Metabolic syndrome in psychiatry: advances in understanding and management

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SUMMARY
Metabolic syndrome comprises a number of cardiovascular risk factors that increase morbidity and mortality. The increase in incidence of the syndrome among psychiatric patients has been unanimously demonstrated in recent studies and it has become one of the greatest challenges in psychiatric practice. Besides the use of psychotropic drugs, factors such as genetic polymorphisms, inflammation, endocrinopathies and unhealthy lifestyle contribute to the association between metabolic syndrome and a number of psychiatric disorders. In this article, we review the current diagnostic criteria for metabolic syndrome and propose clinically useful guidelines for psychiatrists to identify and monitor patients who may have the syndrome. We also outline the relationship between metabolic syndrome and individual psychiatric disorders, and discuss advances in pharmacological treatment for the syndrome, such as metformin.

LEARNING OBJECTIVES
• Be familiar with the definition of metabolic syndrome and its parameters of measurement.
• Appreciate how individual psychiatric disorders contribute to metabolic syndrome and vice versa.
• Develop a framework for the prevention, screening and management of metabolic syndrome in psychiatric patients.

DECLARATION OF INTEREST
None.

Metabolic syndrome is a major public health problem that has been recognised to be a global epidemic by the World Health Organization (WHO) (Potenza 2009). It is a constellation of clinical signs and suboptimal laboratory findings involving five key features: central obesity, elevated blood pressure, hypertriglyceridaemia, low serum levels of high-density lipoprotein (HDL) cholesterol and high serum levels of fasting glucose. It is generally agreed that the presence of at least three of these components is required before a patient can be classified as having metabolic syndrome (Grundy 2004). However, the most widely used definitions of the syndrome focus predominantly on either waist circumference (a surrogate measure of central obesity) or insulin resistance (Table 1) – criteria that apply differently to various ethnic groups.

Given the difficulty in reaching consensus among these definitions, a number of major international bodies came together in an attempt to harmonise diagnostic criteria (Alberti 2009; Kassi 2011). They advised that there should be no obligatory component for metabolic syndrome, but rather that all five individual components should be deemed important in risk prediction. These components are independent risk factors for coronary heart disease, cerebrovascular disease and diabetes.

Prevalence
Metabolic syndrome affects around 20–25% of the population worldwide, and it is associated with a twofold increase in the likelihood of death and threefold increase in the risk of heart attack or stroke (International Diabetes Federation 2006). Metabolic syndrome also has a huge impact on the financial, emotional and psychosocial well-being of those who have the disease and their families. The syndrome is associated with an increased risk of developing psychiatric disorders such as depression, resulting in reduced quality of life. Conversely, long-term psychiatric illnesses can promote metabolic syndrome: its prevalence is 2–3 times higher in people with severe psychiatric illnesses (Holt 2010).

Aetiology
The cause of metabolic syndrome in psychiatric patients is likely to be multifactorial (Box 1) (Grundy 2004). Psychotropic drugs such as second-generation antipsychotics and mood stabilisers are established risk factors. Negative health behaviours such as smoking, excessive alcohol consumption, lack of physical exercise, unhealthy eating habits are also likely to contribute, as are...
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Biological factors such as hypothalamic–pituitary–adrenal (HPA) axis dysregulation and insulin resistance. Inflammation is recognised as an integral component of both metabolic syndrome and psychiatric disorders (Hope 2009; Na 2012), with high serum levels of C-reactive protein (CRP) and proinflammatory cytokines such as interleukin IL-6 and tumour necrosis factor-alpha (TNF-α) in both conditions. Genetic factors such as the presence of specific genes responsible for a predisposition to metabolic problems and variations in the leptin–melanocortin pathway that contribute to heterogeneity in antipsychotic-induced weight gain are also important causes of metabolic syndrome.

The relationship between metabolic syndrome and psychiatric illness is indeed intricate and likely confounded by many issues. Nevertheless, the aim of this article is to highlight some of the mechanisms underlying the two and to outline potential treatment strategies.

Schizophrenia and metabolic syndrome

**Epidemiology**

Metabolic syndrome is common among people with schizophrenia, although the estimated prevalence varies widely, from 8.9 to 68%. This wide range may be attributed to the different age groups and ethnic groups studied and the use of different diagnostic criteria (McEvoy 2005). Nevertheless, the prevalence of metabolic syndrome in people with schizophrenia is still around 5 times higher than that in the general population. Women with schizophrenia have a higher risk of developing metabolic syndrome compared with men (McEvoy 2005). Mortality among people with schizophrenia is two- to threefold higher than in the general population, and this is largely accounted for by cardiovascular morbidity (Koponen 2010).

Schizophrenia is also associated with a greater risk of diabetes mellitus, with a two- to threefold higher prevalence compared with the general population (de Hert 2009). This increase is

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**Table 1** Diagnostic criteria for metabolic syndrome

<table>
<thead>
<tr>
<th>Criteria</th>
<th>WHO</th>
<th>IDF</th>
<th>EGIR</th>
<th>NCEP-ATP III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central obesity/waist circumference</td>
<td>Diabetes plus at least two of the following: (men), &gt;0.85 (women); or BMI &gt;30 kg/m²</td>
<td>Central obesity plus at least two of the following:</td>
<td>Insulin resistance plus at least two of the following: (men), &gt;84 cm (women); or BMI &gt;30 kg/m²</td>
<td>At least three of the following: (men), &gt;88 cm (women); or BMI &gt;30 kg/m²</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≥1.7 mmol/l, or specific treatment for lipid abnormality</td>
<td>&gt;1.7 mmol/l, or specific treatment for lipid abnormality</td>
<td>≥2.0 mmol/l, or treatment for lipid abnormality</td>
<td>&gt;1.7 mmol/l</td>
</tr>
<tr>
<td>High-density lipoprotein (HDL) cholesterol</td>
<td>&lt;0.9 mmol/l (men), &lt;1.0 mmol/l (women)</td>
<td>&lt;1.04 mmol/l (men), &lt;1.29 mmol/l (women); or specific treatment for lipid abnormality</td>
<td>1.0 mmol/l</td>
<td>1.04 mmol/l (men), 1.29 mmol/l (women)</td>
</tr>
<tr>
<td>Blood pressure (systolic/diastolic)</td>
<td>≥140/90 mmHg</td>
<td>Systolic blood pressure &gt;130 or diastolic blood pressure &gt;85 mmHg, or antihypertensive medication</td>
<td>≥140/90 mmHg, or antihypertensive medication</td>
<td>&gt;130/85 mmHg</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>Impaired</td>
<td>&gt;5.5 mmol/l, or previously diagnosed type 2 diabetes</td>
<td>≥6.1 mmol/l</td>
<td>≥6.1 mmol/l</td>
</tr>
<tr>
<td>Urinary albumin</td>
<td>Excretion rate ≥20 µg/min, or albumin/creatinine ratio ≥30 mg/g</td>
<td>Not included</td>
<td>Not included</td>
<td>Not included</td>
</tr>
</tbody>
</table>


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**Box 1** Common risk factors for metabolic syndrome in chronic psychiatric illness

- Excessive alcohol consumption
- Food imbalance and poor dietary habits
- Genetic predisposition
- Hormonal imbalances involving cortisol and leptin
- Second-generation antipsychotics and their related side-effects
- Sedentary lifestyle

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Independent of the use of antipsychotic drugs. Antipsychotic-naive patients were found to have higher insulin resistance, impaired glucose tolerance and increased intra-abdominal fat deposition compared with normal controls (Papanastasiou 2012). In addition, siblings of individuals with schizophrenia were found to have increased glucose intolerance (Fernandez-Egea 2008a), while parents of those with non-affective psychosis had increased prevalence of type 2 diabetes (Fernandez-Egea 2008b). These findings suggest that metabolic abnormality is probably an intrinsic component of schizophrenia, with biological and genetic predisposing factors.

**Common genetic factors**

Research suggests a possible common genetic predisposition to both metabolic syndrome and schizophrenia. An at-risk allele of type 2 diabetes, rs7903146[T], has been found in the transcription factor 7-like 2 (TCF7L2) gene and this genotype is also associated with an increased risk of schizophrenia (Hansen 2011). Associations between weight gain in patients with schizophrenia and various genetic polymorphisms have also been identified. For example, the alpha-1A adrenergic receptor (ADRA1A) gene is related to cardiovascular risk factors such as obesity and hypertension, and a positive association has been reported between the cumulative number of metabolic syndrome components and the presence of the Arg347 allele of ADRA1A (Cheng 2012).

**Chronic inflammation**

Many studies have reported chronic subclinical inflammation to be part of metabolic syndrome (Newcomer 2007). Although inflammatory markers are not currently included in the diagnostic criteria for metabolic syndrome, they have been linked to it, particularly CRP, TNF-α, IL-6, adiponectin and leptin, which are present in visceral fat (Sutherland 2004). Adipose tissue of obese people secretes higher amounts of these inflammatory molecules compared with adipose tissue of lean individuals. In addition, infiltration of macrophages and inflammation-related gene expression in adipose tissue may precede the development of insulin resistance. Insulin resistance in turn has been postulated to promote pro-inflammatory cytokine production (McLaughlin 2002). Adipose-derived hormones such as adiponectin and leptin are important in controlling energy homeostasis and glucose and lipid metabolism. Adiponectin, which is lowered with rising adiposity, is positively associated with insulin sensitivity and has anti-atherogenic properties that prevent the development of atherosclerotic plaques via inhibition of TNF-α production by macrophages. As for leptin, which may impair insulin action, it enhances inflammation by increasing the synthesis of TNF-α and IL-6. There is growing evidence to suggest that inflammation contributes to the development of metabolic syndrome in patients with schizophrenia (Na 2012). Both schizophrenia and obesity demonstrate a decrease in adiponectin and increase in leptin, with raised TNF-α and IL-6. This leads to inflammation, which ultimately confers higher risks of atherosclerosis and coronary artery disease.

