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Antipsychotic Drug Use: Managing Cardiometabolic and Cost Effects

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Introduction

Across the US, 30%, or approximately one third of people meet the criteria for at least one mental illness.¹ Of those with severe mental illness (SMI), namely schizophrenia and bipolar disorder, the mortality rate is more than twofold compared to the general population.² The cardiovascular risk factors that contribute to cardiovascular related deaths, including metabolic disease and type II diabetes, are not only modifiable, but staggeringly higher for those with SMI.³ Though antipsychotic drug prescription is the standard protocol for SMI treatment, such drug effects on cardiovascular risk factors and related deaths exacerbate the much higher mortality rate for the severely mentally ill population. Due to both the prevalence of SMI and the physical comorbidities that it entails, analysis of healthcare costs associated with this population are an essential part of general health and policy improvement for the U.S. Therefore, a breakdown of the healthcare costs of this population requires not only acknowledgment of the modes of treatment for mental illness specifically, but also the identification and cost-analysis of the commonly associated physical comorbidities. This is especially important considering SMI is almost always considered chronic, and many SMI patients qualify for either Medicare, Medicaid, or both. Certain gaps in coverage can lead to lack of preventive care, exacerbating the cost burden.⁴

From a clinician's perspective, assessing relevant scientific studies and reviews to change the relationship between primary care and psychiatry is necessary to dampen the high mortality rate of the SMI population.

From a policy-maker's perspective, analyzing the cause and effect balance between managing costs of care directed at the SMI itself against the adjunct costs from physical comorbidity calls for a change in the structure of therapeutic care and how the SMI population accesses primary care.

The Collaborative Care model is a health care model that unifies psychiatric, behavioral, and primary care to support the mental, behavioral, and physical health of patients. By supporting holistic healthcare, the high cost of care for the SMI population will be diminished. The model includes four parts: patient-centered care, population-based care, measurement-based treatment to target, and evidence-based care. Swapping oral antipsychotics with injectable versions will be especially cost-effective by improving adherence rates, and thus, reducing institutionalization and other hospitalizations. By enforcing the Collaborative Care model through community health center interventions, clinicians and policy makers will be able to work together to effectively leverage the health of the SMI population while eroding the high health care expenditure that this population currently imposes on states.

¹ Marth Ward and Ann Schwartz, "Challenges in Pharmacologic Management of the Hospitalized Patient with Psychiatric Comorbidity," *Journal of Hospital Medicine* 8, no. 9 (2013): 523, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=90096361&site=ehost-live>.

² Kai G. Kahl, Mechthild Westhoff-Bleck, and Tillmann H. C. Krüger, "Effects of Psychopharmacological Treatment with Antidepressants on the Vascular System," *Vascular Pharmacology* 96, (2017): 11, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=125141989&site=ehost-live>.

³ John W. Newcomer, "Comparing the Safety and Efficacy of Atypical Antipsychotics in Psychiatric Patients with Comorbid Medical Illnesses," *The Journal of Clinical Psychiatry* 70 Suppl 3 (2009): 30-31, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=19570499&site=ehost-live>.

⁴ Linda Simoni-Wastila, Ilene H. Zuckerman, Thomas Shaffer, Christopher M. Blanchette, and Bruce Stuart, "Drug use Patterns in Severely Mentally Ill Medicare Beneficiaries: Impact of Discontinuities in Drug Coverage," *Health Services Research* 43, no. 2 (2008): 504, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=31424857&site=ehost-live>.

What is SMI?

Severe mental illness, or *SMI*, represents a select group of diagnoses in the mentally ill population. These SMIs have similarities in their presentation and are oftentimes treated with the same types of psychotropic drugs. Researchers consistently use the label SMI to refer to mental illnesses characterized by psychosis or related episodes; episodes of psychosis are indicative of a break from reality, often in the form of hallucinations or delusions. The two diagnoses that most commonly encompass SMI are schizophrenia and bipolar disorder.⁵

Higher Morbidity through Physical Illness

Morbidity refers to the presence of disease. Multiple clinical studies across various countries have established that those with SMI suffer significantly greater morbidity than the general population.⁶ While some may assume that the leading cause of death for SMI patients is from the mental illness itself, physical impairments are at the forefront, leading to acute cardiovascular events such as heart attack and stroke.⁷ In fact, for the mentally ill population as a whole, cardiovascular disease is the leading cause of death across the United States.⁸

Higher Mortality Due to Drug Use

A mortality rate refers to the rate of death among a population. Countless studies and reviews illustrate that SMI sufferers exhibit a notably higher mortality rate as compared to the general population; one 2009 study found that SMI patients in public hospitals and mental centers lose about 25 to 30 years of potential life,⁹ while another review estimated that they die, on average, 15 to 20 years earlier than those without SMI.¹⁰

Additionally, sudden cardiac death rate doubles among users of first-generation antipsychotics, such as haloperidol, and users of second-generation antipsychotics, like quetiapine.¹¹ Virtually all patients that present with SMI take oral antipsychotics, especially the more modern second-generation antipsychotics, either continuously or at some point in life due to their efficacy and tolerability.¹² Multiple studies have established this conspicuously increased risk of cardiovascular death, and the gap is ever widening.¹³ In fact, approximately 60% of the premature mortality among SMI patients is due to physical illness alone, particular causes being coronary heart disease, atherosclerosis, hypertension, and stroke, which are all metabolically related.¹⁴ Not including suicide, other leading causes of death include respiratory diseases, diabetes, and cancer.¹⁵

What are antipsychotics?

Antipsychotics are typically psychiatrists' first choice for treating mental illnesses that deal with psychosis or related episodes, particularly schizophrenia and bipolar

⁵ Kahl, Westhoff-Bleck, and Krüger, "Effects of Psychopharmacological Treatment with Antidepressants on the Vascular System," 11.

⁶ Ward and Schwartz, "Challenges in Pharmacologic Management of the Hospitalized Patient with Psychiatric Comorbidity," 527.

⁷ Ibid.

⁸ Newcomer, "Comparing the Safety and Efficacy of Atypical Antipsychotics in Psychiatric Patients with Comorbid Medical Illnesses," 30.

⁹ Ibid.

¹⁰ Kahl, Westhoff-Bleck, and Krüger, "Effects of Psychopharmacological Treatment with Antidepressants on the Vascular System," 11.

¹¹ Ward and Schwartz, "Challenges in Pharmacologic Management of the Hospitalized Patient with Psychiatric Comorbidity," 527.

¹² Newcomer, "Comparing the Safety and Efficacy of Atypical Antipsychotics in Psychiatric Patients with Comorbid Medical Illnesses," 32-33.

¹³ Ward and Schwartz, "Challenges in Pharmacologic Management of the Hospitalized Patient with Psychiatric Comorbidity," 527.

¹⁴ Kahl, Westhoff-Bleck, and Krüger, "Effects of Psychopharmacological Treatment with Antidepressants on the Vascular System," 11.

¹⁵ Kahl, Westhoff-Bleck, and Krüger, "Effects of Psychopharmacological Treatment with Antidepressants on the Vascular System," 11.

disorder.¹⁶ Essentially, antipsychotics work to terminate and prevent psychosis and related episodes, such as bipolar mania.¹⁷ The beginning of first-generation antipsychotics, otherwise known as typical antipsychotics, dates back to the 1950s. The more commonly used second-generation antipsychotics, also called atypical antipsychotics, achieved FDA approval in the 1990s.¹⁸ Due to the ability of antipsychotics to subdue episodes of mental illness to a homeostatic level, they are an essential part of the psychiatrist's toolkit, and an essential part of the therapeutic regimen for SMI. And, like all drugs on the market, antipsychotics have the potential to cause adverse side effects. What differentiates antipsychotics from other drugs, however, is the great capacity of cardiovascular risk that comes along with them. In a 2012 review of studies targeting adverse side effects, second-generation antipsychotics were found to frequently cause weight gain, insulin resistance, dyslipidemia (high cholesterol), type II diabetes, and hypertension. What's more is that they did so much more significantly than first-generation antipsychotics.¹⁹ As Newcomer points out in a 2009 paper on safety and efficacy of atypical antipsychotics, "Individual antipsychotic medications are associated with different levels of risk for adverse effects on body weight and body fat [...] In general, as adiposity increases, so does risk for dyslipidemia, hypertension, and hyperglycemia, conditions that all contribute to the risk of [cardiovascular disease]."²⁰ In other words, although antipsychotics in the general sense are more than likely to cause an increase in body fat, which subsequently leads to serious cardiovascular risk factors, certain individual antipsychotics pose a much greater risk than others. Ziprasidone, fluphenazine, and haloperidol are three examples of antipsychotics associated with relatively low risk of weight gain.²¹ Conversely, researchers attribute significant weight increases to the more commonly used second-generation antipsychotics clozapine and olanzapine. Unfortunately, these two are also the ones that seem to offer the greatest therapeutic effect. Clozapine, though linked with the most weight gain as compared to other antipsychotics, has been termed the 'gold standard treatment' for patients with treatment-resistant schizophrenia, as its antipsychotic effects are statistically paramount to the effects of other antipsychotics on treatment resistant types.²²

It seems as if the key problem in the modern psychiatric school of thought lies in the guideline of Western medicine: identify the source of illness and treat it with drugs. This is exactly the function that antipsychotics play in those with SMI – they subdue acute psychotic or manic episodes and can also prevent them. It is the logical framework of psychiatric therapy, and exactly why psychiatrists prefer to prescribe clozapine and the like. However, with such a therapeutic framework, comorbidities arise. Instead of holistically approaching therapeutics by taking a patient's physical risk factors into account, the standard American psychiatrist targets isolated mental disorders and treats them respectively. Unfortunately, this does not mimic the interrelated systems of the body, which affect one another.²³

¹⁶ Siegfried Kasper, "The Metabolic Syndrome and Antipsychotic Treatment," *Annals of General Psychiatry* 7, (2008): 1, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=35703860&site=ehost-live>.

¹⁷ Newcomer, "Comparing the Safety and Efficacy of Atypical Antipsychotics in Psychiatric Patients with Comorbid Medical Illnesses," 32.

¹⁸ "A History of Atypical Antipsychotics," *USA Today* (May 2, 2006): 5a, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=J0E075503181706&site=ehost-live>.

¹⁹ Pavo Filaković, Anamarija Petek Erić, and Ljiljana Radanović-Grgurić, "Metabolic Syndrome and Psychotropic Medications," *Medicinski Glasnik* 9, no. 2 (2012): 181, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=79820876&site=ehost-live>.

²⁰ Newcomer, "Comparing the Safety and Efficacy of Atypical Antipsychotics in Psychiatric Patients with Comorbid Medical Illnesses," 32.

²¹ *Ibid.*, 33.

