Physical health monitoring for people with schizophrenia

SUMMARY

Schizophrenia is a severe psychiatric disorder associated with significant comorbidities and early mortality.

People with schizophrenia have a greater predisposition to the top 6 modifiable global mortality (cardiometabolic) risk factors as defined by the World Health Organization (compared with the general population). These are driven by genetic, lifestyle and disease factors, and obesogenic antipsychotic medications.

Smoking, obesity and type 2 diabetes are the most important modifiable cardiometabolic risk factors for cardiovascular disease in people with schizophrenia.

Enhanced physical health screening, especially for cardiometabolic risk factors, is recommended for people with schizophrenia.

A multidisciplinary holistic approach is recommended for treating people with schizophrenia, using contact with primary care practitioners to review their physical health.

Introduction

Schizophrenia is a severe and complex psychiatric disorder that significantly impacts an individual's biological, psychological and social functioning, and overall wellbeing. Schizophrenia is characterised by positive symptoms (e.g. delusions, hallucinations) and negative symptoms (e.g. social withdrawal, negative affect, reduced speech).

Despite improvements in treatment options for psychosis, people with schizophrenia still face excess morbidity and mortality compared with the general population because of their vulnerability to multiple physical health conditions. This highlights the importance of close physical health monitoring by their primary care practitioners, to improve health outcomes and increase their life expectancy; however, physical health monitoring for patients with schizophrenia can be challenging because of the nature of the illness and its social impacts.

Comorbidity and mortality

People with schizophrenia have reduced life expectancy compared to the general population (18.7 years shorter in men, 16.3 years shorter in women).1 This is largely attributable to physical conditions (e.g. cardiovascular disease [CVD], respiratory disease, cancer) rather than external causes (e.g. suicide, accidents).2

Several factors contribute to the prevalence of comorbidities in people with schizophrenia. First, they have a greater predisposition to the top 6 modifiable global mortality (cardiometabolic) risk factors as defined by the World Health Organization (in order): hypertension, smoking, hyperglycaemia, physical inactivity, obesity and dyslipidaemia.3,4 Second, use of certain antipsychotics predisposes them to metabolic syndrome (defined as 3 or more of: hypertension, hyperglycaemia, abdominal obesity, hypertriglyceridaemia and low high-density lipoprotein cholesterol [HDL-C] concentration).5

Cardiometabolic risk factors

People with schizophrenia have a higher risk of CVD than the general population and CVD is the leading cause of death in this group.² Over half (54.8%) of Australians with a psychotic disorder meet the criteria for metabolic syndrome and approximately one-quarter (24%) already have CVD or are at high risk of CVD.6 This increased risk is addressed in the 2023 Australian guideline and calculator for assessing and managing cardiovascular disease risk; for people living with severe mental illness, consider reclassifying their estimated CVD risk to a higher risk category, particularly if their estimated risk is close to a higher risk threshold.7

Tobacco smoking

Despite increasing health promotion around smoking cessation, approximately two-thirds of people with schizophrenia still smoke (compared with approximately 11% of the general population). 6,8 There is a complex relationship between tobacco use and

David Castle 📵



Professor of Psychiatry¹

Amy Li 🕕

Medical student²

¹University of Tasmania. Hobart

² Monash University, Clayton, Victoria

Keywords

antipsychotics, cardiometabolic risk, hyperprolactinaemia, metabolic syndrome obesity, schizophrenia

Aust Prescr 2023;46:75-9 https://doi.org/10.18773/ austprescr.2023.024

Physical health monitoring for people with schizophrenia

schizophrenia; some studies have correlated continual tobacco use with subsequent onset of schizophrenia.⁹ Some hypotheses regard smoking as a form of self-medication helping people alleviate cognitive and negative symptoms of schizophrenia.⁹

Primary care practitioners are ideally placed to screen for smoking and arrange appropriate treatment; however, studies have shown lower rates of screening in primary care for tobacco use in people with schizophrenia than in the general population.¹⁰

Guidelines for the management of smoking cessation in patients with schizophrenia are similar to those for the general population; however, a specific 'Quitline' intervention for people with mental illness may be more effective than the usual Quitline resources.¹¹ The requirements for nicotine replacement are often higher in this population because they tend to be heavier smokers. Bupropion and varenicline may have adverse mental health effects in the short term and careful monitoring is required in people with schizophrenia.¹²⁻¹⁴ Smoking cessation is associated with decreased metabolism, and thus increased serum concentrations, of certain antipsychotics, notably clozapine and olanzapine.¹² Dose adjustment may be required.

