FEATURE

A healthy heart in mind: defusing a cardiometabolic time bomb in mental illness

KATHERINE SAMARAS MB BS, PhD, FRACP
JACKIE CURTIS MB BS, FRANZCP

Mental illness appears to confer a particular susceptibility to cardiovascular disease. Reasons for this include lifestyle factors, as well as high rates of weight gain and susceptibility to type 2 diabetes, which are related to the presence of schizophrenia and mood disorders, and their treatment per se.

Key points

- **It is important to screen for cardiometabolic risk factors in people with mental illness.**
- **Diagnostic and treatment standards can be used as for any member of the community.**
- **Addressing cigarette smoking, weight or central abdominal weight gain, hypertension, and serum lipid and blood glucose level abnormalities are important in these patients.**
- **Preventing weight gain with an active lifestyle intervention will minimise metabolic complications.**
- **The special needs of the individual person should be considered when advising lifestyle changes in diet and physical activity.**

The physical burden of disease and ill health shouldered by people with mental illness is substantial and frequently inadequately treated. A recently published NSW guideline on 'Physical Health Care of Mental Health Consumers' mandates appropriate physical care of people with mental illness, recognising not only the increased risk and burden of disease, but also the barriers to health (including access to medical services, appropriate living conditions and lifestyle choices).[1]

This article aims to briefly describe the extent of cardiometabolic risk in people with psychosis, detail the underlying and promoting factors and present a simple algorithm for cardiometabolic assessment and intervention. As is the case for many different patient groups, working in partnership with mental health workers, GPs, medical subspecialists and allied health professionals can help improve the physical health of people with psychosis.

CARDIOLOGY TODAY 2011; 1(1): 15-20

Associate Professor Samaras is Associate Professor, Senior Staff Specialist and Consultant Endocrinologist at the Department of Endocrinology, St Vincent's Hospital, Sydney; and Head of the Diabetes and Obesity Clinical Group, the Garvan Institute of Medical Research, Sydney. Dr Curtis is a Senior Staff Specialist Psychiatrist at the Early Psychosis Program, Bondi Centre, and the head of the Youth Mental Health Service, South Eastern Sydney Local Health Network, Sydney; she is also a lecturer at the School of Psychiatry, University of New South Wales, Sydney, NSW.

Scope of the problem

Mental illness appears to confer a particular susceptibility to cardiovascular disease. There are multiple underlying causes for this, including lifestyle factors such as a low-quality diet, cigarette smoking and sedentary lifestyle. Additional factors, including high rates of weight gain, hypertension and susceptibility to type 2 diabetes, appear related to the presence of schizophrenia and mood disorders, and their treatment per se.

At any given time in Australia, one in 200 individuals receives treatment for psychosis.[2] Although suicide in people with schizophrenia is substantially greater than that in the general population, the most common cause of death in this group is cardiovascular disease. This accounts for much of the 20% reduction in life expectancy in people with schizophrenia (that is, from an average of 76 to 61 years of age).[3] Furthermore, the rate of cardiovascular disease in people with schizophrenia is 10 times that of suicide.[4]

Treatment of psychosis with antipsychotic medication is associated with significant weight gain and consequently an adverse cardiometabolic profile. Although there is debate as to whether antipsychotic medications are the cause of the weight gain or whether particular drugs are the culprit, this question is subsumed by the problem confronting us: the individual with a treated psychosis frequently becomes obese and thus develops an adverse cardiometabolic profile. Our imperative and obligation is to intervene and manage the patient's cardiovascular risks to prevent adverse sequelae. Most importantly, the control of the person's mental illness and the improved quality of life from achieving this should outweigh any adverse metabolic effects of treatment.