²² *Ibid.*

²³ Shiv Gautam, "Fourth Revolution in Psychiatry - Addressing Comorbidity with Chronic Physical Disorders," *Indian Journal of Psychiatry* 52, no. 3 (Jul, 2010): 213, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=54556866&site=ehost-live>.

Case Study: Obesity and Antipsychotic Use

In a 2012 study of body mass index and obesity of SMI patients, being overweight or obese was statistically very common in the sample. Additionally, "prescription of antipsychotics was associated with obesity and the total percentage dose of antipsychotic correlated with BMI."²⁴ Essentially, this finding supports the notion that, assuming those prescribed with antipsychotics are indeed taking them, not only are the drugs themselves correlated with BMI, but the correlation is *dose dependent*. In this particular case, the higher the dose of antipsychotics, the higher the patient's BMI.

But what about causation? Was it the antipsychotic medications themselves that *caused* the greater BMI of the sample, or were there more factors at play that directly affected BMI? For this study and many others, the answer remains unclear. What the results seem to show, however, is the presence of factors, other than psychotropic medications, at play. The 2012 study mentioned, "antipsychotic medication, poor diet, and a lack of motivation to exercise," were important contributory factors to the high prevalence of overweight and obese subjects.²⁵ Moreover, the mental health community saw mortality from all causes in schizophrenic patients double between the 1970s and the 1990s, key decades for antipsychotic introduction.²⁶

What is metabolic syndrome?

Metabolic syndrome is a clustered diagnosis that encompasses obesity, hypertension, impaired glucose-tolerance, and dyslipidemia. Due to its constituents, metabolic syndrome is a risk factor for type II diabetes, cardiovascular disease, and cardiovascular related death. The incidence for metabolic syndrome increases with increase in adiposity, meaning that overweight or obese patients are especially at risk.²⁷

How do antipsychotics cause metabolic syndrome?

Psychotropic drugs as a whole may influence weight gain, "through increased food consumption and disruption of satiety signaling system."²⁸ Many times, weight gain is directly caused by second-generation antipsychotics. They can cause fat distribution to concentrate around the abdomen, which, in turn, is a direct cause for insulin resistance, the hallmark of type II diabetes. Since type II diabetes is a well-established risk factor for cardiovascular disease and cardiovascular related death, what is illustrated with antipsychotic drug use is a train of cause and effect with a sour final destination. In fact, the correlations between antipsychotics, metabolic disease, and diabetes are so distinct that the FDA (Federal Food and Drug Administration) asked the producers of second-generation antipsychotics to include a warning on the label of their products. This warning specifies the need for blood sugar tests before treatment and in regular intervals throughout. The American Diabetes Association has similarly published a consensus outlining the higher risks for obesity, type II diabetes, and dyslipidemia associated with some antipsychotics. The Association found the antipsychotics with the highest risk to be clozapine and olanzapine, while those with the

²⁴ C. Haw and S. Bailey, "Body Mass Index and Obesity in Adolescents in a Psychiatric Medium Secure Service," *Journal of Human Nutrition and Dietetics: The Official Journal of the British Dietetic Association* 25, no. 2 (2012): 167, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=21585567&site=ehost-live>.

²⁵ *Ibid.*

²⁶ *Ibid.*

²⁷ Kasper, "The Metabolic Syndrome and Antipsychotic Treatment," 1.

²⁸ Filaković, Erić, and Radanović-Grgurić, "Metabolic Syndrome and Psychotropic Medications," 180.

lowest risk are ziprasidone and aripiprazole.²⁹ In one study of 95 severely mentally ill patients, 100% of patients on a clozapine regimen were overweight or obese, and approximately 90% of the patients on an olanzapine regimen had a raised BMI. The study concluded that clozapine and olanzapine both have the inclination to cause meaningful weight gain in a dose-dependent manner.³⁰ As aforementioned, clozapine is coincidentally the antipsychotic considered to be the 'gold standard' treatment for hard-to-treat types,³¹ and since this is often the case for those with SMI, the prescription of clozapine may be a critical factor in the mortality rate of the SMI population. A particular marker from another study shows that the weight gain resultant from antipsychotic use increases exponentially from the start of treatment and does not reach plateau until several weeks or months from the onset, supporting the causation argument.³² Furthermore, according to Haw and Bailey, the extra weight gained is not prone to come off: "at least 70% of obese adolescents will remain obese as adults,"³³ and the mere presence of obesity in adolescence can cause serious physical comorbidities like diabetes, cardiovascular disease, and cancer. This sequence forges the direct link between adolescent obesity and increased mortality in adulthood.³⁴

Antipsychotics can directly cause weight gain by interfering with signals in the brain that tell the body the stomach is full, more than likely leading to overeating. Additionally, antipsychotics can directly reduce the intensity of physical activity by the same mechanism.³⁵ One such hormone that plays a role in appetite is leptin. Treatment with antipsychotics of high metabolic risk, such as clozapine and olanzapine, can cause a drug-induced resistance to leptin, which indicates satiation to the brain. This phenomenon explains the event that circulating leptin levels double at the onset of treatment with both clozapine and olanzapine, suggesting that the body is not using the leptin in the bloodstream to signal the brain – a drug-induced leptin resistance. Some researchers hypothesize that since leptin and insulin are "mutually coupled in this system,"³⁶ it is possible that the antipsychotics themselves affect insulin in the same way, making insulin resistance potentially independent of weight gain for some patients.³⁷ Other scientific reviews claim that this hypothesis is indeed accepted fact, as insulin dysfunction in those taking clozapine and olanzapine has occurred in patients of a healthy weight, healthy clinical trial volunteers, and animal models.³⁸

How do antipsychotics increase the risk of diabetes?

Two risk factors for diabetes, dyslipidemia and increased insulin resistance, have the potential to be direct effects of some psychotropic drugs; antipsychotics can cause insulin resistance even without weight gain as the causal factor.³⁹

The role of insulin is the distinctive feature in type II diabetes. The body secretes insulin to regulate blood sugar level, which is usually raised during digestion. An absence of insulin allows blood sugar levels to spike, while insulin secretion lowers blood sugar levels by storing the sugar in the liver or as body fat. The hormone can also

²⁹ Ibid., 180-184.

³⁰ Haw and Bailey, "Body Mass Index and Obesity in Adolescents in a Psychiatric Medium Secure Service," 169-170.

³¹ Newcomer, "Comparing the Safety and Efficacy of Atypical Antipsychotics in Psychiatric Patients with Comorbid Medical Illnesses," 33.

³² Filaković, Erić, and Radanović-Grgurić, "Metabolic Syndrome and Psychotropic Medications," 181.

³³ Haw and Bailey, "Body Mass Index and Obesity in Adolescents in a Psychiatric Medium Secure Service," 169-170.

³⁴ Ibid., 169.

³⁵ Filaković, Erić, and Radanović-Grgurić, "Metabolic Syndrome and Psychotropic Medications," 184.

³⁶ Ibid.

³⁷ Ibid.

³⁸ Katrina Weston-Green, Xu-Feng Huang, and Chao Deng, "Second Generation Antipsychotic-Induced Type 2 Diabetes: A Role for the Muscarinic M3 Receptor," *CNS Drugs* 27, no. 12 (2013): 1071.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=24114586&site=ehost-live>.

³⁹ Filaković, Erić, and Radanović-Grgurić, "Metabolic Syndrome and Psychotropic Medications," 180-184.

reduce food intake by interacting with insulin receptors in various parts of the brain, reducing the urge to eat.⁴⁰

Because drugs like clozapine and olanzapine can increase the peripheral resistance to insulin, these and antipsychotics like these can directly cause diabetes.⁴¹ Peripheral resistance to insulin refers to the decreased ability or complete inability of peripheral tissues, meaning muscle and fat, to absorb sugar from the blood.⁴²

One specific hormone receptor that some antipsychotics react with, termed 'M3R,' has been identified as, "a predictor of antipsychotic diabetogenic liability."⁴³ M3R also has a relationship with weight gain. Accumulated results from several studies show that acetylcholine muscarinic receptors – M3R, for example – play important roles in the pathology of SMI and antipsychotic drug efficacy. The affinity of metabolically high risk second-generation antipsychotics (e.g., clozapine and olanzapine) to bind to M3R receptor sites is high, while second-generation antipsychotics that exhibit low M3R binding affinity (e.g., risperidone, ziprasidone, aripiprazole) have much lower adverse metabolic effects. This trend reflects the high M3R binding affinity of a first-generation antipsychotic called chlorpromazine, a foreshadowing of the drug's 'diabetogenic effect.'⁴⁴

Stop the flow of antipsychotics?

From a clinical standpoint, it is fair to say that SMI sufferers need their medications, especially following prior psychotropic drug treatment. Sudden cessation of psychotropic drugs can lead to mild or even life-threatening nervous system complications and/or psychiatric decompensation.⁴⁵ For example, in a study of pregnant women who abruptly stopped their psychotropic drug therapy, as is the standard protocol during pregnancy, nearly one third of the sample population experienced suicidal ideation, one of the primary factors that psychotropic drugs aim to prevent.⁴⁶ Movement disorders resembling parkinsonism, distinguished by tremors, and dyskinesias, which impair voluntary movement, may even occur upon cessation.⁴⁷ With these risks in mind, vacating antipsychotic treatment completely is not the solution to the mortality gap from a clinical standpoint.

Cost implications of SMI treatment

Due to the complexity and largely unknown pathology of SMIs like schizophrenia and bipolar disorder, treatment costs among the population are burdensome to the U.S. healthcare system. From a policy perspective, this poses an economic problem that suggests reform, especially since mental health care in general accounts for about 10% of U.S. Medicaid costs; as of 2013, schizophrenia alone cost Medicaid and other state agencies \$21.4 billion.⁴⁸ Physical comorbidities among SMI sufferers are also correlated with a substantial increase in economic burden for states. Schizophrenia patients alone constitute about 10% of the permanently disabled and are therefore

⁴⁰ Weston-Green, Huang, and Deng, "Second Generation Antipsychotic-Induced Type 2 Diabetes: A Role for the Muscarinic M3 Receptor," 1071.

⁴¹ Filaković, Erić, and Radanović-Grgurić, "Metabolic Syndrome and Psychotropic Medications," 184.

⁴² Ibid.

⁴³ Weston-Green, Huang, and Deng, "Second Generation Antipsychotic-Induced Type 2 Diabetes: A Role for the Muscarinic M3 Receptor," 1072.

⁴⁴ Ibid.

⁴⁵ Ward, Martha and Ann Schwartz, "Challenges in Pharmacologic Management of the Hospitalized Patient with Psychiatric Comorbidity," *Journal of Hospital Medicine* 8, no. 9 (2013): 528.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=90096361&site=ehost-live>.

