Interventions for the metabolic syndrome in schizophrenia: a review

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Abstract: The metabolic syndrome (MetS) is an increasingly prevalent condition in people with schizophrenia. It remains highly prevalent in the general population in developed countries, but recently health promotion campaigns and greater awareness of the high associated mortality rates have resulted in improvements in the rates of cardiovascular risk factors. This is not the case for people with schizophrenia who continue to have more than twice the rates of MetS and significantly higher mortality rates than the general population. Various behavioural and pharmacological interventions have been used to improve conditions that are linked to MetS, mainly smoking and obesity. This review aims to provide an update of the latest knowledge about the behavioural, pharmacological and other interventions that might help to combat this life-threatening problem in people with schizophrenia.

Keywords: Antipsychotic-induced weight gain, cardiovascular risk factors, diabetes, metabolic syndrome, obesity, physical exercise, physical health intervention, schizophrenia, smoking cessation, weight reduction/management

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The metabolic syndrome in schizophrenia: introduction

Schizophrenia is a highly heritable condition which is associated with a dramatic reduction in lifespan. A meta-analysis of existing data revealed a substantial gap between the health of people with schizophrenia and the general population [Saha *et al.* 2007]. Mortality in schizophrenia is largely due to cardiovascular disease [Tandon *et al.* 2009]. Sudden cardiac death, often resulting from cardiac arrhythmias, is also an important cause of mortality [Koponen *et al.* 2008].

Schizophrenia has been associated with an increased risk of diabetes since the nineteenth century [Maudsley, 1979]. Henry Maudsley was one of the first psychiatrists to notice an association between diabetes and schizophrenia. This was prior to the development of antipsychotic treatments. Even today, a significant number of studies have demonstrated that antipsychotic-naïve patients have impaired glucose tolerance, increased insulin resistance and increased visceral fat distribution compared with normal controls [Thakore *et al.* 2002; Venkatasubramanian *et al.* 2007; Fernandez-Egea *et al.* 2009]. More importantly, other studies have shown increased glucose intolerance in the siblings of people with schizophrenia and an increased prevalence of type 2 diabetes in the parents of nonaffective psychosis subjects [Fernandez-Egea *et al.* 2008a, 2008b]. Recently, a Danish study found that having schizophrenia is associated with an at-risk allele for type II diabetes located in the TCF7L2 gene [Hansen *et al.* 2011]. These findings suggest that diabetes and schizophrenia may share familial risk factors or common genetic predisposition.

The metabolic syndrome (MetS; also known as syndrome X, syndrome of chronic cardiovascular disease and Reaven's syndrome) is a constellation of different conditions, including abdominal obesity, insulin resistance, dyslipidaemia and elevated blood pressure (BP). All components of MetS (with obesity holding a central role in its development) have been recognized as independent risk factors for cardiovascular disease. Therefore, the presence of MetS is associated with other comorbidities such as the prothrombotic state, proinflammatory state, nonalcoholic fatty liver disease and reproductive disorders [Cornier *et al.* 2008].

It has been estimated that in the USA as many as 60% of people with schizophrenia meet the criteria for MetS, as opposed to 30% for the general population [Mendelson, 2008]. Numerous studies have

Table 1. Published reviews on healthy living interventions in schizophrenia and severe mental illness.

Authors and year	Type or Review	No of studies reviewed	Type of interventions	Target of interventions
Faulkner *et al.* [2003]	Systematic	16	Pharmacological and behavioural	Weight management in schizophrenia
Werneke *et al.* [2003]	Systematic	13	Behavioural	Management of antipsychotic-induced weight gain
Bradshaw *et al.* [2005]	Systematic	16	Behavioural	Smoking cessation, weight management, exercise, nutritional education in schizophrenia
Faulkner and Cohn [2006]	Selective		Pharmacological and behavioural	Weight and metabolic disturbances management in schizophrenia
Loh *et al.* [2006]	Systematic	23	Behavioural	Weight management in schizophrenia
Faulkner *et al.* [2007]	Systematic	23	Pharmacological and behavioural	Weight management in schizophrenia
Ganguli [2007]	Selective		Behavioural	Weight management in schizophrenia
Strassnig and Ganguli [2007]	Selective		Pharmacological and behavioural	Weight management in schizophrenia
Alvarez-Jimenez *et al.* [2008]	Systematic, meta-analysis	10	Behavioural	Management of antipsychotic-induced weight gain
Beebe [2008]	Selective		Behavioural	Weight management in schizophrenia
Kemp *et al.* [2009]	Selective		Behavioural	Weight management, exercise, nutritional education in mental illness
Banham and Gilbody [2010]	Sytematic	8	Pharmacological and behavioural	Smoking cessation in severe mental illness
Maayan *et al.* [2010]	Systematic, meta-analysis	32	Pharmacological	Management of antipsychotic-induced weight gain and metabolic disturbances
Tsoi *et al.* [2010]	Systematic, meta-analysis	7	Pharmacological	Smoking cessation and reduction in schizophrenia, using bupropion
Roberts and Bailey [2011]	Systematic	12	Behavioural	Weight control, exercise in severe mental illness, incentives and barriers of interventions

shown that overweight and diabetes are in general increased in patients with schizophrenia, with a two- to fourfold increase in the risk of diabetes compared with the general population [Leucht *et al.* 2007].

As the presence of MetS is associated with an increased risk for cardiovascular disease and death, and patients with schizophrenia are increasingly predisposed to develop it, it is of paramount importance to develop and implement strategies which can tackle this problem in this particular group of patients. It is also imperative that the awareness of clinicians is increased regarding this insidious but also potentially lethal condition.

Rationale and objectives of our review

In this review we provide an update about how best to combat MetS in schizophrenia. We aim to explore any pharmacological, behavioural and combined interventions targeting physical health and improving cardiovascular risk factors in patients with schizophrenia.

We set the following objectives at the beginning of our review:

(1) To summarize the interventions currently available, their effectiveness and most importantly to ascertain which interventions appear to be the most effective and therefore should attract clinical interest.
(2) To discuss the importance of monitoring in the early detection of MetS.

Review methodology

Eligibility criteria

We included original articles published in English language up until 2011 that provided evidence on behavioural, pharmacological and combined

interventions. We excluded studies of poor methodological or informative value, such as case reports or pre-experimental observational studies.

