Delusions in Early Intervention for Psychosis: Baseline, Longitudinal and Cross-Cultural Contexts

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November 2020

A thesis submitted to McGill University in partial fulfillment of requirements of degree of Master's of Science (M.Sc.)

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Acknowledgements

I would like to first and foremost thank my thesis supervisors, Dr. Jai Shah and Dr. Patricia Boksa. Along with my advisory committee, they contributed a depth of knowledge, open-mindedness, and enthusiasm that pushed me to think critically about the research process in its entirety. Not only did they strongly support my thesis work, but they encouraged my interests to pursue interdisciplinary learning opportunities and continue my art practice. Both have pushed me to develop my skills, and also the confidence in those skills, as I continue to learn and gradually develop a career in the realm of mental health care. I am also tremendously grateful to have received the unconditional space to mourn and heal after the death of a loved one during my first year. Thank you for creating a healthy working culture that pushed me to grow intellectually and emotionally.

I wish to thank my advisory committee members, Dr. Ian Gold and Dr. Genevieve Gariepy, for their continued encouragement and thoughtful input; Nicole Pawliuk, Kevin Macdonald, and Aarati Taksal for their technical support regarding data. I am very grateful for the unwavering support from past, current and honorary PEPP students and colleagues. Whether sitting around picnic tables under the sun or over zoom once the pandemic started, I will cherish the valuable insight they provided over the countless lunches we enjoyed together. I'd like to give a special thank you to Sarah McIlwaine, a senior student in our lab, who provided unwavering support to the MSc students at PEPP.

This entire process would not have been possible without my partner (Geoff Meugens), close friends, and family. Their love and support have been instrumental towards my well-being, and I am eternally grateful for all of the past and continued discussions around the dinner table

and more recently over phone calls and zoom hangouts – may these discussions continue to be filled with curiosity and compassion.

I am grateful for both SSHRC and FRQS for their generous financial support throughout my masters training.

Finally, it has been an incredible privilege to learn from and work with PEPP participants and the surrounding community – PEPP service users, families, and treatment providers as well as policy and decision makers. Thank you sincerely to each service user for sharing your experiences.

Contributions of Authors

As first author of this thesis, I (**Ann-Catherine Lemonde**) made a significant contribution to the conceptualization, design, data analysis, interpretation of results, and writing of this thesis.

Dr. Srividya N. Iyer contributed significantly to revisions and the implementation of the pre-existing PEPP database used for this thesis, and the conceptualization and design of Chapter 4.

Dr. Ashok Malla contributed significantly to the implementation of the pre-existing PEPP database used for this thesis, and contributed to the revision of Chapter 3.

Dr. Martin Lepage and **Dr. Ridha Joober** contributed significantly to the implementation of the pre-existing PEPP database used for this thesis, and contributed to the revision of Chapter 3.

Dr. Genevieve Gariepy contributed significantly to the data analysis of this thesis.

Dr. Norbert Schmitz contributed significantly to the implementation and data analysis involved in the fourth chapter of this thesis.

Dr. Thara Rangaswamy, Dr. Padmavati Ramchandran, Greeshma Mohan, and **Dr. Howard Margolese** contributed significantly to the implementation (e.g. data collection) of the fourth chapter of this thesis.

Dr. Patricia Boksa provided overall supervision and guidance on the conceptualization, design, data analysis, interpretation of the results, and revisions of this thesis.

Dr. Jai Shah provided overall supervision and guidance on the conceptualization, design, data analysis, interpretation of the results, and revisions of this thesis; and, he was involved with the implementation of the pre-existing PEPP database used for this thesis.

Abstract

Background: During a psychotic episode, patients frequently suffer from unusual and often distressing beliefs known as delusions. The levels of conviction and preoccupation associated with these beliefs can be tremendously afflicting to those experiencing a psychotic episode. Although delusions have been a target of psychiatric research from its inception, little has been reported about their content and severity during the formative stages of illness when patients are relatively young and before exposure to treatments. In addition, there exists minimal research on how social and cultural factors relate to delusions in first episode psychosis.

Objectives: The objectives of the following Master's thesis were 1) to examine how delusions present in a large, minimally medicated, and catchment-based clinical population of individuals experiencing a first episode of affective or nonaffective psychosis (FEP); and 2) to explore the presentation of delusions at baseline and longitudinally in two FEP treatment programs representing different cultural contexts.

Methods: Using descriptive and bivariate statistics, an initial cross-sectional analysis of the content and severity of delusions at presentation to an early intervention setting for psychosis in Montreal, Canada was conducted. Following this, a comparative analysis of baseline and longitudinal data using descriptive and regression statistics was undertaken at similarly organized early intervention programs for FEP in two different contexts: Chennai, India and Montréal, Canada. In both studies the average severity and frequency of each delusional theme was reported using the Scale for Assessment of Positive Symptoms.

Results: Overall, the vast majority of individuals experiencing a FEP developed clinical level delusions, with persecutory, referential and grandiosity being the most common themes. Delusional content was similar across emerging affective and non-affective psychotic illnesses.

Across cultural contexts, the rank-order of thematic content remained relatively consistent although the frequency of clinical-level delusions differed across sites both at baseline and longitudinally.

Discussion: The analyses undertaken in this thesis shed light on the earliest phases of clinically salient delusions; their presentations over time, across diagnoses, and between cultural contexts; and potential predictors of these processes. Perhaps most notable was the similar rank-order of thematic content seen across contexts, indicating a need for future work to consider how the very content of delusions may be useful in understanding the cognitive mechanisms underlying the formation and maintenance of these beliefs.

Résumé

Contexte: Lors d'un épisode psychotique, les patients souffrent fréquemment de croyances inhabituelles et souvent angoissantes, connues sous le concept de délire. Les niveaux de conviction et de préoccupation associés à ces croyances peuvent être extrêmement affligeants pour ceux qui vivent un épisode psychotique. Bien que les délires aient été la cible de la recherche psychiatrique depuis ses débuts, peu de données ont été rapportées sur leur contenu et leur gravité au cours des stades précoces de la maladie lorsque les patients sont relativement jeunes et avant l'exposition aux traitements. De plus, il existe peu de recherches sur la façon dont les facteurs sociaux et culturels sont liés aux délires en ce qui concerne le premier épisode psychotique.

Objectifs: Les objectifs de cette thèse de maîtrise étaient 1) d'examiner la manière dont les délires se présentent au sein d'une population clinique importante, peu médicamentée, et axée sur le recrutement d'individus ayant un premier épisode de psychose (PEP) affective ou non affective; et 2) d'étudier la présentation des délires à un premier niveau de base et longitudinalement dans deux programmes de traitement pour le PEP qui tiennent compte de différents contextes culturels.

Méthodes: À l'aide de statistiques descriptives et bivariées, une première analyse transversale du contenu et de la gravité des délires lors de la présentation initiale à un milieu d'intervention précoce pour la psychose à Montréal, au Canada, a été menée. Par la suite, une analyse comparative des données de base et longitudinale à l'aide de statistiques descriptives et de régression a été entreprise. Cette recherche porte sur des analyses des données obtenues dans le cadre de programmes d'intervention précoce organisés de manière similaire pour le PEP dans deux contextes différents: Chennai, Inde et Montréal, Canada. Dans les deux études, les

moyennes pour la gravité et la fréquence pour chacun des thèmes délirants ont été rapportées à l'aide de l'échelle d'évaluation des symptômes positifs (Scale for Assessment of Positive Symptoms).

Résultats: Dans l'ensemble, la majorité des personnes ayant des expériences de PEP ont développé des délires au niveau clinique, la persécution, le référentiel et la grandiosité étant les thèmes les plus courants. Le contenu délirant était similaire pour les maladies psychotiques affectives et non affectives émergentes. Dans les contextes interculturels, l'ordre de classement du contenu thématique est demeuré relativement cohérent. Cependant, la fréquence des délires au niveau clinique diffère d'un site à l'autre, tant pour le niveau de base que pour les données longitudinales.

Discussion: Les résultats de cette thèse mettent en lumière les premières phases des délires cliniquement saillants; leurs présentations au fil du temps, à travers les diagnostics et les contextes interculturels; et les prédicteurs potentiels de ces processus. Ce qui est le plus remarquable était possiblement la similarité de l'ordre du contenu thématique observé dans tous les contextes. Ceci suggère l’importance de réaliser des recherches futures afin d’examiner comment le contenu délirant peut être utile pour comprendre les mécanismes cognitifs sous-jacents à la formation et au maintien de ces croyances.

CHAPTER 1. Thesis introduction: Literature review and rationale

During an episode of psychosis, a debilitating mental illness found in all corners of the world, patients frequently suffer from strange and distressing beliefs known as delusions. Traditionally conceptualized as 'false but fixed' beliefs emerging from a loss of contact with a shared reality, individuals may nonetheless remain connected to surrounding context; perhaps best exemplified through the socially salient content seen in delusions (i.e. persecution, grandiosity, etc.). While delusions are a core feature of schizophrenia, they are also present in other psychotic and psychiatric disorders (i.e. bipolar disorder and dementia); (Bebbington & Freeman, 2017; Kelly, 2019). While they are paralleled by certain characteristics (i.e. resistance to change) seen in strongly held beliefs in healthy individuals (Upthegrove, S. A., Corlett, Bentall, & Bortolotti, 2018), within clinical and help-seeking populations these beliefs are often associated with impaired functioning and strain social relations. Here is an excerpt from S.A. enclosed in the book *Delusions in Context*:

> *It is said that even Mother Teresa doubted her faith, yet her religious beliefs directly influenced her charitable actions. Unlike Mother Teresa, my delusions had no room for doubt. I was convinced there was a "Challenge" which placed me at the centre of an elaborate scheme to test my suitability for university. "The Challenge" consumed my every being. As part of it I believed people were recording every thought and every word I spoke. I believed that food and drink were poisonous, which led me not to eat or drink for four days. Unlike Mother Teresa, there was no good in my belief systems: only terror, anguish and exhaustion.*
>
> [S.A., 2018, p.2]

S.A.'s experience demonstrates how the levels of conviction and preoccupation associated with these beliefs can result in stress and sheer exhaustion, impacting even everyday mundane experiences such as attending a class or interacting with loved ones. Although delusions have been a target of psychiatric research from its inception, individuals continue to suffer from these maladaptive beliefs and the biopsychosocial mechanisms involved in their formation and maintenance remain poorly understood. In addition, delusions may respond favourably to antipsychotic medication; yet, the mechanisms by which these and other treatments interact with and attenuate delusions remain to be fully illuminated. Further investigation is clearly needed regarding their etiology and course, along with how best to prevent or treat them. In addition, in order to build empathy and reduce stigma surrounding one of the most challenging and persistent of mental illnesses, a clearer understanding of the experience of delusions on the part of sufferers and their families is needed.

1.1 What beliefs do we hold about delusions?

A complete historical analysis of delusions is beyond the scope of this thesis (refer to (Gold & Gold, 2014)); however, it is worth noting that there exists a long tradition of describing the experience and content of delusions. For much of history delusions were conceptualized as the core feature of madness (Gold & Gold, 2014). Those who suffered were too often ostracized; a pain that unfortunately persists as social exclusion continues to affect individuals living with psychotic disorders.

From early descriptions of madness existing in the absence of rational thought, Karl Jaspers continued the tradition of ascribing irrationality as a key characteristic of delusions. The advent of antipsychotic medications in the 1950s led to a new wave of biological psychiatry that birthed the Kraepelinian model of disease classification and subsequent diagnostic models (i.e. DSM-I).

Over the last 40 years there has been a renewed interest in better understanding the cognitive aspects of delusions as symptoms occurring across a range of illnesses, and in their shared overlap with healthy belief frameworks.

One of the most commonly employed definitions for delusions, as laid out by the DSM-5, provides a useful framework to analyze the complex task of defining this phenomenon:

> *A false belief based on incorrect inference about external reality that is firmly held despite what almost everyone else believes and despite what constitutes incontrovertible and obvious proof or evidence to the contrary. The belief is not ordinarily accepted by other members of the person's culture or subculture (i.e., it is not an article of religious faith). When a false belief involves a value judgment, it is regarded as a delusion only when the judgment is so extreme as to defy credibility.*
>
> [American Psychiatric Association, DSM-5, 2013, p. 819]

While this standard definition acts as useful guide towards understanding delusions, a closer look exposes conceptual difficulties. For starters, while some characterize delusions as distinct from 'normal' beliefs, others have recognized them as part of a spectrum of psychosis, favouring a continuity or dimensionality of belief formation (Peters, 2010; So, Tang, & Leung, 2015; van Os et al., 1999). This is perhaps exemplified in literature demonstrating that defining features of delusions (i.e. irrationality) are also apparent in strongly held beliefs seen in healthy individuals (e.g. political ideologies) (Upthegrove et al., 2018). For example, false beliefs can be seen in everyday instances where folks prioritize social commonalities in thinking over individual logic as a means to gain group membership (Bell, Raihani, & Wilkinson, 2019). The continuum of belief formation has led some to abandon the long-standing definition of *false but fixed* beliefs, instead focusing on components such as help-seeking, distress and risk (Upthegrove et al., 2018).

Researchers have even argued that delusions may be somewhat beneficial when considered in the context of a psychotic disorder (Bortolotti, 2015). Elaborating on this more nuanced understanding of delusions, experiential abnormality theories state that delusions are based on an unimpaired inferential process that is applied to anomalous but genuine experiences (Maher, 2005). Fineberg and Corlett create the analogy of a '*doxastic shear pin'* to describe delusions as a cognitive phenomenon that responds to anomalous experiences as a conditional operator, allowing the individual to continue interacting with and functioning with the world around them (Fineberg & Corlett, 2016). This is contrary to some of the earliest accounts which were focused solely on reasoning abnormalities (Von Domarus, 1944) such as a jumping to conclusions bias (Huq, Garety, & Hemsley, 2018). Other investigators have argued that a satisfactory theory of delusions must posit two disorders, one in experience and a second in reasoning processes (Davies, Coltheart, Langdon, & Breen, 2001). A newer theory posits that both delusions and hallucinations develop due to disruptions in the same updating mechanism, namely, aberrant prediction errors; and, because this single deficit likely explains both abnormal perception and belief formation it thus overrides the need for separate reasoning and experiential accounts of delusion formation (Corlett et al., 2007; Fletcher & Frith, 2008).

Garety and Freeman have contributed significantly to the plethora or delusion related work emerging in the last 40 years, and describe the formation of delusional beliefs as multi-factorial process:

"*Both singly and in combination, specific reasoning and information biases, pre-exiting schematic beliefs about the self and others, current emotional disturbance and social factors (i.e. isolation and adversity) are then considered to facilitate maladaptive appraisals of the origins of these anomalous mental states."*

[Garety & Freeman, 2013, p. 328]

In Jasperian tradition, emotional disturbances and psychotic experiences were seen as two distinct issues delineating diagnostic boundaries, with emotion quickly being overlooked once psychotic symptoms emerged (Garety & Freeman, 2013; Jaspers, 1997). For the last 20 years or so, emotional processes have taken a more central role in our understanding of delusions, with anxiety and depression being closely linked to the occurrence and persistence of persecutory delusions (Garety & Freeman, 2013; Opoka, Ludwig, & Lincoln, 2018).

