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A review of current approaches to metabolic consequences of atypical antipsychotics and a description of a potential novel non-pharmacologic strategy

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Dedication

This paper is dedicated to my partner, PJ Redbird Two Ravens, MSW, whose love and support has allowed me to survive and thrive in PA school; and to my mother, Kathleen Frances Sundermeyer, RN, for her never ending encouragement and inspiration.

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Chapter 1: Introduction

Overview of Antipsychotic Medications and Associated Adverse Cardiometabolic Effects

Antipsychotic medications are a diverse and important class of drugs used to treat psychotic symptoms in a wide variety of conditions, primarily schizophrenia, but also bipolar disorder and organic and drug-induced psychoses. They are able to improve mood and reduce anxiety and sleep disturbances and, thus, are commonly used as adjuncts in bipolar disorder and depression. This review will focus on studies pertaining to patients with schizophrenia, as they are the most commonly studied homogeneous population using this class of medications. All antipsychotic medications are dopamine antagonists, though individual receptor binding profiles vary widely, and this leads to a range of desired and undesired effects. These agents are grouped into first generation, or "typical," antipsychotics and second generation, or "atypical," antipsychotics. First generation antipsychotics (FGAs) include phenothiazines (fluphenazine, chlorpromazine) and haloperidol. Particularly for high-potency agents, such as haloperidol, therapeutic doses of FGAs are associated with a high incidence of troublesome movement disorders known as extrapyramidal side effects (EPS), including acute dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia. Second generation antipsychotics (SGAs), including olanzapine, quetiapine, risperidone, clozapine, ziprasidone and others, are more successful in dissociating EPS from antipsychotic action and, as a result, have become much more widely used (Lett et al., 2011; Meltzer, 2012). Unfortunately, many of these atypical antipsychotics are associated with clinically significant weight gain (defined as $\geq$ 7% increase in body weight from baseline) and adverse effects on cardiovascular and metabolic health, including an atherogenic lipid profile, increased fasting glucose, and insulin resistance. Additionally, an increase in inflammatory markers often associated with cardiovascular disease

(CVD), such as C-reactive protein (CRP), has also been noted in patients treated with SGAs (Meyer et al., 2009).

Although research suggests dopamine type 2 (D_2) or histamine type 1 (H_1) receptor binding affinity may play a role, the precise etiology of these adverse cardiometabolic changes and weight gain is still unclear (Lett et al., 2011). A study by Garcia-Tornadu and others (2010) supported the notion that D_2 receptors play a critical role in insulin secretion and glucose metabolism and blockade by SGAs might account for some of the metabolic changes seen. A genome-wide association study searching for single-nucleotide polymorphisms associated with substantial SGA-caused weight gain identified 20 potential sites near the melanocortin 4 receptor (MC4R) gene, which overlaps a region previously associated with obesity in the general population (Malhotra et al., 2012). Others have proposed an alteration in satiety perception or regulation (Leadbetter et al., 1992). Animal models have shown histamine H_1 blockade is associated with appetite stimulation and weight gain via hypothalamic eating centers (Kim, Huang, Snowman, Teuscher, & Snyder, 2007; Stahl, Mignon, & Meyer, 2009) and serotonin $5HT_{2C}$-receptor antagonism leads to hyperphagia and weight gain (Bonhaus et al., 1997; Stahl et al., 2009; Tecott et al., 1995). Regardless of mechanism, these adverse effects have greatly detracted from the therapeutic potential and patient acceptance of SGAs (Bermudes, Keck, & McElroy, 2007; Weiden, Mackell, & McDonnell, 2004).

Complicating the issue, many patients who are routinely prescribed these medications have pre-existing cardiovascular comorbidities or risk factors for cardiovascular and metabolic disease, such as sedentary lifestyle, smoking, poor diet, poverty, and lack of access to health care (Compton, Daumit, & Druss, 2006). A meta-analysis of worldwide studies showed an association between schizophrenia and current cigarette smoking with a weighted average odds

ratio of 7.2 (95% CI [6.1, 8.3]) versus the general population; additionally, heavy smoking (defined as > 1.5 packs per day) was also much more common among patients with schizophrenia (OR 1.9, ranging from 1.7 – 2.1; de Leon & Diaz, 2005). A 2006 study comparing morbidity and mortality statistics of public mental health clients to the general population found that these patients have a two to five times higher standardized mortality rate (SMR) with 13 – 30 years of potential life lost (YPLL) and that they die overwhelmingly of cardiovascular disease (Colton & Manderscheid).

Additionally, disparities exist in treatment of physical illness among people with serious mental illness. A study of a national cohort of Medicare patients hospitalized with acute myocardial infarction examined associations between mental illness and provision of five established quality indicators: reperfusion therapy, smoking cessation counseling, and treatment with aspirin, β-blockers, and angiotensin converting enzyme inhibitors (ACE-I; Druss, Bradford, Rosenheck, Radford, & Krumholz, 2000). They found significant disparities in adherence to these guidelines for patients with schizophrenia, which, after covariate analysis, explained the 34% (HR 1.34, 95% CI [1.01, 1.66]) increase in excess one-year mortality among these patients, particularly those considered "eligible but not ideal" for these therapies (Druss et al., 2000). Extracting data from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study (n = 1460), another group determined that only 69.87% of identified diabetic patients, 37.6% of hypertensive patients, and 12% of patients with hyperlipidemia were receiving pharmacotherapy for these disorders (Nasrallah et al., 2006)

This combination of increased risk factors with disparities in treatment has meant that patients with serious mental illness, specifically schizophrenia, die significantly younger than their peers. Therefore, strategies are needed to mitigate or avoid the unwanted metabolic adverse

effects of SGAs. The following clinical literature review summarizes current pharmacologic and nonpharmacologic approaches to this problem, and it describes a new model for addressing patients who require treatment with SGAs and are likely to experience challenges in maintaining cardiometabolic health.

Chapter 2: Methods

The literature search was carried out using PubMed and Cumulative Index to Nursing and Allied Health Literature (CINAHL) for articles in English language, peer-reviewed journals, preferentially from the last ten years. Medications included in the discussion are FDA-approved therapies currently available in the United States. The following terms were used in varying combinations: *antipsychotic, atypical antipsychotic, second generation antipsychotic,* individual antipsychotic agents *(clozapine, olanzapine, risperidone, quetiapine, aripiprazole, ziprasidone,* and others*), adverse effects, diabetes mellitus, obesity, weight gain, metabolism, metabolic syndrome, MetS, insulin resistance, glucose intolerance, schizophrenia, health at every size, HAES, non-diet, nondiet, intuitive eating, appetite physiology, hunger physiology, diet, feeding behavior, satiation,* and *weight loss*. Additional references were identified via bibliographic searches of retrieved articles. A personal interview was carried out with Brandie Hagaman, MPH, Integrated Health Supervisor of Washtenaw County Community Mental Health Community Support and Treatment Services, to discuss her agency's lifestyle program to address weight gain and other cardiometabolic factors for their consumers. Articles pertaining to SGAs were selected from research populations of adult patients with schizophrenia, as that is the most intensively studied homogeneous population among users of these agents. Additional supporting articles and articles on HAES® approaches were selected from studies of the general adult population. Preference was given to recent (within the last 15 years) double blind, randomized, controlled trials with large sample sizes and systematic reviews and meta-analyses.

Chapter 3: Literature Review of Current Approaches to Prevention and Treatment of Cardiometabolic Effects of Antipsychotics in Patients with Schizophrenia

A wide range of strategies has been utilized to ameliorate the weight gain and cardiometabolic adverse effects of SGAs. In 2007, a systematic Cochrane Database Review examined current pharmacologic and nonpharmacologic approaches to preventing or reversing antipsychotic-associated weight gain and metabolic disturbances (Faulkner, Cohn, & Remington). Pharmacologic strategies reviewed include initial choice of antipsychotic agent, dose and route of administration of the SGA, addition of medications to effect weight loss or prevent weight gain, addition of medications to increase insulin sensitivity and decrease progression to type 2 diabetes, and switching to a less metabolically unfriendly agent. Of the pharmacological interventions, authors concluded that initial medication choice and switching to an SGA with fewer cardiometabolic adverse effects may be the best options for avoiding weight gain and changes in metabolic parameters. Authors also concluded that addition of selective medications may lead to short-term, modest weight loss, but that this strategy should be reserved for patients who do not respond to lifestyle modification strategies. In general, however, the authors advocated for more high quality, long-term studies to determine optimal strategies.

Pharmacologic Strategies

Initial antipsychotic selection.

It has been well established that different SGAs are associated with differing effects on weight and metabolic indicators. The consensus statement issued in 2004 by the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity stated

that current evidence shows that adverse effects on weight gain, risk for diabetes, and worsening lipid profile are strongest with clozapine and olanzapine; intermediate in regard to weight gain and discrepant with regard to risk of diabetes and lipid alterations with quetiapine and risperidone; and lowest with aripiprazole and ziprasidone, which appear to carry no increased risk of diabetes or worsened lipid profiles. This characterization was reinforced by a comprehensive literature review of metabolic effects of SGAs (Newcomer, 2005) and a systematic review and meta-analysis (Rummel-Kluge et al., 2010). This risk stratification by agent was further supported by a large post-marketing multisite analysis that specifically looked at treatment-emergent diabetes in users of FGAs compared with SGAs (Yood et al., 2009). Given the varying liabilities of different agents, choice of initial agent is critical to limit potential adverse effects; findings suggest ziprasidone and aripiprazole are preferred first choice options in this regard.

Subsequent to the publication of the majority of literature reviews and analyses, several new SGAs have been approved and marketed in the U.S.: these include paliperidone (approved in 2006), iloperidone (approved in 2009), lurasidone (approved in 2009), and asenapine (approved in 2010). Although initial data suggest that these agents may have a safer cardiometabolic profile than clozapine or olanzapine, some evidence suggests iloperidone is associated with mild weight gain (Citrome, 2011). However, there are no controlled trials to recommend a first-line status for use of these agents in those concerned about weight gain or metabolic changes at this time.

Medication switch.

