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## Psychosis-risk screening in different populations using the Prodromal Questionnaire - a systematic review

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### Abstract

**Aim**—Diagnosing individuals at Ultra High Risk for psychosis (UHR) can improve early access to treatment, and a two-stage model utilizing self-report screening followed by clinical interview can be accurate and efficient. However, it is currently unclear which screening cutoffs to adopt with different populations.

**Methods**—A systematic review of diagnostic accuracy studies evaluating the Prodromal Questionnaire (PQ) as a preliminary screener for UHR and psychosis was conducted to examine screening effectiveness in different contexts. MedLine, PsycInfo, SCOPUS, and ProQuest Dissertations and Abstracts databases were electronically searched, along with a review screen and citation search of key papers. Findings were summarized in a narrative synthesis.

**Results**—In total, 14 diagnostic accuracy studies and 45 studies using the PQ as a screening tool for UHR and psychosis were included. In all settings, the three different versions of the PQ were all found to accurately identify UHR and full psychosis. Higher cutoff points were required in non-help seeking samples, relative to general help-seeking populations, which in turn were higher than those needed in samples highly enriched with UHR participants.

**Conclusion**—The findings support the use of the PQ as a preliminary screening tool for UHR in different settings, however higher thresholds in lower UHR-prevalence populations are necessary to minimize false positives. Including the distress criteria, rather than just number of symptoms, may improve screening effectiveness. Different thresholds may be appropriate in different contexts, dependent upon the importance of sensitivity versus specificity. Protocol registration: CRD42016033004.

### Keywords

attenuated symptoms; PQ; schizophrenia; screening; ultra-high risk

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## INTRODUCTION

The Ultra-High Risk (UHR) syndrome is a state when sub-threshold psychotic experiences emerge, during which time the risk of developing psychosis is far higher than in the general population (Fusar-Poli et al., 2013). While specialist treatment for UHR can reduce the rate of transition to psychosis (Fusar-Poli et al., 2012), identifying individuals with UHR remains a significant challenge. Structured interviews such as the Structured Interview for Prodromal States (SIPS; Miller et al., 2003) can reliably diagnose UHR syndromes, however they require extensive training to administer and can take hours to complete. As a result, access to assessments are often limited to specialist early intervention clinic referrals (Kline and Schiffman, 2014). This can create a barrier to accurate identification, resulting in a significant proportion of people with UHR being undetected (Ising et al., 2012). In order to improve the efficiency of UHR identification, preliminary screening tools have been developed such the Prodromal Questionnaire (PQ; Loewy et al., 2005), the PRIME screen (Miller et al., 2004) and the Youth Psychosis at Risk Questionnaire (YPARQ-B; Ord et al., 2004). While these self-report scales cannot reliably diagnose UHR, or differentiate between people suffering UHR or psychosis, the evidence suggests they are sufficiently sensitive and specific to identify the majority of those that merit a more comprehensive evaluation for UHR or psychosis (Loewy et al., 2011; Kline and Schiffman, 2014). The advantages of adopting such tools were outlined by Rietdijk and colleagues, who found that using the PQ in secondary mental healthcare services resulted in a three-fold increase in detection of UHR, relative to standard referral methods (Rietdijk et al., 2012).

While the PQ (Loewy et al., 2005), PRIME (Miller et al., 2004) and YPARQ-B (Ord et al., 2004) have all been found to be valid assessment tools for UHR (Kline et al., 2012), in a recent review the PQ has been found to be the most commonly used instrument in the literature (Kline and Schiffman, 2014), and so will be the focus of this investigation. The evidence suggests that while the PQ is successful at identifying UHR individuals in various settings (i.e. Chen et al., 2014; Ising et al., 2012), there is no consensus on what the appropriate cutoff scores should be for screening in these different contexts. It is unlikely that a “one-size fits all” approach would be appropriate due to issues relating to spectrum bias, resulting from differences in the case-mix of participants between different settings (Willis, 2008). Determining appropriate cutoff points is complicated further by the existence of three different iterations of the PQ scale; the PQ-92 (Loewy et al., 2005), the PQ-16 (Ising et al., 2012), and the PQ-B (Loewy et al., 2011), of which each can be scored differently.

In this study, a systematic review of all diagnostic accuracy studies that assess the effectiveness of screening for UHR and psychosis with the PQ was completed, with the aim of producing guidelines specifying what cutoff points should be adopted in different populations. In the second part of the study, a systematic review of studies using the PQ as a screening tool without formal evaluation against gold-standard interview was completed in order to assess the congruency between the research recommendations and current practice.

## METHODS

### Protocol registration

The study protocol is available on the PROSPERO database (ID: CRD42016033004).

### Search strategy

An electronic search of SCOPUS, PsycInfo, PubMed, and ProQuest Dissertation and Abstracts databases was conducted on the 3<sup>rd</sup> of January 2017, containing two parameters. The first included terms defining the UHR state, using “prodrome”, “prodromal”, “clinical high risk”, “ultra high risk” “attenuated psychotic”, “attenuated psychosis”, and “attenuated positive”. The second parameter related to the prodromal questionnaire, including “PQ”, “PQ-92”, “PQ-16”, and “PQ-B”. An additional single search term of “prodromal questionnaire” was also included, which resulted in the article being identified regardless of the previous search. The search was dated to 1<sup>st</sup> January 2005 when the original PQ was first published (Loewy et al., 2005). A screen of all studies which referenced one of the original papers outlining the three different versions of the PQ was completed (Loewy et al., 2005; Loewy et al., 2011; Ising et al., 2012), identified using Google Scholar. Finally, the reference list of all systematic reviews related specifically to UHR screening tools were hand-searched.

