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2	Moving from risk to resilience in psychosis research
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#### 35 36 Abstract

37

<sup>38</sup> Psychosis research has traditionally focused on vulnerability and the detrimental outcomes of

<sup>39</sup> risk exposure. However, there is substantial variability in psychological and functional outcomes

40 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

42 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.

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,

<sup>49</sup> including individuals, institutions, and policy.

# 51 [H1] Introduction

Psychotic disorders, including schizophrenia, are characterized by signs of departure from 52 consensus reality, for example, hallucinations and delusions. This departure is often 53 accompanied by disorganization of thought and behavior and diminished expressivity and 54 motivation. The impact of psychotic disorders, and the discrimination and marginalization that 55 occur in their wake, are tremendous. People diagnosed with schizophrenia have a lower life 56 expectancy in Western countries<sup>1</sup>, higher rates of homelessness worldwide<sup>2-8</sup>, and drastically 57 reduced guality of life<sup>9</sup> compared to those without a diagnosis of schizophrenia. 58 59 Psychotic disorders were historically viewed as irreversible and progressively deteriorating 60 conditions that were inevitably associated with poor outcomes and disability<sup>10</sup>. However, in the 61 past 30 years a more optimistic paradigm focused on psychosis prevention has emerged<sup>11-13</sup>. To 62 this end, there has been a massive effort to identify factors that increase an individual's risk for 63 developing a psychotic disorder, with the hope that targeted interventions might prevent or delay 64 onset. Individuals seeking mental health treatment who are identified as at high-risk for 65 psychosis show markedly increased rates of developing a psychotic disorder, relative to lifetime 66 incidence rates in the general population<sup>14</sup>. However, around two-thirds of help-seeking at-risk 67

individuals are never diagnosed with a psychotic disorder<sup>15</sup>, and around 40% remit from high risk status after 3 years<sup>16</sup>. These findings dovetail with the variability in clinical trajectories of

<sup>70</sup> individuals diagnosed with psychotic disorders—although many have poor long-term outcomes,

over 50% show extended periods of recovery<sup>17-21</sup>. 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.

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There has been comparatively little work examining those factors that might promote

<sup>76</sup> multifaceted positive outcomes in the face of psychosis risk. Understanding the factors that

<sup>77</sup> 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

<sup>79</sup> 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<sup>22</sup>. Thus, a greater

resilience can complement those designed to eliminate preventable risks<sup>22</sup>. Thus, a greate focus on resilience in the context of psychosis risk is critical for advancing the field and

<sup>83</sup> promoting therapeutic discovery<sup>23</sup>.

84

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.

92 93

# 94 [H1] The risk-based approach to psychosis

<sup>95</sup> Converging evidence supports a diathesis-stress etiological model of psychotic disorders,

<sup>96</sup> whereby genetic risk interacts with social and environmental stressors to influence the

<sup>97</sup> development of symptoms<sup>24-26</sup>. 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

<sup>101</sup> monozygotic twins with an estimated heritability of 73% for schizophrenia-spectrum disorders<sup>27</sup>.

Having a parent with a serious mental illness also increases risk for psychosis: a meta-analysis 102 of 33 studies showed that the children of parents with serious mental illness were 6.5 times 103 more likely to develop schizophrenia than the children of parents without serious mental 104 illness<sup>28</sup>. Genome-wide association studies have also identified specific genes that confer 105 areater risk for psychosis, with one report detecting 10 gene variants with odds ratios  $\geq$  3.0 for 106 the development of schizophrenia<sup>29</sup>. Variations in *GRIN2A*, a glutamate receptor, and *SP4*, 107 involved in transcription regulation, have been implicated in multiple reports as carrying greater 108 risk for psychosis and for developmental disorders such as autism<sup>29,30</sup>. 109

In terms of non-genetic risk factors, the earliest stressors might occur during prenatal and perinatal periods<sup>31,32</sup> 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<sup>33</sup>, communication deviations in parents<sup>34</sup>, and delays in sitting, standing, or walking independently<sup>35</sup>) 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 117 (typically in late adolescence and early adulthood) have been summarized and evaluated in 118 several meta-analyses<sup>36</sup> and reviews<sup>32,36,37</sup>. One prominent risk factor during this period is 119 childhood trauma, which has been consistently found at high rates among individuals who later 120 develop psychosis<sup>38,39</sup>. There is also extensive evidence that stressful life events in adulthood 121 are associated with an increased risk for subclinical psychotic symptoms and a psychotic 122 disorder diagnosis<sup>40</sup>. In the past decade, there has been increased focus on the role of 123 discrimination as a risk factor for psychosis. Higher rates of subclinical psychotic symptoms, 124 psychotic experiences, and psychotic symptoms have been found in individuals from 125 communities that have been marginalized on the basis of race and ethnicity<sup>41,42</sup> as well as in 126 sexual and gender minority communities<sup>43</sup>, and structural racism in the United States has been 127 explicitly linked with psychosis risk<sup>44</sup>. Finally, the environment where one lives and who inhabits 128 those spaces plays an important role in the development of psychosis. A meta-analysis of eight 129 studies and nearly 46,000 people found that the risk for schizophrenia was 2.37 times higher in 130 urban areas than in rural environments<sup>45</sup>. Exposure to such environmental stressors might 131 account for the widely replicated finding of increased stress-sensitivity in individuals with 132 psychosis<sup>46,47,48</sup>. Here stress sensitization, whereby the response to some environmental 133 stressor increases in intensity with repeated exposures, transpires and results in enduring 134 alterations in stress-sensitivity. 135

This vast body of evidence describing factors that are associated with an increased risk of 136 psychotic disorder onset has contributed to the development of mental health policies and 137 practices that emphasize the importance of reducing the burden of these disorders in the 138 population <sup>49,50</sup>. Over the past 30 years the clinical high-risk paradigm<sup>13</sup>, which aims to identify 139 individuals in the prodromal phase of a psychotic disorder as part of a preventative approach. 140 has been the major focus within psychosis research. Current criteria define individuals at clinical 141 high-risk as those who have either attenuated psychotic symptoms, full psychotic symptoms for 142 a brief period, or substantial genetic risk paired with functional decline. Formal risk calculators 143 have been created to enhance prediction of which individuals identified at clinical high risk will 144 transition to psychosis<sup>51,52</sup>. These enhanced predictive models represent an important strength 145 of risk-based approaches. Moreover, studies of risk can also help quantify how much risk is 146 conveyed by specific factors. For example, according to meta-analyses the odds of 147 experiencing childhood trauma is almost 3 times higher<sup>37</sup> and the odds of perceived 148 discrimination is almost twice as high<sup>40</sup> among individuals who later develop psychosis 149

compared to controls. A risk-based approach also has important clinical implications for help-150 seeking youth. Early identification permits both preventative care and intervention earlier in the 151 course of illness. This is important because shorter durations of untreated psychosis are 152 associated with better prognosis post-diagnosis<sup>53,54</sup> (but see<sup>55</sup>), and reducing the duration of 153 untreated psychosis is a major emphasis of treatment programs. Finally, identifying individual 154 risk factors can enable increased personalization of treatment on the basis of specific risk 155 exposure. Thus, a focus on risk factors sets the groundwork for treatment development and 156 treatment targets, usually aimed at eliminating preventable risks. 157