Blood serum levels of CRP, TNF-α and homocysteine have been found to be increased in patients with schizophrenia (Hope 2009). C-reactive protein was found to have a positive association with waist circumference and diastolic blood pressure, while homocysteine has a positive association with waist circumference, systolic and diastolic blood pressure, triglycerides and glucose (Vuksan-Cusa 2012). Abnormal baseline levels of IL-6 were found to predict significantly greater elevations in both total cholesterol and low-density lipoprotein (LDL) following a 12-week treatment with olanzapine (Fernandez-Egea 2011). Total white blood cell count, one of the surrogate parameters of inflammation, has been found to be a risk factor for metabolic syndrome, its values positively correlating with the increase in waist circumference and glucose during a 24-week treatment with paliperidone (Na 2012).

**Lifestyle factors**

People with schizophrenia often have a more sedentary lifestyle, with little physical exercise, poor dietary habits and more smoking, all of which contribute to metabolic syndrome (Connolly 2005). These are partly attributed to negative symptoms of schizophrenia, lack of motivation, poor insight into their health, and sedation associated with antipsychotics. Smoking in particular has a negative effect on treatment, as it induces hepatic enzymes, thereby increasing metabolism of psychotropic medications. Thus, higher doses of antipsychotics may be required for smokers than for non-smokers.

**Antipsychotics**

Antipsychotics are the mainstay of management of schizophrenia: there is compelling evidence that they reduce morbidity, suicide and hospital admissions. Compared with first-generation antipsychotics, the second-generation drugs cause fewer extrapyramidal side-effects and offer better...
symptom control and cognitive and affective function. Their use has therefore increased. However, there is evidence that second-generation antipsychotics induce more weight gain than their predecessors, a finding especially pronounced for clozapine and olanzapine (Box 2).

**Antipsychotic-induced weight gain**

The prevalence of metabolic syndrome in patients with first-episode schizophrenia who have been treated with antipsychotics has been estimated at around 10% using the NCEP-ATP III criteria and 18% using the IDF criteria (the criteria are outlined in Table 1) (Saddichha 2008). A recent study has shown an increment of 29.3 points in body mass index (BMI) percentile for children and adolescents up to 16 years of age who were on risperidone for 6 months (Goeb 2010).

The proposed mechanism of antipsychotic-induced weight gain involves multiple pathways. Selective antagonism of antipsychotics at the 5-HT2C, H1 and D2 receptors is contributory. In fact, antagonism at serotonin 5-HT2C receptors increases insulin resistance and reduces glucose uptake by skeletal muscles, thereby heightening the risk of diabetes. Histamine H1 and H3 receptors are recognised as mediators of energy intake and expenditure, and histamine agonists are able to attenuate weight gain. Antipsychotics also have antihistaminergic properties, as they compete with histamine for binding sites on the H1 receptors, which leads to sedation and reduction in metabolism.

Twin studies have led to suggestions of genetic variability in antipsychotic-induced weight gain (Gebhardt 2010). Genetic variations have been proposed for the HTR2C gene, which encodes for 5-HT2C receptors. For example, a single nucleotide polymorphism (SNP) in the coding region 68G/C results in an amino acid substitution (Reynolds 2005). Polymorphisms have been found in other genes, such as the dopamine receptor D2 gene DRD2, brain-derived neurotrophic factor gene BDNF, and ADRA1A (Lee 2011).

Genetic variations involving the satiety pathways have also been implicated (Lee 2011). The leptin system regulates appetite and energy metabolism via the melanocortin system (alpha-melanocyte-stimulating hormone and agouti-related peptide) and neuropeptide Y. Polymorphisms in the leptin gene LEP and leptin receptor gene LEPR are associated with increased risk of developing metabolic syndrome.

Interestingly, clozapine has been found to alter the activity of the AMP-activated protein kinase–acetyl CoA carboxylase–carnitine palmitoyl transferase 1 pathway (the AMPK–ACC–CPT1 pathway) in the rat frontal cortex. This finding suggests that clozapine influences the lipid metabolic regulatory pathway via the central nervous system (Kim 2012). However, further study is necessary to characterise the physiological relevance in human models.

There is an increasing trend of combining different antipsychotics in treating patients with treatment-resistant schizophrenia. Correll et al. (2007) reported that the prescription of multiple antipsychotics was associated with a significant increase in the incidence of metabolic syndrome (50%) compared with antipsychotic monotherapy (34%). Conversely, the combination of clozapine and aripiprazole has been found to reduce triglyceride levels, LDL cholesterol, BMI and waist circumference, as well as negative symptoms, in patients with schizophrenia and metabolic syndrome (Fleischhacker 2010). This is probably because aripiprazole is a partial dopamine agonist that stimulates extracerebral presynaptic D2 receptors, which decreases sympathetic tone and anabolic effects, thereby reducing the risk of metabolic syndrome.

**Depressive disorder and metabolic syndrome**

Metabolic syndrome is associated with increased prevalence of depressive disorder and depressive symptoms, but not anxiety disorder or anxiety symptoms (Takeuchi 2009). The prevalence of metabolic syndrome in patients with depression ranges from 36 to 50%. The syndrome and its components, especially waist circumference, are predictive factors for the development of depressive disorder (Takeuchi 2009). Similarly, the number of components of metabolic syndrome is correlated with higher depression score on the Hospital Anxiety and Depression Scale (Skilton 2007). Capuron et al. (2008) found that depressive symptoms in patients with metabolic syndrome were predominantly neurovegetative (e.g. fatigue, anhedonia and loss of

**Box 2 Second-generation antipsychotics and metabolic syndrome**

Ranking on the basis of relative risk for development of metabolic syndrome:

1. Clozapine (highest risk)
2. Olanzapine
3. Quetiapine
4. Risperidone
5. Aripiprazole
6. Ziprasidone (lowest risk)
energy) and were less likely to be associated with affective and cognitive features.

**Interactive mechanisms**

The interaction between depressive disorder and metabolic syndrome is complex and is mediated by a number of factors. First, people with depression are less likely to abide by dietary restrictions and more likely to be physically inactive. They also tend to adopt unhealthy habits such as smoking and alcohol misuse. This behaviour contributes to obesity and subsequent insulin resistance (Attvall 1993; Wojciech 2007). The lack of exercise may also reduce serotonin synthesis, thus worsening depression. The psychological stress associated with the complications of metabolic syndrome may worsen depressive symptoms.

Second, the activation of the HPA axis increases plasma cortisol levels (Bjomtorp 2000). Chronic elevation of cortisol levels can lead to a pseudo-Cushing’s syndrome, which is characterised by increased visceral adiposity, hyperinsulinaemia, insulin resistance, hypertension and dyslipidaemia, all of which are hallmarks of metabolic syndrome.

Third, the chronic increase of insulin and leptin may activate the sympathetic nervous system. This can result in elevation of the circulating catecholamine level and subsequent faulty glucose metabolism and blood pressure regulation, and accumulation of abdominal fat (Musselman 1998; Anagnostis 2009).

Fourth, the increased levels of proinflammatory cytokines (Howren 2009) and leptin resistance (Patel 2008) found in patients with metabolic syndrome have been shown to be involved in depressive disorder.

Fifth, vascular endothelial dysfunction resulting from decreased levels of vascular endothelial growth factor, which is important in neurogenesis, and the mediating effects of inflammatory cytokines affect cerebral blood flow in distinct areas of the brain, increasing the risk of depressive disorder. Bench et al (1992) found that the severity of depressive mood and psychomotor retardation was inversely correlated with regional cerebral blood flow (rCBF) in the left dorsolateral prefrontal cortex and left angular gyrus. Conversely, the severity of anxiety, insomnia and agitation were positively correlated with bilateral rCBF in the posterior cingulate cortex and inferior parietal lobule.

**Antidepressants**

The use of antidepressants increases the incidence of metabolic syndrome among patients with depression. Tricyclic antidepressants can cause insulin resistance and hypertriglyceridaemia, and patients taking tricyclics such as amitriptyline and doxepin have been reported to experience substantial weight gain (Chokka 2006). Although second-generation antidepressants such as selective serotonin reuptake inhibitors (SSRIs) cause an initial reduction in weight, their long-term use causes weight gain (Chokka 2006). The risk of developing metabolic syndrome is further compounded by reduction in body metabolism in patients with depression. Nevertheless, a trial of 4-week reboxetine treatment demonstrated significant decrease in total cholesterol, LDL cholesterol, BMI and mean systolic blood pressure (Paslakis 2011). The authors suggested that these findings could possibly be attributed to the pharmacological profile of reboxetine in terms of its selective noradrenergic reuptake inhibition and lack of additional undesirable binding properties of other antidepressants (e.g. tricyclic antidepressants and H1-receptor antagonism) (Paslakis 2011). However, the study was limited by its small sample size, lack of control group and short duration of follow-up.

**Bipolar disorder and metabolic syndrome**

The relationship between metabolic syndrome and bipolar disorder has not been much studied, but it is increasingly recognised that patients with bipolar disorder have higher risk of the syndrome than the general population (Chi 2013). The prevalence of metabolic syndrome in bipolar disorder has been estimated to be between 25 and 27% (Lee 2010). The aetiological factors for metabolic disturbances in people with bipolar disorder are multifactorial. Dysregulation of the HPA axis with subsequent glucocorticoid resistance, impaired glucose tolerance and insulin resistance, dysregulation of the sympathetic nervous system, increased proinflammatory cytokine production across both phases of bipolar disorder (Kim 2007) and an unhealthy lifestyle are all implicated.

Several studies have reported that metabolic syndrome tends to be associated with certain characteristics of bipolar disorder (Chang 2009; McIntyre 2010):

- longer duration of bipolar disorder, especially type I
- more lifetime manic and depressive episodes
- more severe first affective episode
- late onset of first manic episode
- late age at first treatment for manic or depressive episode.