During extraction, details regarding participant demographics, study methodology, screening cutoffs, and diagnostic accuracy statistics were recorded on a piloted extraction sheet.

Corresponding authors were contacted for more information where necessary. Extraction was completed independently by two researchers (MS and JDA), both completing 100% of the sample. A third researcher (RLL) was assigned to adjudicate in cases of disagreement.

### Eligibility criteria

In the initial screening case reports, qualitative studies, non-human studies, and those not using the PQ were excluded. In the full-manuscript screening phase, studies where the PQ was not used to screen for UHR or where cutoffs were not reported were excluded. Of this sample, studies which compared the diagnostic accuracy of the PQ to either the SIPS (Miller et al., 2003) or the Comprehensive Assessment of the At-Risk Mental States (CAARMS; Yung et al., 2005) were then selected for the diagnostic accuracy review. Given the PQ is not designed to make a distinction between UHR and full psychosis (see Loewy et al., 2005), but rather to determine whether individuals are experiencing at least attenuated psychotic symptoms to a level where a more thorough evaluation is necessary, participants diagnosed as experiencing full psychosis by either the CAARMS or the SIPS were included in the UHR positive category. In cases where the same diagnostic accuracy data was presented in different articles only the most relevant was retained, with any missing data filled in from the excluded studies. In order to include as broad a pool of studies as possible, grey literature and studies published in any language were considered eligible.

### Assessment tools

The original PQ (Loewy et al., 2005) comprises of 92 yes/no items, including 45 positive, 19 negative, 13 disorganized, and 15 general symptom items. Screening can be completed using

either all 92 items, or the positive symptom subscale alone. In a later version (Loewy et al., 2007) the questionnaire was extended to assess whether symptoms experienced were considered distressing. In this version, a cutoff specifying the number of positive symptoms considered distressing can be used. The PQ-92 scale has not been published previously. Therefore, the full measure with the distress criteria and scoring instructions have been included in the supplementary material (see appendix I).

In order to improve the efficiency and accuracy of UHR identification, two shorter versions of the PQ scale have been produced: the PQ-16 (Ising et al., 2012), and the PQ-B (Loewy et al., 2011). The PQ-16 (Ising et al., 2012) comprises of 16 items, assessed over the responders' lifetime. Nine items cover perceptual abnormalities, five unusual thought content and paranoia, and two negative symptoms. Each item is marked true/false, with endorsed symptoms rated on a scale of distress ranging from 0 (no distress) to 3 (severe). The PQ-16 can be scored by a sum of the distress scores (range 0–48), or the total number of symptoms endorsed (range 0–16). The PQ-B comprises of 21 items, recording positive symptoms experienced over the past month. For each endorsed symptom, responders rate whether they found it distressing or impairing, ranging from 1 (strongly disagree) to 5 (strongly agree), with a 4 or 5 indicating distress. The PQ-B has been adopted as a screening tool using the total number of items endorsed, the number of items which are identified as distressing (both range 0–21), and the total distress score (range 0–105), with the latter the method recommended by Loewy and colleagues.

While the scales have been found to successfully identify potential UHR cases based on the presence of attenuated psychotic symptoms, it is important to note that these instruments do not record family history, the presence of schizotypal personality disorder, nor are able to determine recent functional decline. As a result, while these scales can detect the attenuated positive state (APS) and brief intermittent psychotic state (BIPS) categories which form part of the UHR syndrome, the genetic risk and deterioration syndrome (GRDS), without the additional presence of attenuated symptoms, is unlikely to be identified.

### Assessment of bias

An assessment of bias was based upon a modified version of the QUADAS (Whiting et al., 2003). Studies were evaluated on eight criteria: issues with the participant selection procedure; gold standard selection and execution; the risk of progression, partial, or differential verification bias; whether assessors were blinded to the PQ scores; and whether participant withdrawals were accounted for.

### Analysis plan

Due to anticipated study heterogeneity, and with the SIPS and CAARMS assessments using slightly different criteria to determine UHR status, a meta-analysis of diagnostic test accuracy was not considered feasible. In addition, summary statistics of diagnostic accuracy (presented here as diagnostic odds ratios; DOR) were not compared between studies, given that differences in study design (e.g. sample selection, outcome measurement, method of analysis) were expected to significantly influence the values reported. Instead, a narrative synthesis outlining trends was reported, based upon the optimum sensitivity, specificity and

DOR values at each PQ threshold score within each study. The DOR was selected as the principle measure of diagnostic test effectiveness due to its single value and independence to prevalence, unlike alternatives such as the positive and negative predictive values, which is likely to be very different between the different studies.