⁴⁶ Ibid., 524

⁴⁷ Ward and Schwartz, "Challenges in Pharmacologic Management of the Hospitalized Patient with Psychiatric Comorbidity," 525.

⁴⁸ Zachary S. Predmore, Soeren Mattke, and Marcela Horvitz-Lennon, "Improving Antipsychotic Adherence among Patients with Schizophrenia: Savings for States," *Psychiatric Services (Washington, D.C.)* 66, no. 4 (2015): 343.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=25555222&site=ehost-live>.

dependent on sources of public assistance.⁴⁹ Not only does physical comorbidity compound the treatment costs of SMI patients through adverse cardiovascular events that often lead to costly hospitalizations or tertiary care – it also increases the likelihood that these individuals will be absent in the labor force and unable to help provide for family members such as their children.⁵⁰ Withdrawal from these areas of economic contribution often leads to an even greater cost for the state to financially provide for SMI sufferers and their families.

In order to troubleshoot for healthcare cost issues, it is necessary to review cost analyses and specify expensive components of care for this population. Having SMI, and being actively treated for it, has been found to increase the risk of obesity, cardiovascular disease, and diabetes. Another factor that compounds the cost problem is the finding that while the addressed physical comorbidities are more prevalent in the SMI population, patients are less likely to report them and clinicians are less likely to treat them, posing a primary care discrepancy.⁵¹ In particular, screening rates for obesity and weight-related metabolic disorders is low.⁵² When cardiometabolic conditions such as hypertension are left untreated, adverse events that require costly hospitalizations are more likely to occur. In another cohort study of 67,862 bipolar sufferers in a managed care population, patients taking second-generation antipsychotics alone had an estimated 24% higher cost than the general population, while those taking both mood stabilizers and second-generation antipsychotics, which is the most prominent case for bipolar sufferers, posed an estimated 52% higher healthcare cost. For bipolar sufferers, the key cost components included inpatient care (31%), outpatient visits (16%), prescription drugs (24%), and physician encounters (16%). However, though prescription drug costs and doctor visits were among the most expensive cost components, merely 33% of total treatment costs were specific to bipolar disorder. Instead, the remaining 67% of the costly healthcare provided to bipolar sufferers was allocated for the treatment of comorbidities. To boot, each comorbidity identified individually had a noteworthy impact on cost: there was not an outlier skewing the data.⁵³ Similarly, cost components for the treatment of schizophrenia comprise much more than the direct costs of inpatient psychiatric care and related pharmacotherapy. Although patients diagnosed with schizophrenia make up only 1% of the population, costs to treat them accumulate to 2.5% of the U.S. health care expenditure.⁵⁴ The annual treatment cost of schizophrenia is similar to the cost of treating coronary artery disease across the whole population.⁵⁵ Based on these results and results of various studies on the cost breakdown of healthcare for those with SMI, efforts to control cost must logically target the comorbidities that arise in concurrence with SMI as well as the use of other avenues that can limit hospitalizations.

Implementing Collaborative Care to Manage Costs

⁴⁹ M. Seshamani, "Is Clozapine Cost-Effective? : Unanswered Issues," *European Journal of Health Economics* 3, (2002): 104, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=15205453&site=ehost-live>.

⁵⁰ A-La Park, David McDaid, Prisca Weiser, Carolin Von Gottberg, Thomas Becker, and Reinhold Kilian, "Examining the Cost Effectiveness of Interventions to Promote the Physical Health of People with Mental Health Problems: A Systematic Review," *BMC Public Health* 13, no. 1 (2013): 2, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=90248116&site=ehost-live>.

⁵¹ *Ibid.*, 1.

⁵² *Ibid.*

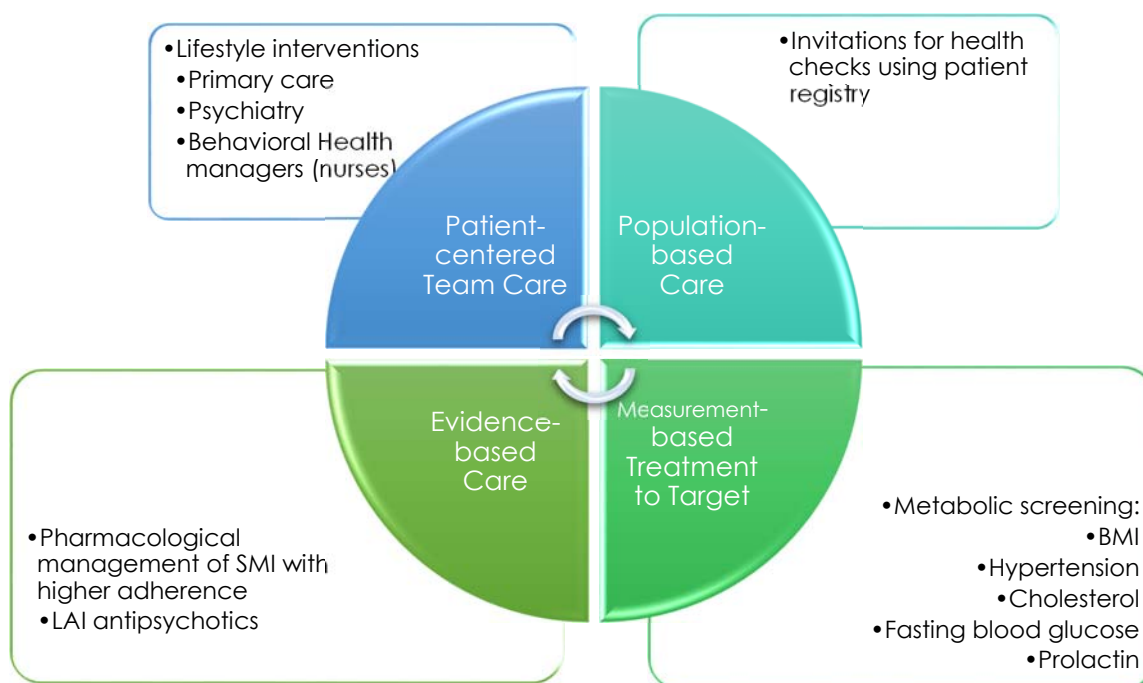
⁵³ Jeff J. Guo, Jr Keck Paul E., Hong Li, Raymond Jang, and Christina M. L. Kelton, "Treatment Costs and Health Care Utilization for Patients with Bipolar Disorder in a Large Managed Care Population," *Value in Health* 11, no. 3 (May, 2008): 419-421, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=32073797&site=ehost-live>.

⁵⁴ Seshamani, "Is Clozapine Cost-Effective? : Unanswered Issues," 104-106.

⁵⁵ *Ibid.*

The increased cardiovascular risk factors and related adverse events among SMI patients relative to the general population is acknowledged by health care providers and researchers. Additionally, policy makers have identified the costly public consequence. Both primary care physicians and psychiatrists face obstacles in the treatment of the SMI population. While general practitioners lack a deep knowledge about the psychiatric features and treatment options for SMI sufferers, psychiatrists lack insight and expertise in managing physical comorbidities that are commonly linked with SMI treatment.⁵⁶ To combat the problem, policy makers and researchers worldwide have teamed up in hopes of finding a resolution. In an important Cochrane review, the Collaborative Care model demonstrated clinical efficacy as well as cost-effectiveness in over 80 randomized controlled trials.⁵⁷

Collaborative Care is an evidence-based model of care that integrates the mental and behavioral health aspects of psychiatry with the primary care setting. In the Collaborative Care health care model, clinicians with concentrations in mental, behavioral, and primary care are team members and take a team-based approach to treating the SMI patient. To implement the collaborative care model, the care team must adhere to four principles: patient-centered team care, population-based care, measurement-based treatment to target, and evidence-based care.⁵⁸



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⁵⁶ Anne Looijmans, Frederike Jörg, Richard Bruggeman, Robert Schoevers, and Eva Corpeleijn, "Design of the Lifestyle Interventions for Severe Mentally Ill Outpatients in the Netherlands (LION) Trial: a Cluster Randomised Controlled Study of a Multidimensional Web Tool Intervention to Improve Cardiometabolic Health in Patients with Severe Mental Illness," *BMC Psychiatry* 17, (2017): 2. <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=afh&AN=122365452&site=ehost-live>.

⁵⁷ Christina Mangurian, Grace C. Niu, Dean Schillinger, John W. Newcomer, James Dilley, and Margaret A. Handley, "Utilization of the Behavior Change Wheel Framework to Develop a Model to Improve Cardiometabolic Screening for People with Severe Mental Illness," *Implementation Science: IS* 12, no. 1 (2017): 2. <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=29137666&site=ehost-live>.

⁵⁸ *Ibid.*

⁵⁹ *Ibid.*, 5.

Patient-Centered Team Care

Lifestyle interventions

Lifestyle interventions in the SMI population are critical, as these patients are less likely to access primary care than the general population.⁶⁰ Particular lifestyle behaviors that are negatively affected by incidence of SMI are lower levels of autonomous motivation towards physical activity, unhealthy diet, non-adherence to medication regimens, poor hygiene, and inadequate maintenance of physical health conditions.⁶¹ Given the troublesome high level of metabolic disease and associated risk for premature death in those with SMI, implementation of lifestyle interventions to tackle the diet, exercise, hygiene, and maintenance of physical disease are of utmost importance.⁶²

In a UK study in which researchers interviewed SMI patients as part of a lifestyle intervention program, there seemed to be a preliminary belief among patients that they were healthy and did not need to immediately confront the risk factors that they possessed. For instance, one interviewee stated that since their doctor performs a yearly blood test review, he or she did not need additional attention paid to risk factors.⁶³ When asked if smoking cessation may prevent further stroke, another patient stated, "No – I don't really think it does – no."⁶⁴ Similarly, another interviewee failed to understand the link between dietary salt intake and high blood pressure. These examples demonstrate the lack of general health knowledge and lack of urgency to change that clinicians need to address among the population via lifestyle interventions. Additionally, participation in a lifestyle intervention is maximized when the initial approach is made by each patient's caseworker. Another UK editorial poses that when patients are admitted to the hospital, mental health services should use the time frame as a window to recommend and explain participation in a lifestyle intervention.⁶⁵

In a Dutch study of SMI patients, lifestyle interventions were shown to be effective for both weight loss and reduction in cardiometabolic risk factors like high blood sugar and cholesterol levels.⁶⁶ In the Dutch model, the three key components of lifestyle interventions include exercise, diet, and behavior. Appointments per patient should be made on a weekly or nightly basis for up to six months with a nurse in a primary care or community health setting.⁶⁷ Psychiatric nurses and therapists use behavioral therapy strategies to improve self-management skills such as goal setting and creation of action

⁶⁰ Robert Pearsall, Susan Hughes, John Geddes, and Anthony Pelosi, "Understanding the Problems Developing a Healthy Living Programme in Patients with Serious Mental Illness: A Qualitative Study," *BMC Psychiatry* 14, no. 1 (2014): 3, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=94426984&site=ehost-live>.

