THE EFFECTS OF ANTIPSYCHOTIC DRUGS ON BODY COMPOSITION AND LIPID PROFILES OF PATIENTS WITH PSYCHOTIC ILLNESSES

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DECLARATION

I hereby declare that the material in this thesis is my own except for the quotations, excepts, equations, summaries and references, which have been duly acknowledged.

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CERTIFICATION

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ABSTRACT

Approximately 50% patients with psychosis illnesses on antipsychotic drugs have an increased risk of obesity. This study aim to determine changes in body weight, body fat percentage and lipid profiles and to stress the importance of early nutrition intervention in the management of psychotic illness patient treated with antipsychotic drugs. This is a prospective longitudinal study conducted for 3 months in Hospital Mesra Bukit Padang, Sabah. Total 150 patients with Diagnostic and Statistical Manual IV (DSM-IV) diagnosis of psychotic illness (either Olanzapine or Risperidone only at any dosage) first started or restarted after a treatment gap of at least 6 months were recruited. Weight, height and body fat percentage measured using Bioelectrical Impedance Analysis (BIA) (Model Omron HBF-375) and blood fasting lipid test were taken from the point of starting medication for 12 weeks. Data were analyzed using repeated measures of ANOVA for statistical method. All variables shows significant mean differences ($p < 0.05$) in increasing pattern throughout the 12 weeks of treatment. However, the total cholesterol of risperidone patients has no significant mean difference from baseline to week 6 ($p=0.282$). It's proven that there is increment in body weight, body fat percentage and lipid profiles among patients on olanzapine and risperidone. The limitation of this study may relate to the drugs' dosage and method used in assessing the body composition. It is suggested that early nutrition intervention is needed to control unnecessary gain of weight, body fat and lipid profiles in the management of patient with psychotic illnesses.

ABSTRAK

KESAN UBAT ANTI PSIKOTIK KE ATAS KOMPOSISI TUBUH DAN LIPID PROFIL PESAKIT YANG MENGHIDAPI PENYAKIT PSIKOTIK

Kira-kira 50% pesakit dengan penyakit psikosis pada ubat antipsikotik mempunyai risiko peningkatan obesiti. Kajian ini bertujuan untuk menentukan perubahan berat badan, peratusan lemak badan dan profil lipid dan menekankan kepentingan intervensi pemakanan awal dalam pengurusan pesakit penyakit psikotik yang dirawat dengan ubat antipsikotik. Ini adalah kajian jangka panjang prospektif yang dilakukan selama 3 bulan di Hospital Mesra Bukit Padang, Sabah. Sejumlah 150 pesakit psikotik dengan Diagnostic and Statistical Manual IV (DSM-IV) (sama ada Olanzapine atau Risperidone pada sebarang dos) baru atau mempunyai jurang rawatan sekurang-kurangnya 6 bulan telah direkrut. Peratusan berat badan, ketinggian dan lemak badan yang diukur dengan menggunakan Bioelectrical Impedance Analysis (BIA) (Model Omron HBF-375) dan ujian lipid puasa darah diambil dari titik permulaan ubat selama 12 minggu. Data dianalisis dengan menggunakan kaedah ANOVA berulang dibuat untuk kaedah statistik. Semua pemboleh ubah menunjukkan perbezaan signifikan ($p<0.05$) dalam peningkatan corak sepanjang 12 minggu rawatan. Walau bagaimanapun, jumlah kolesterol pesakit risperidone tidak mempunyai perbezaan min yang signifikan dari asas ke minggu 6 ($p = 0.282$). Ini terbukti bahawa terdapat kenaikan dalam berat badan, peratusan lemak badan dan profil lipid di kalangan pesakit di olanzapine dan risperidone. Batasan kajian ini mungkin berkaitan dengan dos dan kaedah ubat yang digunakan untuk menilai komposisi badan. Adalah dicadangkan bahawa intervensi pemakanan awal diperlukan untuk mengawal keuntungan berat, lemak badan dan profil lipid yang tidak perlu dalam pengurusan pesakit dengan penyakit psikotik.

