Examining Cardiorespiratory Fitness in Diabetic Individuals with and without Psychotic Illness

by

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A thesis submitted in conformity with the requirements for the degree of Masters of Science

Institute of Medical Science
University of Toronto

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Abstract

Aim: To measure cardiorespiratory fitness (CRF) in diabetic individuals with and without a psychotic illness and healthy controls and determine whether the presence of psychosis increases the risk of cardiovascular disease in Type 2 Diabetes Mellitus (T2DM).

Methods: CRF was assessed using the six minute walk test (6MWT) and self reported questionnaires assessed physical activity, quality of life and perceived exertion.

Results: Individuals with T2DM and a comorbid psychotic illness had a significantly lower CRF when compared to people with T2DM alone. CRF in both T2DM groups was significantly lower compared to previously-collected data on healthy Canadians.

Conclusion: CRF is reduced in T2DM and the co-occurrence of psychotic illness reduces fitness further. More attention needs to be directed at improving CRF in this population, in both primary care and psychiatric settings. Success in improving fitness in this vulnerable population may reduce medical comorbidity, improve quality of life, and prolong lifespan.
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<tbody>
<tr>
<td>6MWT</td>
<td>6 Minute Walk Test</td>
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<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
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<td>ATS</td>
<td>American Thoracic Society</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>BPRS</td>
<td>Brief Psychiatric Rating Scale</td>
</tr>
<tr>
<td>CAMH</td>
<td>Centre for Addiction and Mental Health</td>
</tr>
<tr>
<td>CAPA</td>
<td>Clinical Assessment for Physical Activity</td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary Heart Disease</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CRF</td>
<td>Cardiorespiratory Fitness</td>
</tr>
<tr>
<td>DSM-IV-TR</td>
<td>Diagnostic and Statistical Manual of Mental Disorders-Text Revisions (DSM-IV-TR)</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Glycosylated Hemoglobin</td>
</tr>
<tr>
<td>HDL</td>
<td>High-Density Lipoprotein</td>
</tr>
<tr>
<td>IPAQ</td>
<td>International Physical Activity Questionnaire</td>
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<tr>
<td>LDL</td>
<td>Low Density Lipoprotein</td>
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<tr>
<td>MET</td>
<td>Metabolic Equivalent</td>
</tr>
<tr>
<td>MetSyn</td>
<td>Metabolic Syndrome</td>
</tr>
<tr>
<td>NHANES</td>
<td>National Health and Nutrition Examination Survey</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
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<tr>
<td>---------</td>
<td>-------------</td>
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<tr>
<td>PASIPD</td>
<td>Physical Activity Scale for Individuals with Physical Disabilities</td>
</tr>
<tr>
<td>T2DM</td>
<td>Type 2 Diabetes Mellitus</td>
</tr>
<tr>
<td>SANS</td>
<td>Scale for the Assessment of Negative Symptoms</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
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<tr>
<td>SF-12</td>
<td>Short Form Health Survey</td>
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Chapter 1
Introduction

The main body of your thesis begins here.

1 Review of the literature
1.1 Overview of Psychotic Illness
1.1.1 Definition of Psychotic Illness

The fourth edition of the Diagnostic and Statistical Manual of Mental Disorders-Text Revisions defines persons with a psychotic illness as follows: individuals with a psychotic illness experience symptoms such as catatonic behavior, hallucinations, delusions or disorganized speech (American Psychiatric Association, 2000). Examples of psychotic disorders include schizophrenia, schizoaffective disorder, schizophréniform disorder, bipolar I disorder, major depressive disorder with psychotic features, substance-induced psychotic disorder and psychotic disorder not otherwise specified (American Psychiatric Association, 2000).

Individuals with schizophrenia experience positive symptoms such as delusions and hallucinations as well as negative symptoms such as affective flattening, alogia and avolition (American Psychiatric Association, 2000). These symptoms must also be present for a minimum of 6 months (American Psychiatric Association, 2000). People with schizophréniform disorder experience the same symptoms as schizophrenia except the duration of the illness is present from 1-6 months and there does not need to be impairment in functioning (American Psychiatric Association, 2000). Individuals diagnosed with schizoaffective disorder experience symptoms of
schizophrenia with the presence of a mood disorder (e.g., depressive, manic or mixed episode) (American Psychiatric Association, 2000). Bipolar 1 disorder is a mood disorder where people can experience manic and depressive episodes with psychotic features (American Psychiatric Association, 2000). Individuals with substance-induced psychosis experience psychotic symptoms as a result of a substance such as a drug or medication (American Psychiatric Association, 2000). Lastly, a person with a psychotic disorder not otherwise specified refers to individuals who experience psychotic symptoms; however, do not satisfy the criteria for a specific psychotic disorder (American Psychiatric Association, 2000).

1.1.2 Medical Comorbidities in individuals with Psychotic Illness

In addition to the psychiatric illness, individuals with psychosis are at an increased risk of developing non-psychiatric medical comorbidities. For example, individuals with schizophrenia have an increased prevalence (Bresee, Majumdar, Patten, & Johnson, 2010; Curkendall, Mo, Glasser, Rose Stang, & Jones, 2004) and risk for cardiovascular disease (CVD) (Curkendall et al., 2004). Bresee et al. (2010) found that 27% of individuals with schizophrenia in the province of Alberta had CVD compared to 17% of people without schizophrenia. There was also approximately two times higher prevalence of heart failure and stroke in individuals with schizophrenia when compared to those without the disorder (Bresee et al., 2010). Curkendall et al. (2004) found similar results as individuals with schizophrenia had a significantly higher prevalence of arrhythmias, stroke, transient cerebral ischemia and heart failure, than comparable individuals in the general population. The authors found that the incidence of heart failure, stroke and ventricle arrhythmias was also significantly higher in people with schizophrenia when
compared to those without (Curkendall et al., 2004). Dickey, Normand, Weiss, Drake, & Azeni (2002) also found a significantly higher prevalence of heart diseases in people with psychosis compared to those without. The prevalence of certain CVD risk factors such as hypercholesterolemia, hypertriglyceridemia (Bernardo et al., 2009) and hypertension (Dickey et al., 2002) has also been found to be increased in this population.

The prevalence of Type 2 Diabetes Mellitus (T2DM) is higher in people with psychosis (Bresee et al., 2010; Curkendall et al., 2004; Dickey et al., 2002; Kilbourne et al., 2004) and this independently contributes to risk of premature mortality (Panzram, 1987) as well as increases the risk of incident CVD (Kannel & Mcgee, 1979). Similar trends have also been observed with metabolic syndrome (MetSyn), the prevalence of which is also higher in persons with psychotic illnesses (De Hert et al., 2006; McEvoy et al., 2005).

The prevalence and incidence of chronic obstructive pulmonary disease (COPD) is also higher in people with schizophrenia and other psychotic illnesses (Carney, Jones, & Woolson, 2006; Himelhoch et al., 2004; Hsu, Chien, Lin, Chou, & Chou, 2013; Kilbourne et al., 2004). Hsu et al.(2013) found that there was a significantly higher prevalence as well as incidence of COPD in people with schizophrenia compared to the general population. Himelhoch et al. (2004) found similar results when comparing the prevalence of COPD in people with mental illness (schizophrenia, schizoaffective disorder, major depressive disorder and bipolar disorder) to data from the National Health and Nutrition Examination Survey (NHANES). The authors found that
the prevalence of emphysema and bronchitis was significantly higher in people with mental illness (Himelhoch et al., 2004).

It is hypothesized that the increased prevalence and incidence of these chronic diseases (e.g., CVD, T2DM, MetSyn and COPD) in individuals with a psychotic illness such as schizophrenia contribute to a lifespan that is much shorter than the general population, by approximately 20 years (Hennekens, Hennekens, Hollar, & Casey, 2005; Newman & Bland, 1991). A meta-analysis by Brown (1997) found that approximately 59% of the premature mortality experienced by people with schizophrenia was due to natural causes including cardiovascular diseases, cerebrovascular disease and respiratory diseases. Similar results were found by Prior, Hassall, & Cross (1996) who found that two leading causes of mortality in individuals with psychosis were due to diseases of the circulatory and respiratory systems. The standard mortality ratios for deaths due to CVD and other natural causes have also increased over time in people with schizophrenia (Ösby, Correia, Brandt, Ekbom, & Sparén, 2000). Similar causes of death (e.g., CVD and respiratory disease) have also been observed in people with bipolar disorder (Osby, Brandt, Correia, Ekbom, & Sparén, 2001). The most recent meta-analysis of mortality found that the gap in longevity between people with schizophrenia and the general population appeared to be widening (Saha, Chant, & McGrath, 2007).

1.1.3 Modifiable life style factors which can increase the risk for medical co-morbidities
The Canadian Diabetes Association lists diagnosis of a psychiatric illness (e.g., schizophrenia and bipolar disorder) as a risk factor for T2DM (Ekoé, Punthakee, Ransom, Prebtani, & Goldenberg, 2013). Certain types of antipsychotic medication, commonly used to treat psychotic illnesses can also increase the risk for T2DM (Lambert, Cunningham, Miller, Dalack, & Hur, 2006; Sernyak, Leslie, Alarcon, Losonczy, & Rosenheck, 2002). In addition to the illness itself, the increased prevalence of these chronic diseases and premature mortality experienced by this population can in turn, be related to modifiable life style factors which involve reduced physical activity, unhealthful diets, smoking and weight gain. Yusuf et al. (2004) examined the effect of various risk factors for myocardial infarction in 52 countries. The main findings with respect to modifiable lifestyle factors (e.g., smoking, physical activity, diet, and body weight) that will be discussed in this section are summarized in figure 1. Similar findings were reported by Mokdad, Marks, Stroup, & Gerberding (2004, 2005) who found that the most common attributable causes of death in the United States were due to tobacco, poor diet and physical inactivity (Figure 2) (Mokdad, Marks, Stroup, & Gerberding, 2004, 2005).
Figure 1. The effects of physical activity, obesity, smoking and diet on risk for myocardial infarction in 52 countries. (-) indicate significantly lower odds ratio for myocardial infarction risk, and (+) represent a significantly higher odds ratio for myocardial infarction risk.
Figure 2. Proportion of deaths attributable to common risk factors in the year 2000 within the United States. Data used from Mokdad et al. (2004, 2005).
Several studies have found individuals with schizophrenia and other psychosis to be physically inactive. For example, Daumit et al. (2005) examined the levels of physical activity over the past month in individuals with schizophrenia, schizoaffective disorder, bipolar disorder and major depressive disorder. The authors matched their physical activity to age, race and sex matched controls from the NHANES data (Gail L. Daumit et al., 2005). They found that 25.7% individuals with mental illness were physically inactive compared to 17.5% of people from NHANES data and this difference was significant (Gail L. Daumit et al., 2005). They also found approximately 30% of people with mental illness reported walking as their only exercise and when compared to the NHANES data, people with mental illness had significantly lower reported levels of jogging/running, biking and physical activity performed during gardening or yard work (Gail L. Daumit et al., 2005). Brown, Birtwistle, Roe, & Thompson (1999) compared exercise over the previous week and found that 36% of men and 32% of women with schizophrenia reported no exercise. In a study using accelerometer technology, which provides an objective measure of daily physical activity, it was found that people with schizophrenia and schizoaffective disorder spent approximately 81% of their time being sedentary (Janney et al., 2013). Accelerometer data has also shown that people with bipolar disorder spend approximately 79% of their time in sedentary activities and performed significantly less overall physical activity when compared to data obtained from the NHANES (Janney et al., 2014).

In addition to physical inactivity, another modifiable lifestyle factor for chronic diseases is unhealthy diets. Brown et al. (1999) found that people with schizophrenia consumed diets high in fat and lower in fibre which was significantly different when compared to the general population. In addition, they found that none of their participants consumed at least 5 servings of fruits and
vegetables each day (Brown et al., 1999). Lower consumption of fibre was also observed in a study conducted by Osborn, Nazareth, & King (2007) who found that participants with a mental illness (e.g., schizophrenia, schizoaffective disorder and delusional disorder) consumed significantly lower levels of fibre when compared to people without mental illness. In addition to low fibre and high fat diets, Strassnig, Brar, & Ganguli (2003) found that individuals with schizophrenia also consume significantly higher calories and consume more carbohydrates and fats when compared to data from the NHANES.

According to the Heart and Stroke Foundation, smoking is a modifiable risk factor for heart disease (Heart and Stroke Foundation, 2009). People with mental illness have higher rates of smoking than the general population (Lasser et al., 2000). For example, Brown et al. (1999) found that there were more than twice the number of current smokers in their sample of people with schizophrenia when compared to the general population. Sixty-one percent of men and 42% of women with schizophrenia smoked more than 20 cigarettes each day (Brown et al., 1999). Similar results were found by McCreadie (2003) who found 70% of their participants with schizophrenia were current smokers and 54% of them smoked at least 20 cigarettes each day.

Lastly, weight gain is also a modifiable risk factor for several chronic diseases. Many of the commonly prescribed antipsychotics have been found to be associated with significant risk for weight gain, with olanzapine and clozapine reportedly associated with the highest risk (Allison, Mentore, et al., 1999). These two antipsychotic medications show an approximate increase in body weight by 4kg over 10 weeks (Allison, Mentore, et al., 1999) and this weight gain may be
caused by an increased consumption of calories (Gothelf et al., 2002). The antipsychotics with the greatest risk of weight gain have also been shown to be associated with increased risk of incident T2DM (Gianfrancesco, Grogg, Mahmoud, Wang, & Nasrallah, 2002).

Individuals with psychosis also have a significantly lower knowledge of CVD risk factors (e.g., diet and exercise) when compared to people with no mental illness (Osborn et al., 2007) and have a higher 10 year Framingham CVD risk when compared to the general population (McCreadie, 2003).

Taken together, these factors (e.g., weight gain, physical inactivity, and unhealthy diets) help explain why the prevalence of obesity as well as increased mean Body Mass Index (BMI) in individuals with psychotic illness is higher than the general population (Allison, Fontaine, et al., 1999; G. L. Daumit et al., 2003; Dickerson et al., 2006). Obesity is an established risk factor for both T2DM (Ford, Williamson, & Liu, 1997; Resnick, Valsania, Halter, & Lin, 2000) and CVD (Lavie, Milani, & Ventura, 2009). Individuals with schizophrenia also have a higher waist circumference when compared to the general population (McEvoy et al., 2005). In addition to being associated with T2DM and CVD (Balkau et al., 2007), a higher waist circumference has shown to be a stronger predictor for medical comorbidities (e.g., hypercholesterolemia, MetSyn, high LDL-cholesterol and low HDL-cholesterol) when compared to BMI (Janssen, Katzmarzyk, & Ross, 2004).
Another modifiable risk factor that needs to be examined is Cardiorespiratory Fitness (CRF).