Despite these strengths, relying solely on a risk-based approach for psychosis, where risk is an 158 event or context that is directly associated with poor outcomes, has several shortcomings<sup>56</sup>. For 159 example, relying solely on risk might lead to over-prediction of risk<sup>57</sup> and, accordingly, 160 suboptimal treatment planning such as excessive or unnecessary interventions. Indeed, up to 161 70% of people identified as high-risk do not develop a psychotic disorder within three years<sup>14,58-</sup> 162 <sup>60</sup>. This percentage is even higher in studies that use broader recruitment strategies, resulting in 163 samples that are less biased towards help-seeking individuals with more severe subclinical 164 symptoms<sup>61-67</sup>. Furthermore, opportunities to develop novel treatments might be limited given 165 that the risk factors that have received the most robust support (for example, subclinical 166 psychotic experiences and genetic risk) do not easily lend themselves to therapeutic innovation. 167 Indeed, meta-analytic findings indicate that no specific preventative interventions have yet been 168 identified<sup>13,68</sup>. In addition, an exclusive focus on risk and deficits might exacerbate the stigma 169 associated with psychosis<sup>69-71,72,73</sup>, which is itself linked to poor mental health outcomes<sup>74,75</sup>. 170

Finally, a risk-based perspective spotlights vulnerability and fails to consider the possibility that 171 individuals who are highly sensitive to negative contexts might also be most responsive to the 172 enhancing effects of positive contexts—a pattern described by the differential susceptibility 173 model<sup>76</sup>. That is, individuals at high-risk for psychosis might also be particularly sensitive to the 174 beneficial effects conferred by internal and external resources and assets. A large population-175 based study showed that individuals with high levels of childhood adversity had more dramatic 176 changes in mental health during adulthood as a function of both increases and decreases in life 177 stress across the lifespan compared with individuals with low levels of adversity<sup>77</sup>. These 178 findings suggest that childhood adversity might function as a differential susceptibility factor that 179 increases responsiveness to both negative and positive contexts later in life. 180

In sum, the transition rates of high-risk individuals are higher than incidence rates of psychotic 181 disorders in the general population and therefore a risk-based approach is useful for identifying 182 individuals who will develop a disorder. But an approach purely focused on negative outcomes 183 neglects valuable information about what is protecting those at high-risk from developing 184 psychotic disorders or other severe mental health outcomes and perhaps more importantly-185 what helps people function and thrive despite risk factors<sup>78,79</sup>. Risk-based approaches can be 186 complemented by resilience-based approaches that focus on the access to resources and 187 cultivation of assets and strengths that help people weather atypical risk in ways that yield 188 positive outcomes. 189

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192

# [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.

#### 198

<sup>199</sup> [H2] Defining resilient processes.

Resilience is the process by which a system (an individual, a community, or a biological entity) 200 fares better than expected given exposure to some risk or adversity that threatens 201 functioning<sup>22,80,81</sup>. Central to this definition is that resilience is a process—not a stable trait—in 202 which protective and promotive factors support recovery, persistence, resistance, or adaptation 203 (Figure 1). Furthermore, because human development across the lifespan transpires within a 204 set of interacting systems<sup>82</sup>, individual resilience is inherently multisystemic<sup>83</sup>. Specifically, human resilience can be conceptualized as a network of protective and promotive factors that 206 confer positive outcomes and span multiple interacting subsystems or levels ranging from 207 individual biology (such as genes) to the natural environment (such as green space) 83. 208 209 Resilience can only be studied in the context of risk or adversity. In the context of psychosis, 210 risk might refer to factors that increase the chance of a psychotic disorder diagnosis, the 211 experience of those symptoms (for example, experiencing persistent hallucinations might be a 212 source of psychological distress<sup>84</sup>), or secondary factors that might emerge after a diagnosis of 213

psychotic disorder (for example, poor physical health or discrimination<sup>85,86</sup>). 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<sup>87</sup>. 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<sup>88</sup>. 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.

231

# [H2] Defining positive outcomes.

In the context of mental health, positive outcomes include functioning that aligns with or 233 exceeds developmental or contextual norms. Defining a positive outcome that is indicative of a 234 resilient process is challenging for several reasons. First, positive outcomes are multifaceted 235 and include both developmental competence (for example, academic and occupational 236 achievement, interpersonal competence, completing developmental milestones) and mental 237 health<sup>89</sup>. Importantly, although a person might exhibit resilience in some aspects of functioning 238 or mental health, few people are resilient in all domains<sup>90</sup>. Longitudinal studies of recovery in 239 people with schizophrenia have revealed that positive functional outcomes (such as increased 240 community integration) are independent of mental health outcomes such as reduced 241 depression<sup>91</sup>. There is further nuance within psychological health, which entails both subjective 242 well-being and the absence of distress or diagnosis<sup>92-96</sup>. Indeed, well-being and 243 psychopathology are not two sides of the same coin. For example, some teens exhibit high well-244 being despite significant psychopathology; others conversely exhibit low well-being without 245 significant psychopathology<sup>92</sup>. Positive mental health outcomes in the context of psychosis risk 246 go beyond the absence of distress or formal diagnosis and measurements should include all 247 dimensions of psychological health. 248

249

Second, who defines a positive outcome is shaped by power dymanics<sup>97</sup> and which individuals 250 or systems benefit from a particular outcome must be carefully considered. The priorities of the 251 health care systems, clinical care providers, and families might not always overlap with the 252 priorities of the individual with psychosis. Research in psychosis prevention and recovery has 253 traditionally focused on the absence of clinical psychotic symptoms and identifying the factors 254 that prevent, delay, or reduce psychosis. This narrow definition diverges from the richer 255 gualitative and psychosocial descriptors of well-being in individuals with psychotic disorders. whereby personal recovery is not necessarily contingent on clinical recovery<sup>98-101</sup>. To individuals 257 seeking treatment, symptom remission alone might be insufficient to achieving a positive 258 outcome. Rebuilding or regaining a meaningful life is central to recovery from psychosis, 259 together with symptom management. Qualitative studies suggest that some positive changes at 260 individual, interpersonal, and spiritual levels can occur for many individuals and their caregivers 261 after the first episode of psychosis, despite broadly negative experiences<sup>102</sup>. Furthermore, a rich 262 literature in phenomenological psychiatry has highlighted that some aspects of psychosis, which 263 are considered to be a clinically negative outcome, might in fact provide an individual with 264 meaning and relief and thereby confer resilience. An illuminating example is the case of 265 delusions (Box 2). 266

267

Although objective and subjective indicators of well-being and quality of life are increasingly 268 being used as outcome measures in psychosis research<sup>103</sup>, frequently used scales might not 269 align with the qualitative descriptions provided by mental health service users<sup>104</sup>. Taken 270 together, current metrics of positive outcomes might not fully capture the heterogeneity of 271 individual experience. Whilst efforts to quantify outcomes into categories and metrics are 272 pragmatic and valid solutions to capturing subjective illness experiences, much is lost in the 273 process. The result is that the vast scope and richness of meaning embedded in the internal 274 landscape of individuals with psychosis-spectrum conditions are reduced to impoverished 275 ratings that obscure the phenomenology of lived experience. 276