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LIST OF ABBREVIATIONS

APDs	- Antipsychotic Drugs
DSM-IV	- Diagnostic and Statistical Manual Version 4
GLIMMPSE	- General Linear Multivariate Model Power
HMBP	- Hospital Mesra Bukit Padang
NMRR	- National Medical Research Registry
EER	- Estimated Energy Requirement
Kg	- Kilogram
BMR	- Basal Metabolic Rate
ANOVA	- Repeated measures Analysis of Variance
BMI	- Body Mass Index
LDL	- Low Density Lipoprotein
HDL	- High Density Lipoprotein
LDL	- Low Density Lipoprotein
KCAL	- Kilocalorie
SGAs	- Second Generations Antipsychotic drugs

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CHAPTER 1

INTRODUCTION

1.1 Introduction

DSM-IV defines psychotic illness as 'a clinically significant behavioral or psychological syndrome or pattern that occurs in an individual". It is associated with distress, disability, with a significantly increased risk of suffering death, pain, or an important loss of freedom. Two of the main symptoms of psychotic illness are delusions and hallucinations. There are many types of psychotic illnesses, such as schizophrenia, and these illnesses affect people across the world, including Malaysia. According to National Health and Morbidity Survey 2015, in Malaysia, 29.2% adults and 12.1% children aged 5 to 15 are diagnosed with mental illness, these figures are considered high although they are only based on hospital figures. Another finding by Crabtree and Chong (2000), in both urban and rural areas of Malaysia, the prevalence rate was between 9.6% to 35%. Several previous studies carried out to determine the prevalence of mental illness in Peninsular Malaysia reported high prevalence.

In East Malaysia, the prevalence of psychiatric morbidity lacks consistent data and information, as there were only a few studies, which had been carried out across Sabah and Sarawak. Moreover, there are only a few studies from Sabah that provide information on the prevalence rate of mental illness. Therefore, the prevalence of mental illness remains uncertain in Sabah.

1.1.1 Psychotic Illness

Psychosis is known as a broad category of mental illness which diagnoses a person to enclose some emotional disturbances, causing one to be incapable of staying in contact with the reality (Columbia University, 2008). The symptoms are well

established on the experiences of a subject, such as hearing voices ("hallucinations") and developing unusual belief ("delusions") (Geekie et. al., 2013). Meanwhile, Hinshelwood (2004) discussed the impact of psychosis on one's personal experience, social and careers.

The author claimed that although the cause of psychosis is poorly understood, however, the symptoms are common and similar among the mentally ill patients. Both symptoms of hallucination and delusion should be emphasized while approaching and devising a treatment for psychosis illnesses. As quoted by Hinshelwood (2004),

"In schizophrenia, the world loses meaning, and in place of that loss, a patient reconstructs a new meaning. However, the new meaning comes out of the patient's imagination to form convincing delusions and hallucinations, which populate his world in place of a true interest in the world we all live in." The common treatment given to patients with psychosis illness is antipsychotic drugs (APDs) (Vieweg & Hasnain, 2012). Antipsychotic drugs have two generations, namely the "first-generation" and the "second-generation". The "second-generation" or atypical antipsychotic drugs were initially considered safe to cause any side effects such as involuntary movement that is formally triggered by the "first-generation" antipsychotic drugs (Shireen, 2016). Due to this, atypical antipsychotics are preferable over "first-generation" antipsychotic drugs (Declercq et. al., 2013). However, other side effects such as induced weight gain have rapidly become more evident. This is concerning since these weight gains have been proven to lead the patients into exhibiting obesity. A study conducted by Vreeland, Sharma, Miller, and Mravcak (2013) stated that these APDs are among the factors significantly contributes to the prevalence of obesity among patients with mental illnesses. The researchers added that obesity in patients with psychiatric conditions is often neglected by the patients due to their lack of awareness on their weight problem.

1.1.2 Effects of Drugs

Many clinical books have discussed the effects of APDs which have been introduced to the market around the 1950s. Back then, there are some reported arguments among the researchers regarding the side effects of typical and atypical

APDs. In her book, Geer (2013) discussed the work of Chao Deng that explored the effect of both typical and atypical APDs. Geer (2013) explained the hierarchy of the effects from APDs into three stages: stage 1, an early acceleration of body weight within the first few months of treatment (about 3 months for olanzapine, risperidone and haloperidol); stage 2, a stage where bodyweight steadily increases for a period of one year and above; and stage 3, further treatment resulting in a plateau of weight gain, representing the "ceiling effect" of APDs. This hierarchy is supported by another book, written by Heidelbaugh (2015) where he discussed the symptoms of diabetes patients who had previously been treated with APDs. Furthermore, APDs have also been proven to cause serious metabolic side effects, such as intra-abdominal obesity and hyperglycaemia (Hirsch, 2015). The risks of diabetes have been suggested across various APDs as well in long-term treatment. The author emphasized the key behavioral changes in appetite and food intake as among the side effects related to APD-induced weight gain.

