Coping Strategies In Individuals At Ultra-High Risk Of Psychosis: A Systematic Review

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Abstract

Aim: The impact of dysfunctional coping strategies during the prodromal phase of psychosis has recently been explored by several studies. What has yet to be clarified is whether maladaptive coping is evident in the prodromal phase and the impact that this might have on symptomatic and functional outcomes. The aim of this study was to review the findings on coping in individuals at ultra-high risk of psychosis (UHR) in relation to symptoms and level of functioning.

Methods: Original articles were identified by searching 7 databases using the terms “prodrom*”, “ultra high risk”, “clinical high risk”, “at risk mental state”, “coping style*”, “coping strategies”, “cope”, “coping”, “psychosis”. We included original articles that: (i) reported a measure of coping, (ii) evaluated UHR individuals.

Results: Nine original articles out of 335 that examined coping in individuals at high risk of psychosis were included. UHR subjects were more likely to use maladaptive coping strategies than healthy controls (HC) and were more likely to use emotion-focussed than task-oriented coping. Maladaptive coping was associated with higher levels of negative symptoms, whilst positive coping was associated with fewer negative symptoms. The coping style employed by UHR individuals was found to influence negatively their psychosocial functioning.

Conclusions: It is still unclear whether coping heightens or reduces the likelihood of transition to psychosis in relation to other factors, including environment. Longitudinal studies could clarify whether coping styles remain stable after the onset of psychosis or whether the emerging psychotic symptoms influence the coping strategies.

Keywords: coping strategies, prodromal, psychosis, ultra-high risk.
Introduction

Dysfunctional or maladaptive coping responses to symptoms and environmental stressors are considered an important factor in the development, maintenance and outcome of psychotic disorders (Kessler et al., 1985; Myin-Germeys et al., 2001; Taylor et al., 2007; Phillips et al., 2009). Several environmental stressors have been consistently associated with an increased risk of developing psychosis (Van Winkel et al., 2008) including urban living (Sundquist et al., 2004), migration (Cantor-Graae et al., 2005), discrimination (Morgan et al., 2010), childhood trauma (Read et al., 2005), and drug and alcohol misuse (Niemi-Pynttäri et al., 2013). According to the stress-vulnerability model (Nuechterlein et al., 1984; Walker et al., 1997), biological, cognitive and psychological characteristics of an individual might contribute to increase vulnerability to psychosis when interacting with environmental stressors.

Coping in the context of psychological stress is defined as “the cognitive and behavioural efforts made to master, tolerate, or reduce external and internal demands and conflicts among them.” (Folkman and Lazarus, 1980). Such cognitive processes and behaviours are employed by individuals to minimise distress. According to the model proposed by Lazarus and Folkman (1984), psychological stress is mediated by two components: i) appraisal, an individual’s evaluation of the demands of a situation, and ii) coping, the thoughts and actions employed by an individual to manage those demands. Whenever an individual’s appraisal of the demands of a situation exceeds their perceived available coping resources psychological distress is experienced (Lazarus and Folkman, 1984). Different coping styles in psychosis are known to affect several areas pertaining to symptoms, functioning and quality of life (Jalbrzikowski et al., 2014). More maladaptive types of coping strategies, such as self-blame and denial (Carver, 1997) have been linked to poorer symptomatic and functional outcomes in individuals that have experienced a first-episode psychosis (Phillips et al., 2009) as well as in patients with established schizophrenia (Yanos et al., 2007). For further readings and additional theories on coping, please refer to Zeidner et al., 1996.

In the population with established schizophrenia, coping styles are associated to symptom severity (Meyer, 2001), quality of life (Rudnick et al., 2009), distress associated with the illness (Cooke et al., 2007), cognitive ability (Lysaker et al., 2004) and social functioning (Boschi et al., 2000; Meyer 2001). Research so far suggests that maladaptive coping in people with established psychosis predicts greater distress and poorer symptomatic outcomes while more adaptive coping is associated with better symptomatic outcomes (Boschi et al.,
The impact of dysfunctional coping strategies during the early stages of psychosis has been explored by a number of studies (Phillips et al., 2009; Pruessner et al., 2011; Schmidt et al., 2014). In patients who have experienced a first-episode of psychosis, more adaptive coping styles such as problem-focused coping and seeking social support have been found to be associated with self-efficacy and better cognitive performance (Ventura et al., 2004), better psychosocial functioning (Boschi et al., 2000), less symptoms and improved quality of life (Thompson et al., 2003). In a systematic review on coping in patients with psychosis, Phillips and colleagues (2009) highlighted that no single coping strategy is universally effective and that situational context might influence both the choice of coping strategy used and its efficacy. Supporting this view, Kommescher and colleagues (2017) argued that the evidence suggests that a wide range of coping strategies are associated with better handling of the symptomatic and functioning burden.

Although a number of studies have highlighted the relationship between coping, symptoms and functioning in people that have experienced psychosis, what has yet to be clarified is whether maladaptive coping does influence symptom progression and functional outcome in people at ultra-high risk of developing psychosis.

Therefore, the aims of this systematic review were (i) to identify the most used coping strategies in UHR individuals and (ii) to describe which maladaptive coping affects symptom progression and functioning. The implications for any such findings might help to inform early interventions and potentially delay or prevent transition to psychosis.

**Methods**

**Inclusion and Exclusion criteria**

Original articles were included if (i) they reported a measure of coping; and (ii) if they assessed participants at ultra-high risk of developing psychosis. The status of ultra-high risk of psychosis had to be defined by internationally recognised criteria such as PACE criteria (Yung et al., 2007), SIPS/SOPS criteria (Miller et al., 2003) and basic symptoms (Schultze-Lutter et al., 2010a). The rationale for this was to capture the maximum number of studies covering the population of interest despite the heterogeneity of tools currently being used to define the high-risk status. In the present study we will refer to the clinical high risk population with “ultra-high risk” or “UHR”. Studies investigating coping in individuals at genetic high risk only and
individuals with a diagnosis of schizotypal personality disorder only were not included. Studies investigating individuals with a first episode or established psychosis were not included.

