2-27-2019 10:00 AM

Examining the Relationship between Intrinsic Drivers of Motivation and Functional Outcomes in a Cross-Section of Individuals with Psychotic Disorders

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Epidemiology and Biostatistics

Abstract

Impaired functioning is recognized as a major barrier to recovery among individuals with psychotic disorders. Research on the role of negative symptomatology on functioning has identified avolition (i.e. lack of motivation) as being highly correlated with functional outcomes. However, current measures of avolition fail to consider more intrinsic factors that influence motivation. There is a need for more nuanced research on the drivers of motivation and their relationship with functioning to inform the observed relationship between avolition and impaired functioning. This cross-sectional study uses data obtained from the Prevention and Early Intervention Program for Psychoses, in London, Ontario. 105 clients of PEPP were assessed using validated measures of motivational drivers. Multivariate analyses did not show a statistically significant relationship between the intrinsic drivers of motivation and functional outcomes. Findings demonstrate the need for updated measures of negative symptoms as well as the need for further research on motivation and functional outcomes.

Keywords

psychotic disorders, schizophrenia, negative symptoms, motivation, avolition, functional outcomes

Dedication

I would like to dedicate this thesis to my parents, grandparents, and siblings, who I sincerely thank for their support and for always pushing me to aim higher. To my parents especially, your patience and encouragement throughout these past two have meant so much to me. Words cannot express how appreciative I am for all you have done for me. I love you all and am so thankful to have you all beside me.

This thesis is also dedicated to the memory of my late grandfather, Dr. C. Rajendran, who passed away before I started my postgraduate studies. I wish I could have presented this to you, and I hope I made you proud.

Acknowledgements

Firstly, I would like to acknowledge my thesis supervisors, Dr. Arlene MacDougall and Dr. Kelly Anderson, for their support, guidance and encouragement throughout my graduate program. The knowledge and experiences I gained through my graduate studies have helped me, as both a student and a researcher, tremendously and I would not have been able to complete this thesis without both of your guidance and mentorship. Thank you both for the opportunity to work alongside you and for all the encouraging words you have provided me with throughout these past two years.

I would also like to thank Dr. Ross Norman and the Prevention and the Early Intervention Program for Psychoses for allowing the use of their data and for the client contributions made for this study. I sincerely thank Dr. Norman for his support and guidance through the creation of this thesis.

Last but not least, these last two years would not have been the same without the friends I gained through this graduate program. Thank you to the Society for Higher Epidemiological Thinking for all for the support, advice and unforgettable memories.

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List of Abbreviations

AA= ‘Diminished Experience Domain’

AUDIT= Alcohol Use Disorders Identification Test

CBT= Cognitive Behavioral Therapy

CI= Confidence Interval

CORS=Course of Onset and Relapse Schedule

DAST-20=Drug Abuse Screening Test

DE= ‘Diminished Expression Domain’

DPB=Defeatist Performance Beliefs

DSM-5= The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

DUP=Duration of Untreated Psychosis

EPI=Early Psychosis Intervention

FCS= Fully Conditional Specification Method

GSE=Generalized Self-Efficacy Scale

ICC= Intra-class Correlation

ICD-10= International Classification of Diseases, Tenth Revision

ISEL=Interpersonal Support Evaluation List

MAR= Missing at Random

MCAR= Missing Completely at Random

NMAR= Not Missing at Random

MVN= Multivariate Normal Method

PANSS= Positive and Negative Syndrome Scale

PAS= Premorbid Adjustment Scale

PEPP= Prevention and Early Intervention Program for Psychosis

POMS-SF= Profile of Mood States-Short Form

RFS= Role Functioning Scale

SANS= Scale for the Assessment of Negative Symptoms

SAPS= Scale for the Assessment of Positive Symptoms

SD= Standard Deviation

TEPS= Temporal Experience of Pleasure Scale

VIF= Variance Inflation Factor

Chapter 1

1 Introduction

In this chapter, an overview of the thesis topic is provided in Section 1.1 followed by the research objectives in Section 1.2. Finally, Section 1.3 provides an overview of the structure of this thesis manuscript as well as the role of the student in the research process.

1.1 Overview of Topic

Defined as a loss of contact with reality, people suffering from psychosis often have difficulties distinguishing between what is real and what is not [1]. These breaks from reality, often with a first onset during late adolescence and young adulthood [2], lead to disruptions in academic or professional, personal, and social lives. Psychotic episodes can occur in the context of both primary psychotic disorders as well as mood disorders with psychotic features. Primary psychotic disorders are ones in which psychotic symptomology are the primary symptoms, with disorders such as schizophrenia falling under this category [3-5]. Mood disorders with psychotic features are instances where an individual will have a primary diagnosis of a mood disorder, such as depression, however they also exhibit psychotic symptoms[3-5]. Although no direct cause has been identified as leading to the development of psychosis, a number of possible risk factors have been identified such as substance use, cognitive deficits and other medical conditions[6]. Symptoms of psychotic disorders include delusions and hallucinations, thought disorders, social withdrawal, and lack of motivation - with the majority of symptoms falling into one of two categories, positive or negative symptoms [7-9]. Positive symptoms consist of hallucinations, delusions and disturbances of thought, whereas negative symptoms consist of behaviors such as reduced emotional expressivity and social withdrawal, indicative of a reduction or loss of typical behaviors [10,11]. Although psychotic disorders are considered chronic illnesses, within the last decade advances have been made in regard to treatment options, often consisting of antipsychotic medications in conjunction with psychosocial therapeutic interventions [12]. Our current understanding of treating psychosis recognizes the importance of an early intervention approach [12-17], with past research demonstrating the detrimental effects that a long duration of untreated psychosis can have on disorder progression and outcome [16].

Although symptomatic recovery is often achievable with treatment, functional recovery, defined as a sustained improvement in social and vocational functioning [15], remains more elusive, with impairments being found in both acute and chronic cases of psychotic disorders[18,19]. Growing interest in understanding why functional outcomes are more resistant to treatment has led to a surge in research attempting to pinpoint correlates of poor functioning. Negative symptoms, being one of the two key symptom categories defining psychotic symptomology, have consistently been shown to have a high correlation with functional outcomes [20-25]. Recent evidence has shown that when controlling for other symptoms, such as positive symptoms, depression, and anxiety, negative symptoms remain a strong correlate of functioning[26]. Research has shown that one negative symptom in particular seems to outweigh the others in terms of its correlation to functional outcomes. Specifically, avolition, defined as a lack of motivation, has been identified as a strong correlate of functioning [22,23,25,27-30].

Limitations in the methods used to measure negative symptoms may be inflating the contribution of negative symptoms. Measures of avolition that are currently used, such as the avolition subscale of the Scale for the Assessment of Negative Symptoms (SANS)[31] or the Positive and Negative Syndrome Scale (PANSS)[32], assesses overt behavioral markers rather than intrinsic motivational states. As such, it is highly possible that the strong, positive correlation observed between avolition and functioning may be due to the fact that these measures are assessing the same construct, specifically daily behavioral markers such as personal grooming habits and occupational/academic ability. Given this high degree of overlap between measures of avolition and functioning, there is a need for a more in-depth assessment of motivational deficits and their relationship to functional outcomes to better assess the possible relationship between avolition and impaired functioning.

1.2 Purpose of Thesis and Research Objectives

The overall goal of this thesis was to examine the relationship between the negative symptom of avolition and functional outcomes via intrinsic drivers of motivation in a cross-section of people with primary psychotic disorders. To assess the proposed relationship between motivation and functioning, we used data from 105 clients of an early psychosis intervention program to complete the following objectives:

- To examine the direct relationship between intrinsic drivers of motivation and overall level of functioning, adjusting for covariates; and
- To examine the direct relationship between the intrinsic drivers of motivation and specific subdomains of functioning, specifically working ability, independent living and self-care, immediate social networks, and extended social networks, adjusting for possible covariates.

1.3 Thesis Overview and Student Contribution

In the following chapters, I will present a detailed review of the current literature on psychotic disorders, negative symptoms, and functional outcomes, along with a critical evaluation of related studies assessing motivation and functioning in people with psychotic disorders (Chapter 2). Then I will present the methods used in this thesis, along with information regarding the data source, the multiple imputation method used to address missing data, and the variables and measures used to assess our exposures and outcome (Chapter 3). Subsequently, I will present and summarize the main findings of our analyses along with the results from our additional sensitivity analyses undertaken to assess the robustness of our main analyses (Chapter 4). Finally, I will provide a discussion of our key findings, the overall strengths and limitations of this thesis, and the implications of this study for future research and clinical care.

The student's contribution to the current study consisted of selection of the thesis topic, in collaboration with thesis supervisors, Dr. Arlene G. MacDougall and Dr. Kelly K. Anderson, and Dr. Ross M.G Norman, the principal investigator of the source study and a member of the thesis supervisory committee. Study objectives were formulated with insight from the thesis supervisory committee, and all subsequent phases of the study were developed and produced by the student, from development of the methodological plan to the preparation of this manuscript, in consultation with supervisors Dr. MacDougall and Dr. Anderson.

Chapter 2

2 Literature Review

This chapter will present an overview of psychotic disorders, negative symptoms, and functional outcomes in Sections 2.1, 2.2 and 2.3 respectively. Issues regarding the measurement of negative symptoms, individually and with respect to functional outcome assessments, are discussed in Section 2.4. The search strategy used to identify motivational drivers is reported in Section 2.5, along with the results from our literature search. Gaps in current knowledge are discussed in Section 2.6. Lastly, our study rationale and thesis objectives and hypotheses will be presented in Sections 2.7 and 2.8, respectively.

2.1 Psychosis

2.1.1 Overview

Psychosis can be characterized as disturbances in thought, perception, and behavior [7]. As defined by the Diagnostic and Statistical Manual on Mental Disorders, Fifth Edition (DSM-5) [33] and the International Classification of Diseases, Tenth Revision (ICD-10) [34], psychosis is not a single disorder but rather a spectrum [35,36] categorized by a set of key commonly observed features[37], specifically "common and functionally disruptive symptoms of many psychiatric, neurodevelopmental, neurologic and medical conditions(p715)" [38]. A number of disorders fall within the psychotic spectrum, with the most commonly observed disorders being classified as primary psychotic disorders. Primary psychotic disorders exhibit psychosis as the defining feature, with disorders including schizophrenia, schizoaffective disorder, delusional disorder, schizophreniform disorder and brief psychotic disorder [38]. However, an episode of psychosis can also be observed in other psychiatric conditions such as major depressive disorder and bipolar disorder. Within these disorders, psychotic symptoms such as hallucinations and delusions may occur during manic or depressive phases [38]. Disorders along the psychosis spectrum differ from each other by the type, number, and severity of psychotic symptoms present [38]. Disorders that fall closer to the psychotic side of the spectrum would be schizophrenia spectrum disorders, otherwise considered primary psychotic disorders, whereas disorders that fall closer to the affective side would be bipolar disorder or major depressive disorder where psychotic symptoms are secondary to the main affective symptoms consistent with their diagnosis [3-5]. This concept of

psychosis as a spectrum rather than a single disorder with a set of strict clinical criteria is consistent with population samples in which a large number of individuals report symptoms of psychosis, however they fail to meet the criteria for the clinical diagnosis of a psychotic disorder such as schizophrenia [36]. Given that psychosis is best represented as a spectrum, with a number of diagnoses being placed along this spectrum, it is possible for diagnoses and the presentation of symptoms to evolve over time. This thesis draws on the data of participants who have accessed care in an early intervention program for psychosis with the majority of participants carrying a diagnosis of a primary psychotic disorder, including schizophrenia, schizoaffective disorder, and psychosis not otherwise specified, with a smaller subset of participants diagnosed with bipolar disorder with psychotic features or depression with psychotic features.

2.1.2 Causes of Psychotic Disorders

Although no direct cause has been identified, there are a number of potential risk factors that have been identified to increase the likelihood of developing psychosis. A developmental component has been stated, with models positing that genes involved in neurodevelopment and/or early environmental insults may lead to aberrant brain development, predisposing one to a later onset of psychosis[6]. More recent theories have included the role of social determinants in the development of psychosis, including factors such as childhood adversity, social isolation, and migration [6,39]. Other possible risk factors identified include alcohol and drug misuse, social stress, cognitive deficits, childhood trauma, underlying mental illness and other medical conditions (ex. lupus)[6].

2.1.3 Symptom Classification

In diagnosing psychotic disorders such as schizophrenia, a range of commonly presented symptoms are assessed. Both the DSM-5 and the ICD-10 diagnostic manuals, the two primary diagnostic manuals used to define and diagnose mental disorders, recognize schizophrenia as being comprised of features known as positive and negative symptoms[7-9]. Positive symptoms are categorized by the presence of hallucinations, delusions, and disorganized or bizarre thought patterns[10]. These are collectively referred to as positive symptoms due to them being ‘present’ or ‘added on’ to typical behavior [11]. Hallucinations consist of sensory experiences with which one can see, hear, taste, feel, or smell something without the corresponding external stimulus [38], and

delusions include pervasive false beliefs that are not based in reality [38,40]. In contrast, negative symptoms refer to a reduction or loss of function [11] and consist of blunted affect, alogia, avolition, anhedonia, and asociality. Blunted affect refers to reductions in emotional expression via facial expressions or tone of voice whereas alogia is defined by a reduction in speech [10,41]. Anhedonia refers to a diminished capacity to experience pleasure, regarded as a core feature of schizophrenia [41].Asociality is defined as a reduction in social initiative and an increase in social withdrawal due to decreased interest in forming relationships [10,41] whereas avolition refers to a marked reduction in motivation and motivational behavior [10,11,35]. These symptoms can vary in number and severity depending on the person and their diagnosis. The combination of these symptoms results in distorted perceptions of reality, and people with lived experiences of psychosis describe experiences of unshared perceptions, paranoia, and a loss of sense of having a coherent self [1].

2.1.4 Epidemiology and Burden of Illness of Psychotic Disorders

A first episode of psychosis is typically experienced in between late adolescence and early adulthood, a period marked by numerous changes both personally and academically/professionally [6]. The onset of psychosis has been found to often result in an increase in social isolation and detachment from community and peers, discontinuation of hobbies and school, and impairment in work related activities directly impacting long-term wellbeing. As a result, an episode of psychosis can be highly disruptive to a person's life and negatively impact their growth and development.

The lifetime prevalence of all psychotic disorders has been estimated to be between 3.06% and 3.48% in the general population[42]. The most commonly occurring psychotic disorder, schizophrenia, has an estimated lifetime prevalence of between 0.4% and 0.9% within the general population[42-45], low in comparison to other common mental disorders such as major depression, with an estimate of around 27%[46]. However, despite its relatively low prevalence, schizophrenia and other psychotic disorders result in a significant burden to both the healthcare system and the economy. Schizophrenia is amongst the top 25 leading causes of disability worldwide and people with psychotic illness have an increased risk of premature mortality when compared to the general population [47]. This increase in mortality is due to an increased risk of

suicide along with the numerous co-occurring medical conditions found to be associated with schizophrenia, as well as the under-detection and under-treatment of these medical conditions [47].

Financial costs associated with schizophrenia are higher in comparison to other chronic mental and physical health conditions, with both the direct costs to the healthcare system as well as the indirect costs due to loss of productivity, social service needs, and possible criminal justice involvement [47,48], resulting in an estimated annual cost of $6.85 billion CAN [48].

2.2 Negative Symptoms in Psychotic Disorders

2.2.1 Historical Overview

As previously stated, negative symptoms consist of processes that are unusual in their reduction or absence and may result in a decline in function [1,11,41]. Schizophrenia has been defined as an illness of early and progressive degeneration, with negative symptoms representing the illness' core and possibly the most significant contributing factor in the impaired functioning experienced by people with psychosis [49]. Early descriptions of schizophrenia (1917/1919) emphasized a disturbance of volition or will as the fundamental underlying process in its pathology [50,51].

However from the 1950s up until the 1980s, the treatment of schizophrenia was mainly focused on the alleviation of positive symptoms, namely through the introduction of antipsychotic medications [52]. The distinction between negative and positive symptoms re-introduced by Andreasen in the 1980s marked the beginning of modern research on the subject[53]. This brought about further research and debate on whether the two domains were distinct syndromes. Crow was one of the first to distinguish between negative and positive syndromes, indicating that they were syndromes independent of one another and with differing etiologies and prognoses[54]. Typically, patients exhibiting predominantly positive symptoms were characterized by good premorbid functioning, relatively favorable outcomes, acute onset, good response to treatment, and hyperdopaminergic activity. In contrast, patients exhibiting predominantly negative symptoms were characterized by poor premorbid functioning, impaired cognition, poor response to treatment, and structural brain abnormalities [54]. More recent factor analyses using measures of psychotic symptoms have found support for three-factor, five-factor, and even eleven-factor

models of psychotic symptomology[9,55]. These findings have indicated symptom categories in addition to positive and negative symptoms, such as disorganization symptoms, depression, and anxiety; however, all possible models currently proposed included both positive and negative symptoms as separate and distinct factor domains. Negative symptoms, in particular, have consistently been found to load onto a factor separate from positive symptoms, disorganized symptoms, and affective symptoms, and results from these studies have provided support for the distinctiveness of negative symptoms and its recognition as being an independent target for treatment [9].

2.2.2 Current Conceptualization

The current conceptualization of negative symptoms consists of blunting of affect (i.e. reduced emotional expression), poverty of speech (i.e. alogia), asociality (i.e. apathy or social withdrawal), avolition (i.e. lack of drive or motivation), and anhedonia (i.e. lack of or diminished interest, enjoyment, or pleasure from activities) [44,52,56]. For example, individuals experiencing negative symptoms such as blunted affect and/or alogia may seem artificial or mechanical in movements, with few instances of spontaneous movement, eye contact, or facial expression [57]. Conversations may seem emotionless with few changes in vocal pattern or inflections [57]. Experiences of avolition may be observed through a lack of initiative or self-directed behavior, whereas others may view the individual as being socially withdrawn or without a sense of caring [57]. Recent research on negative symptoms have also proposed that the symptom domain may be better represented using a two-factor model, with one factor being 'diminished expression' (consisting of blunted affect and alogia) and another being 'diminished experience/amotivation' (consisting of avolition, anhedonia and apathy) [8,9,30,35,44,49,58-60]. As described by Foussias and Remington, the diminished experience category involves disturbances of involvement with the surrounding environment, observed via deficits in drive and pleasure, whereas the diminished expression category addresses issues regarding expressivity, observed via deficits in affect and speech[49]. Outcome differences between both domains have been observed among persons with schizophrenia. The diminished expression domain being associated with an earlier onset, diminished cognitive traits and a lower level of education while the diminished experience domain is related to duration of untreated psychosis (DUP), family history of psychosis, work status and global functioning[59]. However, issues regarding the relationship between negative

symptoms subdomains are still present. Along with research showing differential factor loadings between the diminished expression and diminished experience domains, these domains also exhibit a moderate interrelationship, with inter-factor correlation coefficients between 0.47 and 0.57 [49]. Analyses of the Scale for the Assessment of Negative Symptoms (SANS) have also demonstrated moderate interrelationships for affective flattening and anhedonia-asociality subscales (r=0.49 and 0.48, respectively) as well as between alogia and avolition and anhedonia-asociality (r=0.61 and 0.53, respectively) [49]. These findings would seem to suggest that although these domains have distinct phenomenological entities, that they may reflect a common underlying etiology.

In comparison to positive symptoms, negative symptoms are often associated with a more chronic and deteriorating course of illness, with the symptoms persisting even after positive symptoms have been treated and largely reduced [13,44,61,62]. Evidence suggests that negative symptoms contribute to more impaired quality of life and poorer functioning than positive symptoms [22,24,26,63,64]. However, negative symptoms are often not as easily observable and are harder to identify, unlike positive symptoms which are more easily viewed and are often the most prominent and troubling symptoms present at the onset of psychosis. For reasons such as these, positive symptoms were once considered the main defining feature of psychosis and therefore much research was conducted on positive symptoms being a treatment target of psychosis. Only recently have more studies been focused on negative symptoms and their impact on disease progression and outcome.