⁶¹ Looijmans, Anne, Frederike Jörg, Richard Bruggeman, Robert Schoevers, and Eva Corpeleijn, "Design of the Lifestyle Interventions for Severe Mentally Ill Outpatients in the Netherlands (LION) Trial; a Cluster Randomised Controlled Study of a Multidimensional Web Tool Intervention to Improve Cardiometabolic Health in Patients with Severe Mental Illness," *BMC Psychiatry* 17, (2017): 2, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=afh&AN=122365452&site=ehost-live>.

⁶² *Ibid.*, 10.

⁶³ Pearsall, Robert, Susan Hughes, John Geddes, and Anthony Pelosi, "Understanding the Problems Developing a Healthy Living Programme in Patients with Serious Mental Illness: A Qualitative Study," *BMC Psychiatry* 14, no. 1 (2014): 6, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=94426984&site=ehost-live>.

⁶⁴ *Ibid.*, 8.

⁶⁵ *Ibid.*, 8-13.

⁶⁶ Looijmans, Jörg, Bruggeman, Schoevers, and Corpeleijn, "Design of the Lifestyle Interventions for Severe Mentally Ill Outpatients in the Netherlands (LION) Trial; a Cluster Randomised Controlled Study of a Multidimensional Web Tool Intervention to Improve Cardiometabolic Health in Patients with Severe Mental Illness," 2.

⁶⁷ David Osborn, Alexandra Burton, Rachael Hunter, Louise Marston, Lou Atkins, Thomas Barnes, Ruth Blackburn, et al, "Clinical and Cost-Effectiveness of an Intervention for Reducing Cholesterol and Cardiovascular Risk for People with Severe Mental Illness in English Primary Care: A Cluster Randomised Controlled Trial," *The Lancet Psychiatry* (2018): 147, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=29396118&site=ehost-live>.

plans.⁶⁸ Other behavioral measures should include physical activity and diet questionnaires, which the nurse or behavioral health manager should review.⁶⁹

The Dutch lifestyle intervention study used key steps to implement lifestyle interventions. The chart below describes the four most important steps in order.

Lifestyle Intervention Steps ⁷⁰	
1. Identify unhealthy behaviors	Behaviors highly related to health risks
2. Create a lifestyle plan	After discussion with the nurse, patient should set three attainable goals. The nurse's role is to guide realistic goal setting.
3. Evaluate lifestyle goals	Evaluate goals regularly. During every regular care visit, patient and nurse should fill in a new questionnaire to measure progress.
4. Indicate barriers and facilitators in achieving goals	Nurse should guide patient in discussing what factors foster goal achievement and what factors inhibit goal achievement.

While the nurse is present to offer guidance during the intervention, the patient should take leadership in creating a lifestyle plan and setting lifestyle goals. In this way, each individual patient will be able to tailor the lifestyle intervention to his or her specific recovery wishes.⁷¹

In a similar lifestyle intervention study conducted in the UK, the primary outcome was reduction in cholesterol levels, and the intervention was associated with fewer hospital admissions.⁷² Another study on lifestyle interventions across multiple countries determined that supervised walking was highly cost effective in a 16-week randomized trial of a tailored exercise program.⁷³

⁶⁸ Looijmans, Jörg, Bruggeman, Schoevers, and Corpeleijn, "Design of the Lifestyle Interventions for Severe Mentally Ill Outpatients in the Netherlands (LION) Trial; a Cluster Randomised Controlled Study of a Multidimensional Web Tool Intervention to Improve Cardiometabolic Health in Patients with Severe Mental Illness," 2.

⁶⁹ Osborn, Burton, Hunter, Marston, Atkins, Barnes, Blackburn, et al, "Clinical and Cost-Effectiveness of an Intervention for Reducing Cholesterol and Cardiovascular Risk for People with Severe Mental Illness in English Primary Care: A Cluster Randomised Controlled Trial," 147.

⁷⁰ Looijmans, Jörg, Bruggeman, Schoevers, and Corpeleijn, "Design of the Lifestyle Interventions for Severe Mentally Ill Outpatients in the Netherlands (LION) Trial; a Cluster Randomised Controlled Study of a Multidimensional Web Tool Intervention to Improve Cardiometabolic Health in Patients with Severe Mental Illness," 8, table 3.

⁷¹ Ibid., 10.

⁷² Osborn, Burton, Hunter, Marston, Atkins, Barnes, Blackburn, et al, "Clinical and Cost-Effectiveness of an Intervention for Reducing Cholesterol and Cardiovascular Risk for People with Severe Mental Illness in English Primary Care: A Cluster Randomised Controlled Trial," 147-150.

⁷³ Park, McDaid, Weiser, Gottberg, Becker, and Kilian, "Examining the Cost Effectiveness of Interventions to Promote the Physical Health of People with Mental Health Problems: A Systematic Review," 4-8.

What community health/psychiatry needs to change	Implement lifestyle interventions
Who should perform the behavior	Nurses or other behavioral health managers
When to perform the behavior	When seeing patients that take antipsychotic drugs
Where to perform the behavior	At community mental health clinics or primary care offices
How often to perform the behavior	Annually per patient
For whom should they perform the behavior	All patients taking antipsychotic drugs

Population-based Care

Invitations for Health checks

It is commonly understood by the general population that physical health checks should occur at least once a year.⁷⁴ A contributing factor to why SMI sufferers have higher levels of cardiovascular death may be due to the fact that they tend to volunteer symptoms less readily. For this reason, physical comorbidity in the early stages may go unidentified and unmaintained through the course of the morbidity.⁷⁵ Evidence shows that invitations to pre-scheduled health checkups are an intervention method that is both time conducive and cost effective, and positively affects the rate at which SMI patients access primary care.⁷⁶

In an instrumental UK study evaluating SMI patient response to an invitation letter, 70% of the SMI patients invited to a primary care-oriented health checkup attended. One important discrepancy of the study revealed that letters containing an open invitation produced a much lower attendance rate (37%) than the 70% attendance rate produced by invitation letters that indicated a specific date and time for the health check.⁷⁷ Another UK study found that 68.3% of those who received invitation letters attended a health check,⁷⁸ and yet another study provided that 63.3% of

⁷⁴ Misuzu Fujita, Yasunori Sato, Kengo Nagashima, Sho Takahashi, and Akira Hata, "Impact of Geographic Accessibility on Utilization of the Annual Health Check-Ups by Income Level in Japan: A Multilevel Analysis," *PLoS ONE* 12, no. 5 (2017): 1-14, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=122942297&site=ehost-live>.

⁷⁵ Richard Gray and Sheila Hardy, "Is the use of an Invitation Letter Effective in Prompting Patients with Severe Mental Illness to Attend a Primary Care Physical Health Check?," *Primary Health Care Research & Development (Cambridge University Press / UK)* 13, no. 4 (2012): 347-348, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=84125115&site=ehost-live>.

⁷⁶ *Ibid.*, 350-355.

⁷⁷ *Ibid.*, 348.

⁷⁸ Alice S. Forster, Caroline Burgess, Lisa McDermott, Alison J. Wright, Hiten Dodhia, Mark Conner, Jane Miller, Caroline Rudisill, Victoria Cornelius, and Martin C. Gulliford, "Enhanced Invitation Methods to Increase Uptake of NHS Health Checks: Study Protocol for a Randomized Controlled

patients invited to a health check responded.⁷⁹ Since age is not a factor that affects the respondent rate of health check invitation letters, SMI patients of all ages may benefit from this interventional method. Letters should not be sent to those in inpatient care, residential care, or prison, as these patients are rotationally seen by health care professionals.⁸⁰

When patients were sent an invitation letter ten days before the pre-scheduled appointment, 70% attended.⁸¹ A short time period between the disposition of the letter by the office of the physician and acquisition of the letter by the patient is conducive to patient attendance because of the cognitive problems that often accompany SMI or are a side effect of a psychotropic medication regimen. One common problem is poor memory, and consequently, poor planning. If the patient does not attend the health check, the office should send out an invitation for another appointment. When offices send a secondary appointment, an additional 4% of patients attend the health check, reflecting about one sixth of absentees.⁸²

The widespread use of electronic medical records (EMR) by clinicians allows doctors to easily separate patients with SMI from patients without. This ability makes the invitation process an easy, quick, and inexpensive intervention method.

Evidence from related sources suggests that specific changes to health-check invitation letters can critically impact behavioral responses from patients.⁸³ One UK study conducted in 2016 found that four critical changes to health-check invitation letters were particularly instrumental in improving patient attendance. The first was simplification; letters should be shortened to two, one-sentence paragraphs to reduce time and effort on behalf of the patient. The second change is the use of concrete statements and specified instructions. Thirdly, the heading of the letter should be emboldened and state that the intended patient is 'due to attend' a health check, rather than relaying that the patient is 'invited to attend' a health-check. The fourth change is the addition of a tear-off slip for the specified date and time of the appointment with an instruction for the patient to put the slip on their fridge or calendar as a reminder. These small, low cost changes to health check invitation letters were shown to improve patient attendance by 26% as compared to a standard health check invitation letter.⁸⁴

Trial," *Trials* 15, no. 1 (2014): 2.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=110265355&site=ehost-live>.

⁷⁹ Anna Sallis, Amanda Buntten, Annabelle Bonus, Andrew James, Tim Chadborn, and Daniel Berry, "The Effectiveness of an Enhanced Invitation Letter on Uptake of National Health Service Health Checks in Primary Care: A Pragmatic Quasi-Randomised Controlled Trial," *BMC Family Practice* 17, (2016): 2, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=27009045&site=ehost-live>.

⁸⁰ Gray and Hardy, "Is the use of an Invitation Letter Effective in Prompting Patients with Severe Mental Illness to Attend a Primary Care Physical Health Check?," 349-350.

⁸¹ *Ibid.*, 348.

⁸² *Ibid.*, 348-349.

⁸³ Sallis, Buntten, Bonus, James, Chadborn, and Berry, "The Effectiveness of an Enhanced Invitation Letter on Uptake of National Health Service Health Checks in Primary Care: A Pragmatic Quasi-Randomised Controlled Trial," 3.

⁸⁴ *Ibid.*, 3-7.

