Moving from risk to resilience in psychosis research

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Abstract

Psychosis research has traditionally focused on vulnerability and the detrimental outcomes of risk exposure. However, there is substantial variability in psychological and functional outcomes for those at risk for psychosis, even among individuals at high risk. Comparatively little work has highlighted the factors associated with resilience and the processes that might avert serious mental illness and promote positive outcomes. In this Review, we first discuss the prevailing risk-based approach to psychosis. We then outline a resilience-based approach by defining multisystemic mental health resilience and considering what constitutes a positive outcome. Based on this background, we examine evidence of biological, psychological, social and environmental protective and promotive factors that might confer resilience in the context of psychosis risk. A greater understanding of the factors and processes implicated in resilience has the potential to inform psychosis intervention and prevention efforts at multiple levels, including individuals, institutions, and policy.

[H1] Introduction

Psychotic disorders, including schizophrenia, are characterized by signs of departure from consensus reality, for example, hallucinations and delusions. This departure is often accompanied by disorganization of thought and behavior and diminished expressivity and motivation. The impact of psychotic disorders, and the discrimination and marginalization that occur in their wake, are tremendous. People diagnosed with schizophrenia have a lower life expectancy in Western countries[1], higher rates of homelessness worldwide[2-8], and drastically reduced quality of life[9] compared to those without a diagnosis of schizophrenia.

Psychotic disorders were historically viewed as irreversible and progressively deteriorating conditions that were inevitably associated with poor outcomes and disability[10]. However, in the past 30 years a more optimistic paradigm focused on psychosis prevention has emerged[11-13]. To this end, there has been a massive effort to identify factors that increase an individual's risk for developing a psychotic disorder, with the hope that targeted interventions might prevent or delay onset. Individuals seeking mental health treatment who are identified as at high-risk for psychosis show markedly increased rates of developing a psychotic disorder, relative to lifetime incidence rates in the general population[14]. However, around two-thirds of help-seeking at-risk individuals are never diagnosed with a psychotic disorder[15], and around 40% remit from high-risk status after 3 years[16]. These findings dovetail with the variability in clinical trajectories of individuals diagnosed with psychotic disorders—although many have poor long-term outcomes, over 50% show extended periods of recovery[17-21]. These data suggest the presence of internal and/or external assets and resources that can be leveraged to avert serious mental health symptoms in people with or at high-risk for psychotic disorders.

There has been comparatively little work examining those factors that might promote multifaceted positive outcomes in the face of psychosis risk. Understanding the factors that buffer against risk will help elucidate the etiological heterogeneity observed in individuals at-risk for psychosis and offer mechanistic insights into why many of them do not experience negative outcomes. Furthermore, identifying modifiable protective and promotive factors can provide important malleable targets for clinical treatments, and intervention strategies based on resilience can complement those designed to eliminate preventable risks[22]. Thus, a greater focus on resilience in the context of psychosis risk is critical for advancing the field and promoting therapeutic discovery[23].

In this Review, we first briefly summarize the literature on risk factors for psychosis and then describe the strengths and drawbacks of a purely risk-based approach. Next, we present modern conceptualizations of mental health resilience and consider what constitutes a positive outcome. Finally, we describe the factors that might confer resilience in the context of psychosis risk and conclude with recommendations for future directions. Although we focus on psychosis, many of the factors we identify throughout the Review are transdiagnostic and might convey risk and resilience for a host of psychopathological disorders.

[H1] The risk-based approach to psychosis

Converging evidence supports a diathesis-stress etiological model of psychotic disorders, whereby genetic risk interacts with social and environmental stressors to influence the development of symptoms[24-26]. There is strong evidence for a genetic contribution to the onset and maintenance of these disorders. Having a first-degree relative with a serious mental illness is one of the most well-established risk factors for psychosis. In a study of over 30,000 twin pairs spanning 50 years, concordance rates of schizophrenia were approximately 33% in monozygotic twins with an estimated heritability of 73% for schizophrenia-spectrum disorders[27].

Having a parent with a serious mental illness also increases risk for psychosis: a meta-analysis of 33 studies showed that the children of parents with serious mental illness were 6.5 times more likely to develop schizophrenia than the children of parents without serious mental illness[28]. Genome-wide association studies have also identified specific genes that confer greater risk for psychosis, with one report detecting 10 gene variants with odds ratios ≥ 3.0 for the development of schizophrenia[29]. Variations in *GRIN2A*, a glutamate receptor, and *SP4*, involved in transcription regulation, have been implicated in multiple reports as carrying greater risk for psychosis and for developmental disorders such as autism[29,30].

In terms of non-genetic risk factors, the earliest stressors might occur during prenatal and perinatal periods[31,32] and include maternal infection, medical conditions, experiencing stress during pregnancy, and complications during pregnancy or delivery. In early childhood, a variety of factors (such as early hearing impairments[33], communication deviations in parents[34], and delays in sitting, standing, or walking independently[35]) have also been associated with increased risk. These early behavioural risk factors might be secondary to prenatal and perinatal environmental risk exposure.

Social and environmental risk factors during late childhood and more proximally to illness onset (typically in late adolescence and early adulthood) have been summarized and evaluated in several meta-analyses[36] and reviews[32,36,37]. One prominent risk factor during this period is childhood trauma, which has been consistently found at high rates among individuals who later develop psychosis[38,39]. There is also extensive evidence that stressful life events in adulthood are associated with an increased risk for subclinical psychotic symptoms and a psychotic disorder diagnosis[40]. In the past decade, there has been increased focus on the role of discrimination as a risk factor for psychosis. Higher rates of subclinical psychotic symptoms, psychotic experiences, and psychotic symptoms have been found in individuals from communities that have been marginalized on the basis of race and ethnicity[41,42] as well as in sexual and gender minority communities[43], and structural racism in the United States has been explicitly linked with psychosis risk[44]. Finally, the environment where one lives and who inhabits those spaces plays an important role in the development of psychosis. A meta-analysis of eight studies and nearly 46,000 people found that the risk for schizophrenia was 2.37 times higher in urban areas than in rural environments[45]. Exposure to such environmental stressors might account for the widely replicated finding of increased stress-sensitivity in individuals with psychosis[46,47,48]. Here stress sensitization, whereby the response to some environmental stressor increases in intensity with repeated exposures, transpires and results in enduring alterations in stress-sensitivity.

This vast body of evidence describing factors that are associated with an increased risk of psychotic disorder onset has contributed to the development of mental health policies and practices that emphasize the importance of reducing the burden of these disorders in the population [49,50]. Over the past 30 years the clinical high-risk paradigm[13], which aims to identify individuals in the prodromal phase of a psychotic disorder as part of a preventative approach, has been the major focus within psychosis research. Current criteria define individuals at clinical high-risk as those who have either attenuated psychotic symptoms, full psychotic symptoms for a brief period, or substantial genetic risk paired with functional decline. Formal risk calculators have been created to enhance prediction of which individuals identified at clinical high risk will transition to psychosis[51,52]. These enhanced predictive models represent an important strength of risk-based approaches. Moreover, studies of risk can also help quantify how much risk is conveyed by specific factors. For example, according to meta-analyses the odds of experiencing childhood trauma is almost 3 times higher[37] and the odds of perceived discrimination is almost twice as high[40] among individuals who later develop psychosis

compared to controls. A risk-based approach also has important clinical implications for help-seeking youth. Early identification permits both preventative care and intervention earlier in the course of illness. This is important because shorter durations of untreated psychosis are associated with better prognosis post-diagnosis[53,54] (but see[55]), and reducing the duration of untreated psychosis is a major emphasis of treatment programs. Finally, identifying individual risk factors can enable increased personalization of treatment on the basis of specific risk exposure. Thus, a focus on risk factors sets the groundwork for treatment development and treatment targets, usually aimed at eliminating preventable risks.

