# Clinical and functional characteristics of at-risk mental state among non-help seeking adolescents: a cross-sectional study

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# Abstract

*Background* At-risk mental state (ARMS) individuals are at high risk to develop psychosis. In addition to attenuated symptoms, ARMS is associated with cognitive and functional impairment.

*Aim* Our study goal was to explore prevalence rates of ARMS, comorbidities, functioning, and cognitive performance among non-help seeking adolescents.

*Methods* In a cross-sectional design, a sample of high school students were examined with Comprehensive Assessment of At Risk Mental States interview. All participants were administered Kiddie-Schedule for Affective Disorders and Schizophrenia, Social and Occupational Functioning Assessment Scale (SOFAS), KIDSCREEN-52, and a battery of cognitive tests.

*Results* The total of 82 adolescents was enrolled, 21 of them met the ARMS criteria. Subthreshold mental disorders were more frequent in the at-risk mental state positive (ARMS+) group than in the at-risk mental state negative (ARMS-) group. Lower score in (SOFAS) were observed in the ARMS+ group compared to the ARMS- group. In the total sample, high risk symptoms intensity was negatively associated with the SOFAS score. No significant differences in the KIDSCREEN-52 scores or cognitive functioning were found between the groups.

*Conclusion* Our findings suggest that non-help seeking adolescents with at-risk mental state have worse level of functioning compared to controls and higher rates of non-psychotic psychiatric comorbidities. In the management of ARMS individuals, the guidelines recommend non-pharmacological interventions as the first-line option, pharmacotherapy with antipsychotics is reserved for non-responders, more severe, or progressive high-risk symptoms.


# Impact Statements

- In a general population, there is a high prevalence of non-help seeking adolescents who meet at-risk mental state criteria for psychosis, primarily with attenuated psychotic symptoms.
- Individuals with at-risk mental state have poor level of social functioning and low quality of life; they also have higher number of subthreshold comorbid psychiatric conditions.
- Pharmacotherapy with antipsychotics for at-risk mental state is not generally recommended, non-pharmacological interventions are preferred.

# Introduction

Early intervention studies in psychosis, using either pharmacological or non-pharmacological approaches, typically focus on prodromal phase of illness, characterized primarily by the presence of attenuated symptoms [1, 2]. Individuals who meet At Risk Mental State (ARMS) criteria have five times higher chance to be diagnosed with psychotic disorder or schizophrenia [3, 4]. Since the ARMS was developed for a population of help-seeking individuals, the data on prevalence of the ARMS status in

general population are rather scarce [5]. A recent systematic review of nine studies with non-help seeking individuals indicated ARMS prevalence of 1 to 8% [6].

One of the most consistent findings in ARMS research is cognitive impairment [7, 8]. Deficits in general intelligence, attention, executive functions, verbal fluency, working memory, and verbal and visual memory domains, but no impairment in processing speed, were confirmed in a meta-analysis of 1188 ARMS subjects and 1029 controls [9]. Recently, processing speed has been identified as another predictor of transition to psychosis [10, 11]. These results are consistent with those reported in schizophrenia patients [12]. Thus, cognitive impairment can be considered as one of the strongest factors predicting the risk of transition to psychosis [13].

Cognitive impairment correlates with a decline in social and occupational performance measured by the Social and Occupational Functioning Assessment Scale (SOFAS) not only in patients diagnosed with schizophrenia, but also in the ARMS subjects [14]. Deficit in social cognition of the ARMS subjects was found to be associated with low level of overall functioning and poor social skills [15, 16]. Furthermore, a meta-analysis revealed that the functional level of ARMS individuals is closer to that observed in people with psychosis than in healthy individuals [17].

One of the few studies with non-help seeking subjects showed that compared to healthy controls the ARMS subjects recruited from community had impaired cognition, poorer social functioning, and lower Global Assessment of Functioning score [18]. The profile of their cognitive deficit was similar to the cognitive pattern of their help-seeking counterparts.

## Aim

The aim of our study was to examine the prevalence of ARMS among non-help seeking adolescent population and to investigate its relationship to cognition, quality of life, non-psychotic psychopathology and functioning. We hypothesized that non-help seeking ARMS adolescents would have more psychiatric diagnoses, lower level of functioning and quality of live (QoL), and poorer cognitive performance, as compared to non-ARMS adolescents. The severity of ARMS symptoms would be negatively associated with general functioning, QoL, and cognitive performance.

## Ethics Approval

Study protocol was approved by the Ethical Committee of the National Institute of Mental Health, Klecany, Czech Republic. All participants older than 18 years provided written informed consent, for participants younger than 18 years the consent was obtained from their parents/legal representatives.

## Methods

## Study subjects

This was a cross-sectional study. Participating schools were identified through the publicly available registry of high schools in the administrative districts of Prague and Central Bohemia. In total, 82 high schools were approached and 14 (n = 14/82; 17%) agreed to participate in the project in 2019. Study participants were recruited through a two-phase process. The first phase (Phase 1) took place at high-schools and consisted of an educational lecture for students delivered by a study psychiatrist and initial screening for at risk symptoms with Prodromal Questionnaire-Brief version (PQ-BV) [19]. A subset of adolescents from Phase 1 with positive and negative PQ-BV screening (allocation 1:1) was randomly selected, invited into the second phase (Phase 2) and fully assessed (Fig. 1). Methods and primary results of the Phase 1 study are described in detail elsewhere [20]. Here we report the results of the Phase 2 study.

