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Early Intervention in the Real World

The heart of the matter: cardiometabolic care in youth with psychosis

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Abstract

Aim: Weight gain, obesity and metabolic disturbances in youth with psychosis are significant contributors to the health burden of people with psychosis, with a two- to threefold increase in rates compared with the general population and a 20% reduction in life expectancy. Several studies have now described cardiometabolic benefits of a range of interventions, including a structured diet and exercise programmes and metformin for patients receiving antipsychotic medications. Despite the development of Australian consensus guidelines and screening algorithms to detect such metabolic abnormalities, there is a lack of guidelines for clinicians to determine appropriate, timely, targeted prevention and intervention to manage these complications in the youth population.

Methods: The Bondi Early Psychosis Programme targets young people (aged 15–25 years) experiencing their first episode of psychosis. This service has developed a model of metabolic screening and a treatment algorithm to provide clinicians with recommendations for targeted interventions.

Results: Positive Cardiometabolic Health: an early intervention framework for patients on psychotropic medication describes a method for early detection, prevention and intervention strategies targeting antipsychotic-induced metabolic abnormalities and cardiovascular risk factors.

Conclusion: Although further research is required, there is sufficient evidence to support early intervention and prevention strategies to improve physical health outcomes in young people with first-episode psychosis.

Key words: intervention, metabolic syndrome, psychosis, youth.

INTRODUCTION

Approximately one in 200 Australians are being treated for psychosis in any single month, with a peak of onset in adolescents and young adulthood.[1] The standard of optimal care generally includes long-term second generation (or atypical) antipsychotics, in addition to the foundation stones of multidisciplinary psychosocial interventions.[1,2] Use of second-generation antipsychotics avoids the negative side effects that characterize the first generation antipsychotics, such as extrapyramidal symptoms, tardive dyskinesia and tardive dystonia. Second-generation antipsychotics may induce substantive weight gain, obesity and metabolic complications.[3,4] These adverse effects are significant contributors to the health burden of people with psychosis, with an immediate impact on a young individual's development of sense of self and personal life direction, and in the future, on cardiometabolic health.

Disorders of excess weight (overweight and obesity) now affect 30.4% (male) and 35.7% (female) of Australian youth (aged 18–24).[5] Metabolic syndrome, a clustering of central obesity and elevated lipid, glucose and blood pressure, is increasing in prevalence, mostly secondary to obesity.[6] Metabolic syndrome data for Australian youth are lacking; however, US data suggest that 4.5% of youths aged

12–17 years meet diagnostic criteria.[7] Superimposed on this general trend, severe mental illness is associated with a two to threefold greater prevalence of both obesity and metabolic syndrome.[8,9] These 'newcomer' diseases in psychiatry will undoubtedly add to the established 20% reduction in life expectancy of people with schizophrenia.[10] Cardiovascular disease is the major cause of premature death in people with schizophrenia, with a 10-fold higher rate compared with suicide.[11] The impact of an obesity-induced, early life deterioration in cardiometabolic profile on the natural history of heart disease in schizophrenia is not known.

Despite the development of Australian consensus guidelines and screening algorithms with recommendations for identification of diabetes and cardiometabolic monitoring in patients with psychotic disorders,[12,13] significant barriers exist to routine implementation in this patient group.[9]

What is the evidence for weight gain and increased cardiometabolic risk after second-generation antipsychotic initiation in youth?

A great concern to health professionals involved in the care of youth with first-episode psychosis is the rapidity of clinically significant weight gain, associated with premature development of cardiometabolic risk factors.[3,4,14] This was most elegantly shown in a recent prospective study of 272 drug-naïve youths (aged 4–19 years) who received one of four commonly prescribed second-generation atypical antipsychotics, aripiprazole, olanzapine, quetiapine or risperidone for a median of 11 weeks.[3] The average weight gain was 8.5 kg for olanzapine (95% confidence intervals 7.4–9.7), 6.1 kg for quetiapine (95% confidence intervals 4.9–7.2), 5.3 kg for risperidone (95% confidence intervals 4.8–5.9) and 4.4 kg for aripiprazole (95% confidence intervals 3.7–5.2).[3] There was an untreated comparison group with a weight gain of 0.2 kg.[3] Associated with this weight gain were significant increases in total cholesterol, triglycerides and glucose.[3]