Obesity

Multiple factors contribute to the development of obesity in people with schizophrenia, including:

- negative symptoms (e.g. amotivation, reduced self-care)
- obesogenic antipsychotic medication (e.g. clozapine, olanzapine)
- sedentary lifestyle
- · dietary choices.

Approximately three-quarters of people with schizophrenia are classified as overweight or obese. ^{6,15} Certain antipsychotics play a significant role in the development of obesity in this group. Clozapine and olanzapine have been shown to cause the largest weight gains from baseline in patients starting antipsychotics. ^{16,17}

While antipsychotic choice usually is made by the treating psychiatrist together with the patient, the primary care practitioner can promote treatment adherence and emphasise the importance of healthy lifestyle habits.

Type 2 diabetes, hypertension and dyslipidaemia

Type 2 diabetes is often the key cardiometabolic risk factor for people with schizophrenia. They may have a genetic predisposition to diabetes¹⁸ with the risk of type 2 diabetes 2 to 5 times higher than in the general population. The prevalence of type 2

diabetes in people with schizophrenia has been reported between 1.3 and 50%, depending on age and screening method;¹⁹ however, patient awareness of their diagnosis of diabetes is low.¹⁵

Optimising glycaemic management can significantly improve patient outcomes but can be difficult.²⁰

Certain antipsychotics (notably olanzapine and clozapine) have been linked to insulin resistance and dysregulated glucose metabolism.²¹ Additionally, studies suggest high insulin concentrations and low leptin concentrations are often present in the early stages of psychosis, even before antipsychotic treatment has started.²²

There is a high prevalence of hypertension (48.8%) and dyslipidaemia (49.7%) in people with schizophrenia;⁶ however, patient awareness of their diagnoses is low, which suggests screening for cardiometabolic risk factors may be insufficient.¹⁵

People with schizophrenia reportedly have lower adherence to cardiovascular medication compared with the general population. One study reported a 0.37-fold decrease in antihypertensive use, and a 0.47-fold decrease in lipid-lowering drug use, among people with schizophrenia compared with the general population.²³ This suggests that only half of people with schizophrenia and known hypertension or dyslipidaemia are receiving treatment for these manageable conditions.¹⁵

Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is an underrecognised and significant comorbidity in people with schizophrenia.²⁴ OSA presents with various features, including excessive daytime sleepiness, hypertension, snoring, and cognitive deficits (e.g. attention and memory dysfunction).^{25,26} People with schizophrenia commonly have OSA risk factors, such as obesity, smoking and use of sedatives (including alcohol).²⁶⁻²⁸

OSA symptoms may be misidentified as negative symptoms of schizophrenia or antipsychotic adverse effects. People with suspected OSA should have a home-based sleep study or be referred to a sleep physician, to investigate if nocturnal continuous positive airway pressure (CPAP) or other therapy may be of benefit.

A small 2019 pilot study on nocturnal CPAP for OSA in schizophrenia showed improved sleep and blood pressure, and some weight loss over a 6-month period.²⁹

Hyperprolactinaemia

<u>Hyperprolactinaemia</u> is a well-recognised adverse effect of some antipsychotics (e.g. risperidone, paliperidone, amisulpride). Approximately 2 in 5 people

on antipsychotics have high prolactin concentrations, with females more adversely affected than males.²⁶

Antipsychotic-induced hyperprolactinaemia can manifest with galactorrhoea, sexual dysfunction, osteoporosis and amenorrhea. Despite its prevalence, hyperprolactinaemia is under-diagnosed, perhaps because people are embarrassed to discuss their symptoms.

The Royal Australian and New Zealand College of Psychiatrists (RANZCP) clinical practice guidelines for the management of schizophrenia and related disorders recommend assessing prolactin concentration and switching to a prolactin-sparing antipsychotic if necessary, in conjunction with specialist psychiatric and endocrinology input.²⁶

Osteoporosis and low bone mineral density

Osteoporosis and low bone mineral density are significantly associated with schizophrenia, and antipsychotic-induced hyperprolactinaemia. 32,33 Preventive strategies are recommended to reduce the risk of fractures.

