Behavioral Treatments for Weight Management in Schizophrenia

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Introduction

There has been an explosion of articles, in the last decade, calling attention to the high prevalence of metabolic abnormalities such as obesity, diabetes, dyslipidemias and associated problems, in persons with severe mental illness. As pointed out in Chapter xxx by xxx, increasingly robust evidence also indicates that, in Europe and North America, people with schizophrenia and other serious mental illnesses, die 20-25 years earlier, on average, than comparable persons in the general population (McGrath et al., 2008; Saha et al., 2007; Hennekens et al., 2005; Osby et al 2000). There is also evidence suggesting increased prevalence of some of the risk factors for early mortality for cardiovascular disease and diabetes may have been present in individuals with psychotic illnesses, as long as 100 years ago. For example, long before the advent of modern anitipsychotic medications, astute clinicians had noted that recovery in psychotic illness is often accompanied by weight gain (Kraepelin, 1919, Jaspers 1923).

Much of the recent attention to metabolic issues in serious mental illness is often linked to the widespread use of novel antipsychotics. However, patients and some observant practitioners had already highlighted medication-associated weight gain as a common side effect of most antipsychotics from the class to which we now refer to as “first generation antipsychotics” [see Ganguli (1999) for a review]. For example, Buis (1992) reported that weight gain was identified by patients, all of whom were on conventional depot antipsychotics, as one of their most frequent complaints about the side effects of medication. While it does seem clear that some novel antipsychotics, notably clozapine and olanzapine, are associated with especially high risk of weight gain (and insulin resistance and diabetes), all antipsychotics, except molindone, show more clinically significant weight gain than placebo in randomized clinical trials (Casey et al., 2005). Given the long-standing nature of the problem, and its importance to consumers and to their general health status, it is surprising that there have been so few intervention studies, addressing weight gain and its associated risks in people suffering from schizophrenia. From a practical perspective, the interventions which have been used in

persons with schizophrenia have focused almost exclusively on weight reduction. Focusing on weight reduction as a strategy to reduce the risk of cardiovascular disease and diabetes is completely consistent with the approach being taken in studies funded by the NIH like the LOOK-AHEAD study (Ryan et al., 2003; see also LOOK-AHEAD Research Group, 2007) and with NHLBI recommendations (NIH, 1998). Thus in this chapter we will also focus on studies aimed at weight reduction. Obviously other indices of risk for cardiovascular disease and diabetes such as blood pressure, cholesterol, blood sugar etc. have also been tracked in many investigations. With respect to non-pharmacologic approaches to weight reduction the majority of studies have used techniques based on behavior therapy principles, so we will first briefly review the behavioral techniques, common to most weight loss programs.

Principles of Behavioral Approaches to Weight Loss

As reviewed by Wing (2004), the systematic application of behavior therapy techniques to induce weight loss started in the late 1960's. The early studies tended to milder forms of overweight and obesity and focus on stimulus control, rather than on specific caloric intake goals or exercise and activity. In reviewing these early programs, (Wadden And Butryn, 2003) note that weight loss of 4-5 kg was common in programs typically lasting for 10 weeks. Over the next two decades, as the prevalence of obesity grew, treatments became more sophisticated and comprehensive, and tended to last for longer. By the mid 1990's average weight loss in behavioral programs, which typically lasted for 6 months, had risen to about 9 kg, or about double what had been reported in the 1960s (Wing 2004). Probably one of the most persuasive demonstrations of the efficacy of behavioral methods for weight loss was the Diabetes Prevention Trial (DPP) in which over 3,000 overweight or obese individuals with impaired glucose tolerance were randomized to a lifestyle intervention (aimed at weight loss), metformin, or placebo. Not only was significant weight reduction achieved in the lifestyle group, but progression to diabetes was also reduced (Knowler et al. and the DPP Research Group 2002). Furthermore, behavioral treatment was not only twice as effective as metformin

in producing weight loss, but the intervention was so effective in preventing the progression of pre-diabetes to diabetes, that the trial was stopped prematurely (DPP Research Group 2002). The key components for the non-pharmacological management of overweight and obesity are identified in Table 1 [adapted from Jakicic and colleagues (2001)].