2.3 Recovery from Psychotic Disorders

2.3.1 Symptomatic vs. Functional Recovery

Although current approaches, such as pharmacological interventions, have aided patients in achieving some form of symptomatic recovery, it is now understood that recovery from serious mental illness includes both symptomatic recovery and functional recovery. Symptomatic recovery refers to sustained improvement in symptoms of psychosis, whereas functional recovery refers to sustained improvement in social and vocational functioning [15,19,65]. Functional capacity, defined as the ability to perform tasks and activities necessary in daily life, is often significantly impaired in both the acute and non-acute phases of psychotic illness [15,19,66]. Around

75% of people with a first episode of psychosis achieve symptomatic remission with antipsychotic medications, however, functional recovery is achieved by only by a minority [20]. Robinson and colleagues found that among a sample of 118 participants diagnosed with schizophrenia spectrum disorders, around 57% achieved symptomatic remission for 2 years or longer, whereas only 38% achieved adequate functioning and 14% achieved full recovery[67].Similar findings have been demonstrated by other studies [68,69]. With functional recovery found to lag behind clinical remission, impairments in functional capacity have been recognized as a major barrier to full recovery among people with primary psychotic disorders[20].

2.3.2 Negative Symptoms and Functional Outcome

In recent years, studies have assessed functioning among people with schizophrenia to determine factors that are strongly associated with poor functional outcomes. Negative symptoms have been shown to contribute more to impaired functioning than other symptom domains [24,26,66,70]. Rabinowitz and colleagues conducted a study in which they attempted to discern the relative effect of negative symptoms on functioning, in comparison to other symptom domains[24]. They found that both baseline functioning and changes in functioning over time were most strongly related to negative symptoms, suggesting that functioning and the improvement of functioning is most strongly related to negative symptoms.

This association between negative symptoms and functional outcomes has consistently been replicated across a broad range of patient populations, including both first-episode and chronic psychosis [66]. Specifically, studies have shown negative symptoms to be highly correlated with impairments in occupational functioning, household integration, relationships, and recreational activities [70,71]. Fervaha and colleagues assessed the impact of primary negative symptoms on functional outcomes, controlling for other psychopathological factors such as positive symptoms, depression, and anxiety[26]. Findings showed that even when controlling for these symptoms, negative symptoms were a significant contributor to the functional impairment seen in patients with schizophrenia. As well, negative symptoms were found to explain a large portion of the variance in functional status, even after the variance associated with other clinical variables (e.g. depression, anxiety, positive symptoms, extra-pyramidal symptoms) had been accounted for.

Results such as these have highlighted the central role of negative symptoms in functional outcome.

2.3.3 Avolition and Functioning

With the understanding that negative symptoms are significantly associated with functional outcomes – more so than any other symptom domain in psychosis – research has shifted towards understanding the connection between negative symptoms and functional outcomes. Given that negative symptoms can be classified into separate subdomains, the impact that each of these domains has on functional outcomes has been investigated. Among the five symptoms that fall under the category of negative symptoms, the amotivation subdomain has consistently been found to have the strongest association with functional outcomes.

Foussias and colleagues conducted a study assessing each separate subdomain of negative symptoms and its contribution to functional impairment[25]. Among adult outpatients diagnosed with schizophrenia, they found that the amotivation subdomain of the SANS, consisting of avolition, anhedonia and asociality, was the sole predictor of functioning accounting for approximately 74% of the variance in current functioning[25]. This finding was confirmed in separate studies using the Apathy Evaluation Scale, a measure of avolition, with similar results [29,72]. To determine whether motivational deficits were strong contributors to poor functioning, Foussias and colleagues extended past research by assessing the concurrent contributions of motivational deficits in addition to other negative symptoms and other symptom domains at baseline on functional outcomes longitudinally[73]. In a sample of 18 participants diagnosed with schizophrenia, they found that amotivation was the most influential predictor of functioning, at baseline as well as at six-month follow-up; with amotivation accounting for 74% and 72% of the explained variance in functioning, respectively [25,73]. In follow up to this study, a 2014 study by Fervaha and colleagues assessed 754 patients with schizophrenia to determine associations between selected clinical variables and one-year functional outcomes[71]. Their analyses identified several independent predictors, with the strongest being amotivation and neurocognition. A 2015 study by Fervaha and colleagues, assessing the prevalence of motivational deficits and their impact on community functioning among 166 early intervention participants with a diagnosis of schizophrenia, found that motivational impairments were found in more than 75% of participants[22]. Furthermore, these deficits were the most robust and reliable predictor of

functional outcomes at baseline and longitudinally, with an independent predictive value that no other assessed variable exhibited[22].

Chang and colleagues conducted a study to examine the direct effect of avolition and other clinical variables at baseline on one-year functional outcomes in a cohort of people with schizophrenia[27]. A number of significant factors were identified to be correlated with functional outcome at 12 months, including amotivation. However, multiple regression analyses revealed that the amotivation subdomain and cognitive composite scores were the only independent factors associated with functioning at 12 months, with amotivation being the most robustly associated with functioning even after adjusting for cognition, additional negative symptoms, and other symptom dimensions [27]. In a 2015 study by Minchinio and colleagues, the participants categorized as low functioning all exhibited higher levels of negative symptoms, with avolition found to be independently associated with functional outcome [23]. Amotivation has also been associated with level of social activity and social outcomes, such as marriage and gaining competitive employment [74]. In fact, studies have been able to clearly separate people based on their presentation of 'diminished expression' (DE) vs 'diminished experience' (AA) symptom severity, with people with high AA severity experiencing worse functioning in all domains, in addition to more frequent hospitalizations, worse overall psychosis, and social anhedonia [30,70,75].

2.4 Issues in Measurement

Although research has identified negative symptoms, specifically those under the amotivation subdomain, as being highly associated with functional outcomes, there are concerns regarding the validity of these findings based on the measures used to assess these variables.

2.4.1 Measurement of Negative Symptoms

Certain criteria should be met for proper measurement of negative symptoms. Such measures should: (i) assess all domains of negative symptoms while excluding other symptom domains; (ii) be sensitive to change; (iii) demonstrate good reliability; and (iv) be relatively brief for administration purposes [76]. Most importantly, the measures should assess the symptom itself, rather than an outcome of that symptom [76]. However, current measures of negative symptoms differ based on their inclusion of negative symptom subdomains. Two of the most widely used

scales, the Scale for the Assessment of Negative Symptoms (SANS) and the Positive and Negative Syndrome Scale - Negative Subdomain Scale (PANSS), have a substantial degree of overlap, but also exhibit significant differences. These scales, in addition to other negative symptom severity measures, differ in their coverage of the 5 negative symptom domains. As previously mentioned, the current consensus on negative symptoms views the domain as being composed of avolition, anhedonia, asociality, alogia and blunted affect [45,52.56]. Among the measures assessed, only the SANS covers all 5 domains. However, the SANS also includes the domain of inattention, a factor that is no longer considered to be a negative symptom but rather a symptom of the disorganization symptom domain. The SANS also combines anhedonia and asociality, two separate negative symptom categories, into a single domain [77]. The PANSS negative symptom subscale contains items outside the currently viewed negative symptom domains [77]. Given that our current understanding of the relationship between the amotivation subdomain and functional outcomes is reliant on these measures, it is important to examine the specific factors assessed using these tools.

2.4.2 Overlap in Measures of Avolition and Functioning

Our literature review has shown that the amotivation subdomain, consisting of avolition, anhedonia and asociality, is the strongest predictor of functional outcomes in individuals with schizophrenia. Currently, the most commonly used measure of avolition is the SANS amotivation subdomain. But this measure, in addition to other measures of avolition, has a degree of conceptual overlap with measures of functional outcomes due to how avolition is assessed. Measures such as the SANS have items related to avolition that are rated mostly based on behavior and therefore do not take into account the intrinsic and subjective experiences of motivation, which may be intact but not directly observable due to other factors [78]. When looking at the avolition subdomain of the SANS, items assess behavior such as personal grooming habits, with the participant being graded based on the following statement “The patient’s clothes may be sloppy or soiled, and he or she may have greasy hair, body odor, etc.” (Appendix B). An assessment of motivation is therefore made based on the individual’s physical appearance, assuming that a motivated individual would present themselves differently. However, overt behavioral markers such as personal grooming habits are also included as a marker of functional outcome. The Role Functioning Scale (RFS)[79] is a scale used to measure functional outcomes

based on four main functioning domains: working productivity, independent living and self-care, immediate social network, and extended social network. As seen in the RFS Independent Living and Self-Care subdomain (Appendix C), functioning is assessed based on an individual's ability to manage and care for their home and self, with raters making decisions of functional ability based on whether the participant maintains personal grooming and hygiene habits in addition to feeding themselves and maintain the cleanliness and upkeep of their household. This overlap in assessment markers can be observed in other avolition statements such as the "Impersistence at Work or School", which states that the person has difficulties seeking or maintaining work, education, or other meaningful activity. However, assessing the outcome of employment or education does not necessarily measure one's motivation to gain employment or education, which could be hindered due to other factors including systemic barriers such as the stigma around mental illness [80,81]. In fact, this statement more accurately aligns with measures of vocational functioning, as seen in the Role Functioning Scale Working Productivity subdomain. As well, the avolition subdomain assessed using these measures have a limited number of items and therefore this may contribute to the inaccurate measurement of avolition. The SANS only includes three separate markers of avolition, two of which we have shown to overlap significantly with measures of functioning.

Measurement issues can also be found within the anhedonia-asociality subdomain of the SANS. Of the four statements used to assess one's severity of anhedonia, two focus on sexual activity, with statements that the individuals may show a decrease sexual interest, activity or enjoyment and that the person may be unable to form intimate relationships with either the opposite sex or with family. However, one's current sexual activity does not necessarily indicate one's level of anhedonia. In other words, measuring one's level of pleasure does not necessarily measure one's objective capacity for experiencing pleasure [82], with other factors possibly playing a role in the ability to form a sexual/intimate relationship, regardless of whether they themselves want to enjoy said relationship. As well, item 21 asks about the number of friends that the individual has, with a lack of friends being related to a proposed preference to spend time alone. This purports that a lack of a large friend network is consistent with a lack of pleasure gained from friendship, regardless of whether the person wants a larger social group or whether in fact they fail to gain pleasure from friendships. These SANS anhedonia-asociality items do not directly measure one's

ability to experience pleasure but rather the observed behavioral outcomes assumed to be associated with the ability to experience pleasure, as seen in the SANS avolition subdomain statements

The validity of current measures of negative symptoms, with an emphasis on avolition/amotivation subdomains, raises concerns regarding the current evidence base. Here we discussed the SANS specifically, however other measures of avolition currently used demonstrate these issues. Past literature has been consistent in their findings of associations between avolition and functioning, however these associations were drawn from measures that are limited in their operationalization of negative symptomology. When considering validity, these measures focus on measuring the outcome of the construct rather than the construct itself; demonstrating issues in regard to the translation of the symptom constructs into operational measures [83,84]. Construct validity, being the degree to which a measure assesses the construct it claims to be measuring, would therefore be questioned because the items proposed to measure avolition do not assess motivation but rather the behavior assumed to be indicative of motivation [84]. When we look specifically at the content of the items proposed to measure these symptom domains, as seen through the SANS, we see that there are also limitations in how conclusive these measures are in assessing the construct. External observable characteristics are focused upon without the assessment of more internal, psychological markers of motivational drive. With these validity concerns present in measures of negative symptoms in mind, the proposed relationship between avolition and functioning becomes harder to assess. Given that there is a limited number of measures that assess avolition, and that current measures demonstrate these issues in regard to construct validity, there is a need to address more intrinsic aspects of motivation in regard to their impact on functional outcomes to further elucidate the relationship between amotivation and functional outcomes.

2.5 Motivational Drivers and Functional Outcomes in Psychosis

2.5.1 Search Strategy

To identify intrinsic factors that drive motivation, we searched through PsycINFO, EMBASE, and Medline to identify articles examining the association between motivational deficits and

functioning among individuals with psychotic disorders. Articles examining theories regarding motivation, avolition, and negative symptoms were assessed.

2.5.2 Cognitive Model of Negative Symptoms

Until recently, little attention had been given to understanding the possible role that motivational variables have in the development and maintenance of negative symptoms. However, research regarding the effects of cognitive behavioral therapy (CBT) for people with psychotic disorders have found that negative symptoms can be targeted in therapy by focusing on factors such as dysfunctional attitudes, coping style, and self-efficacy [85].

Proposed by Rector, Beck and Stolar, the cognitive model of negative symptoms is a theory regarding the expression and maintenance of negative symptoms [86]. Specifically, the model proposes that people with schizophrenia often experience cognitive impairments that may hinder their normal adjustments in social and academic/occupational domains, thus contributing to poor academic achievement, work performance, and social problems [86,87]. These deficits in social and occupational functioning therefore lead to the formation of dysfunctional attitudes about one's abilities, which in turn can reduce one's motivation or engagement in goal-directed behaviors.

Furthermore, this reduction in engagement and withdrawal from tasks serve as maladaptive techniques employed to avoid expected poor performance and/or failure. In turn, these maladaptive techniques strengthen dysfunctional beliefs by limiting one's ability to participate in future goal-directed tasks, which may have counteracted poor past experiences. In line with this theory, it has been proposed that negative symptoms may develop as a result of this cycle of negative cognitive appraisals regarding one's self, formed as a response to "threatening delusional beliefs, perceived social threat, and anticipated failure in tasks and social activities" [86]. Functioning may then become further impaired with the development and maintenance of negative symptoms.

The model proposes that there are four negative expectancy appraisal domains considered to be characteristic of negative symptomatology in psychotic disorders that contribute to the expression and maintenance of negative symptoms. These four domains include having low

expectancies for pleasure, low expectancies for success, low expectancies for acceptance, and a perception of limited resources.

Low expectancies for pleasure can be explained as the expectations that people with schizophrenia often have that they will not gain or will gain very little pleasure for their efforts at a given activity. Current research supports the theory that people with schizophrenia, in comparison to non-patient controls, do experience more negative emotions and fewer positive emotions in daily life, as well as portraying significantly fewer positive and negative facial expressions in response to emotional stimuli. However, their ability to experience a full range of emotion is intact, with research showing that this perhaps is a function of their participation in fewer activities that are likely to elicit pleasant emotions [86].

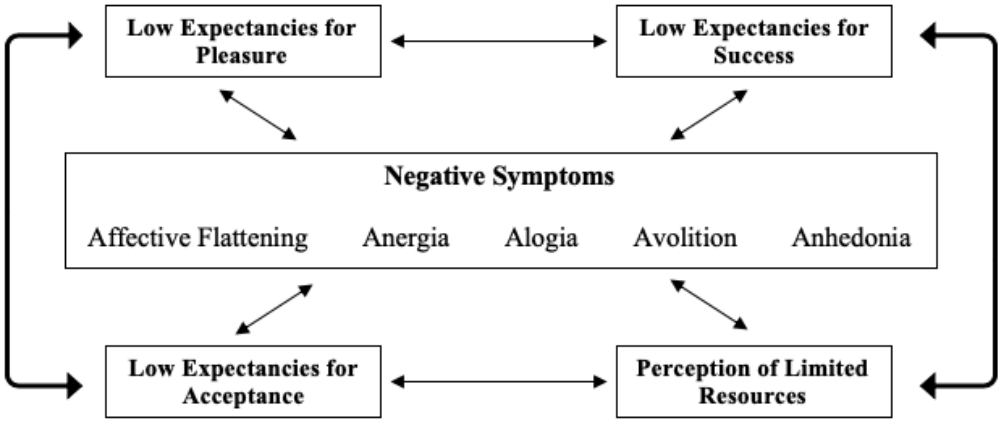

Figure 2.1 The Cognitive Model of Negative Symptoms[86]

Low expectancies for success refer to the poor confidence that people with schizophrenia may have in their ability to perform tasks, and the belief that their performance and abilities are subpar in instances in which they successfully perform tasks [86]. This negative viewpoint affects their motivation to initiate and follow through with goal directed behaviors [86]. This low expectancy for success has been identified to be a significant factor in the maintenance of negative symptoms, with individuals' expectancies for success being positively correlated with negative symptom severity [88].

The domain of *low expectancies for acceptance* refers to the impact that stigma can have on a person's motivation and behavior, with previous studies extensively describing the adverse impact of a schizophrenia diagnosis [86]. This may be compounded by symptom distress and misconstruals by others regarding reasoning behind behavior or lack thereof, that all may lead to negative beliefs about self-worth.

Finally, the *perception of limited resources* appraisal domain refers to the dysfunctional beliefs held by people with schizophrenia about the costs associated with applying energy and effort, which can lead to passivity and avoidance of activities that require effort [86]. This belief in a lack of available resources however may be a symptom of psychosis itself, given that a number of studies have found people with schizophrenia possess a diminished cognitive ability for task relevant cognitive operations. However, this lack of ability may also be exaggerated due to an inflexible and often pessimistic cognitive view [85].

The cognitive model of negative symptoms demonstrates the psychological influences, or drivers, that can increase or diminish one's motivational drive. Negative expectancy appraisals regarding a person's ability to gain pleasure, experience success, experience acceptance, and to gain and develop resources to achieve one's goals can lead to reductions in motivation and engagement in both goal-directed behavior and other enjoyable activities, resulting in social withdrawal and lack of motivation [89].

Use of and support for the cognitive model of negative symptoms has been found in both cross-sectional and longitudinal studies [87,88,90-98]. A number of studies have found associations between increased dysfunctional attitudes, such as defeatist performance beliefs, and negative symptoms in samples of people with schizophrenia [89]. Importantly, these associations have been found even after controlling for other symptom domains, such as depression [22,97].

2.6 Drivers of Motivation

Although research on specific motivational deficits among people with psychotic disorders is sparse, we identified a number of studies and theories discussing possible processes involved in motivational drive, as well as a few studies assessing these processes in regard to negative

symptoms. Motivation has been found to be reliant on a number of processes, revolving around the ability to anticipate rewards, the hedonic experience of rewards, and the ability to form and sustain a mental representation of rewards and work towards that future reward by modifying one's behavior. Through the use of Rector, Beck, and Stolar's cognitive model of negative symptoms and our review of the current evidence base, we identified three psychological factors found to influence motivational drivers.

2.6.1 Self-efficacy

Self-efficacy has been defined by psychologist Albert Bandura as the extent to which we believe ourselves capable of successfully performing a given task to produce a desired outcome[99]. Perceived self-efficacy refers to an individual's belief in his or her ability to influence events that affect the outcome of his or her life [28]. Given that self-efficacious beliefs determine how a person thinks, feels, and behaves, they play a key role in the self-regulation of motivation [99]. As belief in one's own ability to succeed in tasks is influenced by one's perceived self-efficacy, it contributes to the amount of time and effort that one will expend to complete a task, in addition to the number of obstacles or setbacks tolerated before giving up [94]. Self-efficacy beliefs therefore are thought to be important driving factors in one's goal setting, willingness to expend effort and persist at a given activity, and one's resilience to failure [99].

Self-efficacy beliefs influence one's causal attributions – people who regard themselves as highly efficacious attribute their failures to insufficient effort, whereas those who believe themselves to be inefficacious attributing their failure to their own low ability [99]. These causal attributions affect our level of motivation, our performance, and our affective reactions. People who have a low perceived self-efficacy avoid or forego certain tasks which may reinforce their own low expectations, whereas people with a high perceived self-efficacy may be more likely to view difficult tasks as challenges that they can achieve and learn from [99,100]. Although self-efficacy is viewed as a determinant of behavior, it is also possible that one's experiences of success due to their own behavior can influence self-efficacy beliefs, suggesting that there may be a bi-directional relationship between self-efficacy and behavior [99]. This is important to note, given that it would suggest that self-efficacy beliefs are not stagnant and can actively change given one's experiences of goal achievement or failure.

Among individuals with schizophrenia, in both acute and chronic phases of illness, self-efficacy is reduced in comparison to controls [28,89,101]. However, findings have been mixed with respect to the relationship between self-efficacy and negative symptoms in schizophrenia spectrum disorders. Numerous studies have found associations between greater self-efficacy and lower negative symptom severity among people with schizophrenia spectrum disorders [28,85,89,90,94,95,102,103]. A study by Cassar and colleagues used the cognitive model of negative symptoms to assess possible influences on negative symptom development and maintenance[94]. Their findings suggest that low self-efficacy might potentiate negative symptoms, mainly anhedonia and avolition, through a reduction in expectations of success, efforts to obtain rewards, confidence in one's cognitive skills, and a reduced tolerance toward goal obstacles and aversive experiences. However, it is also important to note that a number of studies have failed to find a significant relationship between the two variables [96,100,102,104-107]. Couture and colleagues assessed a number of dysfunctional beliefs in relation to the cognitive model of negative symptoms, with self-efficacy included as a measure of negative expectancy appraisals of one's self; however, the authors failed to find a relationship between self-efficacy and negative symptoms[96].