Other longer-term longitudinal studies of weight gain and metabolic complications following drug initiation support enduring, exaggerated weight gain and progression in metabolic complications.[4,15,16] For example, a study of 230 drug-naïve youths with first episode psychosis (mean age 22 years) received either a first or second-generation antipsychotic medication.[4] At baseline, 6.5% of both cohorts had metabolic syndrome. At 3 years, there was a doubling of metabolic syndrome prevalence in first generation antipsychotic recipients and a fivefold increase in prevalence in those receiving second-generation antipsychotics.[4]

What is the evidence of benefit with intervention?

Several studies have now defined weight and metabolic benefits of a range of interventions, including a supported diet and exercise programme and metformin for patients receiving antipsychotic medications.[17–20] Two randomized physical activity interventions of 12–16 weeks' duration found no benefits in weight in patients with schizophrenia, despite improvement in the severity of negative symptoms.[21,22] However, a randomized controlled trial in a drug-naive first-episode psychosis cohort (mean age 26.8 years) showed that early behavioural intervention (cognitive behaviour therapy, exercise and diet) was effective in attenuating antipsychotic-induced weight gain.[20]

Randomized studies of metformin also indicate benefit. A blinded randomized study of metformin in drug-naive first-episode psychosis patients treated with olanzapine, found metformin-attenuated weight gain by an average of 4 kg in as brief a period as 12 weeks.[18] This study found that metformin prevented any rise in fasting insulin and insulin resistance.[18] In a further randomized, placebo-controlled study, adults with longer-term treated schizophrenia who had already gained >10% baseline weight were assigned to one of four treatment groups for 12 weeks: placebo alone, placebo plus lifestyle intervention, metformin alone or metformin plus lifestyle intervention.[19] Weight gain over 12 weeks with placebo alone ranged 2.4–3.8 kg. In contrast, all other intervention groups lost weight: placebo with lifestyle intervention lost 0.7–2.0 kg; metformin alone lost 2.5–3.9 kg; and metformin with lifestyle intervention lost 3.4–5.7 kg.[19] The mean group difference between placebo and intervention with metformin plus lifestyle was 7.8 kg.[19] It is of interest that both these studies used doses of metformin that we would consider modest compared with those doses that are frequently use in type 2 diabetes mellitus. Some meta-analyses and systematic reviews which have grouped these rather disparate studies (in interventions, drugs and patient groups) have been inconclusive,[23,24] whereas a more recent review supported the use of metformin as an effective adjunctive treatment for the prevention of weight gain in psychiatric populations.[25] In Australia, the NSW Department of Health now mandate physical health care in people with mental health problems.[26] Specifically, all clinicians are now required to ensure

that patients receive intervention for disorders of weight and cardio-metabolic risk factors. As shown previously, young patients experiencing their first episode of psychosis who have commenced a second-generation antipsychotic medication suffer significant health morbidities. We argue that these patients might benefit most from early intervention to prevent weight gain, obesity and metabolic complications associated with initiation of second-generation antipsychotics. Next we outline a model of care we have developed to not only screen, but also actively intervene in young patients with first-episode psychosis. We encourage all clinicians involved in the care of people with mental health problems to take up this challenging but rewarding duty of care, guiding and supporting our young patients and their families or carers in proactive prevention of weight gain, via regular metabolic screening and targeted interventions.