Despite these strengths, relying solely on a risk-based approach for psychosis, where risk is an event or context that is directly associated with poor outcomes, has several shortcomings[56]. For example, relying solely on risk might lead to over-prediction of risk[57] and, accordingly, suboptimal treatment planning such as excessive or unnecessary interventions. Indeed, up to 70% of people identified as high-risk do not develop a psychotic disorder within three years[14,58-60]. This percentage is even higher in studies that use broader recruitment strategies, resulting in samples that are less biased towards help-seeking individuals with more severe subclinical symptoms[61-67]. Furthermore, opportunities to develop novel treatments might be limited given that the risk factors that have received the most robust support (for example, subclinical psychotic experiences and genetic risk) do not easily lend themselves to therapeutic innovation. Indeed, meta-analytic findings indicate that no specific preventative interventions have yet been identified[13,68]. In addition, an exclusive focus on risk and deficits might exacerbate the stigma associated with psychosis[69-71,72,73], which is itself linked to poor mental health outcomes[74,75].

Finally, a risk-based perspective spotlights vulnerability and fails to consider the possibility that individuals who are highly sensitive to negative contexts might also be most responsive to the enhancing effects of positive contexts—a pattern described by the differential susceptibility model[76]. That is, individuals at high-risk for psychosis might also be particularly sensitive to the beneficial effects conferred by internal and external resources and assets. A large population-based study showed that individuals with high levels of childhood adversity had more dramatic changes in mental health during adulthood as a function of both increases and decreases in life stress across the lifespan compared with individuals with low levels of adversity[77]. These findings suggest that childhood adversity might function as a differential susceptibility factor that increases responsiveness to both negative and positive contexts later in life.

In sum, the transition rates of high-risk individuals are higher than incidence rates of psychotic disorders in the general population and therefore a risk-based approach is useful for identifying individuals who will develop a disorder. But an approach purely focused on negative outcomes neglects valuable information about what is protecting those at high-risk from developing psychotic disorders or other severe mental health outcomes and—perhaps more importantly—what helps people function and thrive despite risk factors[78,79]. Risk-based approaches can be complemented by resilience-based approaches that focus on the access to resources and cultivation of assets and strengths that help people weather atypical risk in ways that yield positive outcomes.

[H1] The resilience-based approach

In this section, we define resilience and discuss the challenges in defining positive outcomes in the context of psychosis. Modern research on human resilience originated largely from the child development literature that aimed to identify factors that lead to positive adaptation despite early adversity. We provide relevant background bridging the gap between this developmental literature and the interpretation and contextualization of resilience factors in psychosis.

[H2] Defining resilient processes.

Resilience is the process by which a system (an individual, a community, or a biological entity) fares better than expected given exposure to some risk or adversity that threatens functioning[22,80,81]. Central to this definition is that resilience is a process—not a stable trait—in which protective and promotive factors support recovery, persistence, resistance, or adaptation (**Figure 1**). Furthermore, because human development across the lifespan transpires within a set of interacting systems[82], individual resilience is inherently multisystemic[83]. Specifically, human resilience can be conceptualized as a network of protective and promotive factors that confer positive outcomes and span multiple interacting subsystems or levels ranging from individual biology (such as genes) to the natural environment (such as green space) [83].

Resilience can only be studied in the context of risk or adversity. In the context of psychosis, risk might refer to factors that increase the chance of a psychotic disorder diagnosis, the experience of those symptoms (for example, experiencing persistent hallucinations might be a source of psychological distress[84]), or secondary factors that might emerge after a diagnosis of psychotic disorder (for example, poor physical health or discrimination[85,86]). Vulnerabilities and protective factors moderate the impact of risk and lead to outcomes that are worse or better than expected, respectively (**Box 1**). That is, a vulnerability factor intensifies the maladaptive outcomes in response to risk exposure and a protective factor reduces them[87]. Note that the terms ‘vulnerability factors’ and ‘protective factors’ refer to the mechanisms by which these factors exert their effects on a specific set of outcomes given a specific risk[88]. That is, vulnerability factors are not inherently bad and protective factors are not inherently good. Protective factors are distinguished from promotive factors. Promotive factors are associated with positive outcomes regardless of risk exposure; promotive effects are indicated by a main effect of a particular factor on a positive outcome measure. By contrast, protective factors are associated with positive outcomes in a risk-dependent manner and are indicated by an interaction effect, where the magnitude of association between the factor and the positive outcome is moderated by risk status. For example, social support would be considered a protective factor in the context of psychosis risk if it showed a stronger association with positive outcomes in young adults at clinical high-risk for psychosis than in a population sample of young adults; however, social support would be considered promotive if it was associated with positive outcomes regardless of clinical high-risk status.

[H2] Defining positive outcomes.

In the context of mental health, positive outcomes include functioning that aligns with or exceeds developmental or contextual norms. Defining a positive outcome that is indicative of a resilient process is challenging for several reasons. First, positive outcomes are multifaceted and include both developmental competence (for example, academic and occupational achievement, interpersonal competence, completing developmental milestones) and mental health[89]. Importantly, although a person might exhibit resilience in some aspects of functioning or mental health, few people are resilient in all domains[90]. Longitudinal studies of recovery in people with schizophrenia have revealed that positive functional outcomes (such as increased community integration) are independent of mental health outcomes such as reduced depression[91]. There is further nuance within psychological health, which entails both subjective well-being and the absence of distress or diagnosis[92-96]. Indeed, well-being and psychopathology are not two sides of the same coin. For example, some teens exhibit high well-being despite significant psychopathology; others conversely exhibit low well-being without significant psychopathology[92]. Positive mental health outcomes in the context of psychosis risk go beyond the absence of distress or formal diagnosis and measurements should include all dimensions of psychological health.

Second, who defines a positive outcome is shaped by power dymanics[97] and which individuals or systems benefit from a particular outcome must be carefully considered. The priorities of the health care systems, clinical care providers, and families might not always overlap with the priorities of the individual with psychosis. Research in psychosis prevention and recovery has traditionally focused on the absence of clinical psychotic symptoms and identifying the factors that prevent, delay, or reduce psychosis. This narrow definition diverges from the richer qualitative and psychosocial descriptors of well-being in individuals with psychotic disorders, whereby personal recovery is not necessarily contingent on clinical recovery[98-101]. To individuals seeking treatment, symptom remission alone might be insufficient to achieving a positive outcome. Rebuilding or regaining a meaningful life is central to recovery from psychosis, together with symptom management. Qualitative studies suggest that some positive changes at individual, interpersonal, and spiritual levels can occur for many individuals and their caregivers after the first episode of psychosis, despite broadly negative experiences[102]. Furthermore, a rich literature in phenomenological psychiatry has highlighted that some aspects of psychosis, which are considered to be a clinically negative outcome, might in fact provide an individual with meaning and relief and thereby confer resilience. An illuminating example is the case of delusions (**Box 2**).