277

#### [H1] Resilience factors for psychosis 278

Meta-analyses have highlighted a striking dearth of studies investigating the factors that lead to 279 positive mental health and functional outcomes despite psychosis risk<sup>105,106</sup>. In this section, we 280 review potential promotive and protective factors in the context of psychosis risk with the 281 aforementioned limitations and challenges in defining positive outcomes in mind. Protective and 282 promotive factors are identified as those for which increased levels lead to increases in positive 283 outcomes. We include potential protective and promotive factors that: decrease the chances of 284 being diagnosed with a psychotic disorder in individuals at clinical high-risk and in general 285 population samples; promote well-being and daily functioning and reduce relapse in individuals 286 diagnosed with a psychotic disorder; and distinguish individuals experiencing psychotic 287 symptoms that do and do not require care (such as those for whom auditory hallucinations 288 cause impairment or disability versus those for whom auditory hallucinations are not distressing 289 and often perceived to have a positive impact<sup>84,107</sup>). 290

291

The reviewed promotive and protective factors (**Table 1**) are organized by interacting levels of a 292 biopsychosocial-ecological system that supports resilience of an individual (Figure 2). We 293 include distal factors that might precede the onset of psychosis (for example, those occurring in 294 childhood) as well as factors that would be expected to play a proximal role in promoting 295 positive outcomes and buffering against more immediate risks (for example, current health 296 behaviors). We recognize that these factors do not necessarily fit neatly into one level but rather 297 behave as a cross-level system and are expected to exert their effects via their interactions<sup>83</sup> 298 (Box 3). Finally, this review of resilience factors is not exhaustive but is intended to provide an 299

300 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

<sup>302</sup> 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<sup>31</sup> for a review of prenatal and perinatal factors and refs<sup>108,109</sup> for

reviews of neuroimaging findings.

306

# 307 [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.

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Better sleep quality is associated with better mental health and well-being in the general 312 population<sup>110</sup>, particularly among young adults<sup>111</sup>, and interventions to improve sleep quality 313 decreased paranoia and hallucinations in college students with psychotic-like symptoms<sup>112</sup>. 314 However, sleep quantity has a non-linear relationship with mental health. Although sleep 315 deprivation can precede the onset of psychosis<sup>113</sup> and is associated with impaired cognitive 316 function and reduced physical and mental well-being<sup>114</sup>, excessive sleep quantity is associated 317 with increased depression and negative affect<sup>115</sup>. It is therefore possible that there is an optimal 318 amount of sleep that confers mental health benefits in the context of psychosis risk; however, 319 these optimal sleep parameters still need to be determined. 320

Physical activity also promotes mental health benefits in the general population<sup>116-118</sup> even at lower levels of intensity <sup>119-121</sup> than the current World Health Organization recommendations<sup>122</sup> (but see ref <sup>123</sup>). Physical activity during childhood protects against later psychotic symptoms in

children with multiple adverse childhood experiences<sup>124</sup> and in the general population<sup>125,126</sup>.

Moreover, increased physical activity is associated with increased well-being and functioning,

improved cognitive performance, and reduced psychiatric symptoms in those with psychotic

disorders<sup>127-131</sup>. Akin to sleep quantity, physical activity has protective and promotive effects at low to moderate, but not high, levels<sup>132</sup>.

- Finally, homeostatic regulation of the autonomic nervous system in response to moment-to-329 moment demands might be a biological correlate of adaptive capacity<sup>133,134</sup>. In individuals with 330 normal cardiac function, higher resting state heart rate variability and respiratory sinus 331 arrhythmia are associated with better emotion regulation<sup>133,135</sup> and cognitive performance<sup>136,137</sup>, 332 whereas low heart rate variability and respiratory sinus arrhythmia suggest a rigidity of 333 autonomic response and are associated with poor physical<sup>136,137</sup> and mental health<sup>135,138</sup>. 334 People with psychotic illness have lower resting state heart rate variability and respiratory sinus 335 arrhythmia compared to controls<sup>139-143</sup>, and individual differences in heart rate variability and/or 336 respiratory sinus arrhythmia have been associated with emotion regulation<sup>144</sup>, psychiatric 337 symptom burden<sup>142</sup>, cognitive performance<sup>143,145,146</sup>, and functioning in this clinical population<sup>142-</sup> 338 <sup>146</sup>. Notably, these autonomic responses are malleable through biofeedback training <sup>147-150</sup>, 339 breathing retraining<sup>147,150</sup>, mindfulness practice<sup>151</sup>, and physical exercise<sup>149,152</sup>. Two studies of 340 heart rate variability biofeedback training in individuals at-risk for psychosis suggest potential 341
- <sup>342</sup> benefits to both autonomic activity and clinical symptoms<sup>153,154</sup>.
- 343 [H2] Psychological factors

<sup>344</sup> 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

346 categories: traits and personal characteristics; attitudes, cognitions, and orientations; and

- <sup>347</sup> psychological abilities.
- 348

## [H3] Traits and personal characteristics

Adaptive coping —a cognitive or behavioral process that has long-term benefits for minimizing 350 stress<sup>155,156</sup> — is associated with less severe psychotic-like symptoms in both the general 351 population<sup>157,158</sup> and in at-risk youth<sup>159</sup> and is correlated with reduced symptom severity and 352 increased quality of life in individuals diagnosed with schizophrenia<sup>160-164</sup>. One longitudinal study 353 found that adaptive coping at baseline was associated with attenuated clinical symptom severity 354 and better social functioning one year later in youth at high-risk for psychosis, suggesting a 355 causal effect of adaptive coping on outcomes<sup>165</sup>. Relatedly, some emotion regulation strategies 356 might also confer resilience in the context of psychosis risk. Trait use of reappraisal strategies, 357 which aim to modify the meaning and impact of emotion-eliciting events, is associated with less 358 severe psychotic-like experiences<sup>166</sup> and protects against the distress of these experiences<sup>167</sup>. 359

360

Self-esteem, locus of control, and personality dimensions might also confer beneficial effects. 361 Higher self-esteem is associated cross-sectionally with reduced psychotic and psychotic-like 362 experiences in at-risk youth<sup>168,169</sup>, improved quality of life<sup>170</sup> and reduced suicidality in individuals 363 diagnosed with schizophrenia<sup>171</sup>, and protects against distress associated with persistent 364 psychotic experiences<sup>172</sup>. Longitudinal studies have shown that baseline self-esteem is 365 associated with a lower likelihood of psychosis onset 3 years later in the general population<sup>173</sup>. 366 Internal locus of control refers to the degree to which an individual feels that they are 367 responsible for their own outcomes and is associated with a number of positive outcomes in the 368 context of psychosis risk. Qualitative studies indicate that individuals experiencing their first 369 episode of psychosis identify loss of control as their primary psychosocial problem<sup>174</sup>, and 370 regaining self-efficacy is a major component of recovery<sup>175</sup>. In addition, an internal locus of 371 control might buffer the effect of harsh parenting on later psychotic symptoms<sup>176</sup>. Among 372 individuals with auditory-verbal hallucinations, the ability to exert volitional control over voices is 373 one of the main characteristics that distinguishes individuals who seek treatment from those 374 who do not<sup>177,178</sup>. Finally, broad personality domains such as openness, extraversion, and 375 emotional stability (the inverse of neuroticism) protect against the distress surrounding 376 delusional ideas<sup>179</sup>. In people with schizophrenia, emotional stability, extraversion, and 377 agreeableness are also related to better subjective quality of life and might buffer against some 378 of the negative impacts of traumatic experiences<sup>180-182</sup>. 379 380

# [H3] Attitudes and orientations

<sup>382</sup> In the context of psychosis risk, there are three candidate protective and promotive factors and <sup>383</sup> processes that represent attitudes, cognitions, or orientations that might contribute to positive <sup>384</sup> outcomes: stigma resistance, spirituality and/or religiosity, and meaning-making around unusual <sup>385</sup> experiences. These three factors are a part of a broader category of attitudes and orientations <sup>386</sup> that help people contextualize psychological experiences.