A model of care: the Bondi Early Intervention Model for first-episode psychosis in youth

The Early Psychosis Programme (EPP) is a multidisciplinary community-based team located in Bondi, Sydney that targets 15 to 25-year-olds with first-episode psychosis within 2 years of psychosis onset. As part of the 2-year treatment offered, all clients are invited to participate in the innovative group programme called Recovery and Discovery in Community and Lifestyle ('RaDiCaL'). This programme is co-ordinated by multidisciplinary staff, including clinical nurse specialists, occupational therapists, clinical psychologists and family therapists. The service offers all patients metabolic screening and monitoring as well as individualized lifestyle (exercise and nutrition based) interventions as part of the physical health stream of the RaDiCaL group programme. The metabolic screen is also used as an opportunity to review metabolic changes that may have occurred during the course of the young person's treatment, and administer counselling on issues such as diet, exercise, drugs and alcohol.

In a recent retrospective, naturalistic cross-sectional study of 85 subjects attending the Bondi EPP service, over a third of young patients being treated for their first episode of psychosis either had metabolic syndrome or showed metabolic abnormalities.[27]

Metabolic screening of all clients while drug-naive is the gold standard – but may not occur for example in the context of an acute involuntary admission – and is conducted as soon as possible after entry into the programme. At the initial consultation, there is screening of relevant cardio-metabolic risk factors including ethnicity; a personal history of diabetes (including gestational) and polycystic ovarian disease; a family history of diabetes, obesity and cardiovascular disease which are all recorded on a specifically developed metabolic monitoring chart (available upon request). This chart was developed to capture the relevant cardiometabolic risk factors and ensure regular monitoring of metabolic parameters. Baseline measurement of height, weight, body mass index, blood pressure and waist circumference is documented as well as information about the client's use of cigarettes and estimated current weekly physical activity. As part of the metabolic screen fasting glucose, total cholesterol, high density lipoproteins, low density lipoproteins and triglycerides are performed with levels recorded in the metabolic monitoring form. This form makes it easy to track the progress of each client and can be filled in by any team member. In our service, we aim for routine metabolic screening at three monthly intervals for all patients.

The Bondi model of care: positive cardiometabolic health algorithm

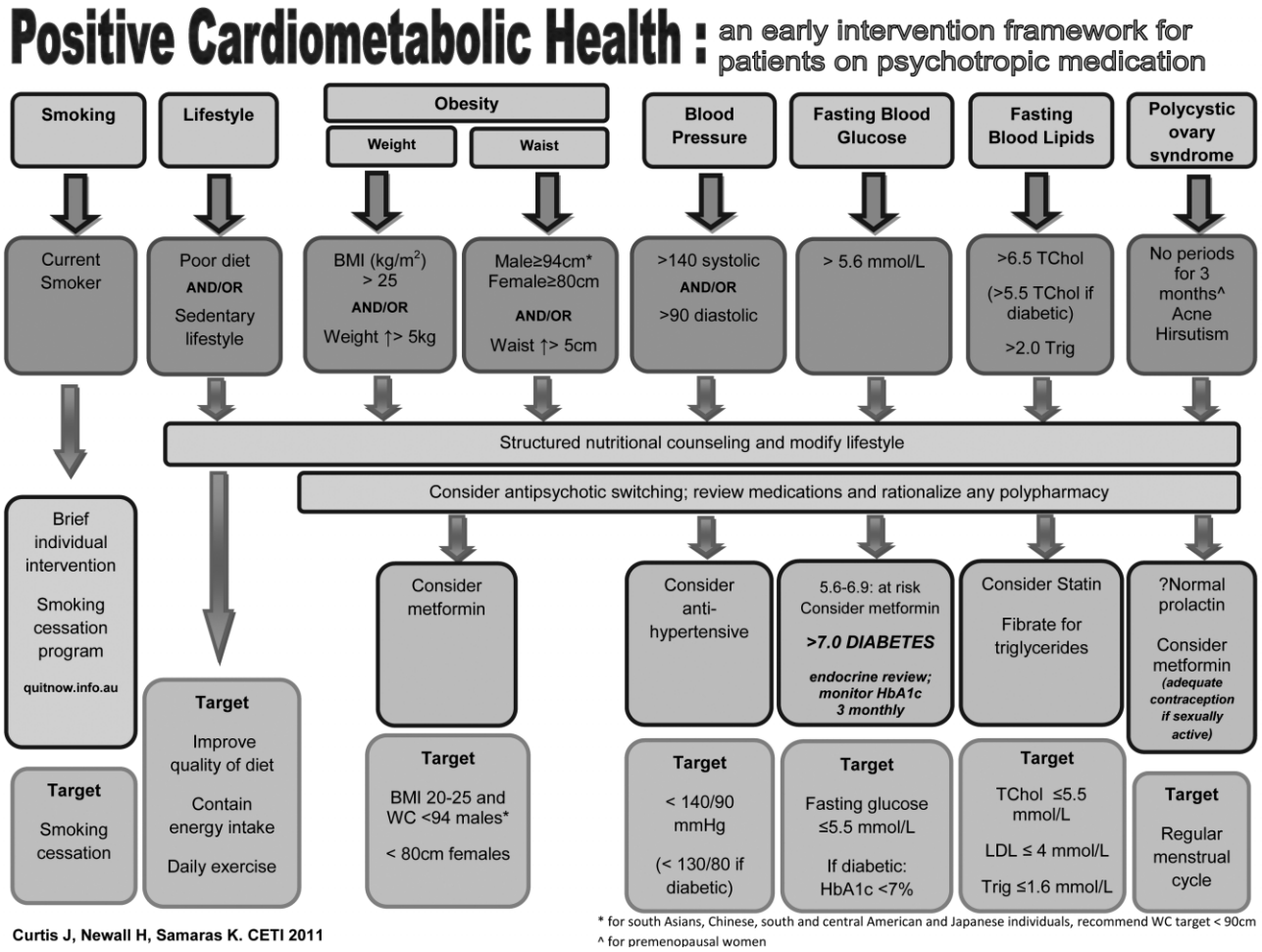
Monitoring, every 3–6 months (refer to algorithm – Fig. 1)