Given the proposed link between negative symptoms, namely avolition, and functional outcomes, it is possible that a relationship between self-efficacy and functional outcomes also exists, given that self-efficacious beliefs are a component of motivation. One might expect that self-efficacy would be the most strongly related motivational driver to the negative symptom subdomain of avolition, and interventions targeting self-efficacy would be useful for alleviating avolition and thereby improving functional outcomes. However, few studies have assessed the role of self-efficacy and functioning in schizophrenia. Pratt and colleagues assessed the role of self-efficacy as a mediating link between negative symptoms, cognition and premorbid adjustment, and functioning as measured by psychosocial status among patients diagnosed with schizophrenia or schizoaffective disorder[103]. Results showed that although self-efficacy was found to have a small but significant correlation with premorbid adjustment, negative symptoms, and functioning, there was no evidence to suggest that self-efficacy mediated the relationship between these factors[103]. Specifically, self-efficacy did not mediate the relationship between

premorbid adjustment or negative symptoms with functioning. However, they did find evidence to suggest that negative symptoms mediated the relationship between self-efficacy and functioning[103].

A study by Kurtz and colleagues built upon these findings by investigating whether self-efficacy mediated the relationship between key illness features, such as negative symptoms and cognition, and performance-based measures of functioning[102]. There was no association between self-efficacy and functional skills, however they did find a moderating effect of illness insight for the relationship between self-efficacy and functioning, where at higher levels of insight, self-efficacy beliefs were linked to measures of functioning. This finding was not present among people with low insight, providing a possible explanation as to why self-efficacy beliefs, which have been shown to play a positive role in achievement outcomes of healthy populations [99], have less of a role in mediating the relationship between key illness features and functioning in schizophrenia. Studies assessing the mediating role of negative symptoms in the relationship between self-efficacy and functioning have been mixed as well, with some lending support to the mediating role of negative symptoms [28,93] whereas others have failed to find a mediation effect [95].

2.6.2 Defeatist Performance Beliefs

As the discussion on motivational deficits and their role in the negative symptoms of schizophrenia has grown in recent years, defeatist performance beliefs (DPB) have received the most empirical support and been consistently found to be associated with negative symptom severity and functional outcomes [87]. DPB refers to a specific form of defeatist beliefs that consists of overgeneralized negative conclusions about one's ability to perform tasks [87]. Consistent with the cognitive model of negative symptoms, defeatist performance beliefs are considered to fall under the category of dysfunctional attitudes, in which people perceive themselves to exhibit inferior task performances. These defeatist beliefs form maladaptive strategies that protect the individual from expected pain and rejection, however they also form barriers for individuals to engage in constructive activities [98].

DPB regarding the planning and execution of tasks can prevent initiation and engagement in motivated, goal-directed behavior. Although the role of DPB in schizophrenia has been

investigated only recently, past research generally focused on the role of dysfunctional attitudes as a general mechanism underlying motivational and pleasure deficits in people with affective disorders. Beck and colleagues built upon this work with the development of the cognitive model of negative symptoms, positing that the development of DPB result in a decreased motivational drive which may contribute to the decline in functional outcomes in schizophrenia [91]. Specifically, Beck and colleagues theorize that DPB leads people with schizophrenia to a false sense of safety, whereby one succumbs to the defeatist beliefs and forms dysfunctional attitudes, and consequently lessen the likelihood of goal-directed behavior further reinforcing their disengagement from society.

Negative performance beliefs have been endorsed by individuals with chronic schizophrenia to a greater extent than healthy controls and have also been found to be associated with negative symptoms [28,98,108]. In relation to self-efficacy as a motivational driver, DPB and self-efficacy have been found to exhibit a moderate inverse correlation to one another, along with each being significantly associated with negative symptoms when adjusting for one another [89]. Cross-sectional studies have found that the occurrence of DPB are associated with elevated cognitive impairments such as deficits in working memory and verbal learning, as well as increased negative symptom severity [96,97]. This positive correlation between DPB and negative symptoms is found to be independent of positive symptoms, as well as depressive symptoms which are often found to be closely tied to negative symptomology [28,96,97]. Importantly, this relationship between DPB and negative symptoms is seen to a larger extent with negative symptoms associated with motivation and pleasure, such as avolition and anhedonia [28,91]. A 2011 study by Couture and colleagues found that when assessing the relationship between DPB and negative symptom domains, a significant relationship was only observed in regard to the 'diminished experience' domain, referring to the negative symptoms of avolition, anhedonia, and asociality, thus lending credence to the theory that DPB play an important role in motivational drive[96].

Research is limited on the relationship between DPB and functional outcomes. Some studies have found an association between increased reports of DPB and reduced functioning in people with schizophrenia. Ventura and colleagues assessed the relationship between dysfunctional attitudes, including defeatist beliefs, and negative symptoms and found them to be significantly

correlated with daily functioning, with negative symptoms found to mediate the relationship[28]. This association was also demonstrated by Kiwanuka and colleagues [109]. As well, Grant and Beck found an increase in defeatist beliefs to be associated with greater negative symptom severity, reduced functioning, and decreased neurocognitive performance[97]. When assessing the mediational role that DPB may play, they found that DPB were mediators in the relationship between negative symptoms and functioning. In a study assessing the use of cognitive therapy at targeting dysfunctional attitudes, Pillny and Lincoln found that a reduction in DPB was associated with a change in functioning 18 months after treatment, and that the use of cognitive therapy to target dysfunctional attitudes was effective in improving motivation and functioning among a sample of individuals with persistent negative symptoms [92].

Although empirical evidence suggests that DPB and functioning are associated, whether they are mediators in the relationship between negative symptoms and functioning, or rather are mediated by negative symptoms, is still unclear. Although other cognitive and emotional mechanisms of negative symptom development and functional outcome decline have been proposed, early evidence suggests that targeting DPB has the potential to reduce negative symptoms and improve functional outcomes [91]. Campellone and colleagues conducted two meta analyses assessing the relationship between DPB and negative symptoms and functional outcome in people with schizophrenia[91]. Findings demonstrated a small effect size for the relationship between DPB and negative symptoms, as well as between DPB and functional outcome[91].

2.6.3 Anticipatory Pleasure Deficits

Anhedonia has been defined as a diminished capacity to experience pleasant emotions, as well as a difficulty in experiencing pleasure [49]. It is a clinically significant aspect of schizophrenia falling under the category of negative symptoms and has been found to be relatively stable and linked with significant impairment in social functioning [82,110]. However, current evidence suggests that people with schizophrenia do not experience a full hedonic deficit. Experimental studies using a wide range of emotion-evoking stimuli demonstrate that people with schizophrenia report intact experiences of emotions, both pleasant and unpleasant, and that these experiences of 'in the moment' emotion are equal in intensity compared to healthy controls [49,110-112]. Interestingly, studies employing the use of self-report or interview-rated measures of

anhedonia have found people with schizophrenia tend to report lower levels of trait-like hedonic experiences [9,110-115]. This 'emotion paradox' has been assessed by considering what constitutes the experience of pleasure. According to Klein (1984), pleasure can be divided into two forms, anticipatory and consummatory, whereby anticipatory pleasure involves motivated behavior and a desire for a future stimulus whereas consummatory pleasure describes the positive emotion experiences at satiation [112,116]. The Temporal Experience of Pleasure scale developed by Gard and colleagues[116]differentiates between anticipatory and consummatory pleasure. Through the use of this scale, studies have shown that people with schizophrenia experience deficits in self-reported anticipatory pleasure but not consummatory pleasure [116,117]. Furthermore, anticipatory pleasure scores were significantly correlated with behavioral activation, response to rewards, drive, and assessments of social and family role functioning, whereas consummatory pleasure was only found to be correlated with physical anhedonia [112,113,116].Foussisas and Remington proposed that people with schizophrenia experience a diminished capacity to anticipate pleasure gained by the pursuit or achievement of a goal[49]. This is indicative of an anticipatory pleasure deficit, suggesting that anhedonia in schizophrenia is closely related to both motivation and goal-directed behavior. Hedonic impairments, therefore, may be considered one facet of motivational deficits [82,117], with these findings supporting the two-factor subdomain structure of negative symptoms with anhedonia and avolition in psychotic disorders being closely related, forming a distinct subdomain separate from other negative symptoms. Specifically, that psychotic disorder symptomology includes motivational deficits, with both avolition and anhedonia being differential expressions of this common underlying process.

Considering the cognitive model of negative symptoms, anticipatory pleasure deficits would align with the cognitive appraisal domain of low expectancies for pleasure. However, studies assessing the link between anticipatory pleasure and motivation are limited. In support of the theory, findings have shown that people with schizophrenia are poor at predicting enjoyment in the distant future and this strongly influences their motivation to seek out a desired outcome [116,117]. As such, these differences in the experience of wanting versus liking (i.e. anticipatory pleasure versus consummatory pleasure) may play a strong motivational role in driving individuals with psychotic disorders to work towards specific stimuli or experiences. A paper by DaSilva and colleagues examining the association between amotivation and hedonic deficits

identified a significant correlation between anticipatory pleasure and amotivation[82]. As well, Chan and colleagues found, in comparison to patients with no negative symptoms, individuals who exhibited negative symptoms reported experiencing less anticipatory pleasure but did not differ in reports on consummatory pleasure[118]. However, findings from Vignapiano and colleagues failed to find an association between low motivation and anticipatory pleasure deficits, demonstrating the mixed findings on the proposed relationship[119].

There is a paucity of studies on the relationship between anticipatory pleasure deficits and poor functioning. Buck and Lysaker found that among a sample of 51 individuals with schizophrenia spectrum disorder, anticipatory pleasure scores at baseline were correlated with poor social functioning at six-month follow-up, as well as emotional discomfort and positive symptoms, however they did not find a correlation between anticipatory pleasure and negative symptoms[110]. However, Mote and colleagues conducted a similar study with findings demonstrating the opposite effect; with anticipatory pleasure scores being negatively correlated with negative symptoms but no significant relationship with functional outcomes were observed[114].

2.7 Knowledge Gap

Although the current evidence base suggests that negative symptoms play a significant role in functional outcomes, specifically via the avolition/anhedonia subdomain, few studies have assessed the relationship between functional and psychological drivers of motivation. Instead, the majority of the studies assessing functional outcome rely solely on measures of avolition that measure overt behavior as a proxy for motivational level. The concern with this approach is that rather than measuring the symptoms itself, the behavioral outcome of functional ability is being assessed. When reviewing the current evidence base, a number of studies were found that assessed motivational factors such as self-efficacy, defeatist performance beliefs and anticipatory pleasure deficits. However, these studies were mainly descriptive in nature and did not control for a full range of potential confounding factors. The few studies that did perform multivariable analyses did not take in to account a wide range of covariates or potential confounders and instead focused mainly on symptom variables, such as positive symptoms and depression. Furthermore, these studies assessed one or two of the identified drivers of motivation, with a different sample being used with each study. Studies comparing these drivers of motivation and

the role they play in regard to functional outcomes within the same sample have not been conducted. Therefore, our current knowledge on the relationship between motivational drivers and functioning does not consider the role or contributions that other psychosocial and clinical variables may have.

Additionally, these prior studies often included measures of negative symptoms within their multivariable models, specifically the negative symptoms that fall within the diminished experience subdomain, which overlap significantly with measures of functioning. As well, a number of these studies assessed the role of the identified drivers of motivation in regard to their indirect effect on functioning, mediated by negative symptoms. However, this approach is concerning given that measures of negative symptoms, namely avolition subdomains, overlap with functional measures. As such, we cannot ascertain whether lack of motivation is associated with poor functioning when both variables are measuring the same overt behavioral markers.

To address these limitations, further study on the role that avolition plays in the development of functional outcomes using multivariable regression models that include a full range of clinical and psychosocial confounding factors, without overlapping negative symptom measures, is warranted.

2.8 Study Rationale and Research Questions

With growing interest in understanding the factors that affect functioning and achieving functional remission in people with psychosis, the identification of modifiable treatment targets to improve functionality is important. Given that avolition has been found to be highly correlated with functioning, the nature of this relationship to functioning needs to be further studied. To better inform the observed relationship between avolition and impaired functioning and address past study limitations, there is a need for more nuanced research on the internal driving factors of motivation and their relationship to functional outcomes. Therefore, the aim of this thesis was to examine the direct effects of internal drivers of motivation and functioning in a cross-sectional sample of people with psychotic disorders, in order to address the following research questions:

1. Is there a relationship between intrinsic, psychological drivers of motivation and functional outcomes?
2. Is there a difference in the relationship between these motivational drivers and specific functional domains?

2.9 Thesis Objectives and Hypotheses

2.9.1 Objective 1

Findings from studies assessing the relationship between clinical variables and functional outcomes in people with psychotic disorders have consistently shown a significant relationship between negative symptoms, namely avolition, and functioning. However, due to methodological and validity issues around the assessment of functional outcomes and avolition, findings are questionable and require the assessment of more intrinsic motivational factors in regard to functioning. Given the need for (a) a better understanding of how to address negative symptoms, (b) more intrinsic measures of motivation that may lead to avolition, and (c) treatment targets to improve functional recovery, we sought to examine and compare the associations between internal drivers of motivation (self-efficacy, anticipatory pleasure capacity, and defeatist performance beliefs) and overall functioning among people with a psychotic disorder, without the confounding effects of avolition and negative symptoms among people with psychotic disorders.

Hypothesis for Objective 1

We hypothesized that there would be a significant association between each identified internal driver of motivation and overall functioning. Specifically, we hypothesized that people with higher self-efficacy, high anticipatory pleasure capacity, and lower defeatist performance beliefs would experience better overall functioning.

2.9.2 Objective 2

To our knowledge, no study to date has examined the role of multiple motivational drivers on specific domains of functioning among people with psychosis. Given that functional outcomes can be divided into separate domains of functioning, we sought to assess the relationships

between the identified internal drivers of motivation and specific domains of functioning, specifically working productivity, independent living and self-care, immediate social networks, and extended social networks in a sample of people with a primary psychotic disorder, adjusting for demographic and clinical covariates.

Hypothesis for Objective 2

Given the exploratory nature of this objective, we did not have any set hypotheses in regard to the relationships between each driver of motivation and each functional domain. However, we expected that there would be observable differences between each driver of motivation within each functional domain, and between domains and hypothesized that drivers of motivation would work independently of each other in regard to their impact on functional sub-domains.

Chapter 3

3 Methods

3.1 Data Source

This cross-sectional, descriptive study uses data from a shared data repository composed of two studies that were conducted by an early psychosis intervention (EPI) program, known as the Prevention and Early Intervention Program for Psychoses (PEPP). Established in 1997, PEPP is an outpatient mental health treatment programme located at Victoria Hospital, London Health Sciences Centre in London, Ontario, Canada. PEPP uses a comprehensive approach to treatment of non-affective psychotic disorders with intensive medical and psychosocial management [14,120]. The PEPP shared data repository consists of (1) a prospective cohort study assessing 10-year outcomes of individuals who were clients of PEPP; and (2) a cross-sectional study assessing the magnitude, nature and determinants of negative symptoms of current clients of PEPP. Both studies received ethics approval from Western University's Health Sciences Research Ethics Board (Appendix A). No additional ethics approval was necessary for the purposes of this thesis as the objectives and methods fell within the scope of the approved protocols.

3.2 Study Setting

PEPP is an integrated clinical and research-based program developed for providing improved care while simultaneously collecting data on patient outcomes, in order to develop an evidence base for improving service delivery and our understanding of psychotic disorders and determinants of outcome [121]. PEPP is geared towards the treatment of non-affective psychotic disorder. At the time of data collection for these studies, PEPP employed strategies to reduce delays in receiving assessment and treatment by using an open referral policy, with a response time for assessment occurring rapidly after initial referral [120]. Following referral, patients are screened by a PEPP clinician for symptoms of psychosis. If presenting with such, patients then undergo a more comprehensive diagnostic assessment by a PEPP psychiatrist. Patients with a primary psychotic disorder who are between the ages of 16 to 40 years (prior to 2014, patients up to 50 years of age were eligible), live within the defined catchment area, and have not received antipsychotic treatment for a period greater than one month are considered eligible and are

accepted into the program once a consent for assessment and treatment is given [120]. Further information on PEPP services can be found within Appendix D.

3.3 Study Procedure

Data from two studies, titled the "Assessment of 10 Year Outcomes for Clients of the Prevention and Early Intervention Program for Psychoses (PEPP)" and the "Understanding Negative Symptoms in Patients of an Early Intervention Program for Psychotic Disorders", are included within our data set with the former being referred to as "the 10-year patient outcome study" and the latter being referred to as "the negative symptom study".

The 10-year outcome study collected data from patients at baseline, one-year follow-up, five-year follow-up and again at 10-year follow-up. This thesis focuses on follow-up assessments conducted at 10 years, as well as assessments conducted in regard to the negative symptom study.

Both studies had assessment periods conducted at similar time points (2014-2015) and with overlapping objectives, namely the assessment of symptomology among individuals with psychosis, the identification of potential covariates, the evaluation of functioning, quality of life and other measures of recovery, and a more detailed assessment of negative symptoms and correlated/predictors of variation in these symptoms. Due to this similarity across study objectives and procedures, we were able to combine the PEPP data sets for our analyses, for a total combined dataset of 105 participants; 69 from the 10-year outcome study and 36 from the negative symptom study.

Participants were provided with a letter of information regarding the nature and purpose of the study as well as a letter of consent in which they agreed to participate in assessment interviews, which were scheduled at a time convenient for the participant. Assessment involved the completion of a battery of clinical and non-clinical outcome measures. Completion of the assessments were split between two days, separated by one to two weeks. A random number system was used to determine which measures would be administered to the participant at each meeting. Written informed consent was obtained from each participant at his/her first assessment

interview. Demographic information was recorded by means of a demographic questionnaire and outcome measures were administered using a semi-structured interview format. All clinical measures were administered by a clinical psychologist or psychiatrist, whereas non-clinical measures were administered by the research coordinator who was trained and supervised by the clinical psychologist.

As assessments were completed, the interviewer paid attention to each participant's demeanor and energy level. In instances where these factors were diminished, participants were encouraged to take a break and complete the rest of the assessments at a subsequent session one to two weeks later.

3.4 Data Set

Access to the PEPP shared data repository was obtained from the principal investigator of the source studies. The principal investigator was tasked with extracting the requested subset of variables from the PEPP shared data repository and creating the data set, which was then transferred for use in the current analyses.

Upon receipt of the data set, SPSS was used to convert the database from SPSS format to SAS format (.sav to .sas7bdat). SAS version 9.4 [122] was then used to 'clean' the data. This step included assessing the distribution of all variables, checking for potential outliers, and re-labeling and re-coding of variables.

3.5 Variables and Measures

3.5.1 Exposure Variables

Self-Efficacy

Self-efficacy is defined as the confidence one has in their ability to perform a behavior or specific task [123]. To assess self-efficacy, the Generalized Self-Efficacy scale (GSE) was used[123]. The GSE is a self-report rating scale consisting of ten items scored using a 4-point Likert scale ranging from one (Not at all True) to four (Very True). Although self-efficacy is understood to be domain specific, meaning that one can have more or less firm self-beliefs in different domains

or situations, the GSE assesses a generalized sense of self-efficacy, which refers to overall confidence in one's ability to cope with a wide range of novel and/or demanding tasks [123]. This concept of generalized self-efficacy consists of a two-part cognitive set composed of a sense of successful agency and pathways [123]. The agency component reflects a goal-directed determination, and the pathways component reflects an ability to plan ways to meet said goals.

The GSE has been used in previous research as a tool to assess self-efficacy and dysfunctional beliefs about one's self, and has demonstrated high internal consistency among 127 outpatients diagnosed with schizophrenia with an ICC value of 0.9 [106]. It also demonstrated a high test-retest reliability with ICC values ranging from 0.69 to 0.8 among multiple samples of university students [123,124]. Along with being parsimonious and reliable, the scale has demonstrated both convergent and discriminant validity.

