The Special Case of Obesity among Persons with Severe Mental Illnesses:
A Paradigm Case for Public Health Action
June 5, 2012

Authors: Erica L. Ahmed, David L. Shern, & Sarah M. Steverman
Editorial Assistance: Hannah-Rose Mitchell

Abstract. We conducted a review of the literature related to obesity and mental illness, synthesizing the existing research. We discussed the prevalence and implications of obesity in the general population, followed by the science of obesity, including environmental, behavioral, and metabolic contributors. The review focused primarily on issues related to adults, but also included a brief description of childhood obesity issues. Special concerns related to individuals with serious mental illnesses were a primary focus of the review. There is an especially high prevalence of obesity among those with serious mental illnesses, which is related to excess morbidity and mortality in this population. Side effects from psychiatric medications are a major contributing factor to weight gain and obesity in this population. While this has been known in the field for some time, the review found new literature related to the common neurobiology of addiction, obesity and mental illnesses, which could have implications for understanding the prevalence of co-occurrence, causes of these conditions, and prevention and treatment strategies. The prevention, intervention, and treatment literature was reviewed for both the general population as well as those with serious mental illnesses. Treatment interventions were found to fall into one of three categories; behavioral (lifestyle change), surgery, and pharmacological. The review concludes with a discussion of the policy implications of the issue, describing policies that support the prevention, early identification, and treatment of obesity for individuals with serious mental illnesses, including several provisions of the Affordable Care Act.

I. Introduction

The burden imposed by obesity is multifaceted and far-reaching, consequently making it a public health priority. It is associated with notable increased risk of more than 20 chronic diseases and health conditions that can yield devastating outcomes such as increased mortality.¹ According to the National Heart Lung and Blood Institute (NHLBI) expert consensus, the full understanding of how and why obesity develops is incomplete, but it is believed to involve the integration of social, behavioral, cultural, physiologic, metabolic and genetic factors.² Obesity prevalence rates have consistently and significantly increased among adults as well as children and adolescents.³ Worldwide, an estimated 1.6 billion adults are overweight and at least 400 million among them are obese.⁴ With an estimated 65 percent of Americans identified as overweight or obese, weight loss has become what at times feels like an insurmountable public health challenge.⁵ If the current rates of overweight and obesity continue, by 2015, 75 percent of adults and almost 25 percent of children and adolescents in the U.S. will be overweight or obese.² In 1990 it was estimated that the total direct cost of obesity-associated morbidity in the U.S. was $45.8 billion, representing nearly seven percent of all health care budget expenditures.³ In 2008, medical spending attributed to obesity is estimated to have been $147 billion, approximately 9.1 percent of annual medical spending.¹ As previously mentioned, obesity is a significant risk factor for increased morbidity and
mortality, but principally from cardiovascular disease (CVD), diabetes, cancer as well as chronic diseases such as depression, sleep apnea, osteoarthritis, and liver and kidney disease. In 2003, the American Cancer Society estimated that nearly 90,000 cancer deaths were related to obesity. While obesity can be an extremely complex health condition to address as it encompasses genetic, developmental and environmental causes, it is treatable. To underscore its' complexity, first we must recognize that unlike other compulsive or addictive disorders such as tobacco or drug addiction, where engaging in the risk inducing behaviors is optional, eating is required to sustain life in addition to being a pleasurable experience like other addictive behaviors. Eating has been shown to activate reward circuits that are also involved in drug addiction. Hence, obesity, like addiction, can be strongly linked with exposure to powerful reinforcing entities. To be clear, food type, portion and quality are some of several contributing factors related to obesity.

**What is Obesity?**

Historically, obesity has been associated with increased mortality and morbidity. Obesity is defined as a body mass index (BMI) greater than or equal to 30kg/m², thus distinguishing it from overweight which is a BMI between 25 and 29 kg/m² of body mass. According to the Centers for Disease Control (CDC), approximately 65 percent of American adults are either overweight or obese (23 percent are considered obese). While obesity is classified as a medical disorder, factors in the development as well as trajectory of the condition strongly suggest that the disease could also be conceptualized as a behavioral disorder with a significant psychiatric component.

The relationship between increased weight gain, age and health risks is curvilinear. This relationship is clearly illustrated in the Framingham Heart Study which demonstrated an increased risk of death by one percent for every pound of weight gained between the ages of 30 and 42 years, and 2 percent between the ages of 50 and 60 years. Regarding a natural history or trajectory of obesity, weight gain occurs until the sixth decade of life; at this time weight appears to stabilize and then decline with age. An elevated BMI in early adulthood appears to increase one’s risk of becoming obese within 15 years.

**The Science of Obesity**

The most essential explanation for the causes of obesity relates to the simple equation involving calories ingested versus calories expended. Social and environmental factors that promote greater calorie intake than calorie expenditure ultimately result in increased weight gain that may eventually result in obesity. As will be discussed below in somewhat more detail, the evolutionary significance of food intake for survival has resulted in biological mechanisms that promote weight gain. While once adaptive, these mechanisms have become troublesome in our current social circumstances of abundant food availability and the commercialization of high calorie, ultra palatable and inexpensive foods. The biology of energy metabolism and appetite control is complicated as both peripheral as well as central mechanisms involving multiple hormones, neurotransmitters, and signaling proteins ensure against starvation and ultimately drive the organism to store energy for use when food is unavailable.
multiple biological systems promote weight gain, very few mechanisms counter excess weight. As previously mentioned, biased energy regulation for storing energy was evolutionarily necessary for survival.\textsuperscript{8} This redundancy of the weight-promoting biological systems tells part of the story regarding the lack of effective obesity medications. Today in the developed world, starvation is rare, but this redundancy of the weight-promoting biological systems is partly responsible for the lack of effective obesity medications despite decades of research.\textsuperscript{8}

While obesity rates are measured in terms of body mass index, increasingly the metabolic syndrome is being used to operationalize the physiological factors that underlie the threats to health related to overweight and obesity. Metabolic syndrome is the name given to a cluster of conditions or risk factors that increase risk for heart disease and other health problems.\textsuperscript{10} The following five characteristics are metabolic risk factors and meeting three criteria is sufficient to make a diagnosis of metabolic syndrome:

1. A large waistline called abdominal obesity or “having an apple shape.” Excess fat in the stomach area is a greater risk for heart disease than excessive fat in other parts of the body.