Another option for those already on an SGA which is causing adverse effects on weight or metabolic parameters is switching to a less obesogenic agent. Specifically, there are studies examining the effects of switching to either aripiprazole or ziprasidone, the agents with lowest risk for weight gain (American Diabetes Association et al., 2004). A multisite randomized controlled trial examined the strategy of switching from olanzapine, quetiapine, or risperidone to aripiprazole, looking at the primary efficacy outcome of non-high-density lipoprotein (HDL) cholesterol and secondary outcomes of efficacy failure (Stroup et al., 2011). Patients that switched had a greater reduction in non-HDL cholesterol, triglycerides (TG), and weight, and switching was not associated with a greater number of treatment failures, although there was a higher discontinuation rate among the switching group. Another trial which randomized patients to different methods of switching to aripiprazole also found that switching was associated with modest weight loss between 1.3 and 1.7 kg among the three switching protocol groups, with some patients achieving "clinically significant" weight loss of ≥ 7% from baseline, ranging from 7 – 15% among three treatment groups (Casey et al., 2003).

Several studies have evaluated switching to ziprasidone. One study compared three six-week, multicenter, randomized, open-label, parallel group trials of switching strategies pertaining to method of discontinuation of prior agent, and also included weight at baseline and endpoint (Weiden, Simpson, Potkin, & O'Sullivan, 2003). Patients were switched from olanzapine (n = 104), risperidone (n = 58), or FGA (n = 108). Patients switched from olanzapine had significant reductions in mean body weight (baseline 205.5 lb [93.4 kg], endpoint 201.5 lb [91.6 kg]; mean change -3.9 lb [1.8 kg], $p < .001$). Patients switched from risperidone had smaller, but still significant, reductions: baseline 192.1 lb [83.7 kg], endpoint 190.3 lb [86.5 kg], mean change -

1.9 lb [-0.9 kg], $p < .05$. No significant changes in weight were seen in patients switched from conventional antipsychotics, and no significant correlations were seen between baseline and endpoint weights. Another article looked at three open-label extension studies of outpatients switched to ziprasidone from risperidone ($n = 43$), olanzapine ($n = 71$), or FGA ($n = 71$) with a maximum total treatment time of 58 weeks, and found significant improvements in weight, BMI, total cholesterol, and triglycerides in patients switched from olanzapine or risperidone, including a mean reduction in weight of 9.8 kg ($p < .002$) for olanzapine and 6.9 kg ($p < .005$) for risperidone (Weiden, Newcomer, Loebel, Yang, & Lebovitz, 2008). Another study (Weiden, Daniel, Simpson, & Romano, 2003) investigated improvements in indices of health status in outpatients with schizophrenia switched to ziprasidone from olanzapine ($n = 104$), risperidone ($n = 58$), or FGA ($n = 108$). In this study, patients switched from olanzapine experienced a mean weight loss of 1.76 kg ($p < .0001$), while those switched from risperidone had a mean weight loss of 0.86 kg ($p = 0.015$) and those switched from FGAs had a small, nonsignificant increase of 0.27 kg ($p = 0.3$). Patients switching from olanzapine also experienced an improvement in TG (-50 mg/dL, $p < .0001$), and patients switching from risperidone had a lesser improvement (-29 mg/dL, $p < .01$; Weiden, Daniel, et al., 2003). Thus, overall, switching from an agent with greater potential for weight gain and dyslipidemia to one with lesser potential appears to be a reasonable approach to partially reversing these negative effects.

Addition of adjunct medications.

Additional pharmacological strategies include addition of adjunct medications to effect weight loss or improve metabolic parameters. Medications tried have included: metformin, an insulin-sensitizing diabetes drug; topiramate, an anticonvulsant; H_2-antagonists such as

famotidine and nizatidine, used to reduce gastric acid secretion; and norepinephrine reuptake inhibitors (NRIs) such as atomoxetine and reboxetine, used as antidepressants and for attention-deficit hyperactivity disorder (ADHD). A 2012 systematic review and meta-analysis of pharmacological interventions for SGA-associated weight gain (Fiedorowicz et al.) found estimated mean weight losses of 2.93 kg with metformin (95% CI [0.97 kg, 4.89 kg], p = .003), 3.95 kg with topiramate (95% CI [1.77 kg, 6.12 kg], p = .0004), as well as nonsignificant losses of 1.78 kg with H_2 antagonists (95% CI [-0.50 kg, 4.06 kg], p = .13) and 1.30 kg with norepinephrine reuptake inhibitors (95% CI [-0.06 kg, 2.66 kg], p = .06). These findings reinforced a 2010 systematic review and meta-analysis (Maayan, Vakhrusheva, & Correll) which found that, compared with placebo, metformin had the greatest weight loss (N = 7, n = 334, -2.94 kg, 95% CI [-4.89 kg, -0.99 kg]) followed by topiramate (N = 2, n = 133, -2.52 kg, 95% CI [-4.87 kg, -0.16 kg]). Other studies have also found promising results for amantadine, an antiparkinsonian agent (Baptista et al., 2008; Deberdt et al., 2005; Faulkner et al., 2007). The 2010 review by Maayan et al. analyzed both intervention trials (after weight gain has occurred) and prevention trials (agent given concomitantly with new SGA); study authors noted greater success in intervention trials, although even among the best adjuncts, treatment effect was only modest, and subjects failed to lose all of the SGA-associated weight gain and return to their pre-SGA baseline weight. A key limitation to all the trials of adjunct medications in the review by Maayan et al. were their generally very short duration (6 – 16 weeks, mean: 13.1), so it was not possible to determine whether any of these agents would have long-term success.

Metformin, which decreases insulin resistance and is a first-line treatment for type 2 diabetes mellitus, is one of the most promising agents being investigated for treatment of SGA-associated weight gain. A systematic review and meta-analysis of metformin use in olanzapine-

induced weight gain (four studies, $n = 105$) showed a weighted mean difference (WMD) for body weight of 5.02% (95% CI [3.93%, 6.10%]) lower with metformin compared with placebo at 12 weeks, and for change in BMI, WMD of -1.82 kg/m^2 (95% CI [-1.44 kg/m^2, -2.19 kg/m^2]) compared with placebo at 12 weeks (Praharaj, Jana, Goyal, & Sinha, 2011). Another systematic review and meta-analysis of metformin for non-diabetic patients on antipsychotic drugs analyzed seven randomized, placebo-controlled studies ($n = 398$) and found that 12 – 14 weeks of metformin therapy significantly reduced body weight in adults compared to placebo by 4.8% (95% CI [1.6%, 8.0%]; Bjorkhem-Bergman, Asplund, & Lindh, 2011). However, they noted significant heterogeneity between studies, and on subgroup analysis, found a marked difference between Asian adults (-7.8%, 95% CI [-4.4%, -11.2%]) and studies comprised primarily of Hispanic adults (-2.0%, 95% CI [-0.7%, -3.3%]). Further, when they restricted analysis to patients with "manifest" weight gain (> 10% initial body weight), a larger weight loss of 7.5% (95% CI [2.9%, 12%]) was observed (Bjorkhem-Bergman et al., 2011). It should be noted, however, that metformin therapy was still found to be less effective than lifestyle interventions (31% v. 58%) for prevention of diabetes in a population not taking SGAs, as shown in the Diabetes Prevention Program Research Group study (Knowler et al., 2002). Additionally, there is concern that metformin increases β-amyloid precursor protein (APP), which is involved in the pathogenesis of Alzheimer's disease (AD), and AD has been shown to be associated with type 2 diabetes (Chen et al., 2009).

Topiramate, an anticonvulsant also used for treatment of migraine, bipolar disorder, and neuropathic pain, is another agent that has shown positive results. It is an antagonist to kainate/ α-amino-3-hydroxyl-5-methylisoxazole-4-propionic acid (AMPA) glutamate receptors and enhances γ-amino butyric acid (GABA) transmission at $GABA_A$ receptors and has been

associated with weight loss (Kim, Yim, & Nam, 2006; White, Brown, Woodhead, Skeen, & Wolf, 2000). A12-week, double-blind, parallel group study of first-episode, drug-naïve inpatients and outpatients randomized subjects to either olanzapine with 100 mg topiramate or placebo and found that the topiramate group had a weight loss of 1.27 kg, whereas the placebo group gained 6.03 kg; additionally, the topiramate group had decreases in leptin, fasting blood glucose (FBG), triglycerides, and systolic and diastolic blood pressures (Narula, Rehan, Unni, & Gupta, 2010). Furthermore, there was a significantly ($p < .001$) greater improvement on the clinical Positive and Negative Syndrome Scale (PANSS) for schizophrenia among those on topiramate adjunct compared to placebo. Another study looked at treatment with either 100 mg or 200 mg topiramate in a 12-week, randomized, placebo-controlled prospective study of overweight (BMI $\geq$ 25 kg/m^2) schizophrenic Korean inpatients ($n = 66$), and found decreases in weight of 2.2% (1.68 kg) in the 100 mg group and 6.8% (5.35 kg) in the 200 mg group, with paresthesia noted as the most common adverse effect (Ko, Joe, Jung, & Kim, 2005). An eight-week study of adjunct topiramate for treatment of schizophrenia (not specifically for weight loss) found improved symptomatology and nonsignificant weight loss, though more side effects, including psychomotor retardation, drooling, and paresthesia (Afshar et al., 2009). Khazaal and colleagues used retrospective chart review of 100 patients to examine the effects of add-on topiramate for psychotropic-induced weight gain (including antipsychotic drugs, lithium, and valproate), and found significant reduction in BMI, from 29.7 kg/m^2 ($SD = 3.6$ kg/m^2) to 28 kg/m^2 ($SD = 3.3$ kg/m^2; Khazaal, Chatton, Rusca, Preisig, & Zullino, 2007). They also reported that the weight loss effect was greatest among those treated with antipsychotic drugs (71% lost weight), which was “almost double” that of those in the lithium and valproate groups. However, they also found a 22% discontinuation rate due to adverse effects.

