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Psychosis

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Abstract

Psychosis is a set of symptoms related to mental health issues that occurs in a range of psychotic disorders. Psychosis in individuals with intellectual disabilities is an underexplored area in research. This chapter provides an overview of psychosis in intellectual disability (ID). Definitions of what psychosis is will be discussed, as well the prevalence and incidence of psychosis. The importance of studying psychosis in ID will be outlined, including a discussion of the difficulties of providing a diagnosis of psychosis in individuals with an ID. Difficulties of diagnosis will be discussed in terms of diagnostic systems and assessment tools, presence of dual diagnosis, similarities in the etiology of challenging behavior and psychiatric disorder, severity of challenging behavior, the level and degree of intellectual disability, and difficulties in self-report. Risk factors of psychosis will be examined, including baseline risks, early-life risks, childhood risks, and risks later in life. Assessment of psychosis will be outlined, including recommendations for the assessment of psychosis in individuals with intellectual disabilities. Pharmacological and psychological treatment of psychosis in ID will be discussed including recommendations for treatment. Finally, future directions for research will be outlined.

Keywords: Psychosis; Intellectual Disability; Risk Factors; Prevalence; Treatment, Pharmacological; Psychological

Introduction

Psychosis is a topic of importance in research in individuals with Intellectual Disabilities (ID). The focus of this chapter is to review the literature on definition, incidence and prevalence of psychosis in individuals with ID. Importance of studying psychosis in ID, difficulties of studying psychosis in ID, assessment of psychosis in ID, and risk factors of psychosis in ID will be discussed. Treatment of psychosis in ID will be presented, including pharmacological and behavioral treatments, and recommendations for treatment will be given. Following this, future directions for research will be outlined.

Definitions of Psychosis

Psychosis is a set of symptoms related to mental health issues that occurs in a range of psychotic disorders, to include Schizophrenia Spectrum Disorder, Bipolar Disorder, Posttraumatic Stress Disorder and Major Depressive Disorder (Doherty & Owen, 2014). Several diagnostic guidelines and assessments exist that can be used to categorize and summarize the dimensional representations of psychosis (Bakken & Høidal, 2014; Cooper & Bailey, 2001; Schűtzwohl et al., 2016; van Os & Tamminga, 2007). Generally, psychosis is defined as an experience that affects a person's concept of reality, wherein their perception of reality differs considerably from those around them (Krishnan, Kraus, & Keefe, 2011; Sass & Parnas, 2003). During a psychotic occurrence, the person may experience either partial or total loss of contact with reality, and symptoms can range from hallucinations, delusions, disorganized confused thinking and speech, abnormal motor behavior to catatonia (Bakken & Høidal, 2014; Canitano & Pallagrosi, 2017; Spauwen, Krabbendam, Lieb, Wittchen, & Van Os, 2006; Yung, Nelson, Thompson, & Wood, 2010). Positive symptoms of psychosis refer to abnormal, disturbing

thoughts, perceptions and behaviors, such as, hallucinations (seeing, hearing, tasting, smelling and feeling things that are not real) and delusions (fixed false beliefs). Negative symptoms refer to disruption to normal emotions or behavior, for example, apathy and lack of emotional reactivity (Doherty & Owen, 2014). Psychosis differs considerably from person to person however the psychotic experience is very real to that person and it is this lack of awareness of reality that can be very distressing and frightening.

The literature often refers to psychosis as a psychotic episode (Cooper et al., 2007a; McCarthy & Barbot, 2016; Tandon et al., 2013). An episode is defined by the duration of time in which the person has developed symptoms that meet the symptomatic criteria of a specific mental health disorder (Tandon et al, 2013). Episodes can differ in accordance with the type of mental health disorder and can include several symptoms, or a quantified severity or frequency of symptoms (Bakken & Høidal, 2014). They are further differentiated into a single (first) episode or recurrence or relapse of multiple episodes (Tandon et al., 2013).

Defining psychosis in a person with an intellectual disability (ID) or Autism Spectrum Disorder (ASD) is a complex process (Cooper et al., 2007a). Quite often a psychotic episode can share core characteristics with repetitive patterns of behaviors, cognitive, social, communication and emotional deficits (Bakken & Høidal, 2014; Canitano & Pallagrosi, 2017; Schűtzwohl et al., 2016), and observable challenging behaviors which are possibly attributed to the person's ID or ASD rather than a psychotic disorder (Cooper et al, 2007a; McCarthy & Barbot, 2016). Even though the core symptoms of psychosis can be difficult to differentiate with the characteristics attributed to varying degrees of ID (Carthy et al., 2010), ID is not a psychiatric disorder, despite being part of the psychiatric classification system (Deb, Matthews, Holt, & Bouras, 2001a).

A person with moderate, severe and profound ID or ASD may have restricted ability to communicate or self-report the symptoms of a psychotic episode (Bakken & Høidal, 2014), which may impede an accurate definition of psychosis. These factors have presented a challenge not only in the diagnosis of psychosis but have also contributed to the lack of explicit ID and ASD psychosis definitions presented within the literature. Researchers have recognized that heterogeneity in cognitive abilities and communication skills of those with an ID and ASD has made it difficult to standardize a definition of psychosis for this population (Canitano & Pallagrosi, 2017; Doherty & Owen, 2014).

Incidence and Prevalence of Psychosis

In general, determining how many people have experienced or are experiencing psychosis can be challenging, especially for individuals with intellectual disabilities, and therefore, estimates on incidence and prevalence can vary (Bagalman & Cornell, 2018; Cooper et al., 2007a; Kildahl, Bakken, Holm, & Helverschou, 2017). Some of the challenges associated with quantifying the prevalence of psychosis in the population include: changing diagnostic criteria over time (especially for schizophrenia and affective disorders), differing diagnostic tools and instruments (across time and geography), and problems in case finding and confirmation (Perälä et al., 2007). For those with ID, the challenges are even greater, and include lack of appropriate assessment tools, difficulties in separating symptoms of comorbid disorders, and barriers for individuals with ID to self-report their symptoms (Cooper et al., 2007a; Hassiotis, Barron, & Hall, 2009; Kildahl et al., 2017). Despite these challenges, a range of studies have examined the prevalence and incidence of psychosis. This section will provide an overview of the key findings in this area.

Prevalence

The lifetime prevalence (LTP) of psychotic disorders in the general population is estimated at just above 3% (Perälä et al., 2007). As psychotic disorders can be severe and impairing, this LTP is substantial and indicates that these conditions likely have a notable impact on public health and well-being. The total LTP corresponds to an approximate LTP of 2.29% for non-affective psychotic disorders and 0.62% for affective psychotic disorders (Perälä et al., 2007). It is thought that psychosis is more prevalent in individuals with ID than in the general population (Cooper et al., 2007a; Hassiotis et al., 2009; Holden & Gitlesen, 2004b; Smiley, 2005; Welch, Lawrie, Muir, & Johnstone, 2011). For example, in Cooper et al. (2007a) in a study of more than 1000 adults with ID, the point prevalence of psychotic disorders in those with ID was found to range between 2.6% (95% CI = 1.8-3.8%) to 4.4% (95% CI = 3.2-5.8%), depending on the diagnostic criteria. Notably, these rates are significantly higher than those of the general population. In the UK general population, the 12-month prevalence was found to only be 0.4%, which is around 10 times less than the reported point prevalence of 2.6% to 4.4% (Cooper et al., 2007a). Further, the prevalence of schizophrenia specifically in the general population is approximately 1%, while the prevalence in individuals with ID is reported around 3% (Hassiotis et al., 2009; Smiley, 2005).

The prevalence of psychotic disorders in individuals with ID likely varies based on the level of ID. It was reported that the point prevalence in adults with mild ID is around 5.8%, while it is around 3.5% in those with moderate to profound ID (Cooper, Smiley, Morrison, Williamson, & Allan, 2007b; Hassiotis et al., 2009). This trend was also confirmed in Holden and Gitlesen (2004b), where it was found that psychosis was more prevalent in those with moderate ID than in those with severe or profound ID; while the difference in prevalence between those with severe ID and profound ID was minor.

In the general population, prevalence estimates have been found to vary based on a wide number of factors (McGrath, Sukanta, Chant, & Welham, 2008), and research has shown that psychosis and schizophrenia do not occur equally across all geographic and demographic groups (Kirkbride et al., 2012; Messias, Chen, & Eaton, 2007; Steel et al., 2014). For example, the prevalence of schizophrenia was found to differ across latitude and economic status, with developed countries having a median prevalence estimate of 3.3 per 1000, with less-developed countries having 2.6 per 1000 (McGrath, Sukanta, Chant, & Welham, 2008). The prevalence was also associated with migration status (McGrath et al., 2008). However, there is still uncertainty in the exact factors that impact prevalence. For instance, in McGrath et al. (2008) the prevalence of schizophrenia was found not to statistically differ between males and females, between urban and rural environments, or over time; while in Messias et al. (2007), schizophrenia was found to be more prevalent among males, with males having a 30-40% higher lifetime risk of developing schizophrenia than females. Despite this, it is clear that schizophrenia affects males and females differently, with varying ages of onset and incidence.

Gender differences in the prevalence of psychotic disorders, along with the subtype of disorder, have also been indicated in individuals with ID, however results have not been consistent across studies and therefore more research is needed in this area (Axmon, Sandberg, & Alhstrom, 2017b). Overall, further investigation in this area is warranted, as individuals with ID may differ from the general population with regards to their interaction with societal factors (Axmon et al., 2017b).

Incidence

Based on a recent international, multisite study, the crude incidence of psychotic disorders in the general population is estimated at 21.4 per 100 000 person-years (95% CI= 19.4

- 23.4) (Jongsma et al., 2018). Of all non-organic psychotic disorders, it was estimated that 78.7% of incident cases are non-affective psychotic disorders and 19.9% are affective (Jongsma et al., 2018). The average age at the first contact with a first diagnosed episode of a non-organic psychotic disorder, was 30.5 years. The first contact age is generally earlier in men (28) than in women (34) (Jongsma et al., 2018). Crude incidence rates of the first episode peaked at 61 per 100,000 person-years for men between the ages of 18 and 24, and decreased sharply after this age range. For women, the peak incidence occurred also at 18-24, however decreased more slowly afterwards with another, more minor, peak between ages 50 and 54 (Jongsma et al., 2018). Similar trends in age were also found in other studies (Kirkbride, et al. 2012; Messias et al. 2007).

In adults with ID, the two-year incidence of psychosis is 1.4% (95% CI = 0.6 – 2.6), and the first-episode incidence is 0.5% (95% CI = 0.1 – 1.3) (Cooper et al., 2007a). The incidence ratio for (first-episode) psychosis in adults with ID is 10 (95% CI = 2.1 – 29.3) relative to the general population (Cooper et al., 2007a; Hassiotis et al., 2009).

However, like prevalence estimates in the general population, the current literature on incidence estimates have shown significantly varying rates across groups (Jongsma et al., 2018; Kirkbride et al., 2012; 2017; McGrath et al., 2008; Messias et al., 2007). Specifically, incidence of psychotic disorders has been demonstrated to vary by sex (Jongsma et al., 2018; Kirkbride et al., 2012; Messias et al., 2007), age (Jongsma et al., 2018; Kirkbride et al., 2012; Messias et al., 2007), migration status and ethnicity (Bourque, vander Ven, & Malla, 2011; Jongsma et al., 2018; Kirkbride et al., 2012 ;McGrath et al., 2008), and geographical region (Jongsma et al., 2018; Kirkbride et al., 2012; 2017; Messias et al., 2007; McGrath et al., 2008). Geographical region variations include across countries and latitudes, along with local variations from urban to

rural regions (McGrath et al., 2008). Socio-economic factors may also impact incidence (Jongsma et al., 2018; Kirkbride et al., 2012).

Notably, individuals with schizophrenia have a two- to three-fold increased risk of death relative to the general population (McGrath et al., 2008). As approximately 7 individuals out of every 1000 may be affected by this condition (McGrath et al., 2008), and it co-occurs with ID three times more than in the general population (Welch et al., 2011), the burden on health is considerable. Overall, while it is clear that there is a degree of heterogeneity in the incidence of psychotic disorders globally, both in the general population and in those with ID (Axmon et al., 2017b; Holden & Gitlesen, 2004b; Steel et al., 2014) further research is needed to examine the impact of the factors that may be responsible for this heterogeneity.