As with any diagnostic tool, adopting a cutoff point is a balancing act between selecting a level sufficiently sensitive to identify an appropriate proportion of cases, but stringent enough in order to minimize the number of false positives. In the original validation study (Loewy et al., 2005), it was proposed that when screening for UHR to identify those eligible for research or specialist evaluation it is usually important to select a symptom cutoff point that prioritizes sensitivity over specificity to minimize the risk of missing UHR individuals. However, to what extent sensitivity should be prioritized over specificity using this tool is largely dependent upon the context in which it is being used, and at present no guidelines exist suggesting what levels may be considered appropriate. In the field of developmental disorder screening, a sensitivity and specificity of at least 70–80% has been suggested, which is lower than many other areas of medicine in recognition of the complexities of measurement (Barnes, 1982). Given measuring and diagnosing sub-threshold psychotic states is also considered a highly complex undertaking (McGorry et al., 2003), we considered adopting a similar threshold appropriate. Therefore, in studies where multiple clinical cutoffs are presented, the one which provides the highest diagnostic odds ratio with a sensitivity of at least 75% was presented. Due to anticipated study heterogeneity, a higher DOR was not considered indicative of a more accurate assessment, relative to other studies.

## RESULTS

### Summary of articles

Fourteen diagnostic accuracy studies and 45 studies using the PQ as a screening tool for UHR were identified (see figure 1), with all eligible studies presented in Table 1. Two diagnostic accuracy studies used the PQ-92, three used the PQ-16, eight used the PQ-B, and one used both the PQ-16 and the PQ-92. Six studies were completed in the USA, three in China, and one in Australia, Finland, the Netherlands, Nigeria, and the UK.

For purposes of analysis, the diagnostic accuracy studies were grouped together into four different categories: non-help seeking populations (typically student samples); populations seeking help for non-specific mental health concerns recruited in secondary mental health care settings; referrals to early intervention services or prodromal clinics (defined as UHR/psychosis enriched populations); and prison populations.

### Optimum cutoff points for the PQ

The optimum cutoff points, and their accompanying sensitivity, specificity and diagnostic accuracy statistics are presented in Table 2. In all 14 studies the PQ was found to be an accurate predictor of UHR diagnosis, with area under the curve (AUC) estimates ranging from between 0.71 (95% CI 0.57 to 0.85) to 0.95 (95% CI 0.94 to 0.95).

**The PQ-92**—Three studies reporting data on the diagnostic accuracy of the PQ-92 were identified. In a general mental health setting a positive subscale cutoff of 18 was supported

by two studies. In a UHR and psychosis enriched sample, the positive subscale was found to be more accurate than the total PQ-92 score, with a cutoff of 8 positive symptoms recommended. No eligible studies evaluating the diagnostic accuracy of the PQ-92 in non-help seeking populations were identified.

**The PQ-16**—Four studies reporting data on the diagnostic accuracy of PQ-16 were identified. In a non-help seeking population a total distress score threshold of 9 was supported, and in general mental health help-seeking populations a lower distress score cutoff of 8 was supported, along with symptom scores of 6 and 5 respectively.

**The PQ-B**—Eight diagnostic accuracy studies using the PQ-B were identified. Of these, three evaluated using the number of distressing symptoms endorsed. In a non-help seeking population a threshold of 8 distressing items was proposed, far higher than the 4 distressing items found most appropriate in a UHR-enriched sample. In a prison population a cutoff of value of 2 distressing symptoms resulted in the highest DOR, however 7 distressing symptoms produced a balance between sensitivity and specificity more appropriate for UHR screening,

Six studies evaluated the total distress score for screening, of which four were completed in UHR/psychosis enriched samples. In samples with a very high prevalence of UHR/psychosis patients (86.5%), a total distress score of 6 was supported, while in similar settings with a much lower prevalence (~40%) a distress score of 18 was recommended. In a general mental health help-seeking population, a total distress score of 24 was found to result in a balance between sensitivity and specificity appropriate for screening.

Four studies adopted the total number of symptoms endorsed, of which two were completed in UHR/psychosis enriched samples. In a sample with a very high proportion of UHR and psychotic participants (86.5%), a cutoff score of 3 symptoms was supported, while in a lower prevalence sample from a similar setting a higher threshold of 9 symptoms endorsed (albeit below the 75% sensitivity threshold). In a general mental health help-seeking population, a clinical cutoff of 7 was supported. In prison populations, a cutoff of 5 was proposed, however this cutoff resulted in very high specificity and low specificity (sensitivity=98%, specificity=24%).

### **Distress versus number of symptoms**

Six studies reported the diagnostic accuracy of the PQ using both the number of symptoms endorsed as a cutoff, and a distress score (either the total distress score, or the number of distressing items). In two studies the AUC was larger when the distress score was adopted, relative to the number of symptoms endorsed (Chen et al., 2014b; Kline et al., 2014). In the four other studies, the specificity was higher when distress was adopted in three of the studies, (Loewy et al., 2011: 68% compared to 58%; Jarrett et al., 2012: 62% compared to 24%; Xu et al., 2016 64% compared to 60%), whilst in the fourth (Okewole et al., 2015) this could not be determined due to insufficient data. These findings suggest that incorporating a measure of distress may be a more appropriate method for UHR screening, particularly when minimizing the volume of false-positives is an important consideration.