Information sources

Articles were retrieved from the ISI Web of Knowledge℠ platform (Thomson Reuters), a comprehensive database that incorporates the Web of Science (1970 to present) and MEDLINE (1950 to present) and also includes articles from PsychINFO and the Cochrane Review Database.

Search

We searched for articles using the terms: Title=(schizophrenia OR severe mental illness OR antipsychotic) AND Title=(exercise OR weight management OR weight reduction OR smoking cessation OR smoking reduction OR health intervention OR well being OR wellness OR caloric restriction OR diet OR nutrition), published up until 2011. Our initial search generated 320 hits. We completed our search by checking against previously published reviews and extracting additional articles (Table 1).

Study selection

Screening of articles was based on titles and abstract reading. Only articles fulfilling our eligibility criteria were included and full texts were subsequently obtained. We originally planned to include randomized controlled trials (RCTs) and other trials of high evidential quality. However, it soon became apparent that by doing so we would inevitably create an important source of bias. By excluding naturalistic studies, leaving us with significantly more pharmacological studies, as the majority of studies describing behavioural interventions are naturalistic, this would consequently disturb the balance we wished to maintain between the two kinds of interventions in our review. Furthermore, naturalistic studies, despite their less robust methodology, often convey valuable information, at a pragmatic level, and we did not want to appear dismissive of their contribution. So in addition to experimental studies (RCTs and non-RCTs) we included some naturalistic studies too.

Outcome

A total of 95 original studies were identified (Tables 2–4). Several researchers have tried to summarize the current evidence of MetS in patients with schizophrenia in numerous systematic or selective reviews. We identified a significant number of reviews that focus on behavioural and pharmacological interventions targeting metabolic disturbances in schizophrenia and severe mental illness. There are a number of reviews that focused on epidemiological studies, which also attempted to address the pathophysiological connections between MetS and schizophrenia. In addition, a group of reviews have focused particularly on studies of metabolic features associated with the use of second-generation antipsychotics. The latter two categories are not covered here as they are beyond the scope of this article.

Description and discussion of studies

Studies of behavioural interventions related to metabolic syndrome in severe mental illness

A total of 42 studies were identified in this category, testing interventions that targeted physical health and cardiovascular fitness, smoking and weight. Behavioural interventions are described in various terms, which may also be used interchangeably or share common concepts. Among the most commonly mentioned are the following:

(1) *Wellbeing programmes*, a holistic approach, which incorporates physical health, checks, physical exercise and dietary advice. They can target specific conditions (smoking, obesity) but also aim at the overall improvement of an individual's quality of life, placing special emphasis on mental health. Their duration varies from a few weeks to several months and they are 'tailor-made' to respond to patients' needs.
(2) *Cognitive behavioural treatment (CBT)*, a broadly used psychological module, which aims primarily to modify erroneous beliefs and behaviours. CBT can have various applications, such as in smoking reduction.
(3) *Nutritional education*, which usually consists of specialist dietary input, focusing on calorie restriction and healthy diet.
(4) *Weight management*, a term used to describe a combination of strategies targeting obesity or overweight, such as physical activity and modification of dietary habits.
(5) *Psycho-education*, usually describing information offered to patients regarding their medication and illness in a manner that can enhance medication adherence and promote relapse prevention.

Table 2. Original articles on behavioural physical health interventions in schizophrenia.

Authors and year	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Sletten *et al.* [1967]	USA	Experimental, crossover	14		SCZ	Calorie restriction	Weight reduction	8 weeks	Yes
Harmatz and Lapuc [1968]	USA	Experimental randomised	21		SCZ	(a) Diet *versus* (b) group therapy *versus* (c) behavioural modification	Weight reduction	10 weeks	No (a), Yes (b, c)
Rotatori *et al.* [1980]	USA	Experimental	7	7	SMI	Counselling, tokens, self-reinforcement	Weight reduction	14 weeks	Not significantly
Lukoff *et al.* [1986]	USA	Naturalistic	28		SCZ	Holistic programme, including stress reduction	Physical health, cardiovascular fitness	10 weeks	Possibly
Mcdougall [1992]	UK	Naturalistic	11		SCZ	Nutritional education	Weight reduction, eating behaviour	8 weeks	No
Pelham *et al.* [1993]	Canada	Naturalistic	11		SCZ	Exercise	Physical health, cardiovascular fitness	8 weeks	Yes
Merriman *et al.* [1995]	UK	Naturalistic	6		SMI	Diet, exercise, self-assertiveness training	Weight reduction	12 weeks	Not significantly
Roll *et al.* [1998]	USA	Experimental, crossover, ABA design	11		SCZ, SCZA	Monetary reinforcement	Smoking cessation/ reduction	3 weeks	Yes (abstinence, reduction)
Aquila and Emanuel [2000]	USA	Retrospective	32		SCZ, SCZA	Low-fat/calorie diet, nutritional education	Weight reduction	18 months	Yes, partially
Ball *et al.* [2001]	USA	Experimental	11	11	SMI	Weight Watchers programme	Weight reduction	10 weeks	Yes, for men only
Cohen *et al.* [2001]	USA	Retrospective chart review	39		Mental retardation	Calorie restriction	Weight reduction	2 years	No
Umbricht *et al.* [2001]	Switzerland	Naturalistic	10		SCZ	CBT, group and individual	Weight reduction	6 weeks	Yes

(Continued)

Table 2. (Continued)

Authors and year	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Feeney *et al.* [2003]	Ireland	Experimental	9	42	SCZ	Weight management programme	Weight reduction	3 years	Yes
Littrell *et al.* [2003]	USA	RCT	35	35	SCZ, SCZA	Psycho-education (wellbeing) *versus* standard care	Weight reduction	6 months	Yes (attenuated weight gain)
O'Keefe *et al.* [2003]	USA	Naturalistic, retrospective chart review	35		SMI	Dietician input, self-directed diet as part of the treatment plan	Weight reduction	84 ± 21 months	Yes
Vreeland *et al.* [2003]	USA	Experimental	31	15	SCZ, SCZA	Nutritional education, exercise, motivational counselling	Weight reduction	12 weeks	Yes
Menza *et al.* [2004]	USA	Experimental	31	20	SCZ, SCZA	Nutritional education, exercise, behavioural strategies	Weight reduction	52 weeks	Yes
Ohlsen *et al.* [2004]	UK	Naturalistic	44		SCZ, SCZA	Weight management programme	Weight reduction	1 year	Not significantly
Beebe *et al.* [2005]	USA	Experimental	6	4	SCZ	Walking group	Weight reduction	16 weeks	Yes
Brar *et al.* [2005]	USA	Experimental, open label, rater blinded, randomized	34	37	SCZ, SCZA	Group behavioural treatment	Weight reduction	14 weeks	Yes
Evans *et al.* [2005]	Australia	RCT	29	22	SCZ, SCZA	Individual nutritional education + OLZ *versus* OLZ	Weight reduction	3 months	Yes (attenuated weight gain)
Fogarty and Happell [2005]	Australia	Naturalistic, quantitative	6		SCZ	Structured exercise programme	Physical health, cardiovascular fitness	3 months	Yes