# Study Assessments

# Clinical characteristics

Basic demographic data (age, sex) were recorded. The Comprehensive Assessment of At Risk Mental States (CAARMS) interview was used to determine the following ARMS criteria: 1) attenuated psychotic symptoms (APS), this criterion identifies young people at risk of psychosis due to the subthreshold psychotic syndrome; 2) brief limited intermittent psychotic symptoms (BLIPS), this criterion identifies young people at risk of psychosis due to a recent history of frank psychotic symptoms that resolved spontaneously; and 3) vulnerability group, this criterion identifies young people at risk of psychosis due to the combination of a trait risk factor and a significant deterioration in psychosocial functioning [21]. The CAARMS assesses the frequency and intensity of psychopathology, including unusual thought content, non-bizarre ideas, perceptual abnormalities, and disorganized speech and predicts onset of psychosis in help-seeking populations with high sensitivity [3].

The Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) was used to obtain the full profile of current mental disorders. Presence of both threshold and subthreshold mental disorders was examined [22].

# Social functioning and QoL

The Social and Occupational Functioning Assessment Scale (SOFAS) was administered to evaluate the current level of social and occupational functioning. The SOFAS is a global rating of current functioning, a score within a range of 0 to 100, with lower values representing poorer functioning [23].

Finally, all subjects were evaluated with the KIDSCREEN-52, a self-report instrument based on the definition of QoL as a multidimensional construct, covering subjectively perceived physical, emotional, mental, social, and behavioral components of well-being and functioning [24].

# Cognitive functioning

Cognition was examined with a battery of tests measuring the following domains:

*Visual Memory.* The Rey complex figure test and recognition trial was administered (RCFT). The figure was placed in front of the participants, who were requested to copy the figure. The immediate recall (3 minutes) and delayed recall (30 minutes) reproductions were scored for the accuracy and placement of the design elements [25].

*Verbal Memory.* The Rey auditory verbal learning test (RAVLT). A 15 noun-word list (list A) was read to the participants. After presentation of 15 words the participants were requested to recall as many words as possible. The procedure was repeated 5 times. The 5 recall trials were summed into a single score. Delayed recall was obtained after 30 minutes [26]. The Logical memory subtest of the Wechsler Memory Scale (WMS-LM). The immediate recall (3 minutes) and delayed recall (30 minutes) scores were recorded [27].

*Processing speed.* Trail Making Test part A (TMT A). Part A requires the participant to connect series of numbered circles arrayed randomly on a sheet of paper using a pencil. The scoring is expressed as time to completion [28]. Trail Making Test part B (TMT B). Part B requires the participant to connect series of both numbered circles and letters arrayed randomly on a sheet of paper using a pencil. The scoring is expressed as time to completion [28]. The Digit Symbol coding test (DS) from the Wechsler Memory Scale – Third Edition. This task consists of rows containing small blank squares, each paired with a randomly assigned number from one to nine. A printed key pairs each number with a different symbol [29].

*Working memory.* The Spatial Span test from the Wechsler Memory Scale – Third Edition (WMS-III). This test consists of a board with ten spatially distributed cubes mounted on top of it. The examiner taps block sequences of increasing length that have to be repeated in the same (forward) or reverse (backward) order. The combined score was recorded [29].

# Statistical Analyses

Descriptive statistics were used to assess socio-demographic characteristics of the sample. We calculated prevalence rates of mental disorders diagnosed by K-SADS. The scores of SOFAS, KIDSCREEN-52, and cognitive tests were expressed as the mean values with standard deviations (SD). The distribution of each variable was tested by the degree of skewness and kurtosis [30]. Unpaired t-tests, Fisher´s exact tests, and Mann-Whitney U tests were used to assess the differences in current mental disorders, functioning, QoL, and cognitive performance between adolescents at-risk mental state positive (ARMS+) and adolescents at-risk mental state negative (ARMS-). Statistical significance for all tests was set at $p < .05$. Standardized effect size for each intergroup difference was calculated as Cohen's d. To analyze associations of CAARMS symptoms severity with functioning, QoL, and cognitive performance in

the total sample, we calculated the CAARMS symptoms severity scale as a sum of frequency scores of unusual thought content, non-bizarre ideas, perceptual abnormalities, and disorganized speech. Then we fitted a multivariate linear regression model to test the effect of CAARMS symptoms severity and the presence of threshold or subthreshold mental disorder on functioning, QoL, and cognitive impairment. Results of a linear regression model were expressed as standardized beta coefficients (β). Quality of model fit was assessed using the adjusted coefficient of determination ($R^2$).

The significant study results were corrected for multiple testing by the Bonferroni correction as follows: 1) SOFAS and KIDSCREEN-52 domain scores p = .05/11 = .0045; 2) Associations between CAARMS symptoms intensity and functioning and QoL p = .05/11 = .0045; 3) Associations between CAARMS symptom subscales and the SOFAS score p = .05/4 = .0125; and 4) Significant associations of respondents' clinical characteristics with the QoL domains - regression models p = 0.05/3 = 0.017. Analyses were conducted in the SPSS software package, version 23.0.

## Results

# Demographics and clinical characteristics

The total of 82 adolescents was enrolled into the study. Twenty-one participants met the ARMS attenuated psychotic symptoms criteria (ARMS+), no case with brief limited intermittent psychotic symptoms nor with the vulnerability traits was detected in the study sample. The ARMS + group and the ARMS- group (n = 61) did not differ in gender (females: 16/21 vs. 36/61; $X^2$ = 1.986; p = .2) and age (mean: 17.5, SD = 0.7 years vs. 17.4, SD = 0.9 years; t = 0.483; p = .7).