387

Public stigma about mental illness, which manifests in negative beliefs and attitudes about 388 people with mental illness and overt discrimination<sup>183</sup>, can result in internalization of those 389 negative attitudes<sup>184</sup>. Self-stigma is associated with negative clinical outcomes<sup>185,186</sup>, whereas 390 the capacity to counteract or be unaffected by stigma (stigma resistance) is related to well-being 391 and quality of life in individuals with psychotic disorders<sup>187-189</sup>. Importantly, cognitions about 392 stigma (for example, rejecting stigma as unfair), rather than perceived stigma (for example, the 393 observed level of stigma against people with mental illness) predicted help-seeking in those with 394 psychosis<sup>190</sup>. Although more work is needed to evaluate interventions that boost stigma 395 resistance in individuals with schizophrenia, there is evidence that self-stigma reduction 396

strategies, such as providing psychoeducation about the illness experience and the 397

consequences of stigma and teaching methods for reducing self-stigmatizing attitudes, can 398 improve psychological outcomes<sup>191,192</sup>. 399

400

Spirituality generally confers benefits to mental health<sup>193,194</sup>. Spirituality (commonly defined as 401 "the search for the sacred"<sup>195</sup>) is related to self-reported adaptation in the face of adversity 402 among individuals diagnosed with a psychotic disorder <sup>196</sup>. Furthermore, sensing the presence 403 of the divine is associated with better social functioning in individuals at clinical high-risk for 404 psychosis<sup>197</sup>. Individuals with non-distressing psychotic experiences report being more spiritual 405 (but not religious) than individuals diagnosed with a psychotic disorder or community controls 406 without a history of psychotic experiences<sup>172</sup> and are more likely to ascribe voices to a spiritual 407 being rather than real people<sup>198</sup>. Although one interpretation of these findings is that spiritual 408 practices increase the likelihood of hearing voices, gualitative and mixed method 409 phenomenological studies instead suggest that spiritual practices and beliefs generally do not 410 precipitate the onset of voices<sup>199,200</sup>. Instead, these practices and beliefs play an important role 411 in controlling voices and interpreting the nature of these experiences, thereby buffering against 412 their potential negative impacts. 413

414

The protective and promotive effects of religion are more complex. Although religion often 415 includes spiritual components, they are enacted in the context of a structured system and 416 sanctioned set of beliefs, practices, and rituals<sup>193</sup>. Religion might act as both a vulnerability 417 factor as well as a protective or promotive factor. On the one hand, religious delusions are 418 common in individuals diagnosed with a psychotic disorder<sup>201</sup>, thereby calling into question the 419 role of religious beliefs and practices in symptom etiology. Indeed, some studies have reported 420 relationships between greater religiosity and more severe symptoms and worse functional 421 outcomes in individuals diagnosed with a psychotic disorder<sup>193,202</sup>. Furthermore, in individuals at 422 clinical high risk, increased participation in religious activities was associated with more severe 423 depressive symptoms<sup>197</sup>. On the other hand, religious involvement within a community of 424 believers wherein beliefs and values have been adopted over generations has also been found 425 to confer benefits to mental health<sup>193</sup>. Qualitative studies<sup>203,204</sup> and data suggesting that religious 426 beliefs protect against suicidal behaviors<sup>205</sup> and promote guality of life<sup>196</sup> attest to a possible 427 protective effect of religious beliefs and practices in individuals diagnosed with schizophrenia. 428 The effects of religion on well-being and mental health might depend on cultural influences. 429 Higher rates of religious beliefs and activity are reported among ethnic minority communities in 430 Europe, the United States, and Australia compared to ethnic majority communities, and there is 431 greater use of religious coping in marginalized and/or socially disadvantaged groups<sup>206-209</sup>. 432

433

Expanding beyond the global meaning structures provided by religion and spirituality, personal 434 appraisals of anomalous experiences influence outcomes in individuals with psychosis or 435 psychotic-like experiences. For example, compared to voice-hearers with a need for care, non-436 treatment seeking voice-hearers often integrate psychotic experiences with their personal 437 context via intra-personal processes or acceptance from others<sup>210,211</sup>, leading them to ascribe 438 meaning and purpose to the experience. Activities whereby individuals with schizophrenia make 439 sense of symptoms and other illness-related experiences and integrate them into their own 440 personal narratives promote well-being<sup>212</sup> and are a central aspect of mental health services 441 associated with positive outcomes<sup>213</sup>. The potential benefits conferred by meaning-making 442 processes are further highlighted by findings from a longitudinal study in India, which found that 443 having insight into one's mental health condition while also holding non-medical explanations for 444 the illness experience was associated with remission within five years following a schizophrenia 445 diagnosis<sup>214</sup>. 446

#### 448

## 449 [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<sup>215</sup>. Social skills training has been found to be protective

against relapse in patients with psychosis<sup>216</sup> and to reduce the risk for and severity of psychotic-

like experiences in individuals with a history of adversity<sup>217,218</sup>

A rich literature suggests that general cognitive functioning (measured using tests of general 457 intelligence) and specific neurocognitive abilities have protective or promotive effects. First, 458 better neurocognitive abilities<sup>219</sup>, particularly verbal fluency, verbal and visual memory, and 459 working memory, are associated with a decreased risk for transitioning to psychosis in high-risk 460 youth<sup>220,221</sup>. Second, individuals with higher general cognitive functioning and better executive 461 functioning early in the course of illness have a greater chance of a resilient illness trajectory<sup>222</sup>. 462 In addition, better general cognitive functioning attenuates the relationship between a history of 463 multiple adverse childhood adverse experiences and later psychotic symptoms<sup>223</sup>. Finally, on 464 average, individuals with persistent psychotic experiences who do not seek help have higher 465 general cognitive functioning than those that do seek help<sup>172</sup>. 466