Many studies have been carried out to show the relationship between the consumption of antipsychotic drugs and obesity among patients with psychosis illnesses, especially schizophrenia patients. Sicras *et al.* (2008) found that obesity was associated with the use of APDs. According to Vieweg and Hasnain (2012), induced weight gains is a common side effect of APDs, however, the real problem lies in the differences of the potential of each antipsychotic agent to induce weight gain. A recent finding by Annamalai, Kosir, and Tek (2017) revealed that APDs may not be the only factor that is responsible for obesity among the Schizophrenia patients. They added that an inherent vulnerability to obesity and diabetes may also contribute to the risk among the patients. From their finding, they found that the prevalence of obesity is high among the patients but there is no significant correlation between APDs and its dosage with obesity. Obesity among patients with psychotic illnesses is a growing concern among our society as it could shorten the patients" life expectancy up to 25 years since obesity is considered as one of the major risk factors for metabolic syndrome, cardiovascular diseases and premature death (Heishanen, 2003). In other words, patients with mental conditions have higher morbidity and mortality rate than average people. The prevalence rate of obesity among patients with schizophrenia is higher than the general population (Susce *et. al.*, 2005; De Hert, Schreurs, Vancampfort, & Van Winkel, 2009). Annamalai and Tek (2015) reported obesity in approximately 50%

of patients with psychosis illnesses. Moreover, compared to a normal person, those with psychosis illness have an increased risk of 1.2 to 1.5 times higher for obesity (Coodin, 2001; McIntyre et. al., 2006). While some argue that obesity associated with schizophrenia"s patients is due to the complex interaction between genetic, environment and effect of atypical drugs (Holt et. al., 2009), others strictly blame the effect of atypical drugs (Alvarez et. al., 2008). Although many types of research have been done to seek for solution to this problem, the mechanism behind the effect is still poorly understood by others (Von Wilmsdorff, M. et. al., 2010).

1.2 Problem Statement

As stated by Teoh *et al.* (2017), despite its low prevalence, psychotic illness can be an economic burden to a country, especially a developing country. Their studies reveal that the magnitude of the economic burden of schizophrenia in Malaysia highlights the need for additional support for people with schizophrenia. The researchers also added that the consequences of psychosis illness could not only result in a higher prevalence of obesity but also added to the productivity loss of a country. Hence, to solve this, Malaysia is urged to provide these people with treatments and solutions. These treatments include the usage of APDs, whether in the long term or the short term. This, unfortunately, only increases the prevalence of obesity in Malaysia if the usage goes unmanaged.

Ghee (2016) emphasized the increasing rate of obesity over the years among Malaysian adults, including Sabah and Sarawak. He further claimed that besides physical inactivity, medication is reported to be one of the significant and common contributing factors for obesity in Malaysia. In Sabah and Sarawak, the people lack the education and awareness on the side effects of this medication, which explains the high prevalence of overweight and obesity, 28.8% and 10.6% respectively. Due to this, Malaysia has been ranked as the second-highest country in Southeast Asia for the prevalence of overweight (Ghee, 2016). According to the National Health and Morbidity Survey (2015), the prevalence of mental illness has increased to 29.2% in Malaysia. The survey also revealed that without proper treatment, mental illness could be the second biggest health problem affecting the

country by 2020 and that the risks factors include rural areas and gender. Ample studies are fundamental to provide clear guidelines on the administration of APDs and their side effects to psychotic patients. Since Sabah has a limited number of studies regarding this topic, this study aims to determine the changes in body composition among patients treated with olanzapine and risperidone.

1.3 Research Questions

In the exploration of the early stage of the study, some research questions arise which motivated the progress of the study itself. The following are the research question of the study.