The ARMS + and ARMS- groups did not differ in the occurrence of major depressive disorder (0/21 vs. 2/61 cases; $X^2$ = 0.706; p = 1.0), anxiety disorders (4/21 vs. 6/61 cases; $X^2$ = 1.238; p = .3), or substance use disorders (3/21 vs. 2/61 cases; $X^2$ = 3.306; p = .1). No case of threshold psychotic disorder was found in the study sample; subthreshold mental disorders were more frequent in the ARMS + group than in the ARMS- group (10/21 vs 14/61 cases; $X^2$ = 4.592; p = .05). For details, see Table 1.

Table 1
Clinical characteristics of study sample.

| | ARMS_AP+ N = 21 | ARMS_AP- N = 61 | p* |
|---|---|---|---|
| **Any current threshold mental disorder, n (%)** | 6 (28.6) | 11 (18.0) | .3 |
| Major depressive disorder | 0 (0) | 2 (3.3) | 1.0 |
| Anxiety spectrum[A] | 4 (19.0) | 6 (9.8) | .3 |
| Psychotic spectrum | 0 (0) | 0 (0) | 1.0 |
| ADHD | 1 (1.6) | 1 (4.8) | .4 |
| Substance abuse[B] | 3 (14.3) | 2 (3.3) | .1 |
| Others[C] | 0 (0) | 0 (0) | 1.0 |
| **Any current subthreshold mental disorder** | 10 (47.6) | 14 (23.0) | .05 |
| Major depressive disorder | 1 (4.8) | 2 (3.3) | 1.0 |
| Anxiety spectrum[A] | 6 (28.6) | 12 (19.7) | .5 |
| ADHD | 1 (4.8) | 1 (1.6) | .5 |
| Others[C] | 2 (9.5) | 1 (1.6) | .2 |
| Abbreviations: | | | |
| ARMS, At Risk Mental State; AP+, Attenuated Psychosis positive; AP-, Attenuated Psychosis negative; ADHD, Attention Deficit Hyperactivity Disorder. | | | |
| **Notes**: | | | |
| * Fisher´s exact test | | | |
| [A] including panic disorder, simple phobia, agoraphobia, generalized anxiety disorder, and adjustment disorder | | | |
| [B] including alcohol and cannabinoids | | | |
| [C] including obsessive-compulsive disorder, eating disorders, behavioral disorders, autistic spectrum disorders, posttraumatic stress disorder | | | |

# Social functioning and QoL

Significantly lower mean SOFAS scores were observed in the ARMS + group than in the ARMS- group (t= -3.888; p < .001; Cohen's d = 0.99). No statistically significant differences in the mean KIDSCREEN-52 scores were found between the ARMS + and ARMS- groups. For details, see Table 2.

Table 2
SOFAS and KIDSCREEN-52 domains scores.

| | ARMS_AP+ N = 21 | ARMS_AP- N = 61 | p* | Cohen's d |
|---|---|---|---|---|
| SOFAS mean (SD) | 70.8 (12.3) | 80.9 (9.4) | < .001 | 0.99 |
| KIDSCREEN-52[A] mean (SD) | | | | |
| Physical Well-being | 43.3 (12.2) | 48.9 (13.1) | .09 | 0.43 |
| Psychological Well-being | 41.4 (8.1) | 44.2 (8.1) | .2 | 0.35 |
| Moods and Emotions | 41.9 (7.5) | 44.7 (7.3) | .1 | 0.38 |
| Self-Perception | 42.4 (11.4) | 45.3 (6.8) | .2 | 0.35 |
| Autonomy | 47.2 (7.9) | 46.4 (8.1) | .7 | 0.10 |
| Parent and Home Life | 42.9 (8.4) | 44.7 (8.8) | .4 | 0.21 |
| Financial Resources | 52.7 (8.0) | 54.3 (8.7) | .5 | 0.19 |
| Social Support and Peers | 46.8 (10.8) | 45.4 (8.0) | .5 | 0.16 |
| School Environment | 43.9 (7.2) | 45.3 (6.4) | .4 | 0.21 |
| Social Acceptance (Bullying) | 48.0 (10.3) | 50.0 (7.6) | .3 | 0.24 |

**Abbreviations:** ARMS, At Risk Mental State; AP+, Attenuated Psychosis positive; AP-, Attenuated Psychosis negative; SOFAS, Social and Occupational Functioning Assessment Scale.

**Notes**:

* unpaired t-test; [A] T-scores according to the Czech general adolescent population data

*Associations between CAARMS symptoms intensity and functioning and QoL in the total sample.*

For the whole study sample, there was a significant negative association between the CAARMS symptoms intensity and SOFAS score (β = − .51; $R^2$ = 0.26; p < .001). In the regression model with CAARMS symptoms subscales ($R^2$ = 0.23, F [4, 77] = 6.987, p < .001), only non-bizarre ideas (β = − .25; p = .03), and disorganized speech (β = − .23; p = .04) were significantly associated with the SOFAS score, but both results lost the statistical significance after the Bonferroni correction. No statistically significant relationship with the presence of current K-SADS threshold/subthreshold diagnoses was found.