1.2 What is CRF and why is it important?

CRF refers to the ability to transport and deliver oxygen to the muscle when performing exercise (D. C. Lee, Artero, Sui, & Blair, 2010). Several non-modifiable factors (e.g., age and sex) as well as modifiable factors (e.g., level of daily physical activity and smoking status) can increase or decrease CRF (Jackson, Sui, Hebert, Church, & Blair, 2009). Physical activity is a predominant modifiable factor which can influence CRF with studies demonstrating that CRF can improve with both changes in physical activity duration and intensity (T. S. Church, Earnest, Skinner, & Blair, 2007; Duscha et al., 2005; Wegner & Bell, 1986). For a detailed review on the effects of physical activity duration, intensity and frequency on CRF, see review by Wegner & Bell (1986).

CRF is commonly assessed using VO\textsubscript{2} max where oxygen consumption is measured while the individual performs exercise at maximum effort on a stationary cycle or on a treadmill (D. C. Lee et al., 2010). Traditional VO\textsubscript{2} max assessments require a facility to deliver the graded exercise test as well as equipment for accurately measuring oxygen and carbon dioxide in inspired and expired air. Due to costs, complexity and the limited availability of VO\textsubscript{2} max measurements in routine clinical care, alternative measurements of fitness have been explored. Field tests of fitness include the 6 minute walk test (6MWT) ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002), the Cooper 12 minute run test (Cooper, 1968) and the 20 meter shuttle test (Leger, Mercier, Gadoury, & Lambert, 1988) have also been used to measure fitness. Significant correlations have been demonstrated between VO\textsubscript{2} max and the distances achieved on the Cooper 12 minute run test (Cooper, 1968), the 20 meter
shuttle test (Palczka, Nichols, & Boreham, 1987) and the 6MWT (Cahalin, Mathier, Semigran, Dec, & Disalvo, 1996b; Cote, Pinto-Plata, Kasprzyk, Dordelly, & Celli, 2007; Ross, Murthy, Wollak, & Jackson, 2010). Field tests, such as the 6MWT are also more feasible as they only require the necessary space for walking and no additional equipment (e.g., treadmills and stationary cycles or measurement of gas concentrations) ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002). In addition to being more practical in clinical settings, sub maximal field tests, such as the 6MWT, may also be a more reasonable proxy for the person’s ability to perform daily life activities (Noonan & Dean, 2000). For a detailed description of other field tests, see the review published by Noonan & Dean (2000).

In recent years, research has been published in the area of CRF, demonstrating its clinical utility beyond measuring individual fitness levels. Results of research on CRF in the general population have found it to be associated with important chronic diseases such as COPD, T2DM, MetSyn and CVD as well as its associated mortality as represented in Figure 3. However, an area where information is currently lacking with respect to CRF is in individuals diagnosed with psychosis (e.g., schizophrenia). This is important as there is an increased risk and prevalence of CVD and its associated risk factors (Bernardo et al., 2009; Bresee et al., 2010; Curkendall et al., 2004) in this population. Type 2 diabetes mellitus is also more prevalent in this population (Bresee et al., 2010; Curkendall et al., 2004), and T2DM increases the risk of premature mortality (Panzram, 1987) and CVD (Kannel & Mcgee, 1979). In addition, there is also an increased risk and prevalence for COPD in this population (Carney et al., 2006; Himelhoch et al., 2004; Hsu et al., 2013). The following sections will examine the relationship between CRF and chronic diseases as well as mortality.
Figure 3. The relationship between low CRF and MetSyn, T2DM, hypertension, CVD and mortality.
1.3 The relationship between CRF and Metabolic Syndrome

Originally proposed by Reaven, under the term “Syndrome X” (Reaven, 1988) MetSyn is a term used for a cluster of factors which increase the risk of developing T2DM and CVD (Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004; P. W. Wilson, D'Agostino, Parise, Sullivan, & Meigs, 2005). Although there has been discussion regarding whether MetSyn actually predicts CVD better than the component risk factors do independently (Kahn, Buse, Ferrannini, & Stern, 2005), the concept is still widely adhered to in the field of CVD and thus discussed here. Components of the current definition are low High-Density Lipoprotein (HDL) cholesterol, elevated triglycerides, elevated blood pressure, abdominal obesity and elevated fasting blood glucose (or evidence of insulin resistance) (Grundy et al., 2004). This section will discuss the work published on CRF and its association with MetSyn.

Kouki et al. (2012) examined this relationship and found an inverse relationship between CRF and MetSyn prevalence in both men and women. The sub-groups with the highest and lowest CRF had the lowest and highest prevalence of MetSyn respectively (Kouki et al., 2012). Similar results were found in a study performed by Lakka et al. (2003) who found that the odds ratio for MetSyn significantly increased with decreasing CRF. When examining each criteria of MetSyn, Kim, Lee, Jung, Kim, & Cho (2011) found that the sub-groups with the highest CRF had a significantly decreased prevalence for waist circumference > 90 cm, fasting glucose ≥ 110 mg/dl, triglycerides ≥ 150mg/dl, systolic blood pressure ≥130mm Hg, diastolic blood pressure ≥ 85 mm Hg in comparison to the low and moderate fitness groups. However, the significant association was not observed for HDL cholesterol levels between the groups (Kim et al., 2011). Orakzai et
al. (2006) also did not find a significant association between CRF and HDL cholesterol but did find significant inverse associations between CRF and other MetSyn criteria (e.g., waist circumference, fasting glucose, triglycerides and systolic blood pressure) (Orakzai et al., 2006). In addition, they found that individuals with low CRF were significantly more likely to have met more criteria for MetSyn compared to individuals with high CRF (Orakzai et al., 2006). This inverse association between CRF and MetSyn was also observed in studies performed by Jurca et al. (2004), Grundy, Barlow, Farrell, Vega, & Haskell (2012), Farrell, Cheng, & Blair (2004), Carroll, Cooke, & Butterly (2000) and Senechal, Bouchard, Dionne, & Brochu (2012). Lastly, MetSyn prevalence is also lower in people with higher CRF independent of body weight (Finley et al., 2006). Finley et al. (2006) found that higher CRF was associated with a lower odds ratio for MetSyn in both overweight and normal weight participants in comparison to participants with lower CRF.

Longitudinal studies shed further light on the association between low CRF and MetSyn. For example, Hassinen et al. (2010) performed a 2 year follow-up on men and women and found higher fitness levels at baseline decreased the risk for developing MetSyn. They also observed that participants who were already diagnosed with MetSyn at baseline were significantly more likely to reverse MetSyn features if they were in the high CRF category in comparison to individuals with low or moderate fitness (Hassinen et al., 2010). In a 5.7 year follow-up study performed by LaMonte et al. (2005), participants were found to have a significantly lower incidence of MetSyn compared to people with low and moderate CRF (LaMonte et al., 2005). Similar results for the inverse relationship between CRF and MetSyn incidence were found by
Shuval et al. (2012) and Carnethon et al. (2003). Carnethon et al. (2003) found that improvements in CRF significantly reduced the risk for developing MetSyn.

1.4 The association between CRF and the lipid profile

This section will highlight the association between CRF and dyslipidemia. Kosola, Ahotupa, Kyrolainen, Santtila, & Vasankari (2012) found oxidized-Low Density Lipoprotein (LDL) cholesterol, LDL cholesterol and total triglyceride levels were significantly higher in men with the lowest CRF in comparison to men with the highest CRF. This association with levels of triglycerides was observed in a study performed by Nagano et al. (2004) where the authors found that levels of triglycerides significantly decreased in their participants moving from low to high CRF groups. In a 7 year follow-up study, Williams (2008) found that higher CRF measured at baseline significantly decreased the incidence of hypercholesterolemia in men and women.

Lastly, the relationship between HDL-cholesterol and CRF has been studied. Kosola et al. (2012) found that subjects with the lowest CRF had significantly lower HDL cholesterol compared to subjects with the highest CRF and these results were supported by findings from a study by Nagano et al. (2004) who found a lower odds ratio for having low HDL-cholesterol in groups with higher CRF. Gando et al. (2010) found a similar relationship between CRF and HDL-cholesterol where HDL-cholesterol was significantly higher in women who were categorized as “fit” by the incremental cycle test in comparison to “unfit” individuals in the same age group. Levels of HDL-cholesterol have also been shown to increase with improvements in CRF (Balducci et al., 2012).
1.5 The associations between CRF and blood pressure

Hypertension can increase the risk of developing coronary heart disease (P. W. F. Wilson et al., 1998). Gando et al. (2010) examined the relationship between CRF and blood pressure in both premenopausal and postmenopausal women. Postmenopausal women who were more fit had significantly lower systolic blood pressure compared to unfit women; however, there was no significant difference in systolic blood pressure between the low and high fitness groups in premenopausal women (Gando et al., 2010). These results were further supported by Krause et al. (2009) who examined the relationship between hypertension prevalence and CRF in 1064 elderly women. The authors found that the women in the two highest CRF groups had a decreased odds of hypertension when compared to the lowest CRF group (Maressa Priscila Krause et al., 2009). Hypertension prevalence also decreased when moving from low to high fitness groups (Maressa Priscila Krause et al., 2009).

Longitudinal data also supports this association between CRF and high blood pressure. In a study performed by Jae et al. (2012), the authors found that there was an inverse association between baseline fitness and the incidence of hypertension during follow-up. Participants with the greatest reductions in CRF had an increased relative risk of hypertension compared to those who improved their CRF the most (Jae et al., 2012). In another study, Barlow et al. (2006) found that the incidence of hypertension was inversely associated with CRF and these results are also supported by studies performed by Chase, Sui, Lee, & Blair (2009), Williams (2008) and Carnethon et al. (2003). After adjusting for factors such as smoking and age, Barlow et al. (2006)
found that participants with high CRF had a significantly lower odds ratio for hypertension compared to subjects with low CRF. They also found that an increase by one metabolic equivalent (MET), an alternative measure of oxygen transport, resulted in a decreased odds of hypertension incidence by 19% (Barlow et al., 2006). The decrease by 19% with a 1 MET increase was also observed in a study by Rankinen, Church, Rice, Bouchard, & Blair (2007).

Higher CRF has also been associated with decreasing the risk of hypertension in individuals who have a parental history of the disease (Shook et al., 2012).

1.6 The association between CRF and T2DM and blood glucose levels

Approximately 90% of individuals with diabetes have T2DM (Stumvoll, Goldstein, & van Haeften, 2005; Zimmet, Alberti, & Shaw, 2001) and the global prevalence of diabetes is expected to reach 300 million people by 2025 (King, Aubert, & Herman, 1998). Many modifiable risk factors already exist for T2DM such as weight gain (Ford et al., 1997; Resnick et al., 2000). Research has shown an inverse relationship between CRF and T2DM as well as T2DM markers.

Research has found T2DM prevalence to decrease with increasing CRF in both men and women (Grundy et al., 2012; Kouki et al., 2012). Cross-sectional data also suggests an inverse relationship between CRF and T2DM and blood glucose levels. Leite, Monk, Upham, Chacra, &
Bergenstal (2009) examined this relationship in 369 individuals who were at a risk for insulin resistance syndrome and T2DM (e.g., presence of risk factors for either condition) in comparison to 177 controls. The authors found that VO$_2$ max was significantly lower in participants at risk of insulin resistance and T2DM in comparison to controls (Leite et al., 2009). VO$_2$ max was inversely associated with insulin resistance (Leite et al., 2009). This data was supported by results from a study by Chen, Chuang, & Wu (2008) who employed a different measure of CRF. Using the 3 minute step test, they found low CRF to predict insulin resistance in their subjects who had a minimum of one risk factor for diabetes (e.g., dyslipidemia) (Chen et al., 2008). The authors also found that CRF was inversely associated with insulin resistance in men and women (Chen et al., 2008). The association between CRF and other measures of glucose homeostasis has also been examined (Gatterer, Ulmer, Dzien, Somavilla, & Burtscher, 2011; Thompson et al., 2007). In a study performed in 200 Native American women, Thompson et al. (2007) found that lower CRF was significantly associated with impaired fasting glucose after adjusting for variables such as BMI. In a separate study in pre-diabetic men and women, Gatterer et al. (2011) did not find any association between CRF and fasting blood glucose; however, lower CRF values were significantly associated with an impaired two-hour plasma glucose in men (Gatterer et al., 2011). The relationship between CRF and T2DM was shown in a separate study where it was found that Brazilian women with the lowest CRF had the highest odds ratio for T2DM compared to women with the highest CRF (Maressa P Krause et al., 2007).

Similar results are also found examining the relationship between T2DM and CRF in longitudinal studies. Sui et al. (2012) examined the effects of CRF on blood glucose over time. They found that individuals with the lowest CRF experienced the highest increase in blood
glucose each year (0.25mg/dl) compared to individuals with high fitness (0.13 mg/dl) (Sui et al., 2012). This effect was observed in individuals over the age of 35 (Sui et al., 2012). In another study, Lee, Sui, Church, Lee, & Blair (2009) measured the incidence of impaired fasting glucose and T2DM in 14 006 men. Results revealed that participants with the highest CRF, had a 25% lower risk of developing impaired fasting glucose and a 70% lower risk of developing T2DM than participants who had the lowest CRF (D. C. Lee et al., 2009). Overall, there was an inverse relationship between CRF and relative risk of T2DM as well as impaired fasting glucose (D. C. Lee et al., 2009). A study published by Wei et al. (1999) showed similar results. The authors found that individuals with lower CRF were at a higher odds ratio for both an impaired fasting glucose and T2DM (Wei et al., 1999). Sawada et al. (2010) found supporting evidence for the association between CRF and T2DM incidence in a Japanese population. In addition, higher baseline CRF has also been shown to protect individuals and decrease the risk and incidence for future T2DM in studies performed by Sui et al. (2008), Goodrich et al. (2012), Williams (2008) and Carnethon et al. (2003). Follow-up studies have also been performed on youth (Dwyer et al., 2009). Dwyer et al. (2009) measured CRF in children in 1985 and followed the participants until 2004-2006. They found that future insulin resistance in their participants was associated with having lower baseline CRF as well as reductions in fitness from baseline to endpoint of the study (Dwyer et al., 2009).

Longitudinal studies are very helpful as they have shown the effects of baseline CRF as well as how changes in CRF are associated with T2DM incidence. Both cross-sectional and longitudinal studies reviewed in this section demonstrate the importance of CRF on glucose homeostasis as well as T2DM prevalence and incidence.
There have been many promising results stemming from studies examining changes to CRF and how it can affect the incidence of T2DM as well as abnormalities in blood glucose. For example, using a 6-month exercise intervention on 251 individuals diagnosed with T2DM, Larose et al. (2011) found that aerobic training alone, and a combined intervention of aerobic and resistance training increased VO$_2$ max in comparison to the control group. More importantly, this increase was significantly associated with a reduction in glycosylated hemoglobin (HbA1c) (Larose et al., 2011). Similar findings were observed in a study where the authors examined the effects of combining aerobic exercise, resistance exercise and exercise counseling in comparison to exercise counseling alone on 606 participants (Balducci et al., 2012). Improvements in VO$_2$ max were associated with improvements in HbA1c (Balducci et al., 2012). These results were supported by findings which compared aerobic versus resistance exercise in 40 participants diagnosed with T2DM (Bachi et al., 2012). The authors found that improvements in VO$_2$ max lowered HbA1c and improved insulin sensitivity (Bachi et al., 2012). Lastly, Senechal et al. (2013) found that after a 9 month exercise program, HbA1c decreased in individuals who increased their fitness from baseline.