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## 468 [H2] Social factors

Social factors are strongly linked with mental health<sup>224</sup>. Greater social support is related to 469 reduced psychotic experiences in young adults with significant psychosis risk factors<sup>124,223,225-227</sup> 470 , and to reduced symptom severity<sup>203,228,229</sup> and improved functioning<sup>229</sup> in people diagnosed 471 with a psychotic disorder. A meta-analysis further indicates that family interventions aimed at 472 improving family support are associated with reduced relapse rates<sup>216</sup>. These benefits are not 473 derived exclusively from receiving support, but also from giving support. Relationship reciprocity 474 (the mutually beneficial exchange of support) is higher in individuals with persistent psychotic 475 experiences that do not have a need for care, versus those who do<sup>230</sup>. Furthermore, help-476 seeking individuals with psychosis reported the highest distress from their symptoms when 477 relationship reciprocity was low, regardless of symptom severity<sup>230</sup>. Relatedly, in individuals with 478 schizophrenia, better relationship quality is related to reduced symptom severity<sup>231</sup> and predicts 479 better functional outcomes three years later<sup>232</sup>. In individuals at clinical high risk for psychosis, 480 better quality of relationships and number of relationships are related to reduced severity of 481 psychotic experiences and better functioning<sup>233</sup>. 482

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Social network size and social interactions are additional factors associated with positive 484 outcomes <sup>234</sup>. For example, interactions with friends predicted two-year clinical recovery in 485 people diagnosed with a psychotic disorder<sup>235</sup>, living with someone else predicted remission in a 486 prospective 20-year follow-up study of individuals experiencing their first episode of 487 psychosis<sup>236</sup>, and the immediate presence of family or friends decreased the moment-to-488 moment risk of mental states associated with delusions in individuals with chronic 489 schizophrenia<sup>237</sup>. Number of relationships is associated with a reduced risk of developing 490 schizophrenia 15 years post-baseline<sup>238</sup> and is further associated with reduced symptom 491 severity in individuals diagnosed with schizophrenia<sup>231</sup>. At broader social levels, involvement in 492 activities that align with interests and values also provides mental health benefits. Withdrawal 493 from extracurricular activities has been found to precede a delusional moment<sup>237</sup>, and holding 494 valued social roles (for example, club membership) prevents relapse in people with 495

496 psychosis<sup>239</sup>.

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- <sup>498</sup> Finally, broader aspects of the social environment play a crucial role in mental health.
- 499 Epidemiological studies have shown that living among people of the same ethnicity reduces the
- <sup>500</sup> chance of developing psychosis<sup>240-242</sup>. However, findings that neighborhood ethnic diversity has
- negative impacts on well-being and health are contested<sup>243,244</sup>, and negative impacts might even
- <sup>502</sup> reverse over longer periods of intergroup contact<sup>245</sup>. The mechanism underlying the association
- <sup>503</sup> between ethnic diversity and psychosis is unclear but is almost certainly culturally-dependent<sup>244</sup>.
- One possibility is that higher ethnic density reduces exposure to discrimination and racism or
- exerts a buffering effect against their negative impacts<sup>242,246</sup>. Alternatively (or in addition), higher ethnic density might increase positive social neighborhood characteristics, at least in the short-
- ethnic density might increase positive social neighborhood characteristics, at least in the short term<sup>244</sup>. These social characteristics of the neighborhood confer beneficial effects in the context
- of psychosis risk, although work here is more limited<sup>244</sup>. Residing in a more socially cohesive
- neighborhood (that is, a neighborhood that fosters a sense of belonging<sup>247</sup>) is associated with a reduced risk for psychotic symptoms in children of mothers diagnosed with schizophrenia<sup>227</sup> and
- attenuates the association between adverse childhood events and later psychotic
- symptoms<sup>124,223</sup>. 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<sup>248</sup>), has been associated with a reduced risk of developing a psychotic disorder<sup>249</sup>-
- <sup>515</sup> <sup>251</sup>, but findings are mixed<sup>252</sup>. Taken together, these findings align with the 'social defeat'
- <sup>516</sup> hypothesis, whereby repeated experiences of social exclusion increase risk for
- schizophrenia<sup>253,254</sup>. Resilience factors at the social environmental level might buffer against
- 518 these risks.

# 520 [H2] Built and natural environments

- 521 Mental health benefits can be conferred by broader aspects of the natural and built
- <sup>522</sup> environment. There is robust evidence that access to green and blue space<sup>255</sup> and exposure to
- <sup>523</sup> natural sounds<sup>256</sup> increase positive affect and social engagement, reduce stress levels and
- negative affect, improve sleep quality and cognition, and enrich meaning in life. Notably,
- <sup>525</sup> epidemiological studies have shown that exposure to natural green and blue space during
- childhood is associated with psychosis risk<sup>257-260</sup>, independent of urbanicity, and increased
- <sup>527</sup> levels of green space density are associated with decreased schizophrenia risk in a dose-
- dependent manner in man-made areas<sup>258</sup>. Furthermore, exposure to green spaces is related to
- <sup>529</sup> better clinical symptoms in individuals diagnosed with schizophrenia<sup>261</sup>.
- 530

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The mechanisms by which green space exert protective or promotive effects are not yet 531 determined. Current theories suggest that natural settings foster restoration from mental 532 fatigue<sup>262</sup>, promote relaxation, and/or enhance well-being owing to an innate preference for life 533 forms and lifelike processes<sup>263</sup>. Qualitative evidence suggests that spending time in open green 534 space might buffer against the stress of living in an urban environment in individuals with 535 schizophrenia<sup>264</sup>. Importantly, forest therapy<sup>265,266</sup> (a guided outdoor healing practice) is broadly 536 promotive for a range of mental health conditions. Even simulated or virtual forest walks might 537 confer psychological benefits<sup>267,268</sup>. A recreational program involving a walk through a suburban 538 forest reduced negative affect and anxiety in individuals hospitalized for psychosis<sup>269</sup>. Given the 539 known beneficial effects of the natural environment on mental health, expansion of green and 540 blue space in urban areas, and even within buildings, seem warranted<sup>270</sup>. 541 542

- <sup>543</sup> Characteristics of the built environment such as walkability, transit access, or housing quality
- have also been shown to contribute to positive mental health outcomes<sup>271-273</sup>. There has been
- 545 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<sup>275-277</sup>, which might in turn lead to mental health

benefits. Furthermore, the built environment influences access to care<sup>278</sup>, 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<sup>274</sup>. These findings underscore the crucial role of judicious urban
 planning, smart policies, and architectural design in public health outcomes.

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# 555 [H1] Limitations of the resilience literature

There are several limitations to the literature reviewed above. First, it does not distinguish 556 protective from promotive factors. Most of the factors associated with positive outcomes in the 557 context of psychosis risk reviewed above are widely regarded as good for health, well-being, 558 and functioning and are potentially promotive factors. Whether these factors also have a 559 differentially positive effect in contexts of heightened risk, particularly in the context of psychosis 560 risk (protective factors), remains unclear<sup>279</sup>. Answering this question would require evaluating 561 whether a given factor was associated with positive outcomes in a risk-dependent manner. For 562 example, spirituality could be considered a protective factor in this context if it showed a positive 563 relationship with subjective well-being in youth identified as clinical high-risk for psychosis, but 564 no relationship in a population sample of young adults. Distinguishing protective and promotive 565 factors is important for developing implementation strategies. Should a factor be broadly 566 promotive, then intervention or prevention efforts aimed at enhancing that factor stand to be 567 effective when delivered to a wide audience through broad public health initiatives. By contrast, 568 strategies aimed at shoring up protective factors in the context of psychosis risk might be most 569 effective when delivered to population subgroups, such as at psychosis specialty clinics. 570

