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Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

For people at potential risk of developing first episode psychosis, what is the most sensitive, valid, reliable and time-effective test for assessing at-risk mental state?

Clarification of question using *PICTRO* structure

Patients:	People at risk of developing first episode psychosis
Intervention:	Test for assessing at-risk mental state
Comparator:	Any other test
Target condition:	Psychosis
Reference standard:	Any reference standard
Outcome:	Sensitivity, validity, reliability and time-effectiveness

Plain language summary

CAARMS has been identified as the most valid tool for assessing "at risk mental state" as it can successfully identify "at risk" patients using its own Ultra High Risk (UHR) criteria. Stronger evidence is needed to support the reliability of other "at risk" assessment tools that have used CAARMS as a point of reference.

Clinical and research implications

There are currently no reliable estimates of the performance of tests to assess at risk mental state.

Future studies should include assessment of test performance using pre-defined cut-off values, i.e. the performance of the test should be independently evaluated in a separate population from that in which its operating characteristics have been determined. Studies should also consider the selection of an appropriate population (one which is representative of the intended use of the test) and an appropriate reference standard. The reference standard used by studies in this summary (Comprehensive Assessment of At-Risk Mental States, CAARMS) is likely to be a valid tool for identifying individuals at increased risk of developing psychosis. However, it should be noted identification of an "at risk" group is not the same as prediction of the actual onset of psychosis; baseline CAARMS alone has a low positive predictive value for psychosis when used in a non-psychotic help seeking population. It may be appropriate to consider undertaking prediction modelling studies, in the target population, to determine which components of CAARMS or other instruments, as well as other risk factors (e.g. socio-economic factors, history of substance abuse, etc.) are independently associated with the development first episode psychosis.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified three studies which were considered to be potentially relevant to this evidence summary.[1,2,3] One study was subsequently excluded because it did not report a reference standard, or any measure of true test performance (see details below).[3] The remaining two studies both reported that they assessed the diagnostic accuracy of screening instruments for detecting at risk mental state in help-seeking general populations,[1,2] however, the first study used an 'enriched' sample, which pre-selected participants who were more likely to be at risk.[1] Both studies used the Comprehensive Assessment of At Risk Mental States (CAARMS) instrument as the reference standard and both defined a positive diagnosis as ultra-high risk (URH)on CAARMS.[1,2] One study reported the development of a brief, 16-item version of the Prodromal Questionnaire (PQ-16), and an assessment of its discriminatory performance in the development population.[1] The second study reported an assessment of the discriminatory performance of various elements of the Community Assessment of Psychic Experience (CAPE) instrument to determine optimal combinations and cut-offs.[2]

Main findings

The first study reported that the 16-item version of the Prodromal Questionnaire (PQ-16) had a sensitivity and specificity of 87% for the prediction of UHR on subsequent CAARMS assessment.[1]The second study reported sensitivity estimates, for various cut-offs and various components of CAPE, of between 63% and 83%; the corresponding specificity values were between 82% and 49%.[2]

Authors' conclusions

Ising 2012 – The authors concluded that the PQ-16 is a good screening instrument for routine use in secondary mental health care, and that the low number of items makes it feasible to screen large help-seeking populations.

Mossaheb 2012 – The authors concluded that their results show promise that CAPE is a valid, simple and cost-effective instrument for detecting individuals at ultra-high risk (UHR) of developing psychosis in a clinical population. They further stated that CAPE is not diagnostic for UHR, but is intended to pre-select individuals for more detailed and intensive clinical interview.

Rausch (2013) – **Excluded: This study describes a theoretical diagnostic/assessment pathway and reports numbers or patients, form the study sample, who were assigned to various categories at each stage. Although the authors conclude that the ERIraos scale provides increased sensitivity for detecting At Risk Mental State (ARMS), the study does not include a reference standard or describe any method of determining the true performance of ERIaos or any of the tests in the pathway.**

Reliability of conclusions/Strength of evidence

Two diagnostic accuracy studies reported estimates of the sensitivity and specificity of two tools, PQ-16[1] and CAPE,[2] for the prediction of UHR on subsequent CAARMS assessment in the help-seeking general population. Both studies had substantial methodological flaws, which mean that neither can provide a reliable estimate of test performance. Both studies reported the development of an instrument and/or optimisation of cut-off values in the same population from which estimates of the instrument's discriminatory performance were then derived. This lack of validation in a new, independent clinical sample is likely to result in overestimations of performance. In addition, the first study also pre-selected participants in the top 20% of the distribution for the original Prodromal Questionnaire (PQ-92) i.e. those who were more likely to be classified as having at risk mental state.[1] This selected population may also result in overestimations of performance and also means that the study is not representative of the 'real life' situation in which a screening test for at risk mental states would be applied. Both study authors drew conclusions about the feasibility,[1] simplicity/ease of use,[2] probable cost-effectiveness,[2] which were not supported by any reported results.