**Search Strategy**

Coping strategies in the UHR population were assessed by conducting a systematic review of published research evidence. The review adhered to published guidance for undertaking systematic reviews from PRISMA 2009 (Moher et al., 2009) and the Cochrane Handbook for systematic reviews (Higgins et al., 2013).

A search on 7 databases (PubMed, ETHOS, Kings Open Portal, EMBASE, MEDLINE, PsycINFO and CINHAL) was performed by two independent researchers (latest search was performed in July 2017) to identify studies investigating coping strategies in UHR individuals. The following search was performed: ((prodrom* OR ultra-high risk OR clinical high risk OR at risk mental state) AND (psychosis)) AND (coping style* OR coping strategies OR cope OR coping). The search strategy was broad and not limited to any particular type of study. Information on studies in progress, unpublished literature and grey literature was sought by searching a range of relevant databases including the ETHOS (http://ethos.bl.uk/) and Kings Open Portal (https://kclpure.kcl.ac.uk/portal/). The reference list section of all articles retrieved and identified as relevant were searched to identify additional articles. The process for selecting studies involved an initial screen of the titles removing any article that was not relevant such as those investigating a different clinical population. The next stage involved assessing the abstracts and checking whether the population met the high-risk for psychosis inclusion criteria. The final stage involved reviewing the original articles and rejecting those that did not provide a measure of coping. The data extracted from the articles included type of study, characteristics of the population and participants, the tools used to identify the ultra-high risk population, the tools used to measure coping and a brief description of the conclusions drawn from each paper focusing on symptoms and functional outcome.
Figure 1. Pubmed, ETHOS and King’s Open Portal Screening process (adapted from Moher et al., 2009)

- Records identified through database searching (n = 73)
- Records after duplicates removed (n=1)
- Records screened (n=74)
- Full-text articles assessed for eligibility (n=65)
- Studies included in qualitative synthesis (n=9)

- Records excluded (not original articles) (n=9)
- Full-text articles excluded (authors not found, articles on different populations, articles not addressing coping, articles without a measure of cooine) (n=56)
Results

Search Results and Screening process (Pubmed, ETHOS and King’s Open Portal)

The electronic search using Pubmed identified 69 citations. The electronic search using ETHOS identified an additional 6 citations. One duplicate was found and removed, this left 74 unique citations to be screened for inclusion (Figure 1). Titles and abstracts were screened to determine their relevance to the review. Nine articles were excluded because they were not original (i.e. reviews, meta-analysis). This resulted in 65 potential citations for which the full text was retrieved. Four unpublished doctoral theses from the ETHOS database were excluded as the authors could not be contacted. After checking whether the remaining articles met the inclusion criteria, 26 articles were excluded as they were based on populations different from the one under investigation. A further 25 articles were excluded as their content was not addressing coping strategies. One article was excluded as it did not provide any measure of coping. Nine original articles were retained for the purpose of this review. In addition, we performed additional searches using other databases (i.e. EMBASE, Medline, PsycINFO, CINAHL), finding 190 entries overall. After removing 11 duplicates, we screened the abstracts and then retrieved the full texts. We did not find any additional article that met our inclusion criteria (see supplementary material 1, PRISMA screening processes flowcharts). Nine original articles were included in this systematic review. The risk of bias was assessed for all included studies using with the Newcastle-Ottawa Scale (Wells et al., 2013), finding an overall low risk of bias (see supplementary material 2).

Characteristics of included studies

Table 1 summarises the original articles investigating coping strategies in UHR individuals. The number of UHR participants ranged from 21 to 143, for a total of 567 UHR participants. The mean age was 20.91 years (range = 11.61–35 years) and 248 (43.74%) were female. Of the 9 suitable articles, seven performed cross-sectional comparisons, two investigated longitudinal changes and one was a randomised controlled trial. Among the longitudinal studies, one study also performed a cross-sectional baseline comparison (Jalbrzikowski et al., 2014). In the other longitudinal study, Phillips and colleagues (2012) used the mean scores of the monthly (for the UHR group), or bi-monthly (for HC) assessment of coping.

Instruments used to identify UHR population

The following instruments were used to identify the UHR population in the included studies:
the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2002), the Structured Interview for Prodromal Syndromes (SIPS; McGlashan et al., 2010), the companion Scale of Prodromal Symptoms (SOPS; Miller et al., 2003) and the Basel Screening Instruments for Psychosis (BSIP; Riecher-Rössler et al., 2008), the Prodromal Questionnaire (PQ; Loewy et al., 2005), the Early Recognition Inventory and Interview for the Retrospective Assessment of the Onset of Schizophrenia (ERIraos; Häfner et al., 2011), the Interview for the Retrospective Assessment of the Onset and Course of Schizophrenia and other Psychoses (IRAOS; Hämpel et al., 1992) and the Structured Clinical Interview for DSM-IV disorders (SCID-I; First et al., 2002).

One study assessed participants based on the presence of basic symptoms (Schmidt et al., 2014) using the Schizophrenia Proneness Instrument - Adult version (SPI-A; Schultze-Lutter et al., 2007) and the Schizophrenia Proneness Instrument - Children version (SPI-CY; Schultze-Lutter et al., 2010b).

**Instruments used to measure coping**

The following instruments were used to measure coping in the UHR population: the Brief COPE (Carver, 1997), the Ways of Coping Scale (WOCS; Folkman and Lazarus, 1988), Korean version of Ways of Coping Questionnaire (K-WCQ; Kim et al., 1987), the adult-version of the Coping Inventory for Stressful Situations (CISS; Endler and Parker, 1990), the German Stress-Coping Questionnaires for adults (SVF-120; Janke et al., 1997) and for children/adolescents (SVF-KJ; Hampel et al., 2001) based on Lazarus and Folkman's (1984) conceptualization of stress appraisal processes.