Weight gain and metabolic syndrome with treatment of psychosis

Several studies document weight gain following the initiation of second generation (atypical) antipsychotic medications.[5,6] A prospective study of 505 drug-naïve youths aged 4 to 19 years reported weight gain over a median of 11 weeks for all of the four antipsychotics examined: aripiprazole, olanzapine, quetiapine and risperidone.[5] Patients taking olanzapine gained an average of 8.5 kg (range: 7.4 to 9.7 kg), quetiapine, 6.1 kg (range: 4.9 to 7.2 kg), risperidone, 5.3 kg (range: 4.8 to 5.9 kg) and aripiprazole, 4.4 kg (range: 3.7 to 5.2 kg).[5] In contrast, an untreated comparison group had a minimal weight gain of approximately 0.2 kg.[5] Of particular concern was that in such a young group, significant increases in total serum cholesterol, triglycerides and glucose levels were also observed.[5]

A second study of 230 drug-naïve youths (mean age 22 years) with first-episode psychosis receiving a first or second generation antipsychotic treatment reported a baseline prevalence of metabolic syndrome of 6.5%. After three years, the prevalence of metabolic syndrome was doubled in the recipients of first generation (typical) antipsychotics compared with a five-fold increase in prevalence in the second generation antipsychotic recipients.[6] Clinically relevant weight gain has been reported within 10 to 16 weeks in 23 to 61% of patients prescribed antipsychotic medications for first episodes of psychosis.[7] Weight gain affects 58 to 100% of patients after one to two years of antipsychotic treatment.[7] Smoking reduction or cessation does not account for this, since most patients will increase their smoking after treatment starts.

A cross-sectional, naturalistic study of an Australian youth cohort with first-episode psychosis found that 55% of males and 42% of females were overweight or obese after a median of eight months of treatment with antipsychotic medication.[8] Body mass indices were related to the length of exposure to antipsychotic medication,[8] and nearly 13% of patients had the metabolic syndrome.[8] These results concur with a separate study that found the incidence of metabolic syndrome to be 13% after 12 months of treatment.[9] A longer-term study reported that the metabolic syndrome affected 30% of patients who had received second generation antipsychotics for three years.[6]

Lipid abnormalities

In a comprehensive review of studies evaluating lipids in patients with first-episode psychosis and a minimal exposure of medication, the serum triglycerides, total cholesterol and LDL cholesterol levels were similar to controls.[10] Lipid abnormalities have been reported to emerge as early as 12 weeks after treatment initiation.[11]