The use of CAARMS as the reference standard is likely to represent the best option currently available to assess the accuracy or new tools for determining at risk status. Data from the pilot evaluation of the CAARMS tool[4] indicated that can identify at risk individuals: baseline CAARMS scores were significantly lower in control subjects than in people defined as UHR by Brief Psychiatric Rating Scale (BPRS)/Comprehensive Assessment of Symptoms and History (CASH)-based criteria ($p < 0.001$); 92% of individuals classified as UHR by BPRS/CASH-based criteria were also classified as UHR by CAARMS and the estimates of 12-month transition rates to psychosis were similar for the two classification methods. By contrast, although in a sample of non-psychotic help seekers, CAARMS positive UHR individuals were found to be at increased risk of developing psychotic disorders (RR 12.44 (95% CI: 1.5 to 103.4), it should be noted that there was considerable uncertainty this estimate. In addition, only 12% of help seeking individuals who were classified as UHR on CAARMS had transitioned to a psychotic disorder at 6 months follow-up. The ability of CAARMS to predict development of psychosis in a general help seeking population is therefore less clear cut.

What do guidelines say?

No guidelines relevant to this evidence summary were identified.

Date question received: 19/08/2015
Date searches conducted: 21/08/2015
Date answer completed: 14/09/2015

References

1. Ising, H. K., Veling, W., Loewy, R. L., Rietveld, M. W., Rietdijk, J., Dragt, S., ... & van der Gaag, M. (2012). The validity of the 16-item version of the Prodromal Questionnaire (PQ-16) to screen for ultra-high risk of developing psychosis in the general help-seeking population. *Schizophrenia bulletin*, 38(6), 1288-1296.

2. Mossaheb, N., Becker, J., Schaefer, M. R., Klier, C. M., Schloegelhofer, M., Papageorgiou, K., & Amminger, G. P. (2012). The Community Assessment of Psychic Experience (CAPE) questionnaire as a screening-instrument in the detection of individuals at ultra-high risk for psychosis. *Schizophrenia research*, 141(2), 210-214.

3. Rausch, F., Eifler, S., Esser, A., Esslinger, C., Schirmbeck, F., Meyer-Lindenberg, A., & Zink, M. (2013). The Early Recognition Inventory ERIraos detects at risk mental states of psychosis with high sensitivity. *Comprehensive psychiatry,* 54(7), 1068-1076.

4. Yung, A. R., Yuen, H. P., McGorry, P. D., Phillips, L. J., Kelly, D., Dell'Olio, M., Francey, S. M., Cosgrave, E. M., Killackey, E., Stanford, C., Godfrey, K. & Buckby, J. (2005). Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. *Australian and New Zealand Journal of Psychiatry*, 39, 964-971.

Results

Primary studies

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Ising et. al. (2012)	**Participants:** Help-seeking adults (18 – 35yrs) from the general population, who were to secondary mental health services by their general practitioners and screened with the Prodromal Questionnaire (PQ-92) between 2008 and 2010. The study used an enriched sample: Participants with a PQ-92 score in the top 20% of the distribution (≥18) were included, and a random sample of 20% of the participants having each PQ-92 score between 12 and 17 was also included. No participants with a PQ score <12 were included Exclusion criteria were: previous use of antipsychotic medication; severe learning disability; psychiatric symptoms of somatic aetiology; insufficient Dutch language fluency; history of psychosis; global assessment functioning score ≥65. **Intervention:**	Initial sample screened using PQ-92: n=3533. Total with PQ-92 score ≥18: n=639 Sample with PQ-92 score <18 selected for inclusion: n=147 Total selected for inclusion: n=786	The stated aim of the study was to develop and test a brief version of the Prodromal Questionnaire (PQ-92) in the general help-seeking population. Participant characteristics were reported for the initial presenting sample (n=3533), which was majority (68%) female and of which 45% were diagnosed with an anxiety or mood disorder. No details of the population selected to develop and evaluate the PQ-16 instrument were reported. Logistic regression analysis was used to select items for inclusion in the PQ-16. The 16-item PQ consists of 9 items from the perceptual abnormalities/hallucinations subscale of PQ-92; 5 items including unusual thought content/delusional ideas/paranoia; 2 negative symptoms. The optimal PQ-16 cut-off score to predict a CAARMS diagnosis of UHR or psychotic disorder was 6. The sensitivity and specificity estimates for the PQ-16 at this cut-off were both 87%; no estimates of variance	The stated aim of the study was to develop and test a brief instrument for use in the general help-seeking population. However, participants included in the study were selected to produce an 'enriched' sample with a greater proportion of at risk individuals than would be likely in a 'real world' setting. This sample is likely to produce an over optimistic assessment of the performance of the instrument.