What primary care/community health needs to change	Send annual health check invitation letters, with specified day and time
Who should perform the behavior	Secretaries or office administration with help of EMR
When to perform the behavior	Ten days before the scheduled appointment
Where to perform the behavior	At administrative offices of community mental health clinics/primary care
How often to perform the behavior	Annually per patient (about 10-15 times per month given a typical community psychiatrist's caseload)
For whom should they perform the behavior	All patients taking antipsychotic drugs

Measurement-based Treatment to Target

Cardiometabolic screening

Since cardiovascular and metabolic health is a target area for cost containment, cardiometabolic screening should be one of the most important measurement-based interventions for SMI patients. Traditionally, physicians screen patients for cardiovascular and metabolic risk factors at the primary care level. However, SMI patients are far less likely to utilize primary care than the general population.⁸⁵ Instead, the care that SMI patients most commonly access originates from community mental health services like clinics.⁸⁶ BMI, blood pressure, glucose and cholesterol monitoring are additionally recommended.⁸⁷ In the UK, recommendations also include tests for liver function and prolactin levels even if symptoms are not present; prolactin testing is in line with UK bipolar disorder treatment guidelines, since certain antipsychotics are associated with elevated levels of the hormone, which can cause breast development in men.⁸⁸

Other areas that overlap with measurement-based treatment to target include previously mentioned lifestyle interventions, as they involve goal tracking and regimented follow up appointments, and annual health checks.

⁸⁵ Mangurian, Niu, Schillinger, Newcomer, Dilley, and Handley, "Utilization of the Behavior Change Wheel Framework to Develop a Model to Improve Cardiometabolic Screening for People with Severe Mental Illness," 2.

⁸⁶ Ibid.

⁸⁷ Gray and Hardy, "Is the use of an Invitation Letter Effective in Prompting Patients with Severe Mental Illness to Attend a Primary Care Physical Health Check?," 348.

⁸⁸ Ibid., 353.

What psychiatry needs to change	Regular assessment of metabolic screening rather than assuming this has been tackled by primary care
Who should perform the behavior	Psychiatrists or nurse practitioners
When to perform the behavior	When seeing patients that take antipsychotic drugs
Where to perform the behavior	At community mental health clinics
How often to perform the behavior	Annually per patient (about 10-15 times per month given a typical community psychiatrist's caseload)
For whom should they perform the behavior	All patients taking antipsychotic drugs

Evidence-based Care

Regarding the SMI population, policy makers are uncertain of which aspects of health care to target for cost-containment. Recent efforts by states such as Maine and New Hampshire have focused on cutting antipsychotic drug costs, a component of care with high economic burden. However, in an effort to resolve the dilemma, evidence-based conclusions from many cohort studies and meta-analysis reviews document that it is the lack of preventive care that leads to costly outcomes, as adverse medical events require in-patient hospitalizations. Therefore, in order to create a cost impact on SMI treatment, measures to make severe mental illnesses and their comorbidities manageable conditions should be the primary focus. Of schizophrenia treatment costs, about 67% is spent on in-patient care, while pharmacotherapies encompass only .6%.⁸⁹ Moreover, due to “financial constraints of government agencies, health insurance plans, and managed care companies, the investment of resources in high-cost residential care limits the amount of money that can be put into community care and pharmacotherapy.”⁹⁰ This finding paints the picture that states concentrate their health care dollars on the cheapest antipsychotics that demonstrate efficacy, with no attention paid to how well patients will adhere to said drugs or how the drugs may affect or exacerbate the physical condition of the SMI population.

Medicaid cost-containment parameters tailored to second-generation antipsychotics lead to antipsychotic nonadherence, illustrating a misallocation of state dollars.⁹¹ Because patients present with low adherence rates and high comorbidity

⁸⁹ Seshamani, "Is Clozapine Cost-Effective? : Unanswered Issues," 105.

⁹⁰ Ibid.

⁹¹ William B. Vogt, Geoffrey Joyce, Jing Xia, Riad Dirani, George Wan, and Dana P. Goldman, "Medicaid Cost Control Measures Aimed at Second-Generation Antipsychotics Led to Less use of all Antipsychotics," *Health Affairs (Project Hope)* 30, no. 12 (2011): 2346, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=22147863&site=ehost-live>.

rates when doctors prescribe the cheapest medications, the up-front cost-cutting measures in pharmacotherapy are actually hurting state economies.

Investing in better adherence for cost-containment

Non-adherence to antipsychotic therapy is the primary reason for relapse and increased institutionalization in SMI patients. Increase in medication adherence could yield more than \$3.28 billion in net savings.⁹² Although a medication adherence initiative projects an 18% increase in prescription drug costs, this increase will be far outweighed by the fruitful 68% savings from lower hospitalization rates; the rest of the savings will come from lower costs of outpatient care and lower rates of patient encounters with the criminal justice system.⁹³

Currently, efforts on the part of state governments and private health insurance plans focus on imposing prior authorization programs and other controls to stabilize drug spending. Prior authorization programs guide psychiatrists to prescribe lower-cost medications before medications that are more-costly to public payers. State governments have targeted second-generation antipsychotics in particular for prior authorization due to their high costs and usage rates among patients with Medicaid.⁹⁴

Between 1999 and 2005, annual spending per Medicaid enrollee on antipsychotics increased by 106%, net of inflation.⁹⁵ In concurrence, prior authorization requirements increased dramatically during the same time frame. What states often overlook is the effect that such utilization management measures have imposed on state-funded healthcare costs. The introduction of prior authorization in Maine, for example, led to antipsychotic nonadherence of 29%.⁹⁶ Studies in New Hampshire and Georgia found that implementation of prior authorization, among other restrictions, did reduce the use of targeted drugs, but effectively increased spending on outpatient and other health services. In one review, the state Medicaid programs that instituted prior authorization exhibited “no significant correlation between the imposition of prior authorization and initial levels of spending,”⁹⁷ as the use of second-generation antipsychotics per Medicaid enrollee still rose by 14% between 1999-2008 in these prior authorization states.⁹⁸

The obvious deterrent for public payers to increase drug spending is the up-front expense of investment. Unwillingness to make this investment, however, leads to higher costs in the end: poor adherence is linked with poorer outcomes and higher treatment costs.⁹⁹ Therefore, the long-term cost-effectiveness of moving towards increased drug spending should offer states an incentive.

Better adherence using LAI antipsychotics

Because non-adherence is a problem, long-acting injectable (LAI) antipsychotics are a treatment option that incentivizes adherence and subsequently lowers healthcare expenditures. LAIs offer a treatment alternative for patients with

⁹² Predmore, Mattke, and Horvitz-Lennon, “Improving Antipsychotic Adherence among Patients with Schizophrenia: Savings for States,” 343-344.

⁹³ *Ibid.*

⁹⁴ Vogt, Joyce, Xia, Dirani, Wan, and Goldman, “Medicaid Cost Control Measures Aimed at Second-Generation Antipsychotics Led to Less use of all Antipsychotics,” 2346-2347.

⁹⁵ *Ibid.*, 2350.

⁹⁶ *Ibid.*, 2350-2351.

⁹⁷ *Ibid.*, 2351.

⁹⁸ *Ibid.*, 2347-2351.

⁹⁹ Predmore, Mattke, and Horvitz-Lennon, “Improving Antipsychotic Adherence among Patients with Schizophrenia: Savings for States,” 343.

chronic non-adherence especially.¹⁰⁰ LAI antipsychotics do come in generic versions, and use of generic LAIs in place of oral antipsychotics could lead to a yearly savings of \$1000 per patient in Medicaid programs according to a 2013 study.¹⁰¹ One large cohort study exhibited that patients who used LAI antipsychotics for more than six consecutive months experienced less relapses, and consequently less hospitalizations than patients who used LAIs for a short duration. In addition, patients who only used LAIs for a short duration had higher rates of comorbidity, logically contributing to more frequent hospitalizations and their resulting costs.¹⁰²

LAI therapy generally requires patients to receive an injection every two to six weeks, completely eliminating the need for oral antipsychotics, which require use one or more times *per day*.¹⁰³ Psychiatrists have the option to administer certain LAI antipsychotics only once every three months.¹⁰⁴ Reducing patients' maintenance responsibility through such injections may offer reprieve from relapse and hospitalizations for sufferers of SMI. For instance, studies report that when bipolar disorder remains untreated due to non-adherence, the relapse rate exceeds 90% for manic episodes and 70% for depressive episodes. Not only have LAIs been shown to reduce risk of antipsychotic cessation in cohort studies, but they also can ensure a more stable blood level of the antipsychotic than an oral version.¹⁰⁵ According to researchers, psychiatrists should target LAI antipsychotic treatment at young, recently diagnosed SMI patients, as they pose the highest risk of antipsychotic non-adherence that contributes to healthcare costs.¹⁰⁶

Though physicians introduced LAI antipsychotics into routine clinical practice decades ago, they are widely underutilized when compared to oral antipsychotics; in a 2007 study of LAI antipsychotic use, only 10% of Medicaid insured patients used them.¹⁰⁷ Some authors hypothesize that the unpopularity may be due to lack of awareness of LAIs as a treatment option or unwillingness to increase medication costs by public payers.¹⁰⁸ Negative patient attitudes towards LAIs are likely due to insufficient information given by physicians, suggesting that educating patients about LAI antipsychotics as a treatment option will increase positive patient attitudes.¹⁰⁹

In a survey of psychiatrists and SMI patients across Australia, Canada, and the United States, physicians reported preference for switching to LAIs from oral antipsychotics for the treatment of both adherent and non-adherent patients, even if efficacy would be reduced as much as 9% for the switch to once-monthly LAIs, and as much as 21% for the switch to LAIs lasting three months.¹¹⁰ As oral antipsychotic

¹⁰⁰ Thomas R. Einarson, Colin Vicente, Roman Zilbershtein, Charles Piwko, Christel Bø N., Hanna Pudas, Rasmus Jensen, and Michiel E. H. Hemels, "Pharmacoeconomics of Depot Antipsychotics for Treating Chronic Schizophrenia in Sweden," *Nordic Journal of Psychiatry* 68, no. 6 (2014): 417, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=24274837&site=ehost-live>.

¹⁰¹ Predmore, Mattke, and Horvitz-Lennon, "Improving Antipsychotic Adherence among Patients with Schizophrenia: Savings for States," 344.

¹⁰² Rimal Bera, Steve Offord, Donna Zubek, Gina Lau, Jay Lin, and Craig Karson, "Hospitalization Resource Utilization and Costs among Medicaid Insured Patients with Schizophrenia with Different Treatment Durations of Long-Acting Injectable Antipsychotic Therapy," *Journal of Clinical Psychopharmacology* 34, no. 1 (2014): 33, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=24135840&site=ehost-live>.

¹⁰³ *Ibid.*, 30.

¹⁰⁵ Gokay Alpak, Bahadır Demir, Ihsan Aksoy, Hilal Kaya, Ahmet Unal, Feridun Bulbul, and Haluk A. Savas, "Both Typical and Atypical Long-Acting Injectable Antipsychotics in Bipolar Disorder: A Retrospective Chart Review," *Journal of Mood Disorders* 4, no. 1 (2014): 21, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=95402041&site=ehost-live>.