Metabolic syndrome appears to affect the course of bipolar disorder. Individuals with bipolar disorder who have diabetes mellitus are
more likely to experience rapid cycling, lower level of functioning and more psychiatric hospital admissions than those without diabetes mellitus (Ruzickova 2003). High rates of lifetime suicide attempts in patients with bipolar disorder and metabolic syndrome have also been reported (Fagiolini 2005).

The prevalence of metabolic syndrome in patients with type II bipolar disorder has been found to be lower than that in type I (Chi 2013). Several factors were postulated for this. For example, patients with hypomania are less likely to receive antipsychotics, and the variation in mood symptomatology may contribute to different degrees of metabolic disturbance. However, data regarding the impact of different mood states on metabolic profile are lacking.

**Mood stabilisers**

Mood stabilisers such as lithium and sodium valproate are first-line agents in the management of bipolar disorder, with augmentation by antipsychotics to achieve optimal mood control. Mood stabilisers, particularly lithium and sodium valproate, have been associated with metabolic syndrome. For example, divalproex, a valproic acid derivative, can cause insulin resistance and weight gain. The simultaneous treatment with mood stabilisers and antipsychotics or the concurrent use of two or three mood stabilisers is associated with significantly higher metabolic disturbances (Chang 2009).

**Cognitive decline, dementia and metabolic syndrome**

Metabolic syndrome is associated with cognitive decline, Alzheimer’s disease and vascular dementia. Elderly people with metabolic syndrome are more likely to develop cognitive impairment than those without the syndrome (Yaffe 2004). Common cognitive deficits that are linked to metabolic syndrome involve memory, visuospatial abilities, executive functioning, processing speed and overall intellectual functioning (Yates 2012). The relationship between metabolic syndrome and mild cognitive impairment (MCI) is less established, but likely to be complex. Roberts et al (2010) have proposed that it depends on the subtype of MCI and the extent of inflammation. For instance, patients with metabolic syndrome and high serum levels of CRP are more likely to develop non-amnestic MCI, not but the other subtypes.

The effects of metabolic syndrome on the brain, and thus on cognitive decline, include neuroinflammation, oxidative stress, impaired glucose metabolism and impairment of vascular reactivity (Yates 2012). In insulin resistance, there is excess production of proinflammatory cytokines such as IL-1β, IL-6 and TNF-α, of which IL-1β and IL-6 stimulate the over-expression of amyloid-β-precursor protein (AβPP) and deposition of amyloid-β in the brain. In turn, amyloid-β leads to further production of proinflammatory cytokines and worsens cognitive function in a vicious circle. Furthermore, these proinflammatory cytokines can accelerate atherosclerosis and potentially lead to irreversible structural brain changes and Alzheimer’s disease (de la Torre 2010), in addition to vascular dementia. It has been increasingly recognised that vascular factors may have a role in the development of Alzheimer’s disease. Impaired cerebrovascular reactivity with increased carotid stiffness and intima-media thickness has also been reported in metabolic syndrome (Koivistoinen 2009). These affect the cerebral blood flow, transportation of nutrients and clearance of metabolic waste, leading to disruptions of neuronal activities and possible progression to cognitive decline.

Interestingly, adiponectin, which is released from adipose tissue, has also been found to be related to cognitive function in several studies. Une et al (2011) discovered that plasma adiponectin was significantly higher in individuals with MCI or Alzheimer’s disease than in normal controls, whereas cerebrospinal fluid adiponectin was significantly higher in those with MCI. Furthermore, the Framingham Heart Study revealed that high plasma levels of adiponectin were a risk factor for all-cause dementia and Alzheimer’s disease in women (van Himbergen 2012).

These findings contradict the commonly accepted belief that a high level of plasma adiponectin is protective of metabolic and cardiovascular functioning. Nevertheless, it is important to note that the renal clearance of adiponectin in the elderly is lower than in younger adults. Thus, plasma adiponectin levels in elderly people should be interpreted with caution. In light of the above evidence, modification of diet and lifestyle as well as appropriate pharmacotherapy for hypertension, dyslipidaemia and hyperglycaemia have important implications in the prevention and treatment of Alzheimer’s disease.

**Other psychiatric disorders and metabolic syndrome**

**Post-traumatic stress disorder**

Post-traumatic stress disorder (PTSD) is associated with cardiovascular risk factors such as hypertension, diabetes and obesity, and chronic and more severe PTSD may be associated with
higher risk of metabolic syndrome (Heppner 2012). Stress-related dysregulation of glucose and lipid metabolism in PTSD can also lead to the development of metabolic syndrome.

**Binge eating disorder**

The reported prevalence of metabolic syndrome in obese individuals with binge eating disorder is between 50 and 60%. Binge eating is associated with excess insulin secretion, impaired fasting glucose and glucose tolerance, and elevated serum lipid levels (Taylor 1999). Bulimia nervosa, which has features of binge eating, is also closely related to the severity of obesity. Furthermore, in obese patients rapid eating is associated with increased serum cholesterol and triglycerides, higher waist/hip circumference ratio and fatty liver (Kral 2001).

**Borderline personality disorder**

The prevalence of metabolic syndrome among people with borderline personality disorder is twice that in primary care patients (Kahl 2013). The increased rate is associated with older age, higher BMI, second-generation antipsychotics, benzodiazepine dependency and binge eating behaviour. Hyperglycaemia is more common in both genders, with central obesity and hypertriglyceridaemia more common in women.

Several aetiologies of the associations between metabolic syndrome and borderline personality disorder have been postulated. Dysregulation of the HPA system has been demonstrated in several studies to result in hypercortisolism, imbalance of pro- and anti-inflammatory cytokines, and lowered feedback sensitivity, with or without major depressive disorder (Kahl 2006; Purnell 2009). Reasons for this phenomenon were not well elucidated, although increased cortisol in people with borderline personality disorder might result from their recurrent state of severe inner stress and tension. Unhealthy lifestyle, comorbid psychiatric conditions and use of psychotropic drugs have also been implicated in metabolic syndrome in this group.

**Alcohol**

Alcohol can either encourage or prevent metabolic syndrome and this is very much dependent on the amount and type of alcohol consumed (Wójcick 2007). Moderate alcohol consumption, in particular red wine, is associated with decreased incidence of metabolic syndrome, with beneficial effects on plasma lipid and glucose levels and waist circumference. This is due to the polyphenols in red wine, which increase the activity of endothelial nitric oxide synthase (eNOS). Decreased activity of eNOS can contribute to hypertension, insulin resistance and dyslipidaemia. In those who misuse alcohol, the distinct disturbances of carbohydrate and lipid metabolism can result in increased risk of hypertension, impaired fasting glucose, high triglyceridaemia and abdominal obesity.

Heavy alcohol consumption is associated with serious health problems, including malnutrition, cardiovascular disease, chronic pancreatitis, cognitive impairment and damage to almost every organ system in the body. When associated with alcoholism, it can also coexist with, contribute to or result from several different psychiatric disorders. It is of particular concern in countries where easy accessibility of alcohol and an accepting and prevalent ‘drinking culture’ facilitate excessive consumption.

Psychiatric disorders commonly associated with alcoholism include major depression, bipolar disorder, schizophrenia, anxiety disorders and personality disorders. It also increases risk of suicide and violence.

**Choosing a psychotropic medication**

The initial selection of a drug to treat a particular psychiatric disorder is important and should be based on risk–benefit profile. Changing medications later in an attempt to reverse metabolic abnormalities may lead to relapse of psychiatric symptoms. This is especially true when the patient has already experienced good clinical response to the prevailing drug regimen. Thus, it is necessary to weigh the benefits and risks of each medication before switching. For example, if the patient has pre-existing metabolic syndrome first-generation antipsychotics should be considered for schizophrenia, given that their metabolic risk profile is more favourable than that of the second-generation drugs. Saddichha et al (2008) recommend that treatment be started with a second-generation drug for a limited period (e.g. 6 weeks) and switched to a first-generation alternative when the risk of developing metabolic syndrome is high.

The data demonstrate an increased incidence of metabolic syndrome in individuals treated with multiple psychotropic drugs, so the combination of psychotropic medications should also be based on careful risk–benefit analysis.

**Screening for metabolic syndrome**

In focusing on the psychiatric needs of their patients, mental health professionals may not address the increased risk of metabolic syndrome, particularly in people receiving long-term antipsychotics. There is little information for
Common signs of metabolic syndrome are illustrated in Fig. 1. Weight gain, especially central obesity, is the most noticeable sign of possible metabolic syndrome. Thus, the quickest and easiest way to identify patients at risk is to measure the waist circumference.

All patients who come to the clinic for follow-up should routinely have their blood pressure and pulse rate measured.

Biological parameters provide an objective indication of the progress of metabolic syndrome. Besides checking fasting blood glucose level, early identification of raised LDL levels among psychiatric patients was recommended by Christoph et al (2006). For psychiatric patients with metabolic syndrome, a target LDL level less than 130 mg/dl is recommended. For those with other comorbid conditions, such as diabetes mellitus, coronary artery disease, abdominal aortic aneurysm and peripheral artery diseases, the recommended target is lower than 100 mg/dl.

It is recommended that alanine aminotransferase (ALT) and γ-glutamyltransferase (GGT) are measured before initiating psychotropic drugs, as this may identify patients with potential risk of developing fatty liver disease and liver damage (Lee 2004; Park 2004). Furthermore, ALT is a predictor for mortality as a result of unrecognised liver disease, and elevated GGT levels are associated with diabetes mellitus, insulin resistance, alcoholism and cardiovascular disease.