	PQ-16 – Brief version of the Prodromal Questionnaire (Dutch language) **Comparator:** PQ-92 – Dutch language version of the original Prodromal Questionnaire **Reference standard:** CAARMS – Comprehensive Assessment of At Risk Mental States. A positive CAARMS diagnosis was defined as ultra-high risk of psychosis (UHR) or diagnosis of a psychotic disorder. **Outcome:** Sensitivity and specificity; internal consistency.		were reported. The overall diagnostic performance of the PQ-92 with the optimal cut-off of 18, as measured by area under the receiver operating characteristic (ROC) curve, was statistically significantly greater than that of the PQ-16 with the optimal cut-off of 6; the area under the curve (AUC) estimates were 0.95 (95% CI: 0.94 to 0.95) and 0.93 (95% CI: 0.92 to 0.94), respectively. The Cronbach's alpha statistic was used to assess internal consistency (no further details reported). Cronbach's alpha for the total score on the PQ-16 was 0.774. No measures of the ease of use of PQ-16, or time taken to complete the instrument, were reported.	The same population appears to have been used to develop the PQ-16 instrument (select criteria from the PQ-92 for inclusion in the new instrument), determine the optimum diagnostic threshold (ROC analysis), and assess the performance of the PQ-16 at this threshold. This approach is likely to produce over optimistic assessments of the performance of the PQ-16. The Q-92 was performed before the reference standard (CAARMS), but it was not clear whether PQ-16 was performed blind to

				CAARMS classification. The ability of the reference standard to correctly classify the target condition was unclear[$], and the reference standard was unlikely to have been applied blind to the index test score (index test score was part of the selection criteria). 219 Of the included participants did not receive a CAARMS assessment.
Mossaheb et. al. (2012)	**Participants:** Help-seeking young people/adults (13 – 24yrs), referred to outpatient clinic for early detection and intervention in psychosis. **Intervention:** CAPE – Community Assessment of Psychic	Initial referred sample: n=256 Response to request to fill in CAPE questionnaire:	The stated aim of this study was to assess whether the Community Assessment of Psychic Experience (CAPE) tool could be used as a screening tool to detect individuals at an increased risk for developing psychosis in a clinical, help-seeking population. The mean age of study participants was 16.2 ± 2.5 yrs and 58% were female. 84 (50.9%) Participants had a	It was not clear whether the initial sample of n=256 was a consecutive or random sample. No exclusion criteria were reported. No information on the

	Experience. **Reference standard:** CAARMS – Comprehensive Assessment of At Risk Mental States. A positive diagnosis was defined as meeting the UHR criteria on CAARMS assessment. **Outcome:** Sensitivity and specificity.	n=191 Included in the analysis: n=165	CAARMS positive (UHR) diagnosis. CAPE is a self-administered tool, comprising three dimensions, assessing positive, negative and depressive symptoms in terms of frequency and associated distress. The sensitivity and specificity estimates for the whole CAPE instrument (cut-off not reported) for the prediction of CAARMS positive (UHR) status were both 64% (no estimate of variance reported). When only the positive symptom dimension of CAPE was considered, the sensitivity and specificity estimates for the optimal cut-off of 3.20 were 67% and 73%, respectively (no estimate of variance reported). Using a lower cut-off (2.80) sensitivity was increased to 83% and specificity was reduced to 49% (no estimate of variance reported). Logistic regression analysis indicated that four items from the positive dimension of CAPE were significantly associated with a positive CAARMS assessment: Item 6: "Do you ever feel as if some people are not what they seem to be?" Item 7: "Do you ever feel as if you are being persecuted in some way?" Item 31: "Do you ever feel as if you are under the	non-responders to CAPE was provided. CAPE was performed before and hence blind to CAARMS assessment. The study reported the derivation of optimal thresholds for CAPE, but no validation of these thresholds in a separate population. The ability of the reference standard to correctly classify the target condition was unclear[$], and it was not clear whether CAARMS assessment was performed blind to the results of CAPE. Two participants with incomplete CAPE questionnaires