Most approaches to the treatment of obesity are described as “behavioral” and based on learning theory (Wing 2004) and the principles of classical conditioning (Wadden and Foster 2000). In the last 20 years or so, cognitive approaches have been added to behavior therapy, to restructure and correct distorted and irrational thoughts which undermine motivation and progress in treatment (Wadden and Foster 2000). Common components of most behavioral weight reduction programs include a) goal-setting, especially on realistic short-term goals (Bandura and Simons 1977); b) self-monitoring (Kazdin 1974) of nutritional intake and physical activity c) a nutritional focus, teaching and demonstrating healthy eating habits (Wing 1989; Brownell 2004), and d) strategies to increase exercise and decrease sedentary behavior (Jakicic 2002; Jakicic and Gallagher 2003; Jakicic, Marcus et al. 2004). Stimulus control, by changing the environment to alter cues so as to increase appropriate (and decrease inappropriate) eating behavior, was also an early component of behavioral programs (Ferster, Nurnberger et al. 1962; Stuart 1967). Problem solving (D'Zurilla and Goldfried 1971) is now also often included to help individuals develop strategies individualized to their own unique situations (Wing 2004). Once weight loss is achieved most programs move participants on to relapse prevention or weight maintenance regimens (Brownell, Marlatt et al. 1986; Jeffery and French 1999; Klem, Viteri et al. 2000; Perri et al. 2001; Wadden, Butryn et al. 2004).Since these strategies are often offered as a package, it is not clear which of these components is essential to the efficacy of the treatments. Recently, cognitive behavior therapy has attempted to distinguish itself from “behavior” therapy, but pointing out that the former specifically includes restructuring cognitive processes (Cooper & Fairburn, 2002).

In the studies of weight loss in schizophrenia, the approaches have included one or more elements of common behavioral approaches, but, in many instances, the precise theoretical underpinnings of the program components have not been specified. A selective review of interventions for weight loss in schizophrenia follows.

BEHAVIORAL AND NUTRITIONAL INTERVNENTIONS IN SCHIZOPHRENIA

One of the earliest published attempts to assist psychotic patients with weight loss was carried out in a State Hospital in the US, over 40 years ago, by Hamatz and Lapuc (1968). This pioneering study was a rigorous behavioral program utilizing negative reinforcement: the patients lost money if they failed to lose weight. Hamartz and Lapuc (1968) used two comparison groups, a group discussion of weight loss strategies with peer-support, and a group who received nutritional counseling. The subjects were randomly assigned to the three arms of the study. The group assigned to contingent negative reinforcement had significantly greater mean weight loss than the other two groups (-7% of initial body weight, over 10 weeks). A second historically important study was carried out by Rotatori and co-workers (1980). They recruited patients, with psychotic illness, residing in community-based group homes. Patients were then randomly assigned to either a 14 week behavioral weight loss group intervention, closely resembling most modern weight loss programs, or to no intervention ("usual care"). In the study by Rotatori and colleagues the group randomly assigned to behavioral treatment lost significantly more weight (mean -7.3 lb) than the control group (mean +.04 lb). The Rotatori et al., study is also notable for their use of a well-developed manual for the delivery of their treatment, and the behavioral techniques employed had already been refined in earlier studies of patients with Downs syndrome. We highlight these early studies because they dealt with populations which are still relevant today: severely mentally ill persons who are in long-stay hospitals as well as those in community residential services. These early (first generation) studies also deserve more recognition for the following reasons. First, they demonstrated that patients with psychotic illnesses could participate successfully in non-pharmacologic

weight loss interventions. Secondly, even though these were pioneering studies, they were well designed randomized trials, in the best traditions of generating evidence for clinical practice. Surprisingly, the second generation of published studies were, for the most part, uncontrolled, or failed to employ random assignment to the intervention or comparison conditions. Fortunately, the most recent generation (third generation) of reports are predominantly from randomized controlled trials, and thus a good evidence base is growing.