Despite some positive results, most reviewers agree that there is not enough evidence to recommend any one pharmacological agent for routine use to prevent weight gain or effect weight loss with SGA usage (Baptista et al., 2008; Faulkner et al., 2007; Maayan et al., 2010), although the most recent review by Fiedorowicz et al. concludes that metformin has the strongest evidence and may additionally improve vascular risk factors (2012). The authors also state that topiramate may offer improvement in psychotic symptoms. However, inconsistent results, short trial duration and concerns for adverse effects remain key limitations of the studies of adjunct medication use and the drugs themselves. While several review articles also mention the use of medications specifically marketed for weight loss (Baptista et al., 2008; Faulkner, 2006; Faulkner et al., 2007; Maayan et al., 2010), all but one of these drugs have subsequently been removed from the market for safety concerns, including sibutramine, phenylpropanolamine, rimonabant, and D-fenfluramine. Prior to July of 2012 when a new combination medication containing phentermine and topiramate was approved, orlistat was the only agent approved for long-term weight loss in the United States (Faulkner, 2006), and it has been shown to be no better than placebo in treatment of antipsychotic-associated weight gain (Maayan et al., 2010). Thus, the phentermine/topiramate combination agent is not included in this review, although based on the inclusion of topiramate in the formulation, it may show promise.

Nonpharmacologic Strategies

Many studies have assessed nonpharmacological or lifestyle modification strategies for addressing metabolic consequences of SGAs, primarily focusing on nutritional education, dietary modification, and exercise (Evans, Newton, & Higgins, 2005; Littrell, Hilligoss, Kirshner, Petty, & Johnson, 2003; Scocco, Longo, & Caon, 2006), with or without additional modalities such as

cognitive-behavioral therapy (Alvarez-Jimenez et al., 2006; Brar et al., 2005; Khazaal, Fresard, et al., 2007; Kwon et al., 2006; McKibbin et al., 2006; Weber & Wyne, 2006) or motivational interviewing (Park, Usher, & Foster, 2011). The primary modifiable risk factors for CVD targeted in these studies are poor diet and sedentary lifestyle (Chacón, Mora, Gervás-Ríos, & Gilaberte, 2011), and the main outcome studied has been weight loss or weight stabilization (De Hert, Schreurs, Vancampfort, & Van Winkel, 2009). As a result, most authors and clinicians have advocated traditional low-fat, restricted calorie diets plus moderate physical exercise. Others have added other components such as food and exercise journals, development and rehearsal of self-monitoring skills to reduce desire to overeat, and development of healthy snacking alternatives.

Six recent reviews have analyzed nonpharmacological interventions (Chacón et al., 2011; Faulkner, 2006; Loh, Meyer, & Leckband, 2006; Megna, Schwartz, Siddiqui, & Rojas, 2011), including two systematic reviews and meta-analyses (Alvarez-Jimenez, Hetrick, Gonzalez-Blanch, Gleeson, & McGorry, 2008; Faulkner et al., 2007). Nine published randomized controlled trials (RCTs) (Alvarez-Jimenez et al., 2006; Brar et al., 2005; Evans et al., 2005; Khazaal, Fresard, et al., 2007; Kwon et al., 2006; Littrell et al., 2003; McKibbin et al., 2006; Weber & Wyne, 2006; Wu et al., 2008) of interventions ranging from 12 weeks to six months have shown that modest weight loss or prevention of weight gain is possible in the short-term. The longest study collected data through an endpoint of six months (Littrell et al., 2003). As with pharmacological interventions, trials are divided among those seeking to prevent weight gain (Alvarez-Jimenez et al., 2006; Evans et al., 2005; Littrell et al., 2003) and those seeking to reverse it (Wu, Wang, Bai, Huang, & Lee, 2007).

Alvarez-Jimenez' et al. 2008 systematic review and meta-analysis examined 10 RCTs of nonpharmacological approaches including six cognitive-behavioral (CBT) interventions (Alvarez-Jimenez et al., 2006; Brar et al., 2005; Khazaal, Fresard, et al., 2007; Kwon et al., 2006; McKibbin et al., 2006; Weber & Wyne, 2006), three nutrition education interventions (Evans et al., 2005; Littrell et al., 2003; Scocco et al., 2006), and one combined nutrition and education intervention (Wu et al., 2007). Four interventions were aimed at prevention of weight gain (Alvarez-Jimenez et al., 2006; Evans et al., 2005; Littrell et al., 2003; Scocco et al., 2006) and six were interventions to reduce weight gained (Brar et al., 2005; Khazaal, Fresard, et al., 2007; Kwon et al., 2006; McKibbin et al., 2006; Weber & Wyne, 2006; Wu et al., 2007). Interventions ranged from eight weeks to six months, with follow-up of two to three months after intervention. They found a statistically significant reduction in mean body weight versus treatment as usual (WMD = -2.56 kg, $p < .001$, 95% CI [-3.20 kg, -1.92 kg]), which was maintained at follow-up (WMD = -4.14 kg, $p < .001$, 95% CI [-5.80 kg, -2.49 kg]). Studies aimed at prevention appeared to show slightly better results (WMD -3.05 kg, 95% CI [-4.16 kg, -1.94 kg]) than studies for weight loss (-2.56 kg, 95% CI [-3.20 kg, -1.92 kg]), though it was not found to be significant on further analysis; similarly, nutritional education seemed to show a slightly larger, though not significant, effect than CBT (WMD = -3.12 kg, $p < .001$, 95% CI [-4.10 kg, -2.14 kg] v. WMD = -2.14 kg, $p < .001$, 95% CI [-2.98 kg, -1.30 kg]). Study authors concluded that focusing efforts on prevention of weight gain at commencement of antipsychotic treatment seems to lead to the best results (Alvarez-Jimenez et al., 2008); additionally, they felt that this approach fits within the clinical staging model which posits that such early treatments should be both more effective and less harmful (McGorry, Hickie, Yung, Pantelis, & Jackson, 2006). Furthermore, they concluded that flexible and multicomponent interventions were associated with better retention

(Alvarez-Jimenez et al., 2006), and they cited one program that used adventure- and recreation-based interventions with 97% treatment adherence and zero dropouts (Voruganti et al., 2006).

A pilot study (n = 17) (Weber & Wyne, 2006) modeled after the Diabetes Prevention Project (DPP) (Knowler et al., 2005) compared a cognitive/behavioral (CBT) lifestyle intervention to treatment as usual in a population of overweight patients with schizophrenia using SGAs at a large urban public mental health clinic in Texas. The intervention consisted of weekly group sessions for 16 weeks and utilized cognitive/behavioral strategies from the DPP to reduce risk of type 2 diabetes, employing role-playing, goal setting, problem solving, and discussions of barriers to change as well as nutritional information and exercise promotion. It was noted that all subjects showed impaired glucose tolerance at the onset of the study, and the majority of study participants were African American or Hispanic and female, unlike most other studies in the literature. Average weight lost by the CBT group was 5.4 lb (2.9% of body weight) versus 1.3 lb (0.6%) in the control group, with a mean change in BMI of 2.9% for the CBT versus 0.8% in the control; unfortunately, the study was inadequately powered to allow significance to be calculated. It was notable that this study had 100% retention in the treatment group, which authors credited to the very motivated CBT participants. Major obstacles to weight loss reported by participants included transportation problems, high crime rate, and low income; a $5.00 per visit transportation stipend likely helped ameliorate the transportation issue. They also noted the significant difficulty patients with low incomes in urban areas have in obtaining healthy, fresh foods, and they helped patients strategize “least harmful” options from what was available.

Another randomized controlled trial (n = 64; McKibbin et al., 2006) of patients over 40 with schizophrenia and type 2 diabetes showed that the 24-week Diabetes Education and

Awareness Training (DART) intervention significantly reduced weight and other factors versus usual care intervention (UCI): mean weight changed from 222.3 lb [*SD* = 49.6 lb] to 217.2 lb [*SD* = 46.8 lb] in the DART group versus 212.1 lb [*SD* = 36.8 lb] to 218.9 lb [*SD* = 37.3 lb] in the UCI group; mean change in BMI from 33.6 kg/m^2 [*SD* = 6.8 kg/m^2] to 32.9 kg/m^2 [*SD* = 6.6 kg/m^2] in the DART group versus 32.9 kg/m^2 [*SD* = 6.2 kg/m^2] to 33.9 kg/m^2 [*SD* = 6.6 kg/m^2] in the UCI group; and mean change in waist circumference from 46.0 in. [*SD* = 7.4 in.] to 45.1 in. [*SD* = 6.9 in.] in the DART group versus 45.4 in. [*SD* = 4.4 in.] to 46.0 in. [*SD* = 4.3] in the UCI group. Clinically meaningful weight loss (defined as ≥ 5% of baseline weight) was achieved by 38% of DART subjects versus 12% of controls. The program adapted educational materials for diabetes self-management for middle-aged and older patients with schizophrenia, using simple guidelines and strategies for change. To assist with potential impaired insight and motivation commonly observed in schizophrenia, study authors incorporated concrete behavioral-change strategies including weekly weigh-ins, pedometers, sampling of health foods, and reinforcements for attendance including raffles for healthy prizes. Study retention in this group was particularly good, with 90% of the subjects completing the study, and authors theorized that this might have been due to greater motivation among patients with diabetes to make positive behavioral changes.

An innovative, multicomponent lifestyle intervention specifically designed for patients with serious mental illness using SGAs (though not solely for patients with schizophrenia) was recently described (Park et al., 2011). Named "Passport 4 Life," this program is composed of previously proven strategies for weight gain prevention including nutrition education, group exercise sessions, nurse support, and motivational interviewing (MI). The twelve-week program is theoretically grounded in health promotion as described by the World Health Organization's

Ottawa Charter, which states that "health is created and lived by people within settings of their everyday life; where they learn, work, play and love" (1986), and is composed of five interlinked components: healthy eating information; nurse-led exercise; diet and exercise journal; goal setting; and motivational interviewing. To address specific challenges patients with serious mental illness face, such as impaired memory and concentration, cognitive difficulties, amotivation, and limited social and living skills, the program was written in easy-to-understand language and incorporated visual reminders, menu planning and low- or no-cost group exercise activities at every session. Support of nurse leaders was used to aid in motivation, while group sharing of experiences and ideas for healthy snacks lent social support. Participants were equipped with pedometers, water bottles, a healthy lifestyle folder and a tote bag, and financial assistance was available to help with transportation costs where needed. Although outcomes are still being studied, the intervention is innovative in its use of multiple components tailored specifically to the needs of patients using SGAs.