## Summary of cutoffs adopted in the literature

A summary of the non-diagnostic accuracy studies which used the PQ as a screening tool is presented in Table 1. Twenty-seven studies used the PQ-92 as a screening tool, primarily in non-help seeking or general mental health help-seeking populations. A threshold of 18 positive symptoms was adopted in 15 studies; nine studies used a threshold of 8 distressing positive symptoms; and four used a threshold of 8 positive symptoms not considering distress. The 18 positive symptom threshold was primarily adopted in general mental health help-seeking samples, while the threshold of 8 distressing symptoms was most commonly used in non-help seeking populations. In the PQ-16, a distress score threshold of 6 score was consistently adopted, both in non-help seeking samples and those recruited in general mental health settings (5 of 7 articles). Seven studies used the PQ-B as a screening tool. In the studies completed in non-help seeking populations, one used a cutoff of one symptom being scored as a '4' or higher on the distress scale, one a score of a '5' on one item, one 8 distressing symptoms, and one a threshold of both 6 symptoms and a distress total score of 29. In two studies completed in general mental health help-seeking population both studies used a cutoff of either 3 symptoms endorsed, or a distress score of 6. In the one study completed in a prison setting a cutoff of 5 symptoms was adopted.

## Bias assessment

An assessment of study bias is presented in the supplementary material (appendix II). In most parameters, the majority of studies were reported in a manner that suggested there was low risk of bias. However, the majority of studies (92.3%) did not report whether the interviewer who conducted the SIPS/CAARMS assessment was blinded to the screening score, and in five studies a non-random selection of participants was followed up with the reference standard, including all those who scored above a pre-specified PQ threshold, but only a selection of those who scored below. This can lead to partial verification bias, which can inflate sensitivity at the expense of specificity (Zhou, 1998).

## DISCUSSION

### Main results

Over all populations examined, the PQ was found to be an accurate screening tool to identify possible UHR cases. In addition, there is some evidence to suggest that incorporating distress may improve the accuracy of screening by minimizing false positives. Higher screening cutoffs appear to be required in non-help seeking samples, relative to general mental health samples, which are in turn higher than those required in highly enriched populations. This is important, given at present the thresholds adopted in the literature appear to be the same regardless of population characteristics, and are often based on diagnostic accuracy studies completed in more enriched samples.

### Recommendations

These recommendations (summarized below and in Table 3) should be considered as only general guidelines, and come with a number of caveats. First, these recommendations are based on relatively few studies, and so are likely to be revised as more studies in the field are

completed; in fact, our primary recommendation is that future research attempt to replicate the same cutoffs to establish reliability. Second, it is unclear what thresholds to adopt in alternative settings such as primary care which may be an important avenue for early identification of psychosis (Cole et al., 1995). Third, given the significant heterogeneity between studies which used different iterations of the PQ these findings cannot provide firm recommendations on which particular scale to use in each setting. That said, given all three were consistently found to be an appropriate screening tool for UHR, the PQ-16 or the PQ-B may be considered preferable over the PQ-92 due to brevity. Fourth, it is important to note that all three iterations of the scale do not measure family history, presence of schizotypal personality disorder, and do measure rate of functional decline. As a result, these scales are unlikely to identify those with GRDS, and so additional information is necessary to identify this particular subgroup of UHR patients to ensure that they are not incorrectly excluded from any screening program. Fifth, the thresholds recommended are based on the premise that a sensitivity of at least 75% is appropriate for preliminary UHR screening, while a different balance between sensitivity and specificity may be more appropriate depending on the context. One example of this may be where a service may anticipate only a small number of referrals but have capacity for a large number of assessments, meaning lower threshold may be appropriate to maximize UHR detection. In such cases, piloting a lower cutoff point would be recommended. Alternatively, a higher specificity may be preferable with limited resources for evaluation of a large screened population, meaning a higher cutoff point should be tested in order to focus on those most likely to be true positives.

**The PQ-92**—The positive symptom subscale may be more appropriate for UHR screening, relative to the whole instrument. Evidence supports a threshold of 8 positive symptoms in highly enriched samples, and 18 positive symptoms in general mental health help-seeking populations. No evidence of an appropriate cutoff point to adopt in non-help seeking populations was identified. However, if the scale is adopted in this setting then a cutoff score of at least 18 positive symptoms would be recommended.

**The PQ-16**—Using the distress scale, rather than the total symptom score, may improve the accuracy of the scale. In non-help-seeking settings a distress score of 9 appears appropriate. In general mental health help-seeking populations a threshold of 8 was supported, however the very high specificity at this level suggests that slightly lower thresholds may also be appropriate. When using the symptom score, a threshold of 5 to 6 appears appropriate in general mental health settings. No appropriate thresholds were identified in highly enriched samples, so careful piloting of any thresholds adopted in this setting would be recommended.

**The PQ-B**—In non-help seeking populations, a threshold of 8 symptoms reported as distressing has been supported. In general mental health settings, either a total distress score of 24, or a symptom total score of 7 was found to be both suitably sensitive and specific. In most UHR/psychosis enriched samples a total distress score of 18 would be recommended, however in populations anticipated to have a high prevalence of UHR/psychotic patients then a lower total distress score may be appropriate (i.e. 6).