There have been numerous reviews of behavioral and nutritional interventions for weight loss in schizophrenia (e.g., Alvarez-Jimenez et al., 2008; Faulkner, Cohn, & Remington, 2007; Faulkner & Cohn, 2006; Ganguli, 2007; Loh, Meyer, Leckband, 2006; Strassnig and Ganguli, 2007; Werneke, Taylor, Sanders, & Wessely, 2003). All reviews conclude that modest short-term weight loss is possible in this population. Examining randomized controlled trials only, a recent meta-analysis (Alvarez-Jimenez et al., 2008) reported a statistically significant reduction in mean body weight for those in the non-pharmacological intervention groups compared with those on treatment as usual (WMD = -2.56 kg, 95% CI -3.20 to -1.92, $p < 0.001$) at the end of treatment. There was a slightly larger effect in studies designed to prevent weight gain but this was not significant. Additionally, there were no statistically significant or practically important differences between therapeutic approaches using individual or group interventions or CBT compared with nutritional counseling (Alvarez-Jimenez et al., 2008).

We will not review each of the included RCTs in detail, but present them in Table 2. In summary, seven of the included trials investigated cognitive–behavioural intervention strategies (Alvarez-Jimenez et al., 2006; Brar et al., 2005; Jean-Baptiste et al., 2007; Khazaal et al., 2007; Kwon et al., 2006; McKibbin et al., 2006; Weber & Wyne, 2006). Three described nutritional counselling interventions (Evans et al., 2005; Littrell et al., 2003; Scocco et al., 2006). Two studies combined nutritional and exercise interventions and compared this to standard care (Wu et al., 2007) or metformin alone or in combination (Wu et al., 2008). Six trials tested group intervention formats (Brar et al.,

2005; Khazaal et al., 2007; Jean-Baptiste et al., 2007; Littrell et al., 2003; McKibbon et al., 2006; Weber & Wyne, 2006) and the remaining six examined individual interventions. Eight studies were designed to treat weight gain while the remaining four studies were designed to prevent weight gain – typically after starting or switching to an atypical antipsychotic (Alvarez-Jimenez et al., 2006; Evans et al., 2005; Littrell et al., 2003; Scocco et al., 2006). Participants were generally outpatients except in three studies which included inpatients (Alvarez-Jimenez et al., 2006; Wu et al., 2007) or a combination (Khazaal et al., 2007). Interventions lasted between 8 to 24 weeks with an average of approximately fifteen weeks. Five studies reported a follow-up assessment ranging from 8 weeks (Littrell et al., 2003), 24 weeks (Evans et al, 2005; Scocco et al., 2006; Khazaal et al., 2007), to six months (McKibbin et al., 2006). In the next paragraphs we will highlight some of these studies which bring up issues that we address in the discussion including two studies not incorporated in the recent meta-analysis (Jean-Baptiste et al., 2007; Wu et al., 2008).

Of the first randomized controlled clinical trials, Litrell et al. (2003) provided a 16-week psychoeducational program focusing on nutrition, exercise, and healthy lifestyle, to patients who had been switched, from other antipsychotics, to olanzapine. That all the patients in this study were on one drug is notable, as in many other studies, treatment effects are potentially confounded by medication effects and interactions. Litrell et al. reported little weight change in the intervention subjects as opposed to a statistically significant weight gain in the control group. Thus the benefit of the intervention might have been to prevent weight gain, rather than to produce weight loss. Since olanzapine carries a very high risk of clinically significant weight gain (Newcomer 2005), and weight gain in adulthood is a powerful predictor of cardiovascular disease (Stamler, Wentworth et al. 1986) prevention of weight gain is a worthwhile benefit of treatment.

Prevention of weight gain was the focus of a study reported by Alvarez-Jimenez and colleagues (2006). In an early behavioral intervention group, 10 to 14 individual sessions were completed with a clinical psychologist within the first 3 months of

antipsychotic treatment. The structure of the sessions consisted of a weight check, agenda setting, review of self-monitoring records, and setting new homework assignments. Modules were available on engagement and assessment, psychoeducation, dietary counseling, exercise, and behavior therapy. Selection of the intervention strategies was based on a collaborative formulation after initial assessment between the therapist and the patient. At the end of treatment, significantly fewer patients in the intervention group increased their baseline weight by more than 7% (39.3% versus 78.8%). All participants randomized completed the trial.