(Continued)

Table 2. (Continued)

Authors and year	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Kalarchian *et al.* [2005]	USA	Naturalistic, chart review	35		SCZ	Behavioural weight control programme	Weight reduction	12 weeks	Yes, sustained
McCreadie *et al.* [2005]	UK	RCT	67	24	SCZ	Provision of fruit and vegetables ± nutritional education	Diet	6 months	Yes, but not sustainable
Skrinar *et al.* [2005]	USA	RCT	10	10	SMI	Exercise	Weight reduction	12 weeks	Not significantly
Alvarez-Jimenez *et al.* [2006]	Spain	RCT	28	33	SMI (FE)	Early behavioural intervention + OLZ/RISP/HAL *versus* OLZ/RISP/HAL	Weight reduction	3 months	Yes (attenuated weight gain)
Baker *et al.* [2006]	Australia	RCT	147	151	SMI	Motivational interviewing + CBT + NR *versus* NR	Smoking cessation/reduction	12 months	Yes (reduction, discontinuation), No (abstinence)
Brown and Chan [2006]	UK	RCT	15	13	SMI	Health promoting intervention	Weight reduction	6 weeks	Yes
Kwon *et al.* [2006]	S. Korea	RCT	33	15	SCZ, SCZA	Weight management + OLZ *versus* OLZ	Weight reduction	12 weeks	Yes
McKibbin *et al.* [2006]	USA	RCT	28	29	SCZ, SCZA	DART *versus* TAU	Weight reduction	24 weeks	Yes
Scocco *et al.* [2006]	Italy	Naturalistic	20		SCZ, SCZA	Psycho-education at an early and late phase of OLZ treatment	Weight reduction	24 weeks	Yes (attenuated weight gain in *late* intervention)
Weber and Wyne [2006]	USA	RCT	8	9	SCZ, SCZA	CBT *versus* TAU	Weight reduction	16 weeks	Yes
Khazaal *et al.* [2007]	Switzerland	RCT	31	30	SCZ, SCZA	CBT *versus* brief nutritional education	Weight reduction	12 weeks	Yes

(Continued)

Table 2. (Continued)

Authors and year	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Pendlebury *et al.* [2007]	UK	Naturalistic	93		SMI	Behavioural treatment programme	Weight reduction	4 years	Yes (increasing dropouts)
Poulin *et al.* [2007]	Canada	Naturalistic	59	51	SCZ, SCZA	Weight control programme	Weight reduction	18 months	Yes
Smith *et al.* [2007]	UK	Naturalistic	966		SMI	Wellbeing support programme (6 consultations)	Weight reduction	2 years	Yes
Wu *et al.* [2007]	Taiwan	Experimental	28	25	SCZ	Low-calorie diet, exercise + CLOZ *versus* CLOZ	Weight reduction	6 months	Yes
Chafetz *et al.* [2008]	USA	RCT	90	109	SMI	Wellbeing training *versus* TAU	Physical health	12 months	Yes (self-reported health status)
Forsberg *et al.* [2008]	Sweden	RCT	24	17	SMI	Healthy living programme *versus* TAU	Weight reduction	12 months	Not significantly, yes for MetS prevalence
Lindenmayer *et al.* [2009]	USA	Naturalistic	275		SCZ, SCZA	Structured wellbeing programme	Weight reduction	36 weeks	Yes
Beebe *et al.* [2011]	USA	RCT	48	49	SCZ, SCZA	Motivational intervention	Physical exercise attendance	16 weeks	Yes
Eldridge *et al.* [2011]	UK	Naturalistic	159		SMI	Wellbeing support programme	Physical health	9–12 months	Yes (blood pressure, BMI)

BMI, body mass index; CBT, cognitive behavioural therapy; CLOZ, clozapine; DART, diabetes awareness rehabilitation training; FE, first episode; HAL, haloperidol; NR, nicotine replacement; OLZ, olanzapine; RCT, randomized controlled trial; RISP, risperidone; SCZ, schizophrenia; SCZA, schizoaffective disorder; SMI, serious mental illness; TAU: treatment as usual.

Table 3. Original articles on pharmacological physical health interventions in schizophrenia.

Authors and year	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Arman *et al.* [2008]	Iran	RCT	11	11	SCZ, C&A	MTF + RISP *versus* PCB + RISP	Weight reduction	12 weeks	Yes
Atmaca *et al.* [2003]	Turkey	RCT	18	17	SCZ	NZT + OLZ *versus* PCB + OLZ	Weight reduction	3 months	Yes
Atmaca *et al.* [2004]	Turkey	RCT	14	14	SCZ	NZT + QUET *versus* PCB + QUET	Weight reduction	8 weeks	Yes (attenuated weight gain)
Ball *et al.* [2011]	USA	RCT	20	17	SCZ, SCZA	ATM *versus* PCB	Weight reduction	24 weeks	No
Baptista *et al.* [2001]	Venezuela	Experimental, crossover, AB design	5		SCZ	MTF *versus* PCB	Weight reduction	12 weeks	No
Baptista *et al.* [2006]	Venezuela	RCT	20	20	SCZ, SCZA	MTF + OLZ *versus* PCB + OLZ	Weight reduction	14 weeks	No
Baptista *et al.* [2007]	Venezuela	RCT	36	36	SCZ	MTF + OLZ *versus* PCB + OLZ	Weight reduction	12 weeks	Yes
Baptista *et al.* [2008]	Venezuela	RCT	13	15	SCZ	MTF + SBT + OLZ *versus* PCB + OLZ	Weight reduction	12 weeks	No
Baptista *et al.* [2009]	Venezuela	RCT	14	15	SCZ	RSL + OLZ *versus* PCB + OLZ	Weight reduction	12 weeks	No
Borovicka *et al.* [2002]	USA	RCT, double-blind	8	8	SCZ	PHENYL + CLOZ *versus* PCB + CLOZ	Weight reduction	12 weeks	No
Bustillo *et al.* [2003]	USA	RCT	15	15	SCZ, SCZA	FLX + OLZ *versus* PCB + OLZ	Weight reduction	4 months	No
Carrizo *et al.* [2009]	Venezuela	RCT	31	30	SCZ	MTF + CLOZ *versus* PCB + CLZ	Weight reduction	14 weeks	Yes
Cavazzoni *et al.* [2003]	USA	RCT	115	60	SCZ, SCZA	NZT + OLZ *versus* PCB + OLZ	Weight reduction	16 weeks	No
Correa *et al.* [1987]	USA	Experimental, crossover, ABA	10		SCZ	AMT	Weight reduction	7 weeks	Yes
Dalack *et al.* [1999]	USA	RCT, crossover	5	5	SCZ	NR	Smoking cessation/ reduction	?	Yes (reduction)
Deberdt *et al.* [2005]	USA	RCT	60	65	SCZ, SCZA	AMT + OLZ *versus* PCB + OLZ	Weight reduction	16 months	Yes