Importance of studying Psychosis in Intellectual Disabilities

Advances in our understanding of psychosis in intellectual disabilities and comorbidity between behavioral profiles and psychiatric disorders may help to identify diagnostic overshadowing i.e. attributing the symptoms of mental ill-health to a person's intellectual disability behavioral profile (Canitano & Pallagrosi, 2017). Psychotic episodes may create a disorganized, frightening, isolated and socially withdrawn environment (Bakken & Høidal, 2014), in which the person with ID and ASD may not have the cognitive, social, emotional and communication capabilities to seek help. Research that focuses on observations of the non-verbal communications and suspected psychotic symptoms of individuals with ID may help to differentiate psychosis from the person's behavioral profile and thus help to improve the diagnostic system (Bakken & Høidal, 2014). In the absence of further research into psychosis and coexisting behaviors associated with ID, there is risk for individuals with ID to receive the incorrect mental health diagnosis (Bakken & Høidal, 2014), and subsequently an inappropriate

ineffective treatment (Allen, 2008). Any treatment outcomes must be considered within the context of improved quality of life, daily functioning and provide relief of physical and perceived emotional pain (Allen, 2008). Implications extend to the provision of mental health care for the person with ID or ASD, who often fall between services, particularly as they transition into adulthood (Selten, Lundberg, & Magnusson, 2015).

Research into psychosis and ID has important implications for psychiatric research. By developing new procedures to detect and identify psychosis we can advance our knowledge of the pathways from genotype to clinical phenotype, which are essential to inform new classification systems and to develop innovative therapeutic treatments (Doherty & Owen, 2014).

Recent research has suggested that prescription of psychotropic medication prescribed to adults with ID results in an overmedicated population with the prescription of antipsychotics drugs (Axmon, Kristensson, Ahlström, & Midlöv, 2017a; McNamara et al., 2017; O' Dwyer et al., 2017; Schűtzwohl et al., 2016) and in some cases the drugs may be ineffective (McNamara et al., 2017; O' Dwyer et al., 2017) and cause adverse effects (O' Dwyer et al., 2017). Prescription of psychotropic medication needs to be re-assessed to evaluate their over use and effectiveness.

Difficulties of diagnosis of Psychosis in Intellectual Disabilities

The identification of psychosis in individuals with intellectual disability (ID) presents considerable challenges. Some of these challenges consist of the limited number of appropriate assessment tools, the presence of dual diagnosis of ID and psychiatric disorders, the level and severity of ID and the difficulty in self-report of diagnostic and/ or psychotic symptoms (Helverschou, Bakken, & Martinsen et al., 2011; Underwood, Kumari, & Peters, 2016). One of the cautionary aspects on which clinicians are particularly advised, is to be careful and pay

special attention in the diagnoses of schizophrenia in the presence of ID (Feinstein, Eliez, Blasey, & Reiss, 2002). The section below describes the complexity and difficulty in diagnosing psychosis in individuals with ID.

Diagnostic Systems and Assessment tools

Several researchers have reported a higher prevalence of psychosis in adults with ID compared to the general population (Buckles, Luckasson, & Keefe, 2013; Cooper et al. 2007a). However, existing diagnostic systems that measure the diagnoses in individuals with ID may not be fully compatible when making a psychiatric diagnosis in them (Watson, 2005). This may be related to the lack of one standardized criterion for psychiatric diagnosis across the whole spectrum of ID (Cohen-Kettenis & Pfäfflin, 2010). Therefore, typical diagnostic systems are not always useful for individuals with intellectual disabilities. Further, the heterogeneity in abilities and communication skills among adults with ID is varied. Some features might not always be apparent, or may be difficult to elicit, making the diagnosis difficult, particularly in those who have severe intellectual disability, and impaired communication (Wing, Gould, & Gillberg, 2011). This explains the reasons why the evidence-based knowledge on the assessment and diagnosis of psychosis problems in individuals with ID is still under-researched (Perry et al., 2018).

It has also been noted that a number of limitations with classification systems such as the *Diagnostic Manual-Intellectual Disability* or *Diagnostic Criteria for Psychiatric Disorders for Use with Adults with Learning Disabilities/Mental Retardation* still exist (Madhavan, 2018). In addition, factors such as gender differences have also been reported as potentially explanatory predictors in understanding psychiatric ill health in the general population (Axmon et al., 2017b; Cohen-Kettenis & Pfäfflin, 2010). But given the social differences in how individuals with ID

are treated in society with regards to accessibility, attitudes and perceptions, this association between gender and psychiatric disorders in individuals with ID will not apply similarly as in the general population (Cohen-Kettenis & Pfäfflin, 2010). What is imperative in the development of assessment tools and systems is a detailed description of specific clinical features of psychiatric illness, with special reference to where these may differ from their presentation in the general population without disabilities. Moreover, a stronger emphasis on reports from support staff and caregivers is often required.

Some tools do aim at screening for psychiatric disorders in individuals with ASD and ID such as the Psychopathology in Autism Checklist (PAC; Helverschou, Bakken, & Martinsen, 2009). The PAC is a behavior checklist that is designed for completion by caregivers or family members, and therefore no general knowledge of psychiatric disorder is required. However, it is unclear whether or not such subjective knowledge influences final scores. Another instrument designed to identify psychiatric symptoms in individuals with ID is the Mini Psychiatric Assessment Schedules for Adults with Developmental Disabilities (Mini PAS-ADD; Prosser et al., 2002; Moss & Hurley, 2014). However, the Mini PAS-ADD may not be sensitive enough to detect symptoms in individuals with no or very limited speech.

The presence of dual diagnosis

Similar deficits exist between developmental disabilities (such as ID and ASD) and psychosis. Therefore, psychosis and developmental disabilities have overlap (Matson, Mayville, Lott, Bielecki, & Logan, 2003). Intellectual disability and psychosis occur 300% more often than would be expected by chance (Cooper et al., 2007b; Turner, 1989). Some note that the psychosis demonstrated by those with ID may be subtly different (Welch et al., 2011). In adulthood, negative symptomology of psychosis shares some similarities with autism spectrum

disorder (Skokauskas & Gallagher, 2010). These populations warrant intervention to address several areas of negative symptoms, which are largely similar to those addressed as adaptive functioning deficits, such as deficits in communication, socialization, daily, adaptive living skills, and deficits in the management of behavior problems.

The manifestation of correlated symptoms of comorbid disorders including psychopathologies other than cognitive impairments have been recognized in individuals with ID (Kozlowski, Matson, Sipes, Hattier, & Bamburg, 2011). It is also evident in the literature that the presence of ID reduces the diagnostic significance of behaviors that normally constitute psychiatric symptoms (Holden & Gitlesen, 2004b). Research often discuss the terms psychosis and ID separately, but make no mention of their possible interrelationship (Allington-Smith, 2006; Clarke, 2006). It is important to review the extent of the correlation between comorbid disorders to address the difficulty in clear and reliable diagnosis of psychotic symptoms.

Similarities in the etiology of challenging behavior and psychiatric disorder

Often, challenging behavior is referred to as the severe level of behavior problems among individuals with ID (Emerson et al., 2001). In particular, aggression towards others, extreme temper tantrums, screaming or shouting, and self-injury are examples of behaviors that may be challenging. A number of authors have suggested that such behavior problems may be indicators of psychiatric disorders in individuals with intellectual disability (Emerson et al., 2001; Moss & Hurley, 2014). Family members, support staff and carers tend to excessively manage these behaviors that may result in social isolation and restricted opportunities for taking part in ordinary social and societal activities. This makes it very difficult to establish a dignified life situation for individuals with disabilities as endorsed by United Nations Convention of the Rights of People with Disabilities (United Nations General Assembly, 2006). Therefore, the

emerging consensus may be accurate that individuals with severe to profound ID may be more prone to psychiatric illness, because they are unable to live normal lives (Munir, 2016). In spite of the parallels, the relation between behavior problems and psychiatric disorders is not entirely clear, given the mixed empirical results that indicate that perhaps studies adopted varied methodologies. What we know is that psychiatry refers to the study of the mind and treatment of disorders of the mind, including but not limited to mood, personality, development and cognition. Psychosis on the other hand, is understood to be a symptom and essentially a flawed ability to perceive reality with the most commonly discussed symptoms being hallucinations and delusions but, this is not all necessarily experienced in a negative way. It is worth considering that in diagnosing psychiatric illness, it is important to differentiate which symptoms can be part of such an illness, and which can be explained by the intellectual disability.

Severity of Challenging behaviors

In recent years, maladaptive and challenging behaviors are increasingly explained by psychiatric disorders, however, because of little or total lack of speech, the diagnosis relies predominantly on more tangible behaviors (Emerson et al., 2001). However, diagnosing psychiatric disorders in individuals with ID, particularly those with severe and profound ID, is more problematic. Individuals with milder levels of disabilities can use self-report measures and can be diagnosed using standard criteria with little modification, but for those with moderate and severe disability, diagnosis is challenging. The severity of behavior problems relates to signs and symptoms common in psychiatric illness such as social withdrawal, excessive agitation, lack of concentration, stereotyped movement disorders, abnormal sleep, and certain other behaviors (Kelly, 2013). These symptoms have been described as the expression of ‘diagnostic

overshadowing', where the diagnostic symptoms are an underlying result from possible brain damage, rather than symptoms of an illness (Mason & Scior, 2004).

The level and degree of intellectual disability

Studies show controversial evidence as to whether or not psychiatric illness is more common among individuals across the spectrum of mild to profound ID (Hove & Havik, 2010). Current research indicates that schizophrenia can be reliably diagnosed in adults with mild ID (Deb et al., 2001b). For example, researchers made a comparison to the general population and there appears to be a higher rate of schizophrenia among adults who have a mild intellectual disability (Kessler, Chiu, Demler, & Walters, 2005). However, studies report the overall rate of psychiatric illness in adults with ID does not differ significantly from that of individuals without ID in the general population if diagnoses like behavioral disorder, personality disorders, ASD, and Attention-deficit/hyperactivity disorder (AD/HD) are excluded (McGough et al., 2005). But the diagnosis of schizophrenia in those with an IQ less than 45 may be difficult or impossible, because of the inability to do an in-depth verbal interview (Friedlander & Donnelly, 2004). In particular the difficulty in diagnosing schizophrenia is of concern, specifically in those with a moderate or more severe intellectual disability (Deb, Thomas, & Bright, 2001b). The diagnosis is based upon the presence of a number of complex subjective symptoms, delusions and thought broadcasting. The diagnosis of psychosis not otherwise specified (NOS) in individuals in particular is associated with moderate or severe ID (Friedlander & Donnelly, 2004).

While psychiatrists tend to use a cluster of symptoms or behaviors that relate with each other, also referred to as syndromic classification, some clinicians believe that the approach of behavioral classification that is more prevalent in the clinical psychology literature may be more appropriate for use in adults with severe intellectual disability (Drake et al., 2001). As a result,

diagnoses of affective disorders are even possible in profound intellectual disability, due to observable behavioral elements of such disorders (Drake et al., 2001).

Difficulties in self-report

Generally, individuals with ID have significant limitations in verbal ability with increasing levels of the degree of ID. However, psychiatric assessment in ID often requires knowledge through verbal expression of the individual's previous functioning, and that can be a very complicated and time-consuming process in individuals with severe to profound ID. It involves investigating and identifying qualitative changes in symptoms related to the level of ID and interpreting atypical symptoms. In addition, investigating of conventional symptoms of psychiatric disorder is also crucial (Helverschou et al., 2011). Consequently, a certain level of communicative ability is needed to describe such symptoms.

Clinical reviews do provide valuable information about the identification, diagnosis and outcome of psychotic symptoms in individuals with low verbal abilities (Friedlander & Donnelly, 2004). In the absence of limited validated tools for assessment of psychosis in individuals with ID, it is noted that conventional assessment tools can be useful in such assessments. However, a full compensation for a lack of self-report is not always possible when relying on conventional assessment tools. It is possible though to partly compensate for lack of self-report by using multiple informers, a process sometimes referred to as triangulation (Yin, 2013). In this instance, it involves including family and professional caregivers as informers, instead of the challenging self-report of the person with ID. As such, a systematic assessment can be initiated with in-depth interviews with family members and caregivers, as well as direct observation by clinicians.

Some anxiety symptoms can be difficult to assess in non-verbal individuals, like excessive worry, unreasonable thoughts, and verbal reports of physiological signs (Bailey & Andrews, 2003). Therefore, the identification of psychiatric disorders in this group is reported to be difficult because of inherent communication and cognitive deficits. As such, giving symptoms a higher score in individuals with more severe ID in order to increase total scores is hardly justified, as there is no gold standard (Mungkhetklang, Crewther, Bavin, Goharpey, & Parsons, 2016). One possibility might be to improve the observational skills of caregivers. However, for behavior to be observed, it must have some strength and clarity related to the specific behavioral symptoms.