Brar et al. (2005), developed a manualized 16 week intervention, adapted from the study conducted by Rotatori et al. (1980). This study also controlled for confounding effects of medication by first switching all subjects to the same antipsychotic (risperidone). This is also one of the few studies to use blinded raters. Participants enrolled because they desired to lose weight. Also of note, regular mental health clinicians, as opposed to specialists in behavior therapy or nutrition, delivered the intervention, following the manual. This latter was an attempt to make the results more likely transferable to routine clinical care. Mean weight loss in this study was larger in those randomly assigned to the intervention, but both groups lost weight and the difference was not statistically significant. However, the proportion of subjects who lost 5% or more of their baseline body weight was three times larger in subjects randomized to the intervention than in controls (32.1% versus 10.8%), and the difference was statistically significant.

Jean-Baptiste et al. (2007), in an outpatient study, used standard behavioral techniques, from a widely accepted program (LEARN, Brownell, 2004). To the standard nutrition and exercise program, they added a novel indirect method of food provision. Subjects were first given lists of “healthy” food choices and subsequently, at weekly group sessions, they were reimbursed for the costs of these foods, provided they had receipts showing that they had purchased these food items in the previous week. There was

statistically significantly greater mean weight loss in the intervention group, as compared to controls. Jean-Baptiste et al. (2007) also conducted a 6 month follow up, and reported continuing weight loss in participants, but the number of subjects was only 12, leaving some uncertainty about the robustness of the results. Nevertheless, this is a promising rigorous evaluation of a "multimodal" approach, and needs to be followed up.

Focusing on patients with both schizophrenia and diabetes, McKibbin et al (2006) recruited patients from board-and-care and community clubhouse settings. Optimal diabetes management requires active self-management, including weight control and weight loss. Patients with schizophrenia often have difficulty accessing, and participating in, comprehensive diabetes management programs. This study illustrates the effectiveness of a well- constructed intervention geared for patients with schizophrenia and diabetes. The 24-wk Diabetes Awareness and Rehabilitation Training Program (DART) was developed in collaboration with a Community Advisory Board comprised of consumers, family members and community clinicians and consisted of weekly, 90 minute group sessions addressing diabetes education, nutrition and exercise. Educational material was adapted by limiting text, introducing one or two topics per session, providing an overview and summary of material, using a teach-and-query training method and mnemonic aids. Concrete behavior change strategies included weekly weigh-ins, pedometers, healthy food sampling and reinforcements (raffle tickets for small health gains). Patients in the intervention group lost a mean of 5 lb compared with a weight gain of 6 lb in those receiving usual care (medical follow-up and written diabetes information). The intervention group also showed significant improvements in diabetes knowledge and self-efficacy, self reported physical activity, but not in fasting plasma glucose or glycosylated hemoglobin.

In the largest study to date, 128 first-episode schizophrenia patients were randomly assigned to 12 weeks of placebo, 750 mg/day of metformin alone, 750 mg/day of metformin and lifestyle intervention, or lifestyle intervention only. The lifestyle

intervention included psychoeducational, dietary and exercise programs. Psychoeducation focused on the role of eating and activity in weight management. Dietary intervention followed the American Heart Association step2 diet which allows less than 30% of total calories from fat (<7% saturated fat and < 200 mg of cholesterol); 55% from carbohydrates; and more than 15% from protein daily with an increase in fiber intake to at least 15 g per 100 kcal. Participants maintained a 3 day food diary at baseline and follow up visits were reviewed by a dietitian who provided feedback. In the first week, exercise sessions were directed by an exercise physiologist and participants performed exercise (walking or jogging) on a treadmill 7 times a week for 30 minutes at each session. After the first week, exercise was home-based with recommendations to exercise 30 minutes per day. At the end of the trial, the lifestyle intervention plus meformin group (-4.7 kg 95% CI -5.7 to -3.4) was superior to both the lifestyle intervention alone (-1.4 kg 95% CI -2.0 to -0.7), and the metformin alone (-3.2 kg 95% CI -3.9 to -2.5) conditions. Metformin alone was more effective in weight loss and improving insulin sensitivity than lifestyle interventions alone.