The Brief COPE (Carver, 1997), WOCS (Folkman and Lazarus, 1988), K-WCQ (Kim et al., 1987), and the SVF-120 (Janke et al., 1997) all refer to the Lazarus and Folkman (1984) model of coping. In this model, two main categories of coping are described. The first is problem-focused coping whereby an individual relies on active ways to directly address the situation or problem causing their psychological stress. Problem-focused coping might include strategies such as enlisting social support or attempting to solve the problems contributing to the stressor. The second is emotion-focused coping whereby individuals try to change their appraisal of a demanding situation or reduce their negative emotional state rather than the situation itself. Examples of emotion-focused strategies might include distraction from the source of stress or using drugs and alcohol.

Two further models of coping underline the Brief COPE. Particularly, the two-category model of the Brief Cope (Meyer, 2001) outlines the types of adaptive and maladaptive
strategies. According to this model, maladaptive coping strategies include denial, substance abuse, behavioural disengagement, self-distraction and self-blame whilst adaptive coping strategies include use of emotional support, active coping, planning and acceptance. The other interpretative model of the Brief COPE is the three-category model (Cooper et al., 2006). This model splits coping into 3 categories: emotion-focused strategies, problem-focused and dysfunctional coping strategies. Emotion-focused strategies include use of emotional support and positive reframing; problem-focused strategies include active coping and planning; dysfunctional coping strategies include denial, substance abuse and self-blame. CISS (Endler and Parker, 1990) is a 48-item self-report inventory which relies on a three-factor model and divides coping in three styles: Task Oriented, Emotion Oriented, and Avoidance Oriented coping. The avoidance scale is in turn divided in two subscales, Distraction and Social Diversions. The authors stated that some of those styles were less-adaptive (i.e. emotion-oriented coping), being associated with neurotic personality traits (see the five-factor model of personality: McCrae and John, 1992) and with clinical depression (Flett et al., 1996). Other styles were considered adaptive (i.e., task-orientated coping) because of their negative association with psychological distress (Flett et al., 1996) and their positive association with social functioning (Jalbrzikowski et al., 2014).

Types of Coping Strategies Employed

Cross sectional comparisons

This section includes the studies that performed a baseline comparison between UHR and HC or first episode psychosis (FEP) groups. Among the seven studies considered, five included a HC group (Lee et al., 2011; Pruessner et al., 2011; Masillo et al., 2012; Kim et al., 2013; Jalbrzikowski et al., 2014) and four included a FEP comparison group (Lee et al., 2011; Pruessner et al., 2011; Schmidt et al., 2014; Kommescher et al., 2017). The samples of two of them (Lee et al., 2011; Kim et al., 2013) partially overlapped, as the subjects assessed in Lee et al., 2011 were fully included in Kim et al., 2013).

Compared to HC, UHR individuals were found to use more emotion-focused (Lee et al., 2011), maladaptive, negative, avoidant (Masillo et al., 2012) or lower active and lower problem-focused coping strategies (Kim et al., 2013). Avoidant coping strategies employed by UHR individuals included social withdrawal, habituation or adaptation to illness and self-medication or engagement with drugs and alcohol (Masillo et al., 2012). Jalbrzikowski and
colleagues (2014) found that UHR individuals were more likely to use maladaptive coping styles than HC. When adaptive coping was used, this was related to fewer negative symptoms and higher level of social functioning.

Compared to FEP patients, UHR individuals showed less active coping strategies (Pruessner et al., 2011). Conversely, Lee and colleagues (2011) reported that UHR and FEP showed a similar pattern in the use of coping strategies. Specifically, both groups relied more on tension reduction and less on problem focus strategies than controls. The UHR group, but not the FEP group, showed also more reliance in wishful thinking than HC. Schmidt and colleagues (2014) reported that compared to FEP, UHR individuals were less likely to use positive coping strategies such as distraction, positive self-instructions, situation control, social support and minimization. Compared to FEP, UHR also presented with higher scores on minimization and lower on situation control, and amongst the negative coping strategies they mainly used avoidance and rumination. Kommescher and colleagues (2017) reported that UHR individuals adopted more frequently negative coping styles (such as social withdrawal, escape tendencies, guilt defence, self-pity, resignation, continued mental preoccupation and self-accusation) than positive ones. On the contrary, FEP patients did not show a marked difference between negative and positive coping and would tend to choose stress control amongst other positive coping styles such as distraction or devaluation. Compared to UHR, FEP individuals appeared to balance more between emotion-oriented and task-oriented styles. Finally, UHR individuals were found to utilise devaluation (which includes guilt defence, trivialization and downplaying by comparison with others) as a cognitive coping strategy.

**Longitudinal comparisons**

The studies included in this section are those that performed a comparison at different time points between the coping strategies of different groups or within the same group. Two studies carried out such a comparison (Philips et al., 2012; Jalbrzikowski et al., 2014). Both had a follow-up period of 12 months and included a comparison with HC.

Philips and colleagues (2012) outlined that UHR individuals coped more poorly than HC, as they reported more to be more affected by stressful events during the whole follow-up period. Moreover, they were more likely to use emotion-focused than task-oriented coping, including distraction, and showed no differences with HC in the use of avoidance to cope with stressors. Jalbrzikowski and colleagues (2014) showed that maladaptive styles were more
likely to change over time, whilst adaptive coping styles scores were stable in UHR participants.

**Randomised controlled trial**

One RCT compared the effectiveness of two therapeutic interventions with UHR individuals (Kommescher et al., 2016). One group was randomised to integrated psychological intervention, which included cognitive behaviour therapy, and the other group was randomised to supportive counselling. Results showed that UHR individuals were more likely to enact negative coping strategies which in turn were associated with a lower perceived ability of handling symptoms and worst clinical outcome. On the other hand, stress control was the most common amongst the positive strategies. At 12 months follow up, results showed that the pre-treatment coping style significantly influenced the clinical outcome in both treatment groups.