Second, although modern conceptualizations of resilience highlight its multisystemic nature<sup>83</sup>, 571 the majority of reviewed studies have focused on biological and psychological factors at the 572 level of the individual and immediate family unit. Assets and activities within broader social and 573 ecological levels that confer substantial mental health benefits have yet to be explored in the 574 context of psychosis risk<sup>272,273,280,281</sup>. Research into the impact of the built environment is 575 particularly scant. Furthermore, most studies have investigated the effects of single factors 576 rather than a constellation of intersecting and multisystemic risk and protective and promotive 577 factors. This makes it impossible to unpack the mechanisms by which these factors come to be 578 associated with resilient outcomes-that is, whether they directly impact outcome measures, or 579 indirectly influence outcomes via other protective, promotive, or vulnerability factors. Moreover, 580 the reviewed factors should be considered on a continuum, whereby optimal levels are 581 protective or promotive and sub-optimal levels confer vulnerability. For example, social support 582 can buffer against risk whereas social isolation might create vulnerability. It is unclear whether 583 there are shared underlying mechanisms, or whether factors operate via distinct pathways at 584 each end of the continuum. 585

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Third, there is little examination of contextual effects in the current psychosis resilience 587 literature. This is a critical gap because when it comes to resilience, one size does not fit all. For 588 example, risk context might influence the degree to which a resource or positive behavior 589 confers benefits. Risk context refers to whether risk occurs in the preliminary circumstances that 590 might lead to a psychotic disorder diagnosis, in distress that emerges from the symptoms 591 themselves, or in secondary risks after diagnosis. The degree of overlap in the factors that 592 promote resilience in the context of these different types of risk and the mechanisms by which 593 they might do so is unclear. Many of the resilience-promoting factors reviewed here, such as 594 positive health behaviors, adaptive coping strategies, or access to green space, reduce the 595 likelihood of being diagnosed with a psychotic disorder. They also engender beneficial effects in 596

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.

#### 601

The benefits conferred by a putative protective or promotive factor might also depend on other 602 contextual factors. Specific factors might have a more profound impact during sensitive periods 603 of brain development characterized by higher plasticity. Notably, the timing of these critical 604 periods are themselves malleable and changed by environmental factors<sup>282-285</sup>. In addition, 605 culture is a critical contextual factor. The definition of a positive outcome and the ways in which 606 resilience at the level of the individual is prioritized relative to other levels of the social ecology 607 are inherently culturally-dependent<sup>286,287</sup>. Furthermore, there are robust cultural and geopolitical 608 differences in the clinical course of psychotic disorders that cannot be explained exclusively by 609 diagnostic differences. For example, individuals in low-income and middle-income regions fare 610 better following a diagnosis of schizophrenia than individuals in high-income regions<sup>288-295</sup>. 611 Finally, the positive effect of engaging in positive coping strategies might be stymied when 612 structural inequalities pose barriers to obtaining basic needs<sup>89</sup>. Indeed, the RAISE-ETP study 613 showed that treatment based on a coordinated specialty care intervention for early psychosis 614 that adopts a strengths and resilience based approach only improved symptoms and quality of 615 life in individuals at the top 25% of the socioeconomic distribution<sup>296, 297</sup>. 616 617

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.

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First, future research should test a comprehensive set of (ideally modifiable) potential protective 633 and promotive factors to identify factors with the strongest associations with positive outcomes 634 both individually and when considered in concert with other factors. Relatedly, future work 635 should test whether putative associations are moderated by psychosis risk, which would 636 distinguish protective from promotive factors. Such research can then be used to identify 637 promising targets for novel and cost-effective interventions. Identifying promotive factors could 638 support the implementation of broad, public health-informed strategies to shore up factors that 639 increase positive outcomes for emerging adults in general<sup>298</sup>. Identifying protective factors could 640 inform clinical staging interventions that acknowledge the 'pluripotential' nature of psychosis 641 risk<sup>299-302</sup>, whereby the identified individuals are at heightened risk for a variety of psychiatric 642 outcomes. Indeed, an increasing number of clinical high-risk research groups are moving 643 toward transdiagnostic clinical staging approaches that focus on youth mental health more 644 generally<sup>299-302</sup>. In addition, future work should examine the co-occurring influences that might 645 moderate the impact of protective and promotive factors. Knowing what factors are associated 646 with positive outcomes, when, and for whom, is central to understanding at what level of a 647

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

Second, future research should re-imagine positive outcomes to be broader than the mere 651 absence of psychological distress and diagnosis. Resilient outcomes are multifaceted, and 652 future work in this field would benefit from considering a wider range of measures that include 653 academic performance, work outcomes, physical health, social functioning, and purpose in 654 addition to mental health. Furthermore, researchers should consider positive outcomes at 655 broader levels of the social ecology and the ensuing impact on individual outcomes-for 656 example, how individual activism might promote transformation of social institutions that in turn 657 engenders more rights and opportunities for those living with mental illness. 658

Third, given the inherent multisystemic nature of resilience, diverse teams that include 659 multidisciplinary scholars as well as individuals who have traditionally been excluded from 660 academic discourse will be critical for gaining a broader perspective on potential protective and 661 promotive factors and on defining positive outcomes. This includes individuals with lived 662 experience of psychosis, families, teachers, and community and religious leaders who often 663 encounter people experiencing or at-risk for mental health emergencies along their pathway to 664 care. Furthermore, more cross-cultural work is needed, as positive outcomes and resilience 665 promoting processes are inherently shaped by culture. Looking beyond the biomedical models 666 of mental health that have dominated scientific discourse might allow us to reshape or refine our 667 conceptualization of positive outcomes, which could potentially uncover additional resilience-668 promoting factors. 669

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Finally, several methodological considerations will likely enhance the study of resilience to 671 psychosis risk. First, mixed methods approaches that link qualitative and quantitative research 672 can provide a springboard for generating testable hypotheses regarding factors that might 673 confer protection against psychotic symptoms and related distress. Second, resilience is best 674 represented as a positive trajectory and therefore not fully captured by a single moment in 675 time<sup>303</sup>. Thus, longitudinal studies are critical for characterizing this trajectory and determining 676 causal relationships between factors and outcomes, particularly as compromised access to and 677 engagement in the promotive and protective factors might be direct consequences of illness. 678 Indeed, prospective longitudinal studies have provided critical data regarding factors that 679 contribute to the development of a psychotic disorder and poor clinical outcomes among high-680 risk individuals<sup>304-307</sup>. Third, more is not always better, and researchers should consider non-681 linear relationships between outcome metrics and both risk and protective and promotive 682 factors. For example, stress is typically considered a risk factor, but might have inoculating 683 effects in small doses <sup>308</sup>. Fourth, natural and passive monitoring approaches, such as 684 ecological momentary assessment and mobility tracking can greatly enhance ecological validity 685 and provide richer assessments that capture the complexity of participants' daily lives<sup>309</sup>. For 686 example, geospatial location and geographical information systems can objectively measure 687 how often and for how long people are exposed to natural or built features of the environment. 688 and how these durations relate to mental health<sup>261,310,311</sup>. Finally, it is paramount to expand 689 beyond help-seeking samples. Individuals identified at clinical high-risk are already experiencing 690 significant clinical distress related to attenuated psychotic symptoms, social and functioning 691 difficulties, depression, and other sources<sup>312</sup>. Identifying individuals in the general population 692 who are at-risk for psychosis owing to attenuated psychotic symptoms or genetic risk but who 693 do not present with a need for care might provide insights into factors that help avert the 694 functional decline that leads young people at-risk for psychosis to seek help in the first place. 695 696

In conclusion, our Review suggests that the 'ordinary magic'<sup>313</sup> that constitutes human resilience promotes positive adaptations in what is generally considered to be the most severe of mental health conditions<sup>314</sup>. Such findings are particularly important given antiquated, but still influential, notions of schizophrenia as a progressively deteriorating illness<sup>315</sup> with its basis in irreversible etiological factors that manifest later in life<sup>316</sup>. 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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#### 1715 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.
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# 1719 Competing interests

The authors declare no competing interests.