Although objective and subjective indicators of well-being and quality of life are increasingly being used as outcome measures in psychosis research[103], frequently used scales might not align with the qualitative descriptions provided by mental health service users[104]. Taken together, current metrics of positive outcomes might not fully capture the heterogeneity of individual experience. Whilst efforts to quantify outcomes into categories and metrics are pragmatic and valid solutions to capturing subjective illness experiences, much is lost in the process. The result is that the vast scope and richness of meaning embedded in the internal landscape of individuals with psychosis-spectrum conditions are reduced to impoverished ratings that obscure the phenomenology of lived experience.

[H1] Resilience factors for psychosis

Meta-analyses have highlighted a striking dearth of studies investigating the factors that lead to positive mental health and functional outcomes despite psychosis risk[105,106]. In this section, we review potential promotive and protective factors in the context of psychosis risk with the aforementioned limitations and challenges in defining positive outcomes in mind. Protective and promotive factors are identified as those for which increased levels lead to increases in positive outcomes. We include potential protective and promotive factors that: decrease the chances of being diagnosed with a psychotic disorder in individuals at clinical high-risk and in general population samples; promote well-being and daily functioning and reduce relapse in individuals diagnosed with a psychotic disorder; and distinguish individuals experiencing psychotic symptoms that do and do not require care (such as those for whom auditory hallucinations cause impairment or disability versus those for whom auditory hallucinations are not distressing and often perceived to have a positive impact[84,107]).

The reviewed promotive and protective factors (**Table 1**) are organized by interacting levels of a biopsychosocial-ecological system that supports resilience of an individual (**Figure 2**). We include distal factors that might precede the onset of psychosis (for example, those occurring in childhood) as well as factors that would be expected to play a proximal role in promoting positive outcomes and buffering against more immediate risks (for example, current health behaviors). We recognize that these factors do not necessarily fit neatly into one level but rather behave as a cross-level system and are expected to exert their effects via their interactions[83] (**Box 3**). Finally, this review of resilience factors is not exhaustive but is intended to provide an

overview to identify trends and offer a basis for future work. Across categories the factors reviewed were chosen based on the breadth of the evidence base (factors that were identified in only a single study are not included). We furthermore focused our review on modifiable factors, which likely have more proximal clinical implications. For a broader discussion of biological resilience factors see ref[31] for a review of prenatal and perinatal factors and refs[108,109] for reviews of neuroimaging findings.

[H2] Biological factors

In this section, we focus on three potentially modifiable protective and promotive factors at the biological level: sleep, physical activity, and homeostatic regulation of the autonomic nervous system.

Better sleep quality is associated with better mental health and well-being in the general population[110], particularly among young adults[111], and interventions to improve sleep quality decreased paranoia and hallucinations in college students with psychotic-like symptoms[112]. However, sleep quantity has a non-linear relationship with mental health. Although sleep deprivation can precede the onset of psychosis[113] and is associated with impaired cognitive function and reduced physical and mental well-being[114], excessive sleep quantity is associated with increased depression and negative affect[115]. It is therefore possible that there is an optimal amount of sleep that confers mental health benefits in the context of psychosis risk; however, these optimal sleep parameters still need to be determined.

Physical activity also promotes mental health benefits in the general population[116-118] even at lower levels of intensity [119-121] than the current World Health Organization recommendations[122] (but see ref [123]). Physical activity during childhood protects against later psychotic symptoms in children with multiple adverse childhood experiences[124] and in the general population[125,126]. Moreover, increased physical activity is associated with increased well-being and functioning, improved cognitive performance, and reduced psychiatric symptoms in those with psychotic disorders[127-131]. Akin to sleep quantity, physical activity has protective and promotive effects at low to moderate, but not high, levels[132].

Finally, homeostatic regulation of the autonomic nervous system in response to moment-to-moment demands might be a biological correlate of adaptive capacity[133,134]. In individuals with normal cardiac function, higher resting state heart rate variability and respiratory sinus arrhythmia are associated with better emotion regulation[133,135] and cognitive performance[136,137], whereas low heart rate variability and respiratory sinus arrhythmia suggest a rigidity of autonomic response and are associated with poor physical[136,137] and mental health[135,138]. People with psychotic illness have lower resting state heart rate variability and respiratory sinus arrhythmia compared to controls[139-143], and individual differences in heart rate variability and/or respiratory sinus arrhythmia have been associated with emotion regulation[144], psychiatric symptom burden[142], cognitive performance[143,145,146], and functioning in this clinical population[142-146]. Notably, these autonomic responses are malleable through biofeedback training [147-150], breathing retraining[147,150], mindfulness practice[151], and physical exercise[149,152]. Two studies of heart rate variability biofeedback training in individuals at-risk for psychosis suggest potential benefits to both autonomic activity and clinical symptoms[153,154].

[H2] Psychological factors

The psychological factors that have garnered significant support as potential protective and promotive factors in the context of psychosis risk can be roughly organized into three main

categories: traits and personal characteristics; attitudes, cognitions, and orientations; and psychological abilities.

[H3] Traits and personal characteristics

Adaptive coping —a cognitive or behavioral process that has long-term benefits for minimizing stress[155,156] — is associated with less severe psychotic-like symptoms in both the general population[157,158] and in at-risk youth[159] and is correlated with reduced symptom severity and increased quality of life in individuals diagnosed with schizophrenia[160-164]. One longitudinal study found that adaptive coping at baseline was associated with attenuated clinical symptom severity and better social functioning one year later in youth at high-risk for psychosis, suggesting a causal effect of adaptive coping on outcomes[165]. Relatedly, some emotion regulation strategies might also confer resilience in the context of psychosis risk. Trait use of reappraisal strategies, which aim to modify the meaning and impact of emotion-eliciting events, is associated with less severe psychotic-like experiences[166] and protects against the distress of these experiences[167].

Self-esteem, locus of control, and personality dimensions might also confer beneficial effects. Higher self-esteem is associated cross-sectionally with reduced psychotic and psychotic-like experiences in at-risk youth[168,169], improved quality of life[170] and reduced suicidality in individuals diagnosed with schizophrenia[171], and protects against distress associated with persistent psychotic experiences[172]. Longitudinal studies have shown that baseline self-esteem is associated with a lower likelihood of psychosis onset 3 years later in the general population[173]. Internal locus of control refers to the degree to which an individual feels that they are responsible for their own outcomes and is associated with a number of positive outcomes in the context of psychosis risk. Qualitative studies indicate that individuals experiencing their first episode of psychosis identify loss of control as their primary psychosocial problem[174], and regaining self-efficacy is a major component of recovery[175]. In addition, an internal locus of control might buffer the effect of harsh parenting on later psychotic symptoms[176]. Among individuals with auditory-verbal hallucinations, the ability to exert volitional control over voices is one of the main characteristics that distinguishes individuals who seek treatment from those who do not[177,178]. Finally, broad personality domains such as openness, extraversion, and emotional stability (the inverse of neuroticism) protect against the distress surrounding delusional ideas[179]. In people with schizophrenia, emotional stability, extraversion, and agreeableness are also related to better subjective quality of life and might buffer against some of the negative impacts of traumatic experiences[180-182].

[H3] Attitudes and orientations

In the context of psychosis risk, there are three candidate protective and promotive factors and processes that represent attitudes, cognitions, or orientations that might contribute to positive outcomes: stigma resistance, spirituality and/or religiosity, and meaning-making around unusual experiences. These three factors are a part of a broader category of attitudes and orientations that help people contextualize psychological experiences.