**TABLE 2** Monitoring schedule for metabolic syndrome in patients with chronic psychiatric illnesses

<table>
<thead>
<tr>
<th>Time</th>
<th>Recommended steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1 History: include previous cardiovascular diseases, family history, smoking, frequency and type of exercise, and dietary habits 2 Physical examination: include blood pressure, weight, waist circumference and body mass index 3 Laboratory tests: include fasting glucose, fasting lipids, total cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides (TG), alanine aminotransferase (ALT) and γ-glutamyltransferase (GGT) 4 Psychoeducation: include advice on smoking cessation, careful food choices and physical activity 5 Choice of psychotropic medication: should be based on the cardiometabolic risk profile of each medication 6 Referral: refer to a primary care physician or specialist if there is at least one abnormal finding at step 2 and/or three abnormal results at step 3</td>
</tr>
<tr>
<td>Week 6</td>
<td>Repeat steps 2, 3 and 4 Monitor consumption of alcohol and cigarettes Review the choice of psychotropic drugs in patients with more than 7% increase in body weight</td>
</tr>
<tr>
<td>Week 12</td>
<td>Repeat steps 2, 3 and 4 Monitor consumption of alcohol and cigarettes</td>
</tr>
<tr>
<td>Week 52</td>
<td>Repeat steps 2, 3 and 4 Monitor consumption of alcohol and cigarettes</td>
</tr>
<tr>
<td>After 1 year</td>
<td>If all the laboratory results are within normal ranges, repeat steps 2, 3 and 4 annually</td>
</tr>
</tbody>
</table>

Sources: de Hert, 2009; Oh, 2011.

**FIG 1** Physical examination of a psychiatric patient presenting with metabolic syndrome.
**Novel biomarkers**

Other novel potential biomarkers for metabolic syndrome, such as high-sensitivity CRP (hsCRP), homocysteine and serum uric acid, have been investigated. The role and association of CRP and homocysteine with metabolic syndrome have been explained earlier. Increased serum uric acid is associated with systemic inflammation, endothelial dysfunction, hypertension and cardiovascular diseases. Simultaneously high serum uric acid and hsCRP levels significantly associate with metabolic syndrome independent of other confounding factors. Thus, the use of these potential biomarkers as routine tests for risk stratification of metabolic syndrome in psychiatric patients should be further evaluated.

**Treatment of metabolic syndrome**

**Lifestyle modification, psychoeducation and self-help groups**

Psychiatrists need to promote healthy lifestyle practices in patients with metabolic syndrome. General recommendations for managing the syndrome are summarised in Box 3. Patients need to be educated about their psychiatric illness and medication, as this is important in enhancing medication adherence and relapse prevention.

If simple advice to eat a balanced diet and take regular exercise is insufficient, patients can be referred to dieticians and weight management specialists for more detailed dietary and exercise advice to help them lose weight. Ideally, patients should have access to holistic well-being programmes that bring these services together. Engaging patients in support groups (e.g. for smoking cessation) can provide patients with additional support. Cognitive–behavioural therapy can be used to modify negative health-related beliefs and behaviours that may be detrimental to health, such as alcohol misuse and cigarette smoking.

**Pharmacological intervention**

The mainstay of pharmacological management of metabolic syndrome is to treat the particular component of the syndrome that is impaired. For hypertension, dyslipidaemia and diabetes, the use of antihypertensive, cholesterol-lowering and diabetic medications is indicated respectively. Such patients should be referred to primary care physicians or appropriate specialists (if there are multiple comorbidities or complications) for continued follow-up and treatment as necessary.

It is important to be mindful of the potential interactions between these drugs and psychotropic medication, which may complicate treatment. For instance, the use of an angiotensin-converting enzyme (ACE) inhibitor to treat hypertension is contraindicated in a patient on lithium, as it can potentiate lithium toxicity. Selective serotonin reuptake inhibitors may increase risk of bleeding in a patient taking warfarin for heart treatment. In addition, some psychotropic medications can worsen control of metabolic syndrome. For example, venlafaxine can increase blood pressure and mirtazapine can increase appetite.

**Weight-loss drugs**

A number of studies have been performed to assess various drugs on their propensity for weight reduction. A meta-analysis of 32 randomised controlled trials that focused on pharmacological intervention for weight loss in antipsychotic-induced weight gain revealed the following order of efficacy, from most to least efficacious: metformin, p-fenfluramine, sibutramine, topiramate, reboxetine, amantadine, nizatidine, orlistat, metformin plus sibutramine, famotidine, dextroamphetamine, fluoxetine, rosiglitazone (Maayan 2010).

**Metformin**

This biguanide, with a dual mechanism of decreasing body weight gain and improving insulin sensitivity, is most efficacious in promoting weight loss in patients with antipsychotic-induced weight gain (McIntyre 2012). Patients with olanzapine-induced weight gain achieved a weight reduction of 5% after metformin treatment (Praharaj 2011). However, metformin seems to be effective only in reducing weight gain once it
has occurred – it does not prevent weight gain if started concomitantly with antipsychotics (Papanastasiou 2012). Although these studies have provided encouraging preliminary evidence on the potential use of metformin in promoting weight loss and improving insulin resistance induced by antipsychotics, further large randomised, placebo-controlled studies are needed to evaluate its use.

**Topiramate** The anti-epileptic topiramate may be helpful in nocturnal eating syndrome and sleep-related eating disorder (McElroy 2009). Its anti-hinge eating and anti-purging effects are particularly useful in patients with binge eating disorders.

**Bupropion plus naltrexone** Another potential treatment is the combination of bupropion and naltrexone. Combined, their mode of action is related to the modulation of hypothalamic pro-opiomelanocortin (POMC) neurons and the mesolimbic pathway, both of which are important in regulation of food intake and body weight (McIntyre 2012).

**Novel drugs** New drugs have been used in the treatment of metabolic syndrome. Endogenous incretins including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotrophic peptide (GIP) regulate insulin secretion (Nauck 2011). As GLP-1 is degraded by dipeptidyl peptidase-4 (DPP-4), DPP-4 inhibitors and synthetic GLP-1 analogs form the basis of incretin-based therapies for type 2 diabetes mellitus. Glucagon-like peptide-1 (GLP-1) analogues such as exenatide and liraglutide are associated with modest reductions in body weight and blood pressure in metabolic syndrome. Thus, it would be worthwhile evaluating these drugs for their safety and efficacy in the management of metabolic syndrome in psychiatric patients.

**Surgical intervention**

Bariatric surgery1 is recommended for severely obese individuals who have a BMI between 35 and 39 and more than one obesity-associated comorbidity, or a BMI >40 without medical comorbidity (Blackburn 2009). It should be noted that surgery reduces the transit time and surface area for absorption of drugs in the gastrointestinal tract, and these postoperative effects on the pharmacokinetics of psychotropic drugs have yet to be investigated in depth.

**Conclusions**

The bidirectional interplay between metabolic syndrome and psychiatric disorders, which involves genetic, pharmacological, inflammatory, endocrinological and behavioural factors, is complex and clinically challenging. Screening, judicious detection and management of metabolic disturbances in psychiatric patients are of paramount importance. It is crucial to recognise and treat metabolic syndrome, as the constellation of symptoms is associated not only with an elevated cardiovascular risk, but also with a higher prevalence of psychotic and depressive symptoms, poor perceived physical health and lower adherence to medications.

Psychiatric patients with metabolic syndrome should ideally be attended by a multidisciplinary team consisting of medical specialists, psychiatrists and dieters, and the patients should assume an active role in their own care. The challenge lies in engaging such patients, who can be more susceptible to impulsivity, risky health behaviour and sedentary lifestyle. Future research is required to develop psychotropic drugs that have lower risk of metabolic syndrome and to evaluate the efficacy and safety of pharmacological agents such as metformin and GLP-1 agonists in treating the syndrome in psychiatric patients.

**References**


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Bipolar Disorder, factor receptor I and von Willebrand factor.


MCQs
Select the single best option for each question stem

1 Which of the following is least likely to be measured in people with severe mental illness?
   a Blood pressure
   b Glucose
   c Lipids
   d Weight
   e None of the above.

2 In bipolar disorder, metabolic syndrome tends to be associated with:
   a early age at first treatment for the affective episode
   b early onset of first manic episode
   c less severe first affective episode
   d more lifetime affective episodes
   e shorter duration of bipolar disorder, especially type II.

3 When a psychiatric patient presents with metabolic syndrome, it is inappropriate to:
   a consider adjusting the psychotropic medication according to its cardiometabolic risk profile and psychiatric condition
   b engage the patient in support groups to increase their motivation to lose weight
   c immediately refer patient to a specialist to manage the metabolic syndrome
   d involve family members early in the treatment
   e educate the patient about healthy lifestyle habits and diet.

4 The possible mechanisms that metabolic syndrome contributes to dementia include:
   a impaired cerebrovascular reactivity
   b impaired glucose metabolism
   c neuroinflammation
   d oxidative stress
   e all of the above.