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1729 Table 1. Summary of reviewed protective and promotive factors.

			1
Level	Factor	Key findings	Considerations for prevention and intervention
Biological	Sleep	Better sleep quality is associated with greater well- being <sup>110,111</sup>	Cognitive behavioral therapy (CBT) for insomnia <sup>317</sup> is the first-line treatment for sleep disturbance and can be effectively delivered
		Sleep quality interventions decrease psychotic-like symptoms <sup>112</sup>	using scalable web-based programs <sup>318</sup>
		Sleep quantity shows a non- linear relationship with well- being <sup>114,115</sup>	Sleep hygiene recommendations as stand-alone interventions without personalization are unlikely to be effective <sup>319</sup>
			Expand beyond the level of the individual and consider how social and environmental determinants might be modified to improve sleep health <sup>320</sup>
	Physical activity	Low to moderate exercise is associated with mental health benefits <sup>116-118</sup>	90 minutes of moderate to vigorous exercise per week can improve mental and physical health <sup>321</sup> among individuals
		Physical activity in childhood is associated with a lower likelihood of developing psychosis later in life <sup>124-126</sup>	diagnosed with psychotic disorders <sup>322</sup> and individuals at clinical high risk <sup>323</sup>
		Physical activity is associated with positive clinical and functional outcomes and subjective well-being in individuals with psychotic disorders <sup>127-131</sup>	Supervised exercise in group settings (versus solitary exercise) maximizes adherence to the exercise intervention in individuals diagnosed with psychotic disorders <sup>322</sup>
			Strategies for addressing barriers to exercise include establishing an incentive structure, using augmented reality, varying the exercise routine, and social support <sup>130</sup>

	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 <sup>135-138</sup> Heart rate variability and respiratory sinus arrhythmia are lower in people with psychotic disorder and individual differences relate to clinical symptoms and daily functioning <sup>142-146</sup>	Heart rate variability and respiratory sinus arrhythmia are modifiable through biofeedback training, breathing retraining, mindfulness practice, and physical exercise in the general population <sup>147-152,324</sup>
		Biofeedback training to enhance heart rate variability is associated with improved clinical symptoms <sup>153,154</sup>	
Psychological	Traits and personal characteristics	Adaptive coping is associated with less severe psychotic and psychotic-like symptoms in the general population <sup>157,158,165</sup> and clinical populations <sup>160-164</sup> Higher self-esteem is associated with reduced psychotic and psychotic-like symptom severity <sup>168,169,173</sup> , improved quality of life <sup>170</sup> and general mental health in clinical populations <sup>170,171</sup> , and reduced distress associated with psychotic experiences <sup>172</sup> Regaining internal locus of control is a major component of recovery in individuals with schizophrenia <sup>175</sup> and is associated with a lower likelihood of developing psychotic symptoms <sup>176</sup> Trait emotional stability, extraversion, and agreeableness are associated with better quality of life in individuals with schizophrenia <sup>180-182</sup>	Fostering coping might be a mechanism of symptom improvement in CBT for psychosis <sup>325</sup> , although CBT does not lead to improvements in quality of life, subjective distress or functioning <sup>326</sup> . There is no evidence to favor any specific preventative treatment of psychosis (including CBT) <sup>327</sup> . 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 <sup>328</sup> . 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 <sup>329</sup> .

Attitudes and orientations	Stigma resistance is related	Stigma reduction strategies that
	to well-being and quality of life in individuals with psychotic disorders <sup>187-189</sup> Spirituality might confer mental health benefits in the general population <sup>193,194</sup> . Religion and religious practices might act as both a vulnerability factor <sup>193,197,202</sup> as well as a protective or promotive factor <sup>196,203-205</sup> . Among individuals diagnosed with a psychotic disorder, spirituality relates to adaptation in the face of adversity <sup>196</sup> , is associated with better social functioning in young people at risk for psychosis <sup>197</sup> , and might buffer against the distress associated with psychotic experiences <sup>172,198</sup> Ascribing meaning to anomalous experiences might buffer against the distress of psychotic experiences <sup>210,211</sup> and promote well-being in individuals diagnosed with schizophrenia <sup>212</sup>	beliefs and attitudes or enhance stigma-coping skills through improvements in self-esteem, empowerment, and help-seeking behavior are effective in reducing self-stigma <sup>330</sup> , particularly when they include a psychoeducation component <sup>331</sup> 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 <sup>206-209</sup> and for whom religious and spiritual resources might be more accessible than other resilience- promoting factors <sup>332,333</sup> .
Abilities	Higher social competence is associated with reduced risk of relapse in patients with psychosis <sup>216</sup> and with reduced risk for and severity of psychotic-like experiences in at-risk individuals <sup>217,218</sup> Better neurocognitive abilities are associated with decreased risk for psychotic symptoms in at-risk youth <sup>219-</sup> <sup>221,223</sup> , a better clinical course in individuals recently diagnosed with a psychotic	Cognitive Behavioral Social Skills Training <sup>334</sup> , Social Cognition Training <sup>335</sup> , and Social Cognition and Interaction Training <sup>336</sup> involve live instruction, role plays, behavioral assignments, and/or computerized programs <sup>337</sup> 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

		against distress associated with psychotic symptoms <sup>172</sup> .	and in individuals at high risk for psychosis <sup>340</sup> , 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 <sup>124,223,225-227</sup> , and to reduced symptom severity <sup>203,228,229</sup> and improved functioning <sup>229</sup> 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 <sup>230</sup> . In individuals with schizophrenia, better relationship quality is related to reduced symptom severity <sup>231</sup> and predicts better functional outcomes three years later <sup>232</sup> . 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 <sup>233</sup>	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 <sup>341</sup> Family interventions aimed at improving family support are protective against relapse <sup>216</sup> . One-to-one peer support improves support provided by personal relationships when adjunctive to usual care for psychosis <sup>342</sup> 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 <sup>343,344</sup>
	Social network size and social interaction	Social interaction promotes positive mental health outcomes in the general population <sup>234</sup> .	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
		relations is associated with	evidence available suggests

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

# 1732 Figure legends

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Figure 1. Trajectories of psychosis risk and resilience. Example trajectories for 1734 psychological distress (top), psychotic and psychotic-like experiences (middle), and subjective 1735 well-being and psychosocial functioning (bottom) in individuals at risk for psychosis. Risk factors 1736 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 1739 health or discrimination). Blue represents an individual presenting with risk factors but not 1740 protective or promotive factors. The grey, yellow, and green trajectories represent different 1741 resilience-promoting processes. Adaptation (grey) occurs when the individual changes in ways 1742 that permit positive outcomes despite the impact of risk. Recovery (yellow) occurs when the 1743 individual initially experiences negative outcomes in response to risk, but later returns to a 1744 previous level of functioning. Finally, resistance and persistence (green) occur when the 1745 individual maintains their current trajectory despite risk. These trajectories are highly 1746 schematized and simplified examples and do not encompass all possible trajectories of an 1747 individual with psychosis risk factors. Rather, they are intended to provide an illustration of how 1748 resilience-promoting processes might be enacted in the context of psychosis risk factors. 1749 1750 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.