**Coping strategies, Symptomatic and Functional Outcomes**

1. **Symptomatic outcome**

Six studies included a HC comparison group (Lee et al., 2011; Pruessner et al., 2011; Phillips et al., 2012; Masillo et al., 2012; Kim et al., 2013; Jalbrzikowski et al., 2014). Lee and colleagues (2011) observed that maladaptive coping patterns such as reliance or wishful thinking, and less reliance on problem-focused coping, were associated with higher levels of negative symptoms, depression and anxiety. Accordingly, lower active coping was associated with higher negative symptoms (Pruessner et al., 2011). In Phillips and colleagues (2012), the UHR group, despite presenting with a good level of social abilities, experienced difficulties and distress due to significant levels of psychiatric symptomatology, mainly negative symptoms such as social withdrawal. Masillo and colleagues (2012) found a significant correlation between interpersonal sensitivity, avoidant coping strategies (such as alcohol and drugs abuse, social withdrawal), depression and anxiety in UHR. Furthermore, compared to HC, UHR were more likely to present with greater level of negative symptoms (Kim et al., 2013). Likewise, adaptive coping in UHR individuals was associated with fewer negative symptoms (Jalbrzikowski et al., 2014).

Six studies examined the relationships between coping strategies and depression (Lee et al., 2011; Pruessner et al., 2011; Masillo et al., 2012; Kim et al., 2013; Kommescher et al., 2016;
Kommescher et al. 2017). Overall, people at UHR for psychosis showed higher levels of depression than other clinical groups or HC. Lee and colleagues (2011) found a strong association between problem-focused coping and wishful thinking and depression, while Pruessner and colleagues (2011) reported that higher stress levels and lower self-esteem were associated to higher depression scores in UHR than FEP patients. Two studies focused on interpersonal sensitivity, outlining that in both UHR and HC it was related to depression (Masillo et al. 2012; Kim et al. 2013). More recently, Kommescher and colleagues (2016, 2017) found that coping strategies such as self-affirmation, distraction and continual mental preoccupation were associated with lower depression scores.

One study examined the relationship between coping strategies and basic symptoms. Lower guilt defences and engaging in more mental preoccupation at baseline was associated with improvements in basic symptoms at follow-up when integrated psychological interventions were given (Kommescher et al., 2017).

Three studies examined the relationship between coping and positive symptoms (Masillo et al., 2012; Jalbrzikowski et al., 2014; Kommescher et al., 2017). Jalbrzikowski and colleagues (2014) underlined the significant relationship between maladaptive coping strategies and higher levels of positive symptoms. Masillo and colleagues (2012) found that positive symptoms were associated with separation anxiety, stronger sensitivity to interpersonal relationships and avoidant coping. The third study found a correlation between positive symptoms and a low cognitive engagement in UHR compared to patients with a FEP or with multiple episode of psychosis (Kommescher et al., 2017).

2. Functional outcomes

Functional outcomes were explored both qualitatively and quantitatively in three of the included studies (Pruessner et al., 2011; Kim et al., 2013; Jalbrzikowski et al., 2014). Pruessner and colleagues (2011) hypothesized an association between active coping and functioning, however, no significant association was found. Nevertheless, adaptive coping style (such as use of emotional support, positive reframing, acceptance, active coping and humour) and resilience were found to be additional independent factors associated with overall psychosocial functioning (Kim et al., 2013). Moreover, UHR individuals employing more adaptive coping strategies tended to have better interpersonal relationships (Kim et al., 2013). Higher reported adaptive coping scores were also associated with a high
level of social functioning (Jalbrzikowski et al., 2014).

Discussion

A person’s experience of stress alongside their vulnerability and ability to cope with such stressors it is suggested to play an important role in the development of psychotic disorders (Walker et al., 1997). Although maladaptive coping has been consistently reported in individuals that have experienced psychosis (Phillips et al., 2009) only recently research focus has shifted towards investigating coping in the population at high risk of developing psychosis.

Results from this review showed that UHR individuals were more likely to use maladaptive, negative, avoidant and fewer active coping strategies than HC (Jalbrzikowski et al., 2014; Kim et al., 2013; Masillo et al., 2012; Lee et al., 2011; Pruessner et al., 2011; Schmidt et al., 2014). UHR were also more likely to use emotion-focussed than task-oriented coping (Phillips et al., 2012), including distraction (Kommescher et al., 2017).

Avoidant coping as main coping strategy was found in three studies (Lee et al., 2011; Phillips et al., 2012; Masillo et al., 2012). Lee and colleagues (2011) argued that those who rely on maladaptive coping strategies might be more depressed and anxious, which in turn might lead to further social withdrawal. In contrast, a longitudinal study (Phillips et al., 2012) observed that there was no overall difference in the use of avoidance as a way of coping with stressors, nor in the use of distraction as a specific avoidance technique in UHR individuals compared to HC. However, compared to controls, the UHR group was less likely to use a more adaptive form of avoidance such as social diversion (i.e. engaging with others) to distract from stressors. This suggests that despite no significant difference was observed in the use of avoidance, UHR individuals might have a smaller range of coping strategies compared to HC. Masillo and colleagues (2012) reported that UHR individuals who scored high in interpersonal sensitivity also scored high in avoidant coping scores, and concluded that this coping style, leading to social withdrawal, might contribute to long-term deficits in social functioning.

Avoidant coping could be a feature of UHR status, and as such could contribute to exacerbate symptoms of paranoia or alternatively it could be an effect stemming from the negative symptoms, suspiciousness and paranoia.