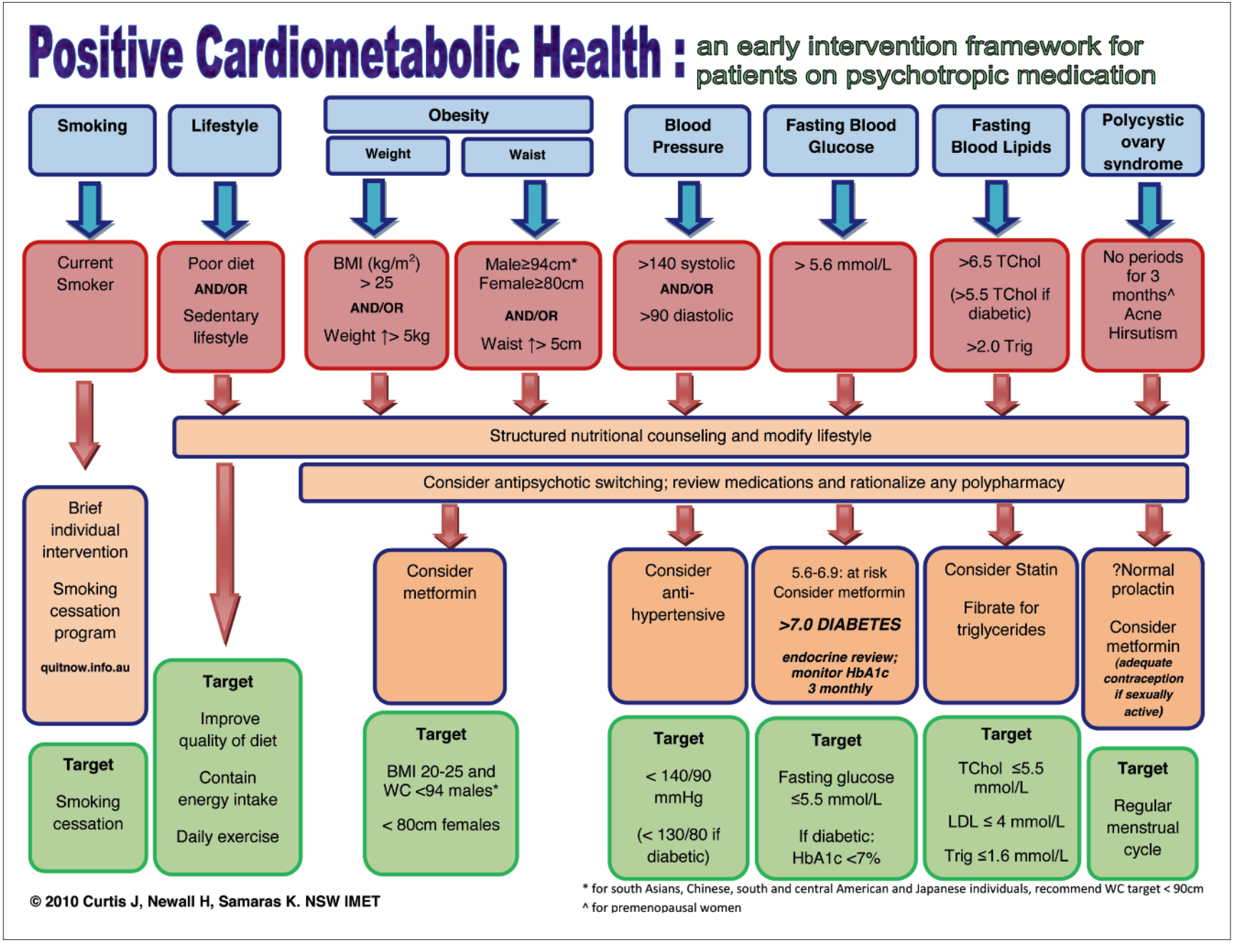
Disturbances in glucose metabolism

Psychosis itself has been associated with disturbances in glucose metabolism, even prior to initiation of antipsychotic medication in some studies[12-15] but not all.[16,17] This suggests that psychosis may be associated with a particular susceptibility to the development of diabetes. Prospective studies have shown, again in youths, an increase in insulin resistance within 12 months of initiation of antipsychotic medications.[18]

Metabolic abnormalities or else cardiovascular risk

Taken together, the above data indicate that weight gain and metabolic abnormalities occur early in the course of treatment. Importantly, many of the studies cited above refer to first-episode psychosis when the evolution of cardiometabolic abnormalities after the initiation of medication can be described. Thus, after treatment initiation, key risk factors are in place that promote cardiovascular disease. Youthfulness confers no protection when it comes to acquiring these risk factors.

The problems are compounded in people with chronic schizophrenia in whom morbid obesity may exist and where social isolation, chronic unemployment, marginalisation and poverty bring their own effects on the burden of disease susceptibility. Studies of people with chronic mental illnesses indicate a very high prevalence of the metabolic syndrome and highly adverse cardiometabolic risk. For example, in a Western Australian cohort, 67% of patients with bipolar or schizoaffective disorder had the metabolic syndrome and the rate in patients with schizophrenia was 51%.[19]



History: smoking, exercise, diet, FHx (diabetes, obesity, CVD), gestational diabetes, ethnicity, Polycystic ovary syndrome

Then at least 3 monthly

Examination: weight, BMI, waist circumference, BP

Investigations: Fasting blood glucose and lipids: total cholesterol (TChol); LDL, HDL, triglycerides (Trig);

Vitamin D (twice per year).

Interventions:

Nutritional counseling: reduce take away and junk food, reduce energy intake to prevent weight gain, stop soft drinks and juices, increase fibre intake.

Physical activity: structured education-lifestyle intervention. Advise daily physical activity: eg 30 minutes of walking.

If unsuccessful after 3 months in reaching targets, then consider switching and medication interventions below

Switching: Consider switching to a more weight neutral medication. Review diagnosis and ensure ongoing need for all psychotropic medications.