## Strengths and Limitations

One strength of the study is the consistency of the findings. All identified studies supported the accuracy of the PQ as a screening tool, and in all three iterations of the scale higher cutoffs were required in settings with a lower prevalence of UHR. The search identified a larger number of studies than anticipated, and included a number of non-English and grey literature studies increasing the generalizability of the findings and minimizing possible publication bias. In the quality assessment a relatively low risk of bias was detected over most of the parameters assessed, supporting the reliability of the findings.

Regarding limitations, it is notable that while a relatively large number of diagnostic accuracy studies were identified (14), split between different settings and scale iterations, each of the recommended cutoffs are based on only a small number of studies. In addition, the 14 identified studies were completed in six different countries, with the PQ translated into five different languages. While all but one outlined a detailed translation procedure suggesting high fidelity to the original scale, including a back-translation with the original author of the PQ (Loewy et al., 2005), it is possible that both cultural and language differences may further limit the generalizability of the findings. Another important consideration is that in four studies a non-random selection of participants was followed up with the reference standard, resulting in possible partial verification bias. This artificially inflates sensitivity at the cost of specificity, so lower cutoffs may be needed than suggested in studies where verification bias may have occurred. Also, in a number of studies the optimum thresholds for UHR screening were not presented, reporting instead the highest average of sensitivity and specificity. Lastly, in one study (Okewole et al., 2015) it was reported that some of the items of the PQ required modification to be appropriate for a Nigerian student population. While it is likely that these changes would have improved the accuracy of the scale for this particular setting, changing the item content limits the generalizability of these findings to other populations.

Finally, as highlighted previously in the methods section it is important to note that these scales do not capture familial history of psychosis, schizotypal personality disorder, nor are designed to capture functional decline. As a result, in any screening program patients with GRDS without additional attenuated psychotic symptoms are unlikely to be identified. While cases are typically rare, it should still be considered a significant issue as using this screening procedure alone may cause sub-groups to be undetected and so therefore not access treatment. As a result, in screening procedures it may be important to ask additional questions relating to familial history and functioning so not to miss potentially eligible patients.

## Implications

Our results support the PQ as a tool to identify people who may meet criteria for UHR, and propose guidelines as to what cutoff points may be the appropriate in different populations. One consistent finding was that higher cutoffs were required in samples with a lower prevalence of UHR and psychosis. However, in our review of the broader screening literature symptom thresholds which have been validated in more enriched samples are commonly being adopted in less UHR-prevalent populations. In a non-help seeking

population for example a distress score of 9 may be the most appropriate for the PQ-16; a figure higher than the 6 used in all three identified studies conducted in this population (Chen et al., 2013; Suna et al., 2015; Wang et al., 2015). Adopting thresholds appropriate for more enriched populations may increase false-positives, reducing screening efficiency. Aside from resource considerations, this is problematic given concerns regarding the possible impact of stigma of being identified as UHR (Yang et al., 2010).

In the review of studies using the PQ as a screening tool, it was notable that a significant proportion were completed in non-help seeking community samples (23 out of 45 studies). With the prevalence rate of psychotic-like experiences in the general population at approximately 5%, with 75–90% disappearing over time (van Os et al., 2009), screening such populations are likely result a high false-positive rate. Furthermore, there have been recent concerns that applying UHR criteria to community samples not otherwise considered at risk may significantly weaken the diagnostic accuracy of the UHR paradigm (Fusar-Poli, 2017). This has led to calls that UHR assessment should be limited to those both seeking help and exhibiting distress (Schultze-Lutter et al., 2015). As a result, more caution should perhaps be exercised in using such screeners in community populations, particularly when measures of symptom distress are not being factored into the screening cutoff. However, with some evidence suggesting that many people who experience concerns regarding their mental health do not actively seek help prior to the onset of full psychotic symptoms (Addington et al., 2002), with factors such as stigma significantly impacting help-seeking behaviors (Clement et al., 2015) there is also an argument that broader screening programs may help identify people who might otherwise may experience a delay in appropriate care.

To improve early identification of psychosis screening both in school systems and primary care settings have been proposed (French et al., 2012; Levitt et al., 2007), however no eligible studies validating the PQ in these settings were identified. In addition, the impact of other socio-demographic and psychopathologies factors on screening effectiveness requires further consideration. For example, very young participants are more likely to report sub-threshold psychotic experiences, and for this to be less associated with psychopathology (Brandizzi et al., 2014; Kelleher et al., 2012). While this may be the case, it was notable that five diagnostic accuracy studies had inclusion criteria allowing for participants to be as young as 12, while none reported any significant difficulties either in their comprehension of the scale, or significantly higher scores relative to older participants. A future evaluation of the PQ and its diagnostic accuracy stratified across different ages may be helpful in determining both at what age is the PQ an effective screener of UHR, and whether the effectiveness of different cutoff points are consistent between older and younger participants. In addition, it is unclear whether different thresholds may be appropriate for different cultures, given some of the items may be indicative of cultural differences rather than positive symptomology (Nuevo et al., 2000). In future work, it would be helpful to determine whether particular PQ items are more predictive of a UHR diagnosis, and to assess whether this is consistent between different populations. Finally, while there is much interest in a screening tool for full psychosis, to date the PQ has not been fully evaluated for this purpose.