1.7 The association between CRF and CVD events

When examining CRF with CVD events in men and women, studies have shown a general inverse relationship (Beatty, Schiller, & Whooley, 2012; Hooker et al., 2008; Kodama et al., 2009; Sui, LaMonte, & Blair, 2007). In a meta-analysis performed the Kodama et al. (2009), the authors found that individuals with low CRF had a significantly higher risk for CVD compared
to individuals with high and intermediate CRF. The authors also found that a 1 MET increase resulted in a reduced risk for CVD by 15% (Kodama et al., 2009). Sui et al. (2007) examined the occurrence of CVD events in men and women diagnosed with hypertension. The authors found that a higher CRF was associated with significantly fewer CVD events (e.g., stroke) compared to participants with low and moderate CRF in both men and women (Sui et al., 2007). In men, this significant inverse relationship was observed between CRF and coronary heart disease (CHD) events as well; however, it was not significant in women (Sui et al., 2007). The relationship between CRF and incidence of stroke was also reported by Hooker et al. (2008). Further support of this relationship between CRF and CVD events comes from studies performed by Talbot, Morrell, Metter, & Fleg (2002) and Beatty et al. (2012). The former found that participants who experienced coronary events had a lower VO\textsubscript{2} max compared to individuals who did not experience coronary events (Talbot et al., 2002). The latter found that individuals with the lowest fitness had the highest percentage of myocardial infarction and heart failure (Beatty et al., 2012).

1.8 The association between CRF and mortality

The relationship between CRF and mortality also needs to be examined. Grundy et al. (2012) found CVD and CHD mortality was inversely associated with CRF. This might be due to several CVD risk factors mentioned above such as low HDL cholesterol which decreased as CRF decreased (Grundy et al., 2012). Farrell, Finley, & Grundy (2012) examined this relationship in men and found that after a 16.7 year follow-up, CHD mortality hazard ratios were higher in individuals with moderate and low CRF when compared to those with higher CRF (Farrell et al., 2012). The low CRF group had 229 deaths, the moderate CRF group had 195 deaths and the high
CRF group had 133 deaths occur due to CHD (Farrell et al., 2012). Similar results were found in a meta-analysis performed by Kodama et al. (2009). The authors found that healthy individuals with high and intermediate CRF had a significantly lower risk for all-cause mortality when compared those with low CRF (Kodama et al., 2009). In addition, an increase in 1 MET reduced all cause mortality risk by 13% (Kodama et al., 2009).

Similar findings between CRF and mortality have been found in hypertensive (Evenson, Stevens, Thomas, & Cai, 2004) and diabetic individuals (Timothy S Church, LaMonte, Barlow, & Blair, 2005) as well as individuals with MetSyn (Katzmarzyk, Church, & Blair, 2004). In a study involving hypertensive and control men and women, Evenson et al. (2004) found that lower CRF resulted in a higher all-cause mortality as well as CVD mortality in participants with and without hypertension. This effect was also observed by Church et al. (2005) in men with diabetes. The authors found that after follow-up, the death rate was higher in men who had low CRF compared to participants with moderate and high fitness and this relationship was observed in subjects who were normal weight, overweight or obese class 1 (Timothy S Church et al., 2005). Katzmarzyk et al. (2004) showed higher fitness levels decreased the risk of all cause mortality as well as mortality due to CVD in both healthy men and men with MetSyn diagnosis. The inverse relationship between CRF and mortality was also observed in studies performed by C. D. Lee & Blair (2002) and Wei, Gibbons, Kampert, Nichaman, & Blair (2000) and improvements in CRF have also been shown to reduce all-cause mortality and CVD mortality (S N Blair et al., 1995).
Studies have also reported a relationship between CRF and mortality in people with COPD. In a minimum 3 year follow-up of people with COPD, Casanova et al. (2008) found that individuals who died had a significantly lower baseline 6MWT distance when compared to those who were alive at follow-up. The 6MWT distance was also a significant predictor of mortality (Casanova et al., 2008). The distance travelled on the 6MWT was also lower in people with COPD who died compared to those who lived after a 2-year follow-up by Pinto-Plata, Cote, Cabral, Taylor, & Celli (2004). The authors found that fitness was a predictor of survival and mortality decreased with increasing distances achieved on the walk test (Pinto-Plata et al., 2004). VO2 max has also been shown to predict mortality in men with COPD (Oga, Nishimura, Tsukino, Sato, & Hajiro, 2003).

1.9 CRF in people with a psychotic illness

The studies examined in the previous sections have highlighted the importance of CRF as it is associated with chronic diseases such as T2DM, MetSyn, CVD and its associated mortality. However, the vast majority of these studies have not included individuals with a psychotic illness diagnosis (e.g., schizophrenia).

This exclusion is important because the prevalence and risk of T2DM (Bresee et al., 2010; Curkendall et al., 2004; Dickey et al., 2002; Kilbourne et al., 2004) and MetSyn (De Hert et al., 2006; McEvoy et al., 2005) and CVD (Bresee et al., 2010; Curkendall et al., 2004; Dickey et al., 2002) are higher in individuals with a psychotic illness when compared to the general
population. This risk and prevalence can be partially due to the higher prevalence (Allison, Fontaine, et al., 1999; G. L. Daumit et al., 2003) of obesity and higher BMI (Dickerson et al., 2006) in individuals with psychosis compared to the general population. The prevalence of obesity, T2DM and CVD can be caused by modifiable life style factors, such as a lack of exercise (Brown et al., 1999; Gail L. Daumit et al., 2005; Faulkner, Cohn, & Remington, 2006; Janney et al., 2014; Janney et al., 2013), consumption of unhealthy diets (Brown et al., 1999; Osborn et al., 2007), increased caloric intake (Strassnig et al., 2003), higher rates of smoking (Brown et al., 1999; McCreadie, 2003), and the side effects of certain antipsychotics (e.g., olanzapine) which can also contribute to weight gain (Allison, Mentore, et al., 1999). The prevalence of these chronic diseases in individuals with psychosis contributes to the premature mortality experienced by this population (Brown, 1997; Osby et al., 2001; Prior et al., 1996).

Even with the vast information on the comorbidities that occur in individuals with psychosis, the body of literature on CRF for this population is small.

There have been studies mentioned above which measured the levels of daily physical activity in people with psychosis (e.g., schizophrenia, bipolar disorder) and physical activity is a major determinant of CRF; however, the studies of physical activity are often based on self-report and research has found that physical activity is often over estimated by participants who complete those questionnaires (Buchowski, Townsend, Chen, Acra, & Sun, 1999; Walsh, Hunter, Sirikul, & Gower, 2004). CRF, on the other hand, provides an objective measure for physical activity. Differences also exist between levels of reported physical activity and CRF in terms of predicting T2DM risk, CVD risk and mortality.
Sieverdes et al. (2010) examined the association between CRF and self-reported physical activity with T2DM incidence in men. They found an inverse association between physical activity and T2DM incidence; however, this association was no longer significant after adjusting for CRF (J. C. Sieverdes et al., 2010). The authors also found an inverse association between CRF and T2DM incidence and this association remained significant after adjusting for physical activity (J. C. Sieverdes et al., 2010). The risk for T2DM also decreased with increasing CRF in men who also had impaired fasting glucose at baseline (J. C. Sieverdes et al., 2010).

The relationship between CRF and self-reported physical activity with CVD risk has also been examined (John C Sieverdes et al., 2011; Paul T Williams, 2001). In a meta-analysis, Paul T Williams (2001) found that relative risk for CVD decreased with increasing levels of self-reported physical activity and CRF. The risk reduction was significantly greater for physical fitness when compared to physical activity at all percentiles greater than the 25th percentile (Paul T Williams, 2001). John C Sieverdes et al. (2011) examined the relationship between CRF and physical activity with the risk of total (fatal and nonfatal) stroke in men. After adjusting for CRF, there was no longer a significant inverse association between physical activity and total stroke; however, the relationship between CRF and total stroke still remained significant after adjusting for physical activity (John C Sieverdes et al., 2011).

D. C. Lee et al. (2011) examined the association between CRF and physical activity with mortality in both men and women. CRF was inversely associated with mortality in both men and women and this relationship was significant; however, physical activity was only significantly
associated with mortality in men (D. C. Lee et al., 2011). After adjusting for CRF, the relationship between physical activity and mortality was no longer significantly associated in men but the relationship between CRF and mortality still remained significant after physical activity was adjusted for (D. C. Lee et al., 2011). In addition, it was found that men and women had a reduced risk of mortality if they were fit regardless of if they met weekly physical activity recommendations (D. C. Lee et al., 2011).

Physical activity, a determinant of CRF has been measured in individuals with psychosis; however, physical activity is based on self-reported questionnaires and is often over-reported (Buchowski et al., 1999; Walsh et al., 2004). As mentioned above, CRF is a better predictor for mortality (D. C. Lee et al., 2011) as well as T2DM (J. C. Sieverdes et al., 2010) and CVD (John C Sieverdes et al., 2011) risk. Despite its importance on predicting chronic diseases and mortality, few studies have measured CRF in people with psychosis. A literature search utilizing the following terms was used to help identify studies which had assessed CRF on individuals with a psychotic illness: “cardiorespiratory fitness”, “physical fitness”, “6 minute walk test”, “schizophrenia”, “schizoaffective disorder”, “schizophreniform disorder”, “bipolar disorder”, “major depression with psychotic features”, “substance-induced psychosis”, “psychosis not otherwise specified” and “psychosis”. We identified 22 studies using this search strategy. These studies are summarized in Table 1.

The sample size ranged from 8 to 120 participants. All studies included participants with schizophrenia or schizophrenia spectrum disorders. However, only three studies included
individuals with other psychoses (e.g., bipolar disorder) (Abdel-Baki, Brazzini-Poisson, Marois, Letendre, & Karelis, 2013; G. L. Daumit et al., 2011; Heggelund, Nilsberg, Hoff, Morken, & Helgerud, 2011).

The first study to be published measuring CRF using the gold standard VO\textsubscript{2} max assessment was performed by Strassnig, Brar, & Ganguli (2011) in 117 overweight or obese individuals who were diagnosed with schizophrenia. They found that only two of the 117 participants had moderate CRF values when compared to the general population (Strassnig et al., 2011). Other cross-sectional studies that compared VO\textsubscript{2} max in individuals with psychosis versus healthy controls consistently found lower CRF in individuals with psychosis (Heggelund, Hoff, Helgerud, Nilsberg, & Morken, 2011; Nilsson et al., 2012; Ozbulut et al., 2013). Using a treadmill test or cycle ergometer, it was found that VO\textsubscript{2} max ranged from 16.26 ml/kg/min to 37.1ml/kg/min in individuals with psychosis (Heggelund, Hoff, et al., 2011; Nilsson et al., 2012; Ozbulut et al., 2013).

Five cross-sectional studies were identified which examined the differences in CRF between individuals with psychosis and healthy controls utilizing the 6MWT (Beebe, 2006; Vancampfort, Probst, De Herdt, et al., 2013; Vancampfort, Probst, Scheewe, et al., 2011; Vancampfort, Probst, Stubbs, et al., 2013; Vancampfort, Probst, Sweers, et al., 2011a). The study conducted by Beebe (2006) found that individuals achieved a 6MWT distance of 1407 feet (428.85m). Other work found that individuals with schizophrenia achieved a distance on the walk test ranging from 573.5m to 583.6m and this was significantly lower than the distance achieved by healthy controls.
Research has also examined the effect of other diseases on CRF. For example, it was found that obese individuals with schizophrenia had a significantly lower 6MWT distance (450.6m) compared to people with schizophrenia who were overweight (580.2m) and normal weight (615.8m) (Vancampfort, Probst, Sweers, et al., 2011a). In addition, individuals with schizophrenia and MetSyn achieved a significantly lower 6MWT distance (527.6m) compared to people with schizophrenia and no MetSyn (610.0m) (Vancampfort, Sweers, et al., 2011). Last, when examining the effects of T2DM in schizophrenia, it was found that people with T2DM achieved a 6MWT distance of 500.3m and this was significantly lower compared to people with schizophrenia and no T2DM (590.7m) (Vancampfort, De Hert, et al., 2013).