2. A high triglyceride level or taking a medication to treat high triglycerides, a type of fat found in the blood.

3. A low HDL cholesterol level or taking a medication to treat low HDL cholesterol as this raises one’s risk for heart disease. It is sometimes referred to as “good” cholesterol as it helps to remove cholesterol from your arteries.

4. High blood pressure or taking a medication to treat high blood pressure. If this pressure rises and is sustained over time, it can damage the heart and promote plaque buildup.

5. High fasting blood sugar or you are taking medication to treat high blood sugar. Mildly high blood sugar can be an early indicator of diabetes.\textsuperscript{10}

Obesity is a common underlying cause of the metabolic syndrome. As obesity rates continue to rise in the U.S., it is predicted that metabolic syndrome will become increasingly common and may even surpass smoking as the leading risk factor for heart disease.
II. Reasons/Explanations for Sustained Obesity Epidemic in U.S.

The expansion as well as the sustainability of the obesity epidemic in the U.S. has multiple causes as this once rare chronic disease becomes the norm. Ultimately, as previously mentioned, overweight and obesity arise as a result of an imbalance between the energy we take in and the energy we expend. The balance as well as imbalance of energy is believed to be influenced by both environmental and genetic factors. It is estimated that 30 to 40 percent of variance in BMI is a result of genetic factors and 60 to 70 percent is believed to be environmental. Moreover, the genotype of obesity may have different phenotypic expression depending on environmental factors such as a sedentary lifestyle, watching television, increased caloric intake, regular fast food consumption as well as sleep deprivation.

Figure 1 – CDC Model of Variables that Impact Health

Figure 1 depicts the factors that affect health, which are involved in the development and persistence of the obesity epidemic in the U.S. The most impactful causes relate to socioeconomic factors including poverty and education. Persons in lower socioeconomic status (SES) groups are overrepresented in obese populations with the potential causal factors related both to general knowledge as well as the environments in which these individuals reside. Poor neighborhoods often have a relatively greater concentration of fast food restaurants that offer...
highly palatable foods that are relatively inexpensive and high in calories, fat and salt. While some recent data indicate that the presence of ‘food deserts’ in poor areas may be less of an explanation for the socioeconomic gradient of obesity, the lack of access to more wholesome, fresh foods has traditionally been cited as frustrating better food choices in low SES neighborhoods. Furthermore, persons who live in poverty are more likely to experience food insecurity and to be exposed to toxic stress and trauma which are also associated with neural and behavioral changes that may interact with the availability of highly palatable food to underwrite the development of obesity.

A helpful model for conceptualizing the SES effects involves food insecurity. According to the U.S. Department of Agriculture (USDA) food insecurity is defined as being periodically uncertain of having or the inability to acquire an adequate amount of food for all household members because of insufficient money or resources. Conceptually, household food insecurity is multidimensional and its definition captures the biological as well as the psychological implications of food insecurity in households. Numerous studies have shown an association between food insecurity and mental well-being, stress, and depression. Inconsistent feeding is stressful and can foster obesity. For example, Lohman et al. (2009) found that increased levels of individual stressors led to an increased chance of obesity, and that youth ages 10-15 from food-insecure households whose mothers experience stress had an increased likelihood of becoming obese. Food insecurity among adults has been associated with being overweight or obese; particularly among women ages 20-26. In 2003, 11.2 percent of U.S. households were at some time food insecure with African American and Hispanic households averaging 25 and 27 percent respectively. According to the Centers for Disease Control and Prevention (CDC), African Americans had a 51 percent higher prevalence of obesity and Hispanics had a 21 percent higher prevalence in comparison to Whites. Furthermore, a USDA report found that most food-insecure households did not reduce their food intake, but rather relied heavily on a small number of basic foods. As a means of avoiding hunger and sustaining energy, poor people consume a significant amount of inexpensive, high calorie, low quality food. This disparity is consistent with generally accepted inequities relative to poverty, as well as diseases such as hypertension, diabetes and obesity among these segments of the population. We now have the science that tells us that cheap, energy dense diets (e.g., tasty processed foods with added sugar and fat) account for nearly 40 percent of the daily caloric intake of people with minimal resources. This strongly suggests that “the obesity epidemic is not so much a failure of biological systems but a social and economic phenomenon.” Or, as alluded to earlier, the convergence of a biological propensity to gain weight in anticipation of starvation coupled with the availability of cheap, tasty, energy dense foods underwritten by a biological system designed to support eating and fat storage add up to big problems.

The second variable highlighted in the figure relates to aspects of the built environment and policy that further protect or compromise health. Safe neighborhoods and neighborhoods with sidewalks help promote exercise while their absence makes it more difficult to stay fit and manage weight. Elimination and/or reduction in the number of physical fitness classes in K-12 education further promote sedentary lifestyles in developing youth. Some government
subsidies of corn, promoting the use of high fructose corn syrup that adds to the hyperpalatability of foods are likely a contributing factor to the problem as well.

The third group of variables highlighted in Figure 1 involves public health measures that increase resilience to disease. Some of these preventive mechanisms will be discussed below. However, the general lack of a systematic approach for implementing behavioral health preventive mechanisms demonstrates another missed opportunity to offer protective factors that would improve health through the development of positive behavioral repertoire and an enhanced ability to cope with chronic stress and trauma.

The clinical and behavioral interventions designed to work with individuals who are already overweight or obese that comprise the last two variables in the pyramid will be discussed later in the context of treatment programs for obesity.

**Childhood Obesity**

Over the last 30 years, the prevalence of obesity has tripled among U.S. children. With the well documented association with increased rates of cardiovascular disease, type 2 diabetes as well as premature mortality and significantly impaired quality of life coupled with a greater likelihood of disability, experts have strongly suggested that there will be profound generational consequences of the obesity epidemic in the U.S. Of particular concern is that obesity in childhood is associated with obesity into adulthood. This underscores the importance of examining the trajectory of obesity across the lifespan. For example, in their analyses, Lee et al. (2010) used the data from the NHANES survey of probability samples of non-institutionalized civilian populations spanning 1971-2006. Beyond just being obese in childhood, this study examined the impact of cumulative exposure to obesity that would likely result in profound implications for future rates of obesity-related chronic diseases and mortality in the U.S. population. In order to address the obesity epidemic across the lifespan in a more meaningful way, it is imperative to understand which individuals are at risk of becoming severely or morbidly obese.