For the purpose of this thesis, we used the GSE as a measure of one's overall sense of self-efficacy. Total scores on this measure range from 10 to 40, with higher scores indicative of a greater sense of self-efficacy. All analyses used the GSE as a continuous variable.

Anticipatory Pleasure Capacity

Anticipatory pleasure is defined as the ability to feel pleasure in regard to future activities, leading to one having the experience of 'wanting' [116]. To assess anticipatory pleasure, the Temporal Experience of Pleasure scale (TEPS) was administered[116]. The TEPS is an 18 item self-report measure that assesses two domains of pleasure, being **anticipatory pleasure** (10 items; e.g. *"When I hear about a new movie starring my favourite actor, I can't wait to see it."*) and **consummatory pleasure** (8 items; e.g. *"I enjoy taking a deep breath of fresh air when I walk outside.").* Anticipatory pleasure has been shown to be more closely linked to motivation and goal-directed behavior, whereas consummatory pleasure has been shown to be closely linked to satiation [116].Therefore, items written to relate to anticipatory pleasure capacities reflect pleasure experiences in anticipation of a positive and/or pleasurable stimulus, whereas items written to relate to consummatory pleasure reflect in-the-moment pleasure in response to a stimulus. Items were written in regard to both specific and general situations that involved all five sensory modalities and that focused on the domain of physical pleasure. Items are rated on a

6-point Likert scale ranging from one (Very False for Me) to six (Very True for Me). Items related to anticipatory pleasure were used to create a total score for one's level of anticipatory pleasure capacity (Appendix E). Total scores on this subscale range from 10 to 60, with higher scores indicative of a higher capacity for anticipatory pleasure.

The TEPS has demonstrated good internal consistency for the total scale as well as both subscales for anticipatory and consummatory pleasure, with a Cronbach's α of 0.87, 0.71 and .78, respectively, among a sample of 86 persons diagnosed with schizophrenia [125]. The test-retest reliability of the scale and subscales have all been found to be high ($r= 0.75$; $p<0.001$) [116]. When tested against scales on pleasure, the TEPS was found to be related but clearly distinguishable from measures of personality, motivation, and pleasure constructs [116].

As previously stated, individuals with psychotic disorders such as schizophrenia have been found to have intact consummatory pleasure capacities, with deficits being observed within the anticipatory pleasure domain. These deficits in anticipatory pleasure have been linked to both negative symptoms and functional outcomes. For the purpose of this thesis, the anticipatory pleasure subscale score was used as a measure of anticipatory pleasure capacity and was used as a continuous variable in all analyses.

Defeatist Beliefs

Defeatist beliefs are defined as overgeneralized negative thoughts about one's ability to successfully perform goal directed behavior [97]. To assess defeatist beliefs, the Defeatist Performance Beliefs scale (DPB) was used[97]. The DPB, a subscale of the Dysfunctional Attitudes Scale, is a 15-item self-report measure that includes statements concerning one's ability to perform tasks and the likelihood of their success (e.g. *"If I do not do as well as other people, it means I am an inferior human being."*) Items are scored using a 7-point Likert scale ranging from one (Totally Agree) to seven (Totally Disagree).

The DPB has been used in previous studies as a measure of defeatist beliefs in patients with psychosis [91,96-98] and has demonstrated high internal consistency, with Cronbach's α of 0.85 [96,98].

For the purpose of this thesis, the total score on the DPB was used as a measure of defeatist performance beliefs. Total scores on this unidimensional measure range from 15 to 105, with lower scores being indicative of a high degree of defeatist performance beliefs. All analyses conducted for this thesis used the DPB as a continuous variable.

3.5.2 Outcome Variable

Functioning

Functioning was assessed using the Role Functioning Scale (RFS)[79], consisting of four single rating scales that are used to evaluate levels of functioning in specific subdomains of everyday life: (1) Working Productivity; (2) Independent Living and Self-Care; (3) Immediate Social Network Relationships; and (4) Extended Social Network Relationships. The RFS is scored using a seven-point Likert scale ranging from one (Minimal Level of Role Functioning) to seven (Optimal Level of Role Functioning), with each of the seven points on the scales accompanied by a behaviorally defined description (e.g. Working Productivity, *"Productivity severely limited; often unable to work or adapt to school or homemaking; virtually no skills or attempts to be productive"*.) The total of the four role scores represents a Global Role Functioning Index, with total scores ranging from 4 to 28. The RFS is administered via a standardized interview, with the patient being evaluated based on a specified time period, such as the previous week.

The RFS has demonstrated its ability to discriminate accurately between psychiatric and non-psychiatric patients of varying functional capacity and shows good inter-item (α=0.92), test-retest (r=0.85 to 0.92) and inter-rater reliability (t=0.64 to 0.820) [79].

For the purpose of this thesis, we used the RFS Global Index score as an overall assessment of functioning as well as the subdomain scores for functional capacity in specified areas of everyday life with higher scores being indicative of better functional outcome. The global index is a composite measure of the four Likert subscales, with each subscale being a 7-point Likert scale, and therefore measured ordinally. However, studies and reviews on the use of Likert data with parametric testing methods have shown that with ordinal measures that have five or more categories, the data can be treated as continuous [126-129]. It has also been demonstrated that parametric testing methods can be used, which are generally more robust than non-parametric

testing methods, especially when there is an adequate sample size and if normality is observed within the data [128,129]. Therefore, for the purposes of consistency with our first objective, we chose to treat the sub-domain scores as continuous for our main analyses.

3.5.3 Potential Covariates

For our main analyses, we controlled for 11 variables that were identified as possible covariates, and were examined in previous studies, through our literature review with information pertaining to the relationship between these variables and our exposure and outcome variables presented below. We were unable to control for four additional variables identified as potential covariates due to their exclusion from assessments within the negative symptom study, specifically age of onset, mode of onset, duration of untreated psychosis and premorbid adjustment. Because these variables were assessed for the 10-year outcome study, we conducted sensitivity analyses on the subset of data from the 10-year outcome study, including these variables and the other identified covariates. Information pertaining to these four additional variables and the measures used for assessment can be found in Appendix F.

Age

Age, measured in years, was assessed at baseline using the demographics questionnaire and was treated as a continuous variable in our main analyses.

Gender

Gender was assessed at baseline using the demographics questionnaire and was treated as a dichotomous variable, with possible response items being either *Male* or *Female*. In comparison to males, females have been associated with a higher level of functioning [20,130-132]. Furthermore, females have been associated with greater premorbid adjustment, a shorter duration of untreated psychosis, and a higher level of education, in comparison to males [130].

Education

Education, measured in years, was assessed using the demographics questionnaire. Higher education has been shown to be associated with greater functional outcomes [20,47,132]. Data on

years of education was used as a proxy indicator of socio-economic status and treated as a continuous variable for all analyses.

Length of Treatment

Length of treatment was defined as the length of time, in years, from the date of admission into PEPP to the date of assessment. These dates were obtained from demographic questionnaires. Given that our data set contained participants from two separate studies, participants' length of treatment varies depending on the study they participated in. In our analyses, length of treatment was used as a continuous variable.

Perceived Social Support

Social support was assessed using the Interpersonal Support Evaluation List (ISEL)[133], a 40-item self-report measure of perceived social support in which items are dichotomously scored (Probably True vs. Probably False). The ISEL calculates total scores as well as subdomain scores assessing four domains of social support including **appraisal** (10 items; e.g. "There are several people that I trust to help solve my problems."), **tangible** (10 items; e.g. "If I needed help fixing an appliance or repairing my car, there is someone who would help me."), **self-esteem** (10 items; e.g. "Most of my friends are more interesting than I am.") and **belonging** (10 items; e.g. "When I feel lonely, there are several people that I can talk to."). Total scores for each subdomain range from 0 to 10, with higher scores indicative of higher perceived social support within that specific domain.

The ISEL has been shown to have a high degree of test-retest reliability after a four-month period ($r=0.83$) as well as internal consistency ($\alpha=0.93$), among a sample of 59 individuals with Bipolar I disorder [134]. Social support has been found to be associated with improved functional outcomes in individuals with schizophrenia [135-137], with the presence of a support system during early stages of illness predicting better functioning [136].

For the purpose of these analyses, the total perceived social support score was computed using the total score from each domain of the ISEL, with the total score used as a continuous variable for all analyses.

Positive Symptoms

Positive symptoms were assessed using the Scale for the Assessment of Positive Symptoms (SAPS)[138]. The SAPS is a 34 item, six-point Likert scale with individual item scores ranging from zero (Absent) to five (Severe). The SAPS provides both a total score as well as subdomain scores pertaining to four positive symptoms, including: (1) **Hallucinations** (7 items; e.g., Auditory Hallucinations, "The patient reports voices, noises, or other sounds that no one else hears."); (2) **Delusions** (13 items; e.g. Persecutory Delusions, "The patient believes he is being conspired against or persecuted in some way."); (3) **Bizarre Behavior** (5 items; e.g. Clothing and Appearance, "The patient dresses in an unusual manner or does other strange things to alter his appearance."); and (4) **Positive Formal Thought Disorder** (9 items; e.g. Derailment, "A pattern of speech in which ideas slip off track onto ideas obliquely related or unrelated.").

As a reference point, all items are answered using the time frame of the past month. Total scores range from 0 to 150, with higher scores indicative of a greater severity of positive symptoms. Subdomain ratings range from 0 to 65, depending on the subdomain, with higher scores indicative of a greater severity of that specific positive symptom.

The SAPS has been used frequently in both research and clinical-based settings and has demonstrated high inter-rater reliability (ICC=0.84) for total summary scores, as well as moderate to high inter-rater reliability for ratings of each subdomain: hallucinations (ICC=0.91), delusions (ICC=0.86), bizarre behavior (ICC=0.50), and positive formal thought disorder (ICC=0.75) [139]. Higher positive symptom severity is associated with, poorer social support[140], a greater level of amotivation [141], and poorer functional outcomes in individuals with psychotic disorders [20,47,72,131,142].

For the purpose of this thesis the total score on the SAPS was used as a measure of positive symptom severity and was computed by summing the total scores on each subdomain of the SAPS. This measure was used as a continuous variable for all analyses.

Negative Symptoms

Negative symptoms were assessed using the Scale for the Assessment of Negative Symptoms (SANS)[31]. The SANS is a 25 item, 6-point Likert scale with individual item scores ranging from zero (Absent) to five (Severe). The SANS provides both a total score as well as subdomain scores pertaining to five negative symptoms, being: (1) **Affective Flattening or Blunting** (8 items; e.g., Unchanged Facial Expression, "The patient's face appears wooden -changes less than expected as emotional content of discourse changes."), (2) **Alogia** (5 items; e.g. Poverty of Speech, "The patient's replies to questions are restricted in amount, tend to be brief, concrete, unelaborated."), (3) **Avolition-Apathy** (4 items; e.g. Grooming and Hygiene, "The patient's clothes may be sloppy or soiled, and he may have greasy hair, body odour, etc."), (4) **Anhedonia-Asociality** (5 items; e.g. Recreational Interests and Activities, "The patient may have few or no interests. Both the quality and the quantity of interests should be taken into account.") and (5) **Attention** (3 items; e.g. Social Inattentiveness, "The patient appears uninvolved or unengaged. He may seem "spacey".").

As a reference point, all items are answered using the time frame of the past month [143]. Total scores range from 0 to 100, with higher scores being indicative of a higher severity of negative symptoms. Subdomain ratings, or global ratings, range from 0 to 25, with higher scores being indicative of a higher severity of that specific negative symptom.

The SANS has demonstrated moderate to high internal consistencies for the five negative symptom domains: affective flattening (α=0.81), alogia (α=0.81), attentional impairment (α=0.84), avolition-apathy (α=0.80), and anhedonia-asociality (α=0.63) [53].

As discussed in chapter two, the SANS total score and subdomain scores demonstrated a high degree of overlap between negative symptoms and functioning, confirmed in the study dataset using Pearson correlation coefficients; therefore, SANS scores were excluded from the main analyses. In the secondary correlation analyses, the SANS total score and subdomain scores were used as a measure of negative symptoms and were treated as continuous variables.

Depression and Anxiety

Depressive and anxiety symptoms were assessed using the Profile of Mood States-Short Form Questionnaire (POMS-SF)[144]. The POMS-SF is a measure of psychological distress consisting of 37 adjectives (e.g. "Tense"), to which responders are asked to describe how often they experience the feeling or mood over the course of the past two to three months [144]. Responses are recorded using a five-point Likert scale, with responses ranging from zero (Not at all) to four (Extremely). Scoring of the POMS-SF yields an overall total mood disturbance score, as well as scores for six subscales: **Fatigue-Inertia** (5 items; e.g. "Worn Out"), **Vigor-Activity** (6 items; e.g. "Lively"), **Tension-Anxiety** (6 items; e.g. "Tense"), **Depression-Dejection** (8 items; e.g. "Unhappy"), **Anger-Hostility** (7 items; e.g. "Grouchy"), and **Confusion-Bewilderment** (5 items; e.g. "Forgetful").

Total mood disturbance scores range from 0 to 148, and subdomain total scores range as follows: 0 to 20 for Fatigue-Inertia, 0 to 24 for Vigor-Activity, 0 to 24 for Tension-Anxiety, 0 to 32 for Depression-Dejection, 0 to 28 for Anger-Hostility and 0 to 20 for Confusion-Bewilderment. Higher scores on the total mood disturbance scale are indicative of greater mood disturbance, and higher scores on each subdomain reflect greater mood disturbance for each specific domain.

Across multiple samples, the POMS-SF demonstrated high internal consistency (α= 0.76 to 0.95) with internal consistency estimates being generally similar to or exceeding the original POMS measure [144]. As well, there was a high degree of reliability across samples for each mood state (r =0.81-0.95) [144].

In individuals with psychosis, both symptoms of depression and anxiety have been found to be correlated with amotivation [145] and poorer functional outcomes [47,72,146,147]. Additionally, the experience of anxiety has been found to be associated with greater positive symptom severity and depressive symptoms [147]. For the purpose of this thesis, only the Depression-Dejection and Tension-Anxiety subdomains were used for our analyses, with these variables being treated as continuous measures.

Drug Use

Drug use was assessed using the Drug Abuse Screening Test (DAST-20)[148]. The DAST is a 20-item self-report measure of drug use within the last three months, with drug use defined as any non-medical use of drugs, not including alcohol (e.g. *"In the last 3 months, have you used drugs other than those required for medical reasons?"*). Items are scored dichotomously, either Yes or No, with a score of one for every Yes response, with three items reverse coded. If the responses for question 1 (i.e. *"Have you used drugs other than those required for medical reason?"*) and 2 (i.e. *"Have you abused prescription drugs?"*) were No, then the remaining items were not to be completed. Total scores on the DAST-20 range from 0 to 20, with higher scores indicative of greater drug use. Comorbid substance use is considered a major obstacle to recovery amongst individuals with psychotic disorders [149], with comorbid substance use being associated with an earlier age of onset, younger age, male gender lower educational attainment and poorer outcomes such as greater symptom severity and employment and housing instability [149,150].

A cut-off score of 6 or above for the DAST-20 has been recommended for detection of substance abuse or dependence among 97 psychiatric patients with an Axis 1 mental disorder other than substance use or dependence (sensitivity, 89-84% and specificity, 68-83%) [151,152]. Psychometric studies on the DAST-20 have shown the DAST-20 to have a high degree of internal consistency (α =0.74-0.95), and test-retest reliability (ICC=0.71) among a sample of 97 psychiatric patients with an Axis 1 mental disorder [151].

Although the DAST-20 has a recommended cut-off score (i.e. 6 or above), we chose to group scores into three categories due to the majority of participants scoring 0 on the DAST-20. Therefore, DAST-20 was treated as an ordinal variable with responses falling into one of three possible categories: no drug use (i.e. DAST-20 score of 0), drug use below the cut-off score (i.e. DAST-20 scores of 1 to 5) or detected drug abuse (i.e. DAST-20 score of 6 or above).

Alcohol Use

Alcohol use severity was assessed using the Alcohol Use Disorders Identification Test (AUDIT)[153]. The AUDIT is a 10-item, self-report measure of alcohol use with the reference point being within the past three months (e.g. *"During the last 3 months, how often did you have*

a drink containing alcohol?"). All items are scored on a five-point Likert scale with scores ranging from zero to four. However, if the response to item one *("During the last three months, how often did you have a drink containing alcohol?"*) is zero, then the remaining nine items are not to be completed. Total scores on this measure can range from 0 to 40, with higher scores indicative of a greater severity of alcohol use. As with drug use, excessive alcohol use is associated with greater symptom severity and a greater risk of mental illness comorbidities [149,150,154], with individuals diagnosed with a substance use disorder being more likely to have depression [154].

The AUDIT has shown high internal consistency when used in a sample of 80 individuals with schizophrenia (α =0.81) [155]. As well, an AUDIT cut-off score of eight was shown to have a sensitivity of 87% and specificity of 90% for detecting alcohol disorders diagnosed by the Composite International Diagnostic Interview among psychiatric patients (n=71) with a diagnosis of schizophrenia [155,156].

For the purpose of this thesis, AUDIT scores were treated as categorical, with responses being grouped into one of three possible categories: no alcohol use (i.e. AUDIT score of 0), use below the cut-off score (i.e. AUDIT score of 1 to 7), and alcohol abuse (i.e. AUDIT score of 8 or above).

Medication Adherence

Medication adherence refers to the use of either first or second-generation antipsychotic medication, and was assessed using the Adherence to Medication Scale, which is a single-item question pertaining to both the past month and year (i.e. *"Based on all available information, approximately what percentage of time has the patient been taking medication as prescribed?"*). For the purpose of this thesis, we chose to use data pertaining to the past month. Development of this question was based on results from studies assessing multiple measures of antipsychotic medication adherence in patients with a first episode of psychosis [157]. In individuals with schizophrenia, non-adherence to antipsychotic medication has been associated with a greater severity of positive symptoms [137], poorer functional outcomes, alcohol dependence and substance use disorders [158] and an increased risk of psychiatric hospitalization [158,159].

The scale is rated by the interviewer based on information obtained from the primary clinician, case manager, family members, and the patient themselves [157]. The estimate is rated using a 4-point scale: 1 (0-25%), 2 (26-50%), 3 (51-75%), and 4 (76-100%). Where there was disagreement between sources on adherence, each case was discussed until a consensus was reached, however the primary clinician's estimate on medication adherence carries the most weight in the decision.

In a comparison study assessing the use of multiple measures of adherence to antipsychotic medication with a sample of 81 first-episode psychosis patients, Cassidy and colleagues found that patient reports, pill counts, and clinical reports had good agreement (ICC=0.84), and that all the measures used were highly correlated to consensus adherence scores (r=0.86 to 0.98)[157].

Due to a lack of variability in scores, we chose to treat the variable as dichotomous instead of categorical. Participant scores were grouped into one of two categories; either less than or equal to 75% medication adherence (i.e. no medication use to a score of 3) or greater than 75% medication adherence (i.e. score of 4).

3.6 Missing Data

To determine the extent of missing data within our sample, we first examined (1) the total number of cases (i.e. participants) with missing observations; (2) the total number of variables with missing observations; and (3) the number of missing observations for the exposure, outcome, and potential covariates. Our findings from these analyses are presented in Table 3.1.

Once the extent of missing data had been determined, we examined the pattern of modality of the missing data. In order to do this, we had to first distinguish between two patterns of missing data (1) Monotone; and (2) Arbitrary [160,161]. A monotone missing data pattern exists if there is a clear, observable pattern among the variables that are missing. If there is no evident pattern observed, then the missing data pattern is said to be arbitrary.