5 Triglyceride and LDL cholesterol levels in patients with schizophrenia and metabolic syndrome can be reduced by a combination of clozapine and:
   a aripiprazole
   b fluoxetine
   c lithium
   d methylphenidate
   e quetiapine.
Chinese translation of:
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Cyrus S. H. Ho, Melvyn W. B. Zhang, Anselm Mak & Roger C. M. Ho

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精神科中的代谢综合征：认识与处理的进展

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摘要
代谢综合征与许多心血管危险因素有关，从而增加了病残病死率。最近的研究表明，代谢综合征在精神科病人中的发病率在增加，而且代谢综合征成为了精神科处理中的挑战之一。除了治疗精神病的药物，诸如基因多态性、感染、内分泌疾病和不健康的生活方式等因素也加强了代谢综合征和精神科疾病之间的联系。在这篇文章中，我们回顾了当前对于代谢综合征的诊断情况，并推荐了实用的临床指南以帮助精神科医生识别和处理那些可能患有代谢综合征的病人。我们也概述了代谢综合征和各个精神科疾病之间的联系，并探讨了代谢综合征药物治疗（比如二甲双胍）的研究进展。

学习目标
- 熟悉代谢综合征的定义及其测量指标。
- 认识各个精神科疾病与代谢综合征的相互作用。
- 明确精神科病人中代谢综合征的预防、筛查和处理的框架体系。

利益关系声明
没有。

代谢综合征是一个重要的公共健康问题，并被世界卫生组织认为是一个全球性问题(Potena 2009)。它由临床表现和实验室检验结果确定，包含 5 个主要特征：向心性肥胖，高血压，高甘油三酯血症，偏低的高密度脂蛋白和偏高的空腹血糖。一般认为，符合这 5 个特征中的至少 3 个就可以认为病人患有代谢综合征(Grundy 2004)。然而，其普遍使用的

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定义主要关注于腰围（向心性肥胖的代理指标）或是胰岛素抵抗性（表 1）--- 这些指标在不同的种族中有不同的标准。

达成一个代谢综合征的统一定义很有难度, 许多主要的国际学术团体曾聚集到一起探讨统一诊断标准的问题(Alberti 2009; Kassi 2011)。探讨的结果是，所有的这 5 个特征对于代谢综合征的风险预测都是非常重要的，但没有哪个固定的特征是代谢综合征必须具备的。这 5 个特征是预测冠心病、脑血管疾病和糖尿病的独立危险因素。

病率

代谢综合征影响到世界人口的 20-25%，并且其增加了 2 倍的死亡风险和增加了 3 倍的心脏病或中风风险 （国际糖尿病联盟 2006）。代谢综合征巨大地影响到了患者及其家人的经济、情感和社会心理健康。代谢综合征也增加了患有精神科疾病（比如抑郁症）的机率，从而降低了生活质量。另外，长期的精神疾病也会促成代谢综合征的发病：患有严重精神疾病的病人中的代谢综合征的患病率比一般人群高出 2-3 倍(Holt 2010)。

病因学

精神科病人中代谢综合征的病因很可能是多因素的(Grundy 2004)。精神病治疗药物（比如二代抗精神病药和情绪稳定剂）是明确的危险因素。不良的生活习惯，比如吸烟、过度饮酒、缺少锻炼和不健康饮食，也会加剧病情。另外，生理因素，比如下丘脑-垂体-肾上腺轴系统失调和胰岛素抵抗，也会影响病情。感染被认为是代谢综合征和精神疾病的共同因素之一(Hope 2009; Na 2012)，在两种情况中均可见血清 C 反应蛋白和促炎细胞因子（比如白介素-6 和肿瘤坏死因子 -α）。遗传因素，比如带有代谢综合征的易感基因和瘦素-黑皮质激素的变异（这导致了抗精神病药物所致体重增加的异质性），也是产生代谢综合征的重要原因。
表 1 代谢综合征的诊断标准

<table>
<thead>
<tr>
<th>诊断标准</th>
<th>世界卫生组织</th>
<th>国际糖尿病联盟</th>
<th>欧洲胰岛素抵抗研究组</th>
<th>美国国家胆固醇教育计划成人治疗组 III</th>
</tr>
</thead>
<tbody>
<tr>
<td>糖尿病</td>
<td>向心性肥胖</td>
<td>胰岛素抵抗</td>
<td>至少两条：</td>
<td>至少两条：</td>
</tr>
<tr>
<td>加上</td>
<td>加上</td>
<td>加上</td>
<td>向心性肥胖</td>
<td>腰/臀比 &gt; 0.90（男）， &gt; 0.85（女）</td>
</tr>
<tr>
<td>最少两条：</td>
<td>腰围：≥94cm</td>
<td>至少两条</td>
<td>至少两条：</td>
<td>至少两条：</td>
</tr>
<tr>
<td>向心性肥胖</td>
<td>腰/臀比 &gt; 0.90（男）， &gt; 0.85（女）</td>
<td>腰围：≥80cm</td>
<td>腰围：≥88cm（女）</td>
<td>腰围：≥102cm（男）</td>
</tr>
<tr>
<td>腰围</td>
<td>0.85（女）或身体质量指数&gt;30kg/m²</td>
<td>≥94cm</td>
<td>指数&gt;30kg/m²</td>
<td>≥88cm（女）</td>
</tr>
<tr>
<td>甘油三酯</td>
<td>≥1.7 mmol/l</td>
<td>≥1.7 mmol/l, 或者在进行针对血脂异常的治疗</td>
<td>≥2.0 mmol/l, 或者在进行针对血脂异常的治疗</td>
<td>&gt; 1.7 mmol/l</td>
</tr>
<tr>
<td>高密度脂蛋白</td>
<td>&lt;0.9 mmol/l (男), &lt;1.04 mmol/l (男), &lt;1.0 mmol/l</td>
<td>&lt;1.04 mmol/l (男), &lt;1.29 mmol/l (女)</td>
<td>&lt;1.0 mmol/l (男), &lt;1.29 mmol/l (女)</td>
<td>&lt;1.0 mmol/l (男), &lt;1.29 mmol/l (女)</td>
</tr>
<tr>
<td>血压</td>
<td>≥140/90 mmHg</td>
<td>收缩压&gt;130或舒张压&gt;85 mmHg, 或者在进行抗高血压治疗</td>
<td>≥140/90 mmHg, &gt;130/85 mmHg</td>
<td>≥140/90 mmHg, &gt;130/85 mmHg</td>
</tr>
<tr>
<td>空腹血糖</td>
<td>受损</td>
<td>≥5.6 mmol/l, 或者在前被诊断为2型糖尿病</td>
<td>≥6.1 mmol/l</td>
<td>&gt; 6.1 mmol/l</td>
</tr>
<tr>
<td>尿白蛋白</td>
<td>排泄率 ≥ 20µg/min, 不包括</td>
<td>不包括</td>
<td>不包括</td>
<td>不包括</td>
</tr>
<tr>
<td></td>
<td>或白蛋白/肌酐比率 ≥30 mg/g</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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来源：Bloomgarden (2004)

格 1 慢性精神病患者中代谢综合征的常见危险因素

- 过度饮酒
- 食物失衡和不良饮食习惯
- 遗传易感性
- 包括皮质激素和瘦素的激素失衡
- 二代抗精神病药物及其相关副作用
- 久坐的生活方式

代谢综合征和精神科疾病的关系非常复杂，而且很可能是很多因素混杂在一起。尽管如此，这篇会尝试阐述这两种疾病的可能机制及处理策略。

精神分裂症和代谢综合征

流行病学

代谢综合征在精神分裂症患者中较常见，患病率估计在8.9%到68%之间。这么大的估计范围可能是因为不同的研究者研究了不同的年龄段和不同的种族，以及使用了不同的诊断标准(McEvoy 2005)。尽管如此，精神分裂症患者中代谢综合征的患病率仍是普通人群的5倍。与男性患者相比，女性患者有更高的风险患上代谢综合征(McEvoy 2005)。精神分裂症患者的死亡率是普通人群的2-3倍，这主要是因为心血管并发症(Koponen 2010)。

精神分裂症患者有更高的风险患上糖尿病，其患病率是普通人群的2-3倍(de Hert 2009)。这个患病率的增加与抗精神病药物的使用是独立的。与对照组相比，未使用抗精神病药物的患者患有更多的胰岛素抵抗、血糖耐受不良和更高的腹内脂肪堆积(Papanastasiu 2012)。另
外，精神分裂症患者的兄弟姐妹有更多的血糖不耐受(Fernandez-Egea 2008a)，且那些非情感性精神病患者有更高的2型糖尿病患病率(Fernandez-Egea 2008b)。这些研究结果表明，代谢异常很可能是精神分裂症的固有表现，其带有生理性遗传倾向的倾向因素。

**常见遗传因素**

研究表明，代谢综合征和精神分裂症可能存在共同的遗传倾向因素。一个2型糖尿病风险等位基因，rs7903146，在转录因子TCF7L2基因上被发现，这一基因型也与精神分裂症的较高发病风险有关(Hansen 2011)。也有研究表明，精神分裂症患者中体重增加和基因多样性有关。比如，ADRA1A基因与心血管风险（诸如肥胖和高血压）有关，代谢综合征的累积患病率与ADRA1A基因上的Arg347等位基因有关(Cheng 2012)。

**慢性炎症**

许多研究表明慢性亚临床炎症是代谢综合征的一部分(Newcomer 2007)。虽然炎症标记物当前还没有列入代谢综合征的诊断标准，但是它们之间存在联系，尤其是在内脏脂肪中存在的CRP、TNF-α，IL-6，脂联素和瘦素(Sutherland 2004)。与较瘦的人群相比，肥胖病人的脂肪组织分泌较高的炎症因子。另外，脂肪组织中巨噬细胞的浸润和炎症相关基因的表达可能发生在胰岛素抵抗之前。据推测，胰岛素抵抗又反过来促进了促炎细胞因子的产生(McLaughlin 2002)。与脂肪相关的激素，比如脂联素和瘦素，在控制能量内稳态和糖类脂肪代谢方面有很大的作用。脂联素在脂肪过多的时候会降低，它与胰岛素敏感性存在正相关性而且有抗动脉粥样硬化的作用，这个作用会通过巨噬细胞抑制TNF-α的途径阻止动脉粥样硬化斑块的形成。对于影响胰岛素功能的瘦素，它会通过增加TNF-α和IL-6的合成而促进炎症的发生。越来越多的证据表明，炎症加剧了精神分裂症患者中代谢综合征的发生(Na 2012)。精神分裂症和肥胖都表现出脂联素的增加和瘦素的下降。与较高的TNF-α和IL-6。这导致了炎症的形成，从而最终使得患上动脉粥样硬化和冠心病的风险增加。