Seven longitudinal studies were identified which examined the effects of exercise interventions on CRF assessed by VO$_2$ max (Abdel-Baki et al., 2013; Dodd, Duffy, Stewart, Impey, & Taylor, 2011; Heggelund, Nilsberg, et al., 2011; Scheewe et al., 2013; Scheewe, Takken, Kahn, Cahn, & Backx, 2012) and the 6MWT (Beebe et al., 2005; G. L. Daumit et al., 2011; Dodd et al., 2011). When measuring the change in VO$_2$ max, two studies (Abdel-Baki et al., 2013; Heggelund, Nilsberg, et al., 2011) found a significant improvements ranging from 12-38%. The studies conducted by Dodd et al. (2011) and Scheewe et al. (2012) also reported increased VO$_2$ max after their exercise intervention; however, these improvements were not significant. The study performed by Scheewe et al. (2013) also found that exercise was able to improve CRF when assessed by the peak work rate.
Three studies also examined the effects of interventions on 6MWT in people with psychosis (Beebe et al., 2005; G. L. Daumit et al., 2011; Dodd et al., 2011). Two of these studies (Beebe et al., 2005; G. L. Daumit et al., 2011) found that the mean 6MWT improved between 104 to 152 feet after the exercise intervention whereas the study conducted by Dodd et al. (2011) did not find improvements in 6MWT.
<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Population diagnosis</th>
<th>Population sample size</th>
<th>Method for assessing CRF</th>
<th>Main findings</th>
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<tr>
<td>Strassnig et al. (2011)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 117</td>
<td>Cycle ergometer using modified Bruce protocol</td>
<td>115 of their participants with schizophrenia diagnosis had low (below the 20th percentile) CRF derived from the Aerobics Center Longitudinal Study.</td>
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<tr>
<td>Heggelund, Hoff, Helgerud, Nilsberg, &amp; Morken (2011)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 33</td>
<td>Treadmill test</td>
<td>VO₂ max was significantly lower in men with schizophrenia compared to control data. People with schizophrenia who were below the VO₂ max threshold for their respective sex, had a higher risk of having at least one CVD risk factor (e.g., hypertension).</td>
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<tr>
<td>Heggelund, Nilsberg, Hoff, Morken, &amp; Helgerud (2011)</td>
<td>Longitudinal</td>
<td>Schizophrenia, schizoaffective disorder, delusional disorder</td>
<td>N = 25</td>
<td>Treadmill test</td>
<td>Significant improvements in VO₂ max (36.0 ± 7.4 ml/kg/min to 40.2 ± 6.6 ml/kg/min) after undergoing a high intensity exercise intervention for 8 weeks. Improvement not observed in the computer game training group.</td>
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<tr>
<td>G. L. Daumit et al. (2011)</td>
<td>Longitudinal</td>
<td>Schizophrenia, schizoaffective disorder, other psychotic diagnosis, bipolar disorder, depression,</td>
<td>N = 63</td>
<td>6MWT</td>
<td>6MWT distance significantly improved from 1358 feet to 1463 feet after the 6 month weight loss intervention. Over 60% of participants improved their 6MWT distance after the intervention. There was also a significant</td>
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<td>Study</td>
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<td>Test</td>
<td>Outcome Description</td>
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<tr>
<td>Beebe et al. (2005)</td>
<td>Longitudinal</td>
<td>Schizophrenia</td>
<td>10</td>
<td>6MWT</td>
<td>Individuals with schizophrenia increased their 6MWT distance after the 16 week exercise intervention from 1412.25 feet to 1564.75 feet. This change in 6MWT distance was greater than the improvement in the control group but not significant. People in the exercise intervention also had a greater reduction in BMI (not significant) and percentage of body fat which was significant.</td>
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<tr>
<td>Beebe (2006)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>11</td>
<td>6MWT</td>
<td>Participants with schizophrenia walked 1407 feet during the 6MWT which was lower than distances from distances obtained from equations designed for in healthy adults.</td>
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<td>Dodd, Duffy, Stewart, Impey, &amp; Taylor (2011)</td>
<td>Longitudinal</td>
<td>Schizophrenia, schizoaffective disorder</td>
<td>8</td>
<td>Submaximal cycle ergometer using YMCA protocol and the 6MWT</td>
<td>Individuals who completed the study had a significant reduction in body weight and BMI; however, there was no significant improvement in VO₂ max or 6MWT after performing exercise intervention for 24 weeks.</td>
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<td>Study</td>
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<td>Martin-Sierra et al. (2011)</td>
<td>Cross-</td>
<td>Schizophrenia, schizoaffective</td>
<td>N = 40</td>
<td>6MWT</td>
<td>Distances achieved on the 6MWT were significantly correlated with the physical health component of quality of life (as measured by the MOS 36-item Short form health survey (SF-36)), levels of physical activity (as measured by the Baecke Physical Activity Questionnaire) and BMI.</td>
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<td>Nilsson et al. (2012)</td>
<td>Cross-</td>
<td>Schizophrenia</td>
<td>N = 20</td>
<td>Submaximal</td>
<td>Significantly lower VO₂ max in individuals with schizophrenia when compared to controls.</td>
</tr>
<tr>
<td></td>
<td>sectional</td>
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<td>exercise test using</td>
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<td></td>
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<td>a cycle ergometer</td>
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<tr>
<td>Scheewe, Takken, Kahn, Cahn, &amp; Backx</td>
<td>Longitudinal</td>
<td>Schizophrenia spectrum disorders</td>
<td>N = 118</td>
<td>Cardiopulmonary</td>
<td>At baseline, healthy controls had a significantly higher VO₂ max when compared to people with schizophrenia. People with schizophrenia assigned to the 6 month exercise intervention did improve CRF; however it was not significant. Individuals with schizophrenia assigned to occupational therapy had a reduction in CRF after the intervention.</td>
</tr>
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<td>(2012)</td>
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<td>exercise test using</td>
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<td></td>
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<td>a cycle ergometer</td>
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<tr>
<td>Vancampfort, Probst, Scheewe, et al.</td>
<td>Cross-</td>
<td>Schizophrenia</td>
<td>N = 100</td>
<td>6MWT</td>
<td>People with schizophrenia had a significantly lower score on the mental health and physical health component of the SF-36, physical activity, and distance achieved on</td>
</tr>
<tr>
<td>(2011)</td>
<td>sectional</td>
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</table>
Individuals with schizophrenia and MetSyn had a lower 6MWT score than people with schizophrenia and no MetSyn. Individuals with schizophrenia had lower 6MWT distances compared to controls. Individuals with schizophrenia who were obese had significantly lower 6MWT distances compared to normal weight and overweight individuals. Individuals with schizophrenia had significantly lower Eurofit test scores on the flamingo balance, plate tapping, sit and reach, shuttle run, and stand broad jump tests. In addition, inactive people with schizophrenia had the poorest Eurofit test scores when compared individuals who were minimally and highly active. People with schizophrenia also had lower levels of physical activity in terms of total minutes of physical activity per week as well as total minutes of moderate and vigorous physical activity and total MET-minutes/week when compared to healthy controls.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Condition</th>
<th>N</th>
<th>Measure</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancampfort, Probst, Sweers, et al. (2011a)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>100</td>
<td>6MWT</td>
<td>the 6MWT compared to healthy controls. Individuals with schizophrenia and MetSyn had a lower 6MWT score than people with schizophrenia and no MetSyn.</td>
</tr>
<tr>
<td>Vancampfort, Probst, Scheewe, et al. (2013)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>120</td>
<td>Eurofit test</td>
<td>Individuals with schizophrenia had lower 6MWT distances compared to controls. Individuals with schizophrenia who were obese had significantly lower 6MWT distances compared to normal weight and overweight individuals. Individuals with schizophrenia had significantly lower Eurofit test scores on the flamingo balance, plate tapping, sit and reach, shuttle run, and stand broad jump tests. In addition, inactive people with schizophrenia had the poorest Eurofit test scores when compared individuals who were minimally and highly active. People with schizophrenia also had lower levels of physical activity in terms of total minutes of physical activity per week as well as total minutes of moderate and vigorous physical activity and total MET-minutes/week when compared to healthy controls.</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Population</td>
<td>Sample Size</td>
<td>Outcome Measures</td>
<td>Findings</td>
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<tr>
<td>Vancampfort, Probst, De Herdt, et al. (2013)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 120</td>
<td>Standing broad jump and 6MWT</td>
<td>Individuals with schizophrenia had a significantly lower standing broad jump, and 6MWT distance when compared to healthy controls.</td>
</tr>
<tr>
<td>Abdel-Baki, Brazzini-Poisson, Marois, Letendre, &amp; Karelis (2013)</td>
<td>Longitudinal</td>
<td>Schizophrenia, schizoaffective disorder, bipolar disorder, psychotic disorder not otherwise specified</td>
<td>N = 25</td>
<td>Treadmill walking test</td>
<td>Individuals with first episode psychosis who completed the 14 week aerobic interval training intervention had a significant decrease in waist circumference, as well as significant improvement in VO2 max by 38%.</td>
</tr>
<tr>
<td>Fogarty and Happell (2005)</td>
<td>Cross-sectional (qualitative study)</td>
<td>Schizophrenia</td>
<td>N = 12 (n = 6 schizophrenia)</td>
<td>Self-report</td>
<td>All participants with schizophrenia reported an improvement in physical fitness after the 3 month exercise program.</td>
</tr>
<tr>
<td>Ozbulut et al. (2013)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 120</td>
<td>Submaximal exercise test using a cycle ergometer</td>
<td>VO2 max was significantly lower in people with schizophrenia when compared to healthy controls.</td>
</tr>
<tr>
<td>Scheewe et al. (2013)</td>
<td>Longitudinal</td>
<td>Schizophrenia, schizoaffective disorder and schizophreniform disorder</td>
<td>N = 63</td>
<td>Cycle ergometer cardiopulmonary exercise test</td>
<td>CRF, measured by peak work rate, significantly improved in people who were assigned to the 6 month exercise intervention compared to individuals who were assigned to occupational therapy. People who received the exercise intervention also significantly improved their CRF from baseline to end point.</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Diagnosis</td>
<td>Sample Size</td>
<td>Measure(s)</td>
<td>Results</td>
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<td>-------------------------------------------</td>
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</tr>
<tr>
<td>Vancampfort et al. (2012)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 93</td>
<td>6MWT</td>
<td>Global assessment of functioning was positively and significantly associated with 6MWT distance. BMI, negative symptoms, depressive, cognitive symptoms and smoking were negatively and significantly associated with 6MWT distance.</td>
</tr>
<tr>
<td>Vancampfort, De Hert, et al. (2013)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 106</td>
<td>6MWT</td>
<td>Individuals with both T2DM and schizophrenia had significantly lower 6MWT distance and levels of reported physical activity when compared to people with schizophrenia and no diabetes.</td>
</tr>
<tr>
<td>Vancampfort, Probst, Stubbs, et al. (2013)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 120</td>
<td>6MWT, Standing broad jump</td>
<td>Individuals with schizophrenia had a significantly lower 6MWT distance, as well as significantly lower forced vital capacity and forced expiratory volume when compared to healthy controls. When compared to healthy controls, people with schizophrenia also had a significantly lower standing broad jump score and levels of physical activity.</td>
</tr>
<tr>
<td>Vancampfort, Sweers, et al. (2011)</td>
<td>Cross-sectional</td>
<td>Schizophrenia</td>
<td>N = 106</td>
<td>6MWT</td>
<td>Individuals with schizophrenia and MetSyn had a significantly lower level of physical activity and distance achieved on the 6MWT.</td>
</tr>
</tbody>
</table>
compared to individuals with schizophrenia and no MetSyn.
Chapter 2
Rationale, Aims and Hypotheses

2 Rationale, Aims and Hypotheses

2.1 Rationale

Low cardiorespiratory fitness (CRF) has been associated with T2DM and CVD risk and is a better predictor for T2DM (J. C. Sieverdes et al., 2010), CVD (John C Sieverdes et al., 2011; Paul T Williams, 2001) as well as mortality (D. C. Lee et al., 2011) when compared to physical activity. As covered in the literature review, research in the general population has also shown protective effects of having a higher CRF on decreasing the risk for chronic diseases and mortality. However, despite the increased risk of T2DM, CVD and mortality in persons with psychotic illnesses such as schizophrenia, the vast majority of studies involving CRF have excluded individuals with this diagnosis. Of the studies which have measured CRF in individuals with a psychotic illness, it remains unclear whether psychosis is further associated with the risk for CVD and mortality in addition to the risk associated with T2DM alone. This is important as T2DM can further put individuals at risk for CVD and mortality. Our study can bridge the gap in knowledge and provide data on this specific population with T2DM and a comorbid psychotic illness. The purpose of this study was to compare CRF in individuals with T2DM and psychotic illness to individuals with T2DM and no psychotic illness. We also compared both groups to physical fitness data published on healthy Canadians.
2.2  Aim #1:

The primary aim was to compare CRF in individuals who are diagnosed with both T2DM and a psychotic illness to individuals diagnosed with T2DM and no psychotic illness.

2.2.1  Hypothesis #1:

It was hypothesized that the individuals with T2DM and a psychotic illness will have a lower 6MWT distance when compared to individuals with T2DM and no comorbid psychotic illness due to their physical inactivity and higher prevalence of smoking.
2.3 Aim #2:

The secondary aim of our study was to compare CRF in both T2DM groups to CRF obtained from data on healthy Canadians. All three groups were matched by sex, BMI and age by decade.

2.3.1 Hypothesis #2:

It was hypothesized that both groups with T2DM will have lower CRF, as represented by the total distance walked on the 6MWT when compared to healthy Canadians.
2.4 Aim #3:

The tertiary aim was to examine the relationship between CRF and physical activity, anthropometrics, quality of life and information obtained from the most recent medical reports regarding glycemic control and lipids in the two T2DM groups.

2.4.1 Hypothesis #3:

It was hypothesized that physical activity would be the best predictor for CRF in our two T2DM groups.
Chapter 3
Research Design and Methods

3  Research Design and Methods

3.1  Study design

Three groups were studied cross-sectionally: 1. Individuals with psychotic illness and T2DM; 2. Individuals with T2DM with no psychotic illness diagnosis and 3. Healthy control data from a published Canadian study (Hill et al., 2011). The comparison between the first two groups of subjects was to determine whether the presence of a psychotic illness was associated with an increased risk for CVD and mortality due to low CRF, beyond that associated with T2DM by itself. The comparisons to previously collected data on healthy Canadians were to verify that there was an adverse effect of T2DM on CRF. CRF was compared across the three groups using the 6MWT following the American Thoracic Society (ATS) protocol. When comparing fitness values between the three groups, we matched for sex, BMI and age by decade. The duration of the study lasted one visit to perform the 6MWT, fill out questionnaires and receive anthropometric measures.

3.2  Recruitment strategy

The healthy control group had been previously studied and we did not obtain any new data for this group. The original data was kindly provided by Hill et al. (2011) with permission to use in
the analysis of this study. We recruited people with T2DM and psychosis from an ongoing randomized control trial for weight loss. People with T2DM and no psychotic illness were recruited from primary care sites for the purpose of this sub study examining CRF.

All participants in the two T2DM groups were first screened through a phone call or in person to ensure they met eligibility criteria. Individuals with T2DM and a psychotic illness were recruited from a clinical trial being performed in our laboratory. Individuals with T2DM and no psychotic illness were recruited using study posters and clinician referrals from diabetes clinics and education programs in Toronto and the Greater Toronto Area.

3.3 Ethics, consent and compensation

The study protocol was approved by the Research Ethics Board at the Centre for Addiction and Mental Health (CAMH) as a sub study within the previously approved randomized control trial protocol for people with T2DM and psychosis. Once recruited, informed consent was obtained from the participants following the procedure approved by the CAMH Research Ethics Board. Participants were compensated for the total time spent performing the study and for transportation costs they had (e.g., TTC tokens).

3.4 Inclusion and exclusion criteria for each study group

3.4.1 Individuals diagnosed with psychotic illness and T2DM

These criteria were determined by the parent study (randomized control trial for weight loss).
Inclusion Criteria

1. Between 18-75 years old (inclusive)
2. DSM-IV-TR diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder, bipolar 1 disorder, major depression with psychotic features, substance-induced psychosis or psychosis not otherwise specified
3. BMI $\geq 25$ kg/m$^2$ at the time of enrollment
4. Documented diagnosis of T2DM in the subject’s medical record
5. Ability to provide informed consent

Exclusion Criteria

1. Inability to provide informed consent
2. Unstable angina and myocardial infarction during the month immediately preceding participation
3. Resting heart rate $> 120$ beats per minute
4. Systolic blood pressure $> 180$ mmHg
5. Diastolic blood pressure $> 100$ mmHg
6. Current enrollment in a weight management program
7. Currently being prescribed medication specifically for weight loss
8. Unstable or active cardiovascular illnesses (myocardial infarction, CHF, etc.), active or end-stage renal disease, unstable thyroid disease, etc.