While research typically centers around the simple presence or absence of delusional beliefs in psychosis, more recent accounts have stressed the importance of considering the content of delusional beliefs. Contrary to earlier views that delusions are not only irrational in nature but "meaningless speech acts" (Berrios, 1996), evidence suggests that the content is personally meaningful to those who experience them (e.g. reflecting life problems and/or life goals; (Jakes, Rhodes, & Issa, 2009), and that certain forms of childhood adversity may be implicated in the development of certain delusion themes (Bentall et al., 2014). In addition, the repetition of themes seen across temporal and cultural dimensions has motivated cognitive theorists to reconsider the content of these phenomenon (Gold & Gold, 2012).

These nuances surrounding our current understanding of delusions should not detract from the very real phenomenon that impacts the lives of those living with psychosis, but they do highlight the need for continued theoretical and conceptual work on the matter.

1.2 Delusions in the earliest phases of psychosis

While delusions have received extensive attention in clinical settings, the relatively new paradigm of early intervention (EI) research offers a unique setting in which to study delusions. The term first episode psychosis (FEP) emerged in the late 1980s to describe the first

presentation of psychotic symptoms, driven by a desire to improve the longitudinal trajectory of psychosis through early detection and treatment. Because of this clinical focus on identifying individuals in the earliest phases of psychotic illness, EI clinical research infrastructures also hold the potential to reduce or even minimize confounding factors such as the effects of long-term illness and treatment exposure (Berkhout, 2018). In addition, studying delusions in their earliest phases is ultimately important to understanding how they arise and are maintained in light of contradictory evidence.

Well-established delusional systems seen in later episodes, or chronic psychoses, are more likely to contain 'secondary' delusions which emerge in response to other psychopathological forms; while the early phases of delusion formation are, at least in theory, more likely to contain the *un-understandable* 'primary' delusions also known as *autochthonous* ideas (Jaspers, 1997; Oyebode, 2015; Wernick, 1906) arising from percepts, memory, atmosphere or even spontaneously. While primary and secondary delusions are not temporally dependent, it is possible that primary delusions emerge through the intensified perceptual and emotional period accompanying the onset of a psychosis (Jaspers, 1997; Maj, 2013; Upthegrove et al., 2018); described as the *Stimmung* by Louis Sass – a phase where objects are "*stripped of familiarity and reality, and of any sense of coherence or connectedness, yet bursting with some profound inner significance that lies just beyond the reach of one's comprehension* (Sass, 1992)." Research has yet to provide mechanistic evidence for the distinction between primary versus secondary delusions, and more recent works have in fact begun to critique the view that delusions are *un-understandable* or irrational in nature, suggesting that this conceptualization has concealed fundamental understandings regarding delusions (Bell et al., 2019). In this sense, perhaps examining the content of delusions, even if traditionally conceptualized as primary, may

contribute to an understanding of the cognitive mechanisms by which individuals navigate their day-to-day interactions.

Another central component of the FEP paradigm, is the period of time between the onset of psychosis and the initiation of treatment, the duration of untreated psychosis (DUP). Extended DUPs have been shown to impact both short- and long-term outcomes – including the severity of symptoms (Marshall et al., 2005). Neurobiological and cognitive models have suggested that delusional beliefs arise and are continually reconsolidated and strengthened due to aberrations of synaptic plasticity (Corlett, Krystal, Taylor, & Fletcher, 2009; Corlett, Taylor, Wang, Fletcher, & Krystal, 2010). These aberrations or prediction errors appear when individuals face a mismatch between their expectations of a given situation and what they actually encounter, signaling the need for updating belief frameworks. It is plausible that prolonged exposure to prediction errors through a longer DUP influences the initial development and severity of delusional themes, strengthening the beliefs so that they persist in light of contradictory evidence and become more intensely preoccupying.

Despite the considerable attention delusions have received in clinical settings, far less has been reported about their content and severity during the formative stages of illness when patients are relatively young and before exposure to treatments. The few studies that have focussed on the first episode are limited by small sample sizes (Kimhy, Goetz, Yale, Corcoran, & Malaspina, 2005; Paolini, Moretti, & Compton, 2016; Rajapakse, Garcia-Rosales, Weerawardene, Cotton, & Fraser, 2011), selected samples (Kimhy et al., 2005; Paolini et al., 2016), and potential confounds (such as treatment effects or lack of clarity regarding antipsychotic exposure) (Ellersgaard et al., 2014; Kimhy et al., 2005; Rajapakse et al., 2011). In addition, the literature focuses almost exclusively on non-affective (schizophrenia-spectrum)

diagnoses, without including delusions in affective psychosis (such as bipolar disorder with psychotic features, or depression with psychotic features) that are frequently indistinguishable in first episode psychosis settings. The elucidation of these presentations through a unique clinical lens could contribute to a much broader and long-standing dialogue among theorists, clinicians, service users, and their families.

1.3 What can context teach us about delusions?

One of the most fascinating and contested findings of our time is that psychosis outcomes are more benign in lower- and middle-income countries (LMICs) compared to higher-income countries (HICs). While earlier works provided suggestive evidence to this effect, it soon became clear that these had methodological shortfalls, necessitating a more rigorous approach that included cross-cultural studies (Lin & Kleinman, 1988; Hopper, Harrison, Janca, & Sartorius, 2007). Yet, direct comparisons between LMICs and HICs remain relatively uncommon, particularly those with similar treatment protocols and outcomes measures. And while there have been more recent assessments of the course of overall positive and negative symptoms in similar early intervention (EI) settings in LMICs and HICs (Malla et al., 2020), specific domains of symptomatology such as delusions remain unexamined.

At present, what is known is that variations in the characteristics and frequency of delusional themes are seen in psychotic episodes across contexts (Gecici et al., 2016; Kim et al., 2001). Similarly, neurocognitive accounts focusing on the core consistencies of delusions across psychiatric diagnoses and in healthy populations have noted commonalities in the themes that emerge across temporal and contextual dimensions (Cannon & Kramer, 2012; Gold & Gold, 2012). Delusions are particularly malleable to culture given that beliefs are themselves cultural representations which shape our shared understandings of reality (Tomasello, 2018); it may be

that while the content reflects the social climate of our time, the broader categories of delusions (e.g. grandiosity, persecutory, somatic, etc.) remain stable. There is no work to date that has systematically investigated delusional content and severity across two services in different countries but with similar treatment protocols. In addition, while studies have long suggested that culture interacts with delusions, there remains the question of what exactly within this *black box* of context (Jenkins & Karno, 1992) interacts with the symptom dimensions of a psychotic episode. We hope to add to the previous literature by moving beyond a homogenous interpretation of positive psychotic experiences and towards a more penetrating understanding of delusions across cultures.

1.4 Objectives

To address the knowledge gaps outlined above, we conducted two studies. The following questions were asked as part of a first manuscript to create a clinical snapshot of delusions in FEP (Chapter 3): 1) How do delusions present, both globally and thematically, in a large, minimally medicated, and catchment-based clinical population of individuals experiencing an affective or nonaffective FEP; and, 2) Are there associations between delusion severity and certain clinical and sociodemographic characteristics in the early phases of psychosis?

In a subsequent manuscript (Chapter 4) we asked: 1) What is the baseline presentation and longitudinal trajectory of delusions in first episode psychosis (FEP) across two similar protocol treatment settings in Montréal (Canada) and Chennai (India); and, 2) Is this trajectory unique to delusions or mirrored by other positive symptom clusters.

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CHAPTER 2. Methods

2.1 Quantitative Study

A cross-sectional and quantitative analysis was first undertaken to set the groundwork for future investigations into delusions at the Prevention and Early Intervention Program for Psychosis in Montreal, Canada (PEPP-Montreal). This sample is catchment-based, meaning that all individuals identified as needing treatment for an early phase psychosis in the catchment were referred to PEPP. The resulting near-treated incidence sample makes this amongst the first to study delusions in all individuals aged 14-35 identified as experiencing a first episode of psychosis (FEP). Delusions were examined across all individuals in the same early phase of their illness, thereby substantially reducing potential confounds such as illness chronicity and treatment exposure. The average severity and frequency of each delusional theme at baseline was reported using the Scale for Assessment of Positive Symptoms (SAPS). To assess frequencies, the presence or absence of delusions was determined by a SAPS rating of >= 3 or <3, respectively. A mix of descriptive and bivariate statistical analyses were untaken to assess delusional severity, both globally and per theme, and to investigate the relationship between delusions and a number of sociodemographic and clinical variables.

2.2 Cross-Cultural Quantitative Study

Given the lack of research directly comparing delusional beliefs in early psychosis across different cultural contexts, a quantitative study was conducted with the aim of investigating the baseline presentation and longitudinal trajectory of delusions in a sample of patients entering an early intervention program for FEP in Chennai (India) and Montréal (Canada) with longitudinal follow-up for two years of treatment. Unique to this study's design was the direct comparison of delusions in programs with similar treatment protocols and outcome measures. Again, delusions

were measured using the SAPS; and, clinical level delusions were considered present with a SAPS rating of >= 3. A series of chi-square analyses and regressions were conducted to assess the baseline presentation and longitudinal trajectory of delusions, to control for confounding effects, and to test for pertinent predictors.

Greater detail on the methodology employed across these two quantitative studies are included in the relevant chapters that follow.

CHAPTER 3. First Manuscript

Title: Delusional Content at Initial Presentation to a Catchment-Based Early Intervention Service for Psychosis

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3.1 Abstract

Background: During a psychotic episode, patients frequently suffer from severe maladaptive beliefs known as delusions. Despite the abundant literature investigating the simple presence or absence of these beliefs, there exists little detailed knowledge regarding their actual content and severity at the onset of illness.

Aim: This study reports on delusions during the initiation of indicated treatment for a first episode psychosis (FEP).

Methods: Data were systematically collected from a sample of 636 patients entering a catchment-based early intervention service for FEP. The average severity and frequency of each delusional theme at baseline was reported using the Scale for Assessment of Positive Symptoms. Delusional severity (globally and per theme) was examined across a number of sociodemographic and clinical variables.

Results: Delusions were present in the vast majority of individuals experiencing onset of a FEP (94.0%), with persecutory (77.7%) being the most common theme. Persecutory delusions remained consistent in severity across diagnoses, but were more severe with older age of onset. No meaningful differences in delusional severity were observed across sex, affective versus non-affective psychosis, or presence/absence of substance abuse or dependence. Globally, delusion severity was associated with anxiety but not depression. Delusions commonly referred to as passivity experiences were related to hallucinatory experiences.

Conclusion: This representative community sample offers a rare clinical lens into the severity and content of delusions in FEP. While delusional severity was consistent across certain sociodemographic and clinical variables, this was not always the case. Future research should consider the course of delusion themes over time.

3.2 Introduction

In psychiatric settings, delusions have been defined as false but fixed beliefs even in the presence of clear and contradictory evidence (APA, 2013). There is a long phenomenological tradition of examining delusional content (Fulford et al., 2013), which is known to reflect socially salient themes (e.g. persecution, grandiosity, etc.) and typically cannot be explained by one's cultural background alone (APA, 2013). While delusions are a core feature of schizophrenia, they are also seen in other psychotic and psychiatric disorders (APA, 2013). More recent literature has demonstrated that defining features of delusions are also apparent in strongly held beliefs seen in healthy individuals (e.g. political ideologies) (Upthegrove, S. A., Corlett, Bentall, & Bortolotti, 2018), leading some to abandon the long-standing definition of *false but fixed* beliefs, instead focusing on components such as help-seeking, distress and risk (Upthegrove et al., 2018). The current debate surrounding the definition of delusions in part indicates the need for improved understanding of this phenomenon.

Well-established delusional systems seen in later episodes, or chronic psychoses, may contain 'secondary' delusions (Oyebode, 2015); while the early phases of delusion formation are, at least in theory, more likely to include 'primary' delusions emerging from intuitions, percepts, memory, and atmosphere (Jaspers, 1997; Oyebode, 2015). However, despite the considerable attention delusions have received in clinical settings, far less has been reported about their underlying content and severity during the formative stages of illness. Investigating delusions in early clinical samples is critical, because their relatively young, treatment-naïve presentations are less likely to be confounded by the effects of long-term illness or previous interventions. Improved knowledge on the content and severity of delusions may also have implications for diagnostic classification and personalizing therapeutic options (Corlett, Taylor, Wang, Fletcher,

& Krystal, 2010; Paolini, Moretti, & Compton, 2016; Picardi, Fonzi, Pallagrosi, Gigantesco, & Biondi, 2018).

The limited prior work undertaken has found relatively high rates of delusions at the first episode of psychosis (FEP) – with the most common themes being persecutory, referential, and grandiose (Paolini et al., 2016; Rajapakse, Garcia-Rosales, Weerawardene, Cotton, & Fraser, 2011). However, this literature is limited by small sample sizes (Paolini et al., 2016; Rajapakse et al., 2011), selected samples (Paolini et al., 2016), and potential confounds (such as treatment effects or lack of clarity regarding antipsychotic exposure) (Ellersgaard et al., 2014; Rajapakse et al., 2011). A brief Australian report examining delusions in FEP was catchment-based, but had a modest study sample (n = 143) and no mention of prior antipsychotic use (Rajapakse et al., 2011). Studies with larger samples (n = 245) have had disproportionately high numbers of African American men (Paolini et al., 2016) or focused on nonaffective psychoses alone (Ellersgaard et al., 2014) (Compton, Potts, Wan, & Ionescu, 2012; Vazquez-Barquero, Lastra, Cuesta Nunez, Herrera Castanedo, & Dunn, 1996). In contrast, an inclusive approach that encompasses both non-affective and affective (e.g. bipolar or major depressive disorder with psychotic features) psychoses may provide valuable insight into how symptoms such as delusions emerge and are maintained, and whether diagnostic grouping impacts these processes: while certain delusional content has been associated with mood, delusions of persecution appear to be broadly dispersed across diagnostic categories in adult patients (Picardi et al., 2018). And in regards to sociodemographic factors, FEP reports have shown a link between persecutory delusions and older age of onset, but not with sex (Hafner, Maurer, Loffler, & Riecher-Rossler, 1993; Paolini et al., 2016). In sum, previous literature on delusional content and severity would

be notably strengthened by data from a large, representative and well-characterized early psychosis patient population.

While the links between symptoms (e.g. anxiety, hallucinations, etc.) and persecutory delusions or delusions as a whole have been researched (Hartley, Barrowclough, & Haddock, 2013), few have rigorously examined the association between other delusion themes (e.g. grandiosity, mind reading, etc.) and symptomatology (Gutierrez-Lobos, Schmid-Siegel, Bankier, & Walter, 2001; Kimhy, Goetz, Yale, Corcoran, & Malaspina, 2005), and even fewer within FEP populations (Paolini et al., 2016). For example, a systematic review demonstrated links between depression, anxiety and overall delusion severity; however, they also called for future research to consider specific subtypes of psychotic symptoms experienced (Hartley et al., 2013). Furthermore, certain delusion themes that have commonly been considered as passivity experiences and/or thought alienation may emerge and persist differently than other themes (Oyebode, 2015). One indicator is that these experiences appear to have a distinct association with hallucinations (Kimhy et al., 2005; Paolini et al., 2016). A more detailed view of the association between clinical factors and delusion severity, both globally and per theme, in a larger and more representative sample may improve psychological models and ultimately interventions.