CAARMS symptoms intensity was associated with Physical Well-being ($R^2$ = 0.11, F [3, 78] = 4.383, p = .007), Psychological Well-being ($R^2$ = 0.13, F [3, 78] = 5.088, p = .003), Moods and Emotions ($R^2$ = 0.17, F [3, 78] = 6.461, p = .001), Self-Perception ($R^2$ = 0.13, F [3, 78] = 5.124, p = .003), and Parent and Home Life ($R^2$ = 0.08, F [3, 78] = 3.228, p = .03). The association between CAARMS symptom intensity and Parent and Home Life lost the statistical significance after the Bonferroni correction. No other significant associations of respondents' clinical characteristics and KIDSCREEN52 domains were detected. For details, see Table 3.

Table 3
Significant associations of respondents' clinical characteristics with the QoL domains.

| **Physical Well-being** | **β** | **p** |
|---|---|---|
| CAARMS symptoms intensity | -0.28 | .01 |
| Presence of current threshold diagnosis | -0.23 | .04 |
| Presence of subthreshold diagnosis | 0.02 | .9 |
| $R^2$ = 0.11; p = .007 | | |
| **Psychological Well-being** | β | p |
| CAARMS symptoms intensity | -0.30 | .005 |
| Presence of current threshold diagnosis | -0.11 | .3 |
| Presence of subthreshold diagnosis | -0.21 | .05 |
| $R^2$ = 0.13; p = .003 | | |
| **Moods and Emotions** | β | p |
| CAARMS symptoms intensity | -0.41 | < .001 |
| Presence of current threshold diagnosis | -0.04 | .7 |
| Presence of subthreshold diagnosis | -0.12 | .3 |
| $R^2$ = 0.17; p = .001 | | |
| **Self-Perception** | | |
| CAARMS symptoms intensity | -0.30 | .006 |
| Presence of current threshold diagnosis | -0.23 | .03 |
| Presence of subthreshold diagnosis | -0.07 | .5 |
| $R^2$ = 0.13; p = .003 | | |
| **Parent and Home Life** | | |
| CAARMS symptoms intensity | -0.22 | .047 |
| Presence of current threshold diagnosis | -0.21 | .06 |
| Presence of subthreshold diagnosis | -0.08 | .4 |
| $R^2$ = 0.08; p = .03 | | |

**Abbreviations**: CAARMS, The Comprehensive Assessment of At Risk Mental States.

# Cognitive functioning

No statistically significant differences in visual memory, verbal memory, processing speed, or working memory were found between the ARMS + and ARMS- groups. With observed effect sizes ranging from Cohen´s d = 0.0 for The Spatial Span test to d = 0.37 for the Trail Making Test part A. For details, see Table 4. Analysis of the total sample did not yield any significant associations between CAARMS symptoms intensity, presence of threshold or subthreshold mental disorder and cognitive performance.

Table 4
Cognitive functioning.

| | ARMS_AP+ N = 21 | ARMS_AP- N = 58 | p | Cohen's d |
|---|---|---|---|---|
| Visual Memory | | | | |
| CFT 3 | 22.1 (7.2) | 21.2 (6.6) | .6[A] | 0.13 |
| CFT 30 | 21.7 (6.9) | 21.1 (6.8) | .7 [A] | 0.09 |
| Verbal Memory | | | | |
| AVLT I-V | 55.4 (6.9) | 53.6 (7.9) | .4 [A] | 0.23 |
| AVLT 30 | 12.0 (2.2) | 11.6 (2.7) | .5 [A] | 0.16 |
| WMS LogM | 47.3 (7.8) | 48.3 (8.9) | .6 [A] | 0.12 |
| WMS LogM 30 | 30.2 (5.0) | 31.5 (7.5) | .5 [A] | 0.19 |
| Processing Speed | | | | |
| TMT A | 25.9 (8.5) | 29.6 (10.6) | .1 [A] | 0.37 |
| TMT B | 62.8 (21.3) | 64.6 (28.8) | .8 [B] | 0.07 |
| WAIS SymbCode | 83.4 (12.8) | 81.7 (13.8) | .6 [A] | 0.13 |
| Working memory | | | | |
| WMS Spatial span | 17.8 (3.2) | 17.8 (3.1) | 1.0 [A] | 0.00 |

**Abbreviations:** ARMS, At Risk Mental State; AP+, Attenuated Psychosis positive; AP-, Attenuated Psychosis negative; CFT, Complex Figure Test; AVLT, Auditory Verbal Learning Test; WMS, Wechsler Memory Scale; TMT, Trail Making Test; WAIS, Wechsler Adult Intelligence Scale.

**Notes**: [A] unpaired t-test; [B] Mann-Whitney U test

# Discussion

Our results revealed in a sample of non-help seeking adolescents drawn from general population high prevalence of individuals with at-risk mental state to develop psychosis (26%), higher than reported previously [6, 31]. Furthermore, ARMS + adolescents had lower social and occupational functioning, and more subthreshold mental disorders compared to ARMS- adolescents. All of the ARMS + subjects belonged to the Attenuated Psychotic Syndrome (APS) group. The

Subclinical psychotic syndrome in the population of non-help seeking adolescents have negative impact on their quality of life. We observed negative association between the severity of CAARMS symptoms and five subscales of KIDSCREEN: Physical Well-being, Psychological Well-being, Moods and emotions, Self-Perception, Parent and Home life. These domains cover crucial aspects of daily life, provide information on general health, life satisfaction, mood, loneliness, and relations with parents. The results further corroborate findings from previous research, which showed with the same QoL instrument that the ARMS subjects had poorer results than controls in Physical Well-being, Psychological Well-being and School Environment [32]. Overall level of functioning, as indexed by the SOFAS score, was similar to the functioning level of non-help-seeking adolescent samples from other studies [31, 33]. The SOFAS score in our sample was mostly affected by the severity of CAARMS symptoms.