(Continued)

Table 3. (Continued)

Authors and year	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Evins *et al.* [2007]	USA	RCT	25	26	SCZ	BPR + NR *versus* PCB + NR	Smoking cessation/ reduction	12 weeks	Yes (reduction)
Fatemi *et al.* [2005]	USA	RCT, cross-over	9	9	SCZ, SCZA	BPR *versus* PCB	Smoking cessation	3 weeks	Not significantly
Floris *et al.* [2001]	Belgium	Naturalistic	12		SMI	AMT (added to OLZ treatment)	Weight reduction	6 months	Yes
George *et al.* [2002]	USA	RCT	16	16	SCZ, SCZA	BPR *versus* PCB	Smoking cessation/ reduction	6 months	Yes (abstinence, reduction)
George *et al.* [2008]	USA	RCT	29	29	SCZ, SCZA	BPR + NR *versus* PCB + NR	Smoking cessation/ reduction	10 weeks	Yes (abstinence)
Goodall *et al.* [1988]	UK	Experimental, double-blind	9	7	SMI	D-FNFL *versus* PCB	Weight reduction	12 weeks	Yes
Graham *et al.* [2005]	USA	RCT	12	9	SCZ, SCZA	AMT + OLZ *versus* PCB + OLZ	Weight reduction	12 weeks	Yes
Henderson *et al.* [2005]	USA	RCT	19	18	SCZ, SCZA	SBT + OLZ *versus* PCB + OLZ	Weight reduction	12 weeks	Yes
Henderson *et al.* [2007]	USA	RCT	11	10	SCZ, SCZA	SBT + CLOZ *versus* PCB + CLOZ	Weight reduction	12 weeks	No
Henderson *et al.* [2009]	USA	RCT	8	10	SCZ, SCZA	RSL + OLZ *versus* PCB + OLZ	Glucose metabolism	8 weeks	Not significantly
Hinze-Selch *et al.* [2000]	Germany	RCT	11	12	SCZ	FLV + CLOZ *versus* CLOZ	Weight reduction	6 weeks	No
Joffe *et al.* [2008]	Finland	RCT	35	36	SMI	ORL + OLZ/CLOZ *versus* PCB + OLZ/ CLOZ	Weight reduction	16 weeks	Not significant, only in men
Kim *et al.* [2006]	S. Korea	Experimental, open label, randomised	23	25	SCZ	TPR + OLZ *versus* OLZ	Weight reduction	12 weeks	Yes (attenuated weight gain)
Klein *et al.* [2006]	USA	RCT	18	20	SCZ, C&A	MTF + OLZ/RISP/ QUET *versus* PCB + OLZ/RISP/QUET	Weight reduction	16 weeks	Yes (weight stabilization)
Ko *et al.* [2005]	S. Korea	RCT	33	20	SCZ	TPR *versus* PCB	Weight reduction	12 weeks	Yes

(Continued)

Table 3. (Continued)

Authors and year	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Lu *et al.* [2004]	Taiwan	RCT	34	34	SCZ	FLV + CLOZ *versus* CLOZ	Weight reduction	12 weeks	Yes (attenuated weight gain)
Modell and Hussar [1965]	USA	RCT	10	10	SCZ	DXA-S *VS* PCB	Weight reduction, eating behaviour	16 weeks	No
Morrison *et al.* [2002]	USA	Naturalistic	19		SMI, C&A	MTF	Weight reduction	12 weeks	Yes
Nickel *et al.* [2005]	Germany	RCT	25	18	SCZ	TPR + OLZ *versus* PCB + OLZ	Weight reduction	10 weeks	Yes
Poyurovsky *et al.* [2002]	Israel	RCT	15	15	SCZ (FE)	FLX + OLZ *versus* PCB + OLZ	Weight reduction	8 weeks	No
Poyurovsky *et al.* [2003]	Israel	RCT	10	10	SCZ	RBX + OLZ *versus* PCB + OLZ	Weight reduction	6 weeks	Yes (attenuated weight gain)
Poyurovsky *et al.* [2004]	Israel	RCT	7	7	SCZ, SCZA (FE)	FMT + OLZ *versus* PCB + OLZ	Weight reduction	6 weeks	No
Poyurovsky *et al.* [2007]	Israel	RCT	31	29	SCZ, SCZA (FE)	RBX + OLZ *versus* PCB + OLZ	Weight reduction	6 weeks	Yes (attenuated weight gain)
Sletten *et al.* [1967]	USA	Experimental, double-blind, crossover	30		SCZ	CHLORPH *versus* PHENME	Weight reduction	15 weeks	Neither drug significantly reduced weight
Tchoukhine *et al.* [2011]	Finland	Naturalistic	44		SMI	ORL + OLZ/CLOZ *versus* PCB + OLZ/CLOZ	Weight reduction	16 weeks	Yes (especially for men)
Weiden *et al.* [2003]	USA	Naturalistic	270		SCZ, SCZA	Switch from FGA, RISP,OLZ to ZIPR	Weight reduction	6 weeks	Yes (RISP, OLZ), No (FGA)
Weiner *et al.* [2011]	USA	RCT	4	5	SCZ, SCZA	VRN *versus* PCB	Smoking cessation	12 weeks	Yes
Wu *et al.* [2008]	China	RCT	18	19	SCZ (FE)	MTF + OLZ *versus* PCB + OLZ	Weight reduction	12 weeks	Yes (attenuated weight gain)