The aim of this study was to systematically examine and describe delusional content and severity, and its clinical and sociodemographic characteristics, in a large, minimally medicated, and catchment-based clinical population of individuals experiencing an affective or nonaffective FEP. We hypothesized that 1) persecutory delusions would be the most common delusion theme across non-affective and affective psychoses in this representative sample; and, that their severity would be positively associated with age of onset, 2) that severity of anxiety and depression

would be positively associated with global severity of delusions, and 3) that passivity experiences and/or thought alienation (e.g. thought insertion, thought withdrawal, thought broadcasting, and being controlled), would be positively correlated with hallucinations.

3.3 Methods

3.3.1 Setting

The study took place at the Prevention and Early Intervention Program for Psychosis (PEPP-Montreal). PEPP is open to youth who are experiencing an FEP within a geographically defined catchment area of roughly 350,000 individuals in an urban setting in southwest Montreal, Canada (Iyer, Jordan, MacDonald, Joober, & Malla, 2015). There are no competing public or private early intervention services in the same catchment; all individuals identified as needing treatment for an early phase psychosis are referred to PEPP, thus forming a near treated incidence sample (Edwards, Rodrigues, & Anderson, 2019). Following intake to the service, PEPP provides a comprehensive standardized assessment battery with longitudinal follow-up for two years of treatment. Written informed consent was obtained from all patients in order to participate in an evaluation and care protocol and as part of various longitudinal FEP outcomes studies, approved by the Institutional Review Board for Human Subjects Research of the Douglas Hospital Research Centre. For those under the age of 18, consent was obtained from parents or guardians.

3.3.2 Study population

Inclusion criteria for participation in PEPP are: age 14 to 35 at the time of referral, diagnosis of an affective or non-affective psychotic illness with the Structured Clinical Interview for DSM-IV, and fluency in either English or French. Patients, both inpatient and outpatient, accepted to PEPP may have received antipsychotic medications for no more than 30 days prior to

referral. For the present sample, the average number of days on antipsychotic medication prior to date of entry was 2.6 days, with the mode being 0 days. Exclusion criteria were IQ < 70, psychotic illness solely related to substance intoxication or withdrawal, or an organic mental disorder. Only data collected at baseline were used for the current analyses.

3.3.3 Instruments and assessments

Initial assessment interviews took place within one month of first intake to the PEPP clinical service. Demographic variables collected included assessments for sex (male/female), age of entry, relationship status (in partnership – yes/no), and education level (completed high school yes/no), and visible minority status. Visible minority status was self-reported as one of six options (Maraj et al., 2018); Table 1), that for further analysis was collapsed to create a binary variable for visible minority status (yes/no). Age of onset and duration of untreated psychosis (DUP) were obtained through the Circumstances of Onset and Relapse Schedule (CORS) (Norman, Malla, Verdi, Hassall, & Fazekas, 2004); DUP was defined as the number of weeks between the onset of threshold-level psychosis and the initiation of antipsychotic medication. The Structured Clinical Interview for DSM disorders (SCID IV) was used to classify each patient's diagnosis as either non-affective (schizophrenia, schizoaffective, delusional disorder, schizophreniform, brief psychotic disorder, or psychosis not otherwise specified [NOS]) or affective psychosis (bipolar II, bipolar I-manic/depressed/mixed, bipolar-NOS, or major depressive disorder) and to determine if the individual had a comorbid substance abuse or dependence disorder (First, 2002). Antipsychotic medication use (number of days) prior to date of entry was acquired during the interview and corroborated with available prescription information in clinical files (Cassidy, Rabinovitch, Schmitz, Joober, & Malla, 2010).

Delusional content was systematically measured using the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984b). The scale measures severity of the following twelve delusion themes: persecutory, jealousy, sin or guilt, grandiose, religious, somatic, reference, being controlled, mind reading, thought broadcasting, thought insertion and thought withdrawal. The severity of each delusion theme is rated on a scale from 0 to 5, as is a global measure of severity. Severity reflects certain aspects of delusional symptoms such as: frequency, complexity, conviction, preoccupation, and interference with functioning.

The SAPS was further used to measure the global rating of positive psychiatric symptoms and separate ratings were compiled for hallucinations, bizarre behaviors, and positive formal thought disorder. The Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1984a) was used to determine the global severity of negative psychiatric symptoms along with separate ratings for affective flattening, alogia, avolition/apathy, and anhedonia/asociality. Attention was excluded as it reflects cognition (Vadhan, Serper, Harvey, Chou, & Cancro, 2001), and this exclusion has been shown to improve reliability of the SANS (Peralta, de Leon, & Cuesta, 1992). Furthermore, the 'inappropriate affect' item was removed as it has been shown to poorly correlate with the overall subscale score (Andreasen, 1982). Depression was measured using the total score from the Calgary Depression Scale (CDS) for schizophrenia (Addington, Addington, & Maticka-Tyndale, 1993). Anxiety was measured using the total score from the Hamilton Anxiety Rating Scale (HAS-A) (Riskind, Beck, Brown, & Steer, 1987).

All diagnostic and symptom data were collected by rigorously trained research assistants with at least an undergraduate degree in psychology or a related health science field. The SAPS training, occurring full-time over a 4-6 week period, included orientation, rating videotapes, role-playing, observing experienced staff leading interviews, and conducting interviews under

supervision. Yearly inter-rater reliability sessions are held to calculate intraclass correlations (ICC), and serve as continuing education for staff. ICCs for the SAPS have consistently been high over the 15 years of data collection (0.73 – 0.80), indicating good to excellent reliability (Cicchetti, 1994).

3.3.4 Statistical analyses

Data from 686 consenting patients entering the program between January 2003 and March 2018 were available for analysis. Those with no SAPS or SANS data collected (n = 11; see Supplementary Table 1 for reasons), over the age of 35 (n = 1), with a purely substance-induced psychosis (n = 9), or an IQ < 70 (n = 3) were excluded from further analyses. Those on medication for more than 30 days prior to the referral date were not included (n = 26) in order to reduce the potentially confounding effects of prolonged medication exposure on delusional context and severity; nonetheless, a post-hoc analysis revealed that there were no significant differences in global delusion severity between those who had taken medication for more than 30 days and those below this cut-off (Supplementary Table 2). Our final sample therefore includes 636 patients.

All statistical testing was performed using SPSS Statistics 24 (Corp., Released 2016). Patient characteristics, both sociodemographic and clinical, were summarized using appropriate descriptive analyses. To further ensure that our final sample was representative of the total population, we identified demographic variables for which greater than 10% of information was missing and examined global delusional severity between subgroups with and without that variable present.

Descriptive statistics were also used to report delusion severity and frequency (globally and per theme) and the co-occurrence of themes. To assess frequencies, we utilized the same

threshold for non-remission (SAPS global scores ≥ 3) recommended by the Working Group on Remission in Schizophrenia (WGRS) (Andreasen et al., 2005). For the most common delusion themes (those with ≥ 100 patients with SAPS global scores ≥ 3), Mann Whitney U-tests and Spearman rank-order correlations were used to describe patterns between delusion severity (both globally and per theme), and demographic and clinical variables (Supplementary Table 4). A Poisson regression was used to analyze the relationship between global delusion severity and the number of delusion themes endorsed; and, to determine if DUP (log transformed) predicts the number of delusion themes present (exponentiated coefficients presented). We further utilized a Spearman rank-order correlation test to demonstrate the relationship between LogDUP and global delusion severity. Where appropriate, confidence intervals were calculated to better represent uncertainty in the results. All analyses were interpreted using the appropriate Bonferroni corrected alpha levels.

3.4 Results

3.4.1 Sample characteristics

Sociodemographic characteristics, as well as diagnosis, comorbid substance abuse and dependence, and antipsychotic medication use (days prior to date of entry) are summarized in Table 1. Of the 636 patients, 191 were female and 444 were male. The average age was 23.8±4.75 years (range 14 to 35). Sixty five percent were diagnosed with a non-affective psychosis (N= 412) and 27% with an affective psychosis (N = 172). Forty five percent (N= 286) of patients had a comorbid substance abuse or dependence diagnosis. We found no significant differences in global rating of delusion severity where missing data were greater than 10% (Supplementary Table 3).

Table 1. Sociodemographic and Clinical Characteristics

Sociodemographic Variable	***n (%)***
Sex	
Female	191 (30.0%)
Male	444 (69.8%)
Missing	1 (0.2%)
Age of entry	
Mean [SD)]	23.8 [4.75]
Range	14-35
Relationship status	
In partnership	66 (10.4%)
No partnership	562 (88.4%)
Missing	8 (1.3%)
Education level	
Completed HS	405 (63.7%)
Did not complete HS	194 (30.5%)
Missing	37 (5.9%)
Visible Minority Status	
White	374 (58.8%)
Black	83 (13.1%)
Asian	49 (7.7%)
Aboriginal	2 (0.3%)
Other	87 (13.7%)
Missing	41 (6.4%)

Clinical Variables	***n (%)***
Diagnosis	
Affective Psychosis	172 (27.0%)
Non-Affective Psychosis	412 (64.8%)
Missing	52 (8.2%)
Comorbid Substance Abuse or Dependence	
Yes	286 (45.0%)
No	259 (40.7%)
Missing	91 (14.3%)
Days on Continuous Antipsychotic Medication prior to Referral	
Mean (SD)	2.6 (5.18)
Mode	0
Missing	116 (18.2%)

3.4.2 Delusional content

Using a SAPS global score ≥ 3 cut-off representing moderate to severe delusions, 598 patients (94.0%) experienced at least one type of delusion. The most commons themes in order were persecutory, reference, and grandiose; the least common were thought broadcasting, thought withdrawal, and jealousy (Table 2a and Figure 1). Delusional themes rarely occurred in isolation, with only 11.9% of patients presenting with one theme (Table 2b and Supplementary Figure 1).

Table 2a. Descriptive Statistics of SAPS Delusion Items

SAPS Item Delusion	*mean* *SAPS severity rating 0-5*	*95% CI for mean*	*n (%)* *SAPS severity rating ≥ 3*	*95% CI for percentage*
Global Rating	4.05	3.98 - 4.12	598 (94.0%)	91.0 - 95.7%
Persecutory	3.44	3.33 - 3.55	494 (77.7%)	74.2 - 80.9%
Reference	2.86	2.73 - 2.99	413 (64.9%)	61.1 - 68.7%
Grandiose	1.83	1.69 - 1.97	256 (40.3%)	35.4 - 44.2%
Religious	1.27	1.14 - 1.40	177 (27.8%)	24.4 - 31.5%
Mind Reading	1.09	0.98 - 1.21	150 (23.6%)	20.3 - 27.1%
Being Controlled	1.01	0.89 - 1.13	125 (19.7%)	16.6 - 23.0%
Somatic	0.92	0.80 - 1.04	107 (16.8%)	14.0 - 20.0%
Guilt or Sin	0.88	0.78 - 0.98	89 (14.0%)	11.4 - 16.9%
Thought Insertion	0.67	0.57 - 0.77	88 (13.8%)	11.3 - 16.8%
Thought Broadcasting	0.56	0.47 - 0.65	72 (11.3%)	9.0 - 14.0%
Thought Withdrawal	0.33	0.26 - 0.40	38 (6.0%)	4.3 - 8.1%
Jealousy	0.23	0.17 - 0.29	21 (3.3%)	2.1 - 5.0%

Table 2b. Descriptive Statistics for Multiple Delusion Themes

Number of delusion themes	*n (%)* SAPS rating ≥ 3	*95% CI for percentage*
0 delusions	37 (5.8%)	4.1 - 7.9%
1	76 (11.9%)	9.5 - 14.7%
2	141 (22.2%)	19.0 - 25.6%
3	137 (21.5%)	18.4 - 24.9%
4	98 (15.4%)	12.7 - 18.5%
5	54 (8.5%)	6.4 - 10.9%
6	48 (7.5%)	5.6 - 9.9%
7	16 (2.5%)	1.4 - 4.1%
8	6 (0.9%)	0.3 - 2.0%
9	7 (1.1%)	0.4 - 2.3%
10	4 (0.6%)	0.2 - 1.6%
11	2 (0.3%)	0.0 - 1.1%
Missing	10 (1.6%)	

3.4.3 Delusion severity

Globally, delusions tended to present at the more severe end of the spectrum, with an overall score that was "marked" ($M = 4.05$, $SD = 0.96$; Supplementary Figure 2). Per theme, however, there were noticeable differences in the distribution of severity (see Supplementary Figure 3). While persecutory and referential delusions were left-skewed, most other themes presented as right-skewed distributions.

3.4.4 Delusions and sociodemographic variables

Older age of onset of a FEP was associated with more severe global ($r_s = 0.15$, 95% CI 0.06 - 0.22) and persecutory delusions ($r_s = 0.12$, 95% CI 0.03 - 0.20), but not delusions of reference, grandiosity, religiosity, mind reading, being controlled and somatic. Visible minority status and sex were not significant predictors of global or thematic delusion severity (Supplementary Table 4).

3.4.5 Delusions and clinical variables

Analyses of global or thematic delusional severity with respect to affective versus non-affective psychosis, or presence/absence of substance abuse or dependence, revealed no differences (Supplementary Table 4); similarly, the severity of all delusion themes, including persecutory, remained consistent across non-affective and affective psychoses.

The global rating for delusion severity was positively associated with anxiety but not with depression. Anxiety was positively associated with persecutory, referential, control, and somatic delusions but not with grandiose, religious or mind reading delusions. While there was no association between depression and global delusion severity, depression was positively associated with the severity of referential, mind reading, control, and somatic delusions.

Grandiose delusions were negatively associated with depression, whereas persecutory and religious delusions had no associations with depression. See Table 3.

Mind reading delusions and delusions of control were positively correlated with hallucinations. Somatic delusions were the only other delusional theme associated with hallucinations.

For every one unit increase in global delusion severity on the SAPS, the number of delusional themes present increased by 1.47 (95% CI 1.32 – 1.56, $p < .001$). However, LogDUP was not associated with the global rating of delusion severity at baseline ($r_s = 0.04$, 95% CI -0.05 - 0.12, $p > .05$) nor to the number of delusion themes present ($B = 0.97$, 95% CI 0.91 – 1.03, p > 5).

