

Breaking the web: life beyond the at-risk mental state for psychosis

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Abstract

Psychiatry's most recent foray into the area of risk and prevention has been spear-headed by work on at-risk mental states for psychotic disorders. Twenty-five years' research and clinical application have led us to reformulate the clinical evolution of these syndromes, blurred unhelpful conceptual boundaries between childhood and adult life by adopting a developmental view and has changed the shape of many mental health services as part of a global movement to increase quality. But there are problems: fragmentary psychotic experiences are common in young people but transition from risk-state to full syndrome is uncommon away from specialist clinics with rarefied referrals and can, anyway, be subtle; diagnostic over-shadowing by the prospect of schizophrenia and other psychotic disorders may divert clinical attention from the kaleidoscopic and disabling range of probably treatable psychopathology with which people with risk syndromes present. We use a 19th Century lyric poem, *The Lady of Shallot*, as an allegory for Psychiatry warning us against regarding these mental states only as pointers towards diagnoses that probably will not occur. Viewed from the fresh perspective of common mental disorders they tell us a great deal about the psychopathological crucible of the second and third decades, the nature of diagnosis, and point towards new treatment paradigms.

Introduction

The at-risk mental state for psychosis and its conceptual cousins, the clinical and ultra-high-risk states (Yung *et al.*, 1996, 2003; Cornblatt *et al.*, 2002) and the Diagnostic and Statistical Manual of Mental Disorders-fifth edition (DSM-5) psychosis risk syndrome proposal (American Psychiatric Association, 2013) are defined largely by the presence of attenuated or fragmentary psychotic experiences. As proto-diagnoses currently considered only within an appendix into DSM-5, these risk states have rightly directed clinical psychiatry and mental health care towards early intervention, and have changed the way we conceptualise the emergence of psychiatric disorders. In fact, they have raised expectations; psychiatric diagnoses may no longer be inevitable and life-long destinations; caught early enough, psychotic disorders may be averted (McGorry and Mei, 2018).

Systematic reviews and evidence synthesis including classic studies in the field show that someone with an at-risk mental state has a 30–40% chance of meeting criteria for an International Classification of Diseases (ICD)/DSM first-episode psychotic disorder over the following years (Fusar-Poli *et al.*, 2012), almost the toss of a coin. However, data from recent studies of briefer mental state abnormalities suggest a different story. Trials of preventative talking therapies (Morrison *et al.*, 2012), specific neuroprotective medications (McGorry *et al.*, 2017) or observations of referrals from primary care (Perez *et al.*, 2015) suggest that the short- to medium-term transition rates are much lower: less than 10%, whereas diagnoses of anxiety and depression are common (Hui *et al.*, 2013; Lin *et al.*, 2015). In addition, only a few people who develop the first-episode psychosis are detected in at-risk mental state clinics (Ajnakina *et al.*, 2017).

This low chance of full-syndrome psychotic illness is great news for young people with the so-called at-risk mental state, especially if those looking after them begin helping with their trans-diagnostic presentation (van Os and Guloksuz, 2017), rather than focusing only on the prospect of a full-syndrome psychotic disorder that they almost certainly will not develop. The apparent paradox in the literature is the familiar one arising from the predictive value of a diagnostic or predictive test, here the identification of an at-risk mental state. Its usefulness for predicting full-syndrome psychosis depends on the prevalence of that target disorder; a test that performs well in the rarefied context of a specialist service accepting referrals whom other experts feel may be developing psychosis (such as in the studies that originally fuelled the at-risk concept) will have disappointing characteristics nearer the general population or even in primary care where the ability to predict

would be valuable but where psychotic disorder is relatively rare. Diagnostic magic is simply more powerful in the hands of specialist wizards than generalist gatekeepers (Mathers and Hodgkin, 1989).

Furthermore, there is usually much more to a first-episode, full-syndrome psychotic disorder than the psychotic phenomena that define it; depression and anxiety almost always lurk close by and may be central. We need to give careful attention to all the symptoms and other problems that people with an at-risk mental state bring into the consultation. Many are dealing with moderate to severe depression, anxiety, substance misuse, recent trauma or vivid echoes of adverse childhood experiences. More often than not these are as much part of their presentation as are the fragments of psychosis in the at-risk state; the psychopathology is often kaleidoscopic, changing day by day and evolving week by week.