Many psychiatric symptoms are a subjective phenomena, for instance hearing voices, and not available to observers unless the individual with ID has the necessary verbal ability to report such experiences. As a result, it is not feasible to reliably diagnose in individuals who are non-verbal or those with limited communication skills. Where an individual's level of functioning and disorganized behavior make self-report impossible, no observer is able to report such symptoms. Treating observational data as interchangeable with self-report data would have led to a serious risk of symptoms being overlooked. Research within behavior analysis indicates that verbal behavior plays a key role in the development and maintenance of psychopathology, not only in anxiety and depression (Tone, Garn, & Pine, 2016).

It is clear that to address the challenges in the diagnoses of psychosis in individuals with ID, an accurate diagnosis will likely not be made from a one-time encounter by a professional. Instead, the diagnosis will rather evolve over time, because a key component of psychosis is based on internal experiences and their description. Thus, a comprehensive assessment and a clear description of the diagnostic criteria used is needed.

Risk Factors of Psychosis

Psychotic disorders are heterogeneous, and as such, a wide range of risk factors and protective factors have been investigated (Radua et al., 2018; Heckers, 2009; Hassiotis et al., 2009). As incidence rates vary significantly across geography and demographics, risk factors are also likely to vary across time and space (McGrath et al., 2008). While many potential risk factors for psychosis have been identified, for some factors the evidence is not conclusive to date. Below is an examination of the potential risk factors for psychosis, and an indication of the level of evidence for each is provided. The risk factors are divided into four broad categories, based on those in Dean and Murray (2005) and in Heckers (2009): i) baseline risks, ii) early-life risks (in utero and during birth), iii) childhood risks, and iv) risks that develop later in life and those that occur close to the incidence of psychosis. It is important to note that for individuals with ID, the risk factors have not been as thoroughly investigated as for the general population (Axmon et al., 2017b; Cooper et al., 2007a; Hassiotis et al., 2009; Smiley, 2005), and as such the risk factors are sometimes extrapolated from those of the general population (Hassiotis et al, 2009). Furthermore, many risk factors for psychosis are also risk factors for intellectual disabilities so it can be difficult to separate the impacts of each (Hassiotis et al., 2009).

Baseline Risks

The baseline risk relates to the level of risk that an individual may have due to their family history, genetics, and place and time of birth. For psychotic disorders, the risk topology for the general population is generally viewed as a complex interaction between environmental risk factors and susceptibility genes (Dean & Murray, 2005; Heckers, 2009; Radua et al., 2018; van Os, Rutten, & Poulton, 2008) and this view is maintained for individuals with intellectual disabilities (Hassiotis et al., 2009).

For schizophrenia in particular, genes are necessary but not the sole operator in developing the condition (Dean & Murray, 2005). However, genetics do play a substantial role in an individual's probability of developing schizophrenia (Heckers, 2009; Messias et al., 2007). For example, the risk of an individual presenting with a psychotic disorder increases several fold if a first-degree relative also has a history with a psychotic disorder (Heckers, 2009). Several genes are being investigated in terms of their link to psychosis (Hassiotis et al., 2009).

Baseline risk factors aside from genetics include gender, culture, residence type (urban versus rural), ethnicity, and immigration status (Dean & Murray, 2005; Heckers, 2009; Messias et al., 2007). In general, men are at increased risk for developing schizophrenia, with a 30-40% higher risk than women (Messias et al., 2007). More research is needed to identify whether this increased risk holds for individuals with ID, however current research does suggest that there are gender differences in this group as with the general population (Hassiotis et al., 2009).

Early-Life Risks (in utero and during birth)

Many risk factors that occur in utero or during birth have been well documented in the general population (Dean & Murray, 2005; Heckers, 2009) and have also been suggested for those with intellectual disabilities (Hassiotis et al., 2009). These risk factors include obstetric complications, such as intrauterine growth restriction (also called fetal growth retardation) or hypoxia, pre- or post-natal infections, maternal malnutrition and maternal stress (Dean & Murray, 2005; Heckers, 2009; Messias et al., 2007). These complications can impact the process of normal brain development (Heckers, 2009).

Childhood Risks

A number of risks that can occur during childhood have been identified in the general population, and may also impact individuals with ID. These include the broad categories of traumatic life events (TLEs) or adverse events or experiences, developmental abnormalities, and infections and immune responses.

In Khandaker et al. (2018) it was reported that exposure to infections can lead to an increased risk of developing non-affective psychoses (with a hazard ratio for an infection during the first year of life of 1.19, with a 95% confidence interval of 1.06 to 1.33). Other studies have linked meningitis to an increased risk (approximately 5x) of developing psychosis and schizophrenia (Messias et al., 2007), and shown that individuals with Toxoplasmosis Gondii antibodies have a higher prevalence of schizophrenia (Messias et al., 2007). In general, it is thought that infections during early childhood may impact typical neurodevelopment (Khandaker et al., 2018).

Childhood developmental delays or abnormalities have also been associated with an increased risk in developing schizophrenia and psychosis (Hassiotis et al., 2009; Khandaker et al., 2018; Messias et al., 2007). The relation between psychosis and IQ has been investigated thoroughly, and studies suggest a linear association between premorbid IQ and schizophrenia (Khandaker et al., 2018). There may be a common risk that links low IQ and psychosis (for example, abnormal brain development), or the link may be causal (Hassiotis et al., 2009). Future research is needed in this area. As early childhood infections are associated with both risk of lower IQ and developing psychosis, these associations may also be causal (Khandaker et al., 2018).

Typically developing children who experience traumatic life events (TLEs) including abuse, trauma, or adverse experiences have increased risk of developing psychosis (Dean & Murray, 2005; Gibson, Alloy, & Ellman, 2016; Radua et al., 2018). Children who have experienced TLEs are at increased risk of psychotic disorders, and such TLEs have been shown to be one of the most robustly associated (environmental) risk factors for psychosis (Bendall, Alvarez-Jimenez, Nelson, & McGorry, 2013; Gibson et al., 2016; Varese et al., 2012). Specifically, the odds of developing a psychotic disorder or psychotic symptoms in individuals with a history of TLEs are between 2.78 and 11.50 (where the value varies based on TLE type and methodology) (Gibson et al., 2016; Varese et al., 2012). Notably, there has been a demonstrated dose-response relationship between TLEs and psychosis (Gibson et al., 2016). Similarly, life events have also been significantly associated with the development of schizophrenia in individuals with ID (Hassiotis et al., 2009; Tsakanikos, Bouras, Costello, & Holt, 2007).

Risks Later in Life

The risks discussed below include risks that occur later in life, and those that occur close to the transition into psychosis and during the symptomatic risk stage. In the general population, studies have shown that there is a robust link between sleep dysfunction and psychosis, but more investigation is needed to establish a causal association (Reeve, Sheaves, & Freeman, 2015). Exposure to drugs, especially marijuana, or drug abuse, are also suggested as risk factors (Dean & Murray, 2005; Hassiotis et al, 2009; Heckers, 2009) for the general population and for individuals with ID. A range of studies across the world have shown higher risk, ranging from 2 times up to 25 times higher for typically developing individuals using cannabis (Messias et al.,

2007). However, this risk is difficult to study in individuals with ID since this population has low rates of usage (Cooper et al., 2007a).

Smoking has been associated with a risk of psychosis in the general population and in individuals with ID, as has visual impairment (Cooper et al., 2007a). However, in individuals with ID, not having comorbid epilepsy was found to correspond with psychosis; while in the general population the opposite appears to be true (Cooper et al., 2007a).

The most significant risk factor for the general population, with the strongest level of evidence of association with psychosis, is the existence or emergence of sub-threshold psychotic symptoms (Heckers, 2009; Yung, Phillips, Yuen, & McGorry, 2004). Individuals already experiencing sub-threshold symptoms, along with a family history of psychotic disorders, were categorized as being at 'ultra-high-risk' (UHR) for developing schizophrenia and other psychotic disorders (Yung et al., 2004). It was found that 34.6% of the individuals at UHR developed obvious psychotic symptoms within 1 year (i.e. the transition rate to disease was 34.6%) and 39.4% developed psychosis eventually.

The identification of such high-risk individuals is of special interest, as this group may benefit in particular from early interventions that aim to prevent the onset of psychosis (Yung et al., 2004). Another recent review found that those individuals with prodromal symptoms were at greater risk for developing a psychotic disorder; however, less than 40% of those actually did (Fusar-Poli et al., 2013). For youths (under age 18) with intellectual disabilities, the early onset of psychotic symptoms led to a later diagnosis of schizophrenia or schizoaffective disorder in more than half of the individuals (Friedlander & Donnelly, 2004) suggesting transition rates for young people with ID may be higher than rates in the general population; but it should be noted

that the sample size in this study was small. Overall, however, transition rates for those at high risk have been highly variable in the literature (Conrad et al., 2017) and more investigation of the role of negative symptoms (as opposed to solely positive symptoms) may provide useful clinical information (Fusar-Poli et al., 2013).

Assessment of Psychosis

As discussed above, an accurate diagnosis of psychotic disorders in individuals with ID is difficult partly because of the cognitive and language difficulties, making it difficult for the individual to describe psychotic symptoms (Helverschou et al., 2011; Myrbakk & von Tetzchner, 2008). However, behavioral phenotypes have been used in identifying psychotic disorders among individuals with ID. For instance, disorganized behavior has been described as potentially being equivalent to disorganized thought or speech in individuals without ID (Bakken, Friis, Løvoll, Smeby, & Martinsen, 2007; Bakken, Eilertsen, Smeby, & Martinsen, 2009; Kildahl et al., 2017).

It has been recommended that clinicians gain knowledge about the person's previous functioning and modes of communication for those with ID referred for concerns of psychosis (Kildahl et al., 2017). This information in addition to behavioral observations will allow the clinical to investigate conventional symptoms of psychiatric disorders (Helverschou et al., 2011). Furthermore, combined knowledge of ID and psychosis/psychiatric disorders are invaluable to the assessment (Kildahl et al., 2017). Although general assessment tools are helpful, they warrant careful interpretation and inclusion of multiple informers (e.g., caregivers, family or other professionals), as this may help to attain a more accurate diagnosis (Kildahl et al., 2017).

Generally, clinicians utilize a combination of structured diagnostic interview as well as assessments of positive and negative symptoms. For example, a structured diagnostic interview

like the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) as well as the use of a structured clinical scale for assessment of positive and negative symptoms such as the Positive and Negative Syndrome Scale (PANSS) or Brief Psychiatric Rating Scale, which have been used in a case study (Kildahl et al., 2017).

Tools aimed at screening for and aiding in the diagnosis of psychotic disorders have been developed. These include the Assessment of Dual Diagnosis (ADD; Matson, 1997), the Diagnostic Assessment for the Severely Handicapped-II (DASH-II; Matson, 1995), and Psychopathology Instrument for Mentally Retarded Adults (PIMRA) (Matson, Kazdin, & Senatore, 1984) among others. The ADD is used for assessment of individuals with mild or moderate intellectual disabilities, while the DASH-II is used with individuals with severe or profound intellectual disabilities. The ADD is a parent/caregiver report measure which contains 79 items and measures comorbid psychopathology such as mania, depression, anxiety, post-traumatic stress disorder (PTSD), substance abuse, somatoform disorders, dementia, conduct disorder, pervasive developmental disorder, schizophrenia, personality disorders, eating disorders, and sexual disorders.

The DASH-II is an 84-item parent/caregiver report measure which assesses psychopathologies such as anxiety, depression, mania, pervasive developmental disorder/autism, schizophrenia, stereotypies, self-injury, elimination, eating, sleeping, sexual, organic, and impulse control. The PIMRA is a 56-item parent/caregiver report measure which assesses schizophrenia, affective disorder, psychosexual disorder, adjustment disorder, anxiety disorder, somatoform disorder, and personality disorder and inappropriate adjustment.

The Mini Psychiatric Assessment Schedule for Adults with Developmental Disability - Mini PAS-ADD (Prosser et al., 2002) and the PAS-ADD Checklist (Moss et al., 2002) have been

used to assess psychotic disorders in individuals with ID. The PAS-ADD checklist consists of 27 items that can be used to help clinicians recognize mental health problems, including psychotic disorders. The Mini PAS-ADD is more elaborate requiring more extensive training in its administration and allows clinicians to gage the presence of psychosis. The Mini PAS-ADD comprises of 86 psychiatric symptoms and generates subscale scores on depression, anxiety, hypomania, obsessive-compulsive disorder, psychosis, unspecified disorder, and pervasive developmental disorders. Both of these measures have been shown to be reliable and valid measure for assessing psychiatric disorders in adults with ID (Prosser et al., 2002; Moss et al., 2002).