Table 3. Correlations between Delusion Severity and Symptomatology

Symptoms	Global Rating			Persecutory			Reference			Grandiose		
	rho	*95% CI*	*sig.*	*rho*	*95% CI*	*sig.*	*rho*	*95% CI*	*sig.*	*rho*	*95% CI*	*sig.*
Anxiety	0.21*	0.12 - 0.29	.000	0.25*	0.17 - 0.33	.000	0.25	0.17 - 0.33	.000	-0.03	-0.11 - 0.06	.564
Depression	0.06	-0.02 - 0.13	.173	0.09	0.01 - 0.17	.026	0.12	0.05 - 0.20	.002	-0.17*	-0.25 - -0.09	.000
Hallucinations	0.10	0.02 - 0.17	.017	0.06	-0.02 - 0.14	.125	0.09	0.01 - 0.17	.020	0.00	-0.08 - 0.08	.985
Bizarre Behavior	0.11*	0.04 - 0.19	.004	0.08	0.00 - 0.15	.051	0.04	-0.04 - 0.11	.366	0.25*	0.18 - 0.33	.000
Positive Formal Thought Disorder	0.09	0.01 - 0.17	.021	-0.06	-0.14 - 0.02	.125	0.09	0.01 - 0.16	.031	0.33*	0.26 - 0.40	.000
SANS	-0.04	-0.12 - 0.04	.313	0.05	-0.03 - 0.13	.220	-0.02	-0.09 - 0.06	.702	-0.19*	-0.27 - -0.12	.000
Affective Flattening	-0.07	-0.14 - 0.01	.096	0.02	-0.06 - 0.09	.696	0.00	-0.08 - 0.08	.968	-0.14*	-0.21 - -0.06	.000
Alogia	-0.11	-0.18 - -0.03	.007	-0.06	-0.14 - 0.01	.105	-0.05	-0.12 - 0.03	.256	-0.10	-0.17 - -0.02	.016
Avolition–Apathy	0.12*	0.05 - 0.20	.002	0.11	0.03 - 0.18	.007	-0.04	-0.12 - 0.04	.286	-0.05	-0.13 - 0.03	.214
Anhedonia–Asociality	0.10	0.02 - 0.18	.010	0.16*	0.08 - 0.24	.000	0.04	-0.04 - 0.12	.344	-0.12*	-0.20 - -0.05	.002

	Religious			Mind Reading			Being Controlled			Somatic		
	rho	*95% CI*	*sig.*	*rho*	*95% CI*	*sig.*	*rho*	*95% CI*	*sig.*	*rho*	*95% CI*	*sig.*
Anxiety	0.00	-0.09 - 0.08	.954	0.10	0.01 - 0.18	.030	0.21*	0.12 - 0.29	.000	0.22*	0.13 - 0.30	.000
Depression	-0.05	-0.13 - 0.03	.186	0.15*	0.07 - 0.23	.000	0.13*	0.05 - 0.21	.001	0.12*	0.04 - 0.20	.003
Hallucinations	0.09	0.01 - 0.17	.022	0.24*	0.17 - 0.32	.000	0.25*	0.17 - 0.32	.000	0.17*	0.09 - 0.24	.000
Bizarre Behavior	0.20*	0.13 - 0.28	.000	0.10	0.02 - 0.17	.015	0.17*	0.09 - 0.25	.000	0.12*	0.04 - 0.20	.002
Positive Formal Thought Disorder	0.22*	0.15 - 0.30	.000	0.04	-0.04 - 0.12	.319	0.03	-0.05 - 0.11	.435	0.09	0.01 - 0.16	.033
SANS	-0.03	-0.11 - 0.05	.435	0.11	0.03 - 0.18	.009	0.09	0.01 - 0.17	.028	0.15*	0.07 - 0.23	.000
Affective flattening	-0.04	-0.12 - 0.04	.287	0.03	-0.05 - 0.10	.497	0.03	-0.05 - 0.10	.516	0.11	0.03 - 0.19	.006
Alogia	0.01	-0.07 - 0.09	.837	0.04	-0.04 - 0.12	.343	0.07	0.00 - 0.15	.065	0.10	0.02 - 0.17	.015
Avolition–Apathy	0.03	-0.05 - 0.10	.520	0.04	-0.04 - 0.11	.371	0.02	-0.05 - 0.10	.541	0.08	0.00 - 0.16	.042
Anhedonia–Asociality	-0.06	-0.14 - 0.02	.143	0.10	0.02 - 0.18	.011	0.03	-0.05 - 0.11	.466	0.13*	0.05 - 0.21	.001

Note. The SANS total score was calculated minus attention and inappropriate affect. *p < .006 (Bonferroni corrected)

3.5 Discussion

In this inventory of systematically collected delusional content and severity in a catchment-based and medication-naïve sample of FEP patients entering early intervention services, the vast majority of individuals presented with delusions of moderate severity, and 80.7% had at least two delusions. As hypothesized, persecutory delusions were the most common delusion theme: these remained consistent in severity across affective and nonaffective diagnoses, and tended to be more severe with older age of onset. Global delusion severity was associated with anxiety but not with depression, with specific relationships emerging per theme. Finally, we found that certain delusional themes that are commonly considered as passivity experiences and/or thought alienation were correlated with hallucinatory experiences.

Our results confirm that persecutory delusions are indeed the most common delusion theme in this near-treated incidence sample of FEP patients (Ellersgaard et al., 2014; Paolini et al., 2016; Rajapakse et al., 2011). Unlike the selective samples, potential confounding due to treatment effects, and/or varying levels of chronicity seen in previous reports (Ellersgaard et al., 2014; Gutierrez-Lobos et al., 2001; Kimhy et al., 2005; Paolini et al., 2016; Rajapakse et al., 2011), this early-stage catchment-based clinical population offers a unique context for the examination of delusions. It has been hypothesized that persecutory delusions are a maladaptive defense mechanism in response to chronic environmental stress (Paolini et al., 2016). Corlett et al. suggested that paranoia and persecutory ideation arise from aberrant prediction errors that create waves of fear and hypervigilance (Corlett et al., 2010), while Gold and Gold explain paranoia in a social-evolutionary framework that accounts for the high prevalence of socially salient themes (Gold & Gold, 2014). It may be that persecutory beliefs emerge in an atmosphere

of tension, uncertainty and uneasiness that often accompanies the prodromal period of FEP (Jaspers, 1997; Upthegrove et al., 2018) and the potential fear and/or stigma associated with this.

As expected, persecutory delusions remained consistent in severity across affective and non-affective diagnoses. Picardi et al. similarly found that persecutory and somatic delusions were evenly distributed across diagnoses (Picardi et al., 2018). However, their consideration for the polarity of mood within affective psychoses may explain their finding that grandiose delusions varied over diagnostic categories. Similar patterns in delusional themes across diagnoses demonstrate the utility of examining their development and maintenance as transdiagnostic phenomena with common underlying cognitive mechanisms (Picardi et al., 2018). Combining this with phenomenological and qualitative analyses that incorporate a more in-depth assessment of delusional content may also be important.

Previous studies have reported that persecutory delusions are more common and severe in older patients (Hafner et al., 1993), even when investigating early psychosis samples with younger age ranges (Paolini et al., 2016); our analyses raise the possibility that this association may be unique to persecutory delusions. Current theories suggest that such delusions are the product of a hyper-inferential state, involving the ability to surmise the intentions of others, a process that is not completely developed by early adolescence (Galdos & van Os, 1995; Paolini et al., 2016). At a neurobiological level, paranoia is postulated to be associated with prediction error dysfunction in certain brain regions, which then plays a role in an individual's ability to infer the intensions of others (Corlett et al., 2010). Consistent with our findings, Hafner et al. showed that adolescents tend to present with undifferentiated delusions, compared with systematized persecutory delusions in later life (Hafner et al., 1993).

Neurobiological and cognitive models have also suggested that delusional beliefs are continually reconsolidated and strengthened due to aberrations of synaptic plasticity (Corlett, Krystal, Taylor, & Fletcher, 2009; Corlett et al., 2010). It is plausible that these extended prediction errors in turn influence the development of more systematized delusions. Thus, a prognostic factor such as the duration of untreated psychosis might impact the initial development and severity of delusional themes. However, in our study DUP was not related to the global severity of baseline delusions nor to the number of delusion themes present in FEP. Future work may wish to consider a different proxy for the complexity and systematization of the delusional system, including perhaps incorporating an analysis of the longitudinal course of delusions in early psychosis.

A systematic review previously highlighted that anxiety and depression were related to the severity, distress, and content of overall psychotic symptoms (Hartley et al., 2013). However, the majority of research has focused on global ratings for delusions and/or solely on persecutory delusions. While our representative sample and findings further strengthen the notion that anxiety and persecutory delusions are related, this association was not present for themes of grandiose, religious, and mind reading. Within the context of depression, there are mixed findings regarding the association with persecutory delusions (Hartley et al., 2013; Paolini et al., 2016) which may reflect different approaches to assessing symptoms (both persecutory delusions and negative affect). For example, previous studies have included measures for anxiety in composite scores for depression (Bentall et al., 2009; Drake et al., 2004); or examined specific content within the overarching persecutory theme (Chadwick, Trower, Juusti-Butler, & Maguire, 2005; Green et al., 2006). In addition, while the Calgary Depression Scale distinguishes depressive and negative symptoms, previous studies measured depression through self-report

questionnaires (Bentall et al., 2009; Chadwick et al., 2005; Green et al., 2006). Our sample also included affective psychoses whereas the CDS was designed for schizophrenia and non-affective psychoses, perhaps influencing our findings. While we did not find an association with persecutory delusions, depression was related to other themes (Table 4). Future work may wish to investigate the onset and course of these clinical states over time in order to better understand their role in the early development of delusions and to study whether interventions targeting negative affect can mediate delusional severity (Sandra M. Opoka, 2018).

As expected, the severity of mind reading delusions and delusions of control were positively correlated with hallucinations. Passivity experiences, characterized by the belief that one's thoughts or actions are influenced or controlled by an external agent, have traditionally been viewed as delusions. However, unlike other delusional themes these experiences may be more consistent with perceptual disturbances (Kelly, 2019). Others have also pointed to a potential source-monitoring bias in which hallucinations and delusions of influence share certain cognitive mechanisms (Paolini et al., 2016).

3.5.1 Strength, Limitations & Future Directions

Major strengths of this study are the unique data collected from a large, catchment-based sample with no competing public or private services, meaning that it is a reasonably representative near-treated incidence sample of all individuals aged 14-35 identified as having a FEP in a defined geographic catchment. Furthermore, due to our cut-off of 30 days for medication use, the results are relatively uninfluenced by confounding factors such as long-term treatment effects or chronicity of illness.

Limitations include the fact that while data were collected as systematically as possible, 20% of patients receiving care did not provide consent to their data being used for research purposes

and were therefore excluded from this analysis (n = 181). Unlike those with missing data, this lack of consent means that we could not examine differences between this group and those included in the study. Symptom assessments also reflect the most acute state of symptoms within the last three months, with corresponding potential for recall bias. Twenty-one percent of baseline assessments were reconstructed at a later date using detailed chart notes. Finally, this study is based on data collected prospectively over a 15-year period, opening up the possibly of inconsistencies in data collection due to multiple raters. However, PEPP-Montreal minimizes these limitations by using standardized assessments, rigorously training research staff, and periodically establishing inter-rater reliability.

Future work may wish to investigate the course of delusions over time, including focusing on specific themes and/or their overlaps. Few have examined how early life factors such as socioenvironmental context relates to the content and severity of delusions at initial presentation for FEP. This also involves integrating smaller samples with in-depth, phenomenologically oriented interviews. Investigating associations between delusional content and sociocultural variables in FEP might prove important for identifying groups that are particularly at-risk and could therefore benefit from improved prevention and early intervention efforts.

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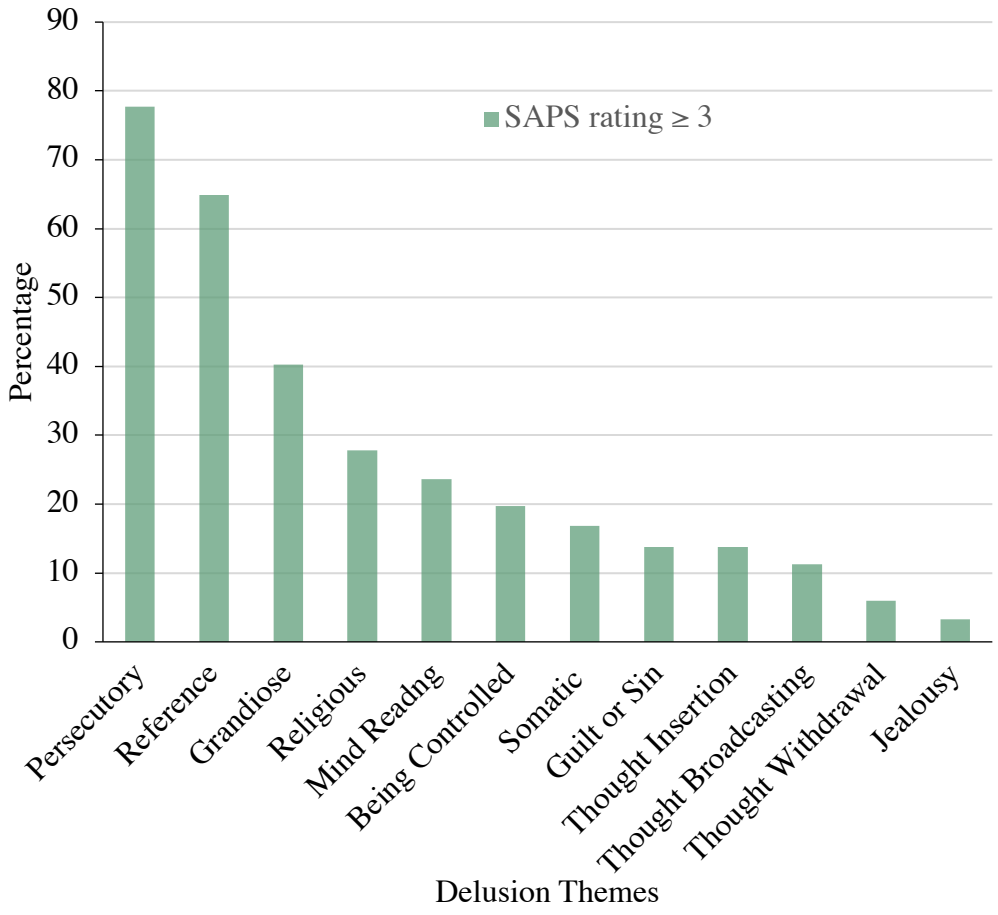
3.7 Figures



F1. Percentage of FEP service users with a specific delusion theme.