1. What are the changes in body composition among the treated patients?
2. Which of the APDs being used has greater potential to induce weight gain?
3. Which of the factors (age, gender or appetite) predict or associated with weight gain among olanzapine and risperidone patients?

1.4 General Objective

The general objective of this study is to investigate the effects of anti-psychotic drugs on body weight, body composition and lipid profile of patients diagnosed with psychotic illnesses. The study is conducted among patients at Hospital Mesra Bukit Padang, Sabah where the drugs are assigned as a treatment to the patients.

1.4.1 Specific Objectives

The following are the specific objectives of the study:

1. To analyze the changes in body composition among patients when treated with olanzapine and risperidone.
2. To compare the potential of olanzapine and risperidone in inducing weight gain.

3. To examine the association between age, gender, and appetite with weight gain among olanzapine and risperidone patients.

1.5 Scope of the study

This study aims to determine the changes in body composition (including body weight and body fat percentage) among patients treated with olanzapine and risperidone. Since APDs are known to induce weight gain among psychotic patients, the potential of inducing weight gain between olanzapine and risperidone is compared and investigated. Olanzapine and risperidone are commonly used in Hospital Mesra Bukit Padang, Sabah where the drugs are assigned as a treatment to patients with psychotic illnesses. The study focuses on the differences in weight gain and other body composition changes between baseline, week 6 and week 12. Approximately 150 patients were recruited for this study where height and body composition were measured during the admission, after 6 weeks and 12 weeks. Overall, the findings will answer the pre-defined research questions and confirm the findings of other empirical research.

1.6 Significance of Study

Despite the importance of research regarding this topic to improve the awareness of APDs side effects, there are a limited number of studies that have been carried out in Malaysia. Without the basic fundamental knowledge of APD side effects, this could further increase the prevalence of obesity among Malaysian. Therefore, this study can become a reference for the comparison of the effect of APDs (olanzapine and risperidone) in patients with psychotic illnesses in Sabah.

Since the mechanism of induced weight gain is not well understood, the results of this study also aim to contribute as a future guideline for to the research on the mechanism behind the effect of APDs on induced weight gain. This study can provide insight for future researchers to further understand the importance of early nutrition intervention in the management of psychotic illness patients.

1.7 Definition of Key Terms

The following are the definitions for some of the key terms being used throughout the study:

Psychotic – Refers to a person suffering from a psychosis and to the symptoms of psychosis.

Psychosis – Refers to a broad category of mental illness which includes emotional disturbances and makes it difficult to stay in contact with reality.

Anti-Psychotic Drugs – Refers to the medications administered to patients with mental illnesses.

Body Composition – Refers to the percentages of fat, bone, water, and muscle in human bodies.

Weight gain – The differences between body weight at baseline and body weight after the treatment period.

1.8 Organization of Report

This report consists of six chapters and structured as follow:

Chapter 1: Introduction

Chapter 1 contains the introduction to this study. This chapter provides information about the origins of the research. In introduction chapter, the main points explain about a brief overview of the background study, problem definition, and research questions, the objectives of the study, significant and research contribution, and lastly the scope and limitation of the study.

Chapter 2: Literature Review

Chapter 2 is a literature review. It will explain about the related works by previous researchers on the comparison of antipsychotic drugs" effect on weight gain and their result. Then, the literature will also focus on the method used to assess weight gain.

Chapter 3: Research Methodology

Chapter 3 discussed the methodologies that utilized as a part of this study to

accomplish the research objectives. It includes research design, research plan, data collection, question design, and data analysis.

Chapter 4: Implementation and Data Analysis

The fourth chapter discussed how the statistical analysis and the data collected will be analyzed.

Chapter 5: Findings and Discussion

Chapter 5 discussed the study's findings, and some discussion regarding the result that will achieve the objectives.

Chapter 6: Conclusion

Chapter 6 gives a summary of this research and study's limitation as well as routes for future research.