Notably, while considerable rigor is required to induce weight loss in terms of maintaining a negative energy balance (see Table 1), in all of the identified RCTs, dropout has generally not been a concern in the treatment arm. This might suggest that patients can be motivated to initiate and then adhere to a lifestyle intervention for weight management at least in the short-term. Drop-out is certainly not as high as reported in a recent review (Loh et al., 2006) although attention must be given to the development of retention strategies to minimize dropout (Faulkner & Cohn, 2006). Furthermore, no adverse effects explicitly linked to participating in a lifestyle intervention program have been reported.

DISCUSSION

The results, from weight loss interventions (WMD = -2.56 kg, Alvarez-Jimenez et al., 2008), achieved in persons with schizophrenia, are within the range of those reportedly obtained by commercial weight loss programs in the general population (Heshka et al.,

2003) although not as great as suggested by a meta-analysis of RCTs of cognitive-behaviour therapy combined with a diet/exercise intervention (WMD = -4.9 kg, CI -7.3 to -2.4; Shaw et al., 2005). However, it is reasonable to question whether such modest improvements actually translate into measurable improvements in health status or risk of cardiovascular disease and diabetes. There is general agreement that even a 5% weight loss, in obese individuals, can produce measurable health benefits. For example, in the Finnish Diabetes Prevention Study, a modest weight loss of 4.8% of initial body weight, was associated with a 58% reduction in the risk of developing diabetes, over the following 3 years (Tuomilehto et al, 2001). In relation to blood pressure, it has been shown that as little as 3-4 Kg of weight loss, over 3 years, results in clinically significant reductions in systolic and diastolic blood pressure (Mertens and Van Gaal 2000). There is also accumulating evidence from prospective observational studies that increasing physical activity is effective in improving the health profile of individuals who are overweight and obese (e.g., Lee et al., 1999). Weight loss might be considered a primary goal but clinicians should keep in mind that small, sustained positive changes in physical activity and dietary intake may be associated with significant health benefits irrespective of weight loss per se.

With very few exceptions, even randomized controlled interventions, have rarely followed patients for longer than 6 months. Weight loss is challenging but even more challenging is weight loss-maintenance (Wing et al., 2006). Hence, the real health benefits of weight loss interventions, even for those who respond to interventions, will only be known when data from longer studies becomes available. Fortunately there are currently several on-going clinical trials which have up to 2 years of follow up in their designs. In addition, obesity is unquestionably a chronic condition, and it is likely that long-term success may require some form of maintenance treatment. Again, it is encouraging that some studies of maintenance treatment are currently in progress. Overall, interventions will probably need to set realistic goals, be highly structured,

provide early and intensive support initially, and offer reduced but continued support over time if not indefinitely (Faulkner & Cohn, 2006).

Most currently published research has evaluated pharmacologic and non-pharmacologic treatments, for weight loss, in separate studies (pharmacologic treatments are reviewed in Chapter xx). However evidence is accumulating that combining behavioral and pharmacologic weight loss interventions can be more effective than either of the approaches by themselves (Wadden et al., 2005). One study has now been published that also demonstrates this in schizophrenia as well (Wu et al., 2008). Given concerns about potential polypharmacy, the demands of adding further medication to an existing medical regimen, and the cost of medication, we suggest however that adjunctive pharmacotherapy for weight loss be reserved for patients who do not respond adequately to lifestyle interventions alone (Faulkner, Cohn, & Remington, 2007). Further studies evaluating the combination of behavioral and pharmacologic weight loss therapies are required before routinely recommending such a dual approach in clinical practice. Switching to an antipsychotic medication with low liability for weight gain has also emerged as an effective strategy for weight loss and metabolic benefit, particularly when the increase in weight was clearly associated with prior antipsychotic treatment (Weiden, 2005a; Weiden and Buckley 2007)(See Chapter xx). No studies to date have investigated the combination of antipsychotic switching and behavioral strategies for weight loss.