Don't just SCREEN → INTERVENE

for all patients in the "red zone"

Screen cardiometabolic risk factors using screening tool (eg Waterreus, et al 2009, Curtis et al 2009 SESIAHS); examine and investigate 3 monthly on all clients on psychotropic medications.

NB additional considerations for those on mood stabilizers & clozapine not included here and need to be performed (eg medication plasma levels, TFT's UEC's, ECHO, etc)

Always involve general practitioner, and, where appropriate and possible refer to specialist (eg dietitian/ physician/ diabetic clinic/ exercise physiologist).

NB: Some drugs used in metabolic disease treatment are contraindicated in pregnancy (eg some antihypertensives and lipid lowering drugs). If your patient on any metabolic medications is considering pregnancy, please discuss with their GP

Specific Pharmacological Interventions:

Consider metformin if:

- impaired glucose
- PCOS
- obesity or rapid weight gain

Metformin therapy: start at 500mg x ½ tablet before breakfast and dinner for two weeks then increase to 500mg bd. If side-effects of nausea, abdominal cramping, shift to after meal.

Lipid lowering therapy: (use PBS guidelines)

Statin initiation doses for cholesterol lowering:

simvastatin 10 mg nocte	atorvastatin 10mg nocte
pravastatin 10mg nocte	rosuvastatin 10 mg nocte

Fibrate therapy for triglyceride lowering:

gemfibrozil 600 mg bd	fenofibrate 145 mg mane

Anti hypertensive therapy: Multiple agents are available. Liaise with the GP who can monitor.

Vitamin D:

- <50 nmol/L: replenish stores: cholecalciferol 4,000 IU per day for one month;
- maintenance: 1,000 IU daily. Target >80nmol/L.
- most vitamin D supplements are 1,000 IU (0.25mcg) each.

References: Alberti K, Zimmet P, Shaw J. The metabolic syndrome - a new worldwide definition. *Lancet*. 2005; 366: 1059-62. De Hert M, Dekker JM, Wood D, et al. Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC). *European Psychiatry*. 2009; 24: 412-24. Newcomer JW, Hennekens CH. Severe Mental Illness and Risk of Cardiovascular Disease. *JAMA*. 2007; 298: 1794-6. Waterreus AJ, Laugharne JD. Screening for the metabolic syndrome in patients receiving antipsychotic treatment: a proposed algorithm. *MJA*. 2009; 190: 185-9. Wu, R. R., J. P. Zhao, et al. 2008. Lifestyle intervention and metformin for treatment of antipsychotic-induced weight gain: a randomized controlled trial. *JAMA* 299(2): 185-193.

For further information or copy right approval please visit; www.imet.health.nsw.gov.au or contact info@imet.health.nsw.gov.au

A 'care can do solution': with a healthy heart in mind

A key to reducing cardiometabolic risk in people with treated psychosis is preventing or reducing the weight gain that occurs at the onset of psychosis treatment. Evidence from randomised controlled studies has shown that metformin at the initiation of antipsychotic therapy can stop weight gain, with a difference between the metformin and placebo groups as substantial as 4 kg in 12 weeks.[20]

A randomised controlled trial investigated the addition of metformin in patients with chronic schizophrenia who were taking long-term antipsychotics. The results showed an ongoing weight gain in the placebo group of 2.4 to 3.8 kg over 12 weeks, compared with 2.5 to 3.9 kg weight loss in those taking metformin and 3.4 to 5.7 kg weight loss if metformin was combined with a lifestyle intervention.[21] Lifestyle intervention alone induced a 0.7 to 2.0 kg loss.[21] Overall, metformin plus lifestyle intervention produced a weight difference of 7.8 kg compared with those receiving placebo.[21] These data indicate that lifestyle intervention should be in place for all people with schizophrenia who receive antipsychotic medication. Furthermore, consideration should be given to metformin treatment in every patient, particularly those who are already overweight or have impaired glucose metabolism.