Table 3.1: Missing Data within the Study Sample

Missing Data Assessment	N (Percentage Missing)
Total number of cases with missing data	50 (47.6%)
Total number of variables with missing data	79 (37.3%)
Exposure Variables	
Generalized Self Efficacy Score	1 (0.9%)
Temporal Experience of Pleasure- Anticipatory Score	2 (1.9%)
Defeatist Performance Beliefs Score	5 (4.8%)
Outcome Variable	
Role Functioning Scale	0 (0.0%)
Work Subscale	0 (0.0%)
Independent Living Subscale	0 (0.0%)
Immediate Social Network Subscale	0 (0.0%)
Extended Social Network Subscale	0 (0.0%)
Potential Covariate Variables	
Age	1 (0.9%)
Gender	0 (0.0%)
Education (years)	10 (9.5%)
Age of Onset *	39 (37.14%)
Mode of Onset *	38 (36.19%)
Duration of Untreated Psychosis (weeks) *	38 (36.19%)
Length of Treatment	1 (0.9%)
Premorbid Adjustment Score *	46 (43.81%)
Perceived Social Support Score	2 (1.9%)
Depressive Symptoms	2 (1.9%)
Anxiety Symptoms	2 (1.9%)
Positive Symptoms	0 (0.0%)
Negative Symptoms	0 (0.0%)
Drug Use	1 (0.9%)
Alcohol Use	1 (0.9%)
Medication Adherence	5 (4.8%)

Note: n= Count; Case = Participant; Total number of observations = 105; Total number of variables=221;
* Variables missing large percentages of data were excluded from main analyses

Once the pattern of modality had been determined, we then determined the mechanism of missing data, of which there are three possible forms: (1) Missing completely at random (MCAR); (2) Missing at random (MAR); and (3) Not missing at random (NMAR) [160,162]. MCAR refers to the case where the probability that a value for a particular variable is missing is not dependent on other measured variables included in the data set and is not related to the value of the missing variable. MAR refers to instances where the probability of a missing data value for a specific variable is related to other measured variables in the data set, however it is unrelated to the value of the missing variable. Finally, NMAR refers to instances where the probability of a missing data value for a variable is dependent on the value of the missing variable [160,163]. From assessing the dataset, we determined that the pattern of missing data was arbitrary, and that the mechanism of the missing data was MAR for all data.

When determining the method to handle missing data, we took into account the pattern, mechanism, and characteristics of the included variables along with our intention to retain the entire sample (n=105). We therefore decided to use multiple imputation to handle the missing data present in our data set. Multiple imputation is a method of accounting for missing data whereby a missing value is imputed multiple times using a set of plausible values sampled from an imputation model [161].

Multiple imputation involves three stages: (1) Imputing, (2) Analyzing, and (3) Pooling. The imputing stage is the first step of the procedure where the missing values are imputed m times to create m complete data set copies. These imputed values are sampled from their predictive distribution based on the observed data. The next step is to analyze the m completed data sets to obtain m sets of parameter estimates and corresponding standard errors for the missing values. These estimates will differ for the m imputed data sets because of the variation introduced during the imputation phase and must be averaged together to give an overall estimate. Therefore, the final stage yields parameter estimates, standard errors, and confidence intervals for each of the m completed data sets that are pooled together to create one overall estimate [160].

To use the multiple imputation method, we had to decide whether we wanted to construct our imputation model using the multivariate normal method (MVN) or the fully conditional

specification (FCS) method [161]. The multivariate normal method assumes that all variables included in the imputation model jointly follow a multivariate normal distribution. Therefore, the imputation stage uses a Bayesian approach to obtain the imputed values from this multivariate normal distribution, which allows for uncertainty in the estimated model parameters [161]. The fully conditional specification method, also known as the chained equations method, has a more flexible approach to multiple imputation in that it does not rely on the assumption of multivariate normality. Conditional distributions are specified for each variable with missing values, and imputations are generated by estimating each of these conditional distributions in turn using observed cases for the variable being considered and imputed values for the other variables at that iteration, thereby imputing the missing values [161]. This again allows for uncertainty in the model parameters. Given that our dataset includes different types of variables (i.e. continuous, binary, and categorical) we decided to use the FCS method due to its ability to model each variable using its own distribution, and therefore our regression models can be tailored appropriately with logistic regression being used for binary variables and linear regression for continuous variables. In terms of the number of imputations (m), we chose 50 imputations (m=50) based on the rule of thumb that the number of imputations should be similar to the percentage of incomplete cases within the data set [164,165].

3.7 Statistical Analyses

All statistical analyses were conducted using SAS version 9.4 [122], with all hypothesis testing using a type 1 error rate set at alpha=0.05, two-tailed.

3.7.1 Descriptive Statistics

Descriptive statistics were summarized for all included participants. Categorical variables were analyzed using counts and percentages, and continuous variables were analyzed using means and standard deviations.

3.7.2 Multicollinearity

Given the inclusion of multiple exposure variables and their relation to the construct of motivation, we assessed for multicollinearity. Multicollinearity describes the situation when one

variable in a regression model can be linearly predicted from the other variables. It occurs when two or more variables that are highly correlated with each other are included in the same regression model and used together to predict the outcome variable [166,167]. Issues arise with multicollinearity due to its impact on effect estimation, with regression coefficients being imprecisely measured and standard errors being high resulting in wide confidence intervals. Taken together, these issues make it difficult to reject the null hypothesis [166,167]. To assess for the presence of a high degree of multicollinearity, we used variance inflation factors with the selected cut-off point of VIF ≥5. The variables were below the selected cut off value, which indicates a low degree of multicollinearity in our regression models. Although no standard cut-off value for VIF exists, various cut-off values have been used in previous research, ranging from scores of five to ten [168,169].

3.7.3 Correlation Assessments

To assess the degree of correlation between study variables, we conducted a series of Pearson correlation matrices to examine the associations between drivers of motivation, avolition, and functional outcomes.

3.7.4 Analysis: Objective 1

Our first objective was to determine the relationship between indicators of motivation and functional outcome among people with primary psychotic disorders. We conducted a series of simple linear regression models to assess the relationship between each exposure and covariate variable and the outcome variable global functioning. We then constructed a multivariable linear regression model to assess the relationship between the identified indicators of motivation (self-efficacy, defeatist performance beliefs, and anticipatory pleasure capacity) and the outcome variable of global functioning, adjusting for potential covariates including age, gender, education, length of treatment, social support, positive symptoms, depression, anxiety, drug use, alcohol use and medication adherence. We hypothesized that there would be a positive association between self-efficacy and functional outcome, a positive association between anticipatory pleasure capacity and global function, and a negative association between defeatist performance beliefs and global function, adjusting for potential covariates.

3.7.5 Analysis: Objective 2

Our second objective was to explore the relationship between these indicators of motivation and specific subdomains of functioning. First, we conducted a series of simple linear regression models to assess the relationship between all four subdomains of functioning and each exposure variable and potential covariates factor. We then constructed four multivariable linear regression models to assess the relationship between the identified indicators of motivation (self-efficacy, defeatist performance beliefs, and anticipatory pleasure capacity) and the sub-domains of the RFS: (i) work, (ii) independent living, (iii) immediate social network, and (iv) extended social network, adjusting for covariate factors. Each model included the three identified indicators of motivation as the exposure variables, one of the four subdomains of functioning as the outcome variable, and the potential covariate variables listed above.

3.7.6 Sensitivity Analyses

We conducted sensitivity analyses to assess the robustness of our findings by repeating objectives one and two using data from the 10-year outcome study, which contains information on additional covariate factors not available in the full dataset, specifically age of onset, mode of onset, duration of untreated psychosis and premorbid adjustment. Using imputed data (n=69) for participants of the 10-year outcome study that included additional information on covariate variables that we were unable to include in our main analyses, we repeated our analyses using these four additional covariates with the variable age being replaced with age of onset. As an additional sensitivity analysis, given that the RFS is a Likert-based scale, we repeated our objective one and two analyses using an ordinal logistic regression models treating the outcome variable as categorical in order to test the robustness of our findings to these methodological decisions.

Chapter 4

4 Results

In this chapter, we present descriptive statistics for our study sample in Section 4.1. In Section 4.2, findings from our analyses of the correlation between negative symptoms, avolition, and functional outcomes are reported. In Section 4.3, the results from our series of simple and multivariable linear regression analyses assessing the association between motivational drivers and global functioning, conducted for objective 1, are presented. This is followed by the results of our series of simple and multivariable linear regression analyses for each subdomain of functioning conducted for objective 2. In Section 4.5, findings from our sensitivity analyses are presented.

4.1 Descriptive Statistics

Socio-demographic and clinical characteristic of our study sample are summarized in Table 4.1. Our sample (n=105) consisted of a higher proportion of males (72%) than females (28%), with a mean age of 34.2 years (SD=9.9), ranging from 19 to 60 years. The majority of participants were European American (85%), single (74%) and had a diagnosis of a primary psychotic disorder (94.3%). Participants were found to be fairly evenly split between being employed (48.6%) and unemployed (45.7%), with a few participants classified as students (2.9%). The majority of participants were living with others (68%) and earning an annual income of $29,999 or less (87%). With respect to the exposure variables within our study sample, participants had a mean generalized self-efficacy score of 30.9 (SD=5.8), a mean anticipatory pleasure capacity rating of 43.6 (SD=7.9) and a mean defeatist performance belief score of 44.3 (SD=15.8).

Overall, our study sample exhibited moderate to adequate levels of functioning, equivalent to a score between 20 and 24, with a mean global functioning score of 20.67 (SD=5.29). Total scores on the RFS ranged from a minimum score of 8 to a maximum score of 28. The distribution of total RFS scores within the sample (n=105) is shown in Figure 4.1. Functional subdomain distributions showed that participants had the lowest levels of functioning in the subdomain of working productivity, with participants scoring a mean of 4.6 (SD=1.8) in comparison to the

other functional domains of independent living (mean=5.6, SD=1.5), immediate social networks (mean=5.4, SD=1.4), and extended social networks (mean=4.9, SD=1.5). However, given the range of possible scores, our study sample exhibited a moderate level of functioning, equivalent to an individual score of 5, in all four subdomains.

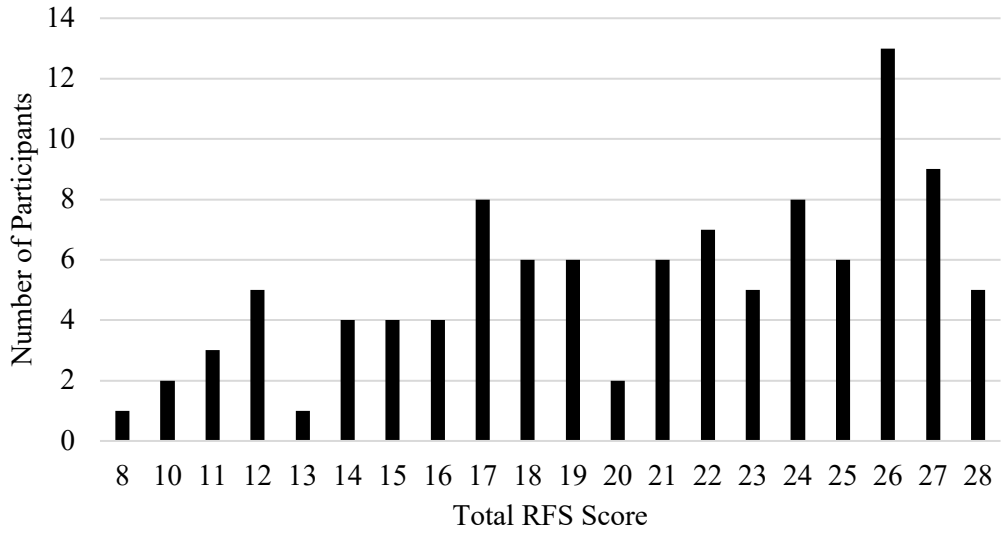

Figure 4.1 Total RFS Scores for sample (n=105)

Table 4.1: Descriptive Statistics of Study Sample (n=105)

Characteristic	*n* (%)		
Gender			
Male	76 (72.38%)		
Female	29 (27.62%)		
Ethnicity			
European American	89 (84.76%)		
African American	4 (3.81%)		
Native American	3 (2.86%)		
Asian/Pacific Islander	5 (4.76%)		
Other	4 (3.81%)		
Marital Status			
Single	78 (74.29%)		
Married/Common Law	20 (19.05%)		
Separated/Divorced/Widowed	7 (6.67%)		
Living Arrangement			
Lives Alone	34 (32.38%)		
Lives with Other(s)	71 (67.62%)		
Employment Status			
Employed	51 (48.57%)		
Unemployed	48 (45.71%)		
Student	3 (2.86%)		
Annual Income			
Less than $10,000 to $29,999	90 (87.38%)		
$30,000 to $49,999	13 (12.62%)		
Primary Diagnosis			
Schizophrenia	94 (89.52%)		
Affective Disorder(s)	4 (3.81%)		
Psychotic Disorder(s)	7 (6.67%)		
Drug Use			
None	68 (64.76%)		
Below Cut off (<6)	22 (20.95%)		
Above Cut off (>=6)	15 (14.29%)		
Alcohol Use			
None	40 (38.10%)		
Below Cut off (<6)	50 (47.62%)		
Above Cut off (>=6)	15 (14.29%)		
Characteristic	**Mean (SD)**	**Median**	**Range**
Age	34.16 (9.86)	33	19 to 60
Education (in years)	13.03 (2.04	13	8 to17
Negative Symptoms	14.39 (15.79)	8	0 to 62
Positive Symptoms	11.81 (13.98)	6	0 to72
Self-Efficacy	30.95 (5.81)	31	10 to 40
Anticipatory Pleasure Capacity	43.55 (7.92)	44	20 to 60
Defeatist Performance Beliefs	44.31 (15.78)	44	15 to 87
Functioning			
Global Functioning Score	20.67 (5.29)	22	8 to 28
Working Productivity	4.63 (1.78)	5	1 to 7
Independent Living and Self-Care	5.63 (1.51)	6	2 to7
Immediate Social Networks	5.44 (1.37)	6	2 to 7
Extended Social Networks	4.97 (1.53)	6	2 to 7

Note: n= count; %=percentage; SD=standard deviation*; Psychotic Disorder= psychosis not otherwise specified (n=3), brief psychotic disorder (n=2), psychosis due to medical condition (n=1), and substance induced psychosis (n=1)*

4.2 Correlation Analyses

In order to assess the degree of overlap between measures of negative symptoms and functioning, we first conducted a series of bivariate correlation analyses. Findings from our correlation analyses can be found in Table 4.2.1, depicting Pearson correlation coefficients between total and subdomain scores of the SANS and RFS.

The Pearson correlation coefficient (r) values revealed significant negative associations between overall functioning and total negative symptoms (r=-0.74, p<0.0001), as well as with the negative symptom subdomains of Avolition (r=-0.75, p<0.0001) and Anhedonia (r=-0.70, p<0.0001). Negative Affect (r=-0.54, p<0.0001), Alogia (r=-0.45, p<0.0001), and Attention (r=-0.57, p<0.0001) were found to have moderate associations with overall functioning. In comparing the negative symptom domain of avolition to the functional subdomains, findings demonstrate that avolition, as measured by the SANS, was more strongly correlated with working productivity (r=-0.70, p<0.0001) than the other functional subdomains. As well, the domains of the SANS demonstrated high correlation between negative symptoms subdomains. Avolition was shown to have a significant positive association with Anhedonia (r=0.755, p<0.0001). Anhedonia however also exhibited moderate positive associations with Alogia (r=0.556, p<0.0001) and Attention (r=0.625, p<0.0001) and Negative Affect also had moderate positive relationships with Alogia (r=0.503, p<0.0001) and Attention (r=0.566, p<0.0001).

Findings from our correlation analyses assessing the relationship between the drivers of motivation, avolition and functional outcomes can be found in Table 4.2.2. Pearson correlation coefficients depicted significant negative associations between avolition and self-efficacy (r=-0.33, p<0.0001) and anticipatory pleasure capacity (r=-0.13, p<0.0001), respectively although associations were small. As well, a small yet significant, positive association was found between avolition and defeatist performance beliefs (r=0.20, p<0.0001).

Correlations between the drivers of motivation and functional outcomes demonstrate small yet significant relationships between each driver of motivation and overall functioning. However, differences between the drivers of motivation can be observed through their relationship to

specific functional subdomains. Self-efficacy was found to have a significant, small association with both working productivity (r=0.23, p<0.05), and extended social networks (r=0.29, p<0.01). Anticipatory pleasure capacity was positively associated with both immediate and extended social networks (r=0.29, p<0.01; r=0.28, p<0.01), respectively, whereas defeatist performance beliefs were negatively associated with independent living and self-care (r=-0.24, p<0.05), and immediate social networks (r=-0.26, p<0.01).

Table 4.2.1: Correlations between Negative Symptoms and Functioning Variables

		Negative Symptoms						*Functional Outcomes*				
		SANS Total	**Avolition**	**Anhedonia**	**Blunted Affect**	**Alogia**	**Attention**	**RFS Total**	**WP**	**ILSC**	**ISN**	**ESN**
Negative Symptoms	**SANS Total**	-										
	Avolition	0.79*	-									
	Anhedonia	0.84*	0.76*	-								
	Blunted Affect	0.66*	0.38*	0.41*	-							
	Alogia	0.83*	0.53*	0.56*	0.50*	-						
	Attention	0.92*	0.59*	0.63*	0.57*	0.81*	-					
Functional Outcomes	**RFS Total**	-0.74*	-0.75*	-0.70*	-0.54*	-0.45*	-0.57*	-				
	WP	-0.61*	-0.70*	-0.56*	-0.49*	-0.36*	-0.45*	0.87*	-			
	ILSC	-0.60*	-0.54*	-0.48*	-0.50*	-0.32*	-0.56*	0.79*	0.57*	-		
	ISN	-0.68*	-0.65*	-0.72*	-0.45*	-0.45*	-0.51*	0.89*	0.66*	0.65*	-	
	ESN	-0.64*	-0.68*	-0.65*	-0.43*	-0.42*	-0.46*	0.87*	0.69*	0.50*	0.77*	-

Note: SANS Total= Total score on the Scale for the Assessment of Negative Symptoms; RFS Total=Total score on the Role Functioning Scale; WP= Working Productivity; ILSC=Independent Living and Self-Care; ISN= Immediate Social Networks; ESN=Extended Social Networks; n=105, *=significant at $p<0.0001$

Table 4.2.2 Correlations between Drivers of Motivation, Avolition and Functional Outcomes

		Motivational Drivers				***Functional Outcomes***				
		GSE	**TEPS-A**	**DPB**	**Avolition**	**RFS Total**	**WP**	**ILSC**	**ISN**	**ESN**
Motivational Drivers	**GSE**	-								
	TEPS-A	0.38**	-							
	DPB	-0.43**	-0.34**	-						
	Avolition	-0.33**	-0.13**	0.20**	-					
Functional Outcomes	**RFS Total**	0.24*	0.20*	-0.21*	-	-				
	WP	0.23*	0.10	-0.13	-	0.87**	-			
	ILSC	0.12	0.04	-0.24*	-	0.79**	0.57**	-		
	ISN	0.18	0.29**	-0.26**	-	0.89**	0.65**	0.65**	-	
	ESN	0.29**	0.28**	-0.13	-	0.87**	0.70**	0.50**	0.77**	-

Note: GSE= Generalized Self Efficacy; TEPS-A=Anticipatory Pleasure Capacity; DPB=Defeatist Performance Beliefs; RFS Total=Total score on the Role Functioning Scale; WP= Working Productivity; ILSC=Independent Living and Self-Care; ISN= Immediate Social Networks; ESN=Extended Social Networks; n=105, *=significant at $p<0.05$, **=significant at $p<0.01$

4.3 Objective 1

Table 4.3 presents the results of our unadjusted and adjusted linear regression models, with the exposure variables being self-efficacy, anticipatory pleasure capacity and defeatist performance beliefs, and the outcome being global functioning.

4.3.1 Exposure Variables

Self-Efficacy

In our unadjusted model, results suggest a positive relationship between self-efficacy and overall functioning (β=0.22, 95% CI: 0.05 to 0.39) with global functioning scores increasing as self-efficacy scores increased. However, when included within the fully adjusted model, this relationship was no longer statistically significant (β=0.14, 95% CI: -0.09 to 0.36).

Anticipatory Pleasure Capacity

Findings from our unadjusted models showed a positive relationship between anticipatory pleasure capacity and overall functioning (β=0.13, 95% CI: 0.00 to 0.26) with global functioning score increasing as one's capacity to experience anticipatory pleasure increased. However, this relationship was no longer statistically significant in the fully adjusted model (β=0.00, 95% CI: -0.15 to 0.15).

Defeatist Performance Beliefs

Results from our unadjusted model showed a negative relationship between defeatist performance beliefs and overall function (β=-0.07, 95% CI: -0.13 to -0.00) with global functioning scores decreasing as defeatist performance beliefs increased. However this relationship was no longer statistically significant when assessed within our fully adjusted model (β=0.01, 95% CI: -0.07 to 0.09).