3.8 Supplementary material

Supplementary Table 1. Reason for Non-Collection of Baseline Data (N = 11)

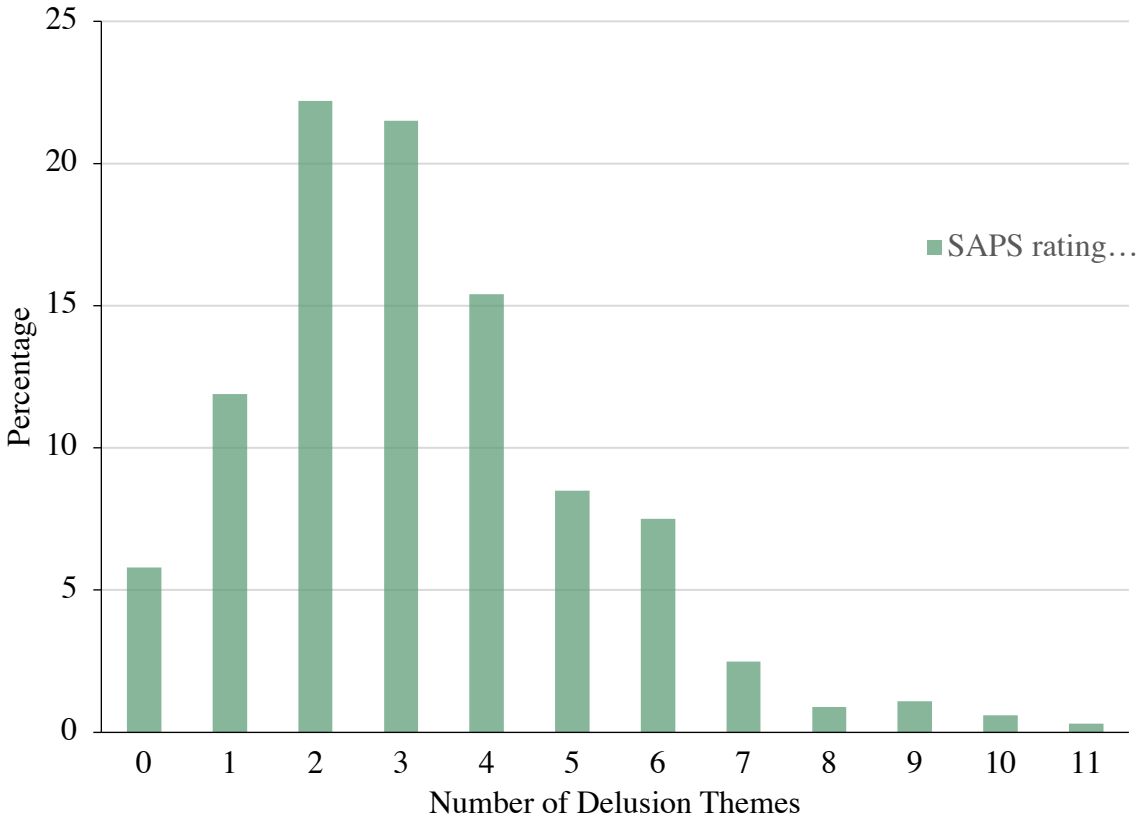
Reason	n (%)
Early drop out	2 (14.3%)
Substance induced psychosis	1 (7.1%)
Previous treatment	5 (35.7%)
Second episode	2 (14.3%)
Unknown	1 (7.1%)

Supplementary Table 2. Comparison of Global Delusion Severity in those Exposed to Antipsychotic Medication for More or Less than 30 Days

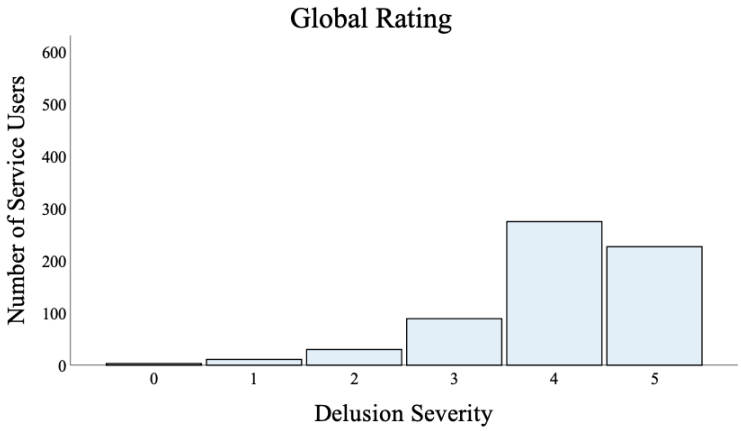
Included: Medication for less than 30 days *Mean (SD)*	Excluded: Medication for more than 30 days *Mean (SD)*	*t-test*	*p-value*
4.05 (0.96)	3.92 (1.13)	-.659	> .05

Supplementary Table 3. Analysis of Variables with Missing Data >10%

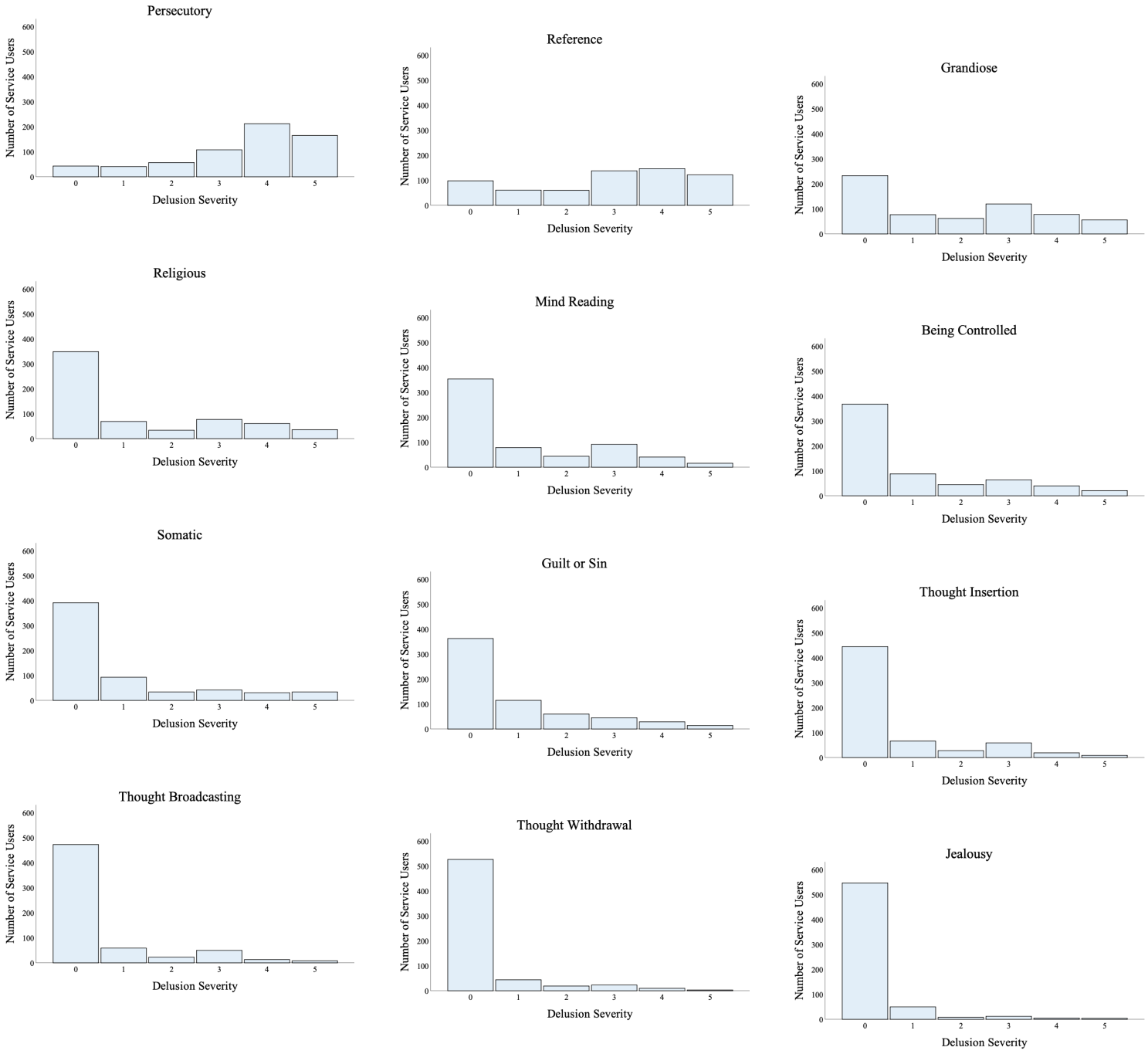
	Global rating of delusion severity			
Sociodemographic or Clinical Variable	Valid *Mean (SD)*	Missing *Mean (SD)*	*t-tests*	*p-value*
Substance Abuse or Dependence	4.05 (0.95)	4.05 (1.04)	.032	> .05
Medication Use	4.05 (0.96)	4.08 (0.94)	.319	> .05



Supplementary F1. Percentage of FEP service users with multiple delusion themes.



Supplementary F2. Distribution of global delusion severity.



Supplementary F3.
Distribution of delusion severity per theme.

Supplementary Table 4. Associations between Delusion Severity & Demographic/Clinical Variables

Demographic/ Clinical Variables	Global Rating		Persecutory		Reference		Grandiose	
	Median	*Mann-Whitney U test*	*Median*	*Mann-Whitney U test*	*Median*	*Mann-Whitney U test*	*Median*	*Mann-Whitney U test*
Sex								
Female	4	41,032	4	41,550	3	40,635	1	37,831
Male	4	p = .560	4	p = .678	3	p = .396	2	p = .026
Visible Minority Status								
	4	38,451	4	39.832	4	40,277	0	39,259
Yes	4	p = .154	4	p = .445	3	p = .597	0	p = .292
No								
Diagnoses								
Affective	4	35,229	4	31,363	3	35,262	2	30,551
Non-Affective	4	p = .946	4	p = .024	3	p = .926	1	p = .007
Substance Abuse or Dependence								
Yes	4	32,449	4	32,895	3	31,668*	2	33,854
No	4	p = .009	4	p = .020	3	p = .003	1	p = .074

	Religious		Mind Reading		Being Controlled		Somatic	
	Median	*Mann-Whitney U test*	*Median*	*Mann-Whitney U test*	*Median*	*Mann-Whitney U test*	*Median*	*Mann-Whitney U test*
Sex								
Female	0	40,258	0	41,265	0	37,027	0	39,104
Male	0	p = .266	0	p = .552	0	p = .019	0	p = .102
Visible Minority Status								
Yes	0	40,430	0	40,949	0	39,237	0	40,532
No	0	p = .626	0	p = .836	0	p = .528	0	p = .695
Diagnoses								
Affective	1	32,188	0	32,055	0	32,939	0	35,075
Non-Affective	0	p = .056	0	p = .045	0	p = .286	0	p = .968
Substance Abuse or Dependence								
Yes	0	37,027	0	32,123*	0	36,219	0	35,033
No	0	p = .995	0	p = .003	0	p = .941	0	p = .274

* $p < .006$ (Bonferroni correction)

CHAPTER 4. Second Manuscript

Title: A Cross-Cultural Examination of Delusions in Early Psychosis

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4.1 Abstract

Introduction: While neurobiological and cognitive accounts have focused on the core consistencies of delusional beliefs, studies have also shown variations across different cultures. Previous work has been carried out across a range of treatment settings and illness stages, resulting in potential confounds. To address these concerns and to examine how culture interacts with illness, this study investigates the baseline presentation and longitudinal trajectory of delusions in first episode psychosis (FEP) across two similar protocol treatment settings in Montréal (Canada) and Chennai (India).

Methods: Data were systematically collected from a sample of patients entering an early intervention program for FEP in Chennai (N = 168) and Montréal (N = 165) with longitudinal follow-up for two years of treatment. Delusions were measured using the Scale for Assessment of Positive Symptoms. Chi-square analyses and regressions were conducted.

Results: At baseline, moderate to severe delusions were more frequent in Montréal than in Chennai (93% versus 80%, respectively; X^2= 12.36 p = .000). Some site differences in the presentation of specific delusional themes emerged; however, the rank-order of delusional themes was similar across sites. Generalized estimating equations revealed a meaningful longitudinal effect of site, whereby clinical-level delusions presented more frequently at yearly follow-ups in Chennai than in Montreal. Finally, this trajectory appears to be unique to delusions in early psychosis when compared to other positive symptom domains.

Conclusion: To our knowledge, this is the first direct comparison of delusional beliefs in similar programs for FEP across two different cultural, health system and economic environments. Delusions varied at initial presentation, and in their trajectories across sites. Future work may wish to consider the substantial overlap in delusion themes seen across cultures.

4.2 Introduction

Contemporary evidence has challenged the Kraepelinian view that outcomes in schizophrenia are unvaryingly bleak (Hopper, Harrison, Janca, & Sartorius, 2007; Kraepelin, 1919; Strauss & Carpenter, 1972), with early intervention paradigms demonstrating improvement across a range of salient outcomes (Correll et al., 2018; Srihari, Shah, & Keshavan, 2012). Similarly arguing against the notion that psychotic illnesses are inevitably progressive are findings that patients in lower and middle-income countries (LMICs) have improved outcomes compared to higher-income countries (HICs) (Harrison et al., 2001; Hopper & Wanderling, 2000; Jablensky et al., 1992; Lin & Kleinman, 1988). Although not without their flaws (Lin & Kleinman, 1988), these reports – supporting the notion that outcomes such as symptomatology, disability and social functioning are favourable in LMICs – appear to hold true in India, a LMIC with a large and diverse population (Hopper et al., 2007).

As of yet, though, direct comparisons of outcomes between LMICs and HICs are uncommon, especially those in which treatment protocols and measures are similar (Cohen, Patel, Thara, & Gureje, 2008). At the onset of illness, Malla and colleagues recently compared the clinical course of patients in similar early intervention services in India and Canada, finding that negative symptoms indeed appear to be improved in India compared to Canada and that family support was an important component of recovery at both sites. Although baseline positive symptoms were found to be more severe in Canada, the longitudinal course of overall/global positive symptoms was similar across site (Malla, Iyer, Rangaswamy, Ramachandran, et al., 2020).

However, specific symptom domains remain to be further investigated. One intriguing symptom is that of delusions – strange and distressing beliefs. In the context of cross-cultural analyses, delusions are intriguing because they are positive psychotic symptoms that have been

shown to vary in thematic content and frequency across cultures (Gecici et al., 2016; Kim et al., 2001). This knowledge is consistent with the notion that delusions are one form of beliefs, which are themselves cultural representations that shape our shared understanding of reality (Tomasello, 2018). However, few have investigated the complex factors behind culture that may impact not only the initial presentation of these delusional beliefs but also their course. For example, family values impact the quantity and quality of social interactions across cultures; in turn, a diminution of social interactions has been suggested as a key contributor to the formation and maintenance of delusional beliefs (Bentall, 2018).

Together, this underscores the importance of examining the earliest clinical presentations of delusions in order to better understand the etiology and subsequent course of these symptoms. Previous cross-cultural work on delusions has reported from varying treatment settings, with a wide range of illness chronicity (Kim et al., 2001; Tateyama, Asai, Hashimoto, Bartels, & Kasper, 1998). Importantly, however, delusions in early intervention settings are less likely to be confounded by the effects of long-term illness or previous interventions. The vast majority of individuals experiencing onset of a psychosis present with delusions, and research has demonstrated that anxiety and age of onset are important predictors of how delusions present in early intervention services (Lemonde et al., 2020).

To our knowledge, there exists virtually no research on how social and cultural factors relate to delusions in first episode psychosis (FEP) specifically; and there are no cross-cultural studies of delusional content in early psychosis. As a result, the aim of this study was to investigate the baseline presentation and longitudinal trajectory of delusions in FEP across two sites with similar (coordinated) treatment settings in Montréal (Canada) and Chennai (India) (Iyer, Mangala, Thara, & Malla, 2010). The resulting dataset offers a rare opportunity to directly examine

delusional content during a formative stage of illness across cultures. Based on prior work investigating outcomes across HICs and LIMCs in early intervention, we hypothesized 1) that at baseline, clinical-level (moderate to severe) delusions would present more frequently in Montreal than in Chennai; 2) that longitudinally, clinical-level delusions would present similarly across sites; and 3) we explored whether the differential trajectory of delusions across contexts was unique, or mirrored by the trajectories of other positive symptoms (hallucinations, bizarre behavior, and positive formal thought disorder).

4.3 Methods

4.3.1 Setting

This longitudinal study was conducted as part of a two-year prospective outcomes study between 2012 and 2018 in Montréal, Canada and Chennai, India. In Montreal, the Prevention and Early Intervention Program for Psychosis (PEPP-Montréal, Canada) (Iyer, Jordan, MacDonald, Joober, & Malla, 2015) is situated at the Douglas Mental Health University Institute, serving a geographically defined catchment area (total population 350,000). In Chennai, the early intervention service is part of the Schizophrenia Research Foundation (SCARF, Chennai, India) (Iyer et al., 2010), a non-governmental organization and a World Health Organization coordinating center which accepts patients across Chennai. During the study, both PEPP and SCARF centers followed identical protocols for treatment of FEP (i.e. open referral systems, intensive case management, second-generation antipsychotic medications in lowest effective dose, family psycho-education, other psychosocial interventions when indicated, and an overall recovery orientation) (Iyer et al., 2010; Malla, Iyer, Rangaswamy, Ramachandran, et al., 2020). All procedures in this study complied with the ethical standards of the relevant national and institutional committees on human experimentation and the Helsinki

Declaration of 1975, as revised in 2008, were approved by the Institutional Review Board (SCARF) or the Research Ethics Board (McGill University).