¹⁰⁴ Dominic Pilon, Erik Muser, Patrick Lefebvre, Rhiannon Kamstra, Bruno Emond, and Kruti Joshi, "Adherence, Healthcare Resource Utilization and Medicaid Spending Associated with Once-Monthly Paliperidone Palmitate Versus Oral Atypical Antipsychotic Treatment among Adults Recently Diagnosed with Schizophrenia," *BMC Psychiatry* 17, (2017): 15, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=123430672&site=ehost-live>.

¹⁰⁷ Bera, Offord, Zubek, Lau, Lin, and Karson, "Hospitalization Resource Utilization and Costs among Medicaid Insured Patients with Schizophrenia with Different Treatment Durations of Long-Acting Injectable Antipsychotic Therapy," 30-34.

¹⁰⁸ Pilon, Muser, Lefebvre, Kamstra, Emond, and Joshi, "Adherence, Healthcare Resource Utilization and Medicaid Spending Associated with Once-Monthly Paliperidone Palmitate Versus Oral Atypical Antipsychotic Treatment among Adults Recently Diagnosed with Schizophrenia," 15.

¹⁰⁹ Alpak, Demir, Aksoy, Kaya, Unal, Bulbul, and Savas, "Both Typical and Atypical Long-Acting Injectable Antipsychotics in Bipolar Disorder: A Retrospective Chart Review," 24.

¹¹⁰ Eva G. Katz, Brett Hauber, Angie Fairchild, Siharri Gopal, Rachel B. Weinstein, Bennett S. Levitan, and Amy Pugh, "Physician and Patient Benefit-Risk

adherence decreased, physician preference for LAIs increased, and physicians would accept higher possible reductions in efficacy that could come along with the medication switch.¹¹¹ Physicians also reported a preference for LAIs that they need only administer once every three months for patients with a history of skipping between 20%-50% of doses. Patients reported preference for LAI antipsychotics for use in non-adherent patients.¹¹²

One particular LAI antipsychotic, 'paliperidone palmitate' (PP1M or PP-LAI) is a once-monthly second-generation LAI antipsychotic that is associated with greater patient adherence levels, lower polypharmacy, reduced frequency of home care services, and lower overall medical costs as compared to treatment with oral second-generation antipsychotics.¹¹³ Administration dates are flexible in an effort to avoid missed monthly doses; physicians may administer PP-LAI ± 7 days before or after the exact monthly mark.¹¹⁴ In a 2014 Swedish study comparing the cost-effectiveness of both first and second-generation antipsychotics, PP-LAI was shown to have the lowest per-patient cost for institutional care, suggesting that the greater adherence that LAIs impose on SMI patients directly causes less institutionalizations.¹¹⁵ In the same study, the cost driver for the SMI patients sampled was institutionalization, comprising 52.5%-80.7% of care, depending on the antipsychotic treatment regimen.¹¹⁶ Although the cost-effectiveness of the LAI 'risperidone' (RIS-LAI) is reasonably comparable to the cost effectiveness of PP-LAI, PP-LAI is paramount due to its longer duration of action, which allows administration to be much less frequent. With fewer administrations, missing a dose is less probable, which supports patient adherence.¹¹⁷ Switching from oral paliperidone palmitate to PP-LAI is easy as well – treatment with PP-LAI can safely begin 1 day after stopping oral PP. When switching from a different LAI antipsychotic, physicians may administer PP-LAI in place of the next scheduled injection.¹¹⁸

Discussion

Episodes of severe mental illness (SMI) are characterized by breaks from reality, among other symptoms that vary according to the diagnosis. Bipolar disorder and schizophrenia are the two most prevalent SMIs. Due to the severity of symptoms and adverse side effects from antipsychotic drug treatment, patients of this population often depend on the public health care system to pay for their medical care, which, per patient, far exceeds the healthcare expenditure as compared to that of the general population.

Antipsychotic drugs may either directly or indirectly cause metabolic disease and increase cardiovascular risk factors and cardiovascular related death. Because antipsychotic drugs are a necessary part of the treatment regimen for SMI patients,

Preferences from Two Randomized Long-Acting Injectable Antipsychotic Trials," *Patient Preference & Adherence* 10, (2016): 2131-2134, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=119302706&site=ehost-live>.

¹¹¹ Ibid.

¹¹² Ibid.

¹¹³ Pilon, Muser, Lefebvre, Kamstra, Emond, and Joshi, "Adherence, Healthcare Resource Utilization and Medicaid Spending Associated with Once-Monthly Paliperidone Palmitate Versus Oral Atypical Antipsychotic Treatment among Adults Recently Diagnosed with Schizophrenia," 14.

¹¹⁴ Mahesh N. Samtani, Srihari Gopal, Cristiana Gassmann-Mayer, Larry Alphs, and Joseph M. Palumbo, "Dosing and Switching Strategies for Paliperidone Palmitate Based on Population Pharmacokinetic Modelling and Clinical Trial Data," *CNS Drugs* 25, no. 10 (2011): 840, <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=69849338&site=ehost-live>.

¹¹⁵ Einarson, Vicente, Zilbershtein, Piwko, Bø, Pudas, Jensen, and Hemels, "Pharmacoeconomics of Depot Antipsychotics for Treating Chronic Schizophrenia in Sweden," 422.

¹¹⁶ Ibid.

¹¹⁷ Ibid., 423.

¹¹⁸ Samtani, Gopal, Gassmann-Mayer, Alphs, and Palumbo, "Dosing and Switching Strategies for Paliperidone Palmitate Based on Population Pharmacokinetic Modelling and Clinical Trial Data," 837.

psychiatrists – especially those working in community health centers – need to pay greater attention to the physical condition of the population in an attempt to reduce the high rate at which SMI sufferers experience cardiovascular morbidity. Conclusions from a variety of cohort studies and meta-analyses suggest that states implement a collaborative health care model in which psychiatrists, primary care physicians, and behavioral health managers (nurses) work together to holistically support the health of the SMI patient using lifestyle interventions, invitations for annual health checks, and cardiometabolic screening. These interventions will not only offer room for physical health improvement and better physical health maintenance, but will also save public payers money by reducing the encounters that SMI patients have with institutionalization, hospitalization, tertiary care, and the criminal justice system.

Because institutionalized care is the highest health cost area for the SMI population, an initial investment on the part of public payers to encourage psychiatrists' prescribing of long-acting injectable (LAI) antipsychotics will be instrumental in increasing medication adherence due to the associated low maintenance regimen as compared to oral antipsychotic therapy. Although injectable antipsychotics will not directly improve cardiometabolic health, they may offer stabilization of side effects such as weight gain, since side effects occur the most quantitatively at the onset of drug therapy. When patients are not consistent with oral antipsychotic therapy, there are more instances of drug onset, as therapy must be restarted. Higher medication adherence among SMI patients will lead to less institutionalizations and effectively reduce the healthcare expenditure for this population. Treatment with paliperidone palmitate (PP-LAI) in particular offers long-term cost savings for Medicaid programs and other state agencies.

SMI patients accrue a large portion of expense for public payers due to their mental illness, cardiometabolic comorbidities, and associated high hospitalization rates. However, primary care interventions and better drug therapies are available and states can implement them in a cost-effective manner. Doing so will not only better the physical health of those with severe mental illness, but will consequently relieve public health care programs of a substantial part of the population's heavy health care burden.

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<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=J0E075503181706&site=ehost-live>.

This short article from May of 2006 lists the second-generation antipsychotics that gained FDA approval in 2002 for adult schizophrenia and bipolar disorder treatment. It also outlines the advantages and risks of second-generation antipsychotics over their first-generation counterparts.

Alpak, Gokay, Bahadir Demir, Ihsan Aksoy, Hilal Kaya, Ahmet Unal, Feridun Bulbul, and Haluk A. Savas. "Both Typical and Atypical Long-Acting Injectable Antipsychotics in Bipolar Disorder: A Retrospective Chart Review." *Journal of Mood Disorders* 4, no. 1 (2014): 20-25.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=95402041&site=ehost-live>.

The authors of this Turkish study reviewed the medical charts of 802 patients diagnosed with bipolar disorder who contribute to research in the Mood Disorders Unit of Gaziantep university, located in Gaziantep, Turkey. The researchers compared the side effects between the 9.88% of the sample population using long-acting injectable antipsychotics (LAIs) and the 90.12% of the sample using oral antipsychotics. To the knowledge of the authors, this study is the first in which both first-generation and second-generation long-acting injectable antipsychotics are studied together. Results show that LAI antipsychotics do not indicate worsened side effects as compared to oral antipsychotic regimens. Recommendation for more studies of larger sample sizes is given.

Bera, Rimal, Steve Offord, Donna Zubek, Gina Lau, Jay Lin, and Craig Karson.

"Hospitalization Resource Utilization and Costs among Medicaid Insured Patients with Schizophrenia with Different Treatment Durations of Long-Acting Injectable Antipsychotic Therapy." *Journal of Clinical Psychopharmacology* 34, no. 1 (2014): 30-35.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=24135840&site=ehost-live>.

Using the Truven Health Analytics MarketScan Research Medicaid database, 5,694 Medicaid-insured schizophrenia patients were identified in this 2010 study evaluating the impact of long-acting injectable (LAI) antipsychotics on health care resource utilization. Both the effects of short-duration and long-duration use of LAI antipsychotics were analyzed as compared to the health care resource utilization of the remaining 2,856 patients using oral antipsychotics. Findings indicate that long-duration use of LAI antipsychotics is associated with a decreased number of hospitalizations, decreased length of hospital stay, and reduced hospital payment than short-duration use of LAI antipsychotics or use of oral antipsychotics.

Einarson, Thomas R., Colin Vicente, Roman Zilbershtein, Charles Piwko, Christel Bø N., Hanna Pudas, Rasmus Jensen, and Michiel E. H. Hemels. "Pharmacoeconomics of Depot Antipsychotics for Treating Chronic Schizophrenia in Sweden." *Nordic Journal of Psychiatry* 68, no. 6 (2014): 416-427.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=24274837&site=ehost-live>.

This year-long Swedish study examined cost-effectiveness of long-acting injectable (LAI) antipsychotics for treatment of chronic schizophrenia. Healthcare consumption costs were measured for patients on LAI versions of paliperidone, olanzapine, risperidone, and haloperidol, as well as oral olanzapine. Results show that treatment with paliperidone palmitate (PP-LAI) followed by olanzapine pamoate (OLZ-LAI) is cost-saving to the healthcare system due to less subsequent resource consumption, such as costly institutionalization.

Filaković, Pavo, Anamarija Petek Erić, and Ljiljana Radanović-Grgurić. "Metabolic Syndrome and Psychotropic Medications." *Medicinski Glasnik* 9, no. 2 (2012): 180-188.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=79820876&site=ehost-live>.