Recommendations for the assessment of psychosis in individuals include the following. First, screening tools should be used in combination with the International Statistical Classification of Diseases and Related Health Problems (ICD-10; World Health Organization, 2004) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013). Second, a biopsychosocial approach should be taken, therefore a multidisciplinary team, including a psychiatrist, psychologist and physician is recommended. Third, medical conditions should be assessed. It is important to assess for pre-existing conditions that may predispose an individual to psychosis. Medication side-effects and drug interactions need to be evaluated. It must be determined if certain symptoms are related to substance use. Assessing for medical conditions may include a complete physical, blood tests and brain scans. Certain medical conditions may display similar symptoms to psychosis including neurological diseases (e.g. Parkinson's disease, Huntington's disease), delirium, brain tumors or cysts, dementia/Alzheimer's disease, HIV and other infections that affect the brain, some types of epilepsy, stroke, hyponatremia, hepatic encephalopathy, uremia, hyperadrenalism,

or Wilson's disease. Genetic disorders that may have a predisposition to psychosis should also be considered, including Velocardiofacial syndrome, Prader-Willi syndrome, Turner's syndrome, Phenylketonuria, or Klinefelter's syndrome. It is possible that psychosis has a medical cause if hallucinations are olfactory, as this may be seizure related. Where hallucinations are tactile, it may be delirium or substance abuse/withdrawal. If hallucinations occur while going to sleep or while waking up, they may be hypnogogic or hypnopompic hallucinations. Fourth, if there is no medical cause for psychosis (such as seizures), the following should be assessed through interview with significant others: Background and life history, current living circumstances, environment, history of presenting symptoms, and changes in presentation of symptoms over time or in different places or situations. Fifth, the following needs to be ruled out: developmentally-appropriate self-talk, imaginary friends, reports that are culturally normative (e.g. seeing relatives who have died) in isolation from other symptoms, and learned behavior that is adaptive to the environment. Sixth, the individual should be observed over time. Accurate diagnosis comes over time and with a multi-disciplinary team. A major reason for the identification of a psychiatric disorder, or a thorough psychiatric assessment may increase the probability of prescribing effective treatment, both pharmacological and psychological.

Pharmacological and Psychological Treatment of Psychosis in ID

There exists limited empirical evidence on the treatment of psychotic disorders in adults with ID. As such, treatment approaches are often extrapolated from research in the general population and from clinical experience. Treatment for most individuals with co-morbid mild ID and major mental illness is delivered predominantly by the mental health services (Patil, Keown, & Scott, 2013). However, inter-agency and/or intensive support approaches providing coordinated and integrated services have been associated with improved clinical outcomes in

some (Lunsky, Bradley, Durbin, & Koegl, 2008; Lunsky, Gracey, Bradley, Koegl, & Durbin, 2011) but not all cases (Martin et al., 2005).

Much like assessment, treatment takes a biopsychosocial approach, including both pharmacological and psychological treatments, which is tailored to the individual's needs. Prior to initiating treatment, it's important to conduct a risk assessment to ensure the clients safety as well as the safety of others.

Pharmacological Treatment

Pharmacological treatments for psychotic disorders include both first and second generation antipsychotic medications. Particularly, antipsychotic drugs are the most frequently prescribed of the psychotic drugs among ID population (Matson & Mahan, 2010). In terms of psychosis, they are used to treat the positive symptoms such as hallucinations and delusions. See Table 1. for a list of first and second generation antipsychotic medications.

First-Generation Antipsychotics (FGAs)

First-Generation Antipsychotics (FGAs) are also known as *typical antipsychotics*, dopamine antagonists, neuroleptics, and classic antipsychotics. These terms have evolved over the years due to historical and conceptual implications. Neuroleptics refers to the ability of a drug to cause "neurolepsis" which includes psychomotor slowing, emotional quieting, affective indifference. These symptoms were initially a reliable sign of antipsychotic efficacy; however, we now know that these effects are not required for drugs to have therapeutic action and that the presence of these symptoms predicts low treatment adherence. Dopamine antagonists act on different regions such as mesolimbic, mesocortical, nigrostriatal and tuberoinfundibular pathways.

Typical Antipsychotics is the most commonly used term in practice and is based on the view that SGA's have atypical properties (e.g., low risk of extrapyramidal symptoms [EPS]). Therefore, drugs that do not have atypical properties are referred to as typical antipsychotics. This original concept of atypicality risk (low EPS) changed to a broader definition that included efficacy for negative and cognitive symptoms in schizophrenia (Grűnder, Hippius, & Carlsson, 2009). This definition was revised after the CATIE (Clinical Antipsychotic Trials Intervention Effectiveness) trial failed to confirm that SGAs are more effective than FGAs, with the exception of clozapine for treatment-resistant schizophrenia. In order to avoid confusions regarding effectiveness in schizophrenia, the World Psychiatric Association suggested the term first-generation antipsychotics.

FGAs are the primary treatment of schizophrenia and related psychotic disorders. The use of FGAs has declined, mainly due to the increase in prescriptions of second-generation antipsychotics. However, they remain a valuable option in the treatment of psychotic disorder as they are considered less expensive. FGAs are associated with higher risk of neurological side effects such as tardive dyskinesia, extrapyramidal side effects (EPSE), and dystonia. For instance, haloperidol is effective in reducing psychotic symptoms; however, they can produce unpleasant sides effects such as drowsiness and EPSE (particularly dystonia, parkinsonism, and akathisia) which can lead to discontinuation of medication and relapse.

Second-Generation Antipsychotics (SGAs)

Second-Generation Antipsychotics (SGAs), also known as *atypical antipsychotic*s. There is a lower risk of EPS associated with the use of clozapine (Leucht, Kissling, & Davis, 2009). Atypical antipsychotics was broadened to include efficacy against negative and cognitive symptoms, lack of prolactin elevation and efficacy in treatment resistant individuals. SGAs also

block D2 receptors (like in FGAs) in addition to their ability to block 5HT2A receptors. Specifically, SGAs are known as dopamine-serotonin antagonists, due to their high affinity for 5HT2A receptors (Sadock & Sadock, 2009). Although SGAs have lower risk of neurological side effects, they have an increased risk of developing metabolic side effects such as hyperglycemia, weight gain, and dyslipidemia.

Clozapine was manufactured by Sandoz in 1959 and was the first of the SGAs to be produced. However, it was later discontinued and withdrawn in several countries following reports of severe blood reactions (i.e., neutropenia) and subsequent death of eight individuals (Crilly, 2007; Hippius, 1999). Clozapine was later re-introduced with a rigid monitoring protocol after several studies showed its efficacy and safety in treatment-resistant schizophrenia. Currently, it is used in the United Kingdom as second-line treatment for schizophrenia after a failed trial with two antipsychotic medications for an adequate time period (Farooq et al., 2011). Though, in some countries it is routinely used as first-line treatment (Tang et al., 2008; Wang & Li, 2012).

Table 1.

List of common First-Generation Antipsychotics (FGAs) and Second-Generation Antipsychotics (SGAs)

FGAs (Typical)	SGAs (Atypical)
Haldol (Haloperidol)	Clozaril (Clozapine)
Loxitane (Loxapine)	Risperdal (Risperidone)
Mellaril (Thioridazine)	Abilify (Aripiprazole)
Moban (Molindone)	Seroquel (Quetiapine)

Navane (Thiothixene)	Zyprexa (Olanzapine)
Prolixin (Fluphenazine)	
Serentil (Mesoridazine)	Invega (Paliperidone)
Stelazine (Trifluoperazine)	Fanapt (Iloperidone)
Thorazine (Chlorpromazine)	Zeldox (Ziprasidone)
Trilafon (Perphenazine)	Saphris (Asenapine)
(Droperidol)	
(Pimozide)	
(Prochlorperazine)	
(Thioridazine)	

Antipsychotics as a Treatment of Challenging Behavior and Comorbid Psychopathology in ID Population

There is a high rate of prescription of psychotropic medication, including antipsychotics, among individuals with an ID (Deb, Unwin, & Deb, 2014; Scheifes, Egberts, Stolker, Nijman, & Heerdink, 2016). In fact, there are about 25-30% of all individuals with ID using services that regularly receive antipsychotics (Brandford, 1994; Holden & Gitlesen, 2004a). This increases to 48% when you include challenging behaviors (Kiernan, Reeves, & Alborz, 1995). There are two main reasons for the use of antipsychotics among this population. First, antipsychotics are used to treat comorbid psychosis. Second, and perhaps more controversially, antipsychotics are used to manage challenging behaviors.

Studies have consistently reported that the rate of prescription of antipsychotics far exceed the expected prevalence of psychoses in individuals with ID (Perry et al., 2018;

Robertson, Emerson, Gregory, Hatton, Kessissoglou, & Hallam, 2000). For instance, of the 74% of the sample who were prescribed antipsychotics, 26% had documented evidence of psychotic features (e.g., bipolar, psychosis) whereas 48% did not (Perry et al., 2018). In a survey of 500 residents with ID, Robertson et al. (2000) reported significantly higher use of all psychotropics, especially typical antipsychotics, in those living in residential campuses (56 %), versus those living in village communities (17 %) or dispersed housing (27 %).

Furthermore, residents having good mobility, challenging behaviors, living in residential campuses, not having been diagnosed with epilepsy and not having moved to the current residence from a family home predicted higher use of antipsychotics (Robertson et al., 2000). Similarly, having a diagnosis of autism and dementia or being older were also associated with the use of antipsychotics in individuals with ID (Sheehan, Hassiotis, Walters, Osborn, Strydom, & Horsfall, 2015). Nevertheless, challenging behaviors are commonly examined as a rationale for the higher use of antipsychotics. For instance, Holden and Gitlesen (2004a) indicate that nearly 50% of individuals with ID have been using psychotropic medications in the treatment of psychiatric disorder and/or challenging behaviors in the last 20 years. As such, although antipsychotic medications are often used to manage psychosis in the general population, it is evident that adults with ID are treated at a rate far exceeding that of recorded mental illness and that individuals with ID and challenging behaviors are significantly more likely to receive antipsychotics (Sheehan et al., 2015).

As such, there is concern that antipsychotics are overused and might often be prescribed for challenging behavior in itself rather than for diagnosed mental illness, despite inconsistent evidence of efficacy (Aman, Buitelaar, Smedt, Wapenaar, & Binder, 2005; Aman, De, Derivan, Lyons, & Findling, 2002; Brylewski & Duggan, 2004; Deb, Sohanpal, Koni, Lenotre, & Unwin,

2007; Duggan & Brylewski, 1999; La Malfa, Bertelli, & Conte, 2001; Scheifes Stolker, Egberts, Nijman, & Heerdink, 2011). In fact, the most common reason for the prescription of antipsychotic medication to individuals with ID is the management of challenging behaviors (Aman, Sarphare, & Burrow, 1995; Matson & Mahan, 2010; Oliver-Africano, Murphy, & Tyrer, 2009). For example, clozapine has been shown to reduce aggression and self-injurious behavior independent of psychiatric diagnosis (Thalayasingam, Alexander, & Singh, 2004).

In a recent review of electronic case records, approximately 92% of a sample of 60 individuals with ID had been on antipsychotic medication. The vast majority of these individuals were prescribed antipsychotics to reduce challenging behaviors or psychotic symptoms; however, some were using them as a mood stabilizer or to reduce anxiety (Thalitaya, Reynolds, & Ismail, 2017). In a similar study exploring the association between prescription of psychotropic drugs, mental illness, and challenging behaviors in individuals with ID, 49% (of a sample of 33,016 adults with ID) had a record prescription of psychotropic drugs (Sheehan et al., 2015). Most antipsychotics were prescribed to individuals without a record of severe mental illness. In fact, challenging behavior was associated with the prescription of antipsychotics after adjusting for psychiatric diagnoses, suggesting that these drugs are being used to manage challenging behavior (Sheehan et al., 2015).

Commonly prescribed antipsychotics include risperidone, aripiprazole, olanzapine, chlorpromazine, clozapine, depixol, fluenthixol, zuclopenthixol, quetiapine, and benperidol (Thalitaya et al., 2017). Similar antipsychotics are reported in the literature as the most frequently reported psychotropic drugs include thioridazine, haloperidol, and chlorpromazine (Aman et al., 1995; Robertson et al., 2000) as well as risperidone, olanzapine, and quetiapine (Connor & Posever, 1998; Williams, Clark, Bouras, Martin, & Holt, 2009). There are concerns

due to whether the antipsychotics are actually effective in controlling challenging behaviors and there are a host of side-effects associated with antipsychotics. Side effects of atypical antipsychotics are commonly identified as a concern with this population (Frighi et al., 2011; Mahan et al., 2010; Matson & Mahan, 2010). Thalitaya et al. (2017) reported common side effects of weight gain, sedation, hyper-salivation, EPSE, hyperprolactinaemia, hypertension, tremors, and hyper-cholesterolaemia.