			control of some force or power other than yourself?" Item 33: "Do you ever hear voices when you are alone?" A positive for items 7, 31 and 33 had a sensitivity of 63% and a specificity of 82% for a CAARMS positive assessment. No measures of the ease of use of CAPE, or time taken to complete the instrument, were reported.	and 15 participants who met the criteria for a diagnosis of psychosis (after CAPE assessment) were excluded from the analysis.
Rausch et. al. (2013)	**Excluded – This study describes a theoretical diagnostic/assessment pathway and reports numbers or patients, form the study sample, who were assigned to various categories at each stage. Although the authors conclude that the ERIraos scale provides increased sensitivity for detecting At Risk Mental State (ARMS), the study does not include a reference standard or describe any method of determining the true performance of ERIaos or any of the tests in the pathway.**			

[$] The CAARMS is a semi-structured interview schedule designed for use by mental health professionals who are already able to assess and evaluate patients' information. It is designed for repeated use over time, i.e. for ongoing monitoring of an individual's mental health/risk .Data from the pilot evaluation of the CAARMS tool[4] indicated that: baseline CAARMS scores were significantly lower in control subjects than in people defined as UHR by Brief Psychiatric Rating Scale (BPRS)/Comprehensive Assessment of Symptoms and History (CASH)-based criteria ($p < 0.001$); 92% of individuals classified as UHR by BPRS/CASH-based criteria were also classified as UHR by CAARMS and the estimates of 12-month transition rates to psychosis were similar for the two classification methods; These results indicate that CAARMS may be useful in identifying individuals at increased risk of developing psychosis. By contrast, although in a sample of non-psychotic help seekers, CAARMS positive UHR individuals were found to be at increased risk of developing psychotic disorders (RR 12.44 (95% CI: 1.5 to 103.4), it should be noted that there was considerable uncertainty this estimate. In addition, only 12% of help seeking individuals who were classified as UHR on CAARMS had transitioned to a psychotic disorder at 6 months follow-up. The ability of CAARMS to predict development of psychosis in a general help seeking population is therefore less clear cut.

Risk of bias:

Primary studies

Study	RISK OF BIAS			
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING
Ishing 2012	☹	☹	?	☹
Mossaheb 2012	?	☹	?	☹
Rausch 2013	**Excluded – This study describes a theoretical diagnostic/assessment pathway and reports numbers or patients, form the study sample, who were assigned to various categories at each stage. Although the authors conclude that the ERIraos scale provides increased sensitivity for detecting At Risk Mental State (ARMS), the study does not include a reference standard or describe any method of determining the true performance of ERIaos or any of the tests in the pathway.**			

☺ Low risk ☹ High risk ? Unclear risk

Search details

Source	Search Strategy	Number of hits	Relevant evidence identified
Systematic Reviews & Primary studies			
MEDLINE	1. Medline; "Health-Status-Indicators".ti,ab; 308 results. 2. Medline; "Outcome-and-Process-Assessment-(Health-Care)".ti,ab; 1 results. 3. Medline; "Outcome-Assessment-(Health-Care)".ti,ab; 8 results. 4. Medline; "Quality-of-Life".ti,ab; 161078 results. 5. Medline; (outcome adj6 measure*).ti,ab; 82825 results. 6. Medline; (health adj6 outcome*).ti,ab; 46821 results. 7. Medline; measure*.ti,ab; 2291988 results. 8. Medline; assess*.ti,ab; 1928439 results. 9. Medline; (score* OR scoring).ti,ab; 585576 results. 10. Medline; index.ti,ab; 504941 results. 11. Medline; indices.ti,ab; 112203 results. 12. Medline; scale*.ti,ab; 504125 results. 13. Medline; monitor*.ti,ab; 560978 results. 14. Medline; 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13; 4779456 results. 15. Medline; outcome*.ti,ab; 946230 results. 16. Medline; 14 AND 15; 476133 results. 17. Medline; exp HEALTH STATUS INDICATORS/; 209001 results. 18. Medline; exp "OUTCOME AND PROCESS ASSESSMENT (HEALTH CARE)"/; 777570 results. 19. Medline; exp "OUTCOME AND PROCESS ASSESSMENT (HEALTH CARE)"/ OR exp "OUTCOME ASSESSMENT (HEALTH CARE)"/; 777570 results. 20. Medline; exp QUALITY OF LIFE/; 127092 results. 21. Medline; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 17 OR 18 OR 19 OR 20; 1160172 results.	52	1