精神分裂症患者的CRP、TNF-α和同型半胱氨酸的血清浓度都有升高(Hope 2009)。C反应蛋白被发现与腰围和舒张血压存在正相关；同型半胱氨酸则与腰围、收缩和舒张血压、甘油三酯和血糖存在正相关(Vuksan-Cusa 2012)。在奥氮平治疗12周后，异常的IL-6初始浓度被发现能显著预测总胆固醇和低密度脂蛋白的升高(Fernandez-Egea 2011)。作为炎症衡量的一个指标，白细胞浓度也被表明是代谢综合征的一个危险因素。在多个使用帕潘立酮治疗24周的研究中，白细胞浓度被表明与腰围和血糖的升高存在正相关(Na 2012)。

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生活方式

精神分裂症患者常常有久坐的生活习惯，缺少身体锻炼，有不良的饮食习惯，而且经常吸烟。所有这些都会导致代谢综合征的发生(Connolly 2005)。这些不良生活方式有部分原因在于精神分裂症的阴性症状，积极性缺失，对自身健康的不良认识和抗精神病药物的镇静作用。吸烟尤其会对治疗产生不良影响，因为它会诱导肝酶，从而增加精神病药物的代谢。因此，与不吸烟者相比，吸烟者可能需要较高剂量的抗精神病药物。

抗精神病药物

抗精神病药是治疗精神分裂症的主要方式。强有力的证据表明抗精神病药能减少病态、自杀和住院率。与一代抗精神病药相比，二代抗精神病药产生的锥体外系副反应较少，提供了更好的控制症状的效果，也有更好的针对认知和情感的功能。因此，它们的使用量得到了提升。然而，有证据表明二代抗精神病药物导致了更多的体重增加，尤其是氯氮平和奥氮平（格2）。

格2  二代抗精神病药和代谢综合征

根据发生代谢综合征的相对风险高低排序：
1 氯氮平 （最高风险）
2 奥氮平
3 奎硫平
4 利培酮
5 阿立哌唑
6 齐拉西酮 （最低风险）

抗精神病药诱发的体重增加
在使用抗精神病药治疗精神分裂症首次发作的患者中，代谢综合征的患病率被估计在10%（使用美国国家胆固醇教育计划成人治疗组 III 标准）和 18%（使用国际糖尿病联盟标准）（这些诊断标准请参见表1）（Saddichha 2008）。在一个最近的对于 16 岁以下的儿童和青少年的研究中，研究者发现这些人群在使用了 6 个月的利培酮之后，其身体质量指数增加了 29.3 个百分点（Goeb 2010）。

当前所推荐的抗精神病药物诱导体重增加的机制包含多种途径。抗精神病药对于 5-HT_{2C}、H_{1} 和 D_{2} 受体的选择性拮抗作用在其中起了一定作用。事实上，对于 5-HT_{2C} 受体的拮抗作用增加了胰岛素抵抗和减少了骨骼肌对糖类的摄取，从而增加了患糖尿病的风险。组织胺受体 H_{1} 和 H_{3} 被认为是能量摄入和消耗的调节者，组织胺受体激动剂能减弱体重增加。抗精神病药有抗组织胺的特性，因为它们能与组织胺竞争 H_{1} 受体的结合点。这导致了镇静作用和代谢减缓。

双胞胎研究提示，基因多样性在抗精神病药诱导的体重增加起一定的作用（Gebhardt 2010）。相关的基因变异被发现是在编码 5-HT_{2C} 受体的 HTR2C 基因上。比如，在 68G/C 编码区的一个单核苷酸多态性导致了氨基酸置换（Reynolds 2005）。基因多态性也被发现存在于其它基因上，比如多巴胺受体 D_{2} 基因 DRD2、NDNF 基因和 ADRA1A 基因（Lee 2011）。

与饱感通路相关的基因变异也与体重增加有关（Lee 2011）。瘦素系统通过黑皮质素系统和神经肽 Y 调节食欲和能量代谢。瘦素基因 LEPR 和瘦素受体基因 LEP 的多态性也与代谢综合征的风险增加有关。

令人感兴趣的是，氯氮平被发现在小鼠的额叶皮质中能改变 AMPK-ACC-CPT1 通路（腺苷磷酸激活的蛋白激酶 - 乙酰辅酶 A 羧化酶 - 肉毒碱棕榈酰转移酶 1 通路）。这一发现提示氯氮平通过中央神经系统影响脂类代谢的调节通路（Kim 2012）。然而，这需要进一步的研究以明确在人类模型上的生理相关特性。

联合使用不同的抗精神病药来治疗难治性精神分裂症越来越成为一种趋势。Correll 等人（2007）报导，与抗精神病药的单药疗法中代谢综合征的发病率（34%）相比，多药联合使用显著增加了代谢综合征的发病率（50%）。相反地，在患有精神分裂症和代谢综合征的患者中联合使用氯氮平和阿立哌唑能降低甘油三酯水平、低密度脂蛋白水平、身体质量指数、腰围和阴性症状（Fleischhacker 2010）。这可能是因为阿立哌唑是激活脑外突触前 D2 受体的多巴胺部分拮抗剂，其降低了交感神经张力和合成代谢效果，从而降低了代谢综合征的风险。
抑郁症和代谢综合征

代谢综合征与抑郁症及其症状的增加有关，而与焦虑症或焦虑症状无关(Takeuchi 2009)。在抑郁症患者中代谢综合征患病率在36%到50%之间。代谢综合征及其症状，尤其是腰围，是抑郁症发病的预测因素(Takeuchi 2009)。符合代谢综合症诊断标准的条数也与医院焦虑抑郁量表的较高得分有关(Skilton 2007)。Capuron 等人(2008)发现代谢综合征患者的抑郁症状主要是植物性神经系统的表现（比如，疲劳、兴趣缺失、精力减退）并很少带有情感和认知方面的特性。

相互作用机制

抑郁症和代谢综合征之间的相互作用非常复杂，并且受到许多因素的调节。首先，抑郁症患者倾向于不遵守饮食限制且很少有身体活动。他们也更易染上不良习惯，比如吸烟喝酒。这些行为导致了肥胖及随后的胰岛素抵抗(Attvall 1993; Wojciech 2007)。运动的缺少也会降低5-羟色胺的合成，从而加剧抑郁症。与代谢综合征有关的心理上的压力也可能会使抑郁症症状恶化。

第二，HPA 轴的激活增加了血浆皮质醇激素的浓度(Bjomtorp 2000)。慢性皮质醇激素的升高会导致假性库欣综合征。假性库欣综合征表现为内脏脂肪过多、高胰岛素血症、胰岛素抵抗、高血压和血脂异常，这些都是代谢综合征的标志。

第三，慢性的胰岛素和瘦素的增加可能会激活交感神经系统。这会导致循环中儿茶酚胺的增加，及随后的糖类代谢和血压调节异常和腹部脂肪堆积(Musselman 1998; Anagnostis 2009)。

第四，代谢综合征患者中升高的促炎细胞因子(Howren 2009)和瘦素抵抗(Patel 2008)被发现与抑郁症有关。

第五，血管内皮细胞生长因子(其对于神经形成很重要)水平的降低导致的血管内皮细胞的功能失常和炎症细胞因子的调节作用会影响到大脑不同区域的血流，从而增加抑郁症的风险。Bench 等人(1992)发现抑郁情绪和精神心理的严重程度与左背外侧前额叶皮质和左侧角回的局部大脑血流呈反向相关性。相反地，焦虑、失眠和烦躁的严重程度与后扣带回和下顶叶的双侧局部大脑血流呈正向相关性。

抗抑郁药
抗抑郁药的使用增加了抑郁症患者代谢综合征的发病率。三环类抗抑郁药会导致胰岛素抵抗和高甘油三酯血症，而且也有报道说服用诸如阿米替林和多虑平之类的三环类抗抑郁药的病人遭受到了严重的体重增加（Chokka 2006）。虽然二代抗抑郁药（比如选择性 5 羟色胺再摄取抑制剂）最初会导致体重下降，但是它们的长期使用会导致体重增加（Chokka 2006）。抑郁症患者中身体代谢减少也增加了代谢综合症的患病风险。然而，一个关于瑞波西汀的 4 周治疗试验表明，这一治疗显著降低了总胆固醇、低密度酯蛋白、身体质量指数和平均收缩压（Paslakis 2011）。作者提出这一结果可能是由于瑞波西汀的药理学特性，因为其有选择性去甲肾上腺素再摄取抑制的特性，而没有其它副作用（比如三环类抗抑郁药和抗组胺受体拮抗剂的副作用）（Paslakis 2011）。然而，这个研究受到小样本量、对照组缺失和随访时间短的限制。

双相情感障碍和代谢综合征

代谢综合征和双相情感障碍之间的关系没有得到很大研究，但是双相情感障碍患者有更高的风险患上代谢综合征的事实被越来越多的认识到 (Chi 2013)。双相情感障碍患者中代谢综合征的患病率被估计在 25% 到 27% 之间 (Lee 2010)。双相情感障碍患者中代谢综合征的病因机制是多因素的。下丘脑垂体肾上腺轴的失调，及随后的糖皮质激素抵抗、糖耐量受损和胰岛素抵抗、交感神经系统失调、促炎因子的过度产生（Kim 207）和不健康的生活方式都与代谢综合征的发病有关。

一些研究表明，代谢综合征倾向于和双相情感障碍的特定表现有关 (Chang 2009, McIntyre 2010):
- 较长的双相情感障碍（尤其是 I 型）发病时间
- 更多的躁狂和抑郁发作
- 更严重的首次情感障碍发作
- 首次躁狂发作的时间较晚
- 患者首次躁狂或抑郁发作的治疗年龄较大

代谢综合征似乎会影响到双相情感障碍的发病进程。与没有糖尿病的双相情感障碍患者相比，患有糖尿病的患者更易于经历快速循环型双相情感障碍，更低的社会功能水平和更多的住院率（Ruzickova 2003）。也有报道表明患有双相情感障碍和代谢综合征的患者有较高的
自杀意向（Fagiolini 2005）。