4.3.2 Covariate Variables

When assessing our unadjusted model, we see that the variables education, perceived social support, positive symptoms, depression and drug and alcohol use were associated with overall functioning. However only education and alcohol use remained statistically significant across our

models. Specifically, in our unadjusted model, we found level of functioning increased with increasing years of education (β=0.88, 95% CI: 0.35 to 1.40). In comparison to individuals with no reported alcohol use, individuals who reported some alcohol use, however not enough to be considered alcohol abuse, were associated with increased overall functioning (β=3.42, 95% CI: 1.28 to 5.56). However, both of these relationships were attenuated within our fully adjusted model (β=0.58, 95% CI: 0.07 to 1.09; β=2.35, 95% CI: 0.09 to 4.62).

Table 4.3: Unadjusted and Adjusted Linear Regression Models with the Outcome of Overall Functional Capacity (n=105)

Variables	Categorical Values	Unadjusted Exposure β (95% CI)	Unadjusted Covariate β (95% CI)	Fully Adjusted β (95% CI)
Exposure Variables				
Self-Efficacy	N/A	0.22 (0.05 to 0.39) *		0.14 (-0.09 to 0.36)
Anticipatory Pleasure	N/A	0.13 (0.00 to 0.26) *		0.00 (-0.15 to 0.15)
Defeatist Performance Beliefs	N/A	-0.07 (-0.13 to -0.00) *		0.01 (-0.07 to 0.09)
Covariates				
Age	N/A		0.06 (-0.05 to 0.16)	0.04 (-0.09 to 0.18)
Gender	Male		-2.13 (-4.39 to 0.13)	-0.94 (-3.43 to 1.55)
	Female		Ref.	Ref.
Education (years)	N/A		0.88 (0.35 to 1.40) *	0.58 (0.07 to 1.09) *
Length of Treatment (years)	N/A		0.08 (-0.10 to 0.26)	-0.06 (-0.31 to 0.19)
Perceived Social Support	N/A		0.22 (0.09 to 0.35) *	0.14 (-0.05 to 0.34)
Positive Symptoms	N/A		-0.10 (-0.17 to -0.03) *	-0.05 (-0.12 to 0.02)
Depressive Symptoms	N/A		-1.56 (-2.96 to -0.16) *	0.46 (-1.93 to 2.84)
Anxiety Symptoms	N/A		-0.92 (-2.07 to 0.23)	-0.26 (-2.11 to 1.58)
Drug Use	None		Ref.	Ref.
	Below Cut-Off		2.93 (0.45 to 5.41) *	0.98 (-1.77 to 3.72)
	Above Cut-Off		-2.32 (-5.19 to 0.56)	-1.97 (-5.28 to 1.33)
Alcohol Use	None		Ref.	Ref.
	Below Cut-Off		3.42 (1.28 to 5.56) *	2.35 (0.09 to 4.62) *
	Above Cut-Off		2.68 (-0.37 to 5.74)	2.32 (-1.04 to 5.68)
Medication Adherence	0-50%		Ref/	Ref.
	50-100%		-0.89 (-4.01 to 2.23)	-1.68 (-4.78 to 1.41)

Note: Unadjusted refers to simple linear regression models; Fully Adjusted refers to multivariable regression models adjusted for additional exposure variables and covariates; R^2=0.33; *Indicates findings significant at p<0.05; β=Beta Coefficient; CI= Confidence Interval; Ref=Reference Group; N/A=Not Applicable

4.4 Objective 2

4.4.1 Working Productivity

Table 4.4 contains the results of our unadjusted and fully adjusted linear regression models, with the exposure variables being self-efficacy, anticipatory pleasure capacity and defeatist performance beliefs, and the outcome being the functioning subdomain of working productivity.

4.4.1.1 Exposure Variables

Self-Efficacy

In our unadjusted model, results suggest a positive relationship between self-efficacy and working productivity (β=0.07, 95% CI: 0.01 to 0.13) with scores on the functional subdomain of working productivity increasing as self-efficacy scores increased. This association remains largely unchanged in the fully adjusted model; however, the 95% confidence interval now includes the null value and is no longer statistically significant (β=0.07, 95% CI: -0.00 to 0.15).

Anticipatory Pleasure Capacity

There was no evidence of a relationship between anticipatory pleasure capacity and the functional subdomain of working productivity (Table 4.4).

Defeatist Performance Beliefs

There was no evidence of a relationship between defeatist performance beliefs and the functional subdomain of working productivity (Table 4.4).

4.4.1.2 Covariate Variables

When assessing our unadjusted model, we see that the variables education, perceived social support, positive symptoms, and alcohol use were associated with one's level of working productivity. However, these associations were no longer statistically significant within our fully adjusted model.

Table 4.4: Unadjusted and Adjusted Linear Regression Models with the Functioning Sub-Domain Outcome of Working Productivity (n=105).

Variables	Categorical Values	Unadjusted Exposure β (95% CI)	Unadjusted Covariate β (95% CI)	Fully Adjusted β (95% CI)
Exposure Variables				
Self-Efficacy	N/A	0.07 (0.01 to 0.13) *		0.07 (-0.00 to 0.15)
Anticipatory Pleasure	N/A	0.02 (-0.03 to 0.06)		-0.02 (-0.08 to 0.03)
Defeatist Performance Beliefs	N/A	-0.01 (-0.03 to 0.01)		0.01 (-0.01 to 0.04)
Covariates				
Age	N/A		0.00 (-0.03 to 0.04)	-0.02 (-0.07 to 0.03)
Gender	Male		-0.56 (-1.33 to 0.20)	-0.51 (-1.39 to 0.36)
	Female		Ref.	Ref.
Education (years)	N/A		0.25 (0.07 to 0.42) *	0.17 (-0.01 to 0.35)
Length of Treatment (years)	N/A		0.02 (-0.04 to 0.08)	0.01 (-0.08 to 0.10)
Perceived Social Support	N/A		0.06 (0.02 to 0.11) *	0.04 (-0.03 to 0.11)
Positive Symptoms	N/A		-0.04 (-0.06 to -0.01) *	-0.02 (-0.05 to 0.00)
Depressive Symptoms	N/A		-0.42 (-0.90 to 0.05)	0.25 (-0.59 to 1.10)
Anxiety Symptoms	N/A		-0.29 (-0.68 to 0.10)	-0.22 (-0.87 to 0.43)
Drug Use	None		Ref.	Ref.
	Below Cut-Off		0.69 (-0.16 to 1.53)	0.08 (-0.88 to 1.04)
	Above Cut-Off		-0.72 (-1.71 to 0.27)	-0.58 (-1.73 to 0.58)
Alcohol Use	None		Ref.	Ref.
	Below Cut-Off		0.82 (0.08 to 1.56) *	0.60 (-0.20 to 1.39)
	Above Cut-Off		0.66 (-0.39 to 1.71)	0.63 (-0.54 to 1.81)
Medication Adherence	0-50%		Ref.	Ref.
	50-100%		-0.33 (-1.38 to 0.72)	-0.65 (-1.73 to 0.43)

Note: Unadjusted refers to simple linear regression models; Fully Adjusted refers to multivariable regression models adjusted for additional exposure variables and covariates; R^2=0.27; *Indicates findings significant at $p<0.05$; β=Beta Coefficient; CI= Confidence Interval; Ref=Reference Group; N/A=Not Applicable

4.4.2 Independent Living and Self-Care

Table 4.5 presents the results of our unadjusted and fully adjusted linear regression models, with the exposure variables being self-efficacy, anticipatory pleasure capacity and defeatist performance beliefs, and the outcome being the functioning subdomain of independent living and self-care.

4.4.2.1 Exposure Variables

Self-Efficacy

There was no evidence of a relationship between self-efficacy and the functional subdomain of independent living and self-care (Table 4.5).

Anticipatory Pleasure Capacity

There was no evidence of a relationship between anticipatory pleasure capacity and the functional subdomain of independent living and self-care (Table 4.5).

Defeatist Performance Beliefs

In our unadjusted model, there was a small negative relationship between defeatist performance beliefs and independent living and self-care (β=-0.02, 95% CI: -0.04 to -0.00) with scores on the functional subdomain of independent living and self-care decreasing as defeatist performance belief scores increased. However, when included within the fully adjusted model, this relationship was no longer statistically significant (β=-0.01, 95% CI: -0.03 to 0.02).

4.4.2.2 Covariate Variables

When assessing our unadjusted model, we see that the variables age, positive symptom severity, depressive symptoms and drug and alcohol use were associated with independent living and self-care. However only drug and alcohol use remained statistically significant across our models. Drug use above the cut-off score, meaning frequent drug use categorized as drug abuse, was found to have a negative association with independent living and self-care (β=-1.05, 95% CI: -1.86 to -0.23) when compared to those that reported no drug use. Alcohol use below the cut-off score, meaning some alcohol use however not enough to be considered alcohol abuse, was found to have a positive association with independent living and self-care (β=0.97, 95% CI: 0.35 to

1.58) when compared to those that reported no alcohol use. These two relationships were attenuated within our fully adjusted model (β=-0.98, 95% CI: -1.94 to -0.01; β=0.85, 95% CI: 0.19 to 1.51) but remained statistically significant.

Table 4.5: Unadjusted and Adjusted Linear Regression Models with the Functioning Sub-Domain Outcome of Independent Living and Self-Care (n=105).

Variables	Categorical Values	Unadjusted Exposure β (95% CI)	Unadjusted Covariate β (95% CI)	Fully Adjusted β (95% CI)
Exposure Variables				
Self-Efficacy	N/A	0.03 (-0.02 to 0.08)		0.01 (-0.06 to 0.07)
Anticipatory Pleasure	N/A	0.01 (-0.03 to 0.04)		-0.02 (-0.06 to 0.03)
Defeatist Performance Beliefs	N/A	-0.02 (-0.04 to -0.00) *		-0.01 (-0.03 to 0.02)
Covariates				
Age	N/A		0.04 (0.01 to 0.06) *	0.03 (-0.01 to 0.07)
Gender	Male		-0.51 (-1.16 to 0.14)	-0.01 (-0.74 to 0.72)
	Female		Ref.	Ref.
Education (years)	N/A		0.18 (0.03 to 0.33) *	0.10 (-0.05 to 0.25)
Length of Treatment (years)	N/A		0.04 (-0.01 to 0.09)	-0.04 (-0.11 to 0.04)
Perceived Social Support	N/A		0.03 (-0.01 to 0.07)	0.00 (-0.05 to 0.06)
Positive Symptoms	N/A		-0.03 (-0.05 to -0.01) *	-0.01 (-0.03 to 0.01)
Depressive Symptoms	N/A		-0.40 (-0.80 to -0.00) *	-0.07 (-0.78 to 0.64)
Anxiety Symptoms	N/A		-0.32 (-0.65 to 0.01)	-0.11 (-0.65 to 0.43)
Drug Use	None		Ref.	Ref.
	Below Cut-Off		0.63 (-0.07 to 1.33)	0.29 (-0.51 to 1.10)
	Above Cut-Off		-1.05 (-1.86 to -0.23) *	-0.98 (-1.94 to -0.01) *
Alcohol Use	None		Ref.	Ref.
	Below Cut-Off		0.97 (0.35 to 1.58) *	0.85 (0.19 to 1.51) *
	Above Cut-Off		0.35 (-0.52 to 1.23)	0.58 (-0.41 to 1.57)
Medication Adherence	0-50%		Ref.	Ref.
	50-100%		-0.07 (-0.96 to 0.82)	-0.15 (-1.06 to 0.75)

Note: Unadjusted refers to simple linear regression models; Fully Adjusted refers to multivariable regression models adjusted for additional exposure variables and covariates; R^2=0.28; *Indicates findings significant at $p<0.05$; β=Beta Coefficient; CI= Confidence Interval; Ref=Reference Group; N/A=Not Applicable

4.4.3 Immediate Social Networks

Table 4.6 contains the results of our unadjusted and fully adjusted linear regression models, with the exposure variables being self-efficacy, anticipatory pleasure capacity and defeatist performance beliefs, and the outcome being the functioning subdomain of immediate social networks.

4.4.3.1 Exposure Variables

Self-Efficacy

There was no evidence of a relationship between self-efficacy and the functional subdomain of immediate social networks (Table 4.6).

Anticipatory Pleasure Capacity

Findings from our unadjusted models showed a positive relationship between anticipatory pleasure capacity and the functional subdomain of immediate social networks (β=0.05, 95% CI: 0.02 to 0.08) with immediate social network scores increasing as one's capacity to experience anticipatory pleasure increased. However, this relationship was no longer statistically significant when assessed within our fully adjusted model (β=0.02, 95% CI: -0.02 to 0.06).

Defeatist Performance Beliefs

In our unadjusted model, results suggest a small negative relationship between defeatist performance beliefs and immediate social networks (β=-0.02, 95% CI: -0.04 to -0.00) with scores on the functional subdomain of immediate social networks decreasing as defeatist performance belief scores increased. However, when included within the fully adjusted model, this relationship was no longer statistically significant (β=-0.01, 95% CI: -0.03 to 0.02).

4.4.3.2 Covariate Variables

When assessing our unadjusted model, we see that the variables education, perceived social support, positive symptom severity and alcohol use were associated with the functional domain of immediate social networks. However, only education, perceived social support and alcohol use remained statistically significant across models. In both our unadjusted and fully adjusted linear regression models, education was found to be associated with the functional subdomain of

immediate social networks (β=0.23, 95% CI: 0.10 to 0.37; β=0.16, 95% CI: 0.03 to 0.30) with immediate social network scores increasing as years of education increased. As with education, in both our unadjusted and fully adjusted linear regression models, perceived social support was found to be associated with the functional subdomain of immediate social networks (β=0.07, 95% CI: 0.03 to 0.10; β=0.06, 95% CI: 0.01 to 0.11) with immediate social network scores increasing as perceived social support increased. Alcohol use below the cut-off was found to have an association with immediate social networks (β=0.90, 95% CI: 0.34 to 1.46; β=0.60, 95% CI: 0.01 to 1.20) when compared to those that reported no alcohol use. Findings demonstrated that the relationships between this functional domain and education and alcohol usage were attenuated when covariate variables were included within the regression model.

Table 4.6: Unadjusted and Adjusted Linear Regression Models with the Functioning Sub-Domain Outcome of Immediate Social Networks (n=105).

Variables	Categorical Values	Unadjusted Exposure β (95% CI)	Unadjusted Covariate β (95% CI)	Fully Adjusted β (95% CI)
Exposure Variables				
Self-Efficacy	N/A	0.04 (-0.00 to 0.09)		-0.00 (-0.06 to 0.05)
Anticipatory Pleasure	N/A	0.05 (0.02 to 0.08) *		0.02 (-0.02 to 0.06)
Defeatist Performance Beliefs	N/A	-0.02 (-0.04 to -0.00) *		-0.01 (-0.03 to 0.01)
Covariates				
Age	N/A		0.01 (-0.02 to 0.04)	0.00 (-0.03 to 0.04)
Gender	Male		-0.40 (-0.99 to 0.20)	-0.11 (-0.75 to 0.54)
	Female		Ref.	Ref.
Education (years)	N/A		0.23 (0.10 to 0.37) *	0.16 (0.03 to 0.30) *
Length of Treatment (years)	N/A		0.03 (-0.02 to 0.07)	0.01 (-0.06 to 0.07)
Perceived Social Support	N/A		0.07 (0.03 to 0.10) *	0.06 (0.01 to 0.11) *
Positive Symptoms	N/A		-0.02 (-0.04 to -0.00) *	-0.01 (-0.03 to 0.01)
Depressive Symptoms	N/A		-0.34 (-0.71 to 0.02)	0.21 (-0.40 to 0.83)
Anxiety Symptoms	N/A		-0.18 (-0.48 to 0.13)	0.07 (-0.41 to 0.55)
Drug Use	None		Ref.	Ref.
	Below Cut-Off		0.63 (-0.03 to 1.29)	0.09 (-0.63 to 0.80)
	Above Cut-Off		-0.44 (-1.20 to 0.33)	-0.30 (-1.16 to 0.56)
Alcohol Use	None		Ref.	Ref.
	Below Cut-Off		0.90 (0.34 to 1.46) *	0.60 (0.01 to 1.20) *
	Above Cut-Off		0.53 (-0.27 to 1.33)	0.32 (-0.55 to 1.20)
Medication Adherence	0-50%		Ref.	Ref.
	50-100%		-0.28 (-1.20 to 0.53)	-0.46 (-1.27 to 0.35)

Note: Unadjusted refers to simple linear regression models; Fully Adjusted refers to multivariable regression models adjusted for additional exposure variables and covariates; R^2=0.34; *Indicates findings significant at $p<0.05$; β=Beta Coefficient; CI= Confidence Interval; Ref=Reference Group; N/A=Not Applicable

4.4.4 Extended Social Networks

Table 4.7 contains the results of our unadjusted and fully adjusted linear regression models, with the exposure variables being self-efficacy, anticipatory pleasure capacity and defeatist performance beliefs, and the outcome being the functioning subdomain of extended social networks.

4.4.4.1 Exposure Variables

Self-Efficacy

In our unadjusted model, results suggest a positive relationship between self-efficacy and the functional subdomain of extended social networks (β=0.07, 95% CI: 0.02 to 0.12) with extended social networks scores increasing as self-efficacy scores increased. However, when included within the fully adjusted model, this relationship was no longer statistically significant (β=0.06, 95% CI: -0.01 to 0.12).

Anticipatory Pleasure Capacity

Findings from our unadjusted models showed a positive relationship between anticipatory pleasure capacity and the functional subdomain of extended social networks (β=0.05, 95% CI: 0.02 to 0.09) with extended social network scores increasing as one's capacity to experience anticipatory pleasure increased. However, this relationship was no longer statistically significant when assessed within our fully adjusted model (β=0.02, 95% CI: -0.02 to 0.06).

Defeatist Performance Beliefs

There was no evidence of a relationship between defeatist performance beliefs and the functional subdomain of extended social networks (Table 4.7).

4.4.4.2 Covariate Variables

When assessing our unadjusted model, we see that the variables gender, education, perceived social support, and drug and alcohol use were associated with the functional domain of extended social networks. However only education remained statistically significant across models. In both our unadjusted and fully adjusted linear regression models, education was found to be significantly associated with the functional subdomain of extended social networks (β=0.21, 95%

CI: 0.06 to 0.37; β=0.15, 95% CI: 0.01 to 0.30) with extended social network scores increasing as years of education increased. Findings demonstrated that this relationship was attenuated when covariate variables were included within the regression model.

Table 4.7: Unadjusted and Adjusted Linear Regression Models with the Functioning Sub-Domain Outcome of Extended Social Networks (n=105).

Variables	Categorical Values	Unadjusted Exposure β (95% CI)	Unadjusted Covariate β (95% CI)	Fully Adjusted β (95% CI)
Exposure Variables				
Self-Efficacy	N/A	0.07 (0.02 to 0.12) *		0.06 (-0.01 to 0.12)
Anticipatory Pleasure	N/A	0.05 (0.02 to 0.09) *		0.02 (-0.02 to 0.06)
Defeatist Performance Beliefs	N/A	-0.01 (-0.03 to 0.01)		0.01 (-0.01 to 0.04)
Covariates				
Age	N/A		0.01 (-0.02 to 0.04)	0.02 (-0.02 to 0.06)
Gender	Male		-0.66 (-1.31 to -0.01) *	-0.30 (-1.03 to 0.42)
	Female		Ref.	Ref.
Education (years)	N/A		0.21 (0.06 to 0.37) *	0.15 (0.01 to 0.30) *
Length of Treatment (years)	N/A		-0.00 (-0.05 to 0.05)	-0.04 (-0.12 to 0.03)
Perceived Social Support	N/A		0.06 (0.02 to 0.10) *	0.04 (-0.02 to 0.10)
Positive Symptoms	N/A		-0.02 (-0.04 to 0.00)	-0.01 (-0.03 to 0.01)
Depressive Symptoms	N/A		-0.39 (-0.80 to 0.01)	0.06 (-0.63 to 0.45)
Anxiety Symptoms	N/A		-0.13 (-0.47 to 0.20)	-0.00 (-0.54 to 0.53)
Drug Use	None		Ref.	Ref.
	Below Cut-Off		0.99 (0.27 to 1.71) *	0.52 (-0.28 to 1.32)
	Above Cut-Off		-0.11 (-0.95 to 0.73)	-0.12 (-1.09 to 0.84)
Alcohol Use	None		Ref.	Ref.
	Below Cut-Off		0.74 (0.11 to 1.36) *	0.30 (-0.36 to 0.97)
	Above Cut-Off		1.14 (0.25 to 2.03) *	0.79 (-0.20 to 1.77)
Medication Adherence	0-50%		Ref.	Ref.
	50-100%		-0.20 (-1.11 to 0.70)	-0.42 (-1.33 to 0.48)

Note: Unadjusted refers to simple linear regression models; Fully Adjusted refers to multivariable regression models adjusted for additional exposure variables and covariates; R^2=0.30; *Indicates findings significant at $p<0.05$; β=Beta Coefficient; CI= Confidence Interval; Ref=Reference Group; N/A=Not Applicable

4.5 Sensitivity Analyses

4.5.1 Sensitivity Analyses Using Additional Variables

4.5.1.1 Objective 1

Results from our sensitivity analyses including an additional four variables, being age of onset, mode of onset, duration of untreated psychosis and premorbid adjustment, were consistent with our main analyses in that no significant relationship was observed between our exposure variables and overall functioning and effect estimates were comparable in magnitude.