In our own mental health service, psychiatrists have become pro-active in prescribing metformin when indicated. Mental health workers are liaising with GPs, who are experienced in the use of this medication. Use of metformin for prevention of weight gain in recipients of atypical antipsychotics is an off-label use, as it is when used to treat prediabetes and polycystic ovarian syndrome. This fact should be discussed with patients, noting the discrepancy between progress in the scientific literature and outdated product information.

Similarly, GPs are well placed to initiate or uptitrate lipid-lowering or antihypertensive medications, as they would in other high cardiovascular risk patients, taking into consideration the need for dose reductions in those with renal impairment.

Lifestyle change, support and supervision

The special needs of patients with mental illness should be considered when advising change in diet and physical activity. These needs include an individual's educational status, social isolation, income limitations, cooking skills, availability of cooking facilities (or lack of) and any cognitive difficulties the person has. Mental health clinicians, including nurses, nutritionists and occupational therapists, have an important role to play in addressing these barriers. Similarly, when a health professional offers exercise advice, the personal barriers preventing that individual from acting on the suggestions need to be addressed. Again, support from occupational therapists, exercise physiologists and other mental health care workers is invaluable.

Smoking cessation and the management of alcohol and illicit drug use is critical. GPs involved in the care of patients with mental illness need to advocate and support smoking cessation at every visit. Excellent resources are available online to support this important behaviour change (see the algorithm on page 17).

Identification and intervention of cardiometabolic risk

Cardiometabolic risk factors require detection and intervention, particularly in people with severe mental illnesses such as schizophrenia. In 2010, we designed the 'Don't just screen – intervene algorithm' (see page 17) as an educational project to assist psychiatry trainees, psychiatrists and mental health workers in the cardiometabolic risk management of their patients. The algorithm was designed as a tool for clinical use and has a 'traffic light' system to highlight action points for each cardiometabolic risk factor, the intervention recommended and the treatment targets. The algorithm addresses cigarette smoking, weight or central abdominal weight gain, blood pressure elevation, and serum lipid and blood glucose levels. The algorithm includes 'how to' suggestions that can be initiated by health workers for each health issue, as well as prescribing advice based on PBS guidelines or published evidence for medical practitioners. NSW Health has adopted this algorithm as part of an educational package soon to be launched and the algorithm is available for download from the IMET website on the psychiatry training link (see: http://ceti.moodle.com.au/ personal login required).

A further useful Australian algorithm for screening metabolic risk in people with mental illness has been developed (available online, see: www.mja.com.au/public/issues/190_04_160209/wat10895_fm.html),[22] and this also provides a practical guideline to monitoring patients treated with antipsychotic medications.[22]

Conclusion

Severe mental illnesses such as schizophrenia can take years of productive life from individuals, as well as their sense of self and their place in the community. Furthermore, mental illness takes away productive members from the community and increases costs to society through ill health, disability and premature loss of life. As individuals engaged in health care across many specialties and skill sets, we can each contribute to the better health of people with mental illness, particularly in areas in which we might already have expertise, such as cardiometabolic risk reduction.

People with mental illness have special needs and these must be taken into consideration when advising lifestyle change. In partnership with mental health colleagues and allied health professionals, GPs are well placed to defuse the cardiometabolic time bomb in people with mental illness. CT

References

A list of references is available on request to the editorial office.

COMPETING INTERESTS: Associate Professor Samaras has accepted honoraria for speaking at meetings from Janssen-Cilag, Merck Sharp and Dohme and ViiV Healthcare Australia. Dr Curtis has accepted honoraria for speaking at meetings from Janssen-Cilag and AstraZeneca.