Studies involving thousands of young people from the general population have demonstrated that psychotic experiences, depressive and anxiety symptoms are best seen as manifestations of a unitary, latent continuum of common mental distress, on which psychotic experiences measure severity (Stochl *et al.*, 2015). Therefore, psychotic experiences may act not only as markers for unlikely future psychotic illness or for rare, affective psychotic disorders to be found in current diagnostic classifications but also for more severe species of common, but disabling mental disorders that are hiding in plain sight beyond the eye of the DSM and ICD (Murray and Jones, 2012). Few people with at-risk mental states will develop a psychotic syndrome but many may suffer from persistent mental ill-health that should be a target for intervention. Therefore, we must not assume that the at-risk mental state is some kind of *chrysalis* that will metamorphose into a *psychosis butterfly*. In the specialist clinic such a transition may be the result of a clinical judgement increasing a rating-scale score by a single point, far from a dramatic metamorphosis. We wonder whether the at-risk mental state for psychosis may represent a hitherto unrecognised *species* trapped in an elaborate disciplinary *web* of knowledge that the field of psychiatrists and researchers has woven over recent decades.

Alfred Lord Tennyson's 'The Lady of Shalott' [Tennyson, 1833 (1857)] is a lyric ballad poem concerning a cursed Lady imprisoned in a tower on the island of Shalott, near Camelot. Forbidden even a single glance from her window onto the real world, she sits each day happily weaving a charming web that represents the fragmentary reflections of real-life that she glimpses through a small mirror in her bedroom-cum-prison cell. Is our own medical speciality similarly fixated? Are we weaving more and more threads of information on an established disciplinary *web* whilst, simultaneously, oblivious to being, ourselves, engulfed by the web as it imposes a restricted view of what we see as an at-risk mental state for psychosis?

To look beyond the current notion of at-risk mental state, we must face the conundrum of breaking a familiar web that psychiatrists and psychologists may be weaving. Closer investigation of our metaphor may be useful.

The web

Representing a modern evolution of prodromal psychotic phenomena described in older versions of current diagnostic manuals (American Psychiatric Association, 1987), the at-risk mental state concept and its operationalisation in clinical high-risk criteria provided a new way to cluster and research the early phases of

psychotic disorders first, in people who clearly met diagnostic criteria and later, in people who had many but not all of their requirements. Thus, the at-risk mental state epistemology and associated research methodology have been built upon two inter-linked paradigms in psychiatry: a categorical nosology and the prediction paradigm. The notion of being 'at-risk' for psychosis implied a heightened likelihood of developing categorical disorders included in diagnostic manuals.

Humans have a yen to classify. Just as sensory perception makes sense of complex, multi-domain stimuli to construct our everyday world (and is prone to illusion), psychiatrists and other mental scientists try to reduce the complex patterns of mental phenomena by grouping them into classes with common characteristics. The reasons behind psychiatric classification are diverse and not so different from other medical specialities. In fact, the most basic function of any medical epistemology is to create distinctions (Sokal, 1974; Berrios, 1999). For many years, psychiatry was in need of robust scientific foundations to avoid further ideological contaminations and divisions. The introduction of categorical diagnostic systems in psychiatry was an innovation that provided clear diagnostic criteria, preventing whimsical changes whilst raising the profile of psychiatry as a medical science. Classifications offered a common language and improved the validity and reliability of our diagnostic constructs. The diagnostic categories had to be valid, reliable, stable and specific (Kendler, 1990). This reductionist approach, mostly based on contemplative medicine, inevitably exposes clinicians to uncertainties around clinical presentations that do not fit into any category, and, therefore, are inexistent from a nosological perspective.

To understand the foundations of categories, we must rewind more than a century to Emil Kraepelin's (1856–1926) categorisation of psychiatric diseases; a landmark that would be endorsed by the DSM-III (American Psychiatric Association, 1980; Shorter, 2015). Kraepelin built taxonomy on the assumption that groups of symptoms were disease-specific (Hoff, 2015). Notably, this view was confronted by contemporaneous German psychiatrists such as Alfred Hoche (1865–1943) or Karl Bonhoeffer (1868–1948). For instance, Bonhoeffer considered that a particular illness may express itself with different psychiatric symptoms and that a single symptom might be the expression of several different psychiatric illnesses. His views countered Kraepelin's assertion that psychiatric phenotypes identify natural disease entities and anticipated the view that these phenotypes are likely to be aetiologically heterogeneous. Bonhoeffer's works provided evidence that psychopathological syndromes for a large variety of somatic and psychological disturbances are limited in number and aetiologically nonspecific (Bonhoeffer, 1908; Ströhle *et al.*, 2008). Bonhoeffer and others presaged the distinction between disease, in which there seem to be an underlying pathological evidence – and illness, in which a person reports symptomatic distress, but no pathological condition can yet be found (Kleinman, 1988).