Among the additional variables assessed, premorbid adjustment and mode of onset were found to be associated with global functioning. Results from our unadjusted models showed a statistically significant relationship between global functioning and premorbid adjustment (β =-7.85, 95% CI: -15.18 to -0.51), however when included within the fully adjusted model this relationship was rendered no longer statistically significant. Mode of onset, although insignificant in our unadjusted model however was significant within our fully adjusted model (β =-4.03, 95% CI: -7.86 to -0.19), demonstrating that when compared to those with an acute onset of psychosis, individuals with an insidious onset of psychosis had poorer functioning overall.

4.5.1.2 Objective 2

Similar findings were observed between our main analyses (n=105) and our sensitivity analyses (n=69) including four additional variables in regard to assessing each functional subdomain. Findings for each of our three exposure variables were consistent with our main analyses across functional subdomains. The magnitude of effect was smaller across all models with a narrower confidence interval.

In regard to the functional subdomain of working productivity, our models did not show evidence of a significant association between age of onset, mode of onset, duration of untreated psychosis or premorbid adjustment with working productivity.

When assessing the functional subdomain of independent living and self-care, although our unadjusted models showed age of onset and premorbid adjustment to be associated with

independent living and self-care (β =0.05, 95% CI: -0.01 to 0.10; β =-2.13, 95% CI: -4.15 to -0.11), these associations did not hold in our full model.

Unadjusted models assessing the functional domain of immediate social networks showed a significant association between the functional domain and premorbid adjustment (β =-2.37, 95% CI: -4.22 to -0.53) however, this relationship did not remain statistically significant within the full model. However, when controlling for the other identified factors, findings from our full model showed mode of onset, being the manner in which psychotic symptoms evolve during the first episode of psychosis, to be significantly correlated with the functional domain (β =-1.06, 95% CI: -2.07 to -0.05). Similar to our findings for immediate social networks, a significant association between mode of onset and extended social networks was present within our full model (β =-1.38, 95% CI: -2.51 to -0.25). Although age of onset was shown to be significant in our unadjusted models, this relationship did not remain when controlling for other factors.

4.5.2 Sensitivity Analyses Treating Outcome as Ordinal

4.5.2.1 Objective 1

Results from our sensitivity analyses treating the outcome of global functioning as measured on an ordinal scale found results consistent with our main analyses. Our exposure variables, being self-efficacy, anticipatory pleasure capacity and defeatist performance beliefs, remained non-significant, although the magnitude of effect was smaller and had narrower associated confidence intervals in comparison with our main analyses.

4.5.2.2 Objective 2

In contrast to the main analyses, results from the sensitivity analyses treating the four functional subdomains, working productivity, independent living and self-care, immediate social networks and extended social networks, as measured on an ordinal scale found a small but statistically significant effect for self-efficacy with working productivity and extended social networks. Specifically, an increase in self-efficacy was associated with a decrease in the odds of being in a lower working productivity category, with an odds ratio of 0.91 (95% CI: 0.84 to 0.99), and a

decrease in the odds of being in a lower functioning category in terms of extended social networks with an odds ratio of 0.87 (95% CI: 0.80 to 0.95).

Chapter 5

5 Discussion

In this concluding chapter, an overview of key study findings, by objective, will be discussed and contextualized within the current evidence base. Section 5.1 will first discuss findings from our analyses examining the correlation between measures of negative symptoms and functioning, followed by a discussion of key findings from our linear regression models assessing the relationship between drivers of motivation and functioning, adjusting for potential covariates. Study strengths and limitations will then be discussed in Sections 5.2 and 5.3, respectively. Finally, translation of results for clinicians and researchers will be discussed in Section 5.4, followed by study conclusions in Section 5.5.

5.1 Overview of Findings

5.1.1 Correlational Analyses

In recent years, a number of studies have examined the relationship between psychotic symptomatology and functional outcomes in individuals with psychotic disorders [20,26,27,29,71,74,92,170]. A relationship between negative symptoms and functional outcomes has been consistently found, with avolition being shown to be the strongest correlate than any other negative symptom subdomain. A 2012 study by Hunter and Barry investigated the relationship between negative symptoms and functioning using multiple measures of functioning. Their findings demonstrated strong, statistically significant correlations between the PANSS and five of six measures of functioning assessed [64]. These scales included the Global Assessment of Functioning scale[171], the Personal and Social Performance scale[172], the Quality of Life Scale[173], the Functional Remission of General Schizophrenia scale[174] and the Psychosocial Remission in Schizophrenia scale[175], as well as the Subjective Wellbeing under Neuroleptics scale[176], which did not significantly correlate with the PANSS scores. With findings such as these, conclusions have been made that negative symptoms are predictive of functional outcomes, specifically with motivational deficits being associated with poorer functioning. However, studies that found this strong correlation have used measures to assess negative symptoms that, although extensively used, do not discriminately measure the construct of negative symptoms separate from functional

outcomes, calling into question the validity of these measures given our current knowledge of negative symptoms. Specifically, when looking at the avolition sub-domain of the commonly used SANS, we see a high degree of overlap between the questions posed to assess one's degree of avolition and measures used to assess functioning itself, as discussed in Chapter 2. For example, the ability to care for one's self in terms of grooming habits is considered a behavioral marker of functioning within the independent living and self-care domain of the RFS however it is also measured as part of the avolition sub-domain of the SANS as a behavioral marker of poor motivation (Appendix B and C). The questions posed to assess avolition fail to truly measure factors related to motivation and focus more on overt behavioral outcomes believed to be indicative of underlying motivation. Current measures of negative symptoms tap into behavioral achievement rather than the symptom itself and possibly fail to adequately address more experiential motivational deficits [9], which has been recognized as a limitation of current assessments of negative symptom domains [29,71].

We conducted a series of Pearson correlation analyses to see whether this relationship was present within our sample. Our analyses demonstrated moderate to strong, significant correlations between all domains of negative symptoms and functional outcomes, consistent with our hypothesis. Total scores on the SANS demonstrated a strong negative correlation to total scores on the RFS (r = -0.737, p<0.001) as well as with each subdomain (Table 4.2).The largest Pearson correlation coefficient was observed between the negative symptom domain of avolition and global functioning (r = -0.754, p<0.001), consistent with our hypothesis that these two domains would be highly correlated due to the high degree of overlap between measures.

Although our correlations are consistent with ongoing discussions on measures of avolition and negative symptoms [23,25-27,29,71-74], we proposed that this association is present due to both domains measuring the same underlying constructs. We believe that our current method of measuring avolition may be erroneously connected to functioning due to the focus on assessing avolition using overt behavioral markers such as grooming habits and difficulty obtaining or maintaining employment - factors that are similarly found within scales assessing functioning. In other words, the strong relationship between negative symptoms, namely avolition, and functional outcomes that has been observed in the literature to date may be due to the two

domains being assessed using similar indicators, resulting in erroneous conclusions formed regarding the role of avolition as a predictor of functional outcomes. Through the literature we identified 3 psychological drivers of motivation that assess intrinsic motivational drivers rather than overt behavioral characteristics. Our correlation analyses demonstrated small yet significant relationships between all three of the drivers and avolition. As well, we observed differences between the motivational drivers and specific functional subdomains, in that certain psychological drivers of motivation were found to have significant associations with one or two functional subdomains rather than all four.

5.1.2 Objective 1

Although recent studies have recognized the issues associated with current measures of avolition in addition to other negative symptoms [29,71], no study to date has directly assessed the influence of motivational factors on functional outcomes, excluding negative symptoms scales. In order to better understand the relationship between avolition and functioning, we aimed to investigate whether drivers of motivation were associated with overall functional capacity in a sample of individuals with psychotic disorders. We had hypothesized that, given the existing literature showing that avolition has a dominant role in the development of poor functional outcomes, our identified drivers of motivation would each demonstrate a statistically significant association with overall functioning, namely that both self-efficacy and anticipatory pleasure capacity would have a significant, positive relationship with overall functioning, and defeatist performance beliefs would exhibit a significant, negative relationship with overall functioning.

When assessing the relationship between the identified drivers of motivation and functioning, we found that each of the drivers assessed had a small but statistically significant relationship with overall functioning. However, when adjusting for our covariates, contrary to our hypothesis, we did not observe any statistically significant relationships between any of the motivational drivers and overall functioning in our fully adjusted model. Our findings therefore seem to be in disagreement with the current evidence base, in that our identified exposure variables, being considered primary indicators of motivation and therefore avolition, were not significantly associated with functioning in our multivariable analyses.

Comparison of our findings to past research assessing functional outcomes suggest that there is a possibility that the previously observed relationship between functioning and avolition was falsely identified due to the overlap between measures of negative symptoms and functioning. Given that our identified drivers of motivation can influence one's degree of motivational deficits and therefore levels of avolition, it would stand to reason that if avolition and functional outcomes were associated with one another, then this relationship would still be observed via these motivational drivers. Buck and Lysaker [110] found that anticipatory pleasure deficits at baseline, as measured by the TEPS, was linked to poorer levels of interpersonal relations at 6-month follow up among people with schizophrenia or schizoaffective disorder (n=51). As well, Ventura and Colleagues [28] conducted a study assessing the relationship between negative symptoms, neurocognition, and daily functioning along with what they termed "attitudinal beliefs" which included self-efficacy and defeatist performance beliefs. They also found strong correlations between self-efficacy and defeatist performance beliefs and global functioning. However, these analyses were univariate and failed to assess motivational drivers while controlling for confounding factors, which may explain the discrepancies between with our findings. Other studies using these drivers of motivation have conducted mediation analyses using negative symptoms as mediators in the relationship between motivational drivers and functioning. Ventura and colleagues [28]conducted one such analysis, where self-efficacy and defeatist performance beliefs were assessed for their indirect effect on functioning via negative symptoms. They found evidence consistent with a model where self-efficacy and defeatist performance beliefs, referred to as 'dysfunctional attitudes', had a partial influence on negative symptoms which in turn significantly influenced daily functioning levels. However, as with the previously stated analyses, no confounding factors were assessed which would likely affect study results, as observed in our analyses where the inclusion of covariates rendered the relationship between drivers of motivation and functioning non-significant. As well, given that these analyses included measures of negative symptoms, which we have shown overlap significantly with functional outcomes, it is possible that these previous findings were inflated.

Although we found no significant relationship between overall functioning and any driver of motivation, results demonstrated that when adjusting for our covariate variables, total years of education and alcohol use exhibited a significant relationship with overall functioning. The

finding of education being significantly associated with overall functioning is consistent with findings reported by Santesteban-Echarri and colleagues,[20] who conducted a meta-analysis assessing predictors of functional recovery in individuals with a first-episode of psychosis, with education being a significant correlate of functioning in 15 of 22 studies examining this variable (r=0.16, 95% CI: 0.11 to 0.20, p<0.00). Taken together, these findings suggest that one's level of education is related to overall functioning and that this association reflects a positive relationship between the two variables.

Interestingly, alcohol usage below what is considered alcohol abuse, in comparison to individuals that reported no alcohol use, was found to have a significant, positive relationship with overall functioning, with individuals reporting some alcohol usage experiencing better overall functioning then those who reported no alcohol use. Although our measure of alcohol use was self-reported, similar findings have been reported with substance use[177]. Similar to our findings, Swartz and colleagues [177]found that compared to individuals who were abstinent, those who used substances (alcohol or illicit drugs) without serious impairment or without diagnosis of a substance use disorder had higher overall psychosocial functioning and equivalent functioning. One potential explanation for these counterintuitive findings is that some degree of initiative, social contact, and organizational skills are required for engaging drug-involved peer and obtaining illicit substances [177].

5.1.3 Objective 2

To our knowledge, no study to date has examined the relationship between motivational drivers and specific subdomains of functioning. We hypothesized that each driver of motivation would have a different relationship with functioning; however, our results showed no statistically significant relationships between any of our drivers of motivation across all functioning subdomains when adjusting for possible covariate factors. Interestingly, we did find differences in our unadjusted models. Self-efficacy, when not controlling for other variables, was found to be significantly correlated with both of the functional subdomains of working productivity and extended social networks. In our sensitivity analyses, these relationships remained significant within our fully adjusted model however effect sizes were small. Defeatist performance beliefs were the only motivational driver that was found to be correlated with the functional domain of

independent living and self-care. Defeatist performance beliefs were also found to have a significant association with extended social network functioning. Anticipatory pleasure capacity was found to be significantly associated with both immediate and extended social network subdomains. Therefore, although our fully adjusted models did not find significant associated between these variables and functioning, we did observe differences between drivers of motivation and functional subdomains.

A number of covariates were found to be associated with the functional subdomains. Both alcohol use and drug use were found to be significantly associated with the functional subdomain of independent living and self-care. Education, social support, and alcohol use were found to have significant associations with the functional subdomain of immediate social networks. However, when assessing extended social networks, only education was found to be significantly correlated with functioning. Overall, education was shown to have the strongest relationship with functioning; being significantly correlated with overall functioning as well as 3 out of 4 subdomains of functional outcomes.

Our main analyses identified small yet significant relationships between all of our drivers of motivation and overall functioning within our unadjusted models, however we did not find a statistically significant relationship between the identified drivers of motivation and functioning after adjusting for covariates. Similar findings were shown in our models of each functional subdomains, with some drivers of motivation being shown to have a small but significant relationship to that functional domain. Our findings, although the first to assess these factors in conjunction with possible covariate factors and without the influence of negative symptoms, goes against previous studies of functional outcomes within a psychosis population. The current evidence base suggests that negative symptoms play an important role in the development of poor functional outcomes. However, our exposure variables, recognized to be factors that influence or “drive” motivation and therefore theoretically should be a direct influence on avolition, failed to support this theory. Self-efficacy, anticipatory pleasure capacity, and defeatist performance beliefs, although each identified as motivational targets, did not support the theory that avolition leads to poor functional outcomes. Therefore, our findings seem to propose that the previously observed relationship between negative symptoms, mainly avolition, and functional

outcomes may be inflated due to the overlapping measures used to measure these constructs and the lack of control for additional factors.

5.2 Study Strengths

This study had a number of strengths. Firstly, to our knowledge this was the first study to assess the relationship between functioning and avolition using measures that directly assess factors known to drive motivation. This effectively allowed for us to observe the relationship between motivation and functioning without overlapping measures which we believe has previously resulted in an inflated association between negative symptoms and functioning. Our study was unique in the consideration of multiple driving factors of motivation rather than a single factor. This allowed us to first assess whether there was in fact a relationship between motivation and functioning, and to ascertain whether certain factors exerted a stronger influence than others.

In contrast to previous studies assessing functional outcomes, we also included a number of potential covariate factors, including sociodemographic and clinical factors. Although a number of studies have been conducted assessing the relationship between negative symptoms and functioning and have found a significant relationship between the two, the majority of these studies did not include a wide range of potential covariates variables, and instead included other symptom domains such as positive symptoms and affective symptoms [26,28,29,71,110,170]. Given that our literature search identified a number of factors that influence functioning, it is important to account for these factors in order to truly assess the relationship between motivation and functioning. Accounting for covariate variables is an important strength to this study as the factors found to be associated with functional outcomes across our models were variables identified as covariates and not our exposure variables. This illustrates that the strongest relationships with functioning were not found with motivational factors but rather variables such as education, length of treatment, alcohol use and drug use. As well, these variables were all analyzed using a series of simple and multivariable linear regression analyses, allowing for us to assess and estimate the independent effect of our exposure variables (self-efficacy, anticipatory pleasure capacity and defeatist performance beliefs), controlling for each other and for our identified potential covariates. Furthermore, the selection of covariates included within our

analyses were guided by our research using previous studies that make up the current evidence base.

Lastly, we also re-assessed our findings for robustness by means of two sensitivity analyses. Given that our outcome of functioning is assessed on a Likert scale, we additionally ran our analyses using an ordinal logistic regression model to assess whether treating our outcome as continuous had affected our results. As well, we used a subset of our total sample to re-assess our exposure variables controlling for four additional variables that we had identified as possible covariates. Both sensitivity analyses were consistent with our main analyses, demonstrating the robustness of findings for this study.

5.3 Study Limitations

Although our study had a number of strengths, there were also some limitations that should be considered. This study design was cross-sectional, with data collection for each participant occurring at one time point. Findings from cross-sectional research is limited when discussing directionality of hypotheses. While the presence of associations, and whether they are positive or negative in nature, can be discussed, the directionality of these associations cannot be determined and any consideration of variables as cause and effect are solely theoretical in nature. Specifically, we cannot determine whether these motivational drivers impact functioning or whether poor functioning impacts motivation. Although we were able to show associations, or lack of, between our exposure variables and outcomes, cross-sectional research is also limited in regard to the statements and conclusions made when discussing causality. Longitudinal models would be better able to assess causality, namely, whether drivers of motivation have a causal role in functional outcomes. In previous studies, self-efficacy and defeatist performance beliefs have been identified as being fluid, with the possibility of change occurring over time. Given this understanding that motivational drivers are not stagnant and therefore motivational level can change, our cross-sectional study only pinpoints motivation at one time point. A longitudinal study assessing motivational drivers and functioning over time would allow one to form more concrete conclusions on the relationship between motivation and functioning in psychosis populations. We also acknowledge that the drivers of motivation were all assessed using self-report measures and therefore may be influenced by response biases and/or factors affecting their

current mindset at the time of assessment such as a recent psychotic episode or increases in depressive symptoms.

Furthermore, within our analyses we controlled for a number of covariates, with a few factors being found to have a significant association with functional outcomes. Although we controlled for these factors, based on our literature review which demonstrated their association with functional outcomes, as with our drivers of motivation we cannot determine the directionality of these variables in regard to both motivation and functioning. We chose to examine the direct effect of motivational drivers on functional outcomes, given the current discussion on avolition being the strongest influence on functioning. However, education was found to be significantly associated with overall functioning within our sample, and when included within our fully adjusted model this covariate remained significant while our motivational drivers did not. One could argue that motivational drivers may impact educational achievement, and consequently influence functional outcomes; thereby acting as a mediator in this relationship, or, that educational achievements may impact motivational drive, in turn affecting functioning. Therefore, there is a possibility that some of our covariates, such as education, depression or social support, may have a more integrated role within the causal pathway between motivational drivers and functioning, and that their inclusion within our fully-adjusted model resulted in over-adjustment. However as indicated in Tables 4.3 to 4.7, our model diagnostics demonstrated that the R^2 values calculated for each regression model ranged between 0.27 and 0.34 depending on the model; demonstrating that approximately 27% to 34% of the total variance was accounted for by our motivational drivers and covariates. Given that only a small proportion of the variance in functional outcomes was accounted for by the motivational drivers and covariates, there may be other factors that were not included within our models that may play an important role in the development of poor functional outcomes. Further research should consider these possibilities, namely through a longitudinal study design to aid the discussion on possible mediational roles within the causal pathway.

It should also be noted that our study was conducted using a sample that had been previously receiving treatment. The duration of untreated psychosis within a subset of our sample had a median value of 23.1weeks (IQR= 52.4), meaning that from the first signs of psychosis over half

of participants did not start receiving treatment for close to 6 months. Duration of untreated psychosis has been shown to be associated with poorer symptomatology and social functioning [16,20]. Given that early psychosis treatment is associated with numerous benefits in terms of symptomatic recovery, reduced risk of relapse and a better ability to preserve and develop psychosocial skills, it is possible that our results may be indicative of a more chronic population and not be generalizable to individuals who are first starting treatment.