Given that the current system of care for persons with severe mental illness is routinely described as underfunded and overburdened (Frank and Glied, 2006), economic considerations may well determine which interventions for weight loss, if any, will make it to the front lines of community mental health. Thus, cost benefit analyses should be included in the evaluation of proposed interventions. At this point, it is fair to say that such analyses are almost entirely missing from the evidence base on this subject. Even without, sophisticated economic analyses, clinicians would be able to evaluate the

potential benefit of investing time and resources in particular interventions, if the published results systematically reported the proportions of subjects who benefitted and preferably also reported number-needed-to-treat, for each threshold of response. Unfortunately, most studies already published limit the results to reporting mean changes in body weight.

CONCLUSIONS

At this time we can conclude that persons with schizophrenia want to and will participate in behavioral weight loss interventions. For unmotivated or difficult to engage individuals, consideration could be given to broader environmental interventions that aim to shape the environment in ways which are conducive to encouraging greater physical activity while restricting energy intake (Gorczynski, Faulkner, Zeglen, & Cohn, 2008). Taken together, the evidence from controlled trials indicates that patients who do participate in weight loss interventions increase their chances of losing weight. The results of simple and practical interventions are modest, but clinically meaningful. The data on long-term maintenance of weight loss is essentially lacking, but some ongoing studies will provide data in the next few years. The data on preventing weight gain, in persons with schizophrenia, is developing and looking positive. With these observations in mind, standard behavioral weight loss interventions should be widely and routinely offered to schizophrenia patients who are overweight or obese. In addition, discussion about the risk of weight gain and monitoring of weight should be routinely offered to all patients with schizophrenia. Given that the current trend is for the rates of obesity to continue to increase, research into enhancing the effectiveness of current interventions, and the development of new approaches to weight loss need to be urgently funded.

Key Clinical Points

- Education about the health hazards of being overweight or of becoming overweight should be included in the psychoeducational interventions offered to persons with schizophrenia along with simple advice about health nutrition and exercise measures

- Regular measurement of body weight should be part of routine care in mental health settings and patients should be given feedback on their own weight regularly. Patients should also be encouraged to weigh themselves.

- Patients who ask for active interventions to help them lose weight should be offered group or individual interventions, preferably within the mental health treatment setting.

- Referral to specialized programs, including the full range of options for severe and/or treatment-resistant obesity should be pursued for patients who are in need of these services

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Table 1. Key components for the management of overweight and obesity [adapted from Jakicic (2001)]

Component	Requirement
Diet	
	Energy intake restriction of 500-1000kcal/day.
	Dietary fat reduced to <30% of energy intake.
	Optimal dose of carbohydrate and protein have not been established.
Exercise	
	Significant health benefits will occur with 150 minutes of moderate (55%-69% of maximum heart rate) exercise per week.
	Overweight and obese individuals should increase this to 200-300 minutes per week.
Behavioural Therapy	
	Associated with improved long term outcomes.
	Training should be given in behavioural concepts (e.g., problem solving, goal setting, social support).

Table 2 Randomized Controlled Trials of Behavioral Interventions for Weight Gain in Schizophrenia