Few studies have looked at individuals who are obese early in life to determine their risk of developing severe obesity in adulthood. Table 1 below highlights results from the National Longitudinal Study of Adolescent Health which is a cohort of adolescents (n = 20,745) drawn from a sample of 80 high schools and 52 middle schools in the United States. Table 1 depicts the relationship between adolescent weight status and obesity as an adult. It shows that overall, severe adult obesity in males occurs in about six percent of the population, but that 37 percent of males who were obese as adolescents became severely obese as adults in contrast to the 1.2 percent of normal weight adolescents who became severely obese. Even more dramatic associations are obtained for women, Blacks and Hispanics. If we are going to manage adult obesity, it is critically important that we proactively intervene and rigorously manage childhood and adolescent overweight and obesity.
III. Special Concerns for People with Severe Mental Illness

The most disadvantaged population in the U.S. regarding life expectancy is not a racial minority, but instead, people with serious mental illnesses (SMI). Persons with mental illness have notably higher rates of metabolic disturbance including diabetes, obesity and dyslipidemia. The high prevalence of comorbid medical conditions among persons with severe mental illnesses is well documented. An already vulnerable population, they are afflicted with obesity, chronic lung disease, diabetes mellitus, HIV and hepatitis B and C at least two to five times as commonly as the general population. In a random sample of selected individuals with SMI receiving outpatient psychiatric treatment (n=169) and an individually matched control group from the NHANES III database, Dickerson et al. found that 50 percent of the female and 41 percent of the male psychiatric sample were obese, compared to 27 percent of women and 20 percent of men in matched comparison groups. Current pharmacotherapies such as antipsychotics are important contributors to this problem. Antipsychotic medications are generally divided into two categories: first generation agents (typical) such as haloperidol and...
second generation agents (atypical) such as risperidone and olanzapine. The primary
difference between the two types of antipsychotics is that the first generation drugs block
dopamine and the second generation drugs block dopamine in addition to affecting serotonin
levels. While we know that second-generation atypical antipsychotic drugs (AAPDs) may have
fewer motor side-effects than earlier anti-psychotic medications, they are not side-effect free.
The most commonly reported side-effect of the second generation agents is weight gain (See
Figure 2).

![Figure 2. Weight change after 10 weeks on standard drug doses, estimated
from a random-effects model](image)

Adapted from Allison et al., 2009

Figure 2 displays the weight gain that is associated with varying types of antipsychotics. Clearly,
on average, these agents promote weight gain. Also, they differ in the degree to which they
promote weight gain over the 10 week period summarized in the Figure. In yet another
study, in short-term trials lasting 8-12 weeks, treatment with multiple antipsychotic
medications yielded a significant range of changes in mean body weight, from <1 kg to >4 kg.
For example, over a 10 week treatment period, weight gains for persons treated with clozapine,
olanzapine, risperidone, and ziprasidone were 4.5, 4.2, 2.1 and .4 kg, respectively.

Among people with schizophrenia, risk factors for metabolic syndrome and type 2 diabetes
mellitus are 1.5-2.0 times as common as in the general population. In the largest study to date,
with more than 50 sites across the United States, researchers compared the baseline metabolic
characteristics of fasting subjects with schizophrenia entering the Clinical Antipsychotic Trials of
Intervention Effectiveness (CATIE) study to the characteristics of age-matched people in the
general population (data from NHANES III).
Adapted from Allison, et al., 2009

As depicted in Table 2, researchers found metabolic syndrome was present in 41 percent of schizophrenia patients overall (51.6 percent in women, 36 percent in men), whereas rates in healthy women and men were 25.1 and 19.7 percent, respectively.  

In another study conducted in 2002 with 644 patients with bipolar disorder, 58 percent of the patients were overweight, 21 percent were obese, and 5 percent were extremely obese.  

Even more disturbing is the association between serious mental illness, obesity and a 20-25 year reduction in lifespan, primarily attributed to premature heart and cerebrovascular disease.  

These high rates of comorbidity of medical disease can be partly attributed to unhealthy behaviors such as smoking, poor diet, substance abuse and sedentary lifestyle. For example, we know that persons with serious mental illness are less likely to be physically active than the general population because of a lack of affordable safe places to exercise as well as the psychomotor retardation that often accompanies affective states such as sadness or depression. Additionally, antipsychotics’ promotion of weight gain underscores the important added risk for obesity and diabetes. We also know that individuals with a severe mental illness such as schizophrenia have alarmingly high mortality rates which can be attributed to obesity related diseases and cardiovascular problems that are largely environmentally driven.  

Moreover, the extent to which weight gain is induced by many antipsychotic agents, including the atypical neuroleptics, has harmful effects on general health as well as quality of life and adherence to antipsychotic medication.  

It is clear that persons with severe mental illnesses are at increased risk for multiple co-occurring general health conditions that ultimately result in dramatically shorter life expectancy. It is also clear that lifestyle choices such as inactivity and tobacco use, which themselves may be related to vulnerabilities of the illnesses, contribute to this excess mortality. The existing medications that are used to treat these conditions further exacerbate the general health problems and, as we will discuss next, may reflect common developmental course.  

Obesity is a common end point for several of these contributing factors and is unequivocally related to increased morbidity and early mortality.
The Neurobiology of Addiction, Obesity and Severe Mental Illness.

As we have come to better understand the neural mechanisms that are associated with obesity, strong parallels have been discovered between them and the processes that characterize drug addiction. Additionally, the pharmaceuticals that are used to treat individuals with schizophrenia and other severe mental illnesses impact some of the same neural systems that are involved in weight management and drug addiction. Many of these medications are known to cause significant weight gain. Finally, traumatic childhood experiences and toxic stress are also known to be associated with both the development of severe mental illnesses as well as increasing the likelihood that an individual will become addicted and/or obese. As might be expected, given the similarities in the mechanisms underlying obesity, addiction and severe mental illnesses and given their common association with childhood trauma and chronic stress, it is perhaps not surprising that these conditions often co-occur. In this section of the paper, we will explore these similarities in etiology and the mechanisms that underlie these conditions and speculate that understanding their common etiological and pathophysiological substrate may help to understand the disorders and suggest prevention, treatment and rehabilitative strategies.