1.9 Summary of the Chapter

This chapter introduces the background knowledge of the topic being studied where a basic understanding of psychotic illness is outlined and defined accordingly. The association of psychotic illness in Malaysia is linked with the currently available treatment, the administration of anti-psychotic drugs. The origin of these drugs and the different types have been discussed and explained thoroughly which brings to the emergence of the problem statement. Since Sabah has limited empirical research regarding the usage of APDs on psychotic patients, this study aims to determine the side effects of olanzapine and risperidone on the patient's body composition. The potential of inducing weight gain among the two APDs is also evaluated and examined.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Psychotic illness is characterized by delusions, hallucinations, and lack of insight, with disturbed behaviour and disordered thinking. Commonly, antipsychotic drugs (APDs) have been used as a treatment towards psychotic illnesses such as schizophrenia. There are two generations of antipsychotic drugs, that are the "first-generation" in which is known as the "typical drugs" that associated with motor side effects such as tremor while another one is the "second-generation" or also called as "atypical drugs". Development of atypical drugs was mainly an improvement on older typical APDs in term of reduced side effects (reduced motoric extrapyramidal side effects - EPS) and various enhanced therapeutic effects (Freedman, 2003). Having these advantageous, atypical agents have been widely used as the first choice of medication. However, the side effects of some of these atypical agents quickly became more evident among treated patients, including weight gain and other complications.

The prevalence of obesity among patients with psychotic illness is higher than the general population (Susceet al 2005). In addition, in people with schizophrenia, obesity is associated with lower self-esteem, poorer psychosocial adaptation (De Hert *et al.,* 2006), reduced quality of life (Allison *et al.*, 2003), non-compliance with antipsychotic medication (Weiden *et al.,* 2003) and increased medication cost (Chwastiak *et al.,* 2009). Obesity is also considered to be one of the major risk factors for metabolic syndrome, cardiovascular diseases and premature death among patients with schizophrenia (Heiskanen, 2003). Due to these problems, research has been carried out to study the association between antipsychotic drugs and weight gain among patients, including

REFERENCES

Allison, D. B., Mackell, J. A., & McDonnell, D. D. 2003 . The Impact of Weight Gain on Quality of Life Among Persons With Schizophrenia. *Psychiatric Services*, 54 (4), 565-567.

Annamalai, A., Kosir, U., & Tek, C. 2017. Prevalence of obesity and diabetes in patients with schizophrenia. *World Journal of Diabetes*, 8(8), 390.

Annamalai, A., & Tek, C. 2015. An Overview of Diabetes Management in Schizophrenia Patients: Office Based Strategies for Primary Care Practitioners and Endocrinologists. *International Journal of Endocrinology* , 1-8.

Arciniegas, D. B. 2015. Psychosis. *Continuum,* 21 (3), 715 - 736

Atmaca, M., Kuloglu, M., Tezcan, E., & Ustundag, B. 2003. Serum Leptin and Triglyceride Levels in Patients on Treatment With Atypical Antipsychotics. *The Journal of Clinical Psychiatry*, 64(5), 598-604.

Borgwardt, S., Fusar-Poli, P., & McGuire, P. 2012. *Vulnerability to psychosis: From neurosciences to psychopathology : Maudsley series*. Taylor and Francis.

Carpenter, A., Pencharz, P., & Mouzaki, M. 2015. Accurate Estimation of Energy Requirements of Young Patients. *Journal of Pediatric Gastroenterology and Nutrition*, 60(1), 4-10.

Chan, Y. Y., Lim, K. K., Lim, K. H., Teh, C. H., Kee, C. C., Cheong, S. M., Ahmad, N. A. 2017. Physical activity and overweight/obesity among Malaysian adults: findings from the 2015 National Health and morbidity survey (NHMS). *BMC Public Health*, 17(1).

Chwastiak, L. A., Rosenheck, R. A., McEvoy, J. P., Stroup, T. S., Swartz, M. S., Davis, S. M., & Lieberman, J. A. 2009. The impact of obesity on health care costs among persons with schizophrenia. *General Hospital Psychiatry*, 31(1), 1-7.

Crabtree, S. A., & Chong, G. 2000. Mental Malaysia. Health and Citizenship in International Social Work, 43 (2), 217 - 226

Columbia University (Ed.). 2008. *The Columbia encyclopedia*. New York: Columbia University Press.

Coodin, S. 2001. Body Mass Index in Persons with Schizophrenia. *The Canadian Journal of Psychiatry*, 46(6), 549-555.