9. Recurrent episodes of diabetic ketoacidosis, seizure or coma without warning, or severe hypoglycemia

10. Weight > 158.75 kg due to technical limitations in obtaining accurate weights

3.4.2 Individuals diagnosed with T2DM and no psychotic illness

Inclusion Criteria (Comparable to the cohort with psychotic illness)

1. Between 18-75 years old (inclusive)

2. No DSM-IV-TR diagnosis of psychotic illness (i.e. schizophrenia, schizoaffective disorder, schizophreniform disorder, bipolar 1 disorder, major depression with psychotic features, substance-induced psychosis or psychosis not otherwise specified) (based on the current treating clinician’s opinion)

3. BMI $\geq 25$ kg/m$^2$ at the time of enrollment

4. Documented diagnosis of T2DM in the subject’s medical record

5. Ability to provide informed consent

Exclusion Criteria (Comparable to the cohort with psychotic illness)
1. Inability to provide informed consent
2. Current or past psychotic illness
3. Unstable angina or myocardial infarction during the month immediately preceding participation
4. Resting heart rate > 120 beats per minute
5. Systolic blood pressure > 180mm Hg
6. Diastolic blood pressure > 100mm Hg
7. Currently enrolled in a formal structured weight management program
8. Currently being prescribed medication specifically for weight loss
9. Unstable or active cardiovascular illnesses (myocardial infarction, CHF, etc), active or end-stage renal disease, unstable thyroid disease, etc.
10. Recurrent episodes of diabetic ketoacidosis, seizure or coma without warning or severe hypoglycemia
11. Weight > 158.75 kg due to technical limitations in obtaining accurate weights

3.4.3 Data on the healthy Canadian Population (Hill et al., 2011)

Fitness values were already obtained for this group. The data that was provided included 77 healthy Canadians. From the data, participants were identified who were between the ages of 45-75 and had a BMI ≥ 25 kg/m². The healthy control data was used solely for comparing fitness values obtained from the 6MWT, age, BMI and information regarding levels of perceived exertion. In addition to the data that was available on this population, we also calculated the mean 6MWT distance expected for a healthy population using the following predictive equation
obtained from the study by Hill et al. (2011): 6MWT distance = 970.7 + (-5.5 X age) + (56.3 X sex). For sex, a value of 1 was inputted for males and a value of 0 for females (Hill et al., 2011). We compared the mean 6MWT distance expected for a healthy population to the mean 6MWT distance achieved by individuals with T2DM and psychosis.

People in this study had to be between the ages of 45-85 and be able to access Canadian health care (Hill et al., 2011).

People in this study were excluded if they: 1. Were not able to understand English; 2. Were previous or current smokers; 3. Had a history of cardiovascular, respiratory, musculoskeletal or neurological disease; 4. In the previous 4 weeks, had an upper respiratory tract infection; 5. Used β-adrenergic blocking agents 6. Had an air flow obstruction; 7. Used a gait aid; 8. Blood pressure (resting) > 150/100 mm Hg and 9. Heart rate (resting) > 100 beats / minute (Hill et al., 2011).

3.5 Variables collected

In the two T2DM groups, we collected information regarding demographics, anthropometrics, physical activity, physical fitness, levels of perceived exertion, tolerability of the 6MWT, quality of life and information from medical reports.
3.5.1 Demographics

A demographic questionnaire developed by the laboratory was used to collect information on age, sex, ethnicity, marital status, number of children, living situation, education, employment status, psychiatric diagnosis, age of first psychiatric diagnosis, number of psychiatric hospitalizations, number of medical hospitalizations, smoking status, current psychotropic medications, concomitant medications, previous psychotropic medications, other physical medical comorbidities, current alcohol/substance use, blood pressure and heart rate.

3.5.2 Determination of psychotic illness and confirmation of T2DM

Medical records were used to confirm diagnosis of psychotic illness for participants with T2DM and psychosis. Study participants who were not clients of CAMH were asked for permission to verify their psychiatric diagnosis through their psychiatrist. Diabetes diagnosis in both groups T2DM was confirmed through the participants’ family physicians. Absence of a psychotic illness for people with T2DM and no psychosis was confirmed by the participant’s family physician.

3.5.3 Anthropometrics

Weight and height were measured using a scale and a wall stadiometer and data on waist and hip circumference was collected using measuring tape. Body mass index was calculated by dividing body weight (measured in kg) by the height (measured in squared meters).
3.5.4 Physical activity measurements

Information regarding physical activity was collected using the International Physical Activity Questionnaire (IPAQ) and the Clinical Assessment for Physical Activity (CAPA). The IPAQ collects information regarding the number of days and total time spent performing vigorous and moderate exercises as well as the number of days and time spent walking during the previous week (Craig et al., 2003). In addition, the IPAQ collects information on time spent sitting on a weekday (Craig et al., 2003) and has been validated in individuals with schizophrenia (Faulkner et al., 2006). This questionnaire was scored to generate the total number of MET-minutes of physical activity achieved per week (Craig et al., 2003). The number of days performing vigorous, moderate and walking physical activity was multiplied by the total time (minutes) spent each day performing those exercises and the Metabolic Equivalent value assigned to that activity (vigorous = 8 MET, moderate = 4 MET and walking = 3.3 MET) (Craig et al., 2003).

The CAPA questionnaire is derived from the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD) (Washburn, Zhu, McAuley, Frogley, & Figoni, 2002). Similar to the IPAQ, the CAPA questionnaire gathers information regarding physical activity over the last 7 days (Washburn et al., 2002). It collects information regarding total time spent walking, performing light sport or recreational activity, moderate or vigorous sport and recreation activities, exercises to increase muscle strength and endurance, as well as physical activity achieved when performing house work, home repairs, yard care, taking care of another person as well as physical activity at work or volunteering (Washburn et al., 2002). In addition, the CAPA
questionnaire collects information for the total time spent performing stationary activities (Washburn et al., 2002). Scoring the CAPA questionnaire is similar to the PASIPD. Each item has a fixed value which is multiplied by a factor that is determined by the number of days spent performing a certain physical activity and by the time spent each day performing that physical activity.

3.5.5 Physical fitness

Physical fitness was assessed using the 6MWT following the ATS protocol ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002). We selected this field test as people with psychosis are very sedentary and might not have the ability to exercise for long periods of time set out by other field tests, such as the Cooper 12 minute run test (Cooper, 1968). The 6MWT has also been shown to be reliable in this population (Vancampfort, Probst, Sweers, et al., 2011b).

Participants were asked to follow the proper preparation recommended by the ATS protocol such as wearing light comfortable clothing ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002). Before each walk test, we checked for any medical contraindications to ensure the test was safe for our participants to complete ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002). Participants performed the 6MWT two times on their visit to CAMH with the higher distance travelled being used for data analysis. Since two walk tests were performed, participants were provided with a
60 minute rest in between. Participants were asked to walk back and forth around two orange fluorescent cones approximately 30 meters apart as fast as possible for 6 consecutive minutes. They were allowed to stop and rest if needed. The number of laps and the distance for the final partial lap was recorded. All distance measurements were made by a trundle wheel and a timer was used to count down 6 minutes with instructions being told to the participant after each minute as instructed by the ATS protocol ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002). After each walk test was completed, participants were asked why they stopped walking (if applicable) and if they experienced any angina, dizziness, hip, leg or calf pain ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002). They were also asked “What, if anything kept you from walking farther” ("American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test," 2002).

This field test has previously been shown to be reliable in this population (Vancampfort, Probst, Sweers, et al., 2011b) and 6MWT distances have been significantly correlated with VO2 max in various populations (Cahalin, Mathier, Semigran, Dec, & Disalvo, 1996a; Cote et al., 2007; Ross et al., 2010). 6MWT data on healthy Canadians was also available (Hill et al., 2011).

### 3.5.6 Perceived exertion

Perceived exertion was measured using the Borg Scale (Borg, 1982). Participants were asked to rate their dyspnea and fatigue before and after each walk test on a scale from 0 – 10 where 0 = Nothing at all and 10 = Very, very severe (Maximal) (Borg, 1982).
3.5.7  Tolerability of the 6MWT

To measure how each walk test was tolerated for people with T2DM, we read out the statement “I had no difficulty performing this walk test” and asked a subsample of our participants to rate the statement on a 5 point likert scale where 1 = Completely Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree and 5 = Completely Agree.

3.5.8  Quality of life

Quality of life was assessed using the short form health survey (SF-12) which measures quality of life for both physical and mental health (Ware, Kosinski, & Keller, 1996). The SF-12 provides information regarding how much physical or mental health limits daily activities such as accomplishing work or climbing several flights of stairs (Ware et al., 1996) and has also been validated and shown to be reliable for people with mental illness (Salyers, Bosworth, Swanson, Lamb-Pagone, & Osher, 2000).

3.5.9  Measures of lipids and glycemic control

We used the most recent laboratory results from the participants’ medical records or communication from their primary care physician to collect information on glycemic control (e.g., fasting glucose and HbA1c) as well as information on lipid profiles (e.g., HDL-cholesterol, LDL-cholesterol and triglycerides).
3.6 Positive and negative symptoms

Positive and negative symptoms were assessed solely in the group of individuals with T2DM and a psychotic illness. Positive symptoms were assessed using the Brief Psychiatric Rating Scale (BPRS) which examines severity for somatic concern, anxiety, depression, guilt, hostility, grandiosity, suspiciousness, hallucinations, unusual thought content, conceptual disorganization, blunted affect, emotional withdrawal, motor retardation, tension, uncooperativeness as well as mannerisms and posturing (Overall & Gorham, 1962). Each item was scored on a scale from 0 to 7, where 0 = not assessed, 1 = not present, 2 = very mild, 3 = mild, 4 = moderate, 5 = moderately severe, 6 = severe, and 7 = extremely severe (Overall & Gorham, 1962).

Negative symptoms were assessed using the Scale for the Assessment of Negative Symptoms (SANS) which assesses the severity of affect flattening or blunting, alogia, avolition-apathy, anhedonia-asociality, and attention (Andreasen, 1984). Each of these five categories contain questions to assess each item where every question is scored on a scale from 0 to 5. Zero represents the symptoms not being present, 1 = questionable, 2 = mild, 3 = moderate, 4 = marked and 5 = severe (Andreasen, 1984).

Scoring for the BPRS and SANS was accomplished by adding the scores for each subcomponent.
3.7 Statistical analyses and sample size calculation

3.7.1 Sample size calculation

This is a pilot study and we have limited data on which to base power and sample size calculations. Thus, we aimed to recruit at least 20 participants in each T2DM group based on practical recruitment targets within the time frame of the Institute of Medical Science Master’s program. Descriptive statistics on the data from this study will allow us to estimate the effect size for future definitive studies.

3.7.2 Statistical analyses

An analysis of variance (ANOVA) test was used when comparing age, BMI and 6MWT distances among the three groups. Bonferroni post-hoc analysis was used to determine if there were statistically significant differences between two groups for these variables (e.g., group 1 compared with group 2; group 1 compared with group 3; and group 2 compared with group 3). An analysis of co-variance was used to determine the effect of BMI on 6MWT distance between the three groups. An independent samples T-Test was used to determine differences in the 6MWT distance for people with T2DM and psychosis compared to the 6MWT distance obtained from the predictive equation. An independent samples T-Test was also used to determine if there were statistically significant differences between the two T2DM groups in terms of levels of reported physical activity, anthropometrics, quality of life and measures of lipids and glycemic control. A paired T-Test was utilized to examine changes in distance from the first to second
walk test as well as changes in exertion (e.g., dyspnea and fatigue) before and after the best walk test. With the exception for examining the change in 6MWT distance from trial 1 to trial 2, all analysis involving the 6MWT distance was performed using the greater distance of the two trials. We also used Pearson correlation analysis to examine possible correlations between 6MWT distance, physical fitness, quality of life, physical activity measures, anthropometrics and information from medical reports in the two T2DM groups. Lastly, within the two groups with T2DM, multiple regression was employed to identify the best predictors of CRF using the 6MWT. SPSS version 15.0 software was used to analyze the data.
Chapter 4
Results

4 Results

4.1 Participant recruitment flow chart

Individuals with T2DM and a psychotic illness were enrolled in a clinical trial in our laboratory. At baseline, 41 participants were approached to participate in this study involving the 6MWT. Data from 23 individuals, between the ages of 45-75 was used in the analysis (Figure 4).

Sixty-nine individuals with T2DM and no psychotic illness were screened through a telephone interview and data from 20 participants in this group was ultimately used in the analysis (Figure 5).

From the control data of healthy Canadians, we identified 25 participants who met our study eligibility criteria and were thus included in the data analysis (Figure 6). As we did not recruit this group, we did not have information regarding how many people were screened or withdrew consent.
Figure 4. Recruitment flow chart for people with T2DM and psychosis.
Figure 5. Recruitment flow chart for people with T2DM and no psychosis.
Figure 6. Recruitment flow chart for healthy controls.

- Obtained healthy control data (n = 77)
- Fifty two participants were excluded for not meeting eligibility criteria
- Twenty five participants met inclusion criteria: ages 45 - 75 and BMI > 25kg/m²
- Twenty five participants included in data analysis after matching age by decade
4.2 Demographic data

Information regarding demographics (e.g., age, age of first psychiatric diagnosis, sex, ethnicity, psychiatric diagnosis, marital status, children, living situation, education, employment, number of psychiatric hospitalizations, number of medical hospitalizations and smoking status) for participants can be found in table 2. The demographic variables were driven by the group comprised of individuals with T2DM and psychosis.

