Psychosis as a continuous phenotype in the general population: the thin line between normality and pathology

van Os and Reininghaus[1] provide a compelling overview of evidence suggesting that psychosis may be perceived as an extreme expression of continuously distributed quantitative traits in the general population, where minor psychotic symptoms, similar but less severe than those observed in affected individuals, can be found in proportions of up to 7%.

The concept of the extended psychosis phenotype offers a number of unique opportunities. Firstly, recognizing the psychosis phenotype as a gradual infusion of quantitative traits into clinical syndromes provides an elegant explanation for variation in the degree of severity of psychosis-like experiences. Secondly, as highlighted by the authors, the extended psychosis phenotype is transdiagnostic in nature, implying that it is not restricted to any specific psychotic disorder but rather represents a continuous expression across the psychosis spectrum. This may explain the overlap in psychopathological presentation observed across mental disorders and therefore provides a foundation for cross-disorder analyses. The latter in turn would tackle the indistinctness of current diagnostic categories, that are marked by lack of clear boundaries between themselves and with normality[2]. While considering psychopathology in terms of a transdiagnostic psychosis dimension with five specific constructs may still be perceived as agnostic with respect to traditional diagnostic systems, using these two approaches in combination may allow for a more accurate classification of affected individuals.

The transdiagnostic approach may also have important advantages for scientific research. In research carried out by our group employing the transdiagnostic psychosis dimension, a degree of specificity was found in the relationships between different types of childhood trauma and psychosis symptom dimensions in adulthood, suggesting that distinct pathways may be involved in the relationship between the childhood trauma and psychosis[3]. Eventually, these findings might feed into interventions targeting high-risk children. Similarly, Jones et al[4] have shown the importance of the transdiagnostic psychosis dimension in exploring how an increased genetic risk for schizophrenia expresses during early teens among the general public. Building on these findings, future studies may shed some light on the pathways between the genetic liability for schizophrenia and the phenotypical expression of this illness in childhood, adolescence and throughout adulthood.

It is asserted that 20% of those who report subclinical psychotic symptoms make the transition to persistent psychosis. If these estimates are accurate, then detecting individuals with subclinical psychotic experiences from the general public would offer a unique opportunity to reduce the duration of untreated psychosis, which in turn has been linked to poor treatment response, increased risk for relapse and overall poorer prognosis[5]. It would also enable early interventions ultimately resulting in diminishing symptom severity from the onset, deferring or preventing the onset of psychosis and reducing the financial and emotional liabilities associated with the lifetime burden of the illness.

Are these estimates accurate? Identification of individuals with subclinical psychotic experiences is reliant on help-seeking behaviour. However, young individuals with an early onset of psychosis are less likely to engage in such behaviours[6]. The likelihood of help-seeking is dependent on the awareness and insight of the earliest manifestations of psychotic symptoms, and even more so on availability of supportive families and strong social networks around at-risk young individuals[6]. Another issue relevant to the calculation of so-called transition rates is the drawing of distinctions between the emergence of psychotic symptoms (marking the onset of the period of untreated psychosis) and the onset of psychotic disorder. The claim that early intervention services reduce the duration of untreated psychosis in comparison to generic clinical services[7] is critically dependent on whether the time between the earliest report of symptoms and the intervention of the former services is taken as the "duration of untreated psychosis" or whether the beginning of "duration of untreated psychosis" is "reset" after such an intervention until the individual is in the unlucky minority and subsequently develops a first episode of full-blown psychosis. Furthermore, preliminary work from our clinic indicates that, when we look back at the journey that first episode psychosis patients took before arriving at generic catchment area clinical services, we find that there are very few who come via prodromal services, suggesting that the scope for reducing or postponing the onset of psychosis is limited. Some people have an onset that is too rapid and severe, while others have an onset that is so insidious that they escape the notice even of services whose philosophy is not at all tied to diagnostic categories and who embrace the dimensional approach[8].

Finally, it has also been argued that subclinical psychotic experiences are more likely to occur in adolescence – the phase in young people's lives that is frequently marked by experimenting with substances or rebellious behaviour[2]. This issue is exacerbated by differing approaches used to elicit psychotic experiences, some of which exclude clinical judgement and others seem to lead the respondent into endorsing such experiences (see David[9] for a discussion). These methodological issues probably contribute to the wide range of estimates of psychotic experiences in the general population.