Optimising monitoring

Primary care practitioners are well placed to monitor physical health for people with schizophrenia. General recommendations for long-term monitoring of physical health in people with schizophrenia are listed in Table 1.³⁴ Some basic preventive strategies for common comorbidities in people with schizophrenia are listed in Table 2.³⁵

Optimising monitoring in clinical practice could include:

- ensuring lifestyle risk factors (e.g. smoking) are identified and appropriate management options are explained to the patient
- empowering patients to monitor their own physical health
- providing patients with a record of their test results
- organising regular review appointments (e.g. every 6 months or annually).

Recommendations for preventive health measures (e.g. vaccinations, dental examination) and screening for the general population (e.g. cancer screening) also apply to people with schizophrenia, but these are less frequently undertaken.^{36,37}

The RANZCP clinical practice guidelines for the management of schizophrenia and related disorders emphasises long-term monitoring of physical health for people with schizophrenia. ²⁶ The RANZCP has produced free downloadable patient education material to support self-management of general physical health.

Table 1 Suggestions for long-term monitoring of physical health in people with schizophrenia

Monitoring parameter	Frequency
blood pressure and heart rate	every 6 months
fasting blood glucose concentration and glycated haemoglobin (HbA1c)	every 6 months
fasting lipid concentrations	every 6 months
weight, waist circumference and body mass index	every 6 months
extrapyramidal effects	every 6 months
electrocardiogram (ECG)	annually, or more frequently if prolonged QT interval is present
full blood count	annually
prolactin concentration	annually, or more frequently if on an antipsychotic known to increase prolactin concentration
sexual and reproductive problems	annually

Adapted from reference 34

Table 2 Preventive strategies for common comorbidities in people with schizophrenia

Comorbidity	Preventive strategies
cardiometabolic disease	smoking cessation healthy diet regular physical activity reduction of alcohol consumption maintenance of healthy body weight
osteoporosis and fractures	falls-prevention strategies (e.g. walking aids) exercise and balance training adequate calcium intake maintenance of vitamin D sufficiency smoking cessation reduction of alcohol consumption maintenance of healthy body weight
poor oral and dental health	maintenance of oral hygiene annual dental review
respiratory conditions	smoking cessation
sleep disorders	good sleep hygiene formal sleep assessment
depression and anxiety	psychosocial interventions to decrease isolation monitoring for substance use
problem use of alcohol, cannabis and other substances	monitoring for substance use discussion about impacts of substance use on medications, relapse of schizophrenia symptoms, self-harm, social situation

Adapted from reference 35

Physical health monitoring for people with schizophrenia

Conclusion

People with schizophrenia usually have similar interest as the general population in wanting to make healthier lifestyle choices but may not have the means or motivation to do so. Support provided by primary care practitioners is critical to significantly improve health outcomes for this particularly at-risk group.²³ ◀

Conflicts of interest: David Castle has received grants for research on schizophrenia and antipsychotics from the National Health and Medical Research Council, Medical Research Future Fund, Barbara Dicker Foundation,
Canadian Institute for Health Information, Brain Canada,
Servier and Boehringer Ingelheim. He has also received
travel support and honoraria for presentations and
consultancy from Servier, Seqirus, Lundbeck, Mindcafe,
Psychscene and Inside Practice. He was a co-author of the
Royal Australian and New Zealand College of Psychiatrists
clinical practice guidelines for the management of
schizophrenia and related disorders (2016), and an
author on Being Equally Well (2021). He founded the
Optimal Health Program and holds 50% of its intellectual
property, and is a part owner (5%) of Clarity Healthcare.