An interview with Brandie Hagaman, MPH, Integrated Health Supervisor of Community Support and Treatment Services at Washtenaw County Community Mental Health (CMH), was conducted to discuss her program's pilot Disease Management Program (personal communication, May 3, 2012). State and federal grants had been obtained to enrich physical health of CMH consumers, who include patients with mental illness, developmental disabilities, and/or substance abuse. Consumers were targeted for interventions through a combination of record review, health care utilization data and self-reported health ratings. The disease management team consists of nurses who coordinate care, a dietitian, a family nurse practitioner who provides medical care and rotates among CMH sites and peer support specialists, who are former consumers who underwent state training. A range of interventions were offered, including

things such as assistance with transport to medical appointments, wellness education classes on diabetes, nutrition, smoking cessation, exercise and other topics, information on obtaining medical supplies and proper use of glucometers and provision of activity and exercise opportunities. Patient education, group support, and personal accomplishments are integral to the program, and all participants are assisted in setting small, measurable personal health goals with the aid of the team.

There are a number of challenges that Ms. Hagaman has observed through the course of her program. A major issue at the outset was the all-too-prevalent view among both providers and consumers that one can have good mental health or good physical health, but that the struggle to obtain both is out of reach, which has led to difficulty getting consumers to invest and partner in their health. With time and success of the program, she has made significant inroads, working with both her staff and consumers. Another issue is stigma and lack of understanding among health care providers. Despite Washtenaw County being an area rich with health care resources, her consumers are often reluctant to seek medical help due to prior poor experiences or feeling as though their voices are not heard or are discounted due to their mental illness. To address this, her program works to identify providers who are both comfortable with and competent to provide care to her consumers.

Throughout the evolution of the program and the relationships it has formed with consumers, she has seen many consumers become more empowered to take control of their health. Some have made vast improvements in their health, with significant weight loss, smoking cessation, and returning to school. Others have managed to make more incremental changes, cutting back from smoking two packs per day to one, or switching from drinking a two-liter of regular soda per day to drinking diet soda or water. Annual celebrations honor consumers who

have been nominated for achieving their goals, large or small, and help to show consumers that change is possible and is happening in their midst with the support the program provides.

Limitations of Current Approaches

While multiple studies have shown that short-term weight loss is possible, longer, more rigorously designed studies with larger samples are needed, as most studies are limited to six months or fewer (Alvarez-Jimenez et al., 2008; Faulkner, 2006; Faulkner et al., 2007; Loh et al., 2006). One non-controlled study of 93 self-referred outpatients (80 with schizophrenia, 13 with affective disorder) did report results on "long-term" maintenance of weight loss in patients with serious mental illness in a behavioral treatment program in the UK for the four years the clinic has existed (Pendlebury, Bushe, Wildgust, & Holt, 2007). The group met weekly and consisted of weigh-ins, group discussion, and various topics on health, nutrition, and exercise. Authors claimed progressive statistically significant reduction in mean weight and BMI, and cited mean final weight loss of 6.2 kg [$SD = 0.6$], though their "long-term" data was based on increasingly smaller numbers of subjects who were available for follow-up, as noted below. Moreover, all patients were self-referred, thus more likely to be highly motivated than patients who would be seen in real world practice.

Another limitation to current approaches is a relatively high rate dropout rate and loss to follow-up, which has been noted as a cause for concern in several reviews (Faulkner et al., 2007; Loh et al., 2006). Despite self-referral, the Pendlebury study reported a dropout rate of 23% within the first 8 weeks, with further decline as follow-up continued; 41 subjects remained at one year, 16 at two years, 7 at three years, and only three at four years (2007). Furthermore, the inconsistent handling of dropout may have biased results in several other studies. Faulkner and

colleagues' 2007 Cochrane Review of 23 pharmacological and nonpharmacological interventions for weight gain in schizophrenia noted, for example, that nine trials analyzed only completers, which may have skewed results more favorably to the intervention, while only eight trials used the more robust intention to treat (ITT) analysis .

Beyond the matters of accounting for dropout in clinical trials, it is likely that results found in these interventions may not be representative of what would be seen in real world practice for another reason: patient preference. Pendlebury et al. noted that weight management programs are often declined when offered to patients and stated that results seen in studies, therefore, may not be generalizable to the larger population of patients with schizophrenia, implying the need for other approaches that would be more appealing (2007). A case series reported by Feeney and colleagues of 51 Irish outpatients with schizophrenia attending either a clozapine or depot clinic reported results of a weight management program three years after induction (2003). They found that nine patients in the weight management program had statistically significant weight loss, reducing their BMI on average by 1.6 kg/m^2 ($p = .025$), compared to an increase of 0.2 kg/m^2 of those not in the program ($n = 42$). Study authors concluded that "sufficiently motivated" patients with schizophrenia were capable of losing weight, but clearly the majority of the patients in this study were either uninterested or unmotivated, as only 9 of the 51 eligible patients chose to participate. Similarly, another study (Beebe et al., 2011) noted a 40% rate of refusal to participate in their exercise intervention, which was consistent with previous studies of patients with schizophrenia (Beebe, 2001; Beebe et al., 2005) and acknowledged that this may lead their study findings to be nonrepresentative of the wider population.

Meyer anonymously surveyed hospital inpatients (largely patients with psychosis) on their perceptions of their weight, possible factors leading to weight gain, level of concern about weight, and opinions about several possible interventions to control weight gain (2002). Interestingly, he noted that while many studies have been done of interventions in this population, it is rare that the explicit preferences of these patients are sought. Results showed that, when offered the choice among several diet options, 24% of obese patients chose no change in diet, 57% chose voluntary dietary restriction, 10% chose a required but not monitored diet, and only 10% chose a mandatory and monitored diet. While evaluating possible strategies for health promotion, it is important to bear in mind that these interventions have to be chosen and implemented by patients in real-world settings. If only a small percentage of patients choose an intervention and are successful only for the short-term, the intervention has failed.

Perhaps the largest limitation to the current non-pharmacologic approaches is that studies have focused primarily or solely upon weight or BMI as proxies for health, rather than more direct measures of metabolic and cardiovascular health, such as insulin resistance, lipid profiles, blood pressure, fasting plasma glucose (FPG), or glycosylated hemoglobin (A1C; Faulkner, 2006). This omission is critical, given "the role of physical inactivity and poor diet as independent risk factors for cardiovascular disease [which] infers the need for nonpharmacologic or lifestyle intervention regardless of weight loss per se" (Faulkner et al., 2007, p. 24). Several large reviews have analyzed the effectiveness of traditional weight loss interventions in the general population. A review by Mann and colleagues (2007) attempted to analyze current hypocaloric/restriction-based approaches ("diets") to long-term weight loss using the well-established GRADE system (Atkins et al., 2004) for qualifying the strength and quality of evidence. They identified seven randomized controlled trials of weight loss with follow-up of at

least two years, and 14 observational studies with follow-up of at least four years. Study authors were able to extract details on weight regain from eight studies, and determined that an average of 41% of subjects weighed more at follow-up than at initiation, ranging from 29% (Pekkarinen & Mustajoki, 1997) to 64% (Wadden, Sternberg, Letizia, Stunkard, & Foster, 1989). Furthermore, authors also noted that this was likely a conservative estimate due to the way in which study dropout and attrition were often selectively reported, and that while positive results (subjects who maintained weight loss) were always reported in studies, only a small minority of studies reported results on those (often the majority) who gained weight. Furthermore, due to very low follow-up rates (averaging 33%), it is likely that the effectiveness of the interventions was even lower than reported, given that those who "fail" and gain back weight are less likely to return for follow-up. This focus on weight loss and restrictive eating can lead to frustration and a sense of futility in patients, who may give up on healthy behavior changes, feeling that if they have not lost weight, they have not benefitted. Furthermore, while it is a topic of some controversy, there is evidence that chronic weight fluctuation is associated with increased cardiovascular morbidity and mortality (Christen, Efstathiadou, Laspa, Johnston, & Godsland, 2007) and predicts atherosclerotic disease (Montani, Viecelli, Prevot, & Dulloo, 2006). Given the lack of evidence that dieting is capable of producing sustained weight loss and the association of diets with weight cycling and weight gain, some researchers go so far as to suggest that clinicians should consider whether advocating for diets for weight loss is ethical (Mann et al., 2007; Schmidt, Voigt, & Wikler, 2010).

Chapter 4: The Health at Every Size®* Approach –

A New Model for Cardiometabolic Health

A new trans-disciplinary movement has arisen that seeks to place focus on healthy behaviors rather than reducing weight, utilizing what is known as the Health At Every Size® (HAES®) approach (HAES®, 2012; Health At Every Size®, 2011). This model draws on the considerable evidence showing that health indicators can be improved with behavioral change even in the absence of weight loss (Gaesser, Angadi, & Sawyer, 2011) and was born partially out of a reaction to the long-term ineffectiveness of traditional weight-loss approaches, which often lead to weight cycling and net weight gain (Bild et al., 1996; Cameron, Killen, Hayward, & Taylor, 1999; Coakley, Rimm, Colditz, Kawachi, & Willett, 1998; French et al., 1994; Korkeila, Rissanen, Kaprio, Sorensen, & Koskenvuo, 1999; Mann et al., 2007). It is based on several key principles: self- and body-acceptance with acknowledgement of a diverse range of healthy body sizes and shapes; promotion of natural and unrestricted "intuitive" eating guided by internal hunger and satiety signals rather than external controls; promotion of pleasurable physical activity for enjoyment and health rather than weight loss; and "the critical contribution of social, emotional, spiritual, and physical factors to health and happiness" (Robison, Putnam, & McKibbin, 2007, p. 185). Within this holistic framework, success is measured by metabolic, cardiovascular, and psychological wellness, as opposed to weight, which may or may not change.