Cope, M. B., Li, X., Jumbo-Lucioni, P., DiCostanzo, C. A., Jamison, W. G., Kesterson, R. A., ... Nagy, T. R. 2009. Risperidone alters food intake, core body temperature, and locomotor activity in mice. *Physiology & Behavior*, 96(3), 457-463.

De Hert, M., Schreurs, V., Vancampfort, D., & Van Winkel, R. 2009. Metabolic syndrome in people with schizophrenia: a review. *World Psychiatry*, 8(1), 15-22.

Declercq, T., Petrovic, M., Azermai, M., Vander Stichele, R., De Sutter, A. I., Van Driel, M. L., & Christiaens, T. 2013. Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia. *Cochrane Database of Systematic Reviews*.

Eder, U., Mangweth, B., Ebenbichler, C., Weiss, E., Hofer, A., Hummer, M., Fleischhacker, W. W. 2001. Association of olanzapine-Induced Weight Gain With an Increase in Body Fat. *American Journal of Psychiatry*, 158(10), 1719- 1722.

Ferrie, S., & Ward, M. 2007. Back to basics: Estimating energy requirements for adult hospital patients. *Nutrition & Dietetics*, 64(3), 192-199.

Freedman, R. 2003. Schizophrenia. *The New England Journal of Medicine*, 349, 1738-1749.

Fountaine, R. J., Taylor, A. E., Mancuso, J. P., Greenway, F. L., Byerley, L. O., Smith, S. R., Fryburg, D. A. 2010. Increased Food Intake and Energy Expenditure Following Administration of olanzapine to Healthy Men. *Obesity*, 18(8), 1646-1651.

Geekie, J., Randal, P., Lampshire, D., & Read, J. 2013. *Experiencing Psychosis: Personal and Professional Perspectives*. Hoboken: Taylor and Francis.

Geer, E. 2013. *Endocrine and Neuropsychiatric Disorders, An Issue of Endocrinology and Metabolism Clinics*. London: Elsevier Health Sciences.

Ghee, L. K. 2016. A Review of Adult Obesity Research in Malaysia. *Medical Journal Malaysia*, *71*(1).

Gordon, P., Louza, M. R., & Xavier. 2013. Weight gain, metabolic disturbances, and physical health care in a Brazilian sample of outpatients with schizophrenia. *Neuropsychiatric Disease and Treatment*, 133.

Gothelf, D., Falk, B., Singer, P., Kairi, M., Phillip, M., Zigel, L., Apter, A. 2002. Weight Gain Associated With Increased Food Intake and Low Habitual Activity Levels in Male Adolescent Schizophrenic Inpatients Treated With olanzapine. *American Journal of Psychiatry*, 159(6), 1055-1057.

Graham, K. A., Perkins, D. O., Edwards, L. J., Barrier, R. C., Lieberman, J. A., & Harp, J. B. 2005. Effect of olanzapine on Body Composition and Energy Expenditure in Adults With First-Episode Psychosis. *American Journal of Psychiatry*, 162(1), 118-123.

Hammer, G. P., Prel, J. D., & Blettner, M. (2009). Avoiding Bias in Observational Studies. *Deutsches Aerzteblatt Online*. doi:10.3238/arztebl.2009.0664

Heckers, S., Barch, D. M., Bustillo, J., Gaebel, W., Gur, R., Malaspina, D., Owen, M. J. 2013. Structure of the psychotic disorders classification in DSM 5. *Schizophrenia Research*.

Heidelbaugh, J. J. 2015. *Type II diabetes mellitus: A multidisciplinary approach*.

Philadelphia: Elsevier.

Heishanen, T., Niskanen, L., Lyytikäinen, R., Saarinen, P. I., & Hintikka, J. 2003. Metabolic syndrome in patients with schizophrenia. *Journal of Clinical Psychiatry*, 64(5).

Henderson, D. C., Cagliero, E., Copeland, P. M., Borba, C. P., Evins, A. E., Hayden, D., ... Goff, D. C. (2005). Glucose Metabolism in Patients With Schizophrenia Treated With Atypical Antipsychotic Agents. *Archives of General Psychiatry, 62*(1), 19. doi:10.1001/archpsyc.62.1.19

Hill, J. O., Wyatt, H. R., & Peters, J. C. (2012). Energy balance and obesity. *Circulation, 126*(1), 126-132.