Public stigma about mental illness, which manifests in negative beliefs and attitudes about people with mental illness and overt discrimination[183], can result in internalization of those negative attitudes[184]. Self-stigma is associated with negative clinical outcomes[185,186], whereas the capacity to counteract or be unaffected by stigma (stigma resistance) is related to well-being and quality of life in individuals with psychotic disorders[187-189]. Importantly, cognitions about stigma (for example, rejecting stigma as unfair), rather than perceived stigma (for example, the observed level of stigma against people with mental illness) predicted help-seeking in those with psychosis[190]. Although more work is needed to evaluate interventions that boost stigma resistance in individuals with schizophrenia, there is evidence that self-stigma reduction

strategies, such as providing psychoeducation about the illness experience and the consequences of stigma and teaching methods for reducing self-stigmatizing attitudes, can improve psychological outcomes[191,192].

Spirituality generally confers benefits to mental health[193,194]. Spirituality (commonly defined as "the search for the sacred"[195]) is related to self-reported adaptation in the face of adversity among individuals diagnosed with a psychotic disorder [196]. Furthermore, sensing the presence of the divine is associated with better social functioning in individuals at clinical high-risk for psychosis[197]. Individuals with non-distressing psychotic experiences report being more spiritual (but not religious) than individuals diagnosed with a psychotic disorder or community controls without a history of psychotic experiences[172] and are more likely to ascribe voices to a spiritual being rather than real people[198]. Although one interpretation of these findings is that spiritual practices increase the likelihood of hearing voices, qualitative and mixed method phenomenological studies instead suggest that spiritual practices and beliefs generally do not precipitate the onset of voices[199,200]. Instead, these practices and beliefs play an important role in controlling voices and interpreting the nature of these experiences, thereby buffering against their potential negative impacts.

The protective and promotive effects of religion are more complex. Although religion often includes spiritual components, they are enacted in the context of a structured system and sanctioned set of beliefs, practices, and rituals[193]. Religion might act as both a vulnerability factor as well as a protective or promotive factor. On the one hand, religious delusions are common in individuals diagnosed with a psychotic disorder[201], thereby calling into question the role of religious beliefs and practices in symptom etiology. Indeed, some studies have reported relationships between greater religiosity and more severe symptoms and worse functional outcomes in individuals diagnosed with a psychotic disorder[193,202]. Furthermore, in individuals at clinical high risk, increased participation in religious activities was associated with more severe depressive symptoms[197]. On the other hand, religious involvement within a community of believers wherein beliefs and values have been adopted over generations has also been found to confer benefits to mental health[193]. Qualitative studies[203,204] and data suggesting that religious beliefs protect against suicidal behaviors[205] and promote quality of life[196] attest to a possible protective effect of religious beliefs and practices in individuals diagnosed with schizophrenia. The effects of religion on well-being and mental health might depend on cultural influences. Higher rates of religious beliefs and activity are reported among ethnic minority communities in Europe, the United States, and Australia compared to ethnic majority communities, and there is greater use of religious coping in marginalized and/or socially disadvantaged groups[206-209].

Expanding beyond the global meaning structures provided by religion and spirituality, personal appraisals of anomalous experiences influence outcomes in individuals with psychosis or psychotic-like experiences. For example, compared to voice-hearers with a need for care, non-treatment seeking voice-hearers often integrate psychotic experiences with their personal context via intra-personal processes or acceptance from others[210,211], leading them to ascribe meaning and purpose to the experience. Activities whereby individuals with schizophrenia make sense of symptoms and other illness-related experiences and integrate them into their own personal narratives promote well-being[212] and are a central aspect of mental health services associated with positive outcomes[213]. The potential benefits conferred by meaning-making processes are further highlighted by findings from a longitudinal study in India, which found that having insight into one's mental health condition while also holding non-medical explanations for the illness experience was associated with remission within five years following a schizophrenia diagnosis[214].

[H3] Abilities

Psychological abilities that might serve as protective or promotive in the context of psychosis include social competence and neurocognitive abilities. Social competence entails having the skills needed for successful social functioning, which include the ability to verbally and non-verbally communicate with others, to interpret communication from others, and to regulate oneself during social interactions[215]. Social skills training has been found to be protective against relapse in patients with psychosis[216] and to reduce the risk for and severity of psychotic-like experiences in individuals with a history of adversity[217,218]

A rich literature suggests that general cognitive functioning (measured using tests of general intelligence) and specific neurocognitive abilities have protective or promotive effects. First, better neurocognitive abilities[219], particularly verbal fluency, verbal and visual memory, and working memory, are associated with a decreased risk for transitioning to psychosis in high-risk youth[220,221]. Second, individuals with higher general cognitive functioning and better executive functioning early in the course of illness have a greater chance of a resilient illness trajectory[222]. In addition, better general cognitive functioning attenuates the relationship between a history of multiple adverse childhood adverse experiences and later psychotic symptoms[223]. Finally, on average, individuals with persistent psychotic experiences who do not seek help have higher general cognitive functioning than those that do seek help[172].

[H2] Social factors

Social factors are strongly linked with mental health[224]. Greater social support is related to reduced psychotic experiences in young adults with significant psychosis risk factors[124,223,225-227], and to reduced symptom severity[203,228,229] and improved functioning[229] in people diagnosed with a psychotic disorder. A meta-analysis further indicates that family interventions aimed at improving family support are associated with reduced relapse rates[216]. These benefits are not derived exclusively from receiving support, but also from giving support. Relationship reciprocity (the mutually beneficial exchange of support) is higher in individuals with persistent psychotic experiences that do not have a need for care, versus those who do[230]. Furthermore, help-seeking individuals with psychosis reported the highest distress from their symptoms when relationship reciprocity was low, regardless of symptom severity[230]. Relatedly, in individuals with schizophrenia, better relationship quality is related to reduced symptom severity[231] and predicts better functional outcomes three years later[232]. In individuals at clinical high risk for psychosis, better quality of relationships and number of relationships are related to reduced severity of psychotic experiences and better functioning[233].

Social network size and social interactions are additional factors associated with positive outcomes [234]. For example, interactions with friends predicted two-year clinical recovery in people diagnosed with a psychotic disorder[235], living with someone else predicted remission in a prospective 20-year follow-up study of individuals experiencing their first episode of psychosis[236], and the immediate presence of family or friends decreased the moment-to-moment risk of mental states associated with delusions in individuals with chronic schizophrenia[237]. Number of relationships is associated with a reduced risk of developing schizophrenia 15 years post-baseline[238] and is further associated with reduced symptom severity in individuals diagnosed with schizophrenia[231]. At broader social levels, involvement in activities that align with interests and values also provides mental health benefits. Withdrawal from extracurricular activities has been found to precede a delusional moment[237], and holding valued social roles (for example, club membership) prevents relapse in people with psychosis[239].