Stress, Mental Illness and Obesity

It is now commonly accepted that genes play an important role in the development of mental illnesses, addictions and body mass. Heritability estimates that reflect the amount of variation in a characteristic that may be attributable to genetic makeup are significant for all three phenomena. However, an individual’s genetic risk is not a definitive factor in developing these conditions. Even for identical twins, the concordance rate for schizophrenia is only about 50 percent implying that environmental variables also play a critical role in the expression of this disorder. Heritability for drug dependence from one large twin study has been estimated at approximately .60 showing an important genetic vulnerability to develop the disorder. However, persons who are never exposed to drugs or alcohol will not become addicted regardless of their genetic makeup. Body mass index is a polygenic trait with estimates of heritability ranging between .45 and .85. This range of estimates for obesity and addiction underlines the importance of particular environmental variables modifying the effect of genotype on the development of obesity and addiction. However, individual differences in genetic vulnerability for each of these three conditions must be considered in any comprehensive understanding of their development. Genotype environment correlation and interaction are critical considerations.

Toxic stress and trauma are one set of environmental factors that have been shown to increase the prevalence of these three conditions as well. Early childhood adverse experiences have been shown to dramatically increase the risk of the development of mental illnesses, addiction and extreme obesity. Anda and his colleagues report adjusted odds ratios of 3.6 for depression, 1.9 for severe obesity (BMI>35), 7.2 for alcoholism and 11.1 for drug addiction for individuals who report four or more adverse childhood experiences relative to persons reporting none. This means that persons who report four or more adverse childhood experiences are 11 times
more likely to develop drug addiction than persons who report none, controlling for other variables that may be correlated with drug addiction. Rodrigues and colleagues further suggest that early traumatic experiences, either pre or post natal, can have profound effects on the development of the central nervous system during critical developmental periods that may predispose individuals to be at higher risk of expressing mental illnesses and/or addiction.\(^{34}\)

While each of the conditions partially underwritten by stress or trauma are likely to have a unique developmental process related to the types of stress experienced, when it is experienced during the lifespan and interaction with the individual’s particular genotype, the general process through which toxic stress and trauma impact neural, endocrine and immune structures has been understood for some time\(^ {35}\). While the specific correlates for mental illness, addiction and obesity are yet to be fully elucidated (particularly in humans) the general theory involves the effects of chronic exposure to stress hormones on neural structure and functioning that may underlie the expression of these three conditions. For example, prolonged exposure to stress hormones involving the hypothalamic-pituitary-adrenal (HPA) axis is believed to have destabilizing effects on the hippocampus which in turn impact the activity of the dopamine system. Increased activity of the dopamine system is associated with the expression of psychosis and anxiety with both stress and psychostimulants increasing the risk of these mental health symptoms as well. Anti-psychotic medications used to treat severe mental illnesses typically act by blocking the Dopamine 2 (D2) receptors thereby counteracting the effects of the dopamine dysregulation that is thought to result in part from changes in the hippocampus. This dysregulation can result from toxic stress or trauma.\(^ {36}\) Interestingly, the agents that block the D2 receptors are associated weight gain. Dopamine regulation is also integrally involved in drug addiction and obesity.

**Neural Correlates of Obesity**

As noted earlier, the ability to obtain food is clearly an important evolutionary characteristic for the survival of the species. It therefore makes sense that mechanisms to help individuals recognize and remember safe foods would be essential for survival. These mechanisms evolved in environments in which high calorie foods were less available than in contemporary developed nations. Similarly, storing calories in body fat was once adaptive in environments with variable access to food. These same mechanisms now may underwrite maladaptive fat storage that results in obesity. Given the slow pace at which genetic changes occur in response to changing environments and the centrality of feeding behavior to survival, it also makes sense that these evolutionarily favored behaviors would be slow to respond to important changes in the environment. The difficulty in modifying these obesity producing behaviors and their associated compulsive qualities makes the control of weight in calorie rich environments a challenge.

With this evolutionary schema as a backdrop, the neural mechanisms that appear to underlie feeding behaviors involve both the reward/pleasure response centers of the brain as well as those involved in decision making and control. As indicated previously, they also strikingly parallel those that are involved with the addiction to alcohol or drugs. While a detailed presentation of these neural mechanisms is beyond the scope and goals of the current paper,
they are increasingly well understood. They involve the response of the brain to food ingestion that stimulates the pleasure response centers of the brain. As a result of this pleasurable response, feeding behaviors can become classically conditioned much like the famous conditioning of Pavlov’s dogs. Food ingestion that produces a pleasurable response becomes conditioned to the sight of food and/or images that are associated with food. Following repeated exposure, the presentation of food related stimuli (e.g., food images in advertising) evokes the conditioned response and prompts food seeking behavior and food consumption. Individuals learn to respond favorably to the sight of palatable food which is associated with craving to ingest the food, regardless of the immediate availability of food and/or the individual’s satiety. Volkow et al. note that vulnerable individuals eating large quantities of highly palatable food can result in increased strength of the reinforcing value of food and decreases in inhibitory control otherwise exercised by the “cortical top down networks ...(which ultimately) ... results in impulsivity and in compulsive food intake.” This compulsive eating is very similar to the compulsivity associated with drug addiction both as it is experienced by the individual and in the basic brain processes that underwrite the response.

Along with some other neurotransmitters and hormones, the neurotransmitter dopamine is critical in modulating reward from food and drugs. Dopamine is a neurotransmitter that is involved in stimulating the pleasure centers of the brain and reinforcing essential evolutionary behaviors such as sexual activity and food ingestion. Individual differences in the architecture of the dopamine system appear to be associated with the cravings and compulsive behaviors that are characteristic of addiction and may account for some of the differences among people in their vulnerability to this ‘addictive’ mechanism. For example, research by Volkow and her colleagues indicates that individuals’ number of D2 receptors is correlated with the degree to which they report a pleasurable response to the administration of an amphetamine. Fewer D2 receptors are associated with a stronger pleasurable response from amphetamine ingestion in non-drug using individuals. Interestingly, individuals with a broad range of addictions (alcohol, cocaine, heroin and methamphetamine) show reduction in the D2 receptors. It is thought that the association of the addiction to drugs and the dopamine system may reflect either changes in the dopamine system in response to the use of drugs (repeated use causes a decrease in the number of receptors) or inborn individual differences in the availability of the D2 receptors may place individuals at greater risk to become addicted to drugs that stimulate this system. Reduced dopamine stimulation of the brain’s reward centers related to reduced D2 receptors when coupled with the classical conditioning associated with the stimulation of the system appears to underlie the addictive response. Drug use helps stimulate these neural circuits which, when stimulated, help compensate for the under stimulation associated with fewer D2 receptors.