We have had examples of *illnesses*, mostly characterised by distress for which underlying aetiologies were (or were not) eventually found. Gulf War Illness (GWI) is a recent and pertinent one, apparently affecting many soldiers who had served in the Gulf War campaign at the beginning of the 1990s. Taking an approach to definition along the lines of cause, form, course and outcome that would have been familiar to Kraepelin, numerous hypotheses to explain the GWI were never confirmed; they included exposure to different toxic agents or weapons and also psychiatric explanations. Despite being inconclusive, they offer some interesting

parallels with the expression of symptoms in the at-risk psychosis syndrome. For instance, the manifestation of GWI, despite having elements of different psychiatric categories, including post-traumatic stress disorder (PTSD), depression, anxiety and somatic symptoms, rarely met all the diagnostic criteria for any of them. Relevant observations confirmed an increase in formal psychiatric disorders, such as PTSD or depression, but they also showed that this increase was insufficient to explain the entirety of an illness that comprised a variety of *a priori* disparate psychiatric and physical symptoms (Wessely and Freedman, 2006). In fact, conditions such as GWI are extraordinarily difficult to investigate given the difficulty to fit a previously inexistent (or never reported) condition into current diagnostic constructs.

By applying the status of psychosis risk broadly, perhaps we have fortuitously discovered another distinctive condition that, in clinical settings, could be called common mental illness including psychotic experiences (Perez *et al.*, 2018), which does not fit into any diagnostic category and challenges the usefulness of the current psychiatric disciplinary *web* for many individuals. Common mental illness including psychotic experiences should not be another uselessly stigmatising label, but a distinctive definition for an unrecognised presentation affecting a distressed and disabled group. Indeed, evidence suggests that psychosis, depression and anxiety share causes and mechanisms (Nishida *et al.*, 2008; Varghese *et al.*, 2011; Kelleher *et al.*, 2012a; Russo *et al.*, 2014); however, current psychiatric diagnostic classifications do not yet acknowledge the presence of psychotic experiences in more common depressive or anxiety disorders. This is in spite of past diagnostic manuals, such as the ICD-9, acknowledging the difficulties clinicians may face in distinguishing between neurosis and psychosis in some presentations (World Health Organisation, 1978).

Ladies of Shalott

The concept of risk is commonly used in other areas of medicine but in psychiatry, it may have gained less traction as it lies on a more speculative knowledge-base (Rothstein, 2008). Psychosis risk follows a conventional medical science framework that keeps accumulating knowledge upon an assumption (the existence of certain clinical phenotypes that increase the likelihood of developing a psychotic disorder) in order to predict more accurately the conversion to psychosis. For many, such as ourselves, who have embarked in this enterprise the ultimate in predicting such conversion has become the Holy Grail; a scientific success that would bring not only patient benefit through preventative interventions but would also contribute to further alignment with the rest of medical specialities. To suffer the first-episode psychosis is irrefutably devastating and we should aim to prevent it; however, this narrowed vision may neglect the here and now. Psychosis risk is often used as a label for many people that will never develop a DSM/ICD psychotic disorder. They may already be suffering from a condition (wrongly named as 'at-risk' for another one) that does not fit into the *web*, but also deserves scientific attention and intervention.

However, a change of focus is not easy, involving a review of paradigms that are deeply entrenched in our scientific communities. According to Thomas Kuhn (1922–1996), deciding between different paradigms can yield good reasons for favouring one over another, but those reasons cannot be codified into an algorithmic scientific method that would decide the point objectively and conclusively. Thus, science is not irrational, but competing paradigms

may be incommensurable: there exists no objective way of assessing their relative merits. This incommensurability precludes the possibility of interpreting scientific development as an approximation to the truth. Scientific revolutions simply result in changes to the ontology. Therefore, a paradigm shift is so much one defying a curse or changing his/her own religion, and the reason to do so is often inscrutable. No matter how much evidence is provided to change the paradigm, it will all come to a time of crisis, a final acceptance that the end of the rainbow cannot be reached. Then, such a change begins to be pursued and endorsed widely, regardless of the outcome; this is the core of any paradigm shift (Kuhn, 1962; Orman, 2016).