Surprisingly, we failed to detect any significant difference in cognitive performance between the ARMS + and ARMS- groups. The data contradict previously reported impairment in processing and motor speed among non-help seeking ARMS subjects [18]. The discrepancy can be partially explained by the different recruitment methods used and/or dissimilar cognitive tests administered. Another possible explanation of our negative findings is a relatively small sample size. Cognitive performance in our study was not associated with the CAARMS symptoms severity, neither with the presence of threshold or subthreshold mental disorder. The lack of associations can be attributed to the lower prevalence of comorbidities.

In our non-help-seeking sample, the prevalence of other psychiatric disorders was lower than reported previously [34]. Although the difference in the prevalence rates of threshold mental disorders between ARMS+/ARMS- subjects did not reach statistical significance, the subthreshold mental disorders were more frequent in the ARMS + group. Their prevalence was similar to that observed in larger samples [35]. Results of a longitudinal study with help-seeking ultra-high risk youth showed that individuals with comorbidities had more severe symptoms, higher distress and lower level of functioning [36]. In addition, those with both comorbid anxiety and depressive diagnoses were more severely functionally impaired.

Recent research suggested that the earliest stages of mental disorders can be described by waxing and waning subthreshold states of depression and anxiety, often accompanied by psychotic-like disturbances of salience or perception and emotional dysregulation [37]. Thus, psychotic experiences can be seen as a transdiagnostic phenomenon, transitory in 80% of individuals, majority of them are diagnosed with a non-psychotic disorder [38].

High prevalence of AMRS + subjects in our sample should be viewed in light of several limitations. First, the onset of psychosis may also occur via previously identified nonpsychotic clinical risk syndromes [39]. Second, most of the individuals who will later develop psychosis (up to 95%) remain undetected at the

time of their ARMS stage [40]. Higher prevalence found in our study subjects can be attributed to the sampling bias, as the subjects with subtle symptoms are more prone to participate in testing. Since there were no adolescents with threshold psychosis detected in our sample, it is possible that some subjects developed psychosis after initial screening and subsequently refused to participate in the study phase two. Finally, false positivity could also play the role.

Study limitation is the absence of assessment of negative symptoms, not covered by the brief version of CAARMS. Negative symptoms are associated more strongly with cognitive, social, and functional impairments in help-seeking individuals than positive or depressive symptoms [15, 41, 42]. Cross-sectional design and a relatively small sample limit generalizability of our results to the entire ARMS population.

The psychosis-predictive ability of CHR criteria in general population is unknown. There is a meta-analytical evidence of overall risk enrichment (pretest risk for psychosis at 38 months = 15%) in help-seeking samples selected for CHR assessment, as compared to the general population (pretest risk of psychosis at 38 months = 0.1%) [43]. The authors emphasised that intensive outreach campaigns and a higher proportion of self-referrals dilute the pretest risk for psychosis. Accordingly, the EPA guidance recommends restricting the CHR assessment to individuals already distressed by mental problems and seeking help [44]. Novel research approaches stress out sequential screening of CHR-P subjects, with future use of prescreening e-health methods [40].

The challenge is what kind of help can we offer and deliver to the non-help seeking ARMS subjects. In general, treatment of the ARMS individuals has two aims: to manage current symptoms and problems, and to reduce the risk of developing a psychotic disorder [45]. Current international guidelines recommend the least restrictive approach, i.e. psychological interventions as the first-line treatment, while the administration of antipsychotics is reserved for patients who do not respond to psychological management or who suffer from severe and/or progressive high-risk symptoms [46, 47]. It is important that the initiation of pharmacotherapy is based on shared-decision making [48, 49]. Moreover, scarce data indicate that cognitive remediation in the ARMS subjects can also improve functional outcome and cognition [50]. Recent meta-analyses concluded that there is a lack of evidence to favour specific effective interventions to prevent psychosis in CHR-P individuals [51, 52].

# Conclusion

In our study, we confirmed that non-help seeking adolescents with at-risk mental state experience significant functional impairment compared to their healthy peers. Moreover, ARMS + individuals had greater number of subthreshold non-psychotic psychiatric comorbidities. Recent research suggested that the earliest stages of mental disorders can be described by waxing and waning subthreshold states of depression and anxiety, often accompanied by psychotic-like disturbances of salience or perception and emotional dysregulation [37]. The risk of transition into psychosis grows along with increasing intensity

of subthreshold psychotic symptoms and decrease in functioning [53]. In the management, non-pharmacological interventions are preferred over pharmacotherapy, as the first-line option.