与 I 型双相情感障碍相比，II 型双相情感患者中的代谢综合征患病率较高（Chi 2013）。一些因素被推测与之有关。比如，轻躁狂患者不太可能服用抗精神病药，而且不同类型的情感障碍表现也会导致不同的代谢障碍。然而，不同类型的情感状态对于代谢的影响的研究数据还是缺失的。

心境稳定剂

心境稳定剂（比如碳酸锂和丙戊酸盐），及其结合抗精神病药的增加效果，是治疗双相情感障碍的一线药物。心境稳定剂，尤其是碳酸锂和丙戊酸盐，与代谢综合征相关。比如，作为丙戊酸盐衍生物的双丙戊酸钠会导致胰岛素抵抗和体重增加。心境稳定剂和抗精神病药的使用，或两到三种心境稳定剂的使用，与显著的代谢综合征增高有关（Chang 2009）。

认知衰退、痴呆和代谢综合征

代谢综合征与认知衰竭、阿尔茨海默症和血管性痴呆有关。与没有代谢综合征的老年人相比，患有代谢综合征的老年人更容易患上认知功能受损（Yaffe 2005）。常见的与代谢综合征有关的认知缺陷包括了记忆、视觉空间能力、执行能力、处理速度和整体智力功能（Yates 2012）。代谢综合征和轻度认知损害的关系还未完全确立，但很可能是比较复杂的关系。Roberts 等人（2010）提议其关系与轻度认知损害的亚型和感染的程度有关。比如，有较高 C 反应蛋白血清浓度的代谢综合征患者更易患上非遗忘性轻度认知损害，而不是其它的亚型。

代谢综合征作用于大脑及其导致的认知衰退的机制包括：神经炎症、氧化应激、糖类代谢受损和血管反应受损（Yates 2012）。在胰岛素抵抗中，促炎细胞因子（比如 IL-1 β, IL-6 和 TNF-α）产生了过度分泌，而且其中的 IL-1 β 和 IL-6 刺激了 A β PP 蛋白的过度表达和 β 淀粉蛋白在大脑中的沉积。反过来，β 类淀粉蛋白导致了更多的促炎细胞因子的分泌，且加剧了认知功能损害。这形成了一种恶性循环。另外，这些促炎细胞因子可以加剧动脉粥样硬化，而且可能导致不可逆的结构性大脑改变和阿尔茨海默症(de la Torre 2010)以及血管性痴呆。研究者们越来越多地认识到血管性因素可能在阿尔茨海默症的发病中起一定的作用。也有研究报导代谢综合征与受损的脑血管反应性、颈动脉硬化和血管中内膜增厚有关（Koivistoinen 2009）。这些因素影响了脑血管血流，营养物质运输和代谢废物清理，从而干
扰了神经元活动和加剧了认知衰退。

令人感兴趣的是，也有许多研究报导，从脂肪组织中分泌的脂联素与认知功能有关。Une等人（2011）发现，与对照组相比，轻度认知损害或阿尔茨海默症患者中的血清脂联素显著升高，而且轻度认知损害患者中脂联素的脑脊液浓度也显著升高。另外，弗雷明汉心脏研究显示，高血清浓度的脂联素是女性中所有痴呆症和阿尔茨海默症的危险因素（van Himbergen 2012）。

普遍认为的观点是脂联素的高血清浓度是代谢和心血管功能的保护因素，但这些研究结果否定了这个观点。值得注意的是，脂联素的肾脏清除率在老年人群中比中年轻人群中低。因此，在理解老年人中的血清脂联素浓度时应多加注意。根据以上的研究证据，饮食和生活习惯的改善以及对高血压、高脂血症和高血糖的药物治疗是预防和治疗阿尔茨海默症的重要措施。

其它精神科疾病和代谢综合征

创伤后应激障碍

创伤后应激障碍与诸如高血压、糖尿病和肥胖之类的心血管风险有关，而且慢性和较严重的创伤后应激障碍可能与更高的代谢综合征风险相关（Heppner 2012）。创伤后应激障碍患者中应激相关的糖类和脂类代谢失调可以导致代谢综合征的发生。

狂食症

患有狂食症的肥胖个体中患有代谢综合征的患病率被报导在50%-60%之间。暴饮暴食与过度胰岛素分泌、空腹血糖和糖耐量受损和血清脂类水平偏高有关（Taylor 1999）。带有暴饮暴食特性的暴食症也与肥胖的严重程度紧密相关。另外，在肥胖病人中，快速饮食与血清胆固醇和甘油三酯升高、偏高的腰/臀比和脂肪肝有关（Kral 2001）。

边缘性人格障碍

边缘性人格障碍患者中代谢综合征的患病率是基础医疗中患者的两倍（Kahl 2013）。增加的患病率与较大的年龄、更高的身体质量指数、二代抗精神病药的使用、苯二氮卓类药物的依赖和暴饮暴食行为有关。高血糖在男性和女性患者中都较常见，而向心性肥胖和高甘油三酯血症则在女性患者中更常见。
目前有一些关于边缘性人格障碍和代谢综合征相关性病因的假设。下丘脑-垂体-肾上腺系统的失调被一些研究证明导致了皮质醇增多症、抗炎和促炎细胞因子的失衡以及与抑郁症无关的更低的反馈敏感性(Kahl 2006; Purnell 2009)。这些现象的原因还没有被很好的阐明，但是边缘性人格障碍患者中增加的皮质醇激素可能是由于他们反复的内心紧张不安所致。不健康的生活方式、并发的精神科疾病以及精神科药物的服用也被表明也这一人群中的代谢综合征相关。

**酒精**

酒精可以加剧也可以预防代谢综合征，这很大程度上取决于饮酒的数量和类型(Wojciech 2007)。适量的饮酒，尤其是饮用红酒，可以降低代谢综合征的发病率，因为其对血清脂类糖类水平和腹围有改善作用。这一作用是因为红酒中的多元酚增加了内皮细胞中一氧化氮合酶的活动。内皮细胞中一氧化氮合酶活动的降低可以导致高血压、胰岛素抵抗和血脂异常。在那些酒精滥用的患者中，糖类和脂类代谢的严重失调可以导致患有高血压、空腹血糖受损、甘油三酯血症和腹型肥胖的风险增加。

重度饮酒与严重的健康问题有关，包括营养不良、心血管疾病、慢性胰腺炎、认知功能受损和几乎所有器官的功能受损。许多不同的精神科疾病可以与酗酒并发，由酗酒导致，或导致酗酒。这在那些很容易获得酒精且流行“饮酒文化”的国家尤其值得关注。

常见的与酗酒相关的精神科疾病包括抑郁症、双相情感障碍、精神分裂症、焦虑症和人格障碍。酗酒也增加了自杀和暴力的风险。

**选择精神药物**

选择一种治疗特定精神科疾病的药物的初始决定是非常重要的，这应该基于收益风险评估来决定。在治疗过程中，为了逆转代谢异常而改换另一种药物的做法可能会导致精神症状的复发。这个现象在那些已经对于某个处方获得良好临床反应的患者中更明显。因此，在每次改换药物之前应仔细衡量利弊。比如，如果病人之前已经患有代谢综合征，那么应该考虑一代抗精神病药，因为其对于代谢的副作用比二代抗精神病药少。Saddichha等人(2008)建议当发生代谢综合征的风险较高时，应该先使用二代抗精神病药一段时期（比如6个星期），然后改换成一代抗精神病药。

研究数据显示多种精神药物的联合使用会增加代谢综合征的风险，因此在精神药物的联
合使用前，要进行细致的风险利益分析。

代谢综合征的筛查

由于在关注患者的精神需求，精神卫生专业人员可能没有较好处理代谢综合征风险增加的问题，尤其是对于那些长期服用抗精神病药的患者。那些指导患者如何调整生活方式以降低代谢综合征的信息很少，而且患有精神科疾病的患者也很少被筛查代谢综合征的症状。比如，一个在英格兰南方实施的调查精神科病人中代谢综合征筛查的研究项目得出了一个令人担心的结果(Holt 2010)。在12个月的研究过程中，被评估的病人由下列部分组成：32%的病人筛查了血压，16%筛查了血糖，9%筛查了血脂，2%筛查了体重。另外，少于一半的住院病人和少于四分之一的门诊病人同意身体检查。这个研究表明，临床医生常常低估了常规筛查和检查代谢综合征的必要性，而且精神科病人常常不愿意进行健康筛查。

筛查时间表和标准化评估

精神科医生应当在精神药物治疗前和治疗中都筛查病人的代谢综合征。推荐的代谢综合征的筛查和监控的时间表见表2。代谢综合征的常见体征如图1所示。体重增加，尤其是向心性肥胖，是代谢综合征中最容易被注意到的体征。因此，发现存在代谢综合征风险病人的最快速简单的方法是测量其腰围。

所有来门诊随访的病人均应常规地被测量血压和脉搏。

生物学指标是评估代谢综合征进展的客观指标。除了检查空腹血糖，Christoph等人(2006)也推荐尽早发现精神科病人中的偏高低密度脂蛋白水平。对于那些患有代谢综合征的精神科患者，低密度脂蛋白水平被推荐在低于130mg/dl。对于那些患有其它疾病（比如糖尿病、冠以病、腹主动脉瘤和外周血管疾病）的患者，推荐的水平是低于100mg/dl。

在开始使用精神药物前，谷丙转氨酶和谷氨酰转移酶也被建议测量，因为这可以发现那些可能存在肝功能损害风险的病人(Lee 2004; Park 2004)。另外，谷丙转氨酶是不明原因的肝脏疾病所至死亡的预测因子，而升高的谷氨酰转移酶与糖尿病、胰岛素抵抗、酗酒和心血管疾病有关。
表 2 慢性精神疾病患者中代谢综合征的监控时间表