## Conclusions

This study further supports the use of the PQ as a screening tool to identify people with UHR presenting with attenuated psychotic symptoms. The findings suggest higher cutoffs are required in lower UHR prevalence populations, whilst incorporating a measure of distress caused by symptoms may improve the accuracy of screening and minimize the rate of false-positives. However, the impact of false-positives and false-negatives may be different depending upon the requirements of the screening. In addition, further studies are required to replicate the presented findings. As a result, these recommendations should be considered as a starting point in selecting which cutoff points to adopt in any future research or clinical practice.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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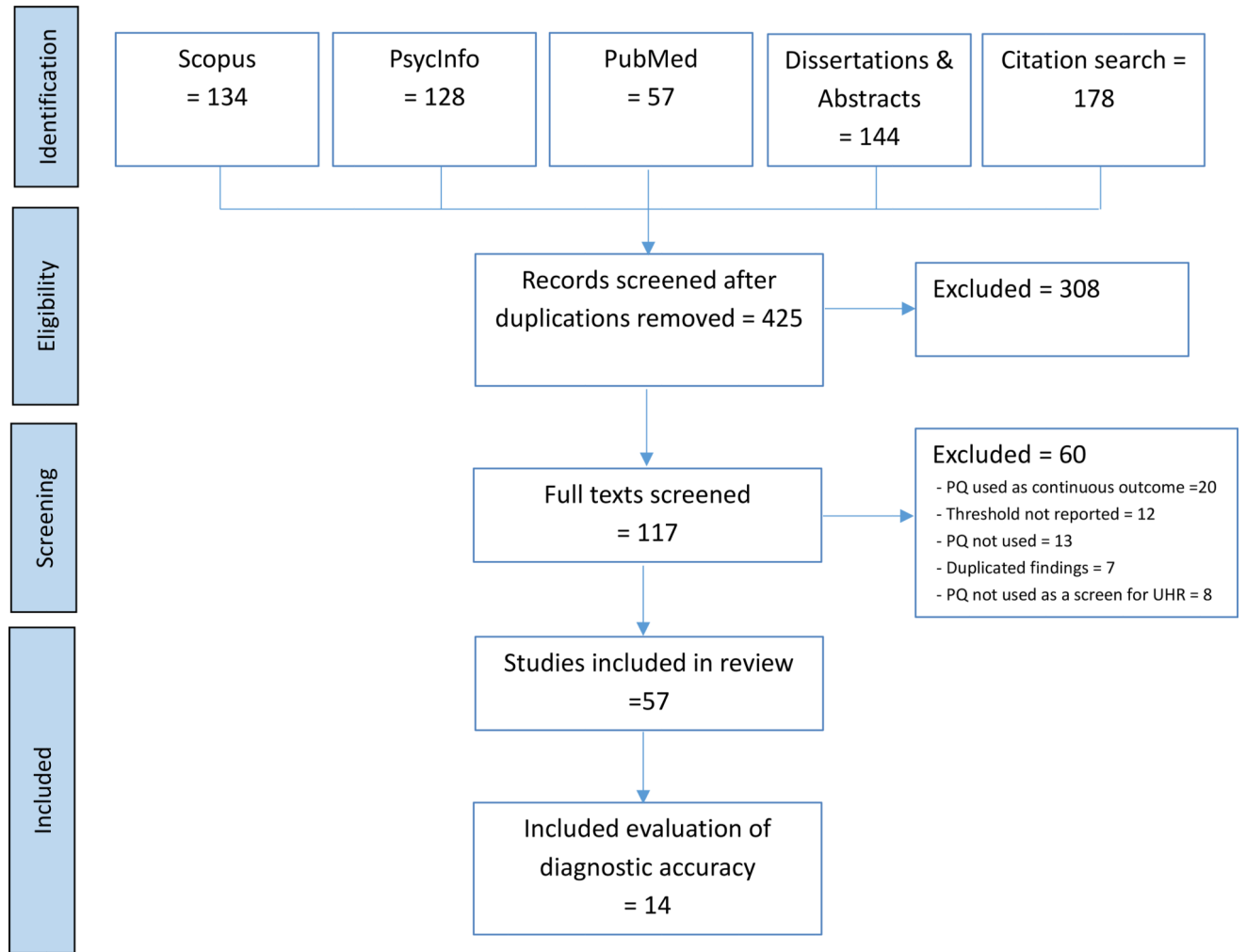
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**Figure 1.**  
PRISMA diagram