Evidence suggests that neurocognitive alterations, dysregulation in top-down processing and reasoning biases may be particularly relevant to the development of psychotic experiences even in non-help seeking populations, and sophisticated imaging analysis techniques may be used to uncover them[10]. These may yet serve as important markers for illness onset. However, it is too early to say how specific these sorts of findings are to psychotic spectrum disorders and to what extent they apply to other mental disorders.

Certainly, the evidence based on family studies suggests that subclinical psychotic experiences are influenced by genetic risk factors. In theory this may offer a unique prospect to develop a screening test based on genetic composition. Indeed, similarly to the asserted nature of the extended psychosis phenotype, the genetic risk for psychosis is distributed on a continuum at the highest end of which are affected individuals followed by their healthy relatives[11]. Although these results support the premise of being able to detect those at risk based on their genetic make-up, recent attempts of linking genetic risk score for schizophrenia to an intermediate phenotype in non-clinical populations have so far been contradictory[12].

The importance of the transdiagnostic and extended psychosis phenotype in relation to diagnosis, aetiology, prevalence and outlining the future direction for research is indeed noteworthy. However, without a clearly established and scientifically validated threshold defining pathology, as well as markers indicative of susceptibility to the illness, the borderline between normality and psychopathology will remain contested.

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Psychotic experiences and their significance

The term "psychotic experiences" generally refers to subthreshold forms of hallucinations and delusions. However, this term is used inconsistently, sometimes referring to psychotic symptoms (i.e., full threshold positive phenomena), at other times including both sub- and full threshold positive symptoms. van Os and Reininghaus[1] use the term "subclinical psychotic experiences" to discuss their views on psychotic experiences along the extended psychosis phenotype. Here we present a clinical perspective from the ultra high risk (UHR) paradigm, that aims to identify people at high risk of psychotic disorder by the presence of psychotic experiences and associated help-seeking and functional impairment.

van Os and Reininghaus assert that "most individuals with psychotic experiences have a current diagnosis, primarily one of mood or anxiety disorder"[1]. We do not believe this is true. For example, Varghese et al[2] found that major depressive disorder was absent in the majority of individuals with psychotic experiences, including those scoring in the highest quartile for these experiences. Similarly, anxiety was absent in most people with psychotic experiences, even for those in the highest quartile. Morgan et al[3] showed that 46% of their community sample with psychotic experiences had no common mental disorder, and a large German general population study found that only 43% of individuals with psychotic experiences at baseline had at least three symptoms of depression 3.5 years later (note that at least three depressive symptoms is not necessarily diagnostic).

In fact, many of the studies cited by van Os and Reininghaus as evidence for their assertion are examining a different research question, that is, the prevalence of psychotic experiences in people with mood and anxiety disorders. Indeed, individuals with common mental disorder *are* more likely to have psychotic experiences than their counterparts with no psychiatric disorder[4], and such experiences in mood and anxiety disorders predict more severe illness course[4].

While psychotic experiences may not always be associated with mental disorder in the general population, some people with psychotic experiences are at increased risk of psychotic disorder, including schizophrenia. This has been shown in both general population studies[5] and the UHR group[6]. A meta-analysis of UHR research found that risk for psychotic disorder was 22% within one year of identification, rising to 36% after three years[6]. Therefore, while van Os and Reininghaus argue that individuals in the community with psychotic experiences are more likely to develop a mood or anxiety disorder than a psychotic disorder, these phenomena actually predict psychotic disorders far more strongly[5]. This is because mood and anxiety disorders are much more common than psychotic disorders and frequently occur in the absence of psychotic experiences[4]. Consistent with this, as van Os and Reininghaus note, evidence from a Danish birth cohort study showed that psychotic experiences at age 11-12 years were strongly associated with a family history of psychotic disorder, but not of common mental disorder. Thus, just as the UHR state is relatively specific to psychotic disorders (compared to non-psychotic disorders)[7], this is also the case with psychotic experiences in the general population.

So, how are we to understand these psychotic experiences? It is important to recognize that not all positive psychotic symptoms are the same. Previous research has identified four factor (persecution, bizarre experiences, hallucinations, and paranormal beliefs/magical thinking)[8] and five factor (hallucinations, delusions, paranoia, grandiosity, paranormal beliefs)[9] models of psychotic experiences. Persecution, bizarre experiences and