4.3.2 Study population

Inclusion criteria for study participants across sites were: age 16 to 35 years; diagnosis of either schizophrenia-spectrum psychotic disorder or affective psychosis using the Structured Clinical Interview for DSM-IV (First, 2002); having received antipsychotic medication for no more than 30 days prior to entry in program; ability to communicate fluently in Tamil or English in Chennai and French or English in Montréal. Exclusion criteria were: IQ < 70; psychosis secondary to an organic mental disorder; or primary diagnosis of substance dependence.

4.3.3 Instruments and assessments

Sociodemographic variables collected included assessments for gender, age at entry, relationship status (in relationship vs single), education level (completed high school yes/no), and living situation (alone; with family; with friends/roommates; residence, group home, or homeless).

Clinical variables that have previously been shown to associate with or predict delusions globally and/or per theme were also recorded, including age of onset, diagnosis, duration of untreated psychosis (DUP), distress (anxiety and depression), substance abuse or dependence, hallucinations, bizarre behavior and positive formal thought disorder. Data on age of onset for psychosis and DUP were obtained via the Circumstances of Onset and Relapse Schedule (CORS) (Malla et al., 2006). DUP was defined as the number of weeks between the onset of threshold-level psychosis lasting for at least 7 days and the initiation of antipsychotic medication. The Structured Clinical Interview for DSM disorders (SCID-IV) was used to classify each patient's diagnosis as either non-affective (schizophrenia, schizoaffective, delusional disorder,

schizophreniform, brief psychotic disorder, or psychosis not otherwise specified [NOS]) or affective psychosis (bipolar II, bipolar I-manic/depressed/mixed, bipolar-NOS, or major depressive disorder with psychosis), and to determine if the individual had a comorbid substance abuse or dependence disorder (First, 2002).

Delusions were systematically assessed using the Scale for the Assessment of Positive Symptoms (SAPS) at baseline, and at months 12 and 24 (Andreasen, 1984). The scale measures global delusion severity and severity of the following twelve delusion themes (rated on a scale from 0 to 5): persecutory, jealousy, sin or guilt, grandiose, religious, somatic, reference, being controlled, mind reading, thought broadcasting, thought insertion and thought withdrawal. The SAPS was further used to measure the global rating for hallucinations, bizarre behavior, and thought disorder, also scored from 0 to 5. Anxiety was measured using the total score from the Hamilton Anxiety Rating Scale (HAS-A) (Riskind, Beck, Brown, & Steer, 1987). Depression was indexed using the total score from the Calgary Depression Scale (CDS) for schizophrenia (Addington, Addington, & Maticka-Tyndale, 1993).

Antipsychotic medication dose at baseline was included as a putative early predictor for the longitudinal course of delusions. In nearly all cases, a daily dose of second-generation antipsychotic medication is prescribed upon entry into the programs (CPZ equivalents computed for analyses). Measured at month 3, family support was included as a measure of support that may predict the course of delusions. An overall score for family support was calculated by multiplying the ratings on the following two questions derived from the Wisconsin Quality of Life Index – Provider Version (Becker, 1995; Malla, Iyer, Rangaswamy, Ramchandran, et al., 2020): “During the past four weeks, this person has received infrequent/moderate/good support” (three-point Likert scale, 1-3); and “How would you describe the quality of this person’s

relationship with his/her family in the last 4 weeks" (six-point Likert scale, 0-5). Higher scores indicate higher levels of family support.

All data were collected by rigorously trained research staff at both sites. The use of the CORS in cross-cultural research and the interrater reliability between raters at the two sites were established on 10 randomly selected cases (intraclass correlation coefficient ICC = 0.89-0.97) in the pilot study (Iyer et al., 2010). Inter-rater reliability across sites was also regularly established for the SAPS using videotaped interviews of FEP patients (two from each site) and assessed by all raters involved with symptom evaluation. The Cronbach's alpha for the SAPS global score ranged from 0.933-0.988.

4.3.4 Statistical analyses

All statistical testing was performed using SPSS Statistics 24 (Corp., Released 2016) and R Studio Version 1.1463 (RStudio, 2015). Patient characteristics, both sociodemographic and clinical, were summarized using appropriate descriptive analyses. Descriptive statistics and chi-square analyses were also used to report delusion severity and frequency (globally and per theme) at baseline. To assess frequency of clinical delusions, we utilized the same threshold for non-remission (SAPS global scores ≥ 3) recommended by the Working Group on Remission in Schizophrenia (WGRS) (Andreasen et al., 2005): namely, a SAPS severity rating of ≥ 3. In order to control for potential confounds, we ran a series of logistic regressions with the presence of delusions at baseline (delusion score ≥ 3 or <3) as a binary outcome variable. Given our modestly sized sample (Bujang, Sa'at, Sidik, & Joo, 2018), we carefully selected no more than five predictors per delusions theme based on previous literature (Lemonde et al., 2020; Paolini, Moretti, & Compton, 2016).

To assess the effects of time and site on the longitudinal course of delusions, we first ran simple chi-square analyses at each time point. Following this, generalized estimating equations (GEE) were employed to assess potential site differences in clinical-level delusions (delusion score ≥ 3) at yearly time points (months 12 and 24) while controlling for confounding effects. DUP and antipsychotic medication dose were transformed using the cube function as opposed to the commonly used LOG function, in order to normalize the data for analyses and retain participants who may present with zero days of untreated psychosis and/or who did not receive antipsychotic medication at baseline. Given prior observations that positive symptoms are more severe in Montreal than in Chennai, we controlled for baseline delusion severity in order to gain precise estimates in our longitudinal analyses (Malla, Iyer, Rangaswamy, Ramachandran, et al., 2020).

Given the presence of missing data, we ran sensitivity analyses; those included in the longitudinal analyses appeared to be representative of the overall sample (Supplementary Table 1). We used the last observation carried forward (LOCF) method to further address the issue of missing data in our outcome variable (positive symptom severity) such that where applicable, positive symptom ratings at each time point were carried forward for the next period (up to a maximum of six months). In order to determine whether the findings were biased by missing data and the LOCF method, we compared the GEE findings between the original results using the original dataset and the LOCF dataset.

4.4 Results

4.4.1 Sample characteristics

Sociodemographic and clinical characteristics per site are summarized in Table 1. Of 333 total service users, 168 were from Chennai and 165 from Montréal. Participants were younger in

Montreal than in Chennai both when considering their age of onset for a FEP and their age of entry into the program. There was a significantly higher proportion of male patients in Montreal. More patients in Chennai were married/in a relationship. While most patients lived with their families across sites, this was more common in Chennai compared to Montreal.

Patients were in both sites more likely to present with a non-affective FEP, although this proportion was significantly higher in Chennai. More individuals met criteria for a concurrent substance abuse disorder in Montreal compared to Chennai. DUP was similar across both sites. The initial dose of antipsychotic medication given in Montreal was higher than in Chennai. Finally, baseline levels of anxiety and depression were significantly higher in Montreal than in Chennai.

Table 1. Sociodemographic and Clinical Characteristics

Sociodemographic Variable	**Montréal** *n (%) / M (SD)*	**Chennai** *n (%) / M (SD)*	**Statistical Test**	**p-value**
Age of entry (years)	24.20 (5.3)	26.60 (5.24)	t(331) = 4.15	<0.001
Gender				
Men	110 (66.7)	82 (48.8)	$X^2(2) = 12.37$	0.002
Women	54 (32.7)	86 (51.2)		
Transgender	1 (0.6)	0 (0.0)		
Education				
Less than HS	44 (27.2)	47 (28.0)	$X^2(1) = 0.03$	0.868
More than HS	118 (72.8)	121 (70.0)		
Relationship Status				
Single	151 (92.1)	106 (63.1)	$X^2(1) = 39.85$	<0.000
In a relationship	13 (7.9)	62 (36.9)		
Living situation				
Alone	16 (10.0)	2 (1.4)	$X^2(3) = 22.95$	<0.001
With family	125 (78.1)	140 (96.6)		
With friends/roommate	16 (10.0)	2 (1.4)		
In residence, group home, or homeless	3 (1.9)	1 (0.7)		
Clinical Variables	*n (%) / M (SD)*	*n (%) / M (SD)*		
Age of illness onset (years)	23.41 (5.67)	25.81 (5.22)	t(318) = 3.94	<0.001
SCID Diagnosis Type				
Non-affective Psychosis	109 (67.3)	150 (90.4)	$X^2(1) = 26.29$	<0.001
Affective Psychosis	53 (32.7)	16 (9.6)		

Substance Abuse or Dependence				
Yes	54 (37.8)	17 (10.2)	$X^2(1) = 32.90$	<0.001
No	89 (62.2)	149 (89.8)		
DUP (weeks) to presenting episode	40.79 (88.46)	25.81 (5.22)	t(287) = -0.63	0.527
Antipsychotic dose at baseline	209.17 (165.04)	169.22 77.20)	t(191) = -2.02	0.044
Baseline anxiety	10.27 (7.76)	4.26 (6.68)	t(298) = 7.21	<0.001
Baseline depression	4.48 (3.76)	3.57 (4.75)	t(307) = 1.89	<0.060

Note. DUP and Antipsychotic dose (CPZ equivalent) are cubed for analyses.

4.4.2 Delusions at baseline

At baseline, delusions were more common in patients at the Montreal site compared to the Chennai site, except for delusions of reference and jealousy (Figure 1; Table 2a). Furthermore, global delusions were more severe in Montreal than in Chennai ($t(302) = 6.92, p < .001$): there was a significant association between site and the presence (SAPS severity >3) of clinical delusions, both globally and for specific delusions (grandiosity, religiosity, mind reading, and jealousy). In almost all cases, these associations were maintained after controlling for confounding effects (Table 2b).

Table 2a. SAPS delusion items at baseline across sites

	Montréal		**Chennai**		
SAPS Item Delusion	$mean \pm SD$ *Delusions*	*n (%) Delusions*	$mean \pm SD$ *Delusions*	*n (%) Delusions*	X^2
Global Rating	4.01 (0.97)	149 (93.1)	3.10 (1.37)	134 (79.8)	12.36*
Persecutory	3.37 (1.51)	121 (75.6)	2.75 (1.64)	113 (67.3)	2.80
Reference	2.48 (1.81)	92 (57.5)	2.51 (1.68)	104 (62.3)	0.78
Grandiose	1.93 (1.78)	65 (40.6)	0.47 (1.12)	16 (9.5)	42.63*
Religious	1.22 (1.65)	44 (27.5)	0.33 (0.98)	13 (7.7)	22.29*
Mind Reading	1.07 (1.43)	38 (23.8)	0.36 (1.00)	13 (7.7)	16.00*
Being Controlled	1.07 (1.47)	34 (21.5)	0.63 (1.35)	26 (15.5)	1.98
Somatic	0.86 (1.48)	25 (15.7)	0.54 (1.19)	17 (10.1)	2.29
Thought Insertion	0.55 (1.07)	17 (10.6)	0.22 (0.80)	9 (5.4)	3.06
Guilt or Sin	0.88 (1.19)	20 (12.5)	0.36 (0.91)	9 (5.4)	5.19
Thought Broadcasting	0.47 (0.98)	15 (9.4)	0.22 (0.80)	8 (4.8)	2.68
Thought Withdrawal	0.34 (0.81)	8 (5.0)	0.08 (0.46)	2 (1.2)	4.02
Jealousy	0.21 (0.58)	3 (1.8)	0.65 (1.30)	26 (15.5)	18.67*

Note. Average severity was calculated using the SAPS severity rating 0-5; frequency was calculated using the SAPS severity cut-off of ≥ 3; *p < .004 (Bonferroni corrected); X^2 calculated using *n (%)*.

Table 2b. SAPS delusion items at baseline across sites: Controlling for confounding effects

Predictors	Global delusions	
	OR	95% C.I.
Site	3.42*	1.08-10.84
Age of onset	1.13*	1.04-1.22
Anxiety	1.06	0.99-1.13
Bizarre behavior	1.62*	1.21-2.18
	Grandiose Delusions	
	OR	95% C.I.
Site	2.19*	1.03-4.68
Depression	0.99	0.91-1.06
Bizarre behavior	1.37*	1.07-1.77
Positive formal thought disorder	1.60*	1.28-1.99
	Religious Delusions	
	OR	95% C.I.
Site	2.04	0.92-4.52
Bizarre behavior	1.16	0.90-1.49
Positive formal thought disorder	1.53*	1.22-1.91
	Mind Reading Delusions	
	OR	95% C.I.
Site	3.16*	1.56-6.40
Depression	1.03	0.96-1.11
Hallucinations	1.23	1.00-1.50
	Delusions of Jealousy	
	OR	95% C.I.
Site	5.95*	1.48-23.91
Relationship	6.40*	2.61-15.73
Substance	3.24*	1.06-9.93
Hallucinations	0.86	0.65-1.12

Note. * indicates OR has meaningful confidence interval.

4.4.3 Longitudinal investigation of clinical delusions

Simple comparisons were first run at each time point to compare the frequency of delusions across sites (Table 3; Figure 2). While clinical delusions (SAPS ≥ 3) were more common at baseline in Montreal, they were significantly more common in Chennai at year 1. There was no difference across sites at year 2.

Table 4 displays the GEE logistic regression regarding the presence or absence of delusions (SAPS >= 3 or <3, respectively) at year 1 and 2. An interaction effect emerged between time and site (Table 4a) which mirrored the findings from Table 3; this interaction was lost when controlling for confounding effects, but a significant main effect of site remained at years 1 and 2 (Table 4b): those in Chennai were more likely to present with clinically significant delusions at annual follow-ups. Older age of onset was independently associated with a higher risk of presenting with clinical delusions over time.

Table 3. SAPS Global Delusions across time and by site

	Montréal		Chennai		
Time	$mean \pm SD$	*n (%)*	$mean \pm SD$	*n (%)*	X^2
Baseline	4.01 (0.97)	149 (93.1)	3.10 (1.37)	134 (79.8)	12.36*
Mth 12	0.85 (1.20)	18 (12.7)	0.83 (1.41)	34 (20.2)	4.29*
Mth 24	0.95 (1.30)	17 (13.0)	0.69 (1.29)	24 (14.3)	0.20

Note. Average severity was calculated using the SAPS severity rating 0-5; frequency was calculated using the SAPS severity cut-off of ≥ 3; $*p < 0.05$; X^2 calculated using *n (%)*.