A major component of the HAES® approach is intuitive eating (sometimes called mindful or attuned eating), which seeks to teach the individual to become more aware of the internal signs of hunger and satiety, rather than relying on external rules, prohibitions, or

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guidelines to steer food choices (Tribole & Resch, 2003). This approach has been shown to be useful for reducing eating disorder symptomatology in the treatment of binge eating disorder (Bacon et al., 2002; Bacon, Stern, Van Loan, & Keim, 2005; Ciliska, 1998; Goodrick, Poston, Kimball, Reeves, & Foreyt, 1998). Intuitive eating has been shown to improve nutrient intake and dietary variety (Smith & Hawks, 2006) and has also been associated with higher HDL, lower triglycerides, improved cardiovascular risk, and lower body mass (Hawks, Madanat, Hawks, & Harris, 2005; Madden, Leong, Gray, & Horwath, 2012). It has also been shown to lead to a reduction in hunger sensations and a subsequent reduction in caloric intake (Leblanc et al., 2012). Furthermore, evidence shows that intuitive eating can be taught effectively (Bacon et al., 2005; Mensinger, Close, & Ku, 2009; Smith & Hawks, 2006). Therefore, an intuitive eating approach may offer patients useful tools to help them discern medication- or emotion-influenced cravings from true hunger, and help them to find alternative ways to cope with these sensations, as an alternative to placing certain foods in "forbidden" categories which can promote later binging.

The HAES® approach has been officially endorsed by The Academy for Eating Disorders, Binge Eating Disorder Association, Eating Disorder Coalition, International Association for Eating Disorder Professionals, and National Eating Disorder Association (National Eating Disorder Association, 2009). HAES®-influenced approaches have also been used in worksite wellness programs (Carrier, Steinhardt, & Bowman, 1994; Putnam, 2006) and community outreach and health promotion endeavors nationally and internationally (Health Canada, 2000; Liebman, 2005; Liebman et al., 2003). This approach has shown particular promise in the treatment of chronic dieters and patients with binge eating disorders (Bacon et al., 2002; Bacon et al., 2005; Ciliska, 1998; Goodrick et al., 1998). Given that SGA treatment has

been described as inducing a state akin to binge-eating disorder in patients (Khazaal, Fresard, Borgeat, & Zullino, 2006; Khazaal, Fresard, et al., 2007; Stahl, 1998; Theisen et al., 2001; Theisen et al., 2003), a HAES® approach may be a particularly useful approach in this population.

Several studies have explored the association between SGA use and binge eating. Theisen and colleagues explored binge eating symptomatology, BMI, and weight gain among adolescent and young adult patients with schizophrenia using either clozapine (n = 57) or olanzapine (n = 17), and found 37 patients (50%) screened positive for binge eating (2003). They found that these patients also had higher BMI (26.8 kg/m^2 [SD = 3.9 kg/m^2] compared to 24.7 kg/m^2 [SD = 3.7 kg/m^2]) and higher change in BMI during SGA treatment (3.9 kg/m^2 [SD = 3.1] compared to 2.6 kg/m^2 [SD = 3.4]) than subjects who did not screen positive for binge eating. Authors concluded that SGA use might induce binge eating in susceptible patients, even suggesting a new Diagnostic and Statistical Manual of Mental Disorders (DSM) category of "medication-induced eating disorders." A case-control study of 40 outpatients with schizophrenia being treated with SGAs and 40 non-psychiatric controls by Khazaal and colleagues in 2006 affirmed a similar proportion of binge eating disorder (BED) and binge eating symptomatology (BS) among severely overweight patients with schizophrenia. Each group of 40 was composed of a subgroup of severely overweight (BMI > 28) subjects and a comparison sample (BMI < 28). They found BED or BS in 60% of severely overweight patients with schizophrenia while only 25% among patients with schizophrenia and BMI < 28; among severely overweight controls, 28% had BED or BS, while those with BMI < 28, only 20% had BED or BS. Authors concluded that BS is not specifically correlated with SGA use alone, but a clinical correlate of high BMI in patients using SGAs, and development of binge eating disorder

or symptomatology may be triggered by weight gain associated with SGA usage among more susceptible patients. Additionally, a six-week double-blind, parallel study of 30 inpatients with schizophrenia, schizophreniform, or schizoaffective disorder randomized to either olanzapine or clozapine therapy by Kluge and colleagues noted that body weight and BMI increased significantly ($p < .05$), and the number of patients reporting binge eating or food craving also significantly increased over time ($p < .05$; clozapine binge eating from zero at baseline to 13% at week 6 and cravings from zero at baseline to 27% at week 6; olanzapine binge eating from zero at baseline to 27% at week 6 and cravings from 7% at baseline to 53% at week 6; 2007). Weight gain was also numerically though not statistically significantly higher among those with these abnormal eating behaviors than among those without; weight gain in patients with food cravings was 1.3 kg [$SD = 4.3$ kg], where weight gain in patients with binge eating was 1.4 kg [$SD = 4.2$ kg]).

An intervention used as a part of an RCT for SGA-associated weight gain included several components remarkably similar to HAES® approaches (Khazaal, Fresard, et al., 2007). Khazaal and colleagues conducted a 12-week RCT of a cognitive behavioral (CB) intervention v. control (brief nutritional education, BNE) to assess effects on eating and weight-related cognitions, binge eating symptomatology, and weight loss in adult patients reporting weight gain with SGA usage ($n = 61$, 73.8% with schizophrenia). The elements of the CB intervention that were similar to HAES® approaches included: teaching meal tasting with attention to sensations and learning to recognize satiety, promoting food moderation without specific food prohibition, and promoting physical activity not for exercise, but to promote self-care. Additionally, it taught self-observation of eating behavior and cognitive restructuring of maladaptive cognitions related to eating and weight. The CB intervention showed significant improvement in binge eating

symptomatology as measured by the Mizes Anorectic Cognitive Questionnaire-Revised (MAC-R; (Mizes et al., 2000) on multivariate analysis (MANOVA), with overall significance *F* for group effect as shown by $p = .006$, $F(5, 15) = 5.10$. Between-subjects effects showed a group effect for MAC-R total score $F(1, 19) = 6.96$, $p = .02$, factor 2 ("rigid weight regulation and fear of weight gain": $F(1, 19) = 6.01$, $p = .02$), and factor 3 ("self-control of weight as the basis of self-esteem" $F(1, 19) = 11.62$, $p = .003$), indicating a decrease in scores in the CB group. Additionally, while both groups lost weight during the 12-week intervention, subjects in the CB group continued to lose weight at 24-week follow-up, while the BNE group had begun to regain weight. Because of significant differences in BMI at baseline, multivariate analysis of covariance (MANCOVA) for repeated measures was performed, controlling for BMI: between weeks 12 and 24, time x group interaction was shown for BMI ($F(1, 19) = 8.60$; $p = .009$) and weight (F (1, 19) = 8.76; $p = .008$), with the mean of the CB group decreasing and the mean of the BNE group increasing (Khazaal, Fresard, et al., 2007). Based upon the success of this intervention, which used principles similar to intuitive eating and promotion of movement as self-care, it may be reasonable to consider a HAES® approach in this population.

The evidence for behavioral change leading to improvement in health indicators in the absence of weight loss is substantial and was delineated in a 2011 review by Gaesser et al. Authors reviewed a number of studies showing improvements in type 2 diabetes risk (Roumen et al., 2008; Salas-Salvado et al., 2011), glucose metabolism and insulin action (Duncan et al., 2003; Estruch et al., 2006; Slentz et al., 2005; Snowling & Hopkins, 2006), blood pressure (Appel et al., 1997; Cornelissen & Fagard, 2005; Estruch et al., 2006; Snowling & Hopkins, 2006; Svetkey et al., 1999), blood lipids (Balducci et al., 2010; Chandalia et al., 2000; Kraus et al., 2002; Slentz et al., 2005), endothelial function and hemostasis (Kadoglou et al., 2010; Ma et

al., 2010; Mestek et al., 2010; Van Guilder et al., 2005), and inflammation (Balducci et al., 2010; Estruch et al., 2006; Kadoglou et al., 2007) with no or only minor weight change. A review by Pederson of 555 articles found that both objective fitness measured by VO_{2max} and subjectively reported level of physical activity, independent of BMI, have prognostic value for all-cause and cardiovascular mortality (2007). Another systematic review by Fogelholm and colleagues compared morbidity, mortality, and cardiovascular and type 2 diabetes risk factors for normal weight and obese persons based on fitness and level of self-reported physical activity, and found that subjects with high BMI and good fitness had lower risk for cardiovascular and all-cause mortality than normal weight subjects with poor fitness (2010). However, in his analysis, high BMI even with high levels of self-reported physical activity was still associated with increased risk for incidence of type 2 diabetes and cardiovascular disease risk factors compared with normal weight subjects with low physical activity. This may have been due, however, to the more protective effects of objectively measured aerobic fitness (VO_{2max}) versus the relative imprecision of self-reported physical activity. In Snowling and Hopkins' meta-analysis of the effects of different modes of exercise (aerobic, resistance, or combined) on glycemic control in type 2 diabetics, small to moderate improvements were made in A1C (-0.7%, 95% CI [-1.0%, -0.4%]; -0.5% [-1.0%, -0.1%]; -0.8% [-1.3%, -0.2%]), fasting (-0.5 mmol/l [-1.0 mmol/l, -0.1 mmol/l]; -0.3 mmol/l [-1.1 mmol/l, 0.6 mmol/l]; -1.5 mmol/l [-2.3 mmol/l, -0.6 mmol/l]) and postprandial blood glucose (-9% [-13%, -5%]; -2% [-13%, 10%]; -6% [-15%, 4%]), insulin sensitivity (28% [9%, 49%]; 12% [-6%, 33%]; 106% [12%, 280%]), and fasting insulin despite only small changes in body mass (-1.5% [-2.1%, -1.0%]; 0.5% [-0.3%, 1.4%]; -5.1% [-7.6%, -2.5%]; 2006). Another meta-analysis of 72 randomized controlled trials of 3936 participants investigating the effect of endurance training on ambulatory blood pressure (BP) showed

significant reduction (-6.9 mm Hg, 95% CI [-9.1 mm Hg, -4.6 mm Hg], $p < .001$] / -4.9 mm Hg [-6.5 mm Hg, -3.3 mm Hg], $p < .001$]) in BP despite only minimal changes in weight (-1.1 kg [-1.6 kg, -0.57 kg]; $p < .001$]) and percent body fat (-0.79% [-1.6%, 0.051%; $p = .062$]; Cornelissen & Fagard, 2005). Additional studies of exercise interventions have shown similar favorable results with minimal or no change in body weight (Balducci et al., 2010; Slentz et al., 2005).