Finally, broader aspects of the social environment play a crucial role in mental health. Epidemiological studies have shown that living among people of the same ethnicity reduces the chance of developing psychosis[240-242]. However, findings that neighborhood ethnic diversity has negative impacts on well-being and health are contested[243,244], and negative impacts might even reverse over longer periods of intergroup contact[245]. The mechanism underlying the association between ethnic diversity and psychosis is unclear but is almost certainly culturally-dependent[244]. One possibility is that higher ethnic density reduces exposure to discrimination and racism or exerts a buffering effect against their negative impacts[242,246]. Alternatively (or in addition), higher ethnic density might increase positive social neighborhood characteristics, at least in the short-term[244]. These social characteristics of the neighborhood confer beneficial effects in the context of psychosis risk, although work here is more limited[244]. Residing in a more socially cohesive neighborhood (that is, a neighborhood that fosters a sense of belonging[247]) is associated with a reduced risk for psychotic symptoms in children of mothers diagnosed with schizophrenia[227] and attenuates the association between adverse childhood events and later psychotic symptoms[124,223]. Finally, higher social capital (a community's bank of trust and expectations regarding reciprocity that fosters and facilitates collective action, generally measured by civic engagement[248]), has been associated with a reduced risk of developing a psychotic disorder[249-251], but findings are mixed[252]. Taken together, these findings align with the 'social defeat' hypothesis, whereby repeated experiences of social exclusion increase risk for schizophrenia[253,254]. Resilience factors at the social environmental level might buffer against these risks.

[H2] Built and natural environments

Mental health benefits can be conferred by broader aspects of the natural and built environment. There is robust evidence that access to green and blue space[255] and exposure to natural sounds[256] increase positive affect and social engagement, reduce stress levels and negative affect, improve sleep quality and cognition, and enrich meaning in life. Notably, epidemiological studies have shown that exposure to natural green and blue space during childhood is associated with psychosis risk[257-260], independent of urbanicity, and increased levels of green space density are associated with decreased schizophrenia risk in a dose-dependent manner in man-made areas[258]. Furthermore, exposure to green spaces is related to better clinical symptoms in individuals diagnosed with schizophrenia[261].

The mechanisms by which green space exert protective or promotive effects are not yet determined. Current theories suggest that natural settings foster restoration from mental fatigue[262], promote relaxation, and/or enhance well-being owing to an innate preference for life forms and lifelike processes[263]. Qualitative evidence suggests that spending time in open green space might buffer against the stress of living in an urban environment in individuals with schizophrenia[264]. Importantly, forest therapy[265,266] (a guided outdoor healing practice) is broadly promotive for a range of mental health conditions. Even simulated or virtual forest walks might confer psychological benefits[267,268]. A recreational program involving a walk through a suburban forest reduced negative affect and anxiety in individuals hospitalized for psychosis[269]. Given the known beneficial effects of the natural environment on mental health, expansion of green and blue space in urban areas, and even within buildings, seem warranted[270].

Characteristics of the built environment such as walkability, transit access, or housing quality have also been shown to contribute to positive mental health outcomes[271-273]. There has been little direct investigation into how aspects of the built environment confer resilience in the context of psychosis risk. However, several studies have shown that neighborhood walkability increases physical activity in individuals with schizophrenia[275-277], which might in turn lead to mental health

benefits. Furthermore, the built environment influences access to care[278], and therefore high-quality built environments might be associated with better outcome trajectories via access and adherence to treatment. Indeed, a study in China showed that individuals with schizophrenia living in neighborhoods with high walkability had lower re-hospitalization rates than those living in less walkable neighborhoods[274]. These findings underscore the crucial role of judicious urban planning, smart policies, and architectural design in public health outcomes.

[H1] Limitations of the resilience literature

There are several limitations to the literature reviewed above. First, it does not distinguish protective from promotive factors. Most of the factors associated with positive outcomes in the context of psychosis risk reviewed above are widely regarded as good for health, well-being, and functioning and are potentially promotive factors. Whether these factors also have a differentially positive effect in contexts of heightened risk, particularly in the context of psychosis risk (protective factors), remains unclear[279]. Answering this question would require evaluating whether a given factor was associated with positive outcomes in a risk-dependent manner. For example, spirituality could be considered a protective factor in this context if it showed a positive relationship with subjective well-being in youth identified as clinical high-risk for psychosis, but no relationship in a population sample of young adults. Distinguishing protective and promotive factors is important for developing implementation strategies. Should a factor be broadly promotive, then intervention or prevention efforts aimed at enhancing that factor stand to be effective when delivered to a wide audience through broad public health initiatives. By contrast, strategies aimed at shoring up protective factors in the context of psychosis risk might be most effective when delivered to population subgroups, such as at psychosis specialty clinics.

Second, although modern conceptualizations of resilience highlight its multisystemic nature[83], the majority of reviewed studies have focused on biological and psychological factors at the level of the individual and immediate family unit. Assets and activities within broader social and ecological levels that confer substantial mental health benefits have yet to be explored in the context of psychosis risk[272,273,280,281]. Research into the impact of the built environment is particularly scant. Furthermore, most studies have investigated the effects of single factors rather than a constellation of intersecting and multisystemic risk and protective and promotive factors. This makes it impossible to unpack the mechanisms by which these factors come to be associated with resilient outcomes—that is, whether they directly impact outcome measures, or indirectly influence outcomes via other protective, promotive, or vulnerability factors. Moreover, the reviewed factors should be considered on a continuum, whereby optimal levels are protective or promotive and sub-optimal levels confer vulnerability. For example, social support can buffer against risk whereas social isolation might create vulnerability. It is unclear whether there are shared underlying mechanisms, or whether factors operate via distinct pathways at each end of the continuum.

Third, there is little examination of contextual effects in the current psychosis resilience literature. This is a critical gap because when it comes to resilience, one size does not fit all. For example, risk context might influence the degree to which a resource or positive behavior confers benefits. Risk context refers to whether risk occurs in the preliminary circumstances that might lead to a psychotic disorder diagnosis, in distress that emerges from the symptoms themselves, or in secondary risks after diagnosis. The degree of overlap in the factors that promote resilience in the context of these different types of risk and the mechanisms by which they might do so is unclear. Many of the resilience-promoting factors reviewed here, such as positive health behaviors, adaptive coping strategies, or access to green space, reduce the likelihood of being diagnosed with a psychotic disorder. They also engender beneficial effects in

those already diagnosed, which is consistent with the fact that these factors promote mental health and well-being in the general population. Other factors, such as stigma resistance and meaning making, might only produce positive outcomes in the context of a mental health diagnosis and clinically significant psychotic experiences.

The benefits conferred by a putative protective or promotive factor might also depend on other contextual factors. Specific factors might have a more profound impact during sensitive periods of brain development characterized by higher plasticity. Notably, the timing of these critical periods are themselves malleable and changed by environmental factors[282-285]. In addition, culture is a critical contextual factor. The definition of a positive outcome and the ways in which resilience at the level of the individual is prioritized relative to other levels of the social ecology are inherently culturally-dependent[286,287]. Furthermore, there are robust cultural and geopolitical differences in the clinical course of psychotic disorders that cannot be explained exclusively by diagnostic differences. For example, individuals in low-income and middle-income regions fare better following a diagnosis of schizophrenia than individuals in high-income regions[288-295]. Finally, the positive effect of engaging in positive coping strategies might be stymied when structural inequalities pose barriers to obtaining basic needs[89]. Indeed, the RAISE-ETP study showed that treatment based on a coordinated specialty care intervention for early psychosis that adopts a strengths and resilience based approach only improved symptoms and quality of life in individuals at the top 25% of the socioeconomic distribution[296, 297].