We researchers working within established paradigms may become *Ladies of Shalott* weaving a charmed web, inspired by what we are allowed to see, but also cursed by our peers if we look beyond that. We may seem confident, in control, but, in reality, we are trapped in someone else's web. Notably, Tennyson's *Lady of Shalott* came to the realisation through a state of crisis when she decided to break through the colourful web she had patiently woven around her (see Fig. 1). Driven by the desire of knowing Lancelot and Camelot in the real world beyond her restricted gaze, she defied the curse and escaped. But what can be done until that sense of crisis and desire for change grips at-risk psychosis researchers, making us, all *Ladies of Shalott*, confront our curse and defiantly break the web?

Breaking the web

There is already a consensus on the high clinical relevance of psychotic experiences in depression and anxiety. This co-occurrence is associated with poor quality of life, bad clinical and functional outcomes, and increased risk of self-harm (Granö *et al.*, 2011; Hutton *et al.*, 2011; Kelleher *et al.*, 2012b; Hui *et al.*, 2013; Fusar-Poli *et al.*, 2014). People suffering from this combination of symptoms are at least seven times less likely to reach remission of depressive symptoms. Psychotic experiences predict poorer response to standard psychological treatments for depression and anxiety, even in combination with pharmacotherapy (Perlis *et al.*, 2011; Wigman *et al.*, 2014; Perez *et al.*, 2018).

Nonetheless, people with common mental illness including psychotic experiences are served badly by current diagnostic classifications and by the aim to perfect a predictive test for psychotic disorders rather than enhancing interventions for current symptoms (Ajnakina *et al.*, 2018; Moritz *et al.*, 2019). As stated before, these people have psychotic experiences as part of what is often a kaleidoscopic and disabling mental state. They may be found in secondary mental health services, placed under the conceptual umbrella of the at-risk mental state, but it is also highly likely that given an overall lower severity of their mental health problems, a very high proportion attends primary care settings or remains untreated in their communities (Perez *et al.*, 2015, 2018). Many of these individuals may find themselves in a service no-man's-land when they seek help, with therapies given in the wrong settings to the wrong people.

Emerging evidence suggest that at least 25% of all the people with common mental disorders treated by the Improving Access to Psychological Therapies (IAPT) programme in England may have this unrecognised condition (Perez *et al.*, 2018). IAPT services sit in primary care and provide access to evidence-based psychological treatments, predominantly within a cognitive-behavioural therapy framework, to over one million people with common mental disorders every year. Also caught



Fig. 1. The Lady of Shalott: Breaking of the Web. William Holman Hunt's illustration to 'The Lady of Shalott' from the Edward Moxon edition of Tennyson's Poems, 1857

"She left the web, she left the loom, She made three paces thro' the room, She saw the water-lily bloom, She saw the helmet and the plume, She look'd down to Camelot."

up in the *web*, these services routinely record patient-reported questionnaires for depression and anxiety but do not measure or treat psychotic experiences (NHS England, 2019). If one-in-four people treated in primary care IAPT services suffer from common mental illness including psychotic experiences, the prospects of recovery for a significant population may be affected by the use of standard talking therapies that do not target all relevant symptoms. This all indicates that, perhaps, the best way to start *breaking the web* is simply trying to improve these people's life. We have got some highly effective, evidence-based interventions for depression and anxiety, and increasingly confident approaches for helping people with psychotic experiences that may ease these phenomena and promote recovery. Effective psychological treatments for common mental illness including psychotic experiences may already exist (Devoe *et al.*, 2019) but, just as the condition is scattered across different chapters of the diagnostic manuals, these treatments are scattered between different clinical settings that are inadequate to assess or treat trans-diagnostic conditions.