REFERENCES

- Laursen TM. Life expectancy among persons with schizophrenia or bipolar affective disorder. Schizophr Res 2011;131:101-4. https://doi.org/10.1016/j.schres.2011.06.008
- Roberts R. The physical health of people living with a mental illness: A narrative literature review. Equally Well; 2019. https://www.equallywell.org.au/media/ [cited 2023 Oct 6]
- Wildgust HJ, Beary M. Are there modifiable risk factors which will reduce the excess mortality in schizophrenia? J Psychopharmacol 2010;24:37-50. https://doi.org/10.1177/ 1359786810384639
- World Health Organization. Global health risks: mortality and burden of disease attributable to selected major risks. Geneva; 2009. https://www.who.int/publications/i/ item/9789241563871 [cited 2023 Oct 6]
- Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640-5. https://doi.org/10.1161/CIRCULATIONAHA.109.192644
- Morgan VA, Waterreus A, Jablensky A, Mackinnon A, McGrath JJ, Carr V, et al. People living with psychotic illness in 2010: the second Australian national survey of psychosis. Aust N Z J Psychiatry 2012;46:735-52. https://doi.org/ 10.1177/0004867412449877
- Commonwealth of Australia. Australian guideline and calculator for assessing and managing cardiovascular disease risk. Department of Health and Aged Care; 2023. https://www.cvdcheck.org.au/ [cited 2023 Oct 6]
- Dickerson F, Schroeder J, Katsafanas E, Khushalani S, Origoni AE, Savage C, et al. Cigarette Smoking by Patients With Serious Mental Illness, 1999-2016: An Increasing Disparity. Psychiatr Serv 2018;69:147-53. https://doi.org/ 10.1176/appi.ps.201700118
- Sagud M, Mihaljevic Peles A, Pivac N. Smoking in schizophrenia: recent findings about an old problem. Curr Opin Psychiatry 2019;32:402-8. https://doi.org/10.1097/ YCO.0000000000000529
- Castillo-Sanchez M, Fabregas-Escurriola M, Berge-Baquero D, Fernandez-SanMartin M, Goday-Arno A. Screening of cardiovascular risk factors in patients with schizophrenia and patients treated with antipsychotic drugs: are we equally exhaustive as with the general population? Clin Exp Hypertens 2017;39:441-7. https://doi.org/10.1080/ 10641963.2016.1267200
- Baker AL, McCarter K, Turner A, Segan C, Castle D, Brophy L, et al. 'Quitlink': Outcomes of a randomised controlled trial of peer researcher facilitated referral to a tailored quitline tobacco treatment for people receiving mental health services. Aust N Z J Psychiatry 2023:48674231181039. https://doi.org/10.1177/00048674231181039
- Mendelsohn CP, Kirby DP, Castle DJ. Smoking and mental illness. An update for psychiatrists. Australas Psychiatry 2015;23:37-43. https://doi.org/10.1177/1039856214562076

- Varenicline for smoking cessation and nicotine dependence.
 In: Therapeutic Guidlines. Melbourne: Therapeutic Guidelines Limited; 2023. https://www.tg.org.au [cited 2023 Oct 6]
- Bupropion for smoking cessation and nicotine dependence.
 In: Therapeutic Guidlines. Melbourne: Therapeutic Guidelines Limited; 2023. https://www.tg.org.au [cited 2023 Oct 6]
- Galletly CA, Foley DL, Waterreus A, Watts GF, Castle DJ, McGrath JJ, et al. Cardiometabolic risk factors in people with psychotic disorders: the second Australian national survey of psychosis. Aust N Z J Psychiatry 2012;46:753-61. https://doi.org/10.1177/0004867412453089
- Kahn RS, Fleischhacker WW, Boter H, Davidson M, Vergouwe Y, Keet IP, et al. Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial. Lancet 2008;371:1085-97. https://doi.org/10.1016/S0140-6736(08)60486-9
- Parsons B, Allison DB, Loebel A, Williams K, Giller E, Romano S, et al. Weight effects associated with antipsychotics: a comprehensive database analysis. Schizophr Res 2009;110:103-10. https://doi.org/10.1016/ j.schres.2008.09.025
- Rouillon F, Sorbara F. Schizophrenia and diabetes: epidemiological data. Eur Psychiatry 2005;20 Suppl 4:S345-8. https://doi.org/10.1016/s0924-9338(05)80189-0
- Ward M, Druss B. The epidemiology of diabetes in psychotic disorders. Lancet Psychiatry 2015;2:431-51. https://doi.org/ 10.1016/S2215-0366(15)00007-3
- Annamalai A, Tek C. An overview of diabetes management in schizophrenia patients: office based strategies for primary care practitioners and endocrinologists. Int J Endocrinol 2015;2015:969182. https://doi.org/10.1155/2015/969182
- Suvisaari J, Keinanen J, Eskelinen S, Mantere O. Diabetes and Schizophrenia. Curr Diab Rep 2016;16:16. https://doi.org/ 10.1007/s11892-015-0704-4
- Mizuki Y, Sakamoto S, Okahisa Y, Yada Y, Hashimoto N, Takaki M, et al. Mechanisms Underlying the Comorbidity of Schizophrenia and Type 2 Diabetes Mellitus. Int J Neuropsychopharmacol 2021;24:367-82. https://doi.org/10.1093/ijnp/pyaa097
- Lahti M, Tiihonen J, Wildgust H, Beary M, Hodgson R, Kajantie E, et al. Cardiovascular morbidity, mortality and pharmacotherapy in patients with schizophrenia. Psychol Med 2012;42:2275-85. https://doi.org/10.1017/ S0033291712000396
- Stubbs B, Vancampfort D, Veronese N, Solmi M, Gaughran F, Manu P, et al. The prevalence and predictors of obstructive sleep apnea in major depressive disorder, bipolar disorder and schizophrenia: A systematic review and meta-analysis. J Affect Disord 2016;197:259-67. https://doi.org/10.1016/ j.jad.2016.02.060
- Malhotra A, White DP. Obstructive sleep apnoea. Lancet 2002;360:237-45. https://doi.org/10.1016/ S0140-6736(02)09464-3
- Galletly C, Castle D, Dark F, Humberstone V, Jablensky A, Killackey E, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. Aust N Z J Psychiatry 2016;50:410-72. https://doi.org/10.1177/ 0004867416641195