The overall finding that UHR individuals are more likely to use emotion-focussed strategies rather than task-oriented strategies suggests that they might have difficulties to cope directly with stressors and that they show a preference in dealing with their emotional distress. This is in line with what was observed in individuals with established psychosis who were also more
likely to use emotion-focussed coping (Van Den Bosch et al., 1992). According to the stress and coping model of Folkman and Lazarus (1980), if an individual believes that a situation can be changed they are more likely to utilise task-oriented coping strategies and, conversely, if they do not believe that a situation can be changed they are more likely to employ emotion-oriented strategies. This is supported by the idea that the locus of control (Rotter, 1966) influences which type of coping strategy will be used. Around the time in which UHR individuals present to the clinical services they are usually reporting attenuated positive psychotic symptoms and a decline in social and occupational functioning. The symptoms burden and the functional impairment are likely to contribute in reducing the psychological resources available to cope directly with environmental stressors.

Even though UHR individuals seem to predominantly employ maladaptive coping strategies, they also use some forms of adaptive coping. Adaptive coping skills, such as use of emotional support and positive reframing (Meyer, 2001) were associated with less severe clinical symptomology and better social functioning overtime (Jalbrzikowski et al., 2014). Older age in both HC and UHR individuals was associated with higher levels of adaptive coping (Jalbrzikowski et al., 2014). Adaptive coping could be implemented by individuals that are less unwell at the time in which they present to the clinical service.

Clinical Implications

The investigation of coping strategies in UHR individuals is of great relevance for the development of effective early interventions. The effectiveness of coping strategies can be enhanced in a clinical setting and this has the potential to improve the course of illness. The evidence that UHR individuals have higher stress levels compared to HC and to FEP patients (Pruessner et al., 2011) and that levels of stress are a predictor of the severity of positive and negative symptoms further supports the provision of interventions that address the management of stress levels. Interventions that teach adaptive coping styles in UHR individuals might be an important target to reduce stress and potentially prevent transition to psychosis. Coping style might correspond to one’s current functioning level or severity of symptoms and might represent an important factor in the process of mediating stress-vulnerability in the therapeutic setting (Jalbrzikowski et al., 2014). More research needs to be carried out to clarify the link between pre-treatment coping and clinical outcomes in UHR individuals.
Those identified as ultra-high risk might have different clinical outcomes, including depression (Rutigliano et al., 2016). Since dysfunctional coping has been associated with depression, interventions that challenge core beliefs and coping strategies in this area might be more appropriate for this population (Schmidt et al., 2014). Additionally, since active coping strategies are associated with increased resilience to negative events, interventions seeking to enhance these might help to reduce distress and potentially prevent transition to psychosis (Schmidt et al., 2014).

Limitations and future directions
This study has five main limitations. Firstly, the included studies had relatively small sample therefore coping in relation to transition to psychosis could not be examined. In addition, the included longitudinal studies reported high drop-out rates and longitudinal changes in the HC comparison group could not be assessed (Jalbrzikowski et al., 2014). Secondly, three studies did not include a HC group (Schmidt et al., 2014; Kommescher et al., 2016; Kommescher et al., 2017). Without exploring coping strategies in a group of matched HC it is not possible to disentangle whether the implemented coping strategies are the expression of a way of coping with the attenuated psychotic symptoms, as opposed to a general way of coping with life stressors in relatively young adults. Thirdly, only two studies had a longitudinal component (Phillips et al., 2012; Jalbrzikowski et al., 2014). One of the key considerations in exploring coping strategies in the UHR population and their associations with symptomatic and functional outcomes is the observation time and the potential changes within it. For example, some studies have shown that coping strategies in FEP differ to those with chronic schizophrenia and UHR individuals (Lewin et al., 2001; Schmidt et al., 2014). It is possible therefore that coping styles might be both dynamic and changeable in function of the symptoms, of the functioning level as well as of individual’s experiences that might shape the selection of coping strategies. Fourthly, there are several theoretical and practical issues that emerge when assessing coping. Coping strategies themselves can change due to interactions between a person and the environment, so they do not represent a single concept but rather an umbrella term that includes interactions between strategies, cognitions and behaviours. Coping can be observed directly or through self-report and can include internal thoughts and external actions (Folkman et al., 2004). A critical survey of measurements of coping (Schwarzer et al., 1996) argued that disentangling coping from coping resources cannot always be possible at an
individual level. For example, an individual’s own hardiness, self-efficacy and social support might hinder whether a behavioural response is due to coping resources, personality trait, cognitive appraisal or a combination of factors. In addition, coping strategies are unlikely to be static and might change from one stressful situation to the next. It is also important to note that the coping strategy employed might be adaptive or maladaptive depending on the situation. For example, seeking social support might be an adaptive strategy when in the context of a person sharing their concerns with someone, however, seeking social support in the form of drug taking or alcohol could be viewed as maladaptive. The fact that an assessment of the number and severity of stressful events in participants’ lives was not included in the available studies means that no exploration could be made into how such events might influence the coping strategy employed or the degree in which an individual is able to cope. Finally, most instruments used to assess coping are self-report scales, which carry potential issues around reliability. Self-report measures are associated with recall and response biases. Even when participants have answered the questions honestly, their levels of introspective ability are likely to be subject to individual differences in accuracy of how they view themselves compared with how others see them. Response biases might also be found where an individual tends to respond either conservatively or otherwise (Austin et al., 1998). To address some of these pitfalls in the existing literature, future studies should investigate the use of coping strategies using more ecologically valid methods, for examples using experiencing sampling method, which would allow collecting multiple measurements of coping overtime as well of environmental information. Using such methodology would also allow to overcome the problem of response and recall biases associated with self-report measures of coping.

Conclusions

UHR individuals use more maladaptive coping strategies than healthy counterparts and they seem to use more maladaptive coping compared to FEP. It is still unclear whether these influence the likelihood of transition to psychosis in relation to factors such as severity of symptomatology, personality traits, genetic vulnerability and environment. Maladaptive coping has a negative effect also on psychosocial functioning. The research available suggests that coping styles are part of a dynamic response to mitigate stress-vulnerability and are not necessarily stable over time nor static for every type of stressful event. Future studies should focus on disentangling such a composite interaction, with more ecological tools, which could
measure people’s coping style in their personal environment.