Several studies have looked at ad-lib dietary changes and shown that improvements in diet quality bring about improvement in health indicators in the absence of significant weight loss. A large multisite RCT of 772 asymptomatic Spanish adults with cardiovascular risk factors by Estruch and colleagues compared the effects of three diets on cardiovascular risk factors: traditional low-fat diet and two ad-lib Mediterranean-style diets, one supplemented with olive oil and one with mixed walnuts, hazelnuts, and almonds (2006). After three months, both Mediterranean diet groups had decreased systolic blood pressure (between-group changes: olive oil v. low-fat: -5.9 mm Hg, 95% CI [-8.7 mm Hg, -3.1 mm Hg], $p < .001$; nuts v. low-fat: -7.1 mm Hg [-10 mm Hg, -4.1 mm Hg], $p < .001$), fasting blood glucose (olive oil v. low fat: -7.0 mg/dL, [-13.0 mg/dL, -1.3 mg/dL], $p = .017$; nuts v. low-fat: -5.4 mg/dL [-10.5 mg/dL, -0.2 mg/dL], $p = .039$), and total cholesterol-HDL cholesterol ratios (olive oil v. low-fat: -0.38 [-0.55, -0.22], $p < .001$; nuts v. low-fat: -0.26 [-0.42, -0.10], $p = .002$); and increased HDL cholesterol (olive oil v. low-fat: 2.9 mg/ dL[1.7 mg/ dL, 4.0 mg/ dL], $p < .001$; nuts v. low-fat: 1.60 mg/dL[0.45 mg/ dL, 2.70 mg/ dL], $p = .006$) without weight gain; additionally, nondiabetic subjects also had lower fasting insulin (olive oil v. low-fat: -16.7 pmol/L [-27.1 pmol/L, -0.4 pmol/L], $p = .001$; nuts v. low-fat: -20.4 pmol/L [-31.9 pmol/L, -9.7 pmol/L], $p < 0.001$) and insulin resistance (Homeostasis Model Assessment [HOMA] index for olive oil v. low-fat: -0.91

[-1.40, -0.46]; nuts v. low-fat: -1.1 [-1.6, -0.55]). Furthermore, inflammatory biomarkers including high-sensitivity C-reactive protein (CRP) improved in the olive oil group (olive oil v. low-fat: -0.54 mg/L [-1.04 mg/L, -0.03 mg/L], $p < .003$; nuts v. low-fat: 0.33 mg/L [-0.19 mg/L, 0.84 mg/L]), while intercellular adhesion molecule-1 (ICAM-1; olive oil v. low-fat: -104 ng/mL [-135 ng/mL, -72 ng/mL]; $p < .003$; nuts v. low-fat: -97 ng/mL [-128 ng/mL, -65 ng/mL]; $p < .003$), vascular cell adhesion molecule-1 (VCAM-1; olive oil v. low-fat: -178 ng/mL [-277 ng/mL, -79 ng/mL]; $p < .003$; nuts v. low-fat: -167 ng/mL [-267 ng/mL, -68 ng/mL; $p < .003$), and interleukin-6 (IL-6; olive oil v. low-fat: -1.6 ng/L [-2.5 ng/mL, -0.6 ng/mL]; $p < .003$; nuts v. low-fat: -1.3 ng/L [-2.3 ng/mL, -0.4 ng/mL]; $p < .018$) were improved in both Mediterranean diet groups, and worsened in the low-fat groups. A follow-up study by Salas-Salvado and colleagues in 2011 found additionally that after four years, there was a 52% (95% CI [27%, 86%]) reduction in type 2 diabetes despite the absence of significant weight change or change in physical activity; diabetes incidence was 10.1% [5.1%, 15.1%] in the Mediterranean diet plus olive oil group, 11.0% [5.9%, 16.1%] in the Mediterranean diet plus nuts group, and 17.9% [11.4%, 24.4%] in the control group . Another small randomized crossover study ($n = 13$) investigated the role of dietary fiber in glycemic control in patients with type 2 diabetes. Patients were instructed to follow two diets in sequence, each for six weeks: the first one moderate in dietary fiber, as recommended by the American Diabetic Association (ADA; total 24 g; 8 g soluble, 16 g insoluble), followed by one high in fiber (total 50 g: 25 g soluble, 25 g insoluble; Chandalia et al., 2000). By the sixth week of the high fiber diet, mean daily preprandial plasma glucose concentrations had decreased by 13 mg/dL (95% CI [1 mg/dL, 24 mg/dL], $p = .04$) compared to the moderate-fiber diet. Additionally, area under the curve (AUC) for 24-hour plasma glucose and insulin concentrations was reduced by 10% ($p = .02$) and 12% ($p = .02$). Plasma total

cholesterol was reduced by 6.7% ($p = .02$), triglycerides by 10.2%, and very-low-density lipoprotein (VLDL) by 12.5% ($p = .01$). Again, these changes were accomplished without significant differences in weight during the last week of each study period (ADA diet 90.7 kg [$SD = 13.3$] v. high fiber diet 90.5 kg [$SD = 12.7$]; $p = .60$).

These findings are similar to the results of the Dietary Approaches to Stop Hypertension (DASH) RCT, which compared 459 adults with untreated systolic blood pressure less than 160 mm Hg and diastolic blood pressure 80 to 95 mm Hg on three diets: a control diet; a diet rich in fruits and vegetables; or combination (DASH) diet rich in fruits and vegetables, low-fat dairy, with reduced saturated fat, total fat, and cholesterol (Svetkey et al., 1999). The DASH diet significantly lowered systolic blood pressure in all subgroups ($p < .008$) and significantly lowered diastolic blood pressure ($p < .01$) in all but two subgroups; it was particularly effective in hypertensive subjects, who had a greater decrease (11.6/5.3 mm Hg; $p < .001$) compared to normotensive subjects (3.5/2.2 mm Hg; $p < .001$), and in African Americans (6.9/3.7 mm Hg; $p < .001$) compared to Caucasians (3.3/2.4 mm Hg; $p < .01$). In this intervention, salt intake and weight were deliberately held constant, thus proving that dietary change alone can bring about favorable changes in blood pressure in the absence of weight loss.

Several randomized controlled trials comparing HAES® approaches to conventional obesity treatments have been conducted. Bacon and Aphramor reviewed current evidence behind HAES® approaches including seven RCTs with explicit HAES® focus (Table 1) and stated that such an approach is associated with statistically and clinically significant improvements in metabolism, health behaviors, and psychological outcomes (2011). A six-month RCT ($n = 78$) by Bacon and colleagues compared a HAES®-based nondiet approach to a traditional weight loss intervention among obese, Caucasian, female chronic dieters (2002).

Each group met weekly for six months and then met monthly for six more months. The HAES® (nondiet) group focused on body acceptance, regulating food intake by listening to innate hunger, appetite, and satiety (intuitive eating), removing barriers to physical activity and finding pleasurable activities to engage in, and social support. The control group was taught to moderately restrict fat and calorie intake, monitor intake with a food journal, weigh themselves weekly, and exercise. Dropout in the control group was significantly higher than the nondiet group (n = 13 [41%] v. n = 3 [8%]; $p < .05$). The nondiet group had no significant change in weight and BMI, while the control group initially lost weight at one year post-aftercare (-5.9 kg [SD = 6.3 kg]; 5.8% of mean body weight) as reported in the original study (Bacon et al., 2002) but regained weight such that, in a subsequent two year follow-up study (Bacon et al., 2005), weight was not significantly different from baseline (101.2 kg [SD = 13.8 kg] initially; 98.0 kg [SD = 14.3 kg] at follow-up; p = .068). Both groups at one year post-aftercare (Bacon et al., 2002) had significantly improved LDL (3.10 mmol/L [SD = 0.63 mmol/L] to 2.87 mmol/L [SD = 0.68 mmol/L], p = .010 in non-diet group v. 3.07 mmol/L [SD = 0.53 mmol/L] to 2.76 mmol/L [SD = 0.73 mmol/L], p = .003 in control), triglycerides (2.03 mmol/L [SD = 1.22 mmol/L] to 1.55 mmol/L [SD = 0.72 mmol/L], p = .005 in non-diet group v. 1.94 mmol/L [SD = 0.82 mmol/L] to 1.41 [SD = 0.85 mmol/L], p = .001 in control), and systolic blood pressure (125.3 mm Hg [SD = 13.0 mmol/L] to 120.8 mm Hg [SD = 14.0 mmol/L], p = .034 in non-diet group v. 126.9 mm Hg [SD = 11.3 mmol/L] to 118.7 mm Hg [SD = 10.2 mmol/L], p = .001 in control), although they significantly worsened in HDL (1.19 mmol/L [SD = 0.25 mmol/L] to 1.05 [SD = 0.22 mmol/L], $p < .001$ in nondiet group v. 1.23 mmol/L [SD = 0.26 mmol/L] to 1.12 [SD = 0.30 mmol/L], p = .003 in control). The nondiet group also had a significant decrease in total cholesterol between baseline and two-year follow-up (4.61 mmol/L [SD = 0.80 mmol/L] to 4.07

mmol/L [*SD* = 0.77 mmol/L]; p = .026). The nondiet group sustained their LDL improvement at two-year follow-up (3.01 mmol/L [*SD* = 0.83 mmol/L] to 2.53 mmol/L [*SD* = 0.51 mmol/L], *p* = .038), while the LDL values for the control group were not significantly different from baseline (2.99 mmol/L [*SD* = 0.95 mmol/L] to 2.63 mmol/L [*SD* = 0.57 mmol/L], *p* = .236); similarly, the non-diet group sustained their improvement in systolic blood pressure (125.8 mm Hg [*SD* = 14.2 mm Hg] to 119.5 mm Hg [*SD* = 11.7 mm Hg], *p* = .043), while the control group did not quite attain significance in sustaining their improvement (127.6 mm Hg [*SD* = 11.1 mm Hg] to 121.3 mm Hg [*SD* = 16.9 mm Hg], *p* = .051; Bacon et al., 2005). In activity measures, the nondiet group had a significant increase in daily energy expenditure from baseline to one year posttreatment, from 3310.8 kcal [*SD* = 416.9 kcal] to 3400.6 kcal [SD = 417.3 kcal], *p* = .047, compared with the control group which had a significant decrease in activity from baseline to one year posttreatment, from 3334.7 kcal [*SD* = 496.1 kcal] to 3191.9 kcal [*SD* = 455.7 kcal], *p* = 0.005 (Bacon et al., 2002). In the two-year followup article, authors state this increased activity in the non-diet group was maintained at two-year follow-up, although explicit details on the increased activity were not included in the article (Bacon et al., 2005). In addition, retention in the non-diet group was significantly higher than that of the control (92% v. 58%), which is particularly useful given the notoriously poor retention of most standard obesity treatments (Bacon et al., 2005).