# Declarations


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### Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

# References


1. Hartmann JA, Nelson B, Ratheesh A, et al. At-risk studies and clinical antecedents of psychosis, bipolar disorder and depression: a scoping review in the context of clinical staging. Psychol Med. 2019;49:177 – 89. doi: 10.1017/S0033291718001435
2. Pelizza L, Azzali S, Paterlini F, et al. The "Reggio Emilia At-Risk Mental States" program: A diffused, "liquid" model of early intervention in psychosis implemented in an Italian Department of Mental Health. Early Interv Psychiatry. 2019;13:1513-24. doi: 10.1111/eip.12851
3. Fusar-Poli P, Rutigliano G, Stahl D, et al. Long-term validity of the At Risk Mental State (ARMS) for predicting psychotic and non-psychotic mental disorders. Eur Psychiatry. 2017;42:49–54. doi: 10.1016/j.eurpsy.2016.11.010
4. McHugh MJ, McGorry PD, Yuen HP, et al. The Ultra-High-Risk for psychosis groups: Evidence to maintain the status quo. Schizophr Res. 2018;195:543-8. doi: 10.1016/j.schres.2017.09.003
5. Nelson B, Fusar-Poli P, Yung AR. Can we detect psychotic-like experiences in the general population? Curr Pharm Des. 2012;18:376 – 85. doi: 10.2174/138161212799316136.
6. Howie C, Potter C, Shannon C, et al. Screening for the at-risk mental state in educational settings: A systematic review. Early Interv Psychiatry. 2020;14:643 – 54. doi: 10.1111/eip.12926
7. Giuliano AJ, Li H, Mesholam-Gately RI, et al. Neurocognition in the psychosis risk syndrome: a quantitative and qualitative review. Curr Pharm Des. 2012;18:399–415. doi: 10.2174/138161212799316019
8. Hou CL, Xiang YT, Wang ZL, et al. Cognitive functioning in individuals at ultra-high risk for psychosis, first-degree relatives of patients with psychosis and patients with first-episode schizophrenia. Schizophr Res. 2016;174:71 – 6. doi: 10.1016/j.schres.2016.04.034

9. Fusar-Poli P, Deste G, Smieskova R, et al. Cognitive functioning in prodromal psychosis: a meta-analysis. Arch Gen Psychiatry. 2012;69:562 – 71. doi: 10.1001/archgenpsychiatry.2011.1592
10. Cannon TD, Yu C, Addington J, Bearden CE, et al. An Individualized Risk Calculator for Research in Prodromal Psychosis. Am J Psychiatry. 2016;173:980-8. doi:10.1176/appi.ajp.2016.15070890
11. Zheng W, Zhang QE, Cai DB, et al. Neurocognitive dysfunction in subjects at clinical high risk for psychosis: A meta-analysis. J Psychiatr Res. 2018;103:38–45. doi:10.1016/j.jpsychires.2018.05.001
12. Bowie CR, Harvey PD. Cognitive deficits and functional outcome in schizophrenia. Neuropsychiatr Dis Treat. 2016;2:531–6. doi:10.2147/nedt.2006.2.4.531
13. Fusar-Poli P, Bonoldi I, Yung AR, et al. Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. Arch Gen Psychiatry. 2012:69;220-9. doi: 10.1001/archgenpsychiatry.2011.1472
14. Higuchi Y, Sumiyoshi T, Seo T, et al. Associations between daily living skills, cognition, and real-world functioning across stages of schizophrenia; a study with the Schizophrenia Cognition Rating Scale Japanese version. Schizophr Res Cogn. 2017;7:13–8. doi:10.1016/j.scog.2017.01.001
15. Glenthøj LB, Fagerlund B, Hjorthøj C, et al. Social cognition in patients at ultra-high risk for psychosis: What is the relation to social skills and functioning? Schizophr Res Cogn. 2016;5:21–7. doi:10.1016/j.scog.2016.06.004
16. Spada G, Molteni S, Pistone C, et al. Identifying children and adolescents at ultra high risk of psychosis in Italian neuropsychiatry services: a feasibility study. Eur Child Adolesc Psychiatry. 2016;25:91–106. doi: 10.1007/s00787-015-0710-8
17. Fusar-Poli P, Rocchetti M, Sardella A, et al. Disorder, not just state of risk: meta-analysis of functioning and quality of life in people at high risk of psychosis. Br J Psychiatry. 2015;207:198–206. doi: 10.1192/bjp.bp.114.157115
18. Haining K, Matrunola C, Mitchell L, et al. Neuropsychological deficits in participants at clinical high risk for psychosis recruited from the community: relationships to functioning and clinical symptoms. Psychol Med. 2020;50:77–85. doi: 10.1017/S0033291718003975
19. Loewy RL, Pearson R, Vinogradov S, et al. Psychosis risk screening with the Prodromal Questionnaire–brief version (PQ-B). Schizophr Res. 2011;129:42 – 6. doi: 10.1016/j.schres.2011.03.029
20. Sebela A, Dorazilova A, Vorackova V, al. Prevalence of high-risk symptoms for psychosis in population of adolescents: Czech version of The Prodromal Questionnaire Brief. Cesk Psychol. 2019;63:430 – 44
21. Yung AR, Yuen HP, McGorry PD, et al. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. Aust N Z J Psychiatry. 2005;39:964–71. doi: 10.1080/j.1440-1614.2005.01714.x.
22. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997;36:980-8. doi: 10.1097/00004583-199707000-00021

23. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: American Psychiatric Association; 2020. ISBN 978-0890420256.
24. Ravens-Sieberer U, Gosch A, Rajmil L, et al. The KIDSCREEN-52 quality of life measure for children and adolescents: psychometric results from a cross-cultural survey in 13 European countries. Value Health. 2008;11:645 – 58. doi: 10.1111/j.1524-4733.2007.00291.x
25. Meyers JE, Meyers KR. Rey complex figure test and recognition trial (RCFT). Odessa, FL: Psychological Assessment Resources; 1995.
26. Schmidt M. Rey auditory verbal learning test: A handbook. Los Angeles, CA: Western Psychological Services; 1996.
27. Abikoff H, Alvir J, Hong G, et al. Logical memory subtest of the Wechsler Memory Scale: age and education norms and alternate-form reliability of two scoring systems. J Clin Exp Neuropsychol. 1987;9:435 – 48. doi: 10.1080/01688638708405063
28. Spreen O, Strauss E. A Compendium of neuropsychological test: Administration, norms, and commentary (3rd ed.). New York, NY: Oxford University Press; 2006. ISBN 978-0195159578
29. Wechsler, D. Wechsler Adult Intelligence Scale—Third edition (WAIS-III). San Antonio, TX: Harcourt Assessment; 1997.
30. Gravetter, F, Wallnau L. Essentials of statistics for the behavioral sciences (10th ed.). Belmont, CA: Wadsworth; 2020. ISBN 978-0357365298
31. Mills JG, Fusar-Poli P, Morgan C, et al. People meeting ultra high risk for psychosis criteria in the community. World Psychiatry. 2017;16:322–3. doi:10.1002/wps.20463
32. Nitka F, Richter J, Parzer P, et al. Health-related quality of life among adolescents: A comparison between subjects at ultra-high risk for psychosis and healthy controls. Psychiatry Res. 2016;235:110-5. doi: 10.1016/j.psychres.2015.11.040
33. Michel C, Schnyder N, Schmidt SJ, et al. Functioning mediates help-seeking for mental problems in the general population. Eur Psychiatry. 2018;54:1–9. doi: 10.1016/j.eurpsy.2018.06.009
34. Kelleher I, Murtagh A, Molloy C, et al. Identification and characterization of prodromal risk syndromes in young adolescents in the community: a population-based clinical interview study. Schizophr Bull. 2011;38:239–46. doi: 10.1093/schbul/sbr164
35. Roberts RE, Fisher PW, Turner JB, et al. Estimating the burden of psychiatric disorders in adolescence: the impact of subthreshold disorders. Soc Psychiatry Psychiatr Epidemiol. 2015;50:397–406. doi: 10.1007/s00127-014-0972-3
36. Lim J, Rekhi G, Rapisarda A, et al. Impact of psychiatric comorbidity in individuals at Ultra High Risk of psychosis - Findings from the Longitudinal Youth at Risk Study (LYRIKS). Schizophr Res. 2015;164:8–14. doi: 10.1016/j.schres.2015.03.007
37. McGorry PD, Hartmann JA, Spooner R, et al. Beyond the "at risk mental state" concept: transitioning to transdiagnostic psychiatry. World Psychiatry. 2018;17:133 – 42. doi:10.1002/wps.20514

38. van Os J, Reininghaus U. Psychosis as a transdiagnostic and extended phenotype in the general population. World Psychiatry. 2016;15:118 – 24. doi:10.1002/wps.20310
39. Lee TY, Lee J, Kim M, et al. Can We Predict Psychosis Outside the Clinical High-Risk State? A Systematic Review of Non-Psychotic Risk Syndromes for Mental Disorders. Schizophr Bull. 2018;44:276 – 85. doi:10.1093/schbul/sbx173
40. Fusar-Poli P, Sullivan SA, Shah JL, et al. Improving the Detection of Individuals at Clinical Risk for Psychosis in the Community, Primary and Secondary Care: An Integrated Evidence-Based Approach. Front Psychiatry. 2019;10:774. doi:10.3389/fpsyt.2019.00774
41. Lee SJ, Kim KR, Lee SY, et al. (2017). Impaired Social and Role Function in Ultra-High Risk for Psychosis and First-Episode Schizophrenia: Its Relations with Negative Symptoms. Psychiatry Investig. 2017;14:539 – 45. doi: 10.4306/pi.2017.14.5.539
42. Meyer EC, Carrión RE, Cornblatt BA, et al. The relationship of neurocognition and negative symptoms to social and role functioning over time in individuals at clinical high risk in the first phase of the North American Prodrome Longitudinal Study. Schizophr Bul.l 2014;40:1452–61. doi:10.1093/schbul/sbt235
43. Fusar-Poli P, Schultze-Lutter F, Cappucciati M, et al. The Dark Side of the Moon: Meta-analytical Impact of Recruitment Strategies on Risk Enrichment in the Clinical High Risk State for Psychosis. Schizophr Bull. 2016;42:732 – 43. doi:10.1093/schbul/sbv162
44. Schultze-Lutter F, Michel C, Schmidt SJ, et al. EPA guidance on the early detection of clinical high risk states of psychoses. Eur Psychiatry. 2015;30:405 – 16. doi:10.1016/j.eurpsy.2015.01.010
45. Yung AR. Treatment of people at ultra-high risk for psychosis. World Psychiatry. 2017;16:207–8. doi:10.1002/wps.20424
46. Schmidt SJ, Schultze-Lutter F, Schimmelmann BG, et al. EPA guidance on the early intervention in clinical high risk states of psychoses. Eur Psychiatry. 2015;30:388–404. doi: 10.1016/j.eurpsy.2015.01.013
47. Addington J, Addington D, Abidi S, et al. Canadian Treatment Guidelines for Individuals at Clinical High Risk of Psychosis. Can J Psychiatry. 2017;62:656 – 61. doi: 10.1177/0706743717719895
48. Younas M, Bradley E, Holmes N, Sud D, Maidment ID. Mental health pharmacists views on shared decision-making for antipsychotics in serious mental illness. Int J Clin Pharm. 2016;38:1191-9. doi: 10.1007/s11096-016-0352-z.
49. Ashoorian DM, Davidson RM. Shared decision making for psychiatric medication management: a summary of its uptake, barriers and facilitators. Int J Clin Pharm. 2021;43:759 – 63. doi: 10.1007/s11096-021-01240-3. Epub 2021 Jan 29. PMID: 33515136.
50. Glenthøj LB, Hjorthøj C, Kristensen TD, et al. The effect of cognitive remediation in individuals at ultra-high risk for psychosis: a systematic review. NPJ Schizophr. 2017;3:20. doi:10.1038/s41537-017-0021-9
51. Davies C, Cipriani A, Ioannidis JPA, et al. Lack of evidence to favor specific preventive interventions in psychosis: a network meta-analysis. World Psychiatry. 2018;17:196–209. doi:10.1002/wps.20526