As outlined, we recommend routine baseline assessment of cardiometabolic risk and then at least three monthly examination and investigations. We recommend a number of trigger points for increased monitoring and more one-on-one intervention. These are listed in Box 1 and should include clinically meaningful weight or waist gains (5 kg or 5 cm) or development of any metabolic abnormality or polycystic ovary syndrome phenotypes.

The Bondi Model of Early Intervention in Youth with Psychosis: Don't Just Screen, Intervene

If metabolic syndrome phenotypes develop as listed in Box 1, we initiate a trial of lifestyle intervention, using self-empowering education, involving (where possible) families and carers who may support, encourage or facilitate transitions to a healthier lifestyle. A multidisciplinary approach is undertaken with liaison between the psychiatrist, general practitioner, dietitian and ideally, where available, occupational therapist and structured exercise programme. When indicated, lifestyle interventions (nutritional and exercise based) are conducted weekly for a minimum of eight sessions where possible. Where there are additional cardiovascular risks such as smoking or pre-existing obesity, these

FIGURE 1. Positive cardiometabolic health algorithm.



BOX 1. Trigger points for increased metabolic screening and intervention.

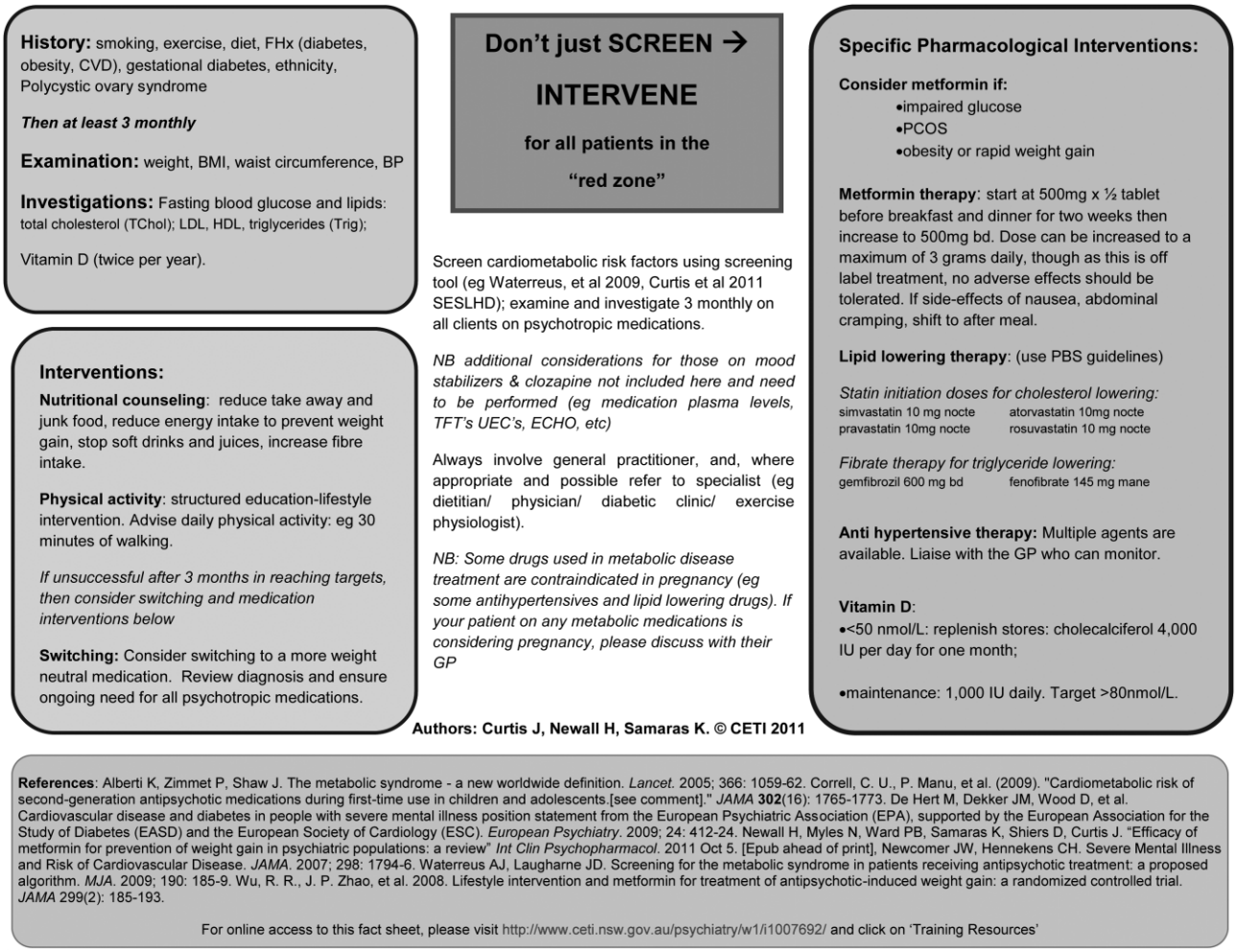
- >5 kg weight gain
- >5 cm increase in waist circumference
- BMI > 25
- Waist circumference ≥ 94 cm (males); females ≥ 80 cm
- Hypertension (systolic > 140 mm Hg or diastolic > 90 mm Hg) on two occasions, measured after 10-min rest
- Increased fasting glucose (>5.6 mmol L^{-1})
- Increased total cholesterol (>6.5 mmol L^{-1}) or triglycerides (>2.0 mmol L^{-1})
- PCOS phenotypes such as oligo-amennorhea, acne or hirsutism

are specifically addressed in a targeted manner, rather than generalized advice.

Weight loss and increased physical activity are cornerstones of intervention, underpinning multiple aspects of recovery in both physical and mental health. These interventions are trialled for a minimum period of 3 months. Individual nutritional and exercise based interventions are complemented by a weekly group physical health stream programme encompassing sport, gym and cooking groups as well as monthly active outdoor adventures.