**Table 1**

## Summary of eligible studies

Study	PQ used	N <sup>†</sup>	Population	Threshold adopted
<b>Diagnostic Accuracy Studies</b>				
Lindgren, 2015	PQ-92	161	General mental health help-seeking population	
Loewy et al., 2005	PQ-92	113	Targeted referrals for possible UHR/FEP	
Chen et al., 2014a	PQ-16	99	Non-help seeking population	
Chen et al., 2014b	PQ-16	101	General mental health help-seeking population	
Ising et al., 2012	PQ-16 & PQ-92	567	General mental health help-seeking population	
O'Donoghue et al., 2016	PQ-16	147	General mental health help-seeking population	
Okewole et al., 2015b	PQ-B	102	Non-help seeking population	
Kline et al., 2015	PQ-B	47	General mental health help-seeking population	
Kline et al., 2012	PQ-B	66	Targeted referrals for possible UHR/FEP	
Kline et al., 2014	PQ-B	85	Targeted referrals for possible UHR/FEP	
Thompson et al., 2013	PQ-B	70	Targeted referrals for possible UHR/FEP	
Loewy et al., 2011	PQ-B	141	UHR/FEP treatment referrals	
		46	Non-help seeking population	
Jarrett et al., 2012	PQ-B	301	Prison services	
Xu et al., 2016	PQ-B	505	General mental health help-seeking population	
<b>Studies which adopt PQ thresholds to screen for UHR</b>				
Anglin et al, 2014	PQ-92		Non-help seeking population	8 positive distressing symptoms
Cooper et al., 2015	PQ-92		Non-help seeking population	8 positive distressing symptoms
Cooper et al., 2016	PQ-92		Non-help seeking population	8 positive distressing symptoms
				8 distressing positive symptoms
Ellman et al., 2013	PQ-92		Non-help seeking population	18 positive symptoms
Ellman & Anglin, 2014	PQ-92		Non-help seeking population	8 positive symptoms
Gibson et al., 2014	PQ-92		Non-help seeking population	8 distressing positive symptoms
				8 positive symptoms
Loewy et al., 2007	PQ-92		Non-help seeking population	14 positive symptoms
				8 distressing positive symptoms
				36 total symptoms
Reeves et al., 2014	PQ-92		Non-help seeking population	8 distressing symptoms
Sandt, 2013	PQ-92		Non-help seeking population	8 distressing positive symptoms
Rockers et al., 2009	PQ-92		Non-help seeking population	8 symptoms (for screening controls)
Shaikh, 2014	PQ-92		Non help-seeking population (control screen)	18 positive symptoms for control screen
Valmaggia et al., 2015a	PQ-92		Non help-seeking population (control screen)	18 positive symptoms for control screen

Study	PQ used	N <sup>†</sup>	Population	Threshold adopted
Valmaggia, et al. 2015b	PQ-92		Non help-seeking population (control screen)	18 positive symptoms for control screen
Wolfe et al., 2016	PQ-92		Non help-seeking population	8 distressing positive symptoms
Bebber et al., 2016	PQ-92		General mental health help-seeking population	18 positive symptoms
Brandizzi et al., 2014	PQ-92		General mental health help-seeking population	18 positive symptoms
Chiu et al., 2010	PQ-92		General mental health help-seeking population	8 positive symptoms
Koren et al., 2013	PQ-92		General mental health help-seeking population	8 positive symptoms
Lindgren et al., 2010	PQ-92		General mental health help-seeking population	18 positive symptoms
Masillo et al., 2016	PQ-92		General mental health help-seeking population	18 positive symptoms
Rietdijk et al., 2012	PQ-92		General mental health help-seeking population	18 positive symptoms
Rietdijk et al., 2013	PQ-92		General mental health help-seeking population	18 positive symptoms
Scheyer et al., 2014	PQ-92		General mental health help-seeking population	8 distressing positive symptoms
Van der Gaag et al, 2012	PQ-92		General mental health help-seeking population	18 positive symptoms
Masillo et al., 2015	PQ-92		Targeted referrals for possible UHR/FEP	18 positive symptoms
Masillo et al., 2016	PQ-92		Targeted referrals for possible UHR/FEP	18 positive symptoms
Eussen et al., 2014	PQ-92		Children with Autistic Spectrum Disorder	18 total symptoms OR 14 positive symptoms
Chen et al., 2013	PQ-16		Non-help seeking population	6 Distress score
Pantlin et al., 2016	PQ-16		Non-help seeking population	6 symptoms endorsed
Shi et al., 2016	PQ-16		Non-help seeking population	6 Distress score
Suna et al., 2015	PQ-16		Non-help seeking population	6 distress score
Wang et al., 2015	PQ-16		Non-help seeking population	6 distress score
Cross et al., 2014	PQ-16		General mental health help-seeking population	6 symptoms endorsed
De Jong et al., 2016	PQ-16		General mental health help-seeking population	6 symptoms endorsed
Drake, 2016	PQ-16		General mental health help-seeking population	6 symptoms endorsed
Van Der Velde et al., 2015	PQ-16		General mental health help-seeking population	6 distress score
Salsabillah et al., 2015	PQ-16		People-receiving care in an HIV/AIDS clinic	6 symptoms endorsed
Fonseca-Pedrero et al., 2016	PQ-B		Non-help seeking population	6 symptoms and 29 distress score
Mittal et al., 2011	PQ-B		Non-help seeking population	1 symptom scored '4 or 5' on distress
Mittal et al., 2012	PQ-B		Non-help seeking population	1 symptom scored '5' on distress
Okewole et al., 2015a	PQ-B		Non-help seeking population	8 distressing symptoms
Zhang et al., 2015	PQ-B		General mental health help-seeking population	3 symptoms endorsed, OR distress score of 6

Study	PQ used	N <sup>†</sup>	Population	Threshold adopted
Zhang et al., 2014	PQ-B		General mental health help-seeking population	3 symptoms endorsed, OR distress score of 6
Evans et al., 2016	PQ-B		Prison Population	5 distressing symptoms
Jarrett et al., 2015	PQ-B		Prison Population	5 symptoms endorsed

PQ, Prodromal Questionnaire; UHR, Ultra High Risk; FEP First Episode of Psychosis.