As such there are international guidelines for prescribing psychotropics for managing challenging behaviors (Deb et al., 2009) and for diagnosing mental health disorders in individuals with ID (Cooper, Melville, & Enfield, 2003; Clarke & Gomez, 1999; Fletcher, Loschen, Stavrakaki, & First, 2007). For example, in 2006, the Royal College of Psychiatrists of the UK suggested that if there is no diagnosis of comorbid mental disorders and the challenging behaviors are a result of psychosocial factors, then use of antipsychotics should be used to alleviate short term risks to self and others, while other non-pharmacological programs are implemented to manage behavior. As such, researchers and clinicians assume that there will be a decline in use of antipsychotics (due to their questionable efficacy with challenging behaviors and reported side effects) and increased use of mood stabilizers, antidepressants, anti-anxiety medications given such international guidelines (Tsiouris, Kim, Brown, Pettinger, & Cohen, 2013). Recently it has been reported that current prescribing practice of antipsychotics in persons with ID in the UK is consistent with evidence-based practice and overall prescribing practice (Paton et al., 2011).

Antipsychotics as a Treatment of Psychosis in ID Population

The diagnosis of psychiatric disorders in individuals with ID is a complex process with difficulties increasing with lower IQ scores and poorer verbal communication (Thalayasingam et

al., 2004). This would also mean that psychiatrists would have similar problems in establishing treatment refractoriness. Given the difficulty with diagnosis and treatment of psychosis in individuals with ID, it is not surprising that limited research exists. Many researchers outline the lack of studies on the efficacy of antipsychotics on schizophrenia or other psychotic disorder in individuals with ID (Duggan & Brylewski, 1999; Malfa, Lassi, Bertelli, & Castellani, 2006; Matson, Bielecki, Mayville, & Matson, 2003). There are also concerns regarding the greater risk of developing side effects and the impact of antipsychotics on learning and cognitive abilities of individuals with ID (Aman, 1993; Frighi et al., 2011; Mahan et al., 2010; Matson & Mahan, 2010).

Not only do individuals with ID receive psychotropic medications at high rates, but these drugs tend to be prescribed for many years (Yen, Lin, Loh, Shi, & Hsu, 2009), and with little or no current data collected to determine treatment efficacy (Matson & Neal, 2009). In a sample of 2,069 adults with ID, almost half of the survey sample (45%) received antipsychotic medication, 39% of which was atypical antipsychotic, and the remaining 6% typical antipsychotic (Tsiouris et al., 2013). Tsiouris et al. (2013) noted the frequent use of antipsychotics for psychosis (70%) and bipolar disorder (67%).

Although typical antipsychotics such as haloperidol or chlorpromazine are most prescribed in ID, on a long-term basis they turn out to be less effective than new antipsychotics (Malfa et al., 2006). For instance, in the abovementioned sample of 2,069 adults with ID, typical antipsychotics such as haloperidol, thioridazine, and chlorpromazine were infrequently prescribed, while atypical antipsychotics like risperidone, olanzapine, quetiapine and aripirprazole were more commonly used (Tsiouris et al., 2013). This finding is consistent with other commonly used SGAs in the literature (Frighi et al., 2011; Malfa et al., 2006; Leucht et al.,

2009). In a sample of 13 adults with mild ID and 8 with moderate ID and comorbid psychiatric disorders (with significant challenging behaviors in 10 cases), olanzapine and risperidone were well tolerated by individuals with ID and psychiatric disorders (with improvements in psychotic features), with only one case where olanzapine was discontinued due to side-effects.

In a review of the literature, Connor and Posever (1998) concluded that atypical antipsychotics appeared better tolerated than typical antipsychotics, but there is a need for more research into their clinical efficacy for individuals with ID. Despite the efficacy for some antipsychotics, a Cochrane review did not find sufficiently detailed randomized controlled trials that examined antipsychotic medication versus placebo for individuals with both ID and psychosis, specifically schizophrenia (Duggan & Brylewski, 2004).

While there is limited evidence of antipsychotic medications, Clozapine has been shown to have a good response on treatment resistant individuals with ID and DSM-IV diagnosis of schizophrenia, schizoaffective disorder, bipolar disorder, delusional disorder or other psychotic disorders (Ayub, Saeed, Munshi, & Naeem, 2015; Chakos, Lieberman, Hoffman, Bradford, & Sheitman, 2004; Farooq et al., 2011; Malfa et al., 2006; Thalayasingam et al., 2004; Singh, Singh, Kar, & Chan, 2010). When at least two antipsychotics are not effective in treating the symptoms of psychosis, it is labelled as treatment-resistant psychosis. Individuals with ID who also suffer from psychosis are at a higher risk of developing treatment-resistant psychosis (Ayub et al., 2015). The extent of treatment resistance in individuals with ID is unclear (Ayub et al., 2015). Much of the evidence for treatment-resistance psychosis in ID is based on the fact that low IQ is a predictor of poor prognosis in psychosis and one manifestation of poor prognosis is treatment resistance (Thalayasingam et al., 2004).

A recent Cochrane review conducted by Ayub and colleagues (2015) revealed poorly designed randomized controlled trials (RCTs) that examined the efficacy and side effects of clozapine in individuals with ID and psychoses. Of 1224 titles and abstracts screens, 38 articles were initially included. However, these articles were subsequently excluded as they did not meet the inclusion criteria. Specifically, these studies were not RCTs. This makes sense as individuals with ID are a very heterogeneous population and psychiatric disorders are difficult to diagnose, which makes randomized controlled trials even more difficult to conduct. Nevertheless, small studies have shown that clozapine appears to efficacious and safe for individuals with ID (Antonacci & de Groot, 2000; Thalayasingam et al., 2004). Thalayasingam et al. (2004) found that clozapine may be used to effectively treat either refractory schizophrenia or bipolar affect disorder in individuals with ID. They highlighted that the dose of clozapine was comparable to those without ID and the effectiveness did not appear to diminish over time.

In line with the international guidelines, careful monitoring of side effects is recommended (Thalayasingam et al., 2004). The effect of psychotropic medication can be different in individuals with ID; that is, antipsychotics can have different (desired and undesired) side effects in different individuals. For instance, individuals with ID are reportedly more prone to side effects (Ayub et al., 2015). Common side effects of the use of clozapine include anemia and leukocytosis, drowsiness, hypersalivation, tremors, syncope, disturbed sleep or nightmares, restlessness, hypokinesia or akinesia, agitation, sedation, seizures, rigidity, akathisia, confusion, fatigue, insomnia, and hyperkinesia (Millar, 2000). Clozapine is also associated with weight gain (Leucht et al., 2009).

Psychological Treatment

Treatment models exist for individuals with comorbid major mental illness and ID. One of which is Assertive Community Treatment (ACT), which was originally designed to support individuals with severe and enduring mental illness (Herman, 2014). The main goals of ACT include maximizing medication compliance, minimizing relapse, meeting basic social and occupational needs, enhancing quality of life, improving social and vocational functioning, promoting independent living skills, reducing carer burden and facilitating community integration (Martin et al., 2005). Research has indicated that benefits are mixed (Balogh, Ouellette-Kuntz, Bourne, Lunsky, & Colantonio, 2008). Raftery et al. (2006) provided an intensive personalized support program for individuals with mild ID and co-morbid psychosis over an 18-month period.

With regards to ecological treatments, these approaches are largely psychoeducational, tailored to particular presentations and levels of intensity. These approaches often target psychosis in a typically developing population, as opposed to in individuals with ID or developmental disabilities. There are no manualized approaches, but instead a variety of strategies are implemented together. Due to the idiopathic nature of psychosis, this approach is appropriate.

With regards to behavioral treatments, Cognitive Behavior Therapy for Psychosis (CBTp) has been implemented for typically developing individuals with psychosis. The Cognitive Behavior Therapy model (combining cognitive exercises and behavioral strategies) has been extended for use with this population. In many ways, the standard CBT approach has been adjusted for use with psychotic thoughts (e.g., delusions, hallucinations). With regards to negative symptoms, a psychoeducational approach is taken, which focuses on behavioral support and traditional skills training. For positive symptoms, a more traditional CBT approach is taken,

which focuses on identifying patterns and thoughts, and opting not to act upon them. The CBT package is not very different to traditional CBT, in that it focuses on both observable behavior and covert behavior. Despite many programs practicing this model, there is not a formalized treatment package available. Much of the research literature is conceptual and practice-based.

Morrison and Barratt (2010) conducted a Delphi study, which highlighted some of the key components of CBTp. It was found that there was not a clear consensus regarding the essential elements of treatment (Morrison & Barratt, 2010). No CBTp package has been found to consistently improve outcomes for individuals with ID and psychosis. Treatment packages that exist for comorbid ID/ASD are not well-defined and are unclear in how they differ.

Support of CBTp for psychosis ranges from supportive to little or no support. Over 30 RCTs demonstrated positive outcomes for CBTp on positive and negative symptoms of schizophrenia (Wykes, Steel, Everitt, & Tarrier, 2008). In their review, Jauhar et al. (2014) found a small therapeutic effect for CBTp. In contrast, a meta-analysis of highly-controlled CBTp found that CBTp does not reliably, if ever, lead to significant outcomes when compared to controls (Jones, Hacker, Cormac, Meaden, & Irving, 2012; Lynch, Laws, & McKenna, 2010; Newton-Howes & Wood, 2013). Various scales have been developed for use in CBTp, including the Cognitive Therapy for At Risk of Psychosis Adherence Scale (Bell et al., 2008), the Cognitive Therapy for Psychosis Adherence Scale (Rollinson et al., 2008), and the Cognitive Therapy Scale for Psychosis (Haddock et al., 2001). There is some evidence that CBTp can be effective in psychosis (with and without ID), though support is very limited. Future research is needed to determine the effectiveness of CBTp in individuals with ID and psychosis.

Support for Acceptance and Commitment Therapy for Psychosis (ACTp) ranges from having some benefit to minimal benefit in the general population. The approach found that there

were some improvements displayed, though not much over psychosocial comparative treatment in typically developing individuals (Shawyer et al., 2017). Bach and Hayes (2002) found positive improvements compared to controls on self-report data in typically developing individuals. The ACTp approach is still in formative stages, though nothing to suggest as of yet that it provides anything beyond what CBTp offers. There are little standardized measures used in ACTp. ACTp is highly experimental at this point, without many well-controlled trials. Future research is needed on ACTp in the typically developing population, as well as expanding this research to include individuals with ID and psychosis.

In summary, ecological treatment models for psychosis (with or without developmental disabilities) do not lead to reliable differences in well-controlled trials. Some studies that indicate improvements with regard to self-reported data, though these are not highly-controlled studies. Ultimately, these studies suggest these approaches lead to arguably small effects on real-world outcomes (e.g., hospital readmissions, symptom counts). No studies exist that directly compare CBTp to ACTp. As can be seen, the psychological treatment of psychosis in individuals with ID is an area where much more research is needed. Predominantly, treatment is pharmacological and therefore, research on psychological treatments are warranted.

Recommendations for Treatment

Recommendations for the treatment of psychosis in individuals include the following. First, the medication type that the individual is prescribed needs to be considered. There needs to be a focus on balancing the individual's needs with treatment and the side effect profile of the medication. Second, regular physical health checks, including cardiovascular and endocrine review should be conducted, for example, an ECG prior to starting antipsychotics and at regular intervals thereafter is useful to monitor any ECG abnormality (like QT prolongation). Third,

medication needs to be monitored. This includes monitoring the benefit and response, as well as the side effects, and the possibility of reducing medication over time and as appropriate. Fourth, clinicians need to familiarize themselves with existing guidelines, such as the National Institute for Clinical Excellence (NICE) guidelines. Fifth, a full diagnostic evaluation with clear description of psychotic symptoms should be conducted. Sixth, there should be a clear statement outlined of the risks and use of anti-psychotics, given the side effects. Seventh, informed consent to treatment needs to be given. Eighth, behavioral supports and therapy should be given, where appropriate.

Future Directions for Research

Research in this area is difficult as the literature is limited by inconsistent definitions, use of small or highly selected samples (Sheehan et al., 2015). Therefore, future researchers are encouraged to better define inclusion criteria (e.g., symptoms, adaptive functioning). Moreover, researchers should focus on RCTs (with double-blind vs. placebo or other medications) for clinical evidence to guide the medication for this population, especially given its use for those with challenging behaviors. Although pharmacotherapy is necessary to alleviate the symptoms of psychiatric disorders, it is only part of a coordinated comprehensive treatment plan.