Data from participant self-evaluations in the study by Bacon et al. were especially revealing and differed significantly between the groups (2002). Responding to "the program has helped me feel better about myself," 51% of the control group endorsed "agree" or "strongly agree," compared to 93% of the nondiet group. Responding to "I feel like I have failed (or am failing) in the program," 38% of the control group endorsed "agree" compared to only 5% of the

nondiet group. All the control group dropouts endorsed "agree" to "I feel like I have failed…," whereas all of the nondiet group dropouts endorsed "disagree," which the authors felt suggested that "redefining success in a treatment program as helping people feel better about themselves, irrespective of whether they succeed at weight loss, may have contributed to the nondiet group's success in maintaining participation" (Bacon et al., 2002, p. 864).

A study by Tanco and colleagues of a nondieting cognitive group treatment (CT) in adult obese women compared with behavioral treatment (BT; traditional weight loss) and wait list control noted significant improvement of depression, $F(2, 34) = 6.04$, $p < .025$; state anxiety scores, $F(2, 34) = 5.12$; $p = .011$; trait anxiety scores, $F(2, 34) = 5.18$; $p = .011$; and eating-disordered pathology, $F(12, 178) = 4.96$; $p < .001$ within the non-dieting CT group (1998). Additionally, weight loss occurred in the CT group, though less than in the BT arm of the study; MANOVA of body weight data indicated a significant group × time interaction, $F(4, 90) = 4.12$, $p < .05$, such that CT $F(2, 90) = 5.34$, $p < .05$, and BT $F(2, 90) = 11.95$, $p < .01$] groups lost weight, whereas the control group did not, $F(2, 90) = .83$; $p > .44$.

A nondiet-focused cognitive-behavioral program (M-CBT) was compared to a standard cognitive-behavioral (S-CBT) program in a ten-week RCT of sixty-three women with BMI ≥ 28 by Rapoport, Clark, and Wardle (2000). The goal of the M-CBT group was weight management (prevention of weight gain) through permanent lifestyle change as well as reduction of psychosocial and medical risks of obesity through encouragement of regular physical activity and healthy eating, while the S-CBT group aimed to reduce weight through caloric restriction of approximately 1200 kcal/day, healthy eating, and increasing exercise. S-CBT showed initially greater weight loss after treatment (3.9 kg v. 1.3 kg), though by 52-week follow-up, mean weight loss had decreased in the S-CBT group to 3.6 kg and increased in the M-CBT group to 2.0 kg,

with a group × time interaction of $F(3, 52) = 3.71$, $p = .02$. At 52-week follow-up, weight loss in both groups had reached significance (M-CBT: $t(29) = 2.41$, $p = 0.02$; S-CBT: $t(29) = 2.32$, $p = 0.03$). Significant changes also occurred in total cholesterol, $F(3, 49) = 2.28$, $p < .001$; LDL-C, $F(3, 49) = 7.44$, $p < .001$; systolic blood pressure, $F(3, 50) = 2.93$, $p = .04$; and diastolic blood pressure, $F(3, 50) = 4.80$, $p = .005$; though no differences in degree of change between groups was evident, and changes in glucose, triglycerides, and waist-to-hip ratio (WHR) were not significant. Psychological factors improved significantly, but there were no group × time interactions. Significant improvements were also noted in depression, $F(3, 52) = 4.32$, $p = .009$; self-esteem, $F(3, 52) = 8.62$, $p < .001$; perceived stress, $F(3, 52) = 3.98$, $p = .013$;, binge eating, $F(3, 52) = 28.81$, $p < .001$; hunger ($F(3, 52) = 10.07$, $p < .001$; disinhibition, $F(3, 52) = 15.46$, $p < .001$; restraint, baseline as covariate, $F(3, 51) = 17.95$, $p < .001$; and body dissatisfaction, $F(3, 54) = 12.44$, $p < .001$. Additionally, there were significant increases in self-reported physical activity, $F(3, 34) = 4.9$, $p < .006$, but again no group × time interaction. Acceptability of treatment was assessed in the M-CBT cohort and ninety percent of the women found the intervention less competitive and less frustrating than other weight-loss programs. Dropout was similar between the two groups. The predicted advantage of the M-CBT with regard to psychosocial variables did not emerge, however, and authors surmised that this might be due to the supportive effects of the group intervention and emphasis on self-acceptance within both groups. Both interventions were judged to be modestly successful in achieving significant though small improvements in dietary and cardiovascular risk factors, with substantial improvement in body image, binge eating, and overall well-being.

Provencher and colleagues explored the differences between a HAES® group, a social support group (SS), and waitlist control on eating behaviors and appetite ratings in 144

premenopausal overweight women (2007; 2009). Authors added a social support group to try to isolate the effect of the HAES® intervention from the possible confounding effect of group support. Additionally, they sought to find out if the intuitive eating component of the HAES® approach had a measurable effect on appetite sensations and eating behavior. The four month HAES® intervention ("Choisir de Maigrir?" – "What about losing weight?") consisted of 13 three-hour evening sessions and one intensive six-hour session led by a registered dietitian and clinical psychologist, supported by lectures, guided self-reflection, and group discussions, and focused on promotion of a healthy lifestyle. Group discussions and a weekly food diary were used to explore recognition of internal cues of hunger and satiety and effects of external influences on eating behavior. Promotion of enjoyable physical activity, healthy nutrition, and acceptance of their own and others' bodies was also emphasized. The social support (SS) group was led by the same staff and explored the same themes as the HAES® group, but staff were merely facilitators in discussion. Control was a wait list of women instructed to continue their usual lifestyle habits. Following the intervention, significant increase in flexible restraint was observed in the HAES® group, with significant decrease in disinhibition and susceptibility to hunger (and all subscales). The SS group also saw significantly decreased scores for some eating behaviors, though HAES® group saw significantly greater decrease in susceptibility to hunger. Additionally, the HAES® group had a greater decrease in external hunger than control. Women in the HAES® group had a higher desire to eat and hunger in fasting state after the intervention, while no significant changes were observed in SS and controls. One hour after the standardized breakfast, desire to eat and hunger significantly decreased among the HAES® group which was significantly different from SS and control, who had slight increases in appetite sensations. Additionally, a significant decrease in weight was observed in the HAES® group (-1.6 kg [*SD* =

2.5 kg], $p < .0001$, 2% of initial weight) while weight loss in the SS and control groups was nonsignificant (SS: -0.8 kg [$SD = 2.2$ kg], $p = .07$; control, -0.4 kg [$SD = 3.0$ kg], $p = .28$). Greater increase in flexible restraint (intuitive eating) was significantly related to larger weight losses in HAES® and SS groups, while among controls larger weight loss was associated with higher increase in cognitive dietary restraint (restrained eating).

An advantage to a HAES® approach is that such approaches are associated with equal or, more commonly, greater retention than traditional approaches. All of the controlled studies (Bacon et al., 2002; Bacon et al., 2005; Ciliska, 1998; Provencher et al., 2007; Provencher et al., 2009) based upon HAES® principles have been associated with higher retention than traditional weight loss programs, with the exception of two which had equal attrition to treatment as usual (Rapoport et al., 2000; Tanco et al., 1998). For example, in the studies by Bacon and colleagues, there was a 42% attrition rate in the diet group versus an 8% rate in the nondiet, HAES®-based group (Bacon et al., 2002; Bacon et al., 2005). Similarly, in studies by Provencher, the attrition rates were 18.8% versus 8.3% (Provencher et al., 2007; Provencher et al., 2009). If this increased retention rate also holds true for patients taking SGAs, then a HAES®-based approach offers a potentially more sustainable and patient-acceptable path to improved health, irrespective of weight.

Additionally, several of the HAES®-influenced interventions are associated with improvements in psychological factors such as depression and anxiety that could be of benefit to patients with psychiatric illness. This is evidenced in numerous of the HAES® studies already described (Bacon et al., 2002; Bacon et al., 2005; Ciliska, 1998; Provencher et al., 2007; Provencher et al., 2009; Rapoport et al., 2000; Tanco et al., 1998). Self-acceptance as taught by HAES® approaches is central to self-care, as articulated in compassion-focused behavior change

theory, and leads people with stronger self-regard to take better care of their bodies and adopt more positive behaviors (Gale, Gilbert, Read, & Goss, 2012; Goss & Allan, 2010; Leary, Tate, Adams, Allen, & Hancock, 2007). This may be particularly useful for patients with schizophrenia, as evidenced in the experience of Ms. Hagaman's disease management program discussed earlier, and as noted by Evans et al.: "interventions that focus on empowering the patient to take control of their diet and activity levels and their health and wellbeing, intuitively offer much more to this group" (2005, p. 480).

Limitations of HAES® Approaches

There are a number of limitations to HAES®-based approaches, most notably the relative paucity of adequately powered RCTs supporting its use, although numerous studies do exist proving the independent effects of behavioral change on health regardless of weight. HAES®-specific studies of greater duration and power are needed to better evaluate whether the apparent short-term benefits of this approach will be shown to have long-term sustainability. Existing studies also evidence a great deal of heterogeneity, as HAES® approaches are loosely based on a set of principles rather than being a defined intervention, and so a standardized HAES® protocol may thus be beneficial.