There were more current and past smokers in the group comprised of people with psychosis and T2DM in comparison to those without psychosis. In addition, individuals with psychosis were less educated and had a higher prevalence of unemployment.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>T2DM and Psychotic Illness (n = 23)</th>
<th>T2DM and no Psychotic Illness (n = 20)</th>
<th>Healthy Controls (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years): mean (± SD)</strong></td>
<td>54.30 (± 6.81)</td>
<td>59.75 (± 7.62)</td>
<td>59.12 (± 9.40)</td>
</tr>
<tr>
<td><strong>Age of first psychiatric diagnosis (years): mean (± SD)</strong></td>
<td>25.14 (± 5.70)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td>13 (56.5%)</td>
<td>7 (35.0%)</td>
<td>15 (60.0%)</td>
</tr>
<tr>
<td>Male</td>
<td>10 (43.5%)</td>
<td>13 (65.0%)</td>
<td>10 (40.0%)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity, n (%)</strong></td>
<td>0</td>
<td>1 (5.0%)</td>
<td>-</td>
</tr>
<tr>
<td>Aboriginal</td>
<td>3 (13%)</td>
<td>2 (10%)</td>
<td>-</td>
</tr>
<tr>
<td>Black</td>
<td>0</td>
<td>1 (5.0%)</td>
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</tr>
<tr>
<td>Chinese</td>
<td>0</td>
<td>1 (5.0%)</td>
<td>-</td>
</tr>
<tr>
<td>Filipino</td>
<td>0</td>
<td>1 (5.0%)</td>
<td>-</td>
</tr>
<tr>
<td>Latin American</td>
<td>0</td>
<td>1 (5.0%)</td>
<td>-</td>
</tr>
<tr>
<td>South Asian</td>
<td>3 (13%)</td>
<td>4 (20.0%)</td>
<td>-</td>
</tr>
<tr>
<td>White</td>
<td>14 (60.9%)</td>
<td>9 (45.0%)</td>
<td>-</td>
</tr>
<tr>
<td>Other</td>
<td>3 (13%)</td>
<td>1 (5.0%)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Diagnosis, n (%)</strong></td>
<td>0</td>
<td>1 (5.0%)</td>
<td>-</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>n</td>
<td>(%)</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-----</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>9</td>
<td>39.1</td>
<td></td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>5</td>
<td>21.7</td>
<td></td>
</tr>
<tr>
<td>Bipolar 1 disorder</td>
<td>6</td>
<td>26.1</td>
<td></td>
</tr>
<tr>
<td>MDD with psychosis</td>
<td>2</td>
<td>8.7</td>
<td></td>
</tr>
<tr>
<td>Substance induced psychosis</td>
<td>1</td>
<td>4.3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marital Status, n (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Married or living with someone as if married</td>
<td>2 (8.7%)</td>
<td>6 (30.0%)</td>
</tr>
<tr>
<td>Widowed</td>
<td>0</td>
<td>4 (20.0%)</td>
</tr>
<tr>
<td>Divorced or annulled</td>
<td>7 (30.4%)</td>
<td>4 (20.0%)</td>
</tr>
<tr>
<td>Separated</td>
<td>3 (13.0%)</td>
<td>1 (5.0%)</td>
</tr>
<tr>
<td>Never married</td>
<td>11 (47.8%)</td>
<td>5 (25.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Children, n (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>10 (43.5%)</td>
<td>11 (55.0%)</td>
</tr>
<tr>
<td>No</td>
<td>13 (56.5%)</td>
<td>9 (45.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Living Situation, n (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Live alone in private dwelling</td>
<td>8 (34.8%)</td>
<td>11 (55.0%)</td>
</tr>
<tr>
<td></td>
<td>Education, $n$ (%)</td>
<td>Employment, $n$ (%)</td>
</tr>
<tr>
<td>--------------------------------------</td>
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<td>---------------------</td>
</tr>
<tr>
<td>Live with spouse and children in private dwelling</td>
<td>2 (8.7%)</td>
<td>8 (40.0%)</td>
</tr>
<tr>
<td>Live with parents in private dwelling</td>
<td>1 (4.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Rooming or boarding home or supportive housing</td>
<td>12 (52.2%)</td>
<td>1 (5.0%)</td>
</tr>
<tr>
<td>Education, $n$ (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 7 to 12 without graduating</td>
<td>8 (34.8%)</td>
<td>2 (5.0%)</td>
</tr>
<tr>
<td>Graduated high school or high school equivalent</td>
<td>7 (30.4%)</td>
<td>5 (25.0%)</td>
</tr>
<tr>
<td>Part college / university</td>
<td>5 (21.7%)</td>
<td>2 (10.0%)</td>
</tr>
<tr>
<td>Graduated 2 year college</td>
<td>3 (13.0%)</td>
<td>6 (30.0%)</td>
</tr>
<tr>
<td>Graduated 4 year undergraduate</td>
<td>0</td>
<td>4 (20.0%)</td>
</tr>
<tr>
<td>Completed graduate / professional school</td>
<td>0</td>
<td>1 (5.0%)</td>
</tr>
<tr>
<td>Employment, $n$ (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed full time</td>
<td>0</td>
<td>6 (30.0%)</td>
</tr>
<tr>
<td>Employed part time</td>
<td>1 (4.3%)</td>
<td>2 (10.0%)</td>
</tr>
<tr>
<td>Employed casually</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Smoking Status, n (%)</td>
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<td>-----------------------</td>
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</tr>
<tr>
<td>Unemployed</td>
<td>22 (95.7%)</td>
<td>12 (60.0%)</td>
</tr>
<tr>
<td>Number of psychiatric hospitalizations, n ( % )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 (4.3%)</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>2 (8.7%)</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>5 (21.7%)</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>1 (4.3%)</td>
<td>-</td>
</tr>
<tr>
<td>5 or more</td>
<td>14 (60.9%)</td>
<td>-</td>
</tr>
<tr>
<td>Number of medical hospitalizations, n (%)</td>
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<td></td>
</tr>
<tr>
<td>0</td>
<td>7 (30.4%)</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>8 (34.8%)</td>
<td>4 (20.0%)</td>
</tr>
<tr>
<td>2</td>
<td>2 (8.7%)</td>
<td>3 (15.0%)</td>
</tr>
<tr>
<td>3</td>
<td>2 (8.7%)</td>
<td>1 (5.0%)</td>
</tr>
<tr>
<td>4</td>
<td>1 (4.3%)</td>
<td>2 (10.0%)</td>
</tr>
<tr>
<td>5 or more</td>
<td>3 (13.0%)</td>
<td>10 (50.0%)</td>
</tr>
<tr>
<td></td>
<td>T2DM and psychotic illness</td>
<td>T2DM and no psychotic illness</td>
</tr>
<tr>
<td>----------------</td>
<td>-----------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Smoker</td>
<td>11 (47.8%)</td>
<td>4 (20.0%)</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>7 (30.4%)</td>
<td>13 (65.0%)</td>
</tr>
<tr>
<td>Previous smoker</td>
<td>5 (21.7%)</td>
<td>3 (15.0%)</td>
</tr>
</tbody>
</table>

**Table 2.** Demographic information for people with T2DM and a comorbid psychotic illness, T2DM and no comorbid psychotic illness as well as healthy control data.
There was no significant difference in age between the 3 groups (Figure 7). The mean BMI for people with T2DM and psychosis was 34.41 (± 5.24) kg/m², for people with T2DM and no psychosis, the mean BMI was 32.58 (± 4.73) kg/m² and 28.32 (± 2.93) kg/m² for the healthy controls. BMI was significantly lower for healthy controls when compared to the two T2DM groups (p < 0.01) (Figure 8). The BMI difference between the two T2DM groups was not significant.
Figure 7. Mean age between people with T2DM and psychosis, T2DM and no psychosis as well as healthy control data.
Figure 8. Mean BMI between people with T2DM and psychosis, T2DM and no psychosis as well as healthy control data. * p < 0.01.
4.3 Primary and secondary aims and hypotheses

Aim #1:

The primary aim was to compare CRF in individuals who are diagnosed with both T2DM and a psychotic illness to individuals diagnosed with T2DM and no psychotic illness.

Hypothesis #1:

It was hypothesized that the individuals with T2DM and a psychotic illness will have a lower 6MWT distance when compared to individuals with T2DM and no comorbid psychotic illness due to their physical inactivity and higher prevalence of smoking.

Aim #2:

The secondary aim of our study was to compare CRF in both T2DM groups to CRF obtained from data on healthy Canadians. All three groups were matched by sex, BMI and age by decade.

Hypothesis #2:

It was hypothesized that both groups with T2DM will have lower CRF, as represented by the total distance walked on the 6MWT when compared to healthy Canadians.
Individuals with T2DM and comorbid psychosis achieved a distance of 469.93 (± 65.17) m on the 6MWT. Individuals with T2DM and but no comorbid psychosis walked a distance of 550.61 (± 84.59) m and the healthy controls walked a distance of 643.56 (± 82.54) m. As hypothesized, individuals with T2DM and a comorbid psychotic illness had a lower 6MWT when compared to people with T2DM alone and this difference was statistically significant (p < 0.01). We computed the effect size of the difference in mean 6MWT results between the subjects with and without psychosis and found an effect size of “1” which, by convention would be considered a large effect (Cohen’s d = -1.07; r = -.472) (Cohen, 1992). People with psychosis also had a significantly lower distance walked when compared to healthy controls (p < 0.01). The healthy control group achieved a significantly higher distance on the walk test when compared to individuals with T2DM and no psychosis (p < 0.01). The results are displayed on figure 9. Individuals with psychosis and T2DM also had a significantly lower 6MWT distance (469.93 (± 65.17) m) compared to values expected for a healthy population of the same age and sex determined from the predictive equation (703.85 (± 42.36) m) (p < 0.01).

Since BMI was significantly higher for people with T2DM, we performed an analysis of covariance to determine the possible effects of BMI on 6MWT distance. We found that after adjusting for BMI, the differences between these groups still remained significant (p < 0.01).
Figure 9. Mean 6MWT distance between people with T2DM and psychosis (469.93 (± 65.17) m), T2DM and no psychosis (550.61 (± 84.59) m) as well as healthy control data (643.56 (± 82.54) m). * p < 0.01.
4.4 Sex differences for fitness, BMI and age

Next we examined the effects of sex on physical fitness. First, we analyzed our entire sample (e.g., all three groups) to examine whether differences existed in CRF between males and females. Males achieved a 6MWT distance of 578.73 (± 103.11) m and females walked 534.97 (± 106.28) m during the 6 minutes; however, this difference was not significant. Males in the entire sample were also older and had a slightly higher BMI when compared to females but these differences were not significant. We also examined the differences in these three variables between males and females in each group individually. For individuals with T2DM (with and without psychosis), there was no significant difference between males and females for age and BMI. Males in the healthy control group had a significantly higher age (p = 0.016) and BMI (p < 0.01) compared to females. The differences in each group between males and females for 6MWT distances are displayed in figure 10-12. In all three groups, males achieved a higher mean 6MWT compared to females; however, this was only significant for individuals with T2DM and no psychotic illness (p < 0.05).
Figure 10. Mean 6MWT distance for males (489.93 ± 49.43 m) and females (443.93 ± 76.13 m) for people with T2DM and a psychotic illness.
Figure 11. Mean 6MWT distance for males (604.11 ± 77.25 m) and females (521.80 ± 76.01 m) for people with T2DM and no psychotic illness. * p < 0.05.
**Figure 12.** Mean 6MWT distance for males (643.84 ± 94.77 m) and females (643.15 ± 64.80 m) for healthy Canadians.
4.5 Effects of smoking status on 6MWT distance

We found that there were no significant differences in 6MWT between current smokers, previous smokers and non-smokers for people with psychosis (Figure 13) and without psychosis (Figure 14).
Figure 13. Mean 6MWT distance for smokers, previous smokers and non-smoking individuals with T2DM and psychosis.
**Figure 14.** Mean 6MWT distance for smokers, previous smokers and non-smoking individuals with T2DM and no psychosis.
4.6 Difference between two walk test distances and change in Borg scale variables

Since two walk tests were performed for our participants, we also examined the change in distance travelled as well as changes in dyspnea and fatigue measured by the Borg Scale. Figures 15-17 show the change in 6MWT distance in the three groups from trial 1 to trial 2. There was a significant increase for distance walked from the first to the second walk test in both T2DM groups (p < 0.05) and healthy controls (p < 0.01). We also examined the changes in variables measured from the Borg Scale before and after completing the best 6MWT in the three groups. There was a significant increase in the reported levels of dyspnea (p < 0.01) and fatigue (p < 0.05) in all three groups. The means (± SD) are listed in table 3 and table 4.
Figure 15. Distance achieved on the 6MWT during trial 1 and trial 2 for people with T2DM and psychosis. * p < 0.05
Figure 16. Distance achieved on the 6MWT during trial 1 and trial 2 for people with T2DM and no psychosis. * p < 0.05
Figure 17. Distance achieved on the 6MWT during trial 1 and trial 2 for healthy controls. *p < 0.01
<table>
<thead>
<tr>
<th></th>
<th>Borg Scale Dyspnea before best 6MWT</th>
<th>Borg Scale Dyspnea after best 6MWT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2DM and Psychotic Illness</td>
<td>0.67 (± 0.86)</td>
<td>1.89 (± 1.42)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>T2DM and no Psychotic Illness</td>
<td>0.50 (± 0.81)</td>
<td>2.05 (± 1.23)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>0.20 (± 0.10)</td>
<td>1.72 (± 1.04)</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

**Table 3.** Changes in dyspnea before and after the best 6MWT for all three groups.
<table>
<thead>
<tr>
<th></th>
<th>Borg Scale Fatigue before best 6MWT</th>
<th>Borg Scale Fatigue after best 6MWT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2DM and Psychotic Illness</td>
<td>1.22 (± 1.23)</td>
<td>1.78 (± 1.37)</td>
<td>0.014</td>
</tr>
<tr>
<td>T2DM and no Psychotic Illness</td>
<td>0.50 (± 0.74)</td>
<td>1.87 (± 1.23)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>0.10 (± 0.29)</td>
<td>1.34 (± 1.25)</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

Table 4. Changes in fatigue before and after the best 6MWT for all three groups.
4.7 Tolerability of 6MWT

In a subset of individuals with T2DM (n = 5) (Groups 1 and 2), we also assessed the tolerability of the 6MWT when read the statement “I had no difficulty performing the walk test”. Results for each group are presented in table 5.
<table>
<thead>
<tr>
<th>Response, n (%)</th>
<th>T2DM and Psychotic Illness (n = 2)</th>
<th>T2DM and no Psychotic Illness (n = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completely disagree</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Disagree</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutral</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Agree</td>
<td>1 (50.0%)</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Completely agree</td>
<td>1 (50.0%)</td>
<td>2 (66.7%)</td>
</tr>
</tbody>
</table>

**Table 5.** Tolerability of the 6MWT in people T2DM and psychosis as well as people with T2DM and no psychosis.
4.8 Correlations

4.8.1 Correlation matrix for people with T2DM

We examined the correlation between the age, BMI, height, weight, waist circumference, hip circumference, IPAQ scores, CAPA scores and quality of life (mental and physical health data from SF-12) variables that were collected in the two T2DM groups. There was a strong correlation between IPAQ and CAPA ($r = 0.658$, $p < 0.001$). The Pearson correlation coefficients are listed in table 6. Bold values indicate statistical significance ($p < 0.05$).
<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>BMI</th>
<th>Height</th>
<th>Weight</th>
<th>Waist Circumference</th>
<th>Hip Circumference</th>
<th>IPAQ</th>
<th>CAPA</th>
<th>SF-12 Physical Health component</th>
<th>SF-12 Mental Health component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.252</td>
<td>-0.276</td>
<td>-0.345</td>
<td>-0.236</td>
<td>-0.193</td>
<td>0.174</td>
<td>0.208</td>
<td>0.117</td>
<td>0.316</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>-0.252</td>
<td>-0.030</td>
<td>0.747</td>
<td>0.841</td>
<td>0.853</td>
<td>0.068</td>
<td>-0.016</td>
<td>-0.205</td>
<td>-0.026</td>
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</tr>
<tr>
<td>Height</td>
<td>-0.276</td>
<td>0.030</td>
<td>-0.673</td>
<td>0.373</td>
<td>0.079</td>
<td>0.249</td>
<td>0.100</td>
<td>0.145</td>
<td>0.052</td>
<td></td>
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<tr>
<td>Weight</td>
<td>-0.345</td>
<td>0.747</td>
<td>0.673</td>
<td>-0.864</td>
<td>0.690</td>
<td>0.214</td>
<td>0.069</td>
<td>-0.048</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>-0.236</td>
<td>0.841</td>
<td>0.373</td>
<td>0.864</td>
<td>-0.743</td>
<td>0.101</td>
<td>0.073</td>
<td>-0.204</td>
<td>-0.013</td>
<td></td>
</tr>
<tr>
<td>Hip Circumference</td>
<td>-0.193</td>
<td>0.853</td>
<td>0.079</td>
<td>0.690</td>
<td>0.743</td>
<td>-0.013</td>
<td>0.067</td>
<td>-0.297</td>
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<tr>
<td>IPAQ</td>
<td>0.174</td>
<td>0.068</td>
<td>0.249</td>
<td>0.214</td>
<td>0.101</td>
<td>0.013</td>
<td>-</td>
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<td>0.267</td>
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<tr>
<td>CAPA</td>
<td>0.208</td>
<td>-0.016</td>
<td>0.100</td>
<td>0.069</td>
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<td>0.067</td>
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<td>SF-12 Physical Health component</td>
<td>SF-12 Mental Health component</td>
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<td>0.054</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.054</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Correlation matrix for variables collected in the two T2DM groups. Bold values indicate statistical significance (p < 0.05).
4.8.2 Correlates of CRF for people with T2DM