- Kalucy MJ, Grunstein R, Lambert T, Glozier N. Obstructive sleep apnoea and schizophrenia – a research agenda. Sleep Med Rev 2013;17:357-65. https://doi.org/10.1016/ j.smrv.2012.10.003
- Al Lawati NM, Patel SR, Ayas NT. Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. Prog Cardiovasc Dis 2009;51:285-93. https://doi.org/10.1016/j.pcad.2008.08.001
- Myles H, Myles N, Coetzer CLC, Adams R, Chandratilleke M, Liu D, et al. Cognition in schizophrenia improves with treatment of severe obstructive sleep apnoea: A pilot study. Schizophr Res Cogn 2019;15:14-20. https://doi.org/10.1016/ j.scog.2018.09.001
- Kelly DL, Wehring HJ, Earl AK, Sullivan KM, Dickerson FB, Feldman S, et al. Treating symptomatic hyperprolactinemia in women with schizophrenia: presentation of the ongoing DAAMSEL clinical trial (Dopamine partial Agonist, Aripiprazole, for the Management of Symptomatic ELevated prolactin). BMC Psychiatry 2013;13:214. https://doi.org/10.1186/1471-244X-13-214
- Byerly M, Suppes T, Tran QV, Baker RA. Clinical implications of antipsychotic-induced hyperprolactinemia in patients with schizophrenia spectrum or bipolar spectrum disorders: recent developments and current perspectives. J Clin Psychopharmacol 2007;27:639-61. https://doi.org/ 10.1097/jcp.0b013e31815ac4e5

- Kishimoto T, De Hert M, Carlson HE, Manu P, Correll CU. Osteoporosis and fracture risk in people with schizophrenia. Curr Opin Psychiatry 2012;25:415-29. https://doi.org/10.1097/ YCO.0b013e328355e1ac
- Yokoyama S, Wakamoto S, Tanaka Y, Nakagawa C, Hosomi K, Takada M. Association Between Antipsychotics and Osteoporosis Based on Real-World Data. Ann Pharmacother 2020;54:988-95. https://doi.org/10.1177/1060028020913974
- 34. Antipsychotic adverse effects. In: Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; 2021. Updated August 2022. https://www.tg.org.au [cited 2023 Sep 20]
- Principles of treating psychoses including schizophrenia. In: Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; 2021. https://www.tg.org.au [cited 2023 Sep 20]
- Lord O, Malone D, Mitchell AJ. Receipt of preventive medical care and medical screening for patients with mental illness: a comparative analysis. Gen Hosp Psychiatry 2010;32:519-43. https://doi.org/10.1016/j.genhosppsych.2010.04.004
- 37. Mitchell AJ, Pereira IE, Yadegarfar M, Pepereke S, Mugadza V, Stubbs B. Breast cancer screening in women with mental illness: comparative meta-analysis of mammography uptake. Br J Psychiatry 2014;205:428-35. https://doi.org/10.1192/bjp.bp.114.147629