References


Table 1 Summary of included studies with coping strategies employed, clinical and functional outcome

<table>
<thead>
<tr>
<th>Authors</th>
<th>Participant</th>
<th>Age of UHR participants (years)</th>
<th>Gender of UHR participants (years)</th>
<th>Method of identifying at risk group</th>
<th>Method of assessment of coping and study design</th>
<th>Coping strategies</th>
<th>Clinical outcome</th>
<th>Functional outcome</th>
</tr>
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<tbody>
<tr>
<td>Jalbrzikowski et al., 2014</td>
<td>UHR (n=88), HC (n=53)</td>
<td>12-35 (mean 17.9)</td>
<td>M 58, F 30</td>
<td>SIPS</td>
<td>Brief COPE. Longitudinal study over 12 months period, performing both cross-sectional and longitudinal comparisons</td>
<td>UHR individuals used less adaptive coping strategies relative to HC. Adaptive ones were more stable over time.</td>
<td>Adaptive coping was associated with fewer negative symptoms. No relationship between maladaptive coping and clinical variables.</td>
<td>In UHR, higher adaptive coping was associated with a higher level of social functioning. No relationship was found between maladaptive coping and social variables.</td>
</tr>
<tr>
<td>Kim et al., 2013</td>
<td>UHR (n=60), HC (n=47)</td>
<td>15-35 (mean 19.7)</td>
<td>M 35, F 25</td>
<td>SIPS</td>
<td>K-WCQ, Cross-sectional study</td>
<td>Maladaptive coping strategies not specified.</td>
<td>Negative symptoms were higher in UHR compared with HC and were lower in those UHR with higher interpersonal functioning.</td>
<td>Adaptive coping and resilience was found to be an additional independent factor associated with overall psychosocial functioning.</td>
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<tr>
<td>Kommescher et al., 2016</td>
<td>UHR (n=91)</td>
<td>17-35 (mean 25.5)</td>
<td>M 57, F 34</td>
<td>ERsRaos, IRAOS</td>
<td>SVF-120. RCT over 12 months</td>
<td>All participants at baseline employed more negative than positive coping strategies.</td>
<td>Basic symptoms score: less guilt defence and more continual mental preoccupation at baseline was associated with improvements to basic symptoms at follow-up in the integrated psychological intervention</td>
<td>For global functioning scores, coping strategies were not able to predict changes over 12 months of interventions.</td>
</tr>
<tr>
<td>Kommescher et al., 2017</td>
<td>UHR (n=39), FEP (n=19), MEP (n=52)</td>
<td>17-35 (mean 24.74)</td>
<td>M 27, F 12</td>
<td>ERIraos</td>
<td>SVF-120. Cross-sectional study</td>
<td>UHR put in act more negative than positive coping strategies, followed by patients with MEP. FEP showed a more balanced pattern between negative and positive coping styles.</td>
<td>In UHR there was no significant correlations between coping strategies and psychopathology (including positive, negative symptoms and depression), unlike the FEP and MEP groups.</td>
<td>Did not look at functional outcomes.</td>
</tr>
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</tr>
<tr>
<td>Lee et al., 2011</td>
<td>UHR (n=33), FEP (n=22), HC (n=33)</td>
<td>15-35 (mean 19.3)</td>
<td>M 16, F 17</td>
<td>SIPS</td>
<td>K-WCQ. Cross-sectional study</td>
<td>Passive maladaptive coping patterns, greater reliance on tension-reduction and Maladaptive coping patterns and less reliance on problem-focussed coping were associated with No functioning scores were measured, however social avoidance was noted as a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Group</td>
<td>Sample Size</td>
<td>Gender</td>
<td>Measure</td>
<td>Study Type</td>
<td>Findings</td>
<td></td>
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</tr>
<tr>
<td>Masillo et al., 2012</td>
<td>UHR (n=62), HC (n=39)</td>
<td>14.35 (mean 22.63)</td>
<td>M 37, F 25</td>
<td>CAARMS</td>
<td>WCQ, Cross-sectional study</td>
<td>Lower reliance on problem-focused coping in UHR group. Higher levels of negative symptoms, depression and anxiety. Maladaptive coping strategies employed by some subjects.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phillips et al., 2012</td>
<td>UHR (n=143), HC (n=32)</td>
<td>14.30 (mean 18.69)</td>
<td>M 66, F 77</td>
<td>CAARMS</td>
<td>CISS, Longitudinal study over 12 month period</td>
<td>The UHR group were less likely to utilise task-oriented coping strategies and more likely to use emotion focussed strategies. They were significantly less likely to use social diversion (engaging with others) to distract themselves from stressors.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>UHR Group</td>
<td>FEP Group</td>
<td>HC Group</td>
<td>Mean Age</td>
<td>Gender</td>
<td>CAARMS</td>
<td>COPQ</td>
<td>SVF</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Pruessner et al., 2011</td>
<td>UHR (n=30), FEP (n=32), HC (n=30)</td>
<td>Mean 20.33</td>
<td>M 16, F 14</td>
<td>CAARMS</td>
<td>Brief COPE. Cross-sectional study</td>
<td>Lower active coping was found in the UHR group compared to HC.</td>
<td>Lower active coping was associated with higher negative symptoms in UHR. Stress levels independently predicted positive and depressive symptoms.</td>
<td>No correlation was found between active coping and functioning, although UHR tend to have higher ratings because of continued employment or enrolment in education and less severe symptoms.</td>
</tr>
<tr>
<td>Schmidt et al., 2014</td>
<td>UHR (n=21), FEP (n=22)</td>
<td>11.61–27.49 (mean 19.44)</td>
<td>M 7, F 14</td>
<td>SIPS and/or SPI-A or SPI-CY</td>
<td>SVF-120 and SVF-KJ. Cross-sectional study</td>
<td>UHR participants used more negative coping strategies than FEP.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Key:* CAARMS = Comprehensive Assessment for At Risk Mental States; CISS = Coping Inventory for Stressful Situations, Adult version; CHR = Clinical High Risk; ERIraos = Early Recognition Inventory and Interview for the Retrospective Assessment of the Onset of Schizophrenia; FEP = First Episode Psychosis; IRAOS = Interview for the Retrospective Assessment of the Onset and Course of Schizophrenia and other Psychoses; K-WCQ = Korean version of Ways of Coping Questionnaire; MEP = Multiple Episodes of Psychosis; SIPS = Structured Interview for Prodromal Symptoms; SPI-A = Schizophrenia Proneness Instrument, Adult; SPI-CY = Schizophrenia Proneness Instrument, Child version; SVF-120 = Stress-Coping Questionnaire, adult version; SVF-KJ = Stress-Coping Questionnaire, child version; UHR = Ultra-High Risk; WCQ = Ways of Coping Questionnaire.
Supplementary Material 1: Screening Process