Hillier, S. E., Beck, L., Petropoulou, A., & Clegg, M. E. (2014). A comparison of body composition measurement techniques. *Journal of Human Nutrition and Dietetics, 27*(6), 626-631. doi:10.1111/jhn.12197

Hinshelwood, & R.D. 2004. *Suffering Insanity: Psychoanalytic Essays on Psychosis*. Taylor & Francis.

Hirsch, I. B. 2015. *Diabetes management*. Philadelphia, PA: Elsevier.

Jamaiyah H., 2000 *Community mental health in Malaysia: marriage of psychiatry and public health.* Jurnal Kesihatan Masyarakat, 6 (S). pp. 155-166.

Khalaf, M. M., & Thanoon, I. A. 2013. Effects of olanzapine versus risperidone on body mass index, BMI, serum leptin and lipid profile in schizophrenia patients. *African Journal of Pharmacy and Pharmacology*, 17(8), 1137-1143.

Kreidler, S. M., Muller, K. E., Grunwald, G. K., Ringham, B. M., Coker-Dukowitz, Z., Sakhadeo, U. R., Glueck, D. H. 2013. GLIMMPSE: Online Power Computation for Linear Models with and without a Baseline Covariate. *Journal of Statistical Software*, 54(10).

Konarzewska, B., Stefańska, E., Wendołowicz, A., Cwalina, U., Golonko, A., Małus, A., Ostrowska, L. 2014. Visceral obesity in normal-weight patients suffering from chronic schizophrenia. *BMC Psychiatry*, 14(1).

Lamont, B. J., Waters, M. F., & Andrikopoulos, S. 2016. A low-carbohydrate high-fat diet increases weight gain and does not improve glucose tolerance, insulin secretion or β-cell mass in NZO mice. *Nutrition & Diabetes*, 6(2), e194-e194.

Lato, M. M., Currier, M. B., Villaverde, O., & Gonzalez-Blanco, M. 2005. The Relation Between Body Fat Distribution and Cardiovascular Risk Factors in Patients With Schizophrenia: A Cross-Sectional Pilot Study. *The Primary Care Companion to The Journal of Clinical Psychiatry*, 07(03), 115-118.

Lenander, C., Midlöv, P., Viberg, N., Chalmers, J., Rogers, K., & Bondesson, Å. 2017. Use of Antipsychotic Drugs by Elderly Primary Care Patients and the Effects of Medication Reviews: A Cross-Sectional Study in Sweden. *Drugs - Real World Outcomes*, 4(3), 159-165.

MacGill, M. 2017. Psychosis: Causes, symptoms, and treatments. Retrieved from https://www.medicalnewstoday.com/articles/248159.php at 21st February 2016

McIntyre, R. S., Konarski, J. Z., Wilkins, K., Soczynska, J. K., & Kennedy, S. H. 2006. Obesity in bipolar disorder and major depressive disorder: results from a national community health survey on mental health and well-being. *Canadian Journal of Psychiatry*, 51, 274-280.

Minet-Ringuet, J., Even, P. C., Lacroix, M., Tomé, D., & De Beaurepaire, R. 2006. A model for antipsychotic-induced obesity in the male rat. *Psychopharmacology*, 187(4), 447-454.

Mozaffarian, D., Hao, T., Rimm, E. B., Willett, W. C., & Hu, F. B. 2011. Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men. *New England Journal of Medicine*, 364(25), 2392-2404.

Mulat, E., Mossie, A., Negash, A., & Ibrahim, M. 2017. Effect of Antipsychotic Drugs on Body Composition in Patients Attending Psychiatry Clinic, Jimma, Ethiopia. *Journal of Psychiatry*, 20(3).

Murashita, M., Inoue, T., Kusumi, I., Nakagawa, S., Itoh, K., Tanaka, T., Koyama, T. 2007. Glucose and lipid metabolism of long-term risperidone monotherapy in patients with schizophrenia. *Psychiatry and Clinical Neurosciences*, 61(1), 54-58.

Park, S., Yi, K., Kim, M., & Hong, J. 2013. Effects of ziprasidone and olanzapine on body composition and metabolic parameters: an open-label comparative pilot study. *Behavioral and Brain Functions*, 9(1), 27.