AMT, amantadine; ATM, atomoxetine; BPR, bupropion; C&A, children and adolescents; CBT, cognitive behavioural therapy; CHLORPH, chlorphenetermine; CLOZ, clozapine; D-FNFL, D-fenfluramine; DXA-S, dextroamphetamine sulphate; FE, first episode; FGA, first-generation antipsychotics; FLV, fluvoxamine; FLX, fluoxetine; HAL, haloperidol; MTF, metformin; NR, nicotine replacement; NZT, nizatidine; OLZ, olanzapine; ORL, orlistat; PCB, placebo; PHENME, phenmetrazine; PHENYL, phenylpropanolamine; QUET, quetiapine; RBX, reboxetine; RCT, randomized controlled trial; RISP, risperidone; RSL, rosiglitazone; SBT, sibutramine; SCZ, schizophrenia; SCZA, schizoaffective disorder; SMI, serious mental illness; TAU, treatment as usual; TPR, topiramate; VRN, varenicline; ZIPR, ziprasidone.

Table 4. Original articles on mixed physical health interventions in schizophrenia.

Authors	Country	Design	Study group (*N*)	Control group (*N*)	Diagnoses	Intervention	Target	Length of intervention	Effectiveness
Ziedonis and George [1997]	USA	Naturalistic	24		SCZ	Behavioural group therapy, individual motivational enhancement, NR	Smoking cessation/ reduction	10 weeks	Yes, partially (abstinence, reduction)
Addington *et al.* [1998]	USA	Naturalistic	50		SCZ, SCZA	Positive reinforcement, anxiety reduction, NR	Smoking cessation/ reduction	7 weeks	Yes (abstinence)
George *et al.* [2000]	USA	RCT	28	17	SCZ, SCZA	American Lung Association group therapy *versus* specialized group therapy for schizophrenia smokers (+NR on each arm)	Smoking cessation/ reduction	12 weeks	Yes, partial reduction, especially combination of nicotine replacement and atypical antipsychotics
Evins *et al.* [2001]	USA	RCT	9	9	SCZ	BPR + CBT *versus* PCB + CBT	Smoking cessation/ reduction, weight reduction	3 months	Yes (reduction)
Weiner *et al.* [2001]	USA	Experimental, crossover, A/A + B/B design	9		SCZ, SCZA	BPR + GT	Smoking cessation/ reduction	14 weeks	Yes (reduction)
Evins *et al.* [2005]	USA	RCT	25	28	SCZ, SCZA	BPR + CBT *versus* PCB + CBT	Smoking cessation/ reduction	12 weeks	Yes but not sustainable
Meyer *et al.* [2005]	USA	Experimental, open label, rater blinded, randomized	34	37	SCZ, SCZA	Switch from OLZ to RISP then BT + RISP *versus* RISP	Prevalence of MetS	20 weeks	Yes (switching), No (BT)
Weiner *et al.* [2007]	USA	RCT	16	16	SCZ	BPR + SGT *versus* PCB + SGT	Smoking cessation/ reduction	12 weeks	Unclear
Wu *et al.* [2008]	China	RCT	64	64	SCZ	MTF + LFI *versus* MTF *versus* LFI + PCB *versus* PCB	Weight reduction	12 weeks	Yes (MTF + LFI→MTF → LFI → PCB)

BPR, bupropion; BT, behavioural therapy; CBT, cognitive behavioural therapy; LFI, lifestyle intervention; MTF, metformin; OLZ, olanzapine; PCB, placebo; RCT, randomized controlled trial; SCZ, schizophrenia; SCZA, schizoaffective disorder; SGT, supportive group therapy; SMI, serious mental illness; TAU, treatment as usual.

Studies on physical health and cardiovascular fitness. Some naturalistic studies provided limited evidence that wellbeing support programmes, holistic approaches or exercise can generally improve physical health and cardiovascular fitness in patients with severe mental illness (SMI) or schizophrenia [Lukoff *et al.* 1986; Pelham *et al.* 1993; Fogarty and Happell, 2005; Eldridge *et al.* 2011]. An RCT comparing wellbeing training with standard care showed improved rates of self-reported heath status following a 12-month wellness training intervention [Chafetz *et al.* 2008]. Another recent RCT showed that a motivational intervention in patients with schizophrenia spectrum disorders significantly increased their attendance to a physical exercise programme [Beebe *et al.* 2011].

Studies on smoking cessation/reduction. An RCT showed that CBT added to nicotine replacement (NR) works better than NR alone for smoking reduction or discontinuation; however, abstinence was not achieved [Baker *et al.* 2006]. Another experimental study, employing an ABA crossover design (alternation of treatment 'B' and nontreatment 'A' phases within the same subjects) showed that monetary reinforcement can lead to both reduction and abstinence [Roll *et al.* 1998].

Studies on weight reduction/diet. Most of the studies on behavioural interventions targeted weight reduction, of which almost a third used an RCT design. This group of studies is utterly versatile, not only in terms of design but also with regards to the type of particular interventions tested (or combinations of these), duration of intervention or period of observation, number of participants and specification of intervention (weight reduction in general or in the context of antipsychotic medication). Although details of all these studies are included in the relevant tables, for the purposes of our discussion, we will not take into account studies with very small sample sizes (i.e. <10).

Wide availability of fruit and vegetables can improve diet but this effect was not sustained [McCreadie *et al.* 2005]. Calorie restriction, alone or combined with nutritional education and some behavioural or motivational strategies, appears to be effective in tackling weight gain [Sletten *et al.* 1967; Aquila and Emanuel, 2000; O'Keefe *et al.* 2003; Vreeland *et al.* 2003; Menza *et al.* 2004]. Diet and exercise can cause patients taking clozapine to lose weight [Wu *et al.* 2007], and individual nutritional education can attenuate weight gain in patients taking olanzapine, as shown by a recent RCT [Evans *et al.* 2005]. Despite these encouraging results, a 2-year retrospective chart review failed to show any weight reduction by calorie restriction only.

Comprehensive weight management programmes, including diet, exercise and counselling on lifestyle modifications, can also prove helpful in reducing weight, as shown by a naturalistic study and an RCT [Kwon *et al.* 2006; Poulin *et al.* 2007]. However, another naturalistic study showed no significant outcomes following a similar nurse-led programme in patients with schizophrenia spectrum disorders [Ohlsen *et al.* 2004].