Similarly, Volkow and colleagues demonstrated that morbidly obese individuals showed lower than normal D2 receptor availability when compared with normal weight individuals. As in drug addiction, D2 receptor availability was negatively related to eating behavior (e.g. fewer receptors more food consumption). Decreased D2 receptor availability is also related to decreased activity in those brain areas that are associated with inhibitory control – making it more difficult to resist the craving for drugs and/or food. A circular reinforcing cycle therefore
is established in which drug or excess food consumption is associated with decreased D2 receptor availability which, in the context of the learned response to food or drug stimuli, helps to provoke craving and food or drug ingestion. At the same time, stimulation of those areas of the brain that are involved in controlling these impulses is reduced. This circular reinforcing mechanism makes behavioral change particularly difficult for both food and drug addiction and helps to explain the persistence of obesity as a chronic medical problem in the face of negative social and health consequences.

Given the relationship between the availability of dopamine receptors and obesity, and the action of antipsychotic agents blocking D2 receptors, the weight gain attributed to antipsychotics is consistent with the neural mechanisms underlying obesity in non-mentally ill populations. Persons treated with these drugs, therefore, are at a particular disadvantage in trying to control their weight since the medication used to control their psychosis also creates a neural substrate that calls for increased dopamine stimulation particularly as related to the evolutionarily necessary consumption of food. Similarly, drugs or alcohol may be used to stimulate the release of dopamine. Persons with schizophrenia or other psychotic disorders have triple threats to their health. Newer treatments that don’t exert the same influence on the dopamine system and/or alternative treatments that help to manage the side effects of the antipsychotic agents would be extremely helpful in improving the health status of persons with these disorders.

Understanding the role of these common neurological mediators and the shared risk factors of trauma and chronic stress that predispose individuals to develop obesity, severe mental illnesses and addictions, may suggest both avenues for further research and a rationale for increased deployment of evidence-based interventions that are designed to reduce stress and trauma as well as foster resilience. The relationship between the development of mental illnesses and addictions, and the metabolic syndrome associated with obesity and their further relationship to cardiovascular, immune and endocrine disorders is intriguing. Could it be that a common pathway exists among these conditions, suggesting that the interaction of genetic vulnerability and environmental insult launches a disease cascade that ultimately results in death and disability? In this model, the mental illnesses, with a median age of onset of 14 \textsuperscript{40}, would be the earliest signs of deteriorating health status followed by the addictions and subsequently by obesity and the metabolic syndrome. Neuronal changes associated with early life trauma might initially be reflected in emotional and cognitive dysfunction with later problems with addictive substances used in an attempt to compensate for the neuronal dysregulation attendant with the stress and trauma. Drugs and alcohol further destabilize the neuronal control mechanisms. Given the similarities in the processes underlying drug and food addiction and the ubiquitous availability of highly palatable, high calorie foods, addiction to food, possibly resulting in obesity, might follow as would the development of the metabolic syndrome and later disorders associated with it. A novel and integrative way to think about the intimate relationship between diseases once thought to inhabit different provinces (e.g. of the mind versus the body) and high leverage strategies to improve overall health by increasing resilience and reducing stress/trauma would be the new prescription of improved overall
health – a strategy that would likely benefit other dimensions of human capital and productivity.

The recent increase in childhood obesity may suggest an important variant of this explanation that reflects the changing environments in which stress and trauma might respond to self-soothing associated with eating. The availability of inexpensive, palatable food and the social processes reinforcing its consumption may now predispose obesity to be the first developmental disorder associated with these social pathologies. This developmental model of disease is quite consistent with the well understood impact of the social determinants of health suggesting that impacts of the social environment are at least as important as an individual’s genotype (zip code as important as genetic code). Fortunately, we have several well understood interventions that can help to ameliorate the effects of social disadvantage and bolster the resiliency of the general population.\(^\text{12}\) This emerging general theory of the developmental trajectory of health and illness along with our increasing understanding of the relationships among the shared biological processes that underlie mental illnesses, obesity and drug addiction, highlight the importance of efforts to effectively deploy prevention and treatment technologies that are now available, to study their deployment and long term effects on overall health and productivity and further refine our understanding of the biological mechanisms through which these social interventions are mediated.

**IV. Prevention, Intervention and Treatment Technologies**

From a public health perspective, prevention is always the ideal treatment. In using this framework, we are able to see the applicability of primary, secondary and tertiary efforts as they relate to obesity and its co-morbidities.\(^\text{28}\)

**Primary prevention**— Reduce the risk of the onset of the disease since many of the risk factors can be modified (quantity and composition of food intake, physical activity, etc) and offering antipsychotic medications with the least weight gain potential.

**Secondary prevention**— Early detection of weight gain followed by immediate treatment to limit or eliminate disease progression; metabolic monitoring of patients on antipsychotics.

**Tertiary prevention**— Intervention initiated after the individuals become obese with the goals of preventing damage and disability and the restoration of health to the greatest extent possible. Weight loss programs and pharmacotherapies are generally in this category.

Since we know that obesity is a complex disease involving multiple interactions between genetic as well as environmental and cultural factors, it is critical that the treatment of obesity begins by examining the pathophysiologic processes leading to weight gain.\(^\text{4}\) As in the treatment of drug addiction, the scientific evidence regarding the involvement of multiple brain circuits (reward, motivation, learning, cortical inhibitory control) suggests the need for a multimodal approach to the treatment of obesity. In treating both obesity and addiction, some of the most promising pharmacological interventions may be those that interfere with various
processes, including the reinforcing value of the substance (food or drug). Safe and effective pharmacotherapies should be a component of a “treatment buffet” along with healthy eating, caloric reduction and exercise.