52. Devoe DJ, Farris MS, Townes P, et al. Interventions and Transition in Youth at Risk of Psychosis: A Systematic Review and Meta-Analyses. J Clin Psychiatry. 2020;81:17r12053. doi:10.4088/JCP.17r12053
53. Valmaggia LR, Stahl D, Yung AR, et al. Negative psychotic symptoms and impaired role functioning predict transition outcomes in the at-risk mental state: a latent class cluster analysis study. Psychol Med. 2013;43:2311-25. doi: 10.1017/S0033291713000251

# Figures

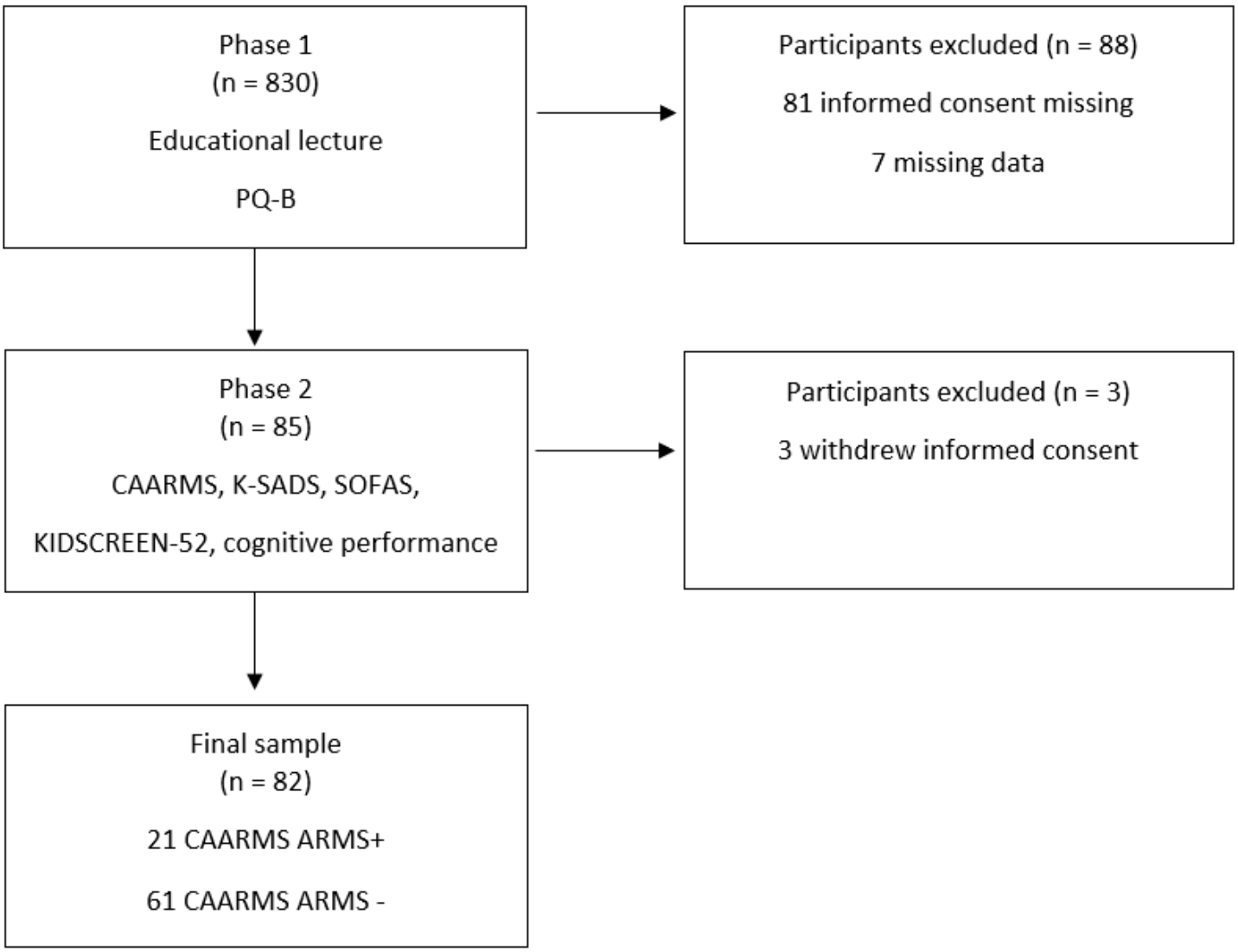


**Figure 1**

**Study flow, recruitment and assessment pathway**

**Abbreviations:** PQ-B, Prodromal Questionnaire-Brief version; CAARMS, The Comprehensive Assessment of At Risk Mental States; K-SADS, Kiddie Schedule for Affective Disorders and Schizophrenia; SOFAS, Social and Occupational Functioning Assessment Scale; ARMS, At Risk Mental State.