Several other interventions, including behavioural components and psychoeducation, have shown various degrees of effectiveness in dealing with overweight obesity and improving antipsychotic-induced weight gain [Littrell *et al.* 2003; Brar *et al.* 2005; Kalarchian *et al.* 2005; Alvarez-Jimenez *et al.* 2006; Brown and Chan, 2006; McKibbin *et al.* 2006; Scocco *et al.* 2006; Pendlebury *et al.* 2007; Forsberg *et al.* 2008]. Some studies even demonstrated a relative advantage of behavioural techniques compared with diet or brief nutritional information [Harmatz and Lapuc, 1968; Khazaal *et al.* 2007]. Of note are two large naturalistic studies of structured wellbeing programmes (targeting both physical and mental health with emphasis on healthy lifestyle promotion) which showed weight reduction or improvements in lifestyle habits [Smith *et al.* 2007; Lindenmayer *et al.* 2009]. Smith and colleagues employed a multistep approach to provide a combination of assessment of physical health, lifestyle and medication side effects; feedback offered to clients; and referral to weight management/physical activity groups in a total of 956 outpatients with SMI lasting for up to 2 years. They noticed significant improvement in levels of physical activity, smoking, diet and self-esteem, though there were no changes in mean body mass index (BMI) or cardiovascular risk factors. Lindenmayer and colleagues described a 36-week inpatient programme for 275 chronically ill patients, offering a combination of psychoeducation, dietary advice and physical exercise and targeting primarily obesity and metabolic abnormalities. They found a significant decrease in BMI, especially in patients with diabetes.

Studies of pharmacological interventions related to metabolic syndrome in severe mental illness

A total of 44 studies were identified in this category, testing interventions that target smoking and weight. The majority of studies adopted a robust RCT design.

Studies on smoking cessation/reduction

Bupropion. Four RCTs tested bupropion (BPR) *versus* placebo, on its own or as an adjunct treatment to CBT or NR. They favoured BPR for either abstinence or smoking reduction; however, outcomes are not always sustainable [George *et al.* 2002, 2008; Fatemi *et al.* 2005; Evins *et al.* 2007].

Nicotine replacement. One RCT showed NR to be effective in smoking reduction [Dalack and Meador-Woodruff, 1999].

Varenicline. One RCT showed improved abstinence in patients receiving varenicline; however, it involved a very small sample of nine patients in total [Weiner *et al.* 2011].

Studies on weight reduction. A large number of RCTs tested various agents for weight reduction, usually in the context of antipsychotic medication. In a 2010 systematic review and meta-analysis of 32 RCTs of pharmacological interventions to attenuate antipsychotic-related weight gain, Maayan and colleagues ranked a number of medications according to their efficacy in reducing weight (from the most efficacious to the least): metformin, d-fenfluramine, sibutramine, topiramate, reboxetine, amantadine, nizatidine, orlistat, metformin plus sibutramine, famotidine, dextroamphetamine, fluoxetine, rosiglitazone [Maayan *et al.* 2010]. Specific findings per agent are briefly described below.

Dextroamphetamine sulphate. This medication did not modify appetite [Modell and Hussar, 1965].

Amantadine. Amantadine attenuated olanzapine-induced weight gain [Correa *et al.* 1987; Floris *et al.* 2001; Deberdt *et al.* 2005; Graham *et al.* 2005].

Atomoxetine. Atomoxetine was not effective in reducing weight gain associated with olanzapine or clozapine treatment [Ball *et al.* 2011].

Chlorphenetermine, phenmetrazine. When compared with each other, neither drug significantly reduced weight [Sletten *et al.* 1967].

D-Fenfluramine. This medication attenuated neuroleptic-induced obesity [Goodall *et al.* 1988].

Fluvoxamine. Contradictory findings were reported from two RCTs assessing fluvoxamine's efficacy in reducing clozapine-induced weight gain [Hinze-Selch *et al.* 2000; Lu *et al.* 2004].

Fluoxetine. Fluoxetine did not attenuate olanzapine-induced weight gain [Poyurovsky *et al.* 2002; Bustillo *et al.* 2003].

Famotidine. Famotidine did not attenuate olanzapine-induced weight gain [Poyurovsky *et al.* 2004].

Metformin. Most studies point towards metformin being efficacious in attenuating olanzapine-, clozapine-, risperidone- and quetiapine-induced weight gain [Morrison *et al.* 2002; Klein *et al.* 2006; Baptista *et al.* 2007; Arman *et al.* 2008; Wu *et al.* 2008a; Carrizo *et al.* 2009]. Only a few studies provided contradictory findings, also when metformin was combined with sibutramine [Baptista *et al.* 2001, 2006, 2008].

Nizatidine. Contradictory findings were reported from three RCTs about the efficacy of nizatidine in attenuating olanzapine-induced weight gain [Atmaca *et al.* 2003; Cavazzoni *et al.* 2003]. Although it appears to attenuate quetiapine-induced weight gain [Atmaca *et al.* 2004].

Orlistat. Orlistat appears to be more efficacious for olanzapine- or clozapine-induced weight gain in men [Joffe *et al.* 2008; Tchoukhine *et al.* 2011].

Phenylpropanolamine. This medication did not attenuate clozapine-induced weight gain [Borovicka *et al.* 2002].

Reboxetine. Reboxetine attenuated olanzapine-induced weight gain [Poyurovsky *et al.* 2003, 2007].

Rosiglitazone. This medication did not attenuate olanzapine-induced weight gain or improve glucose metabolism [Baptista *et al.* 2009; Henderson *et al.* 2009].

Sibutramine. Sibutramine attenuated olanzapine-induced weight gain but not clozapine-induced weight gain [Henderson *et al.* 2005, 2007].

Topiramate. This medication attenuated olanzapine-induced weight gain [Ko *et al.* 2005; Nickel *et al.* 2005; Kim *et al.* 2006].

Switching antipsychotic agents. A naturalistic study showed that switching from risperidone or olanzapine to ziprasidone led to weight reduction, however this effect was not observed when switching from first-generation antipsychotics to ziprasidone [Weiden *et al.* 2003].