EMBASE Screening process (adapted from Moher et al., 2009)

Records identified through database searching (n = 100)

Records after duplicates removed (n=41)

Records screened (n=59)

Full-text articles assessed for eligibility (n=43)

Studies included in qualitative synthesis (n=0)

Records excluded (not original articles, not articles but posters) (n=16)

Full-text articles excluded (articles on different populations, articles not addressing coping, articles without a measure of coping) (n=43)
MEDLINE Screening process (adapted from Moher et al., 2009)

Records identified through database searching (n=44) → Records after duplicates removed (n=37) → Records screened (n=8) → Full-text articles assessed for eligibility (n=2) → Studies included in qualitative synthesis (n=0) → Records excluded (not original articles) (n=6) → Full-text articles excluded (articles on different populations, articles not addressing coping) (n=2)
PsycINFO Screening process (adapted from Moher et al., 2009)

1. Records identified through database searching (n=40)
2. Records after duplicates removed (n=26)
3. Records screened (n=14)
   - Records excluded (not original articles, not an article but abstracts from a Congress) (n=2)
4. Full-text articles assessed for eligibility (n=12)
   - Full-text articles excluded (articles on different populations, articles not addressing coping) (n=12)
5. Studies included in qualitative synthesis (n=0)
CINAHL Screening process (adapted from Moher et al., 2009)

- Records identified through database searching (n=6)
- Records after duplicates removed (n=6)
- Studies included in qualitative synthesis (n=0)
**Supplementary Material 2 – Assessment of Risk of Bias**

The risk of bias assessment was performed using the Newcastle - Ottawa Quality Assessment Scale (Wells et al., 2013) for Non-Randomised Studies (cohort studies and case-control studies), and the Risk of Bias Assessment Tool from Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2013) for one Randomised Clinical Trial.

1. **COHORT STUDIES**

   **Jalbrizowski et al., 2014**

**Selection**

1) Representativeness of the exposed cohort  
a) somewhat representative of the average CHR in the community

2) Selection of the non exposed cohort  
a) drawn from the same community as the exposed cohort

3) Ascertainment of exposure  
b) structured interview

4) Demonstration that outcome of interest was not present at start of study  
a) yes

**Comparability**

1) Comparability of cohorts on the basis of the design or analysis  
a) study controls matched for age  
b) study controls matched for IQ

**Outcome**

1) Assessment of outcome  
c) written self report

2) Was follow-up long enough for outcomes to occur  
a) yes (12 months)

3) Adequacy of follow up of cohorts  
c) follow up rate < 50% and no description of those lost provided
Selection

1) Representativeness of the exposed cohort
   b) somewhat representative of the average UHR in the community

2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort

3) Ascertainment of exposure
   b) structured interview

4) Demonstration that outcome of interest was not present at start of study
   a) yes

Comparability

1) Comparability of cohorts on the basis of the design or analysis
   a) study controls matched for age
   b) study controls matched for education

Outcome

1) Assessment of outcome
   c) written self report

2) Was follow-up long enough for outcomes to occur
   a) yes (12 months)

3) Adequacy of follow-up of cohorts
   b) subjects lost to follow up unlikely to introduce bias - small number lost (> 50 % followed up), and a description of those lost was provided
2. **CASE CONTROL STUDIES**

Kim et al., 2013

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

**Selection**

1) Is the case definition adequate?
   a) yes, with independent validation

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases

3) Selection of Controls
   a) community controls

4) Definition of Controls
   a) no history of disease (endpoint)

**Comparability**

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls matched for age
   b) study controls matched for gender

**Exposure**

1) Ascertainment of exposure
   d) written self report

2) Same method of ascertainment for cases and controls
   a) yes

3) Non-Response rate
   a) same rate for both groups
Kommescher et al., 2017

Selection

1) Is the case definition adequate?
   a) yes, with independent validation

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases

3) Selection of Controls
   b) hospital controls

4) Definition of Controls
   b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for education

Exposure

1) Ascertainment of exposure
   d) written self report

2) Same method of ascertainment for cases and controls
   a) yes

3) Non-Response rate
   a) same rate for both groups
Selection

1) Is the case definition adequate?
   a) yes, with independent validation

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases

3) Selection of Controls
   a) community controls

4) Definition of Controls
   a) no history of disease (endpoint)

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls matched for education

Exposure

1) Ascertainment of exposure
   d) written self report

2) Same method of ascertainment for cases and controls
   a) yes

3) Non-Response rate
   a) same rate for both groups
Selection

1) Is the case definition adequate?
   a) yes, with independent validation

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases

3) Selection of Controls
   a) community controls

4) Definition of Controls
   a) no history of disease (endpoint)

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls matched for age
   b) study controls matched for ethnicity