<table>
<thead>
<tr>
<th>时间</th>
<th>推荐的步骤</th>
</tr>
</thead>
</table>
| 起初  | 1. 病史：包括之前的心血管疾病、家族史、吸烟史、身体锻炼的类型频率和饮食习惯  
      2. 体格检查：包括血压、体重、腰围和身体质量指数  
      3. 实验室检查：包括空腹血糖、空腹血脂、总胆固醇、低密度脂蛋白、高密度脂蛋白、甘油三酯、谷丙转氨酶和谷氨酰转移酶  
      4. 心理教育：包括停止吸烟的建议、良好的食物选择和身体锻炼  
      5. 精神药物的选择：应根据每种药物的心血管代谢特性决定  
      6. 会诊：如果在步骤 2 中发现至少一个异常 和/或 在步骤 3 中发现三个异常，应当求助于社区医院医生或请专科医生会诊 |
| 第 6 周 | 重复步骤 2, 3 和 4  
      检查饮酒和吸烟情况  
      对于那些体重增加 7%的病人，检查其精神科药物 |
| 第 12 周 | 重复步骤 2, 3 和 4  
      检查饮酒和吸烟情况 |
| 每 52 周 | 重复步骤 2, 3 和 4  
      检查饮酒和吸烟情况 |
| 1 年后 | 如果实验室检查在正常范围内，每年重复一次步骤 2, 3 和 4 |

来源：de Hert 2009; Oh, 2011

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图1 患有代谢综合征的精神科病人的体格检查
新型生物标志物

其它潜在的新型生物标志物（比如高敏感度 C 反应蛋白、同型半胱氨酸和血清尿酸浓度）也得到了研究。C 反应蛋白和同型半胱氨酸的作用已经在前文提及。升高的血清尿酸浓度与全身炎症反应、内皮细胞功能失调、高血压和心血管疾病有关。同时升高的高敏感度 C 反应蛋白和同型半胱氨酸与代谢综合征的显著相关性与其它混合因素无关。因此，这些生物标志物常规用于精神科病人中代谢综合征风险定性的可行性还需更进一步的衡量。

代谢综合征的治疗

生活方式改良、心理教育和自助团体

精神科医生需要在代谢综合征患者中推广健康的生活方式。关于代谢综合征处理的大致推荐方法概括于格 3 中。病人需要知道他们的精神疾病和药物，因为这对于药物依从性和复发预防很重要。

如果均衡日常饮食和常规身体锻炼的简单建议还不够，可以让病人去看营养学家和体重控制专家获得更详细的饮食和锻炼建议。理想的条件下，病人应该能得到整合了所有这些服用的整合性健康项目。让病人参与支持小组（比如减肥小组）可以激励病人保持健康。在早期就让家庭成员和照料者参与其中很重要，这可能提供病人额外的支持。认知行为疗法可以用于改变健康相关的不良信念和有害健康的行为（比如饮酒和吸烟）。
格 3 关于处理代谢综合征的一般建议

- 饮食调整 --- 建议病人：
  避免饱和脂肪酸摄入（比如红肉、蛋黄和油炸食物）
  食用低热量食物
  食用新鲜水果和绿色蔬菜
- 鼓励适量运动（比如散步、游泳和骑车），每天 30-40 分钟，
  一周 3-4 次
- 为病人制定在每次门诊随访之间的减肥目标
- 使用 β 阻断剂将病人的血压控制在 140/80mmHg 以下
- 通过饮食或其他类药物改善脂类水平：目标是控制空腹低密度
  脂蛋白低于 3mmol/l; 高密度脂蛋白高于 1 mmol/l 甘油三酯低于 20 mmol/l

(Gurnell 2001)

药物干预

药物治疗代谢综合征的主要方法是治疗该综合征中受损的健康环节。对于高血压、血脂
异常和糖尿病，抗高血压药物、降脂药物和糖尿病药可以分别使用。这些病人也应该去看社
区医院或是专科医生（如果存在多种并发症或合并症），以能得到继续的随访和必要的治疗。

留心于这些药物和精神药物的相互作用是很重要的，虽然这可能会使治疗复杂化。比如，在
服用碳酸锂的病人中使用血管紧张素转换酶抑制剂来治疗高血压是禁忌的，因为这可能会
导致碳酸锂中毒。对于一个服用华法令治疗心脏病的患者，选择性 5-羟色胺再摄取抑制剂的使用可能增加出血的风险。另外，有些精神药物会恶化代谢综合征的控制。比如，文拉法新会升高血压，米氮平会增加食欲。

**减肥药物**

许多研究评估了一些药物在减肥方面的效果。有研究者对 32 个随机对照研究进行了荟萃分析，这 32 个研究关注于对于抗精神病药物诱发的体重增加的药物干预。这个研究得到的药物的减肥效果顺序是（从高到低）：二甲双胍、D芬氟拉明、西布曲明、托吡酯片、瑞波西汀、金刚烷胺、尼扎替丁、奥利司他、二甲双胍加上西布曲明、法莫替丁、右旋安非他命、氟西汀、罗格列酮(Maayan 2010)。

**二甲双胍** 这个双胍类药物具有降低体重和增加胰岛素敏感性的双重作用，从而是治疗抗精神病药诱发的体重增加的最有效药物(McIntyre 2012)。患有奥氮平诱发的体重增加的病人在使用二甲双胍治疗后，体重下降了 5%(Prahraj 2011)。然而，二甲双胍似乎只能在体重增加发生的时候才有降低体重的效果 — 如果和抗精神病药同时开始服用，二甲双胍不能防止体重增加(Papanastasiou 2012)。虽然这些研究提供了二甲双胍在促进体重下降和改良胰岛素抵抗方面地潜在应用，但也需要更大且含有对照组的研究来进一步评估二甲双胍的效果。

**托吡酯片** 抗癫痫药托吡酯片可能对夜间进食综合征和睡眠相关性进食障碍有所帮助(McElroy 2009)。它的抗暴食和抗清泻效果在狂食症患者中尤其明显。

**安非他酮加上纳洛酮** 另一种可能的治疗方法是安非他酮和纳洛酮的联合使用。当它们联合使用时，其作用机制与下丘脑的促阿黑皮素原神经元和中脑边缘通路的调节有关，这两者在食物摄入和体重调节中起很重要的作用(McIntyre 2012)。

**新型药物** 一些新型的药物已被用于治疗代谢综合征。内源性的肠促胰岛素（包括胰高血糖素样肽-1 和葡萄糖依赖性促胰岛素肽）能调节胰岛素分泌(Nauck 2011)。因为胰高血糖素样肽-1 是由二肽肽酶-4 降解，所以二肽肽酶-4 抑制剂和合成胰高血糖素样肽-1 类似物是基于肠促胰岛素的治疗 2 型糖尿病的基本原理。胰高血糖素样肽-1 类似物（比如艾塞那肽和利拉鲁肽）能适度降低代谢综合征患者的体重和血压。因此，评估这些药物在治疗精神科病
人中代谢综合征的安全性和有效性是非常值得的。

手术干预

减肥手术适用于重度肥胖的患者：身体质量指数在35到39之间且有至少一个肥胖相关并发症，或是没有并发症但身体质量指数大于40（Blackburn 2009）。值得注意的是，减肥手术减少了药物在胃肠道的通过时间和胃肠道对药物的吸收面积，而且这种术后效应对于精神药物的药代动力学还没有被深入研究。

结论

代谢综合征和精神科疾病的双向作用是复杂且具有临床挑战性的，其互相作用的方面包含了基因、药物、感染、内分泌和行为的因素。筛查、认识和治疗精神科病人中的代谢综合征是至关重要的。识别和治疗代谢综合征之所以重要，是因为其症状不仅与心血管疾病的风险增加有关，也与精神错乱和抑郁症状的患病率增高、不良的自感健康状况和较差的药物依从性有关。

理想的条件下，患有代谢综合征的精神科患者应该由一支包含医学专家、精神科医生和营养学家组成的多学科医疗组来进行治疗，而且患者应积极主动参与其中的治疗活动。调动这些病人的积极性很有挑战性，因为他们易冲动而且有不良的健康习惯和久坐的生活方式。总之，需要更多的研究来研发对于代谢综合征风险较低的精神药物，也需要后续的研究来评估治疗精神科中代谢综合征的药物（比如二甲双胍和胰高血糖素样肽-1）的有效性和安全性。

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多项选择题

请根据每个题干选择一个最佳选项

1. 在患有严重精神疾病的病人中，以下哪个最不会被测量？
   A. 血压
   B. 血糖
   C. 血脂
   D. 体重
   E. 以上都不是

2. 在双相情感障碍中，代谢综合征常常关联于：
   A. 首次情感障碍发作时的年龄较小
   B. 首次躁狂症的早期发作
   C. 首次情感障碍发发作时严重程度较低
   D. 在一生中更多的情感障碍发作次数
   E. 双相情感障碍（尤其是 II 型）的持续期较短

3. 当一个精神科病人患有代谢综合征时，不恰当的做法是：
   A. 根据药物的心血管代谢风险情况和精神科病情调整精神药物
   B. 将病人加入支持小组以增加他们减肥的动力
   C. 立即请专科医生会诊以治疗代谢综合征
   D. 治疗早期请家庭成员加入治疗活动
   E. 教育病人相关健康生活方式和饮食

4. 代谢综合征导致老年痴呆的可能机制是：
   A. 受损的脑血管反应性
   B. 受损的糖类代谢
   C. 神经炎症
D 氧化应激
E 以上所有

5 在患有代谢综合征的精神分裂症患者中甘油三酯和低密度脂蛋白胆固醇可以被联合使用氯氮平和以下哪种药物降低：
A 阿立哌唑
B 氟西汀
C 碳酸锂
D 哌醋甲酯
E 奎硫平

多项选择题答案
1D  2D  3C  4E  5A