The great majority of study subjects have been Caucasian women, which leaves considerable cultural and gender bias (Miller & Jacob, 2001). Indeed, it has been proposed that men may be more naturally intuitive eaters, and so may not reap as much benefit from a HAES® model (Gast, Madanat, & Nielson, 2012), and it is unclear whether other cultures and ethnicities may respond as robustly. Furthermore, HAES® approaches have been primarily studied among subjects with eating disorders, which presumes a baseline of eating disorder psychopathology

which may not be present in other populations, and therefore may not respond to these techniques.

Most importantly, while HAES® approaches have been studied in subjects with eating disorders, they have not been studied in those with severe psychiatric illness, as proposed here; indeed, in most studies, severe psychiatric illness has been an exclusion criterion. Therefore, a HAES® approach would need to be thoroughly explored in randomized, controlled trials in populations of patients with schizophrenia, perhaps compared to a treatment-as-usual lifestyle interventions.

Challenges specific to the population of patients with schizophrenia would need to be addressed in any intervention, and include amotivation, sedative effects of medications, poor insight, and reduced social and cognitive functioning (Faulkner, 2006; Menza et al., 2004); Beebe et al. particularly stressed the importance of addressing motivation (2011); the flexibility of a HAES® approach in encouraging all manners of movement beyond conventional "exercise" may be especially helpful here. Existing interventions in this population have proved that successful interventions are possible. It is likely that a HAES® approach may be adapted to existing group or individual interventions, and with its focus on self-acceptance may help empower patients towards positive change.

Chapter 5: Conclusion

Given the well-known adverse effects of SGAs as well as the existing disparities in treatment outlined earlier in this review, health status of all patients using these medications should be carefully monitored according to existing guidelines, including blood pressure, fasting plasma glucose, and lipids, and not merely body weight/BMI (Sernyak, 2007). Because treatment with SGAs is most commonly initiated by mental health providers, it is important that they take responsibility to ensure proper monitoring and care of any metabolic consequences that arise and coordinate with primary care providers as needed (Vreeland, 2007). Conversely, all primary care providers should be familiar with SGAs and their adverse effects and confirm that any of their patients using these agents are receiving adequate monitoring and treatment, and coordinate their care with mental health providers (Gold, Kilbourne, & Valenstein, 2008).

For patients commencing treatment with an SGA or wishing to mitigate metabolic consequences of SGA treatment, a HAES® strategy may offer a sustainable, patient-acceptable approach for long-term behavioral change. Even in the absence of adverse effects from SGAs, all patients with schizophrenia may benefit from improved health behaviors such as offered by a HAES® approach. However, as stated before, specific trials in the population of patients with schizophrenia are needed to determine the possible utility of a HAES® approach and elucidate any modifications that may be needed to maximize its benefit in this population.

Future directions for research, as well as further exploring HAES®-based interventions, should include investigations into SGA receptor binding and effects on hunger and satiety sensation, effects on inflammatory markers, and most importantly, search for new agents with fewer adverse effects. All studies should be adequately powered and have longer follow-up periods, ideally two to five years, to properly evaluate long-term success. Additionally, new

studies of interventions should include as their endpoints direct measures of cardiometabolic health rather than relying solely on weight or BMI as a proxy for health.

Furthermore, as called for by Faulkner, adoption of a "broader ecologic framework" is needed to address the frequently "obesogenic environment" in which many patients with schizophrenia must live, with institutional environments offering scarce opportunities for physical activity, few fresh fruits and vegetables, and confined living spaces (2006, p. 508). The role of "active embodiment" within HAES® approaches, wherein people strive to be more active in all realms of their life through simple acts such as taking stairs rather than elevators, may help with some aspects of this, but administrators, mental health workers, and architects should work to improve the health of the environments in which patients must live as well. This framework must also be expanded more broadly to the rest of society, to include more walkable communities, easily available healthy foods, farmers' markets, bike paths, and transit options for all.

All health care practitioners can help their patients adopt a HAES® approach by:

- Respecting body diversity and avoiding assumptions of health status based on weight, BMI, or body shape.
- Encouraging self-acceptance, recognizing that positive change is nourished via self-care, not self-hate.
- Encouraging the patient in activities they enjoy (dance, nature hiking, roller derby, yoga, tai chi) for the joy of movement and caretaking of the body, and not as punishment or for weight loss.

- Teaching intuitive eating: listening for hunger and satiety, tasting food and responding to how it makes one feel, avoiding eating mindlessly while doing other activities, and abandoning good/bad food categories.
- Placing the emphasis for all patients, regardless of weight, on well-being, quality of life, and direct measures of health such as blood pressure, lipids, and fasting blood glucose, rather than BMI or weight.

Suggested resources for providers who want to know more about HAES® or HAES®-like approaches include:

- The Association for Size Diversity and Health (ASDAH): international professional organization which has links to and resources for HAES®-friendly providers: http://sizediversityandhealth.org/
- The Intuitive Eating website has lists of providers and resources for certification in Intuitive Eating: http://www.intuitiveeating.org/
- Linda Bacon, PhD, has many resources at her website: http://www.lindabacon.org/
- National Association to Advance Fat Acceptance (NAAFA): a non-profit civil rights organization dedicated to ending size discrimination: http://www.naafa.org
- The HAES® Community Resource List website lists resources, providers, and programs: http://www.haescommunity.org/resources.php

Suggested HAES®-based resources for patients include:

- *Health At Every Size: The Surprising Truth About Your Weight* (Bacon, 2010)
- *Intuitive Eating: A Revolutionary Program That Works* (Tribole & Resch, 2003) and the

Intuitive Eating website, which has online support groups and workshops: http://www.intuitiveeating.org/

- *Eat What You Love, Love What You Eat: How to Break Your Eat-Repent-Repeat Cycle* (May, 2009) and *Am I Hungry? What to Do When Diets Don't Work* (May, 2005): http//amihungry.com
- *Secrets of Feeding a Healthy Family: How to Eat, How to Raise Good Eaters, How to Cook* (Satter, 2008): http://www.ellynsatter.com/
- *Don't Weight, Eat Healthy and Get Moving NOW!* (Bliss, 2002): http://www.kellybliss.com/
- *The Fat Chick Works Out! (Fitness that's Fun and Feasible for Folks of all Ages, Sizes, Shapes and Abilities)* (Bliss, 2002): DVDs also available at http://www.thefatchick.com/
- *Every Body Dance Now*, by Ragen Chastain, professional dancer and blogger at http://danceswithfat.wordpress.com/: Fun, easy to follow, non-intimidating, choreography-based classes on DVD with options to suit dancers of all levels
- The Fat Nutritionist: intuitive eating advice blog and online classes: http://www.fatnutritionist.com/
- *Weigh This Instead! Life After Emotional & Binge Eating* blog and membership circle: http://www.aweighout.com/binge-eating-membership-circle/blog

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Tables

Table 1

Table 1 Randomized controlled HAES studies reported in peer-reviewed journals

Investigation	Group type[a] (n)	Population	Number of treatment sessions	Follow-up (number of weeks post treatment)	Attrition	Improvements			Decre-ments
						Physio-logic	Health behaviors	Psycho-social	
Provencher, et al., 2009 [17] **and 2007**[20]	**HAES** (n = 48); social support (n = 48); control (n = 48)	Overweight and obese women	15	26	8%; 19%; 21%	Not evaluated	Eating behaviors	Not evaluated	None
Bacon et al, 2005 [11] **and 2002**[19]	**HAES** (n = 39); diet (n = 39)	Obese women, chronic dieters	30	52	8%; 42%	LDL, systolic blood pressure	Activity, binge eating	Self esteem, depression, body dissatisfact-ion, body image, interoceptive awareness	None
Rapaport et al., 2000[16]	**Modified cognitive-behavioral treatment** (n= 37); cognitive behavioral treatment (n= 38)	Overweight and obese women	10	52	16%; 16%	Total cholesterol[b], LDL cholesterol[b], systolic blood pressure[b], diastolic blood pressure[b]	Activity[b], dietary quality[b]	Emotional well-being[b], distress[b]	None
Ciliska, 1998 [12]	**Psycho-educational** (n = 29); education only (n = 26), waitlist control (n = 23)	Obese women	12	52	14%; 23%; 41%	Diastolic blood pressure	Binge eating	Self-esteem, body dissatisfact-ion, depression	None
Goodrick et al., 1998[13]	**Nondiet** (n = 62); diet (n = 65); wait-list control (n = 58)	Overweight and obese women, binge-eaters	50	78	Not reported	Not evaluated	Binge-eating, exercise[b]	Not evaluated	None
Tanco, et al., 1998[14]	**Cognitive group treatment** (n = 20); weight loss (n = 21); waitlist control (n = 19)	Obese women	8	26	10%; 10%; 32%	Not evaluated	Not evaluated	Depression, anxiety, eating-related psycho-pathology, perception of self-control	None

[a] HAES group listed first and in bold. (The names reflect those used in the publication.)

[b] Improvement in HAES group, but not statistically different from the control.

From "Weight science: Evaluating the evidence for a paradigm shift," by L. Bacon and L. Aphramor, *Nutrition Journal*, 10(1), 1-13. doi: 10.1016/j.jada.2005.03.011, p. 3.

Abstract

BACKGROUND: Second generation antipsychotics (SGAs) are used in schizophrenia, bipolar disorder, and other conditions, and are associated with weight gain and cardiometabolic disturbances. This article reviews current approaches to these effects and investigates feasibility of the Health At Every Size® (HAES®) model in this population.

METHODS: MEDLINE, CINAHL, and bibliographic searches were conducted for articles on adults with schizophrenia.

RESULTS: Of current strategies, initial choice of agents with better adverse effect profiles is most effective. Evidence may also support adjunct metformin. Traditional lifestyle approaches appear effective short-term but have high dropout and poor long-term data. HAES® studies in non-SGA populations show sustained improvement in cardiometabolic measures regardless of weight loss and have lower dropout than traditional approaches, though studies in SGA populations are lacking.

CONCLUSION: All patients can benefit from healthy behaviors; a HAES® strategy may offer a more sustainable, patient-acceptable approach. However, specific trials in this population are needed.