Studies of mixed interventions related to metabolic syndrome in severe mental illness

A limited number of studies attempted to test the efficacy of combinations of behavioural and pharmacological interventions or even compare

different kinds of interventions. Only nine studies were identified in this category. Two naturalistic studies showed that behavioural techniques (group therapy, motivational enhancement, positive reinforcement and anxiety reduction) can help maintain abstinence from smoking when combined with NR [Ziedonis and George, 1997; Addington *et al.* 1998]. When group therapy was added to NR, in order to reduce smoking, there was no difference between modules specially designed for patients with schizophrenia and those aimed at the general public. However, it seems that combining NR with atypical antipsychotic agents provided better outcomes [George *et al.* 2000]. BPR appeared quite a promising intervention when combined with either group therapy or CBT to reduce smoking [Evins *et al.* 2001, 2005; Weiner *et al.* 2001, 2007]. Switching from olanzapine to risperidone significantly reduced prevalence rates of MetS. However, adding behavioural treatment to risperidone did not add to this effect [Meyer *et al.* 2005]. Finally, an RCT comparing metformin and a lifestyle intervention (LFI) in weight reduction found a combination of the two interventions to be more effective than either intervention alone. Metformin was superior to LFI [Wu *et al.* 2008b].

Findings from reviews of healthy-living interventions in schizophrenia and severe mental illness

Behavioural interventions

In 2003, Werneke and colleagues systematically reviewed 13 studies on behavioural management of antipsychotic-induced weight gain; none of these studies were RCTs [Werneke *et al.* 2003]. They found that behavioural approaches, including diet, exercise and modification of treatment were possibly effective, considering limited evidence and methodological flaws.

In 2003, Bradshaw and colleagues published a systematic review of 16 studies of healthy living interventions in schizophrenia, including smoking cessation, weight management, exercise and nutritional education [Bradshaw *et al.* 2005]. They acknowledged the poor quality of the majority of studies; however, they noted that most studies showed positive outcomes.

In 2006, Loh and colleagues published another systematic review of 23 articles on interventions for weight management in schizophrenia [Loh *et al.* 2006]. Despite the fact that most of the literature was not methodologically sound, some controlled studies suggested that behavioural interventions could prevent weight gain and in some cases promote weight loss.

In 2007, Ganguli published a selective review of weight loss therapy in schizophrenia, confirming the above findings and also suggesting that weight can be controlled on a long-term basis [Ganguli, 2007].

In a 2008 systematic review and meta-analysis of 10 RCTs of nonpharmacological management of antipsychotic-induced weight gain, Alvarez-Jimenez and colleagues showed that individual, group, cognitive-behavioural or nutritional counselling interventions were effective in reducing or attenuating weight gain and maintaining treatment effects over time [Alvarez-Jimenez *et al.* 2008].

In a 2008 selective review of obesity in schizophrenia, assuming a nurses' perspective, Beebe noted that measures such as diet teaching (adapted to the cognitive capacities of patients) and exercise could be effective in dealing with obesity in schizophrenia [Beebe, 2008].

In another 2009 selective review of weight management, exercise and nutritional education in mental illness, Kemp and colleagues found that most studies reported modest success during the period of intervention. However, this effect is not generally sustainable [Kemp *et al.* 2009]. They commented that even limited success could significantly reduce the likelihood of development of physical comorbidities.

Finally, in 2011 Roberts and Bailey presented a systematic review of 12 quantitative and qualitative studies of LFIs in SMI, including weight control and exercise [Roberts and Bailey, 2011]. They also identified possible barriers (illness symptoms, treatment effects, lack of support, negative staff attitude) and incentives (symptom reduction, peer and staff support, knowledge, personal attitudes) to these interventions.

Mixed behavioural and pharmacological interventions

Faulkner and colleagues reviewed the evidence for both pharmacological and behavioural interventions for weight management in schizophrenia

by publishing two systematic reviews of 16 studies and 23 RCTs respectively and one selective review published between 2003 and 2007 [Faulkner *et al.* 2003, 2007; Faulkner and Cohn, 2006]. They concluded that, although difficult, the prevention of weight gain and promotion of weight loss is not impossible and can be achieved with a combination of medication and LFIs.

In a similar selective review published in 2007, Strassnig and colleagues found that antiobesity drugs, behavioural approaches, and in some cases bariatric surgery may all lead to significant weight loss in patients with obesity and schizophrenia [Strassnig and Ganguli, 2007]. The authors emphasized the need for rigorous studies to determine whether weight loss achieved in short-term interventions is maintained.

Finally, in 2010 Banham and Gilbody published a systematic review of eight RCTs of both pharmacological and behavioural interventions for smoking cessation in SMI [Banham and Gilbody, 2010]. They concluded that treating tobacco dependence is effective in patients with SMI, and the same treatments are effective in the general population and those with mental illness. They also found that treating tobacco dependence in patients with stable psychiatric conditions does not worsen their mental state.

Pharmacological interventions

In 2010, Maayan and colleagues published a systematic review and meta-analysis of 32 RCTs of pharmacological interventions to attenuate antipsychotic-related weight gain and metabolic abnormalities [Maayan *et al.* 2010]. Across a total of 1482 subjects, 15 different medications were tested: amantadine, dextroamphetamine, d-fenfluramine, famotidine, fluoxetine, fluvoxamine, metformin, hizatidine, orlistat, phenylpropanolamine, reboxetine, rosiglitazone, sibutramine, topiramate, and the combination of metformin and sibutramine. Compared with placebo, metformin showed the greatest weight loss, followed by d-fenfluramine, sibutramine, topiramate and reboxetine. Weight loss was found to be significant with metformin after weight gain had occurred, but not when started concomitantly with antipsychotics.

In a 2010 systematic meta-analysis, Tsoi and colleagues examined the efficacy of BPR for smoking cessation and reduction in schizophrenia, comparing data from seven RCTs. These authors found that biochemically verified self-reported smoking cessation rates (measuring expired carbon monoxide levels) after BPR were significantly higher than placebo at the end of the treatment. They concluded that BPR increases rates of abstinence in smokers with schizophrenia, without jeopardizing their mental state [Tsoi *et al.* 2010].