Finally, the bulk of research to date on resilience factors for psychosis has focused somewhat narrowly on clinical outcomes such as diagnosis and relapse, with resilience in non-clinical domains remaining largely unaddressed. Relatedly, conceptual models of resilient outcomes that guide current research might not necessarily align with those of individuals with lived experience of psychosis.

[H1] Summary and future directions

Resilience models stand to enhance, refine, and complement what has been learned from traditional risk-based approaches to psychosis. Moreover, understanding modifiable factors that lead to resilience in the face of psychosis risk will be central to therapeutic innovation. Existing research highlights several promising modifiable protective and promotive factors in the context of psychosis risk, including health behaviors, psychological strengths, attitudes, and abilities, social interactions, support, and cohesion, and access to green space. Future research must now bridge the critical gaps we identified in the current literature.

First, future research should test a comprehensive set of (ideally modifiable) potential protective and promotive factors to identify factors with the strongest associations with positive outcomes both individually and when considered in concert with other factors. Relatedly, future work should test whether putative associations are moderated by psychosis risk, which would distinguish protective from promotive factors. Such research can then be used to identify promising targets for novel and cost-effective interventions. Identifying promotive factors could support the implementation of broad, public health-informed strategies to shore up factors that increase positive outcomes for emerging adults in general[298]. Identifying protective factors could inform clinical staging interventions that acknowledge the ‘pluripotential’ nature of psychosis risk[299-302], whereby the identified individuals are at heightened risk for a variety of psychiatric outcomes. Indeed, an increasing number of clinical high-risk research groups are moving toward transdiagnostic clinical staging approaches that focus on youth mental health more generally[299-302]. In addition, future work should examine the co-occurring influences that might moderate the impact of protective and promotive factors. Knowing what factors are associated with positive outcomes, when, and for whom, is central to understanding at what level of a

biopsychosocial-ecological system resilience-promoting assets and activities yield better individual-level outcomes, to developing tailored interventions, and to understanding heterogeneity in outcomes.

Second, future research should re-imagine positive outcomes to be broader than the mere absence of psychological distress and diagnosis. Resilient outcomes are multifaceted, and future work in this field would benefit from considering a wider range of measures that include academic performance, work outcomes, physical health, social functioning, and purpose in addition to mental health. Furthermore, researchers should consider positive outcomes at broader levels of the social ecology and the ensuing impact on individual outcomes—for example, how individual activism might promote transformation of social institutions that in turn engenders more rights and opportunities for those living with mental illness.

Third, given the inherent multisystemic nature of resilience, diverse teams that include multidisciplinary scholars as well as individuals who have traditionally been excluded from academic discourse will be critical for gaining a broader perspective on potential protective and promotive factors and on defining positive outcomes. This includes individuals with lived experience of psychosis, families, teachers, and community and religious leaders who often encounter people experiencing or at-risk for mental health emergencies along their pathway to care. Furthermore, more cross-cultural work is needed, as positive outcomes and resilience promoting processes are inherently shaped by culture. Looking beyond the biomedical models of mental health that have dominated scientific discourse might allow us to reshape or refine our conceptualization of positive outcomes, which could potentially uncover additional resilience-promoting factors.

Finally, several methodological considerations will likely enhance the study of resilience to psychosis risk. First, mixed methods approaches that link qualitative and quantitative research can provide a springboard for generating testable hypotheses regarding factors that might confer protection against psychotic symptoms and related distress. Second, resilience is best represented as a positive trajectory and therefore not fully captured by a single moment in time[303].Thus, longitudinal studies are critical for characterizing this trajectory and determining causal relationships between factors and outcomes, particularly as compromised access to and engagement in the promotive and protective factors might be direct consequences of illness. Indeed, prospective longitudinal studies have provided critical data regarding factors that contribute to the development of a psychotic disorder and poor clinical outcomes among high-risk individuals[304-307]. Third, more is not always better, and researchers should consider non-linear relationships between outcome metrics and both risk and protective and promotive factors. For example, stress is typically considered a risk factor, but might have inoculating effects in small doses [308]. Fourth, natural and passive monitoring approaches, such as ecological momentary assessment and mobility tracking can greatly enhance ecological validity and provide richer assessments that capture the complexity of participants' daily lives[309]. For example, geospatial location and geographical information systems can objectively measure how often and for how long people are exposed to natural or built features of the environment, and how these durations relate to mental health[261,310,311]. Finally, it is paramount to expand beyond help-seeking samples. Individuals identified at clinical high-risk are already experiencing significant clinical distress related to attenuated psychotic symptoms, social and functioning difficulties, depression, and other sources[312]. Identifying individuals in the general population who are at-risk for psychosis owing to attenuated psychotic symptoms or genetic risk but who do not present with a need for care might provide insights into factors that help avert the functional decline that leads young people at-risk for psychosis to seek help in the first place.

In conclusion, our Review suggests that the ‘ordinary magic’[313] that constitutes human resilience promotes positive adaptations in what is generally considered to be the most severe of mental health conditions[314]. Such findings are particularly important given antiquated, but still influential, notions of schizophrenia as a progressively deteriorating illness[315] with its basis in irreversible etiological factors that manifest later in life[316]. The factors reviewed here are modifiable, thereby reinforcing the notion that illness course can be changed. The identified modifiable resilience factors provide valuable data that can inform therapeutic development, including individual prevention and intervention efforts, institutional programs, and broader policy.

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Author contributions

K.N.T., A.M., K.S.M., C.S.H., & S.P wrote the article. All authors researched data for the article, contributed substantially to discussion of the content, and reviewed and/or edited the manuscript before submission.

Competing interests

The authors declare no competing interests.

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Table 1. Summary of reviewed protective and promotive factors.

Level	Factor	Key findings	Considerations for prevention and intervention
Biological	Sleep	Better sleep quality is associated with greater well-being[110,111] Sleep quality interventions decrease psychotic-like symptoms[112] Sleep quantity shows a non-linear relationship with well-being[114,115]	Cognitive behavioral therapy (CBT) for insomnia[317] is the first-line treatment for sleep disturbance and can be effectively delivered using scalable web-based programs[318] Sleep hygiene recommendations as stand-alone interventions without personalization are unlikely to be effective [319] Expand beyond the level of the individual and consider how social and environmental determinants might be modified to improve sleep health[320]
	Physical activity	Low to moderate exercise is associated with mental health benefits[116-118] Physical activity in childhood is associated with a lower likelihood of developing psychosis later in life[124-126] Physical activity is associated with positive clinical and functional outcomes and subjective well-being in individuals with psychotic disorders[127-131]	90 minutes of moderate to vigorous exercise per week can improve mental and physical health[321] among individuals diagnosed with psychotic disorders[322] and individuals at clinical high risk[323] Supervised exercise in group settings (versus solitary exercise) maximizes adherence to the exercise intervention in individuals diagnosed with psychotic disorders[322] Strategies for addressing barriers to exercise include establishing an incentive structure, using augmented reality, varying the exercise routine, and social support[130]