Author Participants	**Intervention**	**Number of Participants, Outcome at final assessment** (weight change [kg]), **Compliance, & Attrition**
Littrell et al. (2003) Prior conventional antipsychotics, commencing olanzapine at study entry	Weekly one-hour group sessions for 16 weeks of diet and exercise education versus usual care. Two-month follow-up.	N =70. Intervention = -0.3 kg; usual care = +4.3 kg. There was a compliance rate of 92% to the program sessions. No dropout reported.
Brar et al. (2005) BMI over 26, switched from olanzapine to risperidone	Two sessions per week for six weeks then one session per week for eight weeks of diet and exercise education versus usual care (encouraged to lose weight)	N=72. Intervention = -2.0 kg; usual care = -1.1 kg (not significant). Five per cent weight loss in 32.1% of intervention subjects vs. 10.8% in control group. 15/ 28 patients attended all 20 sessions. 21% dropout in the treatment group.
Evans et al. (2005) Commenced olanzapine within 12 weeks of study entry	Six one-hour individual nutrition education sessions over three months (every two weeks) versus usual care (+ passive nutrition information).	N=51. Intervention = +2.0 kg, usual care = +9.9 kg. Compliance not reported. 21% dropout in the treatment group. Fewer patients in the experimental group (13%) than in the control group (64%) increased initial body weight by more than 7%.
Alvarez-Jimenez et al (2006) First episode psychosis < 6 wk prior antipsychotic. Treated: risperidobe, olanzapine, haldol	10 – 14 individual sessions (psycho-education, behaviour therapy, dietary counseling, exercise program) for 3 months versus usual care	N=61. Intervention = + 4.1 kg, usual care = + 6.9 kg. Fewer patients in the experimental group (39.3%) than in the control group (78.8%) increased initial body weight by more than 7%. Compliance not reported. No dropout and all of the patients completed the study.
Kwon et al. (2006) More than 7% body weight gain on olanzapine	Weekly individual sessions with dietician and exercise coordinator over 12 weeks (weekly for first 4 weeks then every 2 weeks) versus usual care	N=48. Intervention = - 3.9kg, usual care -1.5 kg Compliance: Diet all were over 80% compliant; Exercise 36% were over 80% compliant Dropout: 33% in treatment group
McKibbin et al. (2006) Schizophrenia and diabetes diagnosis	Weekly 90 minute group sessions for 24 weeks focused on diabetes education, nutrition and exercise versus usual care (plus passive information)	N=64. Intervention = - 2.3 kg, usual care = + 3.1kg. Five per cent weight loss in 38% of intervention subjects vs. 12% in control group. 80% of treatment group attended at least one half of all intervention sessions. No difference in drop out rate between intervention group and usual care
Scocco et al. (2006) Patients switched to	Eight-week individual dietary intervention provided by a nutritionist	N=20. Intervention = 0.99 kg, control = 2.96 kg. Dropout: 20% in control group. Compliance not clearly reported. Dropouts: intervention 0/10, control 2/10.

Olanzapine from conventional antipsychotics		
Weber & Wyne (2006) Second generation antipsychotics, BMI>25	Weekly one-hour groups sessions for 16 weeks of diet and exercise education versus usual care.	N=17. Intervention = -2.5 kg, usual care = -0.6 kg (not significant). Compliance not reported. No dropout in treatment group.
Jean-Baptiste et al. (2007) BMI >30, on antipsychotic (any)	Weekly group sessions for 16 weeks. Psychoeducation, goal setting, self monitoring. $25/wk for healthy foods.	N=18. Intervention = -2.8 kg, usual care = + 2.7 Compliance not reported.14/18 completed the intervention
Khazaaal et al. (2007) > 2kg weight gain over 6 months on antipsychotic (any)	Weekly two-hour group cognitive behavioral therapy plus psychoeducation for 12 weeks versus a single 2-hr nutrition education session	N=61. Intervention = - 2.9 kg, usual care = - 0.8 kg. At end of treatment, 16.1% of experimental group vs. 13.3% of control group had lost 5% or more of their initial BMI. This increased to 22.6% and 16.7% at 12 week follow-up. Follow up (12 weeks post intervention) Intervention = - 3.5 kg, usual care = + 1.7 kg. Compliance not reported. Dropouts: intervention 8/31, control 7/30.
Wu et al. (2007) Clozapine (≥300mg/day)for at least 1 year, BMI≥ 27	Diet (inpatients) reduced by 200 to 300 kcal/day. Walking (level and stairs) for 60 minutes three days a week for six months	N= 56. Intervention = -4.2 kg, usual care = + 1 kg Compliance not reported. No dropouts in the treatment group.
Wu et al. (2008) First episode schizophrenia, gained more than 10% of predrug body weight	Psychoeducation, diet and exercise (lifestyle intervention) over 12 weeks versus usual care (placebo), metformin (met), and lifestyle plus met	N=128. Lifestyle intervention = -1.4 kg, usual care +3.1 kg Met. = -3.2 kg, lifestyle plus met. = -4.7 kg Compliance: Diet 61-84%, excercise 50-60% Dropouts : Lifestyle plus met. 2/32, lifestyle only 3/32