Ricciardi, R., & Talbot, L. A. (2007). Use of bioelectrical impedance analysis in the evaluation, treatment, and prevention of overweight and obesity. *Journal of the American Academy of Nurse Practitioners*, *19*(5), 235-241. doi:10.1111/j.1745-7599.2007.00220.x

Romieu, I., Dossus, L., Barquera, S., Blottière, H. M., Franks, P. W., & Willett, W. C. 2017. Energy balance and obesity: what are the main drivers? *Cancer Causes & Control*, 28(3), 247-258.

Rummel-Kluge, C., Komossa, K., Schwarz, S., Hunger, H., Schmid, F., Kissling, W., Leucht, S. (2012). Second-Generation Antipsychotic Drugs and Extrapyramidal Side Effects: A Systematic Review and Meta-analysis of Head-to-Head Comparisons. Schizophrenia Bulletin, 38(1), 167-177.

Saddichha, S., Manjunatha, N., Ameen, S., & Akhtar, S. 2007. Effect of olanzapine, risperidone and haloperidol on weight and BMI in first episode schizophrenia patients in India. *Journal Clinical Psychiatry*, 68(11).

Schwartz, M. W., Woods, S. C., Porte, D., Seeley, R. J., & Baskin, D. G. 2000. Central nervous system control of food intake. *Nature*, 404(6778), 661-671.

Sharpe, J., Stedman, T., Byrne, N. M., & Hills, A. P. 2010. Prediction of resting energy requirements in people taking weight-inducing antipsychotic medications. *Nutrition & Dietetics*, 67(3), 166-170.

Shireen, E. 2016. Experimental treatment of antipsychotic -induced movement disorders. *Journal of Experimental Pharmacology*, Volume 8, 1-10.

Sidik, S. M., & Ahmad, R. 2004. Childhood Obesity: contributing factors, consequences and intervention. *Malaysian Journal of Nutrition*, 10(1), 13-22.

Skrede, S., Fernø, J., Vázquez, M. J., Fjær, S., Pavlin, T., Lunder, N., Steen, V. M. 2012. olanzapine, but not aripiprazole, weight-independently elevates serum triglycerides and activates lipogenic gene expression in female rats. *International Journal of Neuropsychopharmacology*, 15(2), 163-179.

Sicras-Mainar, A. 2008. Relationship between obesity and antipsychotic drug use in the adult population: A longitudinal, retrospective claim database study in Primary Care settings. *Neuropsychiatric Disease and Treatment*, 219.

Sugawara, N., Yasui-Furukori, N., Tsuchimine, S., Fujii, A., Sato, Y., Saito, M., Kaneko, S. 2012. Body composition in patients with schizophrenia: Comparison with healthy controls. *Annals of General Psychiatry*, 11(1), 11.

Von Wilmsdorff, M., Bouvier, M., Henning, U., Schmitt, A., & Gaebel, W. 2010. The impact of antipsychotic drugs on food intake and body weight and on leptin levels in blood and hypothalamic ob-r leptin receptor expression in wistar rats. *Clinics*, 65(9), 885-894.

Vreeland, B., Sharma, M., Miller, M., & Mravcak, S. 2013. Obesity in Patients With Psychiatric Conditions. *Psychiatric Times*, 30(7).

Venkatasubramanian, G., Chittiprol, S., Neelakantachar, N., Shetty, T. K., & Gangadhar, B. N. 2010. A Longitudinal Study on the Impact of Antipsychotic Treatment on Serum Leptin in Schizophrenia. *Clinical Neuropharmacology*, 33(6), 288-292.

Weiden, P. J., Kozma, C., Grogg, A., & Locklear, J. 2003. Partial Compliance and Risk of Rehospitalization Among California Medicaid Patients With Schizophrenia. *Psychiatric Services*, 55(8), 886-891.

Wysokinski, A., & Kloszewska, I. 2014. Mechanisms of Increased Appetite and Weight Gain Induced by Psychotropic Medications. *Journal of Advanced Clinical Pharmacology*, 1(1), 12-33.

Zhang, Z., Yao, Z., Liu, W., Fang, Q., & Reynolds, G. P. 2004. Effects of antipsychotics on fat deposition and changes in leptin and insulin levels. *British Journal of Psychiatry*, 184(01), 58-62.