	Homeostatic regulation of the autonomic nervous system	Higher heart rate variability and respiratory sinus arrhythmia (within the normal range) are associated with better mental and physical health[135-138] Heart rate variability and respiratory sinus arrhythmia are lower in people with psychotic disorder and individual differences relate to clinical symptoms and daily functioning[142-146] Biofeedback training to enhance heart rate variability is associated with improved clinical symptoms[153,154]	Heart rate variability and respiratory sinus arrhythmia are modifiable through biofeedback training, breathing retraining, mindfulness practice, and physical exercise in the general population[147-152,324]
Psychological	Traits and personal characteristics	Adaptive coping is associated with less severe psychotic and psychotic-like symptoms in the general population[157,158,165] and clinical populations[160-164] Higher self-esteem is associated with reduced psychotic and psychotic-like symptom severity[168,169,173], improved quality of life[170] and general mental health in clinical populations[170,171], and reduced distress associated with psychotic experiences[172] Regaining internal locus of control is a major component of recovery in individuals with schizophrenia[175] and is associated with a lower likelihood of developing psychotic symptoms[176] Trait emotional stability, extraversion, and agreeableness are associated with better quality of life in individuals with schizophrenia[180-182]	Fostering coping might be a mechanism of symptom improvement in CBT for psychosis[325], although CBT does not lead to improvements in quality of life, subjective distress or functioning[326]. There is no evidence to favor any specific preventative treatment of psychosis (including CBT)[327]. Individualized Resiliency Training is a psychosocial intervention to enhance well-being among people with psychosis that focuses on education and skills training to foster adaptive coping strategies[328]. Face-to-face or scalable web-based CBT and reminiscence-based interventions that focus on reflecting upon autobiographical memories are associated with improved self-esteem[329].

	Attitudes and orientations	Stigma resistance is related to well-being and quality of life in individuals with psychotic disorders[187-189] Spirituality might confer mental health benefits in the general population[193,194]. Religion and religious practices might act as both a vulnerability factor[193,197,202] as well as a protective or promotive factor[196,203-205]. Among individuals diagnosed with a psychotic disorder, spirituality relates to adaptation in the face of adversity[196], is associated with better social functioning in young people at risk for psychosis[197], and might buffer against the distress associated with psychotic experiences[172,198] Ascribing meaning to anomalous experiences might buffer against the distress of psychotic experiences[210,211] and promote well-being in individuals diagnosed with schizophrenia[212]	Stigma reduction strategies that either attempt to alter stigmatizing beliefs and attitudes or enhance stigma-coping skills through improvements in self-esteem, empowerment, and help-seeking behavior are effective in reducing self-stigma[330], particularly when they include a psychoeducation component[331] Religion and spirituality might offer resources for support and meaning and/or exacerbate psychological distress. Thus, they should only be incorporated into psychotherapy after careful consideration. Incorporating religion and spirituality into treatment might be particularly important for individuals from underserved and minoritized backgrounds who have higher rates of religious beliefs and greater use of religious coping than the general population [206-209] and for whom religious and spiritual resources might be more accessible than other resilience-promoting factors[332,333].
	Abilities	Higher social competence is associated with reduced risk of relapse in patients with psychosis[216] and with reduced risk for and severity of psychotic-like experiences in at-risk individuals[217,218] Better neurocognitive abilities are associated with decreased risk for psychotic symptoms in at-risk youth[219-221,223], a better clinical course in individuals recently diagnosed with a psychotic disorder[222], and might buffer	Cognitive Behavioral Social Skills Training[334], Social Cognition Training[335], and Social Cognition and Interaction Training[336] involve live instruction, role plays, behavioral assignments, and/or computerized programs[337] to foster skills in emotion and social perception, theory of mind, and social problem solving in individuals with psychotic-spectrum illness. Cognitive remediation improves cognition and daily functioning in individuals with schizophrenia[338,339]

		against distress associated with psychotic symptoms[172].	and in individuals at high risk for psychosis[340], particularly when they include an active and trained therapist, repeated practice, structured development of cognitive strategies, and techniques to maximize transfer of cognitive improvement to real-world settings. Delivery in group and individual settings is equally effective.
Social	Social support and relationship quality	Greater social support is related to reduced psychotic experiences in young adults with significant psychosis risk [124,223,225-227] , and to reduced symptom severity[203,228,229] and improved functioning[229] in people diagnosed with a psychotic disorder. Mutually beneficial exchange of support (relationship reciprocity) is higher in individuals with persistent psychotic experiences that do not have a need for care versus those that do[230]. In individuals with schizophrenia, better relationship quality is related to reduced symptom severity[231] and predicts better functional outcomes three years later[232]. In individuals at clinical high risk for psychosis, better quality of relationships and number of relationships are related to reduced severity of psychotic experiences and better functioning[233]	Group and individual interventions in adolescents and adults aimed at enhancing the availability of social support through social skill development or increasing the degree of perceived support through cognitive restructuring show preliminary effectiveness. But results are mixed and methodological limitations preclude a definitive interpretation of these results[341] Family interventions aimed at improving family support are protective against relapse[216]. One-to-one peer support improves support provided by personal relationships when adjunctive to usual care for psychosis [342] Targeting families of children at higher risk for psychosis by increasing parental social support and parent training can enhance the quality of familial support provided to the child[343,344]
	Social network size and social interaction	Social interaction promotes positive mental health outcomes in the general population[234]. Interactions with close relations is associated with	Social participation interventions aim to build social networks and improve community integration for individuals with mental illness through activities that facilitate social interactions. The limited evidence available suggests

		improved psychotic symptoms[235-237] Number of relationships is associated with a reduced risk of developing schizophrenia 15 years post-baseline[238] and with reduced symptom severity in individuals diagnosed with schizophrenia[231].	potential benefit of social participation interventions for social networks. However, further work is needed[345].
	Social roles	Engagement in activities related to valued social roles reduces clinical symptoms and prevents relapse[237,239].	
	Broader social environment	High ethnic density[240-242], neighborhood social cohesion[124,223,227], and neighborhood social capital[249-251] are associated with reduced risk of developing a psychotic disorder.	Data reporting individual outcomes are limited, but modifications to physical neighborhood features (for example, increasing walkability) can increase opportunities for social interactions and improve civic engagement and collective efficacy[346,347]
Built and natural environment	Built environment characteristics	Characteristics of the built environment (for example, walkability and housing quality) contribute to positive mental health outcomes in the general population[271-273]. No studies have directly examined the impact of aspects of the built environment on positive outcomes in the context of psychosis risk.	Environmental modifications aimed at increasing public access to green space (for example, planting street trees and greening vacant lots) might broadly improve health outcomes[348-350]. Neighborhood walkability increases physical activity in individuals with schizophrenia[242-244]
	Exposure to natural space	Exposure to natural green and blue space during childhood is associated with reduced psychosis risk in adulthood[257-259] Exposure to green space is related to decreased severity of clinical symptoms in individuals diagnosed with schizophrenia[261] and might buffer against stress of urban environment[264]	Group and individual interventions to increase time spent in green space promote mental and physical health [265,266], including among individuals hospitalized for psychosis[269] and even in simulated or virtual formats[267,268].

Figure legends

Figure 1. Trajectories of psychosis risk and resilience. Example trajectories for psychological distress (top), psychotic and psychotic-like experiences (middle), and subjective well-being and psychosocial functioning (bottom) in individuals at risk for psychosis. Risk factors include the circumstances that increase the likelihood of being diagnosed with a psychotic disorder, the distress associated with the experience of psychotic symptoms themselves, and secondary events associated with a diagnosis of psychotic disorder (for example, poor physical health or discrimination). Blue represents an individual presenting with risk factors but not protective or promotive factors. The grey, yellow, and green trajectories represent different resilience-promoting processes. Adaptation (grey) occurs when the individual changes in ways that permit positive outcomes despite the impact of risk. Recovery (yellow) occurs when the individual initially experiences negative outcomes in response to risk, but later returns to a previous level of functioning. Finally, resistance and persistence (green) occur when the individual maintains their current trajectory despite risk. These trajectories are highly schematized and simplified examples and do not encompass all possible trajectories of an individual with psychosis risk factors. Rather, they are intended to provide an illustration of how resilience-promoting processes might be enacted in the context of psychosis risk factors.