Cardiometabolic risk is re-evaluated after 3 months. If the profile is no better or has worsened, additional interventions are considered, in addition to ongoing lifestyle change. These include drug

FIGURE 1. (continued)



therapy for lipids and hypertension when these parameters are elevated above recommended cut-off ranges as indicated by the algorithm, as per national recommended guidelines. Metformin for glucose disturbances in the pre-diabetic, impaired glucose range and weight gain is 'off-label'. Metformin is approved for use under the Pharmaceutical Benefits Scheme only for type 2 diabetes; however, it is a cheap medication; further, there is substantial, long-term safety evidence, even in non-diabetic children and adolescents with up to 7 years of safety data from intervention trials[28,29]

It is desirable for patients to have 25 hydroxy vitamin D and vitamin B12 levels checked, as low levels of both contribute to mood disturbance and fatigue. Further, hypovitaminosis D is common in overweight or obese people. A regimen for vitamin D replacement is included in the algorithm.

As for many other medical conditions where lifestyle intervention is essential, a close doctor–patient relationship is beneficial for intervention and follow-up. Identifying patients who lack medical supports and engaging them in supported health care may improve chances of success in lifestyle change and risk factor management. This is a particularly difficult challenge for resource- and advocate-poor patients with psychosis. Ensuring the patient has a general practitioner (GP) is essential, although it is not uncommon for young clients to not identify having a GP. This model provides an opportunity for closer collaboration between primary care and specialist mental health care in the shared goal of reducing cardiovascular risk factors in this population.[30]

As, yet, definitive evidence-based guidelines do not exist. In the absence of accepted guidelines, we propose it is unethical not to intervene to prevent metabolic complications in young patients with psychosis receiving atypical antipsychotic medications. Relative youth is insufficient justification to

prevent aggressive tackling of cardiometabolic risk factors with at least lifestyle change, as we would for other patients at higher risk of cardiovascular disease without psychiatric disease or older patients on long-term antipsychotics. It is of course necessary for all models of care to be evaluated. This process is ongoing in the service in which this model is being implemented. There is ongoing work within the service to ensure routine screening and accurate recording of all clinical outcome data for cardiometabolic risk factor management. This can be challenging where clients move from inpatient to community settings and in the absence of an integrated electronic file. Regular file audits need to be carried out as a matter of routine in any model of preventative physical health care implemented in a mental health service environment, in addition to ongoing staff training and education about the importance of such initiatives.

As health practitioners, lifestyle change and weight reduction, particularly in the face of severe mental health issues, may seem secondary and overwhelming. Many of these young people suffer greatly due to their mental health problems; the additional burden of metabolic complications is likely to silently erode future health. Excess weight gain also disables both physical and mental rehabilitation. All are serious problems. If our mandate is to assist these patients, we need to address not only the needs created by mental health, but the acquired health needs induced by effective drug treatment. This is in practice in other medical specialties where essential drugs come with unwanted adverse effects; for example, addressing adverse cardiometabolic risks associated with antiretroviral agents for HIV infection with preventive intervention.[31]

Healthcare practitioners from many different streams can contribute positively to the future physical health of young people with psychosis. Health gains in this early stage of life can be seen as an investment for the economic future of the nation: productive adults, workforce participation, along with reduced future disability and reduced health costs. Moreover, insisting on improved health for youth affected by psychosis is an index of our society's belief in the value of the most vulnerable individual.

CONCLUSION

Metabolic syndrome is epidemic in the mentally ill population and can be expected to widen the substantial 20% gap in life expectancy between this population and the general public. Antipsychotics contribute directly to weight gain, dyslipidaemia, hyperglycaemia, central obesity and hypertension, although lifestyle circumstances caused by poor mental health also contribute. The presence of metabolic syndrome in the adolescent population is of particular concern, as patients who are overweight as adolescents have greatly increased mortality from all causes in adulthood regardless of adult weight.[32]

It is clear that better monitoring and intervention practices for metabolic syndrome are needed in the medicated mentally ill population to reduce the alarmingly high rates of death and disability caused by cardiovascular disease and diabetes. The Bondi model provides an effective model of physical health care for young people with psychosis.

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