Treatment interventions to achieve and maintain weight loss include the following:

(1) Behavioral-based interventions to facilitate lifestyle change (dietary restriction, increased physical activity, or both)
(2) Surgery
(3) Pharmacotherapy

The following chart, adapted from the work of O'Grady & Capretta (2012), documents the characteristics of various obesity prevention and weight loss interventions. The chart includes the name and type of intervention (behavioral, surgery, pharmalogic), the setting of the intervention, a brief description, the cost per Quality-Adjusted Life-Year (QALY) saved by preventing or reducing obesity, and percentage of weight reduction, if available. For comparison with the costs per QALY, researchers in the United States generally use $100,000 as a reasonable cost for saving one QALY. So while these interventions do not necessarily save money, they are quite cost-effective in comparison to what is generally accepted as reasonable.

### Table 3. Differential Cost Effectiveness of Various Weight Control Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Setting</th>
<th>Description</th>
<th>Cost/QALY Saved</th>
<th>% Weight Reduction</th>
<th>Cost/QALY Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coordinated Approach to Child Health (CATCH)</td>
<td>School-based</td>
<td>Comprehensive intervention in elementary schools includes health and physical education curricula, school nutrition, and family home activities</td>
<td>$900</td>
<td>Control: Over three years, at-risk for overweight or overweight prevalence increased by 9% for boys and 13% for girls Intervention: Prevalence increased by 1% for boys and 2% for girls</td>
<td>Brown et al., 2007^42</td>
</tr>
<tr>
<td>Wheeling Walks</td>
<td>Community-based</td>
<td>Community-wide campaign using paid media to encourage walking among sedentary adults</td>
<td>$14,286</td>
<td>N/A</td>
<td>Reger-Nash et al., 2005^43</td>
</tr>
<tr>
<td>Treatment</td>
<td>Type</td>
<td>Description</td>
<td>Cost</td>
<td>Effectiveness</td>
<td>Study</td>
</tr>
<tr>
<td>-----------</td>
<td>------</td>
<td>-------------</td>
<td>------</td>
<td>--------------</td>
<td>-------</td>
</tr>
<tr>
<td>Xenical (orlistat)</td>
<td>Pharmacological</td>
<td>Anti-obesity drug that inhibits absorption of, and promotes excretion of dietary fat</td>
<td>$8,327</td>
<td>Weight loss at year 1 of diet and medication from pre-treatment: 81.4% experienced ≥ 5%; 52.3% experienced ≥ 10%</td>
<td>Maetzel, Ruof, Covington, &amp; Wolf, 2003&lt;sup&gt;45&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bariatric bypass</td>
<td>Surgical</td>
<td>Limits food intake by reducing the effective size of the stomach and bypassing part of the small intestine</td>
<td>$5,000-$16,100 for women; $10,000-$35,600 for men</td>
<td>Weight loss at year 2 of diet and medication: 63.6% experienced ≥ 5%; 35.0% experienced ≥ 10% (Rissanen, et al., 2003)&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Craig &amp; Tseng, 2002&lt;sup&gt;46&lt;/sup&gt;</td>
</tr>
<tr>
<td>Workplace Wellness</td>
<td>Behavioral</td>
<td>Workplace/community</td>
<td>A meta-analysis was conducted of evaluations done on employer-sponsored wellness plans. The typical interventions include baseline health indicators, educational materials, and exercise.</td>
<td>$3.27 drop in medical expenses for every $1 spent on wellness programs</td>
<td>Baicker, Cutler, &amp; Song, 2010&lt;sup&gt;47&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Ideally, behavioral-based clinical interventions provide information on safe physical activity and nutrition for weight loss with cognitive as well as behavioral management tools to support participants making and maintaining healthy lifestyle changes.<sup>8</sup> There are also a growing number of interventions as well as city wide campaigns that are showing promise. For example, Shape Up Sommerville is a city wide campaign that began as a community based...
research study at Tufts University targeting 1st through 3rd graders in the Sommerville Public schools. It later evolved into a campaign targeting all segments of the community—schools, city government, civic organizations, community groups, businesses and other people who live, work and play in Somerville, to increase daily physical activity and healthy eating through programming, physical infrastructure improvements, and policy work.48

Another intervention based in Somerville, MA, The Live Well project acknowledged and addressed the role of culture in the fight to prevent obesity and other co-morbidities. According to Tufts principal investigator Chris Economos, “Often stressed and short on time, immigrants “begin to eat an American diet that consists of the worst food we have to offer - fast food and sugary drinks.”49 The Live Well project focused on moderating or reducing weight gain in mother/child dyads of new immigrants. As such, this innovative study design combines community-based participatory research with clinical trials.50

Medications currently approved in the U.S. for the management of obesity, including weight loss as well as the maintenance of weight loss in conjunction with a reduced caloric intake are orlistat, phentermine, and diethylpropion.8 These medications are recommended for obese patients with a BMI of ≥30 kg/m² or ≥27 kg/m² in the presence of other risk factors such as diabetes, dyslipidemia, or controlled hypertension. These pharmacotherapies vary in how they are able to facilitate weight loss. For example, orlistat decreases fat digestion by inhibiting pancreatic lipases, resulting in increased fecal fat excretion. Sympathomimetic drugs such as phentermine and diethylpropion block the reuptake of norepinephrine and serotonin into nerve terminals, leading to early satiety and a reduction in food intake.8 Phentermine has been shown to be effective in meta-analysis in reducing weight by an average of 3.6 kg greater than placebo control, while diethylpropion resulted in 3.0 kg weight loss in studies ranging from six to 52 weeks.51 Orlistat is the only drug approved for long term use in the U.S. Two anti-convulsive agents, zonisamide and topiramate, have not been approved for use in the U.S. but are used off-label and have been reported to result in weight loss of 5 and 6.5 percent of body weight. Like the aforementioned, metformin (not FDA approved for weight management) is utilized in an off-label capacity as well. This oral hypoglycemic has been tested and found to be more favorable as a treatment for antipsychotic-induced weight gain in comparison to sibutramine and topiramate which each had high discontinuation rates due to side effects.52 Other drugs are in the approval process at this time. Only limited FDA approved pharmacotherapies are therefore available to assist individuals for who are at elevated risk for adverse effects of obesity.8

While there is a paucity of research regarding obesity prevention, particularly as it relates to adults, a growing body of evidence suggests that obesity can be prevented, managed and treated. Like many other chronic and debilitating conditions, obesity develops over time, and once a person becomes obese, treatment can be challenging but not impossible. Organized approaches to treatment that involve a menu of options including behavioral (lifestyle) interventions, social support, pharmaceutical and surgical options have been demonstrated to be effective during short to intermediate term research trials. Prevention and treatment information and services should be readily accessible in primary care settings, schools,
workplaces as well as places of worship. Increasing the dissemination of evidence-based practices in a variety of community settings along with improved public awareness of the dangers of obesity can provide a framework for successfully addressing this public health problem in the general population.