There is limited research into cognitive impairment related to ID and psychotic disorders (McCarthy & Barbot, 2016), and as such further research is required to enable a better understanding of psychosis experienced by a person with ID. Further evidence is required to initiate effective, suitable treatment based on strong empirical evidence (McCarthy & Barbot, 2016).

Additional research is required to provide information about the extent to which existing support systems meet the needs of adults with ID with mental health disorders (Schűtzwohl et al., 2016). Research that contributes relevant information to the literature regarding mental health service provisions for adults with mild, moderate and profound ID is essential to guiding future policies. By creating a greater awareness of psychosis and the related genetic and environmental factors (Doherty & Owen, 2014; McCarthy & Barbot, 2016) we may help to accumulate evidence that could support high quality clinical practice for those with ID and ASD (Allen, 2008; Canitano & Pallagrosi, 2017). Research evaluating a range of support systems would allow for comparison and consequently an improved understanding of the fundamental factors which contribute to an effective service provision for individuals with an ID or ASD who are diagnosed with psychotic mental health problem (Schűtzwohl et al., 2016). Further research into psychosis and ID could focus on support for health care practitioners, carers and individuals with ID in reducing antipsychotic medication, if possible (McNamara et al., 2017; O' Dwyer et al., 2017).

Conclusion

This chapter has provided an overview of psychosis in individuals with ID. Definitions of psychosis was discussed, as was the incidence and prevalence of psychosis in individuals with ID. The importance of studying psychosis was given, as well as the difficulties in diagnosing psychosis in individuals with ID. The risk factors of psychosis were given including baseline risks, early-life risks (in utero and during birth), childhood risks and risks that develop later in life. Assessment of psychosis in ID was outlined, including recommendations for assessment. Following this, pharmacological and psychological treatment for psychosis in individuals with ID was discussed, including recommendations for treatment. Finally, future directions for

research were suggested. In conclusion, psychosis in individuals with ID is an area where much more research is needed in order to better assess, understand and treat psychosis.

References

Allen, D. (2008). The relationship between challenging behaviour and mental ill-health in people with intellectual disabilities: a review of current theories and evidence. *Journal of Intellectual Disabilities, 12*(4), 267-294.

Allington-Smith P. (2006). Mental health of children with learning disabilities. *Advanced Psychiatric Treatment, 12*, 130–140.

Aman, M. G. (1993). Efficacy of psychotropic drugs for reducing self-injurious behavior in the developmental disabilities. *Annals of Clinical Psychiatry, 5*(3), 171-188.

Aman, M., Buitelaar, J., Smedt, G. D., Wapenaar, R., & Binder, C. (2005). Pharmacotherapy of disruptive behavior and item changes on a standardized rating scale: Pooled analysis of risperidone effects in children with subaverage IQ. *Journal of Child and Adolescent Psychopharmacology, 15,* 220–232.

Aman, M. G., De, S. G., Derivan, A., Lyons, B., & Findling, R. L. (2002). Double-blind, placebo-controlled study of risperidone for the treatment of disruptive behaviors in children with subaverage intelligence. *American Journal of Psychiatry, 159,* 1337–1346.

Aman M. G., Sarphare, G., & Burrow, W. H. (1995). Psychotropic drugs in group homes: prevalence & relation to demographic/psychiatric variables. *American Journal on Mental Retardation, 99,* 500-509.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.) (DSM-5).* American Psychiatric Association: Arlington, VA.

Antonacci, D.J. and de Groot, C.M. (2000). Clozapine treatment in a population of adults

with mental retardation. *The Journal of Clinical Psychiatry*, *61*(1), 22-25.

Axmon, A., Kristensson, J., Ahlström, G., & Midlöv, P. (2017). Use of antipsychotics, benzodiazepine derivatives, and dementia medication among older people with intellectual disability and/or autism spectrum disorder and dementia. *Research in developmental disabilities*, *62*, 50-57.

Axmon, A., Sandberg, M., & Ahlström, G. (2017). Gender differences in psychiatric diagnoses in older people with intellectual disability: a register study. *BMC psychiatry*, *17*(1), 192.

Ayub, M., Saeed, K., Munshi, T. A., & Naeem, F. (2015). Clozapine for psychotic disorders in adults with intellectual disabilities. *The Cochrane database of systematic reviews*, (9), CD010625-CD010625.

Bach, P., & Hayes, S. C. (2002). The use of acceptance and commitment therapy to prevent the rehospitalization of psychotic patients: A randomized controlled trial. *Journal of Consulting and Clinical Psychology*, *70*(5), 1129–1139.

Bagalman, E., & Cornell, A. S. (2018). Prevalence of Mental Illness in the United States: Data Sources and Estimates. *Congressional Research Service Report*. R43047.

Bailey, N. M., & Andrews, T. M. (2003). Diagnostic Criteria for Psychiatric Disorders for Use with Adults with Learning Disabilities/Mental Retardation (DC-LD) and the diagnosis of anxiety disorders: a review. *Journal of Intellectual Disability Research*, *47*(s1), 50-61.

Bakken, T.L., Eilertsen, D.E., Smeby, N.A., & Martinsen, H. (2009). The validity of of disorganized behavior as an indicator of psychosis in adults with autism and intellectual disability: a single case study. *Mental Health Aspects of Developmental Disabilities*, *12*(1), 17-22.

Bakken, T.L., Friis, S., Løvoll, S., Smeby, N.A. & Martinsen, H. (2007). Behavioral

disorganization as an indicator of psychosis in adults with intellectual disability and autism. *Mental Health Aspects of Developmental Disabilities, 10*(2), 37-46.

Bakken, T. L., & Høidal, S. H. (2014). Asperger syndrome or schizophrenia, or both? Case identification of 12 adults in a specialized psychiatric inpatient unit. *International Journal of Developmental Disabilities, 60*(4), 215-225.

Balogh, R., Ouellette-Kuntz, H., Bourne, L., Lunsky, Y., Colantonio, A., (2008). Organising health care services for persons with an intellectual disability. *Cochrane Database of Systematic Reviews, 4,* Art. No.: CD007492.

Bell, K., Startup, M., French, P., Morrison, A. P., Bucci, S., & Fowler, D. (2008). Therapist treatment adherence in Cbt for people at ultra-high risk for psychosis: development of a new rating scale. *Early Intervention in Psychiatry, 2*.

Bendall, S., Alvarez-Jimenez, M., Nelson, B., & McGorry, P. (2013). Childhood trauma and psychosis: new perspectives on aetiology and treatment. *Early Intervention in Psychiatry, 7*(1), 1–4.

Bourque, F., vander Ven, E., & Malla, A. (2011). A meta-analysis of the risk for psychotic disorders Substantial Variation in the Treated Incidence of Psychotic Disorders among first- and second-generation immigrants. *Psychological Medicine, 41*(5), 897-910.

Branford, D. (1994). A study of the prescribing for people with learning disabilities living in the community and in National Health Service care. *Journal of Intellectual Disability Research, 38*(6), 577-586.

Brylewski, J., & Duggan, L. (2001). Antipsychotic medication for challenging behaviour in people with learning disability. *The Cochrane database of systematic reviews*, (3), CD000377-CD000377.

Buckles, J., Luckasson, R., & Keefe, E. (2013). A systematic review of the prevalence of psychiatric disorders in adults with intellectual disability, 2003–2010. *Journal of Mental Health Research in Intellectual Disabilities, 6*(3), 181-207.

Canitano, R., & Pallagrosi, M. (2017). Autism spectrum disorders and schizophrenia spectrum disorders: excitation/inhibition imbalance and developmental trajectories. *Frontiers in psychiatry*, *8*, 69.

Carthy, J., Hemmings, C., Kravariti, E., Dworzynski, K., Holt, G., Bouras, N., & Tsakanikos, E. (2010). Challenging behavior and co-morbid psychopathology in adults with intellectual disability and autism spectrum disorders. *Research in Developmental Disabilities*, *31*(2), 362-366.

Chakos, M., Lieberman, J., Hoffman, E., Bradford, D., & Sheitman, B. (2004). Effectiveness of second-generation antipsychotics in patients with treatment-resistant schizophrenia: a review and meta-analysis of randomized trials. *Focus, 158*(1), 518-121.

Clarke, D. (2006). Psychiatric disorders and challenging behaviour. In: A. Roy, M. Roy M, & D. Clarke (eds). *The Psychiatry of Intellectual Disability.* Oxford: Ratcliffe Publishing, pp.21–31.

Clarke, D. J., & Gomez, G. A. (1999). Utility of modified DCR-10 criteria in the diagnosis of depression associated with intellectual disability. *Journal of Intellectual Disabilities Research*, *43*(5), 413–420.

Cohen-Kettenis, P. T., & Pfäfflin, F. (2010). The DSM diagnostic criteria for gender identity disorder in adolescents and adults. *Archives of sexual behavior*, *39*(2), 499-513.

Conrad, A. M., Lewin, T. J., Sly, K. A., Schall, U., Halpin, S. A., Hunter, M., & Carr, V.J. (2017). Utility of risk-status for predicting psychosis and related outcomes: evaluation of a 10-year cohort of presenters to a specialised early psychosis community mental health service. *Psychiatry research*, *247*, 336-344.

Cooper, S. A., & Bailey, N. M. (2001). Psychiatric disorders amongst adults with learning disabilities-prevalence and relationship to ability level. *Irish Journal of Psychological Medicine*, *18*(2), 45-53.

Cooper, S. A., Melville, C. A., & Einfeld, S. L. (2003). Psychiatric diagnosis, intellectual disabilities and diagnostic criteria for psychiatric disorders for use with adults with learning disabilities/mental retardation (DC-LD). *Journal of Intellectual Disabilities Research*, *47*(Suppl 1), 3–15.

Cooper, S. A., Smiley, E., Morrison, J., Allan, L., Williamson, A., Finlayson, J., ... & Mantry, D. (2007a). Psychosis and adults with intellectual disabilities. *Social psychiatry and psychiatric epidemiology*, *42*(7), 530-536.

Cooper, S. A., Smiley, E., Morrison, J., Williamson, A., & Allan, L. (2007b). Mental ill-health in adults with intellectual disabilities: prevalence and associated factors. *The British Journal of Psychiatry*, *190*(1), 27-35.

Connor, D. F., & Posever, T. A. (1998). A brief review of atypical antipsychotics in individuals

with developmental disability. *Mental Health Aspects of Developmental Disabilities*, *1*, 93-101.

Crilly, J. (2007). The history of clozapine and its emergence in the US market: a review and analysis. *History of psychiatry*, *18*(1), 39-60.

Dean, K., & Murray, R. M. (2005). Environmental risk factors for psychosis. *Dialogues in Clinical Neuroscience*, *7*(1), 69-80.

Deb, S., Kwok, H., Bertelli, M., Salvador-Carulla, L.U.I.S., Bradley, E., Torr, J., ... & Guideline Development Group of the WPA Section on Psychiatry of Intellectual Disability. (2009). International guide to prescribing psychotropic medication for the management of problem behaviours in adults with intellectual disabilities. *World Psychiatry*, *8*(3), 181-186.

Deb, S., Matthews, T., Holt, G., & Bouras, N. (2001a). *Practice guidelines for the assessment and diagnosis of mental health problems in adults who have intellectual disability*. London: European Association for Mental Health in Mental Retardation (EAMHMR).

Deb, S., Sohanpal, S. K., Soni, R., Lenotre, L., & Unwin, G. (2007). The effectiveness of antipsychotic medication in the management of behaviour problems in adults with intellectual disabilities. *Journal of Intellectual Disabilities Research, 51,* 766–777.

Deb, S., Thomas, M., & Bright, C. (2001b). Mental disorder in adults with intellectual

disability. 1: Prevalence of functional psychiatric illness among a community-based population aged between 16 and 64 years. *Journal of Intellectual Disability Research*, *45*(6), 495-505.

Deb, S., Unwin, G., & Deb, T. (2014) Characteristics and the trajectory of psychotropic medication use in general and antipsychotics in particular among adults with an an intellectual disability who exhibit aggressive behaviour. *Journal of Intellectual Disability Research 59,* 11–25.

Doherty, J. L., & Owen, M. J. (2014). Genomic insights into the overlap between psychiatric disorders: implications for research and clinical practice. *Genome medicine*, *6*(4), 29.

Drake, R. E., Essock, S. M., Shaner, A., Carey, K. B., Minkoff, K., Kola, L., Lynde, D., Osher, F.C., Clark, R.E. & Rickards, L. (2001). Implementing dual diagnosis services for clients with severe mental illness. *Psychiatric services*, *52*(4), 469-476.

Duggan, L., & Brylewski, J. (1999). Effectiveness of antipsychotic medication in people with intellectual disability and schizophrenia: A systematic review. *Journal of Intellectual Disability Research, 43,* 94–104.