Figure 2. Protective and promotive factors across the biopsychosocial-ecological system. Potential protective and promotive factors in the context of psychosis risk identified in the Review are organized within levels of a biopsychosocial-ecological system. The factors placed at the border of adjacent levels indicate that different aspects of these factors are best conceptualized as operating at multiple levels of the biopsychosocial-ecological system.

Box 1. Beyond semantics in the shift from risk to resilience

A shift away from risk and towards resilience could be perceived as merely semantic—that a focus on strengths and protection is more hopeful-sounding but conceptually identical to a risk-focused approach to prevention and intervention. But resilience scholars have presented several arguments supporting the idea that a shift from risk to resilience is more than an inversion of language[87]. First, a high 'dose' of a particular variable that buffers against the effect of risk exposure might do so via different processes or mechanisms than those by which a low 'dose' of that same variable exacerbates the effect of risk[22,87]. For example, physical activity (generally considered a promotive factor) has a non-linear relationship with mental health, such that more physical exercise is related to improved mental health up to a threshold, after which it increases the likelihood of poor mental health[351-354]. Those aspects of exercise at low to moderate 'doses' that confer benefits are likely not the same aspects that confer vulnerability at high doses.

Second, context matters: a particular factor or process that has protective or promotive effects in one context, group, or individual might operate as a vulnerability factor in another[87]. For example, participating in high school sports is protective against alcohol use in Black girls, but is associated with increased alcohol use in Black boys and white girls and boys[355]. Third, the 'active ingredient' by which a particular factor confers benefits might lie in the positive end of that factor. For example, in women raised in institutional care, being in a supportive marital relationship was related to improved parental quality as compared to women who were not in a supportive marital relationship; however, parenting quality was equivalent in women raising a child without a partner and women raising children in the context of a poor marital relationship. In other words, a supportive marital relationship was a protective or promotive factor, but there was no analogous vulnerability caused by a poor marital relationship[356]. Thus, focusing on the protective end of a variable— supportive marital relationship, in this example—might elucidate the mechanism or process by which variation in exposure to a given factor might buffer the negative effects of risk. Finally, outcome variables do not lie on a unidimensional spectrum. Presence of resilience factors is not equivalent to an absence of risk factors. In a similar way, positive and negative emotions represent different constructs[357] and 'feeling good' is not the same as 'not feeling bad'. Thus, a paradigmatic shift from risk to resilience represents a change in approach and framework, not just a matter of emphasis on language and terms.

Box 2. The case of delusions

Delusions (false and fixed beliefs that are not amenable to change despite conflicting evidence[359]) are a defining symptom of schizophrenia and are understood as harmful and dysfunctional. Delusions are also considered an important treatment target that is central to recovery from psychosis. Current explanatory models of delusions adopt neurocognitive approaches to belief formation, whereby delusions are thought to arise from normative reasoning in the context of anomalous experiences or reflect abnormalities in a normative belief formation process (for a review see [358]). These approaches have led to the development of cognitive-behavioral therapy (CBT) for delusions [359], which treat delusions as beliefs that can be challenged through standard techniques of reality testing and evaluation. However, the efficacy of CBT for delusions appears to be modest and its therapeutic ingredients remain unclear [360,361].

Delusions are notoriously difficult to dispel. However, the current definition and operationalization of delusions are fraught with epistemic hurdles that make it difficult to determine the borders of pathology [362,363]. Framing delusions as harmful beliefs that must be eliminated to achieve recovery from psychosis fails to consider the lived experience of the phenomenon and the broader sociocultural and psychological context. Specifically, some delusions might serve an adaptive purpose, at least temporarily [364,365]. This proposition is not intended to romanticize delusions or to downplay their seriousness. Indeed, delusions—particularly persecutory delusions—are associated with tremendous personal distress [366], and anger secondary to delusions has been found to increase an individual's risk for violent behavior [367].

To best grapple with these clinical realities, clinicians and researchers must consider that delusions might be an adaptive response in some cases, and notions of recovery and treatment must be reframed accordingly. Indeed, a meta-analysis indicated the improvements in positive symptoms (like delusions) with CBT were related to increases in hopelessness[326]. Quotes from a qualitative study wherein individuals with schizophrenia with a longstanding delusional belief were asked what their life would be like without their delusional belief further illustrate this point[368]:

> "It would all have been for nothing…it would be sadness…it would be wrong, I wouldn't accept it…that's futility - I would really miss it. A waste of a life, all my lives, all the way through."

> "I can't see that ever happening - psychic activity is part of my structure - my heart. If I lost it, I would be inert. I'd have to start all over again."

An alternative phenomenological account of delusions incorporates the phenomenology of the variety of reality experiences to fathom how individuals with delusions might evaluate and discover meaning in these experiential alterations[362]. Moving away from a purely mechanistic model of delusions that fails to acknowledge or incorporate the subjective, phenomenological illness narratives will be essential to defining recovery and positive outcomes in a manner that leaves intact the person's sense of self and ability to find meaning in experience[365,369]. From the perspective of the person with lived experience, delusions are not necessarily an irrational or false representation of reality; rather, such beliefs might bring a sense of meaningfulness to their life [369]—which might confer resilience.

Box 3. Integrating risk and resilience factors

Our categorization of potential protective and promotive factors reflects the current literature that tends to study factors in isolation or within a small selection of other risk or resilience factors. However, this approach obscures the fact that it is the interactions between various assets and abilities together with risk factors that engender the conditions under which resilience can occur[83]. First, interactions between various risk and resilience promoting factors can occur within levels. For example, the biological resilience promoting factors reviewed here (sleep quality, physical activity, and homeostatic regulation of the autonomic nervous system) influence each other through reciprocal interactions via physiological and psychological pathways[370] and might exert their impact on positive mental health outcomes via a common process, such as reducing stress reactivity[371-373]. Second, extensive interactions occur between levels. For example, physical activity is influenced by the walkability of the built environment[374], self-esteem increases perceived social support[375], and exercise promotes cognitive abilities[376]. Furthermore, these resilience promoting factors might also reduce exposure to stressors. For example, for individuals from minoritized ethnic groups, the protective effect of living in neighborhoods wherein their ethnic identity is well-represented might reduce the degree of discrimination they experience in day-to-day life[246]. Finally, the access or ability conferred by resilience promoting resources might be compromised by the illness itself. For example, qualitative studies indicate that symptoms and the sedative effects of medication pose barriers to engaging in physical activity[377]. Similarly, stigma and structural discrimination together with psychosocial disability might limit employment opportunities and thereby reduce opportunities to access resilience promoting resources associated with wealth (such as access to green space, which is less available in low-income neighborhoods[378]), and to engage in social networks.

Table of Contents blurb

Psychosis research has traditionally focused on vulnerability and the detrimental outcomes of risk exposure. In this Review, Thakkar et al. consider an alternative resilience-based approach focused on resources and strengths that might help protect against negative illness course among people at risk.