Exposure

1) Ascertainment of exposure
   d) written self report

2) Same method of ascertainment for cases and controls
   a) yes

3) Non-Response rate
   a) same rate for both groups
Selection

1) Is the case definition adequate?
   a) yes, with independent validation

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases

3) Selection of Controls
   c) no description

4) Definition of Controls
   a) no history of disease (endpoint)

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls matched for gender

Exposure

1) Ascertainment of exposure
   d) written self report

2) Same method of ascertainment for cases and controls
   a) yes

3) Non-Response rate
   a) same rate for both groups
Schmidt et al., 2014

Selection

1) Is the case definition adequate?
   a) yes, with independent validation

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases

3) Selection of Controls
   b) hospital controls

4) Definition of Controls
   a) no history of disease (endpoint)

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls matched for age

Exposure

1) Ascertainment of exposure
   d) written self report

2) Same method of ascertainment for cases and controls
   a) yes

3) Non-Response rate
   c) rate different and no designation
### Risk of Bias Table
from Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2013)

**Kommescher et al., 2016**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>YES</td>
<td>Quote: “This study was a prospective, randomized trial with two parallel groups, which were assigned to alternative outpatient interventions: either IPI, including CBT, or SC.”</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>YES</td>
<td>Quote: “Randomization was accomplished by using computer-generated block randomization.”</td>
</tr>
<tr>
<td>Blinding? (Post-therapy psychopathological changes)</td>
<td>NO</td>
<td>Impossible, as the interventions were psychotherapies.</td>
</tr>
<tr>
<td>Incomplete outcome data addressed? (Outcome post-treatment)</td>
<td>YES</td>
<td>Quote: “128 participants were randomized in the original study, as 22 refused research participation, 15 refused treatment, 2 were lost during assessment and 1 person developed psychosis during assessment.”</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>YES</td>
<td>Every assessment has been reported.</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>NO</td>
<td>Probably the sample is too small. There is no non-psychotic control group. There is no no-treatment control group.</td>
</tr>
</tbody>
</table>
References


stress and coping between young people at risk of psychosis and a non-clinical cohort. 
Behavioural and Cognitive Psychotherapy, 40(01), 69-88.

factors in individuals at ultra-high risk for psychosis, first episode psychosis and healthy 

Differences in coping, self-efficacy, and external control beliefs between patients at-risk for 
psychosis and patients with first-episode psychosis. Psychiatry Research, 219(1), 95–102.

Wells, G., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M. & Tugwell, P. The 
Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-
# PRISMA 2009 Checklist

<table>
<thead>
<tr>
<th>Section/topic</th>
<th>#</th>
<th>Checklist item</th>
<th>Reported on page #</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TITLE</strong></td>
<td></td>
<td><strong>#</strong></td>
<td><strong>Checklist item</strong></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
<td>1</td>
</tr>
<tr>
<td><strong>ABSTRACT</strong></td>
<td></td>
<td><strong>#</strong></td>
<td><strong>Checklist item</strong></td>
</tr>
<tr>
<td>Structured summary</td>
<td>2</td>
<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
<td>1</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td></td>
<td><strong>#</strong></td>
<td><strong>Checklist item</strong></td>
</tr>
<tr>
<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>4</td>
</tr>
<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td>4-5</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td></td>
<td><strong>#</strong></td>
<td><strong>Checklist item</strong></td>
</tr>
<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
<td>/</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.</td>
<td>4</td>
</tr>
<tr>
<td>Information sources</td>
<td>7</td>
<td>Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.</td>
<td>5</td>
</tr>
<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td>5</td>
</tr>
<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td>5</td>
</tr>
<tr>
<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td>5</td>
</tr>
<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td>5</td>
</tr>
<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td>6</td>
</tr>
<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>/</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I², for each meta-analysis).</td>
<td>/</td>
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</tbody>
</table>
## PRISMA 2009 Checklist

<table>
<thead>
<tr>
<th>Section/topic</th>
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<tbody>
<tr>
<td>Risk of bias across studies</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td>6</td>
</tr>
<tr>
<td>Additional analyses</td>
<td>16</td>
<td>Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.</td>
<td>/</td>
</tr>
<tr>
<td><strong>RESULTS</strong></td>
<td></td>
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</tr>
<tr>
<td>Study selection</td>
<td>17</td>
<td>Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.</td>
<td>6</td>
</tr>
<tr>
<td>Study characteristics</td>
<td>18</td>
<td>For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.</td>
<td>Table 1</td>
</tr>
<tr>
<td>Risk of bias within studies</td>
<td>19</td>
<td>Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).</td>
<td>Supplementary material 2</td>
</tr>
<tr>
<td>Results of individual studies</td>
<td>20</td>
<td>For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.</td>
<td>/</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>21</td>
<td>Present results of each meta-analysis done, including confidence intervals and measures of consistency.</td>
<td>/</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>22</td>
<td>Present results of any assessment of risk of bias across studies (see Item 15).</td>
<td>/</td>
</tr>
<tr>
<td>Additional analysis</td>
<td>23</td>
<td>Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).</td>
<td>/</td>
</tr>
<tr>
<td><strong>DISCUSSION</strong></td>
<td></td>
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</tr>
<tr>
<td>Summary of evidence</td>
<td>24</td>
<td>Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).</td>
<td>8-11</td>
</tr>
<tr>
<td>Limitations</td>
<td>25</td>
<td>Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).</td>
<td>14-15</td>
</tr>
<tr>
<td>Conclusions</td>
<td>26</td>
<td>Provide a general interpretation of the results in the context of other evidence, and implications for future research.</td>
<td>15</td>
</tr>
<tr>
<td><strong>FUNDING</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Funding</td>
<td>27</td>
<td>Describe sources of funding for the systematic review and other support (e.g., supply of data), role of funders for the systematic review.</td>
<td>/</td>
</tr>
</tbody>
</table>


For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org).