**V. Proven Interventions for Persons with Severe Mental Illnesses**

As noted earlier, persons with severe mental illnesses are at increased risk for obesity and its subsequent significant health problems owing to a number of environmental factors which are further exacerbated by their use of anti-psychotic medications - many of which are associated with significant weight gain. While almost all antipsychotics carry some risk of weight gain, the risk factors vary across the classes of medication (see Figure 2).28

Clearly, psychiatrists as well as internists providing care for people taking antipsychotic medications must be cognizant of the potential for metabolic dysfunction resulting from these varied treatments. When selecting specific interventions for the treatment of antipsychotic-induced metabolic abnormalities, providers have the options of (1) switching to an antipsychotic drug with fewer metabolic side effects and initiating therapeutic lifestyle change (TLC) therapy, and (2) adjunctive treatment with behavioral and medical interventions targeting the side effects of weight gain. A recent review identified 18 randomized controlled trials (RCTs) of pharmacological weight control in people being treated with second-generation antipsychotic agents (SGAs) and found modest significant treatment effects for some agents.23 According to this review there is insufficient data to support the general use of pharmacologic interventions for weight management in people diagnosed with schizophrenia.23 Moreover, given the inconsistent results in this meta-analysis of RCTs coupled with the lack of understanding of the potential exacerbation of psychotic symptoms through the use of anti-obesity agents, this review supports the conclusion that the general use of pharmacological interventions for overweight individuals with schizophrenia cannot be supported even if such interventions are beneficial to some.29 Faulkner and colleagues (2003) did note however, that all behavioral interventions including diet and exercise showed small reductions or maintenance of weight in persons at risk to substantial weight gain. They conclude that these behavioral health interventions within a systematic behavior modification scheme should be adopted.29

Behavioral weight-loss interventions for persons with chronic mental illness face serious challenges including competing demands in treatment such as the management of active mental health symptoms, accommodating possible cognitive deficits, social support issues in housing, employment and education, substance abuse or other personal and social issues. This underscores the need for traditional evidence-based interventions that are effective in the general population to be altered to meet the needs of persons with serious mental illnesses.22 For example, in a single-arm pilot study conducted at two psychiatric rehabilitation day programs in Maryland, persons with serious mental illness participated in a six-month weight-loss intervention including three components: weight management counseling sessions, group physical activity sessions and education for kitchen staff to provide healthier on-site meals. From a decrease in weight and waist circumference as well as dietary sugar and fat, to an
increase in endurance as demonstrated by 69 percent of the participants increasing the distance they walked in six minutes by an overall mean of eight percent, this study, like a growing number of others, demonstrates that relatively brief behavioral interventions can be effective for this population. Another intervention, In SHAPE, was designed exclusively for persons with mental illness who were grappling with diabetes, obesity, and heart disease and ultimately dying in their forties and fifties. In SHAPE works by pairing a personal health mentor with a participant to support them in getting fit, making sound nutritional decisions in addition to serving as a motivator when needed. During the pilot study, the following outcomes were identified among the 300 participants in 35 towns across New Hampshire:

(1) Significant increase in the number of hours they reported exercising per week
(2) Decrease in waist measurements and psychiatric symptoms
(3) Significant increase in their overall activity and their participation in vigorous activities
(4) Significant increase in reported satisfaction with their physical fitness
(5) Significant increase in reported confidence in social situations

Regarding bariatric surgery, there are reports of favorable outcomes among patients with severe mental illness who were stable on medication as well as adherent to treatment. With that being said, consensus-panel guidelines suggest that severe, untreated psychiatric disorders are contraindicated for surgery as there appears to be an increased risk for suicide. It is unclear if the risk can be attributed to pre-existing mental disorders, severe adjustment problems during the post-operative period, or other unknown factors.

Research regarding weight-management treatment for individuals with severe mental illness or other psychiatric disorders is still relatively rare. While initial efforts appear promising, much more research is needed to determine the effectiveness of various approaches for people with mental disorders.

**VI. Policy and Practice**

Given the epidemic of obesity experienced in the U.S., and the state of our knowledge, what policy and practice options should be adopted? These are particularly important questions for persons with severe mental illnesses given their heightened risk for weight related illnesses and excess mortality from these health conditions. Policies that encourage the prevention and treatment of obesity are critically important. By implementing policies that reconfigure the healthcare delivery system into one that is responsive to the multiple and complex issues people with serious mental illnesses and obesity confront, we can make important progress in addressing these issues both for these special populations and for the general population.

**Programmatic Interventions and Policies to Address Obesity for those with SMI**
While screening and intervention services for persons with SMI should be developed, tested, implemented and reimbursed, it is also important to continue to pursue universal prevention strategies that have been shown to be effective in reducing population weight status. These programs will benefit all. Given the association of early life trauma and chronic stress to a myriad of health consequences, prevention programs that reduce levels of trauma (e.g. Nurse Family Partnership54) or assist individuals in managing chronic stress should be available. Finally, given the strong socioeconomic gradient for the expression of obesity, addiction and mental illnesses, government policies that address poverty and lack of equitable access to valued social resources such as educational and occupational attainment should be aggressively pursued. These root causes for problems in the general population and for persons with severe mental illnesses are high leverage strategies that will benefit all.