The 2016 NHS Access & Waiting Time Standard for people with an at-risk mental state in England (NHS England, 2016) is resulting in more people with psychotic experiences referred to

secondary care psychosis services. This is contrary to research on transition rates, especially in people referred from primary care (Hui *et al.*, 2013; Perez *et al.*, 2015), the limited capacity of these services and their users' needs, many of whom have common mental illness including psychotic experiences. Accommodating them and providing an effective therapy in low-stigma IAPT services will allow specialist early intervention services to concentrate on first-episode psychotic disorders (van Os and Guloksuz, 2017; Perez *et al.*, 2018). If the available treatments were reconfigured and assembled into a practical therapeutic toolbox for use in primary care settings, e.g. IAPT services, where most people with the condition are already seeking help and where they would receive their treatment, prospects for recovery could be greatly improved.

The UK National Institute for Health Research (NIHR) recently funded the TYPPEX programme (National Institute for Health Research, 2018). This national programme primarily aims to provide effective treatment to a vulnerable group in the lowest possible stigma setting. It will develop and test a tailored psychological therapy and training for therapists in IAPT services to detect and treat people with common mental illness including psychotic experiences in their caseloads more effectively. Bold and

iconoclastic, it should provide trans-diagnostic evidence beyond the inadequate boundaries of the diagnostic web, and guide further applied health research on treatments and mental health services for this population.

Conclusion

Current psychiatry is built upon accepted paradigms. Proto-diagnoses, such as the at-risk mental state for psychosis, remain loyal to our long-standing categorical nosology and risk and prediction paradigms mostly adopted from other medical specialities. Despite transition rates in people with the at-risk mental state have declined over the years, especially in samples referred from primary care settings, we continue perfecting prediction tools to whittle down populations in order to detect those at the highest risk. This whittling exercise forbids us from perceiving features in a wider horizon where we may have unwittingly discovered another condition that could be called common mental illness including psychotic experiences.

The at-risk mental state, considered but ultimately shelved by the DSM-5, is the exemplar that should make us break free of the entire diagnostic web. However, such a shift of vision would imply defying the spell preventing us from any attempt to think differently. Tennyson's poem ends with the Lady of Shalott breaking the web that she carefully wove over the years, but dying on a boat just before reaching Camelot. She did not manage to see the real world in its entirety, as by breaking a curse she triggered another one. This outcome also reflects the nature of paradigm shifts. No new paradigm is better than an old one; it simply continues enriching our knowledge until gradually turns into another course that prevents us from finding the truth.