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# 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 1761 focus on strengths and protection is more hopeful-sounding but conceptually identical to a riskfocused approach to prevention and intervention. But resilience scholars have presented 1763 several arguments supporting the idea that a shift from risk to resilience is more than an 1764 inversion of language<sup>87</sup>. 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<sup>22,87</sup>. For example, physical activity 1767 (generally considered a promotive factor) has a non-linear relationship with mental health, such 1768 that more physical exercise is related to improved mental health up to a threshold, after which it increases the likelihood of poor mental health<sup>351-354</sup>. Those aspects of exercise at low to 1770 moderate 'doses' that confer benefits are likely not the same aspects that confer vulnerability at 1771 high doses.

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Second, context matters: a particular factor or process that has protective or promotive effects 1774 in one context, group, or individual might operate as a vulnerability factor in another<sup>87</sup>. For 1775 example, participating in high school sports is protective against alcohol use in Black girls, but is 1776 associated with increased alcohol use in Black boys and white girls and boys<sup>355</sup>. Third, the 1777 'active ingredient' by which a particular factor confers benefits might lie in the positive end of 1778 that factor. For example, in women raised in institutional care, being in a supportive marital 1779 relationship was related to improved parental quality as compared to women who were not in a 1780 supportive marital relationship; however, parenting quality was equivalent in women raising a 1781 child without a partner and women raising children in the context of a poor marital relationship. 1782 In other words, a supportive marital relationship was a protective or promotive factor, but there 1783 was no analogous vulnerability caused by a poor marital relationship<sup>356</sup>. Thus, focusing on the 1784 protective end of a variable- supportive marital relationship, in this example-might elucidate 1785 the mechanism or process by which variation in exposure to a given factor might buffer the 1786 negative effects of risk. Finally, outcome variables do not lie on a unidimensional spectrum. 1787 Presence of resilience factors is not equivalent to an absence of risk factors. In a similar way, 1788 positive and negative emotions represent different constructs<sup>357</sup> and 'feeling good' is not the same as 'not feeling bad'. Thus, a paradigmatic shift from risk to resilience represents a change 1790 in approach and framework, not just a matter of emphasis on language and terms. 1791 1792

## 1793 Box 2. The case of delusions

Delusions (false and fixed beliefs that are not amenable to change despite conflicting 1794 evidence<sup>359</sup>) are a defining symptom of schizophrenia and are understood as harmful and 1795 dysfunctional. Delusions are also considered an important treatment target that is central to 1796 recovery from psychosis. Current explanatory models of delusions adopt neurocognitive 1797 approaches to belief formation, whereby delusions are thought to arise from normative 1798 reasoning in the context of anomalous experiences or reflect abnormalities in a normative belief 1799 formation process (for a review see <sup>358</sup>). These approaches have led to the development of 1800 cognitive-behavioral therapy (CBT) for delusions <sup>359</sup>, which treat delusions as beliefs that can be 1801 challenged through standard techniques of reality testing and evaluation. However, the efficacy 1802 of CBT for delusions appears to be modest and its therapeutic ingredients remain unclear <sup>360,361</sup>. 1803

Delusions are notoriously difficult to dispel. However, the current definition and 1804 operationalization of delusions are fraught with epistemic hurdles that make it difficult to 1805 determine the borders of pathology <sup>362,363</sup>. Framing delusions as harmful beliefs that must be 1806 eliminated to achieve recovery from psychosis fails to consider the lived experience of the 1807 phenomenon and the broader sociocultural and psychological context. Specifically, some 1808 delusions might serve an adaptive purpose, at least temporarily <sup>364,365</sup>. This proposition is not intended to romanticize delusions or to downplay their seriousness. Indeed, delusions-1810 particularly persecutory delusions—are associated with tremendous personal distress <sup>366</sup>, and 1811 anger secondary to delusions has been found to increase an individual's risk for violent behavior 1812 367 1813

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<sup>326</sup>. 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<sup>368</sup>:

- 1821"It would all have been for nothing...it would be sadness...it would be wrong, I wouldn't<br/>accept it...that's futility I would really miss it. A waste of a life, all my lives, all the way<br/>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 1826 variety of reality experiences to fathom how individuals with delusions might evaluate and 1827 discover meaning in these experiential alterations<sup>362</sup>. Moving away from a purely mechanistic 1828 model of delusions that fails to acknowledge or incorporate the subjective, phenomenological 1829 illness narratives will be essential to defining recovery and positive outcomes in a manner that 1830 leaves intact the person's sense of self and ability to find meaning in experience<sup>365,369</sup>. From the 1831 perspective of the person with lived experience, delusions are not necessarily an irrational or 1832 false representation of reality; rather, such beliefs might bring a sense of meaningfulness to 1833 their life <sup>369</sup>—which might confer resilience. 1834

### 1836 Box 3. Integrating risk and resilience factors

Our categorization of potential protective and promotive factors reflects the current literature that 1837 tends to study factors in isolation or within a small selection of other risk or resilience factors. 1838 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 1840 occur<sup>83</sup>. First, interactions between various risk and resilience promoting factors can occur 1841 within levels. For example, the biological resilience promoting factors reviewed here (sleep 1842 quality, physical activity, and homeostatic regulation of the autonomic nervous system) influence 1843 each other through reciprocal interactions via physiological and psychological pathways<sup>370</sup> and 1844 might exert their impact on positive mental health outcomes via a common process, such as 1845 reducing stress reactivity<sup>371-373</sup>. Second, extensive interactions occur between levels. For 1846 example, physical activity is influenced by the walkability of the built environment<sup>374</sup>, self-esteem 1847 increases perceived social support<sup>375</sup>, and exercise promotes cognitive abilities<sup>376</sup>. Furthermore, 1848 these resilience promoting factors might also reduce exposure to stressors. For example, for 1849 individuals from minoritized ethnic groups, the protective effect of living in neighborhoods 1850 wherein their ethnic identity is well-represented might reduce the degree of discrimination they 1851 experience in day-to-day life<sup>246</sup>. Finally, the access or ability conferred by resilience promoting 1852 resources might be compromised by the illness itself. For example, qualitative studies indicate 1853 that symptoms and the sedative effects of medication pose barriers to engaging in physical 1854 activity<sup>377</sup>. Similarly, stigma and structural discrimination together with psychosocial disability 1855 might limit employment opportunities and thereby reduce opportunities to access resilience 1856 promoting resources associated with wealth (such as access to green space, which is less 1857 available in low-income neighborhoods<sup>378</sup>), and to engage in social networks. 1858

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# 1865Table of Contents blurb

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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.