For individuals with serious mental illnesses, there are programs and supporting policies that can be implemented to promote the prevention, early intervention, and treatment of obesity.55, 56 Since the risks for significant weight gain for persons treated with antipsychotic agents are well understood, quality measures related to screening for individuals who are newly diagnosed with severe mental illness must be established and implemented widely by mental health and/or primary care providers. These screenings must be reimbursed within all health insurance programs but especially Medicaid. Funders should monitor these quality indicators and condition performance reimbursement on their availability. Establishing screening and intervention measures and procedures will help prevent and/or mitigate weight gain among persons with SMI who are likely to develop obesity due to lifestyle and the side effects of psychiatric medications.

Once individuals are screened and made aware of the potential weight gain associated with both their illness and aspects of its treatment, programs must be implemented that help prevent or mitigate weight gain. As we noted earlier, behavioral health programs have been shown to be effective in helping to reduce or manage weight but research in this area is thin. Programs should be encouraged to use existing literature and the National Institutes of Health (NIH) should be encouraged to prioritize research on intervention programs that are specifically designed for persons with severe mental illnesses to enrich the portfolio of treatments that are available. Research both in behavioral interventions as well as in the basic science regarding the neural mechanisms of these disorders and the intersection between the neural mechanisms that underlie severe mental illnesses, addictions and obesity should be rigorously explored. This research hopefully will identify new targets for pharmaceutical interventions as well as a better understanding of the developmental pathways that underlie the development of these conditions further bolstering prevention strategies.

Given the relative lack of pharmaceutical interventions and the significant toll that obesity and related conditions exact from persons with severe mental illnesses, the Food and Drug Administration (FDA) should carefully examine the balance of risks and benefits in their drug approval processes. We don’t propose that these be changed precipitously, but rather that given the predictable mortality related to obesity and its metabolic sequelae, rebalancing risks and benefit estimation should be considered.
Weight loss and weight management programs that have been or will be demonstrated to be effective must be available for people with SMI who may be overweight or obese. Behavioral interventions promoting lifestyle change in nutrition and exercise are being implemented in psychiatric rehabilitation centers serving individuals with SMI, and these programs have preliminary results showing weight management and loss for participants.\textsuperscript{56} Policies that support the financing and implementation of such programs, as well as education of communities and providers regarding the need for these programs, should be supported by the Substance Abuse and Mental Health Services Administration (SAMHSA) and the Health Resources and Services Administration (HRSA) with appropriate service reimbursement mechanisms from Medicaid and other insurers. Post-secondary education of mental and general health providers is a logical venue for improving practice. Accreditation organizations should assure that adequate curricular time be devoted to whole person treatment including the management of general health with weight management as a featured educational component.

Relatedly, individuals with serious mental illnesses should have access to a wide range of obesity treatments, provided they are safe and effective. This may include preventive and treatment interventions that address lifestyle and environmental change, but can also include medications and surgery. Medications such as orlistat and phentermine have been approved by the FDA for weight loss, and we assert that any drug approved by the FDA should be available to patients as a covered benefit in private and public insurance plans. Bariatric surgery has also been found to reduce weight and should be made available to all individuals with obesity, including those with serious mental illnesses, and used when appropriate and safe for the individual patient.

### Health Care Settings to Support Interventions

The integration of behavioral health and primary care is a critical mechanism through which prevention, screening, early intervention, and obesity treatment can be promulgated for individuals with serious mental illnesses. Policies that support the co-location of and/or collaboration between behavioral health and primary care providers may be integral to effectively managing the multiple chronic illnesses many individuals with SMI experience, including obesity. They are a potential venue for facilitating prevention and screening activities for newly diagnosed individuals and could provide treatment expertise for both mental health and obesity related issues. Many general and mental health care settings have found the use of peer wellness specialists to be especially useful for addressing issues of multiple chronic illnesses with consumers of mental health services.\textsuperscript{57, 58}

In addition to health care delivery within an integrated system, primary care and behavioral health providers must have the appropriate education regarding available preventive and treatment options for individuals with SMI. This may entail education of these providers through increased content on obesity in medical, nursing, and other allied health education settings. Obesity treatment should also be a part of continuing medical education for physicians and continuing education for other health professionals.
As part of the integrated care delivery system, primary care and behavioral health providers must have mechanisms in place for referral and care coordination with obesity specialists. For individuals who need more complicated or extensive weight management and obesity treatment interventions than can be provided within the behavioral health and/or primary care setting, their providers should have the ability to easily and appropriately refer them to a specialist that can work with them to meet their weight loss goals.

**ACA Provisions of Note**

The Affordable Care Act has several provisions that promote the integration of behavioral health and primary care and incentivize models of health care delivery that facilitate the management and treatment of obesity and related chronic illnesses for individuals with SMI. Several of these provisions are briefly highlighted below:

1. **Medicaid Incentives for Prevention of Chronic Disease** – Administered by the Centers for Medicare and Medicaid Services (CMS), this program provides $85 million over five years to test the effectiveness of prevention programs. These programs include financial and non-financial incentives to promote health behavior change. As of January, 2012, ten states had received funding for this program.

2. **Health Homes** - States have been given the option to develop health homes for Medicaid beneficiaries who have two or more chronic illnesses, a chronic illness and are at risk for a second, or a serious mental illness. In addition to mental health conditions, the health home model specifies that those that are overweight are considered to have a chronic condition. CMS provides a temporary 90 percent federal match rate for health home services. As of April, CMS had approved state plan amendments in four states to provide these services and several other states have submitted proposals to develop health homes.

3. **Center for Medicare and Medicaid Innovation** – States have been provided flexibility to integrate care and financing for individuals who are eligible for both Medicaid and Medicare. Twenty-six states are currently working with CMS to gain approval and implement these programs which would focus on improving care coordination and testing models of integrated care

Persons with severe mental illnesses and their associated co-morbidities are the ‘poster children’ for the problems with multiple chronic illnesses. Research, policy and practice that better address the needs of this population will ultimately benefit them as well as the vast majority of Americans who are likely to develop multiple co-occurring illnesses throughout their life spans. It is therefore in our enlightened self-interest to dedicate considerable efforts toward addressing these problems with both universal preventive interventions as well as those aimed at early identification and effective treatment. Given the difficulty in changing personal behaviors like those associated with drug addiction and obesity, improved techniques for treatment of them – both lifestyle, pharmacotherapies and surgery for obesity – will further assist all of our public health efforts aimed at changing the behaviors that underlie some of our most challenging health concerns.