Table 4a. GEE Logistic Regression Evaluation of Delusions at Mth 12 & 24: Unadjusted Odds Ratios

Variable	OR	95% C.I.
Time*site		
Mth 12		
Montreal	Reference	
Chennai	2.74*	1.44-5.21
Mth 24		
Montreal	1.01	0.53-1.92
Chennai	1.67	0.86-3.26
Baseline delusions	1.41*	1.10-1.79

Table 4b. GEE Logistic Regression Evaluation of Delusions at Mth 12 and 24: Adjusted Odds Ratios

Variable	OR	95% C.I.
Time		
Month 12	Reference	
Month 24	0.71	0.49-1.03
Site		
Montreal	Reference	
Chennai	2.65*	1.22-5.68
Diagnosis		
SSD	Reference	
Affective	0.96	0.41-2.24
Baseline delusions	1.34*	1.01-1.77
Age of onset	1.08*	1.02-1.15
DUP (cubed)	1.09	0.88-1.34
Baseline antipsychotic dose (cubed)	0.86	0.70-1.04
Family support (Mth 3)	0.95	0.88-1.02

Note. Table 3a has 8.1% missing data, and Table 3b has 32.1%.
* indicates OR has meaningful confidence interval.

4.4.4 Is this trajectory unique to delusions?

Comparisons were first run to compare the frequency of positive symptoms across sites for different time points (Table 5). All positive symptom types presented more frequently (i.e. with SAPS severity ≥ 3) in Montreal than in Chennai at baseline; however, at months 12 and 24, there were no site differences for other (non-delusional) positive symptomatology. This was further supported by the adjusted odds ratios from the GEE logistic regressions in Table 6. Hallucinations diminished with time, but no other effects emerged for time and/or site.

Table 5. SAPS Global Delusions across time and by site

		Montréal		Chennai		
Symptom	Time	$mean \pm SD$	*n (%)*	$mean \pm SD$	*n (%)*	X^2
Delusions	Baseline	4.01 (0.97)	149 (93.1)	3.10 (1.37)	134 (79.8)	12.36*
	Mth 12	0.85 (1.20)	18 (12.7)	0.83 (1.41)	34 (20.2)	4.29*
	Mth 24	0.95 (1.30)	17 (13.0)	0.69 (1.29)	24 (14.3)	0.20
Hallucinations	Baseline	2.87 (1.69)	101 (63.1)	1.93 (1.65)	78 (46.4)	9.22*
	Mth 12	0.59 (1.19)	18 (12.6)	0.47 (1.05)	14 (9.0)	1.02
	Mth 24	0.53 (1.14)	11 (8.4)	0.39 (0.95)	9 (5.5)	0.95
Bizarre Behavior	Baseline	2.88 (1.30)	113 (70.6)	1.54 (1.37)	48 (28.6)	57.99*
	Mth 12	0.71 (1.05)	9 (6.3)	0.37 (0.91)	11 (7.1)	0.06
	Mth 24	0.78 (1.09)	12 (9.2)	0.29 (0.77)	6 (3.7)	3.79
Positive Formal Thought Disorder	Baseline	1.92 (1.53)	77 (48.1)	0.52 (1.06)	10 (6.0)	74.30*
	Mth 12	0.47 (0.97)	9 (6.9)	0.09 (0.50)	4 (2.4)	2.50
	Mth 24	0.40 (0.90)	9 (6.9)	0.17 (0.67)	6 (3.6)	1.52

Note. Average severity was calculated using the SAPS severity rating 0-5; frequency was calculated using the SAPS severity cut-off of ≥ 3; *$p < 0.05$; X^2 calculated using *n (%)*.

Table 6. GEE Logistic Regression Evaluation of other Positive Symptoms

	Delusions		Hallucinations		Bizarre Behavior		Positive Formal Thought Disorder	
Variable	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Time								
Mth 12	Reference		Reference		Reference		Reference	
Mth 24	0.71	0.49-1.03	0.47*	0.30-0.73	0.86	0.51-1.45	0.75	0.36-1.55
Site								
Montreal	Reference		Reference		Reference		Reference	
Chennai	2.65*	1.22-5.68	1.31	0.53-3.27	1.86	0.72-4.81	2.18	0.59-8.02
Diagnosis								
SSD	Reference		Reference		Reference		Reference	
Affective	0.96	0.41-2.24	0.57	0.16-2.01	0.95	0.33-2.74	1.62	0.57-4.57
Baseline symptom	1.34*	1.01-1.77	1.29	0.99-1.67	1.72	1.07-2.76	1.65*	1.11-2.45
Age of onset	1.08*	1.02-1.15	0.99	0.93-1.06	0.97	0.89-1.05	0.99	0.90-1.09
DUP (cubed)	1.09	0.88-1.34	1.13	0.83-1.54	1.05	0.75-1.50	1.10	0.82-1.48
Baseline AP (cubed)	0.86	0.70-1.04	0.81	0.65-1.01	0.90	0.75-1.07	0.94	0.76-1.17
Family support (Mth 3)	0.95	0.88-1.02	0.89*	0.80-0.99	0.88	0.77-1.01	0.83*	0.73-0.95

Note. * indicates OR has meaningful confidence interval.

4.4.5 Sensitivity analyses

When comparing the GEE findings between the original results using the original data set (see Supplementary Table 2) and the LOCF dataset (Table 4), the effects and the marginal covariate effects remained consistent across all models.

4.5 Discussion

To our knowledge, this is the first direct comparison of delusional beliefs across similar clinical programming in two different cultural, health system and economic contexts. Most striking was the discovery that the rank-order of delusion themes was almost identical across sites. Consistent with a recent finding that clinical level positive symptoms (SAPS ≥ 3) were more frequent at baseline in HICs compared to LMICs, we found that moderate to severe delusions presented more frequently in Montreal than in Chennai at baseline. Contrary to our hypothesis, clinical-level delusions were more frequent in Chennai than in Montreal at yearly follow-ups. Finally, unlike delusions, other positive symptoms domains (hallucinations, bizarre behavior, and positive formal thought disorder) remained consistent across sites over time.

Initial work on this same study cohort found higher levels of overall positive symptoms upon entry to a FEP program in Montreal than in Chennai (Malla, Iyer, Rangaswamy, Ramchandran, et al., 2020). In the current paper, clinical-level delusions also presented more frequently at baseline in Montreal but (contrary to prior work that has shown favourable illness trajectories in LMICs) were less frequent in Montreal than in Chennai across a two-year longitudinal follow-up. This remained the case even after controlling for factors such as diagnosis and baseline antipsychotic dose. It may have been that ongoing differential exposure to antipsychotic medication accounts for the higher frequency of delusions in Chennai.

At baseline, higher delusions of jealousy were partially explained by relationship status and substance abuse. This was the only delusion theme that presented more frequently in Chennai than in Montreal, potentially linked to higher rates of marriage in Chennai. Grandiose and mind reading delusions were more common in Montreal; however, all other delusion themes presented consistently across sites and followed a similar rank-order. This rank-order mirrors a large body of evidence investigating delusions in chronic episodes of schizophrenia across contexts and time – wherein delusions of persecution, reference and grandiosity are consistently the most common (Kim et al., 2001; Suhail & Cochrane, 2002). Our data also strengthens the notion that delusional content tends to be overwhelmingly socially and relationally themed in both LMIC and HIC contexts. Future work could explore how this sheds light on socio-cognitive processes that form and maintain beliefs in psychosis (Bell, Raihani, & Wilkinson, 2019).

Older age of onset was marginally associated with a heightened risk of presenting with delusions over time. This follows our findings from a large baseline sample of early psychosis patients, in which the association was unique to persecutory delusions (Lemonde et al., 2020). Perhaps surprisingly, duration of untreated psychosis did not predict the longitudinal course of delusions, in contrast to suggestions that a longer DUP might lead to a more crystalized delusional system that integrates these beliefs into larger cognitive schemas (Corlett, Taylor, Wang, Fletcher, & Krystal, 2010; Kapur, 2003). Although the use of antipsychotic medication may mitigate prediction errors and speed the treatment process along, the shift away from a highly integrated belief framework likely takes time and other factors such as psychological strategies, family/friend support, and reduced societal stigma are also vital (Kapur, 2003). Our findings also did not support the notion that the quantity and quality of family relationships plays a role in the course of delusions. Since our measure of family support may not fully reflect the

complex nature of social relationships and their interaction with illness (Norman et al., 2005), future work should expand the notion of support to include familial and non-familial relationships.

Although our analysis provides some initial answers to the question of what exactly sits within the *black box* of context (Jenkins & Karno, 1992), it remains unclear precisely how context interacts with clinical symptom dimensions during a psychotic episode to yield outcome differences across settings. Interestingly, a recent cross-national comparison using a community sample across 13 countries found that most psychotic experiences (e.g. paranoia and grandiosity) were perceived as less distressing in LMICs compared to HICs (Wusten et al., 2018). Although the relationship between distress and psychotic symptoms is not clear-cut (Lemonde et al., 2020; Vracotas, Schmitz, Joober, & Malla, 2007), delusion-related distress has been identified as one key point of distinction between clinical and non-clinical samples, even more so than delusional frequency and conviction (So, Tang, & Leung, 2015). Further research is needed regarding the role that distress plays in the initial presentation of positive symptoms, particularly across LMICs and HICs. In our sample, anxiety – a possible indicator of distress – did not account for the higher presence of delusions in Canada at baseline, and while delusions did present more severely and frequently in Montreal at baseline, this was not the case longitudinally.

Luhrmann and colleagues discuss how people living with psychotic disorders may interact differentially with abnormal perceptual experiences based on *cultural invitations* or variations in ways that people think about phenomena like minds and spirits (Luhrmann, Padmavati, Tharoor, & Osei, 2015); for example, they found that voices were more often described as intrusive and unreal in California while patients in Chennai were more likely to view hallucinations as providing useful guidance. While this pertains to hallucinations, it has been proposed that

symptoms interact within networks that can become self-sustaining, especially within densely connected networks (Borsboom, 2017). In addition, hallucinations and persecutory ideas may be more central to these networks than other symptoms in psychosis; LMICs have been shown to have less densely connected symptom networks than HICs, potentially making individuals more resilient and yielding favourable outcomes (Wusten et al., 2018). Future work may, therefore, wish to consider the interconnection of delusions with other psychotic symptoms in early psychosis across cultures.

While it is worth noting that positive symptom remission has previously been associated with functional outcomes (Jordan et al., 2014), it cannot be forgotten that delusions and even symptomatology as a whole are only one dimension of the recovery process. The aim of this paper was not to view delusions through a recovery lens but simply to understand their initial presence and course across two similar treatment FEP programs in LMICs and HICs. Future work may wish to conduct qualitative research to better understand how today's youth experience delusions and how these beliefs interact with their recovery process.

4.5.1 Strengths and limitations

Amongst the most notable strengths of this project is the considerable effort that has led to the creation of similar treatment protocols in Chennai, India and Montreal, Canada. Research staff were rigorously trained, and regularly evaluated inter-rater reliability across sites. Other than the cost of medications, mental health services were provided at no charge to users or their families at both sites. Furthermore, due to our cut-off of 30 days for antipsychotic medication use, the results are relatively uninfluenced by confounding factors such as long-term treatment effects and illness chronicity.

Scholars have warned against the use of population-level categories in mental health research (Kirmayer & Ban, 2013); even within one country there are complex and meaningful variations – for example, religious, health system, and economic environments. Even with those caveats in mind, however, such comparisons may contribute to a better understanding of delusions and ultimately informing care for youth experiencing a FEP.

It is possible that differences seen in the early presentation and course of delusions result from a sampling bias; Montreal has a catchment-based sample and is therefore theoretically more representative of the overall population seeking care. While there were substantial differences in key patient characteristics at baseline, these do not appear to explain the differential outcomes seen in our later analyses. However, our measure for antipsychotic dose was limited to baseline, whereas a longitudinal measure might be relevant for explaining the year 1 and year 2 findings. Finally, future work should consider a more inclusive measure for social support that encompasses non-kin relationships as well as familial relationships: our measure was limited to the quality and quantity of family support.

4.5.2 Conclusion

Whether in LMICs or HICs, psychoses are distressing and impairing mental experiences that frequently have recognizable features such as delusions. Directly comparing delusions in an LMIC (Chennai, India) with a HIC (Montreal, Canada) revealed a relatively consistent rank order of themes across contexts. At baseline, clinical level delusions were more frequent in Montreal; conversely, longitudinally, delusions were more common in Chennai. The substantial overlap seen in delusional themes across cultures perhaps demonstrates that there is something universal and socially salient about our ability to form beliefs even in challenging circumstances, such as the onset of a FEP. Our hope is that this study may contribute to a richer understanding

of delusions in early psychosis, in order to inform context-sensitive recovery and to ameliorate the lives of people living with psychosis.

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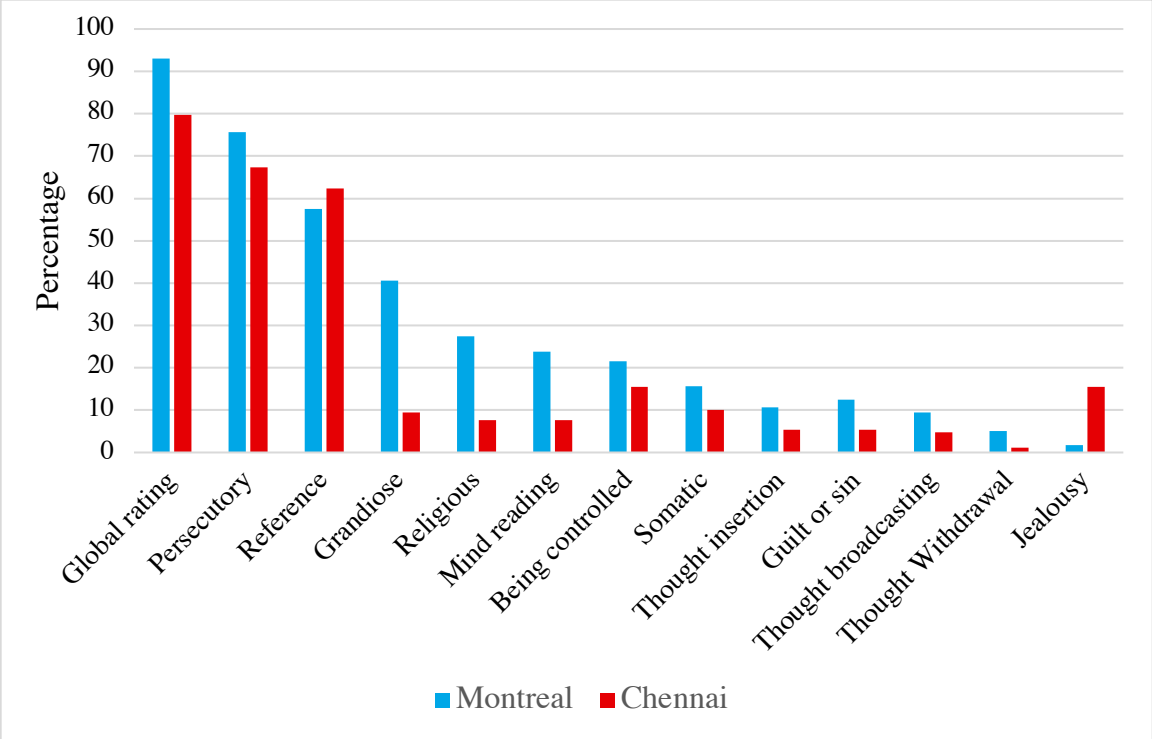
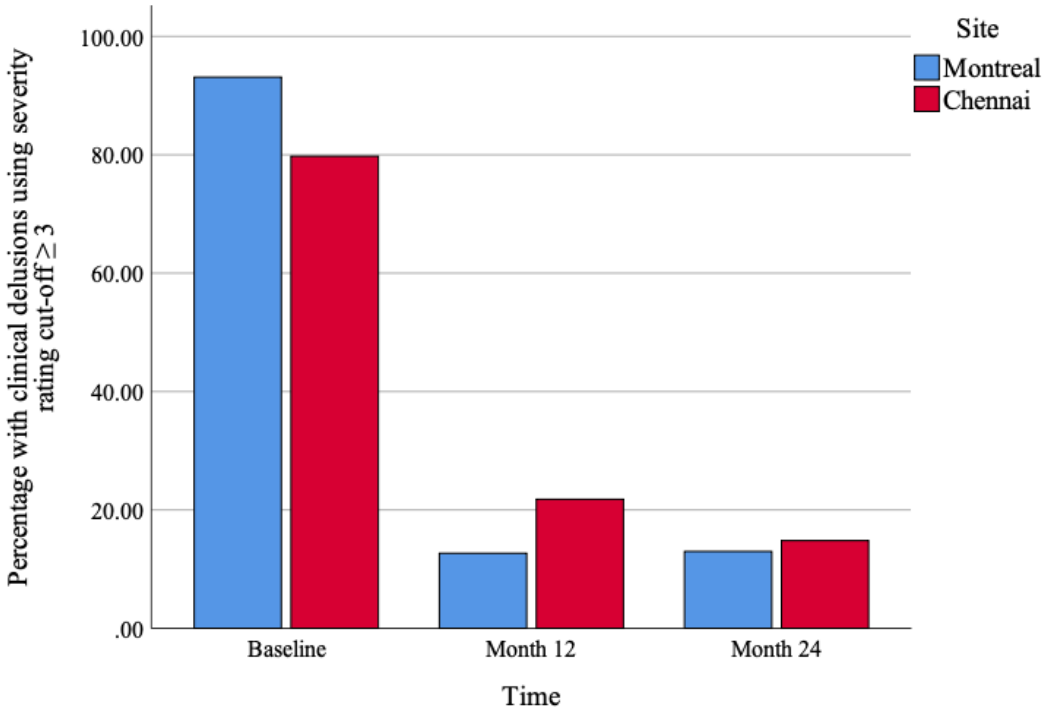
4.7 Figures



F1. Percentage of FEP patients with a specific delusion theme (SAPS severity rating of ≥) at baseline across sites.