	22. Medline; 16 OR 21; 1393756 results. 23. Medline; "at risk mental state*".ti,ab; 261 results. 24. Medline; 22 AND 23; 52 results.		
EMBASE	1. EMBASE; exp HEALTH SURVEY/; 176116 results. 2. EMBASE; exp QUALITY OF LIFE/; 310728 results. 3. EMBASE; exp OUTCOMES RESEARCH/; 71151 results. 4. EMBASE; "health outcome*".ti,ab; 32767 results. 5. EMBASE; "quality of life".ti,ab; 252853 results. 6. EMBASE; "outcome measure*".ti,ab; 192132 results. 7. EMBASE; measure*.ti,ab; 2889443 results. 8. EMBASE; (score* OR scoring).ti,ab; 859171 results. 9. EMBASE; index.ti,ab; 672788 results. 10. EMBASE; indices.ti,ab; 133971 results. 11. EMBASE; scale*.ti,ab; 653399 results. 12. EMBASE; monitor*.ti,ab; 736298 results. 13. EMBASE; assess*.ti,ab; 2600547 results. 14. EMBASE; 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13; 6095204 results. 15. EMBASE; outcome*.ti,ab; 1442733 results. 16. EMBASE; 14 AND 15; 805527 results. 17. EMBASE; 1 OR 2 OR 3 OR 4 OR 5 OR 6; 771178 results. 18. EMBASE; 16 OR 17; 1294956 results. 19. EMBASE; "at risk mental state*".ti,ab; 671 results. 20. EMBASE; 18 AND 19; 124 results.	124	0
PsycINFO/CINAHL	1. PsycInfo; exp TREATMENT OUTCOMES/; 32211 results. 2. PsycInfo; exp MEASUREMENT/; 284031 results. 3. PsycInfo; exp PSYCHOLOGICAL ASSESSMENT/; 35920 results. 4. PsycInfo; exp QUALITY OF LIFE/; 31819 results. 5. PsycInfo; ((outcome* OR process*) adj3 assessment*).ti,ab; 10324 results.	58	2

	6. PsycInfo; (health ADJ status ADJ indicator*).ti,ab; 75 results. 7. PsycInfo; "health status".ti,ab; 13792 results. 8. PsycInfo; "health outcome*".ti,ab; 12972 results. 9. PsycInfo; "quality of life".ti,ab; 44649 results. 10. PsycInfo; "outcome measure*".ti,ab; 28060 results. 11. PsycInfo; measure*.ti,ab; 570779 results. 12. PsycInfo; assess*.ti,ab; 553891 results. 13. PsycInfo; (score* OR scoring).ti,ab; 267605 results. 14. PsycInfo; index.ti,ab; 73647 results. 15. PsycInfo; indices.ti,ab; 24087 results. 16. PsycInfo; scale*.ti,ab; 287647 results. 17. PsycInfo; monitor*.ti,ab; 66358 results. 18. PsycInfo; 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17; 1225289 results. 19. PsycInfo; outcome*.ti,ab; 270183 results. 20. PsycInfo; 18 AND 19; 143712 results. 21. PsycInfo; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9; 381518 results. 22. PsycInfo; 20 OR 21; 479333 results. 23. PsycInfo; "at risk mental state*".ti,ab; 289 results. 24. PsycInfo; 22 AND 23; 58 results		
CENTRAL	Search Hits #1 MeSH descriptor: [Health Status Indicators] explode all trees 16439 #2 MeSH descriptor: [Outcome and Process Assessment (Health Care)] explode all trees 104242 #3 MeSH descriptor: [Quality of Life] explode all trees 15335 #4 OUTCOME ADJ6 MEASURE* 407 #5 health adj6 outcome* 386 #6 measure* 231532 #7 assess* 258305 #8 score* or scoring 114985	7	0

	#9 index 138919 #10 indices 9001 #11 scale* 85425 #12 monitor* 47366 #13 #6 or #7 or #8 or #9 or #10 or #11 or #12 484393 #14 outcome* 236934 #15 #13 and #14 186520 #16 #1 or #2 or #3 or #5 119372 #17 #15 or #16 221961 #18 "at risk mental state*" 28 #19 #17 and #18 14		

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