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References

- Ajnakina O, Morgan C, Gayer-Anderson C, Oduola S, Bourque F, Bramley S, Williamson J, MacCabe JH, Dazzan P, Murray RM and David AS (2017) Only a small proportion of patients with first episode psychosis come via prodromal services: a retrospective survey of a large UK mental health programme. *BMC Psychiatry* **25**, 308.
- Ajnakina O, David AS and Murray RM (2018) At risk mental state' clinics for psychosis - an idea whose time has come - and gone!. *Psychological Medicine* **26**, 1–6.
- American Psychiatric Association (1980) *The Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III)*. Washington, DC: American Psychiatric Association Publishing.
- American Psychiatric Association (1987) *The Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised (DSM-III-R)*. Washington, DC: American Psychiatric Association Publishing.
- American Psychiatric Association (2013) *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Revised (DSM-5)*. Washington, DC: American Psychiatric Association Publishing.
- Berrios GE (1999) Classification in psychiatry: a conceptual history. *Australian and New Zealand Journal of Psychiatry* **33**, 145–160.
- Bonhoeffer K (1908) Zur frage der klassifikation der symptomatischen psychosen. *Berliner Klin Wochenschr* **45**, 2257–2260.
- Cornblatt B, Lencz T and Obuchowski M (2002) The schizophrenia prodrome: treatment and high-risk perspectives. *Schizophrenia Research* **54**, 177–186.
- Devoe DJ, Farris MS, Townes P and Addington J (2019) Attenuated psychotic symptom interventions in youth at risk of psychosis: a systematic review and meta-analysis. *Early Intervention in Psychiatry* **13**, 3–17.
- Fusar-Poli P, Bonoldi I, Yung AR, Borgwardt S, Kempton MJ, Valmaggia L, Barale F, Caverzasi E and McGuire P (2012) Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. *Archives of General Psychiatry* **69**, 220–229.
- Fusar-Poli P, Nelson B, Valmaggia L, Yung AR and McGuire PK (2014) Comorbid depressive and anxiety disorders in 509 individuals with an at-risk mental state: impact on psychopathology and transition to psychosis. *Schizophrenia Bulletin* **40**, 120–131.
- Granö N, Karjalainen M, Souminen K and Roine M (2011) Poor functioning ability is associated with high risk of developing psychosis in adolescents. *Nordic Journal of Psychiatry* **65**, 16–21.
- Hoff P (2015) The Kraepelinian tradition. *Dialogues in Clinical Neuroscience* **17**, 31–41.
- Hui C, Morcillo C, Russo DA, Stochl J, Shelley GF, Painter M, Jones PB and Perez J (2013) Psychiatric morbidity, functioning and quality of life in young people at clinical high risk for psychosis. *Schizophrenia Research* **148**, 175–180.
- Hutton P, Bowe S, Parker S and Ford S (2011) Prevalence of suicide risk factors in people at ultra-high risk of developing psychosis: a service audit. *Early Intervention in Psychiatry* **5**, 375–380.
- Kelleher I, Keeley H, Corcoran P, Lynch F, Fitzpatrick C, Devlin N, Molloy C, Roddy S, Clarke MC, Harley M, Arseneault L, Wasserman C, Carli V, Sarchiapone M, Hoven C, Wasserman D and Cannon M (2012a) Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. *British Journal of Psychiatry* **1**, 26–32.
- Kelleher I, Lynch F, Harley M, Molloy C, Roddy S, Fitzpatrick C and Cannon M (2012b) Psychotic symptoms in adolescence index risk for suicidal behavior: findings from 2 population-based case-control clinical interview studies. *Archives of General Psychiatry* **69**, 1277–1283.
- Kendler KS (1990) Toward a scientific psychiatric nosology. *Archives of General Psychiatry* **47**, 969–973.
- Kleinman A (1988) *Patients and Healers in the Context of Culture: An Exploration of the Borderland Between Anthropology, Medicine, and Psychiatry*. Berkeley, CA: University of California Press.
- Kuhn T (1962) *The Structure of Scientific Revolutions*. Chicago: Chicago University Press.
- Lin A, Wood SJ, Nelson B, Beavan A, McGorry P and Yung AR (2015) Outcomes of non-transitioned cases in a sample at ultra-high risk for psychosis. *American Journal of Psychiatry* **172**, 249–258.
- Mathers N and Hodgkin P (1989) The Gatekeeper and the Wizard: a fairy tale. *British Medical Journal* **298**, 172–174.
- McGorry PD and Mei C (2018) Ultra-high-risk paradigm: lessons learnt and new directions. *Evidence Based Mental Health* **21**, 131–133.
- McGorry PD, Nelson B, Markulev C, Yuen HP, Schäfer MR, Mossaheb N, Schlögelhofer M, Smesny S, Hickie IB, Berger GE, Chen EY, de Haan L, Nieman DH, Nordentoft M, Riecher-Rössler A, Verma S, Thompson A, Yung AR and Amminger GP (2017) Effect of ω -3 polyunsaturated fatty acids in young people at ultrahigh risk for psychotic disorders: the NEURAPRO randomized clinical trial. *JAMA Psychiatry* **74**, 19–27.
- Moritz S, Gawęda Ł, Heinz A and Gallinat J (2019) Four reasons why early detection centers for psychosis should be renamed and their treatment targets reconsidered: we should not catastrophize a future we can neither reliably predict nor change. *Psychological Medicine* **24**, 1–7.
- Morrison AP, French P, Stewart SL, Birchwood M, Fowler D, Gumley AI, Jones PB, Bentall RP, Lewis SW, Murray GK, Patterson P, Brunet K, Conroy J, Parker S, Reilly T, Byrne R, Davies LM and Dunn G (2012) Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. *British Medical Journal* **344**, e2233.
- Murray GK and Jones PB (2012) Psychotic symptoms in young people without psychotic illness: mechanisms and meaning. *British Journal of Psychiatry* **201**, 4–6.