Duggan, L., & Brylewski, J. (2004). Antipsychotic medication versus placebo for people with both schizophrenia and learning disability. *Cochrane Database of Systematic Reviews* 4 (Art. No.: CD000030).

Emerson, E., Kiernan, C., Alborz, A., Reeves, D., Mason, H., Swarbrick, R., Mason, L., & Hatton, C. (2001). The prevalence of challenging behaviors: a total population study. *Research in developmental disabilities*, *22*(1), 77-93.

Farooq, S., Nazar, Z., Irfan, M., Akhter, J., Gul, E., Irfan, U., & Naeem, F. (2011). Schizophrenia medication adherence in a resource-poor setting: randomised controlled trial of supervised treatment in out-patients for schizophrenia (STOPS). *The British Journal of Psychiatry*, *199*(6), 467-472.

Feinstein, C., Eliez, S., Blasey, C., & Reiss, A. L. (2002). Psychiatric disorders and behavioral problems in children with velocardiofacial syndrome: usefulness as phenotypic indicators of schizophrenia risk. *Biological psychiatry*, *51*(4), 312-318.

Friedlander, R. I., & Donnelly, T. (2004). Early-onset psychosis in youth with intellectual disability. *Journal of Intellectual Disability Research*, *48*(6), 540-547.

Frighi, V., Stephenson, M. T., Morovat, A., Jolley, I. E., Trivella, M., Dudley, C. A., ... & Barrow, B. (2011). Safety of antipsychotics in people with intellectual disability. *The British journal of psychiatry*, *199*(4), 289-295.

Fletcher, R., Loschen, E., Stavrakaki, C., & First, M. (2007). *Diagnostic Manual-Intellectual Disability (DM-ID): A textbook of diagnosis of mental disorders in persons with intellectual disability.* NADD Press: Kingston, New York.

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., ... & Valmaggia, L. (2013). The psychosis high-risk state: a comprehensive state-of-the-art review. *JAMA psychiatry*, *70*(1), 107-120.

Gibson, L. E., Alloy, L. B., & Ellman, L. M. (2016). Trauma and the psychosis spectrum: A review of symptom specificity and explanatory mechanisms. *Clinical Psychology Review, 49*, 92–105.

Gründer, G., Hippius, H., & Carlsson, A. (2009). The'atypicality'of antipsychotics: a concept re-examined and re-defined. *Nature Reviews Drug Discovery*, *8*(3), 197.

Haddock, G., Devane, S., Bradshaw, T., McGovern, J., Tarrier, N., Kinderman, P., ... & Harris, N. (2001). An investigation into the psychometric properties of the cognitive therapy scale for psychosis (CTS-Psy). *Behavioural and Cognitive Psychotherapy*, *29*(2), 221-233.

Hassiotis, A., Barron, D. A., & Hall, I. (2009). *Intellectual Disability Psychiatry: A Practical Handbook, 1st edition.* Chichester, West Sussex, UK: Wiley-Blackwell.

Heckers, S. (2009). Who Is at Risk for a Psychotic Disorder? *Schizophrenia Bulletin*, *35*(5), 847–850.

Helverschou, S.B., Bakken, T.L., & Martinsen, H. (2011). Psychiatric disorders in people with autism spectrum disorders: phenomenology and recognition, in Matson, J.L. and Sturmey, P. (Eds), *International Handbook of Autism and Pervasive Developmental Disorders.* Springer Science & Business Media, New York, NY, pp. 53-74.

Helverschou, S. B., Bakken, T. L., & Martinsen, H. (2009). The psychopathology in autism checklist (PAC): A pilot study. *Research in Autism Spectrum Disorders*, *3*(1), 179-195.

Herman, D. B. (2014). Transitional support for adults with severe mental illness: Critical time intervention and its roots in assertive community treatment. *Research on Social Work Practice*, *24*(5), 556-563.

Hippius, H. (1999). A historical perspective of clozapine. *The Journal of Clinical Psychiatry, 60*(Suppl 12), 22-23.

Holden, B., & Gitlesen, J. P. (2004a). Psychotropic medication in adults with mental

retardation: prevalence, and prescription practices. *Research in Developmental Disabilities*, *25*(6), 509-521.

Holden, B., & Gitlesen, J. P. (2004b). The association between severity of intellectual disability and psychiatric symptomatology. *Journal of Intellectual Disability Research*, *48*(6), 556-562.

Hove, O., & Havik, O. E. (2010). Developmental level and other factors associated with symptoms of mental disorders and problem behaviour in adults with intellectual disabilities living in the community. *Social psychiatry and psychiatric epidemiology*, *45*(1), 105-113.

Jauhar, S., McKenna, P. J., Radua, J., Fung, E., Salvador, R., & Laws, K. R. (2014). Cognitive–behavioural therapy for the symptoms of schizophrenia: systematic review and meta-analysis with examination of potential bias. *British Journal of Psychiatry*, *204*(01), 20–29.

Jones, C., Hacker, D., Cormac, I., Meaden, A., & Irving, C. B. (2012). Cognitive behavioural therapy versus other psychosocial treatments for schizophrenia. *The Cochrane database of systematic reviews*, *4*, CD008712.

Jongsma, H. E., Gayer-Anderson, C., Lasalvia, A., Quattrone, D., Mulè, A., Szöke, A., ... & Berardi, D. (2018). Treated incidence of psychotic disorders in the multinational EU-GEI study. *JAMA psychiatry*, *75*(1), 36-46.

Kelly, M. (2013). Understanding psychosis in individuals with intellectual disabilities. Regional Support Services, Presentation, September 7, 2013.

Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, severity,

and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of general psychiatry*, *62*(6), 617-627.

Khandaker, G. M., Dalman, C., Kappelmann, N., Stochl, J., Dal, H., Kosidou, K., ... & Karlsson, H. (2018). Association of Childhood Infection with IQ and Adult Nonaffective Psychosis in Swedish Men: A Population-Based Longitudinal Cohort and Co-relative Study. *JAMA psychiatry*, *75*(4), 356-362.

Kiernan, C., Reeves, D., & Alborz, A. (1995). The use of anti-psychotic drugs with adults with learning disabilities and challenging behaviour. *Journal of Intellectual Disability Research*, *39*(4), 263-274.

Kildahl, A. N., Bakken, T. L., Holm, O. K., & Helverschou, S. B. (2017). Assessment of psychosis in ASD/ID: a case study. *Advances in Mental Health and Intellectual Disabilities*, *11*(1), 17-23.

Kirkbride, J. B., Errazuriz, A., Croudace, T. J., Morgan, C., Jackson, D., Boydell, J., ... & Jones, P. B. (2012). Incidence of schizophrenia and other psychoses in England, 1950–2009: a systematic review and meta-analyses. *PloS one*, *7*(3), e31660.

Kirkbride, J. B., Hameed, Y., Ankireddypalli, G., Ioannidis, K., Crane, C. M., Nasir, M., ... & Spyridi, S. (2017). The epidemiology of first-episode psychosis in early intervention in psychosis services: findings from the social epidemiology of psychoses in East Anglia [SEPEA] study. *American Journal of Psychiatry*, *174*(2), 143-153.

Kozlowski, A. M., Matson, J. L., Sipes, M., Hattier, M. A., & Bamburg, J. W. (2011). The relationship between psychopathology symptom clusters and the presence of comorbid psychopathology in individuals with severe to profound intellectual disability. *Research in Developmental Disabilities*, *32*(5), 1610-1614.

Krishnan, R. R., Kraus, M. S., & Keefe, R. S. (2011). Comprehensive model of how reality distortion and symptoms occur in schizophrenia: Could impairment in learning-dependent predictive perception account for the manifestations of schizophrenia? *Psychiatry and Clinical Neurosciences*, *65*(4), 305-317.

La Malfa, G., Bertelli, M., & Conte, M. (2001). Fluvoxamine and aggression in mental retardation. *Psychiatric Services*, *52*(8), 1105-1105.

Leucht, S., Kissling, W., & Davis, J. M. (2009). Second-generation antipsychotics for schizophrenia: can we resolve the conflict? *Psychological medicine*, *39*(10), 1591-1602.

Lunsky, Y., Bradley, E., Durbin, J., & Koegl, C. (2008). A comparison of patients with intellectual disability receiving specialised and general services in Ontario's psychiatric hospitals. *Journal of Intellectual Disability Research*, *52*(11), 1003-1012.

Lunsky, Y., Gracey, C., Bradley, E., Koegl, C., & Durbin, J. (2011). A comparison of outpatients with intellectual disability receiving specialised and general services in Ontario's psychiatric hospitals. *Journal of Intellectual Disability Research*, *55*(2), 242-247.

Lynch, D., Laws, K. R., & McKenna, P. J. (2010). Cognitive behavioural therapy for major psychiatric disorder: does it really work? A meta-analytical review of well-controlled trials. *Psychological Medicine*, *40*(1), 9–24.

Madhavan, G. P. (2018). Psychotic symptoms in people with intellectual disability. *British Medical Journal*, *360*.

Mahan, S., Holloway, J., Bamburg, J. W., Hess, J. A., Fodstad, J. C., & Matson, J. L. (2010). An examination of psychotropic medication side effects: Does taking a greater number of psychotropic medications from different classes affect presentation of side effects in adults with ID? *Research in Developmental Disabilities*, *31*(6), 1561-1569.

Malfa, G. L., Lassi, S., Bertelli, M., & Castellani, A. (2006). Reviewing the use of antipsychotic drugs in people with intellectual disability. *Human Psychopharmacology: Clinical and Experimental*, *21*(2), 73-89.

Matson, J.L. (1997). *The Assessment for Dual Diagnosis (ADD).* Baton Rouge, LA: Disability Consultants, LLC.

Matson, J.L. (1995). *The Diagnostic Assessment for the Severely Handicapped revised (DASH-II).* Baton Rouge, LA: Disability Consultants, LLC.

Mason, J., & Scior, K. (2004). 'Diagnostic overshadowing' amongst clinicians working with people with intellectual disabilities in the UK. *Journal of Applied Research in Intellectual Disabilities*, *17*(2), 85-90.

Matson, J. L., Bielecki, J., Mayville, S. B., & Matson, M. L. (2003). Psychopharmacology research for individuals with mental retardation: Methodological issues and suggestions. *Research in Developmental Disabilities*, *24*(3), 149-157.

Matson, J. L., Kazdin, A. E., & Senatore, V. (1984). Psychometric properties of the Psychopathology Instrument for Mentally Retarded Adults. *Applied Research in Mental Retardation, 5,* 81-89.

Matson, J. L., & Mahan, S. (2010). Antipsychotic drug side effects for persons with intellectual disability. *Research in Developmental Disabilities, 31,* 1570–1576.

Matson, J. L., Mayville, E. A., Lott, J. D., Bielecki, J., & Logan, R. (2003). A comparison of social and adaptive functioning in persons with psychosis, autism, and severe or profound mental retardation. *Journal of Developmental and Physical Disabilities*, *15*(1), 57-65.

Matson, J. L., & Neal, D. (2009). Psychotropic medication use for challenging behaviors in persons with intellectual disabilities: An overview. *Research in Developmental Disabilities*, *30*(3), 572-586.

Martin, G., Costello, H., Leese, M., Slade, M., Bouras, N., Higgins, S., & Holt, G. (2005). An exploratory study of assertive community treatment for people with intellectual disability and psychiatric disorders: conceptual, clinical, and service issues. *Journal of Intellectual Disability Research*, *49*(7), 516-524.

McCarthy, J. B., & Barbot, B. (2016). The Need for Research on Intellectual Disabilities and Severe Psychiatric Disorders in Children and Adolescents. *Journal of Mental Disorders and Treatment*, *2*(112), 2.

McGough, J. J., Smalley, S. L., McCracken, J. T., Yang, M., Del'Homme, M., Lynn, D. E., & Loo, S. (2005). Psychiatric comorbidity in adult attention deficit hyperactivity disorder: findings from multiplex families. *American Journal of Psychiatry*, *162*(9), 1621-1627.

McGrath, J., Sukanta, S., Chant, D., & Welham, J. (2008). Schizophrenia: A Concise Overview of Incidence, Prevalence, and Mortality. *Epidemiologic Reviews*, *30*(1), 67-76.

McNamara, R., Randell, E., Gillespie, D., Wood, F., Felce, D., Romeo, R., ... & Meek, A. (2017). A pilot randomised controlled trial of community-led ANtipsychotic Drug REduction for Adults with Learning Disabilities. *Health Technology Assessment*, *21*(47), 1-92.

Miller, D. D. (2000). Review and management of clozapine side effects. *The Journal of Clinical Psychiatry*, *61*(Supple 8), 14-17.