When examining correlations with the best 6MWT, Pearson correlation analysis revealed significant negative correlations between 6MWT distance and BMI and hip and waist circumference and well as significant positive correlations between IPAQ and the physical health component of the quality of life questionnaire. The strongest correlation was found between the 6MWT and the physical health component of the SF-12 ($r = 0.461$, $p = 0.002$). The correlation coefficients and p-values between the best 6MWT distance, age, BMI, height, weight, waist circumference, hip circumference, IPAQ, CAPA, quality of life, glycemic control and lipids are listed in table 7.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Best 6MWT distance</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.159</td>
<td>0.309</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.339</td>
<td><strong>0.026</strong></td>
</tr>
<tr>
<td>Height</td>
<td>0.251</td>
<td>0.104</td>
</tr>
<tr>
<td>Weight</td>
<td>-0.093</td>
<td>0.553</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>-0.316</td>
<td><strong>0.039</strong></td>
</tr>
<tr>
<td>Hip Circumference</td>
<td>-0.311</td>
<td><strong>0.042</strong></td>
</tr>
<tr>
<td>IPAQ</td>
<td>0.312</td>
<td><strong>0.042</strong></td>
</tr>
<tr>
<td>CAPA</td>
<td>0.286</td>
<td>0.063</td>
</tr>
<tr>
<td>SF-12 Physical Health component</td>
<td>0.461</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>SF-12 Mental Health Component</td>
<td>0.206</td>
<td>0.190</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>0.272</td>
<td>0.109</td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.031</td>
<td>0.852</td>
</tr>
<tr>
<td></td>
<td>Correlation Coefficient</td>
<td>p-value</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-0.078</td>
<td>0.652</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>-0.247</td>
<td>0.146</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>0.229</td>
<td>0.187</td>
</tr>
</tbody>
</table>

Table 7. Correlation coefficients between the best 6MWT distance and variables collected in the two T2DM groups. Bold values indicate statistical significance.
4.8.3 Correlates of CRF with data from the BPRS and SANS for people with T2DM and psychosis

Symptoms, such as a decreased motivation may be present in individuals with psychosis and therefore affect distance achieved on the 6MWT. Thus, we also examined correlations between positive and negative symptoms with the 6MWT in people with T2DM and psychosis. There was a negative correlation between the BPRS and the 6MWT as well as between the SANS and the 6MWT; however, these correlations were not significant. We performed a Pearson correlation between the 6MWT distance and the Avolition-Apathy subcomponent of the SANS. There was a negative correlation between these two variables; however, it was not significant. The correlation coefficients and p-values are listed in table 8.

<table>
<thead>
<tr>
<th></th>
<th>Best 6MWT distance</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPRS</td>
<td>-0.248</td>
<td>0.254</td>
</tr>
<tr>
<td>SANS</td>
<td>-0.194</td>
<td>0.374</td>
</tr>
<tr>
<td>Avolition-Apathy subcomponent of SANS</td>
<td>-0.183</td>
<td>0.403</td>
</tr>
</tbody>
</table>

Table 8. Correlation coefficients between BPRS, SANS and avolition apathy subcomponent of the SANS with the best 6MWT distance in people with T2DM and psychosis.
4.9 Aim and hypothesis #3

Aim #3:
The tertiary aim was to examine the relationship between CRF and physical activity, anthropometrics, quality of life and information obtained from the most recent medical reports regarding glycemic control and lipids in the two T2DM groups.

Hypothesis #3:
It was hypothesized that physical activity would be the best predictor for CRF in our two T2DM groups.

We employed two models of regression to determine the best predictors of physical fitness for participants with T2DM. Two regression models were employed as we assessed physical activity through two self-report questionnaires, the IPAQ and CAPA, and wanted to examine if one of these two self-report physical activity questionnaires was a better predictor for CRF in people with T2DM. We included variables in both models which are modifiable or non-modifiable factors for CRF. Model one included age, sex, BMI, IPAQ, quality of life (SF-12), smoking status and study group (e.g., diabetic individuals with and without psychosis). Model two included age, sex, BMI, CAPA, quality of life (SF-12), smoking status and study group. In both models, study group was the best predictor with a large beta (Model 1: beta = 0.573, B = 96.807 \( p > 0.01 \); Model 2: beta = 0.619, B = 104.67, \( p < 0.01 \)). Therefore, we performed the regression...
in each model without including the study group to further explore the potential effect of other predictors across the entire cohort of people with T2DM.

In all people with T2DM in model 1 ($R^2 = 0.531$), the best predictors for fitness were age, BMI, and the physical health component of quality of life and physical activity measured by the IPAQ ($p < 0.05$) (Table 9). In model 2 ($R^2 = 0.530$), the best predictors for fitness were age, BMI, the physical health component of quality of life and physical activity assessed by the CAPA questionnaire ($p < 0.05$) (Table 10). Both the IPAQ and CAPA performed well as predictors for CRF in people with T2DM.

In another exploratory analysis, we examined if waist circumference was a predictor for CRF. Waist circumference was not included in the models in tables 9 and 10 as it was significantly correlated with BMI. In model 1 (age, sex, waist circumference, IPAQ, quality of life (SF-12) and smoking status; $R^2 = 0.520$), the best predictors for CRF were age (beta = -0.429, $p < 0.01$), waist circumference (beta = -0.376, $p < 0.01$), physical activity (beta = 0.277, $p < 0.05$) and the physical health component of the SF-12 (beta = 0.281, $p < 0.05$). In model 2 (age, sex, waist circumference, CAPA, quality of life (SF-12) and smoking status; $R^2 = 0.517$), the best predictors for CRF in people with T2DM were age (beta = -0.418, $p < 0.01$), waist circumference (beta = -0.340, $p < 0.05$) and the physical health component of the quality of life measure (beta = 0.305, $p < 0.05$).
<table>
<thead>
<tr>
<th>Model 1</th>
<th>Unstandardized Coefficients</th>
<th>Standardized coefficients</th>
<th>t</th>
<th>P – value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Standard Error</td>
<td>Beta</td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>782.34</td>
<td>137.37</td>
<td>5.69</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Age</td>
<td>-5.06</td>
<td>1.48</td>
<td>-0.45</td>
<td>-3.42</td>
</tr>
<tr>
<td>Sex</td>
<td>-5.04</td>
<td>22.69</td>
<td>-0.03</td>
<td>-0.22</td>
</tr>
<tr>
<td>BMI</td>
<td>-6.29</td>
<td>2.12</td>
<td>-0.38</td>
<td>-2.97</td>
</tr>
<tr>
<td>IPAQ</td>
<td>0.01</td>
<td>0.005</td>
<td>0.29</td>
<td>2.25</td>
</tr>
<tr>
<td>SF12 – Physical health component</td>
<td>2.38</td>
<td>1.01</td>
<td>0.31</td>
<td>2.34</td>
</tr>
<tr>
<td>SF12 – Mental health component</td>
<td>1.74</td>
<td>1.01</td>
<td>0.22</td>
<td>1.73</td>
</tr>
<tr>
<td>Smoking status</td>
<td>22.36</td>
<td>14.69</td>
<td>0.19</td>
<td>1.52</td>
</tr>
</tbody>
</table>

**Table 9.** Linear regression analysis used to determine the best predictors of CRF in the two T2DM groups; self reported physical activity measured by IPAQ. Bold values indicate statistical significance, p < 0.05.
<table>
<thead>
<tr>
<th>Model 2</th>
<th>Unstandardized Coefficients</th>
<th>Standardized coefficients</th>
<th>P – value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Standard Error</td>
<td>Beta</td>
</tr>
<tr>
<td>Constant</td>
<td>778.14</td>
<td>137.41</td>
<td>5.66</td>
</tr>
<tr>
<td>Age</td>
<td>-4.93</td>
<td>1.45</td>
<td>-0.43</td>
</tr>
<tr>
<td>Sex</td>
<td>-20.69</td>
<td>22.18</td>
<td>-0.12</td>
</tr>
<tr>
<td>BMI</td>
<td>-5.73</td>
<td>2.09</td>
<td>-0.34</td>
</tr>
<tr>
<td>CAPA</td>
<td>3.86</td>
<td>1.73</td>
<td>0.27</td>
</tr>
<tr>
<td>SF12 – Physical health component</td>
<td>2.55</td>
<td>1.01</td>
<td>0.33</td>
</tr>
<tr>
<td>SF12 – Mental health component</td>
<td>1.53</td>
<td>1.03</td>
<td>0.19</td>
</tr>
<tr>
<td>Smoking status</td>
<td>20.84</td>
<td>14.62</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Table 10. Linear regression analysis used to determine the best predictors of CRF in the two T2DM groups; self reported physical activity measured by CAPA. Bold values indicate statistical significance, p < 0.05.
4.10 Difference in anthropometrics, blood pressure and heart rate for individuals with T2DM with and without psychosis

We found that people with T2DM and a comorbid psychotic illness had a significantly higher waist circumference ($p < 0.01$) and resting heart rate ($p < 0.05$) when compared to people with T2DM and no psychosis. Means for height, weight, BMI, waist and hip circumference, blood pressure and heart rate in each group can be found in table 11.
<table>
<thead>
<tr>
<th></th>
<th>T2DM and Psychotic Illness</th>
<th>T2DM and no Psychotic Illness</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm) (± SD)</td>
<td>166.83 (± 9.19)</td>
<td>161.76 (± 10.99)</td>
<td>0.112</td>
</tr>
<tr>
<td>Weight (kg) (± SD)</td>
<td>95.96 (± 17.89)</td>
<td>85.91 (± 16.84)</td>
<td>0.065</td>
</tr>
<tr>
<td>BMI (kg/m²) (± SD)</td>
<td>34.41 (± 5.24)</td>
<td>32.58 (± 4.73)</td>
<td>0.235</td>
</tr>
<tr>
<td>Waist Circumference (cm) (± SD)</td>
<td>116.70 (± 12.36)</td>
<td>106.50 (± 11.46)</td>
<td><strong>0.008</strong></td>
</tr>
<tr>
<td>Hip Circumference (cm) (± SD)</td>
<td>114.30 (± 11.64)</td>
<td>113.77 (± 10.99)</td>
<td>0.881</td>
</tr>
<tr>
<td>Resting Systolic Blood Pressure (mmHg) (± SD)</td>
<td>122.43 (± 13.69)</td>
<td>119.85 (± 17.93)</td>
<td>0.603</td>
</tr>
<tr>
<td>Resting Diastolic Blood Pressure (mmHg) (± SD)</td>
<td>81.57 (± 9.45)</td>
<td>76.75 (± 9.78)</td>
<td>0.110</td>
</tr>
<tr>
<td>Resting Heart rate (beats/minute) (± SD)</td>
<td>87.44 (± 15.37)</td>
<td>78.20 (± 13.96)</td>
<td><strong>0.045</strong></td>
</tr>
</tbody>
</table>

*Table 11.* Mean height, weight, BMI, waist circumference, hip circumference, systolic blood pressure, diastolic blood pressure and heart rate for the two T2DM groups. Bold values indicate statistical significance.
4.11 Difference in physical activity and quality of life for individuals with T2DM with and without psychosis

Individuals with T2DM and no psychosis had significantly higher levels of reported physical activity on the CAPA questionnaire when compared to people with psychosis ($p < 0.01$). Means for the CAPA, IPAQ and physical and mental health component of quality of life can be found in table 12.
<table>
<thead>
<tr>
<th></th>
<th>T2DM and Psychotic Illness</th>
<th>T2DM and no Psychotic Illness</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPAQ (MET-minutes/week) (± SD)</td>
<td>1431.80 (± 1962.28)</td>
<td>2601.52 (± 2751.07)</td>
<td>0.123</td>
</tr>
<tr>
<td>CAPA (± SD)</td>
<td>4.76 (± 4.68)</td>
<td>11.01 (± 5.93)</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>SF-12 Physical Health Component (± SD)</td>
<td>36.76 (± 10.83)</td>
<td>38.29 (± 11.82)</td>
<td>0.667</td>
</tr>
<tr>
<td>SF-12 Mental Health Component (± SD)</td>
<td>45.56 (± 11.59)</td>
<td>48.70 (± 10.09)</td>
<td>0.354</td>
</tr>
</tbody>
</table>

Table 12. Mean IPAQ, CAPA and quality of life scores for the two T2DM groups. Bold values indicate statistical significance.
4.12 Difference in glycemic control and lipids for individuals with T2DM with and without psychosis

Lastly, we compared information regarding glycemic control and triglycerides from recent medical reports in the two T2DM groups. Individuals with T2DM and psychosis had significantly lower fasting glucose levels ($p < 0.01$) and LDL-cholesterol ($p < 0.05$). The means for fasting glucose, HbA1c, HDL-cholesterol, LDL-cholesterol and triglycerides can be found in table 13.
<table>
<thead>
<tr>
<th></th>
<th>T2DM and Psychotic Illness</th>
<th>T2DM and no Psychotic Illness</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose (mmol/L) (± SD)</td>
<td>7.08 (± 2.20)</td>
<td>10.11 (± 3.69)</td>
<td>0.007</td>
</tr>
<tr>
<td>HbA1c (± SD)</td>
<td>0.07 (± 0.01)</td>
<td>0.08 (± 0.02)</td>
<td>0.050</td>
</tr>
<tr>
<td>Triglycerides (mmol/L) (± SD)</td>
<td>1.90 (± 1.23)</td>
<td>1.99 (± 0.97)</td>
<td>0.810</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L) (± SD)</td>
<td>1.09 (± 0.26)</td>
<td>1.31 (± 0.39)</td>
<td>0.056</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/L) (± SD)</td>
<td>1.78 (± 0.86)</td>
<td>2.54 (± 1.02)</td>
<td>0.024</td>
</tr>
</tbody>
</table>

Table 13. Mean values for fasting glucose, HbA1c, HDL-cholesterol, LDL-cholesterol and triglycerides for the two T2DM groups. Bold values indicate statistical significance.
Chapter 5
Discussion

5 Discussion

5.1 Discussion

As we hypothesized, participants with both T2DM and a comorbid psychotic illness had lower physical fitness when compared to people with T2DM and no psychosis and healthy controls. The magnitude of the difference between those with and without psychosis was over one standard deviation suggesting that this difference is likely to be of clinical significance. In addition, people with psychosis and T2DM also had a significantly lower 6MWT distance when compared to the expected 6MWT distances for a healthy population obtained using the predictive equation. These results also support previous findings made by Strassnig et al. (2011) who found that approximately 98% of their sample comprised of people with schizophrenia had low CRF. Heggelund, Hoff, et al. (2011) found that VO\textsubscript{2} max was lower in men and women with schizophrenia when compared to healthy controls. Although both studies measured CRF using the gold standard VO\textsubscript{2} max assessment, the former (Strassnig et al., 2011) utilized a cycle ergometer and the latter (Heggelund, Hoff, et al., 2011) utilized a treadmill test to measure CRF. When compared to healthy controls, VO\textsubscript{2} max was also found to be significantly lower in people with schizophrenia by Martín-Sierra et al. (2011), Nilsson et al. (2012) and Ozbulut et al. (2013) as well as schizoaffective disorder (Martín-Sierra et al., 2011).