References

1. Physical health care of Mental Health Consumers. Guideline; NSW Department of Health, 2009. Available online at www.health.nsw.gov.au/policies/gl/2009/pdf/GL2009_007.pdf (accessed March 2010).
2. McGorry P, Killackey E, Lambert T, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of schizophrenia and related disorders. Aust N Z J Psychiatry 2005; 39: 1-30.
3. Hennekens CH, Hennekens AR, Hollar D, et al. Schizophrenia and increased risks of cardiovascular disease. Am Heart J 2005; 150: 1115-1121.
4. Hennekens CH. Increasing global burden of cardiovascular disease in general populations and patients with schizophrenia. J Clin Psychiatry 2007; 68: 4-7.
5. Correll CU, Manu P, Olshanskiy V, Napolitano B, Kane JM, Malhotra AK. Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. JAMA 2009; 302: 1765-1773.
6. De Hert M, Schreurs V, Sweers K, et al. Typical and atypical antipsychotics differentially affect long-term incidence rates of the metabolic syndrome in first-episode patients with schizophrenia: a retrospective chart review. Schizophr Res 2008; 101: 295-303.
7. Alvarez-Jimenez M, Gonzalez-Blanch C, Crespo-Facorro B, et al. Antipsychotic-induced weight gain in chronic and first-episode psychotic disorders - A systematic critical reappraisal. CNS Drugs 2008; 22: 547-562.
8. Curtis J, Henry C, Watkins A, Newall, H, Samaras, K, Ward P. Metabolic abnormalities in an Early Psychosis Service: A retrospective, naturalistic cross-sectional study. Early Inter Psychiatry (in press, 2011 accepted 18/10/10).
9. Patel JK, Buckley PF, Woolson S, et al. Metabolic profiles of second-generation antipsychotics in early psychosis: Findings from the CAFE study. Schizophr Res 2009; 111: 9-16.
10. Foley DL, Morley KI. Systematic review of early cardiometabolic outcomes of the first treated episode of psychosis. Arch Gen Psychiatry 2011 Feb 7. [Epub ahead of print]
11. Perez-Iglesias R, Crespo-Facorro B, Amado JA, et al. A 12-week randomized clinical trial to evaluate metabolic changes in drug-naive, first-episode psychosis patients treated with haloperidol, olanzapine, or risperidone. J Clin Psychiatry 2007; 68: 1733-1740.
12. Fernandez-Egea E, Bernardo M, Donner T, et al. Metabolic profile of antipsychotic-naive individuals with non-affective psychosis. Br J Psychiatry 2009; 194: 434-438.
13. Ryan MC, Collins P, Thakore JH. Impaired fasting glucose tolerance in first-episode, drug-naive patients with schizophrenia. Am J Psychiatry 2003; 160: 284-289.
14. 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: 342-347.
15. Spelman LM, Walsh PI, Sharifi N, et al. Impaired glucose tolerance in first-episode drug-naive patients with schizophrenia. Diabet Med 2007; 24: 481-485.
16. Verma SK, Subramaniam M, Liew A, et al. Metabolic risk factors in drug-naive patients with first-episode psychosis. J Clin Psychiatry 2009; 70: 997-1000.
17. Sengupta S, Parrilla-Escobar MA, Klink R, et al. Are metabolic indices different between drug-naive first-episode psychosis patients and healthy controls? Schizophr Res 2008; 102: 329-336.
18. Perez-Iglesias R, Mata I, Pelayo-Teran JM, et al. Glucose and lipid disturbances after 1 year of antipsychotic treatment in a drug-naive population. Schizophr Res 2009; 107: 115-121.
19. John AP, Koloth R, Dragovic M, et al. Prevalence of metabolic syndrome among Australians with severe mental illness. Med J Aust 2009; 190: 176-179.
20. Wu RR, Zhao JP, Guo XF, et al. Metformin addition attenuates olanzapine-induced weight gain in drug-naive first-episode schizophrenia patients: a double-blind, placebo-controlled study. Am Journal of Psychiatry 2008; 165: 352-358.
21. Wu RR, Zhao JP, Jin H, et al. Lifestyle intervention and metformin for treatment of antipsychotic-induced weight gain: a randomized controlled trial. JAMA 2008; 299: 185-193.
22. Waterreus, AJ, Laugharne JD. Screening for the metabolic syndrome in patients receiving antipsychotic treatment: a proposed algorithm. Med J Aust 2009; 190: 185-189.