Discussion

Can metabolic syndrome be prevented? The role of clinicians and monitoring

Prevention (when feasible) is better than cure, and in the case of MetS, this can be achieved by relatively inexpensive means. The fact that MetS can quickly develop as a response to antipsychotic medication renders the role of clinicians paramount in its early detection, and the only way to do this is using a rigorous monitoring plan. The level of monitoring in many cases is far from being satisfactory, especially in the community. A large audit of 48 assertive outreach teams in the UK, including 1966 patients, revealed that more than 60% of this population had no evidence of screening for BP, obesity, blood glucose and lipid profile [Barnes *et al.* 2008]. However, those numbers significantly improved 1 year after implementing a blend of approaches to influence the behaviour of mental health professionals. Various research teams have suggested different approaches to the monitoring challenge.

The Belgian Consensus Group. This group recommended the following monitoring for basic features of MetS [De Nayer *et al.* 2005]:

(1) Weight and waist circumference (WC): weekly in hospital care, monthly in ambulatory care.
(2) Fasting plasma glucose (FPG): monthly in patients with a family history of diabetes/obesity or who are overweight/have obesity or impaired fasting glucose; at 6 and 12 weeks then every 3 months in patients without risk factors.
(3) Fasting plasma lipids (FPLs): every 3 months for the first year of treatment, then monthly.
(4) BP: every 3 months.

The British Association of Psychopharmacology. This group recommended a thorough evaluation of risks of developing MetS in all patients

receiving antipsychotic medication, followed by individual tailoring of pharmacological treatment to minimize metabolic risk and education/advice [Barnett *et al*. 2007]. Their suggested monitoring includes:

(1) Personal family history: at baseline.
(2) Height/weight and BMI: baseline, 4 weeks, 8 weeks, 12 weeks, 6 months then annually.
(3) BP: at baseline, 12 weeks then every 6 months.
(4) FPG: at baseline, 4 weeks, 8 weeks, 12 weeks then every 6 months.
(5) FPL: at baseline, 12 weeks then every 6 months.

The European Psychiatric Association, supported by the European Association for the Study of Diabetes and the European Society of Cardiology. These organizations recommended a comprehensive four-step monitoring and management algorithm [De Hert *et al*. 2009]:

(1) Step 1 (history including previous diseases, family history, smoking, exercise, dietary habits): at baseline, 12 months, then annually.
(2) Step 2 (BP, weight, WC, BMI): at baseline, 6 weeks, 12 weeks, 12 months then annually.
(3) Step 3 (FPG, FPL, ECG): at baseline, 6 weeks, 12 weeks, 12 months then annually.
(4) Step 4 (advice on smoking cessation; food choices; physical activity): at baseline, 6 weeks, 12 weeks, 12 months then annually.

The Maudsley Prescribing Guidelines. These are detailed guidelines on antipsychotic profiles with regards to hypertension, weight gain, diabetes/impaired glucose tolerance and dyslipidaemia [Taylor *et al*. 2009]. The authors recommended a comprehensive schedule of monitoring covering a variety of physiological parameters for patients receiving antipsychotic medications:

(1) Urea and electrolytes (U&Es): at baseline then annually.
(2) Full blood count (FBC): at baseline then annually.
(3) FPL: at baseline, 3 months then annually.
(4) FPG: at baseline, 4–6 months then annually.
(5) Weight, BMI: at baseline, every 3 months for the first year then annually.
(6) Electrocardiogram (ECG): at baseline, after dose increases.
(7) BP: at baseline, frequently during dose titration.
(8) Prolactin: at baseline, 6 months then annually.
(9) Liver function tests (LFTs): at baseline then annually.
(10) Creatinine phosphokinase: at baseline, then if neuroleptic malignant syndrome is suspected.

What we need to emphasize here is that physical monitoring has to be treated as the responsibility of not only physicians and general practitioners but also treating psychiatrists. It is very important that a 'metabolic monitoring toolkit' consisting of screening for BMI, FPG, FPL and BP is incorporated into the regular follow up of patients, along with the standard psychiatric evaluation [Meyer and Stahl, 2009]. Even if adherence to the above-mentioned guidelines (and any others used locally) often proves problematic, the concept of physical checking patients with schizophrenia, especially those receiving antipsychotic medication, needs to be deeply embedded in the routine practice of psychiatrists.

Is metabolic syndrome in schizophrenia a manageable condition?

A variety of behavioural interventions were considered with regards to cardiovascular fitness, smoking and weight gain in patients with schizophrenia. Most studies in this area employed either a naturalistic or experimental design of poor methodology (non-RCT) and were unable to prove one intervention to be superior to another. Among the interventions studied were wellbeing programmes, CBT, nutritional education and diet, weight management and exercise programmes, and various other combinations. Almost all interventions appeared to have some benefit for patients, either towards improving their physical health or their health perception and views.

Pharmacological interventions mainly target smoking behaviour and antipsychotic-induced weight gain, and were supported by more robust studies, mostly of RCT design. BPR and NR appear to work in smoking cessation and reduction; however outcomes were hardly sustainable.

Among various agents tested for antipsychotic-related weight gain, metformin, d-fenfluramine, sibutramine and topiramate seem to be the most effective in attenuating this side effect.

Few studies focused on mixed behavioural and pharmacological interventions. The results appear to be quite inconsistent and limited in this area, with some studies favouring pharmacological interventions over behavioural ones, while others show better outcomes by combining both kinds of interventions.

Monitoring, monitoring, monitoring

The cornerstone of early detection and effective management of MetS in schizophrenia is comprehensive monitoring, and a variety of guidelines provide structured schedules for this. Despite the introduction of guidelines for metabolic screening in schizophrenia, metabolic monitoring in routine clinical practice is still unusual. In their impressive meta-analysis of 48 studies, Mitchell and colleagues reviewed changes in monitoring of patients receiving antipsychotics before and after the implementation of relevant guidelines [Mitchell *et al.* 2012]. They concluded that although guidelines can increase monitoring, most patients still do not receive adequate tests.

Apart from the basic features of MetS (BMI, FPG, FPL, BP), other tests such as ECG and routine blood tests (U&Es, LFTs, FBC, prolactin levels) can complement the laboratory and physical checks of patients with schizophrenia, especially those in receipt of antipsychotic medication. A medical and family history should also be included in this monitoring, and in most cases it is useful to accompany the whole process with regular advice on healthy living. The frequency of monitoring can vary and be adapted to the individual needs of patients. However, it is more important that this process is incorporated in regular psychiatric follow up. The findings that certain ethnic groups, female sex, family history and type of medication all increase the risk of developing MetS can be used by practitioners to identify and target certain individuals who are likely to be at greater risk of life-threatening cardiovascular disease should they develop schizophrenia.

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