Our results are supported by research studies which examined CRF using the 6MWT. The first study to use the 6MWT on people with psychosis was conducted by Beebe et al. (2005) who
found that people with schizophrenia could increase their 6MWT distance after completing a 16-week walking exercise program. Since then, additional studies have found that people with schizophrenia achieve a lower distance on the 6MWT when compared to healthy controls, in accord with our findings from this study (Vancampfort, Probst, De Herdt, et al., 2013; Vancampfort, Probst, Scheewe, et al., 2011; Vancampfort, Probst, Stubbs, et al., 2013; Vancampfort, Probst, Sweers, et al., 2011a). These studies found that the 6MWT distance in people with schizophrenia ranged between 573.5m and 583.6m whereas the healthy controls in these studies had a 6MWT distance of 710.6m (Vancampfort, Probst, De Herdt, et al., 2013; Vancampfort, Probst, Scheewe, et al., 2011; Vancampfort, Probst, Stubbs, et al., 2013; Vancampfort, Probst, Sweers, et al., 2011a). Our cohort comprised of individuals with T2DM and psychosis had a lower walk test distance compared to individuals with schizophrenia in these studies. In addition, our sample of people with T2DM and psychosis had a lower 6MWT distance (469.93m) compared to individuals in others studies with MetSyn (527.6m) (Vancampfort, Sweers, et al., 2011), T2DM (500.3m) (Vancampfort, De Hert, et al., 2013) as well as individuals who were overweight (580.2m) (Vancampfort, Probst, Sweers, et al., 2011a) with schizophrenia. Our results suggest that the presence of both T2DM and psychosis is associated with a greater risk for chronic diseases as well as mortality. However, the participants in our study achieved a higher 6MWT distance compared to obese individuals (450.6m) with schizophrenia (Vancampfort, Probst, Sweers, et al., 2011a).

Other methods for assessing CRF have also been employed such as Eurofit test where it was found that people with schizophrenia have lower scores on exercises such as the flamingo balance, plate tapping, sit and reach, shuttle run (Vancampfort, Probst, Scheewe, et al., 2013) and

We can only speculate on the factors which may explain the low levels of physical fitness in people with psychosis and T2DM in comparison to the other two study groups. First, there was a higher prevalence of current and past smokers who had T2DM and psychosis when compared to those with T2DM and no psychotic illness. Second, levels of physical activity were significantly lower in people with psychosis and T2DM compared to those with T2DM and no psychosis. Smoking and physical inactivity are two modifiable factors which can reduce CRF (Jackson et al., 2009). Smokers were also excluded in the study in which we obtained the healthy control data which may have contributed to the significantly higher 6MWT distance achieved by this group. No significant differences were found in 6MWT distances in each T2DM group between smokers, non-smokers and previous smokers and this is likely due to the small sample size. Third, we found that the physical health component of the SF-12 questionnaire was lower in people with psychosis compared to those without. This may have affected the results as previous work has shown the physical health component positively and significantly correlated with 6MWT distance in people with psychosis (Martín-Sierra et al., 2011). Fourth, mean BMI was higher in people with psychosis and T2DM compared to people with T2DM and no psychosis as well as healthy controls. We kept the BMI inclusion at ≥ 25kg/m²; however, differences may have been detected due to the higher prevalence of obese individuals with psychosis. These support the findings from (Allison, Fontaine, et al., 1999) who found that the prevalence of BMI > 28 kg/m² higher in people with schizophrenia compared to the general population. Age did not differ significantly between the three groups as we matched age by decade. The presence of other diseases such as joint diseases in this population may have affected their performance; however,
this was not assessed in our study. In addition, when compared to people with T2DM and no psychosis, individuals with psychosis had a higher prevalence of unemployment and the majority of individuals with psychosis did not have an education higher than a high school level. It has been shown that higher socioeconomic status is associated with higher levels of physical activity and lower physical activity declines during follow-up (Droomers, Schrijvers, & Mackenbach, 2001; Ford et al., 1991; Shaw & Spokane, 2008). The lower socioeconomic may have also contributed in the poorer fitness for individuals with psychosis.

In all of the three groups, men had higher CRF when compared to women which was expected as men have more muscle mass, stroke and blood volume as well as higher levels of hemoglobin (Fletcher et al., 2001). We also found a significant improvement from the first walk test to the second walk test in all three groups and this is can be a result of practice and learning.

We found a significant correlation between the two measures of physical activity (IPAQ and CAPA) in people with T2DM. This is expected as there is overlap in questions in both questionnaires (e.g., total time spent walking and performing moderate and vigorous exercises). The score from the IPAQ was positively and significantly correlated with the 6MWT distance. There was a positive correlation between the CAPA score and 6MWT distance but not significant. We also found a significant correlation between the 6MWT distance and the score obtained from the physical health component of the SF-12 questionnaire. This questionnaire provides information on the degree to which physical health limits or interferes with daily activities such as climbing stairs. If participants have difficulty performing daily activities due to their physical health, performance on an exercise test may be affected.
Our third aim was to determine the best predictors for CRF in our two T2DM groups. We hypothesized that the best predictor would be physical activity. The best predictors for CRF in the two T2DM groups were age, BMI and the physical health component of the SF-12 questionnaire and physical activity measured by both IPAQ and CAPA. CRF declines with age (Hawkins & Wiswell, 2003; Jackson et al., 2009) and research has shown that people with a higher BMI have a lower CRF (Jackson et al., 2009). Physical activity is a modifiable factor which can influence CRF (T. S. Church et al., 2007; Duscha et al., 2005; Jackson et al., 2009; Wegner & Bell, 1986). In a separate exploratory analysis, waist circumference was also found to be a strong predictor of CRF in people with T2DM.

Lastly, when comparing variables between the two T2DM groups (e.g., anthropometrics, information from laboratory reports), we found individuals with psychosis had a significantly higher waist circumference, lower levels of physical activity and significantly lower levels of Hb1Ac and LDL-cholesterol. A higher waist circumference is associated T2DM (Balkau et al., 2007), CVD (Balkau et al., 2007; de Koning, Merchant, Pogue, & Anand, 2007) and mortality (Jacobs et al., 2010; Koster et al., 2008). Lower levels of reported physical activity have been previously reported in this population (Brown et al., 1999; Gail L. Daumit et al., 2005; Faulkner et al., 2006; Janney et al., 2014; Janney et al., 2013); however, these studies compared physical activity to the general population and we found less physical activity when comparing people with T2DM and psychosis to individuals with T2DM and no psychotic illness. Contrary to what most people would expect, individuals with psychosis had better control of LDL-cholesterol and fasting glucose. This is in contrast to previous work which found that people with psychosis (e.g., schizophrenia) are more sedentary, consume high caloric diets, have a higher prevalence of obesity and a high prevalence of poor diabetes treatment (Nasrallah et al., 2006). However, one
study found that people with schizophrenia and schizoaffective disorder had more adherence to their hypoglycemic medication compared to those without either of these psychoses (Kreyenbuhl et al., 2010). A possible explanation for this finding is that people with psychosis are more likely to have social workers or other individuals involved in health care monitoring their medication adherence.

5.2 Strengths

This is the largest study to date of objectively-measured physical fitness in people with T2DM and psychotic illness. An earlier study (Vancampfort, De Hert, et al., 2013) also examined physical fitness in people with T2DM and schizophrenia as well as in people with schizophrenia and no T2DM, but with a smaller sample and without comparison groups (e.g., T2DM and no psychosis and healthy controls).

The physical fitness assessment used in our study can be performed with minimal equipment or facilities, making the test more suitable for incorporating into clinical practice. Other studies, as reviewed earlier, have also demonstrated that individuals with psychosis can engage successfully in the 6MWT. In addition, the 6MWT has been proven to be a robust predictor of outcomes such as cardiovascular disease in people with stable coronary heart disease (Beatty et al., 2012) and left ventricular dysfunction (Bittner et al., 1993) as well as mortality in people with primary pulmonary hypertension (Miyamoto et al., 2000), left ventricular dysfunction (Bittner et al., 1993) and COPD (Casanova et al., 2008; Pinto-Plata et al., 2004).
Access to previously collected data on healthy Canadians was an additional strength of this study. This normative data showed the gradient of CRF from the healthy Canadian population to people with T2DM alone and individuals with both T2DM and psychosis.

Another strength of our study was the collection of data on quality of life, physical activity and perceived exertion using instruments which were easy to administer, readily available online and have been previously validated and shown to be reliable in people with psychosis.

In contrast to previous studies, we also included a qualitative measure to provide information on how people with T2DM were able to tolerate the 6MWT. Our findings are that the test is well tolerated by most participants and this suggests that it would not be difficult to incorporate the 6MWT into clinical practice.

5.3 Limitations

There are several limitations of this research which need to be acknowledged. First, the sample size was appropriate for a pilot study; however, argues for replication preferably in a larger population. Despite the modest sample size, the difference in physical fitness between those with and without psychosis was a highly statistically significant result. The magnitude of the difference suggests that the results might be robust and clinically significant.
We did not measure physical fitness using VO$_2$ max, which is regarded as the gold standard for assessing CRF; however, there is adequate research showing an acceptable level of correlation between the 6MWT and VO$_2$ max in various populations (Cahalin et al., 1996a; Cote et al., 2007; Ross et al., 2010).

In addition, sampling of the two cohorts comprised of individuals with T2DM was not random. The group with psychosis and T2DM were participants who had agreed to participate in a randomized control trial lifestyle intervention. The group comprised of people with T2DM and no psychosis were recruited from primary care clinics based on matching the participants with psychosis on age and sex. The healthy control data had previously been collected and contained a small sample size after we matched age by decade and included people with a BMI $\geq 25$ kg/m$^2$. This small sample makes it difficult to generalize to a healthy population.

We also did not assess diseases such as cardiac, pulmonary or joint diseases. This is important as the presence of these factors may have influenced the fitness results.

5.4 Future Directions

Future research is needed on strategies to mitigate the adverse risk associated with the poor physical fitness in people with a psychotic illness. We found that people with psychosis willingly
participated in the 6MWT and reported no difficulties associated with performing this test. This suggests that they may also be willing to engage in interventions aimed at increasing their physical fitness; however, this needs to be evaluated prospectively.

There has been an increase in clinical trials examining lifestyle interventions aimed at reducing obesity and overweight in individuals with psychosis (Cabassa, Ezell, & Lewis-Fernández, 2010). However, there have been relatively few systematic attempts to increase physical fitness in people with psychosis but most that have attempted to do so have succeeded in increasing CRF (Abdel-Baki et al., 2013; G. L. Daumit et al., 2011; Heggelund, Nilsberg, et al., 2011). Nevertheless, in the clinical management of psychosis there is little evidence that fitness is often discussed with clients and less evidence that objective physical fitness testing is attempted. When our results are published, we hope that they will stimulate clinicians to incorporate the discussion of physical activity and fitness and its health benefits with their patients. In addition to publishing these results in the literature, presentations to both scientific and clinical audiences will be used to disseminate the urgent need to address the health risk posed by low levels of physical fitness in this population. Individuals with psychosis are interested in becoming more active (Gorczynski, Faulkner, Greening, & Cohn, 2010) and say they would become more active if instructed to do so by their doctor (Ussher, Stanbury, Cheeseman, & Faulkner, 2007). Clinicians need to encourage their clients with mental illness to become more active and try to achieve the recommended amount of weekly physical activity. There are several guidelines available, for example, they should encourage their clients with psychosis and T2DM to achieve at least 150 minutes of physical activity at a moderate to vigorous intensity (e.g., brisk walking,
jogging) as well as at least two days of resistance training (e.g., weight exercises) per week (Sigal et al., 2013).

In addition, fitness testing, using field tests such as the 6MWT, is cheap and feasible which might encourage the inclusion of this measure into the clinical setting to assess and objectively monitor improvements in CRF for people with psychosis.

There is almost no data on addressing metabolic issues for people with a psychotic illness in primary care settings (Nover & Jackson, 2013). We hope that this study and others which may follow would increase the inclusion of physical fitness evaluation and efforts to improve it in the primary care setting, where individuals with psychosis and medical comorbidities (e.g., T2DM) receive non-psychiatric medical services.

It has been shown that the largest reduction in relative risk and age adjusted mortality occurs from the lowest CRF (where most of our participants were) to second lowest CRF category (Steven N Blair et al., 1989). This indicates that we may only need a small increase in physical activity throughout the course of the day to improve CRF and reduce the risk for mortality in this population. The relative risk for mortality has also been shown to decrease with the presence of other traditional risk factors (e.g., hypertension, smoking, BMI) with increases in CRF (Steven N Blair et al., 1989). S. N. Blair et al. (1996) found that individuals who were fit but also had the presence of other mortality risk factors (e.g., systolic blood pressure ≥ 140mmHg, currently
smoking and cholesterol ≥ 6.2mmol/L) had lower mortality rates compared to individuals classified as having low fitness with none of these risk factors. This information is particularly important for people with psychosis as the prevalence and incidence of medical comorbidities (Bernardo et al., 2009; Bresee et al., 2010; Dickey et al., 2002) as well as the prevalence of smoking (Brown et al., 1999; McCreadie, 2003) is higher in this population compared to the general population. In addition, improvements in CRF has also been shown to significantly lower risk for CVD mortality and all-cause mortality compared to individuals who did not improve their fitness (S N Blair et al., 1995). It was also found that improvements in CRF resulted in greater all-cause mortality risk reduction when compared to reductions in systolic blood pressure, reduction in cholesterol and smoking cessation (S N Blair et al., 1995). Future studies need to follow-up of individuals with psychosis in order to correlate changes in fitness with changes in chronic disease risk as well as risk for mortality. These findings need to be communicated to clinicians who treat people with a psychotic illness, care givers and advocates for this population so that more attention can be focused on improving fitness in this population.
References