- National Institute of Health Research (NIHR)** (2018) Innovative mental health study launches in eastern region. Available at <https://www.nihr.ac.uk/news/innovative-mental-health-study-launches-in-eastern-region> (Accessed 31 May 2019).
- NHS England** (2016) Implementing the Early Intervention in Psychosis Access and Waiting Time Standard: Guidance. Available at <https://www.england.nhs.uk/mentalhealth/wp-content/uploads/sites/29/2016/04/eip-guidance.pdf> (Accessed 31 May 2019).
- NHS England** (2019) Adult Improving Access to Psychological Therapies programme. Available at <https://www.england.nhs.uk/mental-health/adults/iapt/> (Accessed 31 May 2019).
- Nishida A, Tani H, Nishimura Y, Kajiki N, Inoue K, Okada M, Sasaki T and Okazaki Y** (2008) Associations between psychotic-like experiences and mental health status and other psychopathologies among Japanese early teens. *Schizophrenia Research* **99**, 125–133.
- Orman TF** (2016) “Paradigm” as a central concept in Thomas Kuhn’s thought. *International Journal of Humanities and Social Science* **6**, 47–52.
- Perez J, Jin H, Russo DA, Stochl J, Painter M, Shelley G, Jackson E, Crane C, Grafty JP, Croudace TJ, Byford S and Jones PB** (2015) Clinical effectiveness and cost-effectiveness of tailored intensive liaison between primary and secondary care to identify individuals at risk of a first psychotic illness (the LEGs study): a cluster-randomised controlled trial. *The Lancet. Psychiatry* **2**, 984–993.
- Perez J, Russo DA, Stochl J, Clarke J, Martin Z, Jassi C, French P, Fowler D and Jones PB** (2018) Common mental disorder including psychotic experiences: trailblazing a new recovery pathway within the Improving Access to Psychological Therapies programme in England. *Early Intervention in Psychiatry* **12**, 497–504.
- Perlis RH, Uher R, Ostacher M, Goldberg JF, Trivedi MH, Rush AJ and Fava M** (2011) Association between bipolar spectrum features and treatment outcomes in outpatients with major depressive disorder. *Archives of General Psychiatry* **68**, 351–360.
- Rothstein WG** (2008) *Public Health and the Risk Factor: A History of an Uneven Medical Revolution*. Rochester: University of Rochester Press.
- Russo DA, Stochl J, Painter M, Dobler V, Jackson E, Jones PB and Perez J** (2014) Trauma history characteristics associated with mental states at clinical high risk for psychosis. *Psychiatry Research* **220**, 237–244.
- Shorter E** (2015) The history of nosology and the rise of the diagnostic and statistical manual of mental disorders. *Dialogues in Clinical Neuroscience* **17**, 59–67.
- Sokal RR** (1974) Classification: purpose, principle, progress, prospects. *Science* **185**, 1117–1119.
- Stochl J, Khandaker GM, Lewis G, Perez J, Goodyer IM, Zammit S, Sullivan S, Croudace TJ and Jones PB** (2015) Mood, anxiety and psychotic phenomena measure a common psychopathological factor. *Psychological Medicine* **45**, 1483–1493.
- Ströhlle A, Wrase J, Malach H, Gestrich C and Heinz A** (2008) Karl Bonhoeffer (1868–1948). *American Journal of Psychiatry* **165**, 5–6.
- Tennyson A** (1857) *Poems. The Lady of Shallot*. London: Edward Moxon.
- van Os J and Guloksuz S** (2017) A critique of the “ultra-high risk” and “transition” paradigm. *World Psychiatry* **16**, 200–206.
- Varghese D, Scott J, Welham J, Bor W, Najman J, O’Callaghan M, Williams G and McGrath J** (2011) Psychotic-like experiences in major depression and anxiety disorders: a population-based survey in young adults. *Schizophrenia Bulletin* **37**, 389–393.
- Wessely S and Freedman L** (2006) Reflections on Gulf War illness. *Philosophical Transactions of the Royal Society of London B Biological Sciences* **361**, 721–730.
- Wigman JT, van Os J, Abidi L, Huibers MJ, Roelofs J, Arntz A, Kelleher I and Peeters FP** (2014) Subclinical psychotic experiences and bipolar spectrum features in depression: association with outcome of psychotherapy. *Psychological Medicine* **44**, 325–336.
- World Health Organisation** (1978) *The International Classification of Diseases*, 9th Edn. Geneva: World Health Organisation.
- Yung AR, McGorry PD, McFarlane CA, Jackson HJ, Patton GC and Rakkar A** (1996) Monitoring and care of young people at incipient risk of psychosis. *Schizophrenia Bulletin* **22**, 283–303.
- Yung AR, Phillips LJ, Yuen HP, Francey SM, McFarlane CA, Hallgren M and McGorry PD** (2003) Psychosis prediction: 12-month follow up of a high-risk (“prodromal”) group. *Schizophrenia Research* **60**, 21–32.