<sup>†</sup>Number of participants assessed both with the PQ and the reference standard.

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Table 2

Accuracy statistics for optimum screening cutoffs adopted in each identified study<sup>†</sup>

Study	Sample	Diagnosis tool used	% UHR/ Psychotic	Score type	Optimum cutoff	Sensitivity (%)	Specificity (%)	DOR
<b>Thresholds adopted using the PQ-92</b>								
Lindgren, 2015a	General MH service users	SIPS	33.54 <sup>‡</sup>	Positive symptoms	18	80	40	2.63
Ising, 2012	General MH service users	CAARMS	36.68 <sup>‡</sup>	Positive symptoms	18	90	90	81.00
Loewy, 2005	UHR/Psychosis enriched	SIPS	67.30 <sup>‡</sup>	Positive symptoms	8	90	49	8.53
Loewy, 2005	UHR/Psychosis enriched	SIPS	67.30 <sup>‡</sup>	Total score	19	91	38	6.20
<b>Thresholds adopted using the PQ-16</b>								
Chen, 2014a	Non-help seeking	SIPS	3.45 <sup>§</sup>	Distress score	9	85	87	37.92
Chen, 2014b	General MH service users	SIPS	ns	Distress score	8	78	91	ns
Ising, 2012	General MH service users	CAARMS	36.68 <sup>‡</sup>	Symptom score	6	87	87	44.79
Chen, 2014b	General MH service users	SIPS	Ns	Symptom score	5	81	61	ns
O'Donoghue, 2016	General MH service users	CAARMS	43% <sup>‡</sup>	Symptom score	6	90	54	10.96
<b>Thresholds adopted using the PQ-B</b>								
Okewole, 2015b	Non-help seeking	SIPS	ns	Total distressing items	8	89	67	ns
Jarrett, 2012	New prisoners	CAARMS	19.90 <sup>‡</sup>	Symptom score	5	98	24	15.47
Jarrett, 2012	New prisoners	CAARMS	19.90 <sup>‡</sup>	Total distressing items	2	97	29	13.21
Xu, 2016	General MH service users	SIPS	38.40 <sup>§</sup>	Symptom score	7	84	60	6.96
Kline, 2012	General MH service users	SIPS	40.82 <sup>§</sup>	Distress score	6	95	28	5.43
Xu, 2016	General MH service users	SIPS	38.40 <sup>§</sup>	Distress score	24	82	64	7.35
Kline, 2014	UHR/Psychosis enriched	SIPS	39.39 <sup>‡</sup>	Symptom score	9	69	70	5.19
Loewy, 2011	UHR/Psychosis enriched	SIPS	86.52 <sup>§</sup>	Symptom score	3	89	58	11.17
Kline, 2014	UHR/Psychosis enriched	SIPS	39.39 <sup>‡</sup>	Distress score	18	77	68	7.11
Thompson, 2013	UHR/Psychosis enriched	SIPS	44.28 <sup>§</sup>	Distress score	18	84	67	10.66
Kline, 2015	UHR/Psychosis enriched	SIPS	38.90 <sup>‡</sup>	Distress score	6	95	47	16.85
Loewy, 2011	UHR/Psychosis enriched	SIPS	86.52 <sup>§</sup>	Distress score	6	88	68	15.58

Study	Sample	Diagnosis tool used	% UHR/ Psychotic	Score type	Optimum cutoff	Sensitivity (%)	Specificity (%)	DOR
Kline, 2014	UHR/ Psychosis enriched	SIPS	39.39 <sup>‡</sup>	Total distressing items	4	73	83	1.3.20

UHR, Ultra High Risk; DOR, diagnostic odds ratio; MH, Mental Health; ns, not specified; PQ, Prodromal Questionnaire; SIPS, Structured Interview for Prodromal States; CAARMS, Comprehensive Assessment of At-Risk Mental States.

<sup>‡</sup>Where multiple thresholds are reported, the selection is based on the threshold with the highest diagnostic odds ratio with sensitivity of at least 75%.

<sup>‡</sup>Sample includes participants identified as UHR only (Psychotic participants removed)

<sup>§</sup>Sample includes participants identified as UHR and psychotic by the CAARMS/SIPS

**Table 3**

Screening threshold recommendations for each version of the PQ in three different settings

PQ Type	Non-help seeking samples	General MH service users	UHR/Psychosis enriched samples
<b>PQ-92</b>			
Positive symptoms		18	8
Total symptoms			19
<b>PQ-16</b>			
Distress score	9	8	
Total symptoms		5 – 6	
<b>PQ-B</b>			
Number distressing items	8		4 <sup>†</sup>
Total symptoms		7	3
Distress score		24	6 – 18

PQ, Prodromal Questionnaire; UHR, Ultra-high risk.

<sup>†</sup>Sensitivity below pre-specified 75% level (73%)