By retrospectively reviewing data found through electronic databases between 2002-2012, the authors of this Croatian study estimated the prevalence and pathology of metabolic syndrome in patients with mental illness as well as the effects of psychotropic drugs on risk factors for metabolic syndrome. Authors recommend lifestyle alterations in diet and exercise regimen for mentally ill patients with metabolic syndrome, or at risk for it, with indications for behavioral lifestyle modification programs and physician consideration of weight loss surgery for morbidly obese patients.

Forster, Alice S., Caroline Burgess, Lisa McDermott, Alison J. Wright, Hiten Dodhia, Mark Conner, Jane Miller, Caroline Rudisill, Victoria Cornelius, and Martin C. Gulliford. "Enhanced Invitation Methods to Increase Uptake of NHS Health Checks: Study Protocol for a Randomized Controlled Trial." *Trials* 15, no. 1 (2014): 342-348. <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=110265355&site=ehost-live>.

Conducted in the UK, this retrospective controlled trial tested the hypothesis that enhanced invitation methods will increase the uptake of NHS Health Checks as compared to standard invitation methods employed by providers. NHS Health Checks is a UK-run program geared toward the prevention of cardiometabolic risk factors and other risk factors. Authors conclude that small changes to invitation methods, such as inclusion of specified day and time of appointment, are correlated with higher health check attendance rates.

Fujita, Misuzu, Yasunori Sato, Kengo Nagashima, Sho Takahashi, and Akira Hata. "Impact of Geographic Accessibility on Utilization of the Annual Health Check-Ups by Income Level in Japan: A Multilevel Analysis." *PLoS ONE* 12, no. 5 (2017): 1-14. <http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=122942297&site=ehost-live>.

The goal of this Japanese study was to assess whether there is an income dependent relationship or geographically-dependent relationship with the utilization of annual health checks. Results show that low income and low geographic density are associated with lower utilization of health checks. Authors pose that better geographical accessibility in areas of low population

density could both increase the utilization of health checks and decrease the income-related difference in utilization.

Gautam, Shiv. "Fourth Revolution in Psychiatry - Addressing Comorbidity with Chronic Physical Disorders." *Indian Journal of Psychiatry* 52, no. 3 (Jul, 2010): 213-219. doi:10.4103/0019-5545.70973.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=54556866&site=ehost-live>.

This article pulls upon information from multiple studies that link mental illness and physical health problems. The author suggests that the body and mind are inseparable, and that each influences the other. It is suggested that there can be biochemical explanations for such comorbidities, and that current day psychiatry practice neglects, in large part, the bidirectional relationship between physical and mental states. Physical comorbidities that are most commonly seen in mental illness are explored, particularly cardiac, respiratory, gastrointestinal, endocrinal, and neurological disorders, as well as a greater perceived risk of STDs. Strategies to meet the challenges of such comorbidities are indicated.

Guo, Jeff J., Jr Keck Paul E., Hong Li, Raymond Jang, and Christina M. L. Kelton.

"Treatment Costs and Health Care Utilization for Patients with Bipolar Disorder in a Large Managed Care Population." *Value in Health* 11, no. 3 (May, 2008): 416-423. doi:10.1111/j.1524-4733.2007.00287.x.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=32073797&site=ehost-live>.

Using a multistate MCO claims database, bipolar patients were selected and followed in this study to measure total treatment cost. Findings exhibit that the greatest source of treatment dollars are attributed to physical comorbidities of the mentally ill patients, rather than directly for the treatment of their mental illnesses. In the study, the cost was divided into about 2:1, respectively.

Furthermore, higher total costs are associated with mental health comorbidities to bipolar disorder, specifically personality disorders. Author gives the recommendation for more closely monitored associations between psychotropic drug regimens and physical health conditions.

Hardy, Sheila, and Richard Gray. "Adapting the Severe Mental Illness Physical Health Improvement Profile for use in Primary Care." *International Journal of Mental Health Nursing* 19, no. 5 (2010): 350-355.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=20887609&site=ehost-live>.

This UK study outlines the purpose of the Health Improvement Profile online tool as well as providing in-depth directions on how the tool should be used.

Recommendations for the assessment of specific cardiometabolic risk factors and means to both document and follow-up treatment are given by the authors for psychiatric nurses to attend to the physical health needs of mentally ill patients.

Hardy, Sheila, and Richard Gray. "Is the use of an Invitation Letter Effective in Prompting Patients with Severe Mental Illness to Attend a Primary Care Physical Health Check?" *Primary Health Care Research & Development (Cambridge University Press / UK)* 13, no. 4 (2012): 347-352.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=84125115&site=ehost-live>.

This retrospective study compared the rate of response to health check invitation letters between patients with severe mental illness (SMI) and patients with diabetes. The aim of the study was to explore whether patients with SMI would respond to physical-health related invitations as compared to those who have physical morbidity without psychiatric morbidity. Annual physical health checks are recommended for those with SMI, since the SMI population is at a higher risk for cardiometabolic disease compared to the general population. Authors conclude that although the response rate to invitation letters is lesser in SMI patients than diabetes patients, invitation letters are still significantly correlated with greater health check attendance in the SMI population.

Haw, C. and S. Bailey. "Body Mass Index and Obesity in Adolescents in a Psychiatric Medium Secure Service." *Journal of Human Nutrition and Dietetics: The Official Journal of the British Dietetic Association* 25, no. 2 (2012): 167-171.

doi:10.1111/j.1365-277X.2011.01164.x.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=21585567&site=ehost-live>.

This article proposes that interventions are needed to reduce high BMIs, especially in young people, to prevent the associated physical complications, namely diabetes and hypertension. This proposal is based on a study conducted with overweight and obese subjects. A relationship between obesity and psychotropic drugs is established, and higher rates of diabetes and hypertension are noted in obese subjects compared to overweight subjects.

Kahl, Kai G., Mechthild Westhoff-Bleck, and Tillmann H. C. Krüger. "Effects of Psychopharmacological Treatment with Antidepressants on the Vascular System." *Vascular Pharmacology* 96, (2017): 11-18. doi:10.1016/j.vph.2017.07.004.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=125141989&site=ehost-live>.

This review was written to inform clinicians about the direct and indirect effects, both beneficial and adverse, of many antidepressant medications. This information is meant to assist clinicians to choose medications suited to the physical health comorbidities that are often present in mentally ill patients. Data from 2000-2017 on the relationship between antidepressants and the vascular system was used. Charts were created to show the benefits and risks of each antidepressant medication studied in order to make comparison comprehensible.

Kasper, Siegfried. "The Metabolic Syndrome and Antipsychotic Treatment." *Annals of General Psychiatry* 7, (2008): 1. doi:10.1186/1744-859X-7-S1-S33.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=35703860&site=ehost-live>.

This short article informs the clinician about the diseases that constitute metabolic syndrome, as well as the correlation between metabolic syndrome and mental illness due to both lifestyle factors and psychotropic drug use. Metabolic syndrome encompasses obesity, hypertension, high cholesterol, and impaired glucose tolerance. Smoking, sedentary lifestyle, and obesity can

proliferate metabolic syndrome. Obesity and sedentary lifestyle is higher among the severely mentally ill (SMI) population as compared to the general population. Rates of smoking are consistently higher with SMI patients than with the general population.

Katz, Eva G., Brett Hauber, Angie Fairchild, Srihari Gopal, Rachel B. Weinstein, Bennett S. Levitan, and Amy Pugh. "Physician and Patient Benefit-Risk Preferences from Two Randomized Long-Acting Injectable Antipsychotic Trials." *Patient Preference & Adherence* 10, (2016): 2127-2139.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=119302706&site=ehost-live>.

This 2008 study used experiment surveys to determine satisfaction with the efficacy, safety, and mode of administration of paliperidone palmitate long-acting injectable antipsychotic (PP-LAI) by both severely mentally ill (SMI) patients and treating physicians. Both patient and physician respondents reported preference for LAI antipsychotics over oral versions. Moreover, physicians and patients were willing to use injectable versions, even if they performed with lesser efficacy than oral formulations, in order to increase patient adherence. Low adherence rates are linked to higher rates of adverse effects and institutionalizations.

Looijmans, Anne, Frederike Jörg, Richard Bruggeman, Robert Schoevers, and Eva Corpeleijn. "Design of the Lifestyle Interventions for Severe Mentally Ill Outpatients in the Netherlands (LION) Trial; a Cluster Randomised Controlled Study of a Multidimensional Web Tool Intervention to Improve Cardiometabolic Health in Patients with Severe Mental Illness." *BMC Psychiatry* 17, (2017): 1-13.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=afh&AN=122365452&site=ehost-live>.

The aim of this 12-month 2017 Dutch randomised controlled trial was to explore whether lifestyle interventions, using a web tool, were effective in reducing the cardiometabolic health of SMI patients. Psychiatric nurses of five Dutch mental health organizations were trained as motivational coaches to impact lifestyle behavior awareness, lifestyle knowledge, and goal setting among the SMI patients they were treating. Results yield that lifestyle interventions result in decreases in waist circumference and other cardiometabolic risk factors. Cost-effectiveness is discussed. Authors pose that attention to physical health in the SMI population requires more acute intervention by clinicians.

Mangurian, Christina, Grace C. Niu, Dean Schillinger, John W. Newcomer, James Dilley, and Margaret A. Handley. "Utilization of the Behavior Change Wheel Framework to Develop a Model to Improve Cardiometabolic Screening for People with Severe Mental Illness." *Implementation Science: IS* 12, no. 1 (2017): 134.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=29137666&site=ehost-live>.

Authors of the 2017 study recognize the limited evidence base for integrative care models in mental health centers. The paper describes the application of an integrative care model to improve cardiovascular outcomes for the severely mentally ill (SMI) population. Termed the "Behavior Change Wheel framework," the theory-driven approach uses topics such as capability, motivation, opportunity, and behavior to build an intervention framework to screen for

cardiovascular risk factors and treat the physical morbidity present in the SMI population. The paper emphasizes the importance of psychiatrists in expanding their scope of practice to include responsibility for cardiovascular health.

Newcomer, John W. "Comparing the Safety and Efficacy of Atypical Antipsychotics in Psychiatric Patients with Comorbid Medical Illnesses." *The Journal of Clinical Psychiatry* 70 Suppl 3 (2009): 30-36. doi:10.4088/JCP.7075su1c.05.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=19570499&site=ehost-live>.

Newcomer's 2009 review of meta-analyses regarding the cardiometabolic effects of second-generation antipsychotics illustrates the relationship between the medications and modifiable cardiovascular risk factors such as high cholesterol, high blood sugar, hypertension, smoking, and obesity. Clinical guidelines are given to address the disparity of physical health care access in the severely mentally ill (SMI) population, and the author recommends that prescribers consider the physical attributes of each individual patient in the treatment decision-making process; some medications with similar efficacy have significant differences in adverse side effects. Monitoring of cardiometabolic health by clinicians is also recommended.