Additionally, our study sample was recruited from an early psychosis intervention program that had their own inclusion criteria, and the majority of study participants were male and Caucasian. Therefore, our conclusions may be limited to these clinical and demographic populations. Specifically, our findings may not be generalizable to individuals receiving treatment in other settings, females, individuals with affective psychotic disorders, or other ethnic minority groups who may face additional socio-economic barriers in regard to functioning. Notably, our study population also exhibited moderately high functioning with median global functioning scores of 22 out of a possible score of 28. It is therefore possible that our study findings would not be generalizable to a more functionally-heterogeneous population. Future studies should address these limitations in more diverse samples.

Although our sample was relatively large given the population and previous studies in the same field, our sample only included 105 participants whose data were used for our main analyses. However, within this sample we had to exclude data on four variables we identified as possible covariates, including age of onset, duration of untreated psychosis, premorbid adjustment and mode of onset. These variables were excluded from our main analyses because they were not assessed for the subset of our sample that were enrolled in the negative symptom study and therefore were assumed to be *Missing Not at Random*. This prohibited us from imputing these variables, given that the mechanism of missing data required for multiple imputation is for data to be *Missing at Random*. Although we were able to include these four variables in our sensitivity analyses, our sample size was reduced to include only those participants who were enrolled in the 10-year outcome study, a total of 69 individuals. Furthermore, given that we had a small sample size and controlled for a number of covariates, there is a possibility that we over-fitted our models resulting in misleading findings regarding the relationship between our

identified drivers of motivation and functioning. The use of a small sample size for our main analyses, and a loss of sample size for our sensitivity analysis, reduces our statistical power, therefore further research on the topic using a larger sample size is needed.

5.4 Study Implications and Future Directions

The current evidence base suggests that negative symptoms, more so than any other factor, are significantly associated with level of functioning, both in the early stages of illness and in more chronic populations. However, our study using more intrinsic measures of motivation rather than measures of avolition, failed to support these findings and lends credence to the growing opinion that the current measurement of avolition specifically, and negative symptoms more broadly, is lacking. This calls for a greater recognition that there are other factors that may play a role in the extent of poor functioning observed within populations with psychosis. A growing evidence base has suggested that neurocognition is strongly associated with functional outcomes [178-182]. Furthermore, a relationship between motivational deficits, neurocognitive elements and functioning has been proposed, with motivational deficits and neurocognitive factors influencing functional outcomes [183,184]. Within our study, we focused on negative symptoms primarily and excluded neurocognitive variables; however, given that our analyses did not find a relationship between motivational drivers and functioning, future research should build upon past studies assessing the relationship between neurocognitive variables and functioning.

Our study was the first to assess a number of different motivational factors and their relationship with functional outcomes, however, there are other possible factors that may influence one's motivation level. Alternative variables such as self-stigma and fear of negative evaluations from others could affect one's perception of ability in regard to goal achievement. Therefore, future research should address other types of motivational influences to form a better understanding of the impact of motivation on functioning.

As well, our analyses showed that education, social support, and alcohol use were associated with functioning, highlighting the important role of social determinants on health outcomes. This reflects the need to also address recovery through socioeconomic engagement and participation, as well as the future development and implementation of health and social policy initiatives to

address the socioeconomic and health inequalities observed within psychosis populations [185,186]. Enhancement of social participation, through engagement with community activities and connecting individuals with peer groups to form social support networks and develop social skills, in combination with current pharmacological/psychological treatment methods may provide additional benefits in regard to recovery, both symptomatic and functional.

Importantly, findings from this study demonstrate a need for updated measures of avolition and negative symptoms. With motivational drive being composed of multiple factors, both intrinsic and extrinsic, there is a need for measures to include a broader assessment of motivational influences. Furthermore, the development of these measures should be conducted in a manner that takes into account the individual experiences of motivation, and what drives motivation, from individuals with experiences of avolition.

5.5 Conclusions

To our knowledge, this study was the first to assess the relationship between multiple drivers of motivation and functioning among people with psychotic disorders, in addition to formally recognizing the overlap between measures of negative symptoms and functioning. Findings from our study suggest that the relationship between avolition and negative symptoms may be artificially inflated due to the way avolition is measured, given that our more intrinsic measures of motivation failed to find effects similar to past studies that employed the use of avolition measures that overlapped with functioning measures. Other social determinants, such as education, substance use, and social support, were shown to have a stronger relationship with functioning, more so than any other factor included within our models. Further research examining drivers of motivation within a large prospective dataset is necessary to solidify our understanding regarding the influence of motivational drivers on functional outcomes.

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Appendices

Appendix A. Copies of Western REB Approval

Western Research

Research Ethics

Use of Human Participants - Ethics Approval Notice

Principal Investigator: Dr. Ross Norman
File Number:104041
Review Level: Delegated
Approved Local Adult Participants:100
Approved Local Minor Participants:0
Protocol Title: Assessment of 10 year outcomes for clients of the Prevention and Early Intervention Program for Psychoses (PEPP)
Department & Institution: Schulich School of Medicine and Dentistry\Psychiatry,London Health Sciences Centre
Sponsor: Schizophrenia research fund

Ethics Approval Date: August 16, 2013 **Expiry Date:**August 31, 2014
Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Instruments	List of assessment instruments to be used	
Instruments	Copies of assessment instruments part 1	
Instruments	Copies of assessment instruments part 2	
Western University Protocol		2013/07/11
Response to Board Recommendations		
Revised Letter of Information & Consent		
Revised Letter of Information & Consent		

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature

Ethics Officer to Contact for Further Information

Erika Basile (ebasile@uwo.ca)	Grace Kelly (grace.kelly@uwo.ca)	Vikki Tran (vtran@uwo.ca)	Stanley Walcott (swalcott@uwo.ca)

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Research Ethics

Western Research

Western University Health Science Research Ethics Board
HSREB Delegated Initial Approval Notice

Principal Investigator: Dr. Ross Norman
Department & Institution: Schulich School of Medicine and Dentistry\Psychiatry, London Health Sciences Centre

HSREB File Number: 106232
Study Title: Understanding negative symptoms in patients of an early intervention program for psychotic disorders
Sponsor:

HSREB Initial Approval Date: March 25, 2015
HSREB Expiry Date: March 25, 2016

Documents Approved and/or Received for Information:

Document Name	Comments	Version Date
Instruments	Appendix IV Instruments	2014/12/17
Western University Protocol		2015/02/26
Letter of Information & Consent	Appendix II: LOI & Consent	2015/02/26
Instruments	Appendix III: Table & Scales Binder	2015/02/26
Advertisement	Appendix I: Poster	2015/03/24

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Ethics Officer, on behalf of Dr. Marcelo Kremenchutzky, HSREB Vice Chair

Ethics Officer to Contact for Further Information

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Appendix B. Scale for the Assessment of Negative Symptoms -Avolition/Apathy and Anhedonia/Asociality Subdomains

AVOLITION - APATHY

14.	**Grooming and Hygiene** The patient's clothes may be sloppy or soiled, and he or she may have greasy hair, body odour, etc.	**0 1 2 3 4 5**
15.	**Impersistence at Work or School** The patient has difficulty seeking or maintaining employment, Completing school work, keeping house, etc. If an inpatient, cannot persist at ward activities, such as OT, playing cards, etc.	**0 1 2 3 4 5**
16.	**Physical Anergia** The patient tends to be physically inert. He or she may sit for hours and not initiate spontaneous activity.	**0 1 2 3 4 5**
17.	**Global Rating of Avolition - Apathy** Strong weight may be given to one or two prominent symptoms if particularly striking.	**0 1 2 3 4 5**

ANHEDONIA – ASOCIALITY

18.	**Recreational Interests and Activities** The patient may have few or no interests. Both the quality and quantity of interests should be taken into account.	**0 1 2 3 4 5**
19.	**Sexual Activity** The patient may show decrease in sexual interest and activity, or enjoyment when active.	**0 1 2 3 4 5**
20.	**Ability to Feel Intimacy and Closeness** The patient may display an inability to form close or intimate relationships, especially with opposite sex and family.	**0 1 2 3 4 5**
21.	**Relationships with Friends and Peers** The patient may have few or no friends and may prefer to spend all of his her or her time isolated.	**0 1 2 3 4 5**
22.	**Global Rating of Anhedonia - Asociality** This rating should reflect overall severity, taking into account the patient's age, family status, etc.	**0 1 2 3 4 5**

Appendix C. Role Functioning Scale

ROLE FUNCTIONING SCALE (Goodman *et al.*, 1993)

ID # _____ DATE: _____

	Working Productivity	Independent Living, Self Care	Immediate Social Network Relationships	Extended Social Network Relationships
Score	**Rate the client primarily in the most appropriate expected role (i.e., homemaker, student, wage earner)**	**(Management of household, eating, sleeping, hygiene care)**	**(Close friends, Spouse, Family)**	**(Neighbourhood, community church, clubs, agencies, recreational activities)**
1	Productivity severely limited; often unable to work or adapt to school or homemaking; virtually no skills or attempts to be productive	Lacking self-care skills approaching life endangering threat; often involves multiple and lengthy hospital services; not physically able to participate in running a household	Severely deviant behaviours within immediate social networks (i.e., often with imminent physical aggression or abuse to others, or severely withdrawn from close friends, spouse, family; often rejected by immediate social network)	Severely deviant behaviours within extended social networks (i.e., overtly disruptive, often leading to rejection by extended social networks).
2	Occasional attempts at productivity unsuccessfully; productive only with constant supervision in sheltered work, home or special classes.	Marked limitations in self-care/independent living; often involving constant supervision in or out of protective environment (e.g., frequent utilization of crisis services).	Marked limitations in immediate interpersonal relationships (e.g. excessive dependency or destructive communication or behaviours).	Often totally isolated from extended social networks, refusing community involvement or belligerent to helpers, neighbours, etc.
3	Limited productivity; often with restricted skills/abilities for homemaking, school, independent employment (e.g., requires highly structured routine).	Limited self-care/independent living skills; often relying on mental/physical health care; limited participation in running household.	Limited interpersonally; often no significant participation/ communication with immediate social network.	Limited range of successful and appropriate interactions in extended social networks (i.e., often restricts community involvement to minimal survival level interactions).
4	Marginal productivity (e.g., productive in sheltered work or minimally productive in independent work; fluctuates at home, in school; frequent job changes).	Marginally self-sufficient; often uses REGULAR assistance to maintain self-care/ independent functioning; minimally participates in running household.	Marginal functioning with immediate social network (i.e., relationships are often minimal and fluctuate in quality).	Marginally effective interactions; often in a structured environment; may receive multiple public system support in accord with multiple needs.
5	Moderately functional in independent employment, at home or in school. (Consider very spotty work history or fluctuations in home, in school with extended periods of success.)	Moderately self-sufficient; i.e., living independently with ROUTINE assistance (e.g., home visits by nurses, other helping persons, in private or self-help residences).	Moderately affective continuing and close relationship with at least one other person.	Moderately affective and independent in community interactions; may receive some public support in accord with need.
6	Adequate functioning in independent employment, home or school; often not applying all available skills/abilities.	Adequate independent living & self-care with MINIMAL support (e.g., some transportation, shopping assistance with neighbours, friends, other helping persons).	Adequate personal relationship with one or more immediate members of social network (e.g., friend or family).	Adequately interacts in neighbourhood or with at least one community or other organization or recreational activity.
7	Optimally performs homemaking, school tasks or employment-related functions with ease and efficiency.	Optimal care of health/hygiene, independently manages to meet personal needs and household tasks.	Positive relationships with spouse or family and friends; assertively contributes to these relationships.	Positively interacts in community; church or clubs, recreational activities, hobbies or personal interests, often with other participants.

Appendix D. Additional Information Pertaining to the Psychosis and Early Intervention Programme (PEPP) Services

After admission, an individualized treatment plan is developed in collaboration with the client, and whenever possible, their family [121]. Treatment plans are based on an assertive case management model which involve both medication management, involving the initiation of antipsychotic medication combined with psychosocial management, such as family interventions, group interventions, and individualized therapies provided by a nurse or case manager [120,121]. Case managers assess, treat, and work through the patient's recovery from psychosis which is achieved through working closely with patients and their families with the aim to reintegrate the patient to his or her full potential over a two-year period[120,121]. Patients may stay in this core intensive treatment programme for a minimum of two years with patients not recovered sufficiently to assume independent functioning and/or not in remission being provided with extended case management for an additional one to three years [14,120]. However, the majority of patients graduate from this programme. All patients will continue with medical management with their respective psychiatrists for up to a total of five years with most patients being seen every one to three months while stable[120,121].

Appendix E. Anticipatory Pleasure Subdomain Questions of the TEPS

TEMPORAL EXPERIENCE OF PLEASURE SCALE (TEPS)

(Gard, *et al.*, 2006)

ID # _____

DATE: _____

INSTRUCTIONS: Please read each statement carefully and decide how true that statement is for YOU in general. Please respond to ***all items***. In the rare case where you have ***never*** had the experience described, think about the most similar experience you've had and make your response. Do ***not*** leave any blank. Choose only ***one*** response to each statement. Don't worry about being consistent in your responses. Choose from the 6 response options and **CIRCLE** your response.

1. When I hear about a new movie starring my favorite actor, I can't wait to see it.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

2. I enjoy taking a deep breath of fresh air when I walk outside.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

3. The smell of freshly cut grass is enjoyable to me.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

4. I look forward to a lot of things in my life.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

5. I love it when people play with my hair.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

6. **Looking forward to a pleasurable experience is in itself pleasurable.**

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

7. **A hot cup of coffee or tea on a cold morning is very satisfying to me.**

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

8. **When I think of something tasty, like a chocolate chip cookie, I have to have one.**

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

9. **I appreciate the beauty of a fresh snowfall.**

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

10. **I get so excited the night before a major holiday I can hardly sleep.**

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

11. **When I'm on my way to an amusement park, I can hardly wait to ride the roller coasters.**

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

12. **I really enjoy the feeling of a good yawn.**

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

13. I don't look forward to things like eating out at restaurants.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

14. I love the sound of rain on the windows when I'm lying in my warm bed.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

15. When I think about eating my favorite food, I can almost taste how good it is.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

16. When ordering something off the menu, I imagine how good it will taste.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

17. The sound of crackling wood in the fireplace is very relaxing.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

18. When something exciting is coming up in my life, I really look forward to it.

1	2	3	4	5	6
very false for me	moderately false for me	slightly false for me	slightly true for me	moderately true for me	very true for me

Appendix F. Additional Covariate Variables

Age of Onset

Age of onset refers to one's chronological age at the time of the first onset of psychotic symptoms, with psychotic symptoms being identified by hallucinations, delusions or gross disorganization [187]. A younger age of onset has been found to be associated with poorer premorbid functioning [188] however, findings are mixed regarding the effect a younger age of onset has on functional outcomes [131,132,137,189-191]. Age of onset was calculated via the Topography of Psychotic Episode (TOPE) section of the Course of Onset and Relapse Schedule (CORS)[192], a structured interview that assesses lifetime history of illness prior to the onset of the current psychotic episode, using date of birth and date of initial behavioral changes. The CORS consists of 5 sections: (1) Identifying Information, (2) Demographic Information, (3) Family Structure and Health, (4) Pathways to Care, and (5) Topography of Psychotic Episode.

The CORS was completed at baseline for the 10-year outcome study via information obtained from family members and the referral source however, this measure was not used for the negative symptom study. Given that a significant portion of our data set does not have data on age of onset, we were unable to include the variable in our main multivariable regression analyses and therefore only used the CORS as a continuous measure of age of onset for our descriptive statistics and sensitivity analyses.

Mode of Onset

Mode of onset refers to how quickly psychotic symptoms evolve during the first episode of psychosis [193]. Mode of onset was calculated using the CORS by subtracting the date of onset of psychosis from the date of initial behavioral changes.

The CORS was completed at baseline for the 10-year outcome study via information obtained from family members and the referral source however, this measure was not used for the negative symptom study. Given that a significant portion of our data set does not have data on mode of onset, we were unable to include the variable in our multivariable regression analyses and therefore only used the CORS as a dichotomous measure of mode of onset for our descriptive statistics and sensitivity analyses, with participants being categorized as having either

an acute or insidious mode of onset. An acute mode of onset was defined as a period of less than or equal to one month, whereas an insidious mode of onset was defined as more than one month. In individuals with psychotic disorders, an insidious onset of psychosis is associated with a greater duration of untreated psychosis [194]and poorer functional outcomes[193].

Duration of Untreated Psychosis

Duration of untreated psychosis was defined as the length of time, in weeks, from the onset of psychotic symptoms (e.g. hallucinations) to the date of two months post initiation of antipsychotic therapy. Information regarding the date of onset of symptoms and date of treatment were obtained from the CORS at baseline for the 10-year outcome study. Duration of untreated psychosis has been found to be associated with greater symptom severity [195,196], an insidious mode of onset [194], and poorer functional outcomes [16,20,195,196].

The CORS has demonstrated high inter-rater reliability (ICC=0.86 to 0.90) for its ability to calculate duration of untreated psychosis [197] and has been used in studies of participants with a first episode of psychosis [198-200]. Duration of untreated psychosis was treated as a continuous variable.

Given that a significant portion of our data set does not have data on duration of untreated psychosis, we were unable to include the variable in our multivariable regression analyses and therefore only used the CORS as a continuous measure of duration of untreated psychosis for our descriptive statistics and sensitivity analyses.

Premorbid Adjustment

Premorbid adjustment refers to one's psychosocial functioning prior to the onset of psychotic symptoms and was assessed using the Premorbid Adjustment Scale (PAS) [201] at baseline for the 10-year outcome study. The PAS is a series of rating scales that evaluate five domains of functioning: (1) **Sociability and Withdrawal**, (2) **Peer Relationships**, (3) **Scholastic Performance**, (4) **Adaptation to School**, and (5) **Social-sexual Aspects of Life**. All or some of these domains of functioning are then assessed over four separate life periods including childhood (up to age 11), early adolescence (12 to 15), late adolescence (17 to 18) and adulthood

(19 and above). Social-sexual aspects of life is not assessed during the childhood life period, along with scholastic performance and adaptation to school being not assessed during the adulthood life period. Along with the four separate life periods, there is a general section which assesses variables including education, employment, school, establishment of independence, highest level of functioning, social-personal adjustment, degree of interest in life and energy level.

Given that onset of illness typically occurs within the late adolescence and adulthood periods, these sections were excluded from our analyses to reduce the effects of confounding [187]. Therefore, the ratings from the childhood and early adolescence periods were the section used for our analyses to assess premorbid adjustment. Each item of this scale is rated using a Likert-type scale with responses ranging from 0 to 6. To calculate total scores for each psychosocial domain, ratings were summed for all items and divided by the total possible score, which resulted in total scores ranging from 0 to 6, with higher scores being indicative of worse adjustment. For all ratings, the premorbid period was used as a reference frame [201]. Information on psychosocial functioning during this period was obtained from patient reports and reports from family members. Poorer premorbid functioning is associated with greater negative symptom severity [137,189,196,202], amotivation [141]and poorer functional outcomes [20,130,132,137,202,203].

Brill and colleagues conducted a study to test the predictive and concurrent validity of the PAS within a sample of 91 males diagnosed with either schizophrenia or schizoaffective disorder[204]. Their findings demonstrate a high degree of correlation between the PAS late adolescence scores and Draft Board assessments at age 17 years in terms of estimating premorbid functioning in schizophrenic persons. The correlation of the PAS in terms of school achievements and school adjustment items with the Draft Board assessments for functioning in structured environments were r=0.71 and r=0.72, respectively, for concurrent ratings and r=0.4 and r=0.47, respectively for the ratings obtained at the age of 17 [204]. The PAS was also found to have good reliability with a weighted ICC for absolute agreement and consistency of 0.77 [204].

For our analyses, we used the total premorbid adjustment scale rating for the childhood and early adolescence period and treated the score as a continuous variable for our descriptive statistics

and sensitivity analyses. However, we were unable to include the variable in our main multivariable regression analyses due to its exclusion in the negative symptom study resulting in a high degree of missing data and overall lack of variability within our data set.

Curriculum Vitae

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