F2. Percentage of FEP patients with clinical global delusions across time and by site.

4.8 Supplementary Material

Table 1. Comparison of key baseline characteristics across missing versus valid data in longitudinal analyses

Key outcome variables of interest	Valid *Mean (SD)* N (%)	Missing *Mean (SD)* *N (%)*	*t-tests* *Chi-Sq.*
Baseline global delusion rating			
Original dataset	3.52 (1.32)	3.60 (1.16)	-.477
LOCF	3.52 (1.32)	3.61 (1.12)	-.550
Site			
Original dataset	234 (70.3%)	99 (29.7%)	2.77
LOCF	246 (73.9%)	87 (26.1%)	.050
Diagnosis			
Original dataset	234 (71.3%)	94 (28.7%)	2.99
LOCF	246 (75.0%)	82 (25.0%)	5.14*
SSD	187 (76.0%)	72 (87.8%)	
Affective	59 (24.0%)	10 (12.2%)	

*$p < 0.05$

Table 2a. GEE Logistic Regression Evaluation of Delusions at Mth 12 and 24 using original dataset (no LOCF): Unadjusted odds ratios

Variable	OR	95% C.I.
Time*site		
Mth 12		
Montreal	Reference	
Chennai	2.61*	1.33-5.11
Mth 24		
Montreal	0.98	0.50-1.95
Chennai	1.65	0.83-3.28
Baseline delusions	1.38*	1.08-1.77

Table 2b. GEE Logistic Regression Evaluation of Delusions at Mth 12 and 24 using original dataset (no LOCF): Adjusted odds rations

Variable	OR	95% C.I.
Time		
Mth 12	Reference	
Mth 24	0.72	0.49-1.06
Site		
Montreal	Reference	
Chennai	2.69*	1.22-5.89
Diagnosis		
SSD	Reference	
Affective	1.03	0.43-2.44
Baseline delusions	1.32	1.00-1.75
Age of onset	1.09*	1.02-1.16
DUP (cubed)	1.09	0.88-1.34
Baseline antipsychotic dose (cubed)	0.89	0.73-1.09
Family support (Mth 3)	0.94	0.87-1.02

Note. Table 2a and 2b have 12.6% and 34.5% missing data, respectively.

CHAPTER 5. General Discussion and Conclusions

This thesis employed quantitative methods 1) to examine the baseline presentation of delusional content and severity in a catchment-based early intervention service for psychosis, and 2) to explore the comparative themes and longitudinal trajectories of delusions over two years of similar early intervention programming in Chennai, India and Montreal, Canada. Overall, the vast majority of individuals experiencing a FEP developed clinical level delusions, with persecutory, referential and grandiosity themes being the most common across both contexts. This concluding chapter will summarize our findings on delusions in early psychosis through the unique lens offered by our methodology. I will also address how our findings sit within the current and broader discussions being held in the field of delusion research, and present potential avenues for future research.

5.1 Summary of main findings

The results of the first quantitative analysis addressed an important knowledge gap regarding delusional content and severity in the earliest phases of psychosis. Given that there were no competing public or private early intervention services in the same catchment, all individuals identified as needing treatment for an early phase psychosis were referred to PEPP; thus, a major strength of this project was the reasonably representative near-treated incidence sample of all individuals aged 14-35 identified as experiencing a FEP. The study also examined delusions across individuals experiencing the same early phase in their illness, thereby addressing potential confounds such as illness chronicity and treatment exposure. Delusions of persecution, reference and grandiosity were the most common in individuals experiencing onset of a FEP, and occurred similarly across affective and non-affective psychotic illnesses. Older age of onset and

heightened levels of anxiety were both associated with more severe global delusions, particularly for persecutory delusions.

The subsequent quantitative study built off of our first manuscript by investigating whether delusional and severity was consistent cross-culturally, both at baseline and longitudinally in two similar FEP settings in Canada and India. To our knowledge, this is the first direct comparison of delusional beliefs across similar clinical programming sites in two different cultural contexts, and revealed that delusions may have differential trajectories in these two sites as compared to the trajectories of other positive psychotic symptoms. Interesting, delusions were more severe and frequent in Montreal than in Chennai at baseline but over time became more common in Chennai than Montreal. While site differences emerged in the baseline presentation of delusional content, the rank-order of thematic content remained relatively consistent across sites.

5.2 Synthesis of two studies and implications

Together, findings from our two studies contribute a great deal to the existing literature by providing a unique clinical snapshot of delusions in the earliest days of their clinical presentation, relatively unconfounded by intervention effects. One notable element was the similar rank-order of delusional themes seen in FEP across Canada and India. This strengthens a long standing and larger body of work on delusions in non-affective psychosis that has found relatively consistent rank-order and frequencies of delusional themes across continents (Kim et al., 2001; Suhail & Cochrane, 2002); and suggests that while specific delusional content and the severity of those first delusional symptoms may vary, there exists a relatively stable set of delusional forms across cultures (Gold & Gold, 2014): "*the universality of the mechanisms is supported by the fact that the same handful of motifs recurs in different historical periods and cultures*." In Chapter 3, we discussed theories as to why persecutory delusions are prevalent in

psychotic disorders, and how studies restricted to persecutory ideation overlook other common themes such as grandiosity or somatic delusions. More recently, findings regarding socially and relationally themed content have inspired researchers to investigate the socio-cognitive processes that form and maintain beliefs in psychosis (Bell, Raihani, & Wilkinson, 2019).

Beliefs themselves are culturally salient representations which form our shared understanding of reality (Tomasello, 2018); we come to believe information from both individualistic and social sources of evidence (Miyazono & Salice, 2020). In order to cooperate and survive, beliefs are formed through processes that are influenced by people *and* surrounding social structures (e.g. the in-group in high school, parental authority, political atmosphere); thus, delusions may occur when there is a breakdown in the cognitive mechanisms which have evolved to help us navigate our social worlds (Bell et al., 2019). In addition, early childhood adversity (e.g. bullying, sexual abuse, neglect) has been linked with heightened persecutory ideation in psychosis, suggesting that delusions may arise from trauma-related negative beliefs about one's social environment (Bailey et al., 2018). More work is clearly needed to understand the relationship between social cognition and delusional beliefs, as most social cognitive theories of delusions are born from non-clinical data and work is still needed in the context of psychosis. At the same time, others have shown that non-social processes, such as unexpected uncertainty and poor non-social belief updating, may explain the presence of persecutory delusions (Reed et al., 2020).

Researchers have also posited that the quantity and quality of social interactions may impact both the development and maintenance of these maladaptive beliefs (Bell et al., 2019; Bentall, 2018). The process of believing something is negotiated through our interactions and conversations with others over time (Miyazono & Salice, 2020); Bentall suggests that delusional

beliefs may differ from radical or strongly held beliefs because they develop in isolation from social interactions, making them less likely to undergo revisions (Bentall, 2018). While individuals in the early stages of developing psychosis may lack certain capacities or resources needed to engage in their social world (e.g. theory of mind), Bentall speculates that social isolation may also impact the development of delusions. Part of our cross-cultural analysis was precisely geared towards testing whether the trajectory of delusions is impacted by familial support, and whether this support explains differing trajectories in psychosis outcomes between HICs and LMICs. In our work, family support was not a meaningful predictor of delusional outcomes. It may be that our measure did not adequately reflect the complexity of social interactions existing in our sample (e.g. our measure did not consider non-kin relationships); or, it may be that non-social processes are also key towards differentiating between clinical delusions and strongly-held beliefs seen in healthy populations (Corlett & Fletcher, 2012; Reed et al., 2020).

In Chapter 4 we speculated as to why delusions were more severe and frequent in Montreal than in Chennai at baseline. Yet perhaps more surprising – and contrary to the overarching theory that psychosis outcomes are relatively benign in lower- and middle-income countries (LMICs) compared to higher-income countries (HICs) – we discovered that delusions were more frequent in Chennai than in Montreal at yearly follow-ups. While our methodology may have permitted the elucidation of a more nuanced understanding of the relative outcomes in LMICs compared to HICs, there are nonetheless important factors to consider in this synthesis. Our measure for antipsychotic dose was limited to baseline and it may be that ongoing differential exposure to antipsychotic medication accounts for the higher frequency of delusions in Chennai longitudinally. At the same time, delusions are only one component of recovery. For

example, in a paper using the same sample as our study, Malla et al. found that individuals in Chennai showed better negative symptoms outcomes compared to Montreal (Malla et al., 2020). Another study investigating psychotic experiences in non-clinical populations showed that given equal frequency levels, psychotic experiences are perceived as less distressing in LIMCs compared to HICs (Wusten et al., 2018). These and other factors are likely to impact the overall process of recovery and outcomes in a variety of ways.

Delusion themes in our first paper rarely occurred in isolation, making it necessary to not only consider individual themes but the ways in which they connect to form systems (Rhodes, Jakes, & Robinson, 2009). Two studies have previously derived 5 domains underlying the 12 SAPS delusion items in FEP samples (Kimhy, Goetz, Yale, Corcoran, & Malaspina, 2005; Paolini, Moretti, & Compton, 2016); for example, delusions of *jealousy* and *sin or guilt* loaded onto a factor entitled *negative affect delusions*. An analysis to derive underlying delusion domains was not conducted within the scope of this thesis. However, our sample offers a unique opportunity for future analyses, especially given the larger sample sizes, selected samples and potential confounds compared to prior work (Kimhy et al., 2005; Paolini et al., 2016). Since global positive symptom measures have yet to be matched with meaningful neurobiological underpinnings, Kimhy et al. argue that studying domains of delusional themes may help neurobiologists link delusions to putative underlying mechanisms (Kimhy et al., 2005).

On reflection, much of the twentieth century (as exemplified by DSM) was characterized by rigid diagnostic boundaries that regarded schizophrenia as a single disorder. Researchers have since become increasingly flexible in their conceptualization of psychotic disorders, focusing on traits that overlap diagnostic categories and are even found in non-clinical populations (Garety & Freeman, 2013). Unfortunately, to date there are still relatively few studies that investigate

clinical delusions in populations other than those suffering from schizophrenia, and even fewer that consider the transdiagnostic presentation of delusional content (Picardi, Fonzi, Pallagrosi, Gigantesco, & Biondi, 2018). In our work, delusional themes were comparable across affective and non-affective psychoses, and these diagnoses did not impact the longitudinal course of global ratings of delusions. Neuropsychologists have suggested that we study polythematic delusions in a similar fashion as monothematic delusions by moving away from the dichotomous categorization of 'psychiatric' and 'neurological' delusions, and by studying polythematic delusions more broadly as a symptom occurring in many disorders as opposed to solely in schizophrenia (Coltheart, 2013).

Moreover, Garety and Freeman have discussed the need for specific interventions that target symptoms like paranoia or grandiosity by centering the clinical interaction around the experience of the patient as opposed to the diagnosis (Garety & Freeman, 2013). While traditionally delusional content has received little attention, often labeled as irrational or insignificant (Berrios, 1996), there is evidence to suggest that these highly varied and meaningful experiences should themselves be considered in the design of psychological interventions (Jones, Read, & Wood, 2020; Rhodes & Jakes, 2000). For example, the content of delusions may in some cases reflect the personal goals of individuals living with psychosis (Rhodes & Jakes, 2000). In our work, diverse relationships emerged between specific delusion themes and clinical factors such as anxiety and depression. For example, anxiety was most modestly associated with delusions of persecution, somatization, and control, but not with the remaining themes in our analysis. Promising studies have shown that emotion-focused interventions targeting negative affect could impact the severity of delusions (Opoka, Ludwig, & Lincoln, 2018). Understanding

how negative affect is differentially related to delusional content, as seen in our analyses, may further inform tailored therapeutic options.

5.3 Future directions

It may be of interest to consider how additional temporal dimensions interact with delusional content. For example, are delusion themes consistent across successive cohorts (e.g. early 2000s versus now)? Delusional content has been investigated across history but in widely varying settings and/or with inconsistent measures; FEP programming sites that have systemically measured delusions over the last few decades offer a unique opportunity to investigate delusions across a period of vast change (e.g. technological growth).

At the individual level, do service users show concordance or discordance in delusional content between first and subsequent episodes? Neurocognitive models have suggested that the psychotic state itself acts as a contextual cue for old delusional beliefs to re-emerge (Corlett, Krystal, Taylor, & Fletcher, 2009). It has long been suggested that delusions are firmly held *(Jaspers, 1997)*; however, there is also evidence that they are quite fluid (Appelbaum, Robbins, & Vesselinov, 2004; Ellersgaard et al., 2014; Sinha & Chaturvedi, 1989). Currently, there exists a relatively small body of work on the course of delusions, and investigating the effects of time on the content of delusions may help fill important knowledge gaps.

Finally, the early psychosis literature on delusions is largely quantitative in nature. How do those with lived experiences understand their delusions in the earliest phases of psychosis and throughout recovery? How is knowledge regarding delusions being communicated between youth with lived experiences, their communities, and the research milieu? There are also potential avenues for research that involves integrating those with lived experiences more actively into the research process. For example, formats such as digital storytelling have the

potential to innovatively capture the complexity of delusions through subjective experience. My hope is to see the field actively engaging with and integrating findings from both quantitative and qualitative work on delusions, in order to promote understanding, empathy and ultimately healing.

5.4 References

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