Osborn, David, Alexandra Burton, Rachael Hunter, Louise Marston, Lou Atkins, Thomas Barnes, Ruth Blackburn, et al. "Clinical and Cost-Effectiveness of an Intervention for Reducing Cholesterol and Cardiovascular Risk for People with Severe Mental Illness in English Primary Care: A Cluster Randomised Controlled Trial." *The Lancet.Psychiatry* (2018): 147.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=29396118&site=ehost-live>.

This 2018 British randomized controlled trial included severely mentally ill (SMI) patients aged 30-75 years who had high cholesterol and one or more modifiable cardiovascular risk factors. The "Primrose Intervention" encompassed appointments with a trained primary care clinician in order to personalize interventions to better cardiovascular health. After participants had been studied over the course of a year, cholesterol levels did not differ between the Primrose group and the control group. However, authors note the association between the Primrose intervention and reduction in psychiatric hospital admissions, which may demonstrate cost-effectiveness.

Park, A-La, David McDaid, Prisca Weiser, Carolin Von Gottberg, Thomas Becker, and Reinhold Kilian. "Examining the Cost Effectiveness of Interventions to Promote the Physical Health of People with Mental Health Problems: A Systematic Review." *BMC Public Health* 13, no. 1 (2013): 1-17.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=90248116&site=ehost-live>.

This 2013 analysis of 11 studies on physical health interventions calls attention to the possibility that measures to reduce the risk of physical comorbidities may be particularly cost-effective for the severely mentally ill (SMI) population. Authors note that there may be lack of incentives in primary care to regularly monitor the physical health of the SMI population. The reviewed lifestyle-based interventions to promote physical health included exercise programs, diet advice, smoking cessation programs, and similar group interventions. Supervised exercise

programs and smoking cessation programs are shown to be particularly cost-effective by reducing health care resource utilization overall.

Pearsall, Robert, Susan Hughes, John Geddes, and Anthony Pelosi. "Understanding the Problems Developing a Healthy Living Programme in Patients with Serious Mental Illness: A Qualitative Study." *BMC Psychiatry* 14, no. 1 (2014): 1-17.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=94426984&site=ehost-live>.

This UK qualitative study consisted of interviews between researchers and thirteen severely mentally ill (SMI) patients over a period of six months. The mean age of patients was 54.6 years. Approximately half the patients were male and half female. Results of the study show that patients are reluctant to independently participate in healthy living programs, are often indifferent about longevity of life, and are relatively unaware of the risks of certain factors, such as smoking and high sodium intake, to their cardiovascular health. Researchers found that when patients were confronted by their own community caseworker about participation in a lifestyle intervention, they were more likely to be recruited.

Pilon, Dominic, Erik Muser, Patrick Lefebvre, Rhiannon Kamstra, Bruno Emond, and Kruti Joshi. "Adherence, Healthcare Resource Utilization and Medicaid Spending Associated with Once-Monthly Paliperidone Palmitate Versus Oral Atypical Antipsychotic Treatment among Adults Recently Diagnosed with Schizophrenia." *BMC Psychiatry* 17, (2017): 1-18.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=123430672&site=ehost-live>.

This study examines the use of paliperidone palmitate (PP-LAI), a second-generation long-acting injectable antipsychotic that has shows promising increases in adherence rates, reduction in hospitalizations, and lower overall health care costs as compared to oral formulations of second-generation antipsychotics. The 2017 study compared adherence rates, Medicaid spending, and healthcare resource utilization between patients diagnosed with schizophrenia beginning treatment with PP-LAI versus an oral antipsychotic. Patients ranged from 18-25 years. Comparisons in spending and resource utilization were also made between the PP-LAI group and the general population. Findings suggest that patients on PP-LAI preparations have better adherence and significantly lower medical costs as compared to patients on oral antipsychotic drug regimens. Additionally, the health care utilization cost savings resulting from PP-LAI use offset the greater prescription cost of long-acting injectables as compared to oral versions.

Predmore, Zachary S., Soeren Mattke, and Marcela Horvitz-Lennon. "Improving Antipsychotic Adherence among Patients with Schizophrenia: Savings for States." *Psychiatric Services (Washington, D.C.)* 66, no. 4 (2015): 343-345.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=25555222&site=ehost-live>.

Authors of this 2015 article estimated the costs of health care utilization and criminal justice system involvement among patients taking antipsychotic drugs. Estimations were formulated using a financial model on data that had been previously published. This data analysis allows quantification of potential net savings to Medicaid programs and other state agencies. Results estimate that

increased antipsychotic drug adherence could yield \$3.28 billion dollars yearly in net savings to states.

Sallis, Anna, Amanda Buntin, Annabelle Bonus, Andrew James, Tim Chadborn, and Daniel Berry. "The Effectiveness of an Enhanced Invitation Letter on Uptake of National Health Service Health Checks in Primary Care: A Pragmatic Quasi-Randomised Controlled Trial." *BMC Family Practice* 17, (2016): 35.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=27009045&site=ehost-live>.

This 2016 UK study aimed to compare attendance to health check appointments by using a standard health check invitation letter – commonly employed by the National Health Service (NHS) – as a control. The intervention letter used enhancements that included simplification of language and behavioral instruction through action focused language, among other tweaks. Results show that there is an increased uptake of 4.2% among those that receive the intervention letter as compared to those that receive the control letter for health check attendance.

Samtani, Mahesh N., Srihari Gopal, Cristiana Gassmann-Mayer, Larry Alphs, and Joseph M. Palumbo. "Dosing and Switching Strategies for Paliperidone Palmitate Based on Population Pharmacokinetic Modelling and Clinical Trial Data." *CNS Drugs* 25, no. 10 (2011): 829-845.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=a9h&AN=69849338&site=ehost-live>.

This review explores the dosage and withdrawal effects of commonly prescribed antipsychotics to formulate dosage and switching strategies for patients that are switching their regimen to include paliperidone palmitate (PP-LAI). Since PP-LAI has been shown to be as efficacious as other commonly prescribed antipsychotics without increased adverse effects, and with better adherence rates as compared to many other antipsychotics, the switch to PP-LAI is something that many psychiatrists will likely move towards with their patients. Dosage and time interval recommendations associated with switching to PP-LAI are different for each prior antipsychotic regimen.

Seshamani, M. "Is Clozapine Cost-Effective? : Unanswered Issues." *European Journal of Health Economics* 3, (2002): 113.
<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=15205453&site=ehost-live>.

This 2002 analysis focuses on the cost-effectiveness of clozapine, a second-generation antipsychotic drug that is considered to be the "gold standard treatment," for treatment-resistant schizophrenia. Six key studies were analyzed on the topic. Because schizophrenia-related health care costs equate to about 2.5% of the national healthcare expenditure, cost-effective treatments are imperative. The review suggests that treatment with clozapine improves the quality of life for patients with schizophrenia, and patients taking clozapine have a reduction in hospitalizations as compared to schizophrenic patients who do not, which allows for cost savings. Additionally, the study provides that patients receiving clozapine experience a decrease in overall health care spending.

Simoni-Wastila, Linda, Ilene H. Zuckerman, Thomas Shaffer, Christopher M. Blanchette, and Bruce Stuart. "Drug use Patterns in Severely Mentally Ill Medicare Beneficiaries:

Impact of Discontinuities in Drug Coverage." *Health Services Research* 43, no. 2 (2008): 496-514.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=31424857&site=ehost-live>.

This three-year long cohort study of severely mentally ill (SMI) Medicare beneficiaries discovered the extent of drug coverage among beneficiaries to determine whether discontinuities in drug coverage affect the use of antidepressant and antipsychotic medications. Authors conclude that the vulnerability of Medicare beneficiaries to Medicare Part D benefit design may be exacerbated by SMI status, ranging between no coverage and discontinuous coverage.

Vogt, William B., Geoffrey Joyce, Jing Xia, Riad Dirani, George Wan, and Dana P. Goldman. "Medicaid Cost Control Measures Aimed at Second-Generation Antipsychotics Led to Less use of all Antipsychotics." *Health Affairs (Project Hope)* 30, no. 12 (2011): 2346-2354.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=22147863&site=ehost-live>.

This 2011 study involved the collection of information on drug use and utilization management strategies in thirty state Medicaid programs between 1999 and 2008. Prior authorization is found to be one of the most common drug utilization management strategies, as it allows for restrictions and barriers to more expensive prescription drugs. The study found that prior authorization was not offset by the substitution of other less-costly first-generation or second-generation antipsychotics. This finding suggests that initial cost-savings of prescription drugs does not carry over into long-term savings.

Ward, Martha and Ann Schwartz. "Challenges in Pharmacologic Management of the Hospitalized Patient with Psychiatric Comorbidity." *Journal of Hospital Medicine* 8, no. 9 (2013): 523-529.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=her&AN=90096361&site=ehost-live>.

Authors conducted a literature review to obtain data relevant to the effects of psychotropic medication discontinuation, or nonadherence, in order to assist hospital physicians in making informed decisions about discontinuation of patients' psychotropic drug regimens during hospital stay. Many of the studies reviewed demonstrate that mental illness relapse rates are high upon temporary discontinuation of psychotropic medications in patients diagnosed with mood disorders, schizophrenia, and anxiety disorders. Physical withdrawal symptoms may also occur upon abrupt psychotropic drug discontinuation. To boot, continuation of psychotropic drug regimen when the patient is released from the hospital, in combination with discharge medications prescribed to the patient by the hospitalist, may cause dangerous interactions. To assist in medication regimen decision making, hospitalists should refer to all available resources, such as pharmacists and consult-liaison psychiatrists.

Weston-Green, Katrina, Xu-Feng Huang, and Chao Deng. "Second Generation Antipsychotic-Induced Type 2 Diabetes: A Role for the Muscarinic M3 Receptor." *CNS Drugs* 27, no. 12 (2013): 1069-1080.

<http://search.ebscohost.com.providence.idm.oclc.org/login.aspx?direct=true&db=cmedm&AN=24114586&site=ehost-live>.

This 2013 review analyzes the potentiality of the acetylcholine muscarinic M3 receptor (M3R) to be a possible therapeutic target for insulin resistance. Second-generation antipsychotics, which are widely prescribed to severely mentally ill (SMI) patients, can directly and indirectly cause insulin resistance, which is the hallmark of type 2 diabetes. The ability of second-generation antipsychotics to bind to M3R is a risk for diabetes, especially among clozapine and olanzapine. Due to the high prescription rates of both drugs for SMI patients, increased risk for diabetes is realized in a significant portion of SMI patients.