Messias, E., Chen, C-Y., and Eaton, W. W. (2007). Epidemiology of Schizophrenia: Review of Findings and Myths. *Psychiatric Clinics*, *30*(3), 323-338.

Morrison, A. P., & Barratt, S. (2010). What Are the Components of CBT for Psychosis? A Delphi Study. *Schizophrenia Bulletin*, *36*(1), 136–142.

Moss, S., & Hurley, A. D. (2014). Integrating assessment instruments within the diagnostic process. In *Handbook of psychopathology in intellectual disability* (pp. 43-61). Springer, New York, NY.

Moss, S., Prosser, H., Costello, H., Simpson, N., Patel, P., Rowe, S., Turner, S., & Hatton, C. (2002). Reliability and validity of the PAS-ADD Checklist for detecting psychiatric disorders in adults with intellectual disability. *Journal of Intellectual Disability Research*, *42*, 173-183.

Munir, K. M. (2016). The co-occurrence of mental disorders in children and adolescents with intellectual disability/intellectual developmental disorder. *Current opinion in psychiatry*, *29*(2), 95.

Mungkhetklang, C., Crewther, S. G., Bavin, E. L., Goharpey, N., & Parsons, C. (2016). Comparison of measures of ability in adolescents with intellectual disability. *Frontiers in psychology*, *7*, 683.

Myrbakk, E., & von Tetzchner, S. (2008). Psychiatric disorders and behavior problems in people with intellectual disability. *Research in Developmental Disabilities*, *29*(4), 316-332.

Newton-Howes, G., & Wood, R. (2013). Cognitive behavioural therapy and the psychopathology of schizophrenia: Systematic review and meta-analysis. *Psychology and Psychotherapy: Theory, Research and Practice*, *86*(2), 127–138.

Oliver-Africano, P., Murphy, D., & Tyrer, P. (2009). Aggressive behaviour in adults with intellectual disability. *CNS drugs*, *23*(11), 903-913.

O' Dwyer, M., Peklar, J., Mulryan, N., McCallion, P., McCarron, M., & Henman, M. C. (2017). Prevalence, patterns and factors associated with psychotropic use in older adults with intellectual disabilities in Ireland. *Journal of Intellectual Disability Research*, *61*(10), 969-983.

Patil, D., Keown, P., & Scott, J. (2013). A rising tide: the increasing age and psychiatric length of stay for individuals with mild intellectual disabilities. *Journal of Intellectual Disability Research*, *57*(8), 783-790.

Paton, C., Flynn, A., Shingleton-Smith, A., McIntyre, S., Bhaumik, S., Rasmussen, J., ... & Barnes, T. (2011). Nature and quality of antipsychotic prescribing practice in UK psychiatry of intellectual disability services. *Journal of Intellectual Disability Research*, *55*(7), 665-674.

Perälä, J., Suvisaari, J., Saarni, S. I., Kuoppasalmi, K., Isometsä, E., Pirkola, S., ... & Härkänen, T. (2007). Lifetime prevalence of psychotic and bipolar I disorders in a general population. *Archives of general psychiatry*, *64*(1), 19-28.

Perry, B.I., Cooray, S.E., Mendis, J., Purandar, K, Wijeratne, A.…& Kwok, H.F. (2018). Problem behaviours and psychotropic medication use in intellectual disability: A multinational cross-sectional survey. *Journal of Intellectual Disability Research, 62*, 140-149.

Prosser, H., Moss, S., Costello, H., Simpson, N., Patel, P., & Rowe, S. (2002). Reliability and validity of the Mini PAS-ADD for assessing psychiatric disorders in adults with intellectual disability. *Journal of Intellectual Disability Research, 42*(4), 264-272.

Radua, J., Ramella-Cravaro, V., Ioannidis, J., Reichenberg, A., Phiphopthatsanee, N., Amir, T., ... & McGuire, P. (2018). What causes psychosis? An umbrella review of risk and protective factors. *World Psychiatry*, *17*(1), 49-66.

Raftery, M. Burke, K., Murray, N., O'Duinn, O., Murray, I. & Hallahan, B. (2006). An intensive personalised support approach to treating individuals with psychosis and co-morbid mild intellectual disability. *Irish Journal of Psychological Medicine*, 1-11.

Reeve, S., Sheaves, B., & Freeman, D. (2015). The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review. *Clinical Psychology Review, 42,* 96-115.

Robertson, J., Emerson, E., Gregory, N., Hatton, C., Kessissoglou, S. & Hallam, A. (2000). Receipt of psychotropic medication by people with intellectual disability in residential settings. *Journal of Intellectual and Disability Research, 44,* 666-676.

Rollinson, R., Smith, B., Steel, C., Jolley, S., Onwumere, J., Garety, P. A., … Fowler, D. (2008). Measuring Adherence in CBT for Psychosis: A Psychometric Analysis of an Adherence Scale. *Behavioural and Cognitive Psychotherapy*, *36*(2), 163–178.

Sadock, B. J., & Sadock, V. A. (2009). *Concise textbook of child and adolescent psychiatry* Philadelphia: Lippincott Williams & Wilkins.

Sass, L. A., & Parnas, J. (2003). Schizophrenia, consciousness, and the self. *Schizophrenia bulletin*, *29*(3), 427-444.

Scheifes A., Egberts T. C., Stolker J. J., Nijman H. L. & Heerdink E. R. (2016)

Structured medication review to improve pharmacotherapy in people with intellectual disability and behavioural problems. *Journal of Applied Research in Intellectual Disabilities 29,* 346–55.

Scheifes, A., Stolker, J. J., Egberts, A. C., Nijman, H. L., & Heerdink, E. R. (2011). Representation of people with intellectual disabilities in randomised controlled trials on antipsychotic treatment for behavioural problems. *Journal of Intellectual Disabilities Research, 55,* 650–664.

Schützwohl, M., Koch, A., Koslowski, N., Puschner, B., Voß, E., Salize, H. J., ... & Vogel, A. (2016). Mental illness, problem behaviour, needs and service use in adults with intellectual disability. *Social psychiatry and psychiatric epidemiology*, *51*(5), 767-776.

Selten, J. P., Lundberg, M., Rai, D., & Magnusson, C. (2015). Risks for nonaffective psychotic disorder and bipolar disorder in young people with autism spectrum disorder: a population-based study. *JAMA psychiatry*, *72*(5), 483-489.

Shawyer, F., Farhall, J., Thomas, N., Hayes, S. C., Gallop, R., Copolov, D., & Castle, D. J. (2017). Acceptance and commitment therapy for psychosis: randomised controlled trial. *The British Journal of Psychiatry: The Journal of Mental Science*, *210*(2), 140–148.

Sheehan, R., Hassiotis, A., Walters, K., Osborn, D., Strydom, A. & Horsfall, L. (2015). Mental illness, challenging behaviour, and psychotropic drug prescribing in people with intellectual disability: UK population based cohort study. *BMJ, 351,* 1-9.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta,

T., Baker, R. & Dubar, G. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry, 59*(20), 22-33.

Singh, S. P., Singh, V., Kar, N., & Chan, K. (2010). Efficacy of antidepressants in treating the negative symptoms of chronic schizophrenia: meta-analysis. *The British Journal of Psychiatry, 197*(3), 174-179.

Skokauskas, N., & Gallagher, L. (2010). Psychosis, Affective Disorders and Anxiety in Autistic Spectrum Disorder: Prevalence and Nosological Considerations. *Psychopathology*, *43*(1), 8–16.

Smiley, E. (2005). Epidemiology of mental health problems in adults with learning disability: an update. *Advances in Psychiatric Treatment*, *11*(3), 214-222.

Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H. U., & Van Os, J. (2006). Impact of psychological trauma on the development of psychotic symptoms: relationship with psychosis proneness. *The British Journal of Psychiatry*, *188*(6), 527-533.

Steel, Z., Marnane, C., Iranpour, C., Chey, T., Jackson, J. W., Patel, V., & Silove, D. (2014). The global prevalence of common mental disorders: a systematic review and meta-analysis 1980–2013. *International journal of epidemiology*, *43*(2), 476-493.

Tandon, R., Gaebel, W., Barch, D. M., Bustillo, J., Gur, R. E., Heckers, S., ... & Van Os, J. (2013). Definition and description of schizophrenia in the DSM-5. *Schizophrenia research*, *150*(1), 3-10.

Tang, Y.L, Mao, P.X., Jiang, F., Chen, Q., Wang, C.Y., Cai, Z.J., Mitchell, P.B. (2008). Clozapine in China. *Pharmacopsychiatry, 41*, 1–9.

Thalayasingam, S., Alexander, R.T., and Singh, I. (2004) The use of clozapine in adults with intellectual disability. *Journal of Intellectual Disability Research, 48,* 572-579.

Thalitaya, M.D., Reynolds, C., & Ismail, I. (2017). Study on the use of antipsychotic medication in an intellectual disability: Community caseload. *Psychitria Danubiana, 29,* 578-583.

Tone, E. B., Garn, C. L., & Pine, D. S. (2016). Anxiety regulation: a developmental psychopathology perspective. *Developmental Psychopathology*, 1-34.

Tsakanikos, E., Bouras, N., Costello, H., & Holt, G. (2007). Multiple exposure to life events and clinical psychopathology in adults with intellectual disability. *Social Psychiatry and Psychiatric Epidemiology*, *42*(1), 24-28.

Tsiouris, J. A., Kim, S. Y., Brown, W. T., Pettinger, J., & Cohen, I. L. (2013). Prevalence of psychotropic drug use in adults with intellectual disability: positive and negative findings from a large scale study. *Journal of autism and developmental disorders*, *43*(3), 719-731.

Turner, T. H. (1989). Schizophrenia and mental handicap: an historical review, with implications for further research. *Psychological Medicine*, *19*(2), 301–314.

Underwood, R., Kumari, V., & Peters, E. (2016). Appraisals of psychotic experiences: an experimental investigation of symptomatic, remitted and non-need-for-care individuals. *Psychological medicine*, *46*(6), 1249-1263.

United Nations General Assembly (2006). *United Nations Convention on the Rights of Persons with Disabilities (UNCRPD).* New York: UN General Assembly.

van Os, J., Rutten, B. P., & Poulton, R. (2008). Gene-environment interactions in

schizophrenia: review of epidemiological findings and future directions. *Schizophrenia Bulletin*, *34*(6), 1066-82.

van Os, J., & Tamminga, C. (2007). Deconstructing psychosis. *Schizophrenia Bulletin*, *33*(4), 861-862.

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., ... & Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective-and cross-sectional cohort studies. *Schizophrenia Bulletin*, *38*(4), 661-671.

Yung, A. R., Nelson, B., Thompson, A., & Wood, S. J. (2010). The psychosis threshold in Ultra High Risk (prodromal) research: is it valid? *Schizophrenia research*, *120*(1), 1-6.

Yung, A. R., Phillips, L. J., Yuen, H. P., & McGorry, P. D. (2004). Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. *Schizophrenia Research*, *67*(2), 131–142.

Wang, C., & Li, L. (2012). Proper use of clozapine: experiences in China. *Shanghai archives of psychiatry*, *24*(2), 108.

Watson, D. (2005). Rethinking the mood and anxiety disorders: a quantitative hierarchical model for DSM-V. *Journal of abnormal psychology*, *114*(4), 522.

Welch, K. A., Lawrie, S. M., Muir, W., & Johnstone, E. C. (2011). Systematic review of the

clinical presentation of schizophrenia in intellectual disability. *Journal of Psychopathology and Behavioral Assessment*, *33*(2), 246-253.

Williams, H., Clarke, R., Bouras, N., Martin, J., & Holt, G. (2009). Use of atypical antipsychotics Olanzapine and Risperidone in adults with intellectual disability. *Journal of Intellectual Disability Research, 44,* 164-169.

Wing, L., Gould, J., & Gillberg, C. (2011). Autism spectrum disorders in the DSM-V: better or worse than the DSM-IV? *Research in developmental disabilities*, *32*(2), 768-773.

World Health Organization. (2004). *International statistical classification of diseases and related health problems* (Vol. 1). World Health Organization.

Wykes, T., Steel, C., Everitt, B., & Tarrier, N. (2008). Cognitive Behavior Therapy for Schizophrenia: Effect Sizes, Clinical Models, and Methodological Rigor. *Schizophrenia Bulletin*, *34*(3), 523–537.

Yen, C. F., Lin, J. D., Loh, C. H., Shi, L., & Hsu, S. W. (2009). Determinants of prescription drug use by adolescents with intellectual disabilities in Taiwan. *Research in Developmental Disabilities, 30*(6), 1354-1366.

Yin, R. K. (2013). Validity and generalization in future case study evaluations. *Evaluation, 19*(3), 321-332.