing Interest

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