Introduction

There are two key approaches for identifying people with early signs that may suggest a high risk of developing psychosis or schizophrenia. The first approach is based on Huber’s Basic Symptoms which focuses on a detailed way of describing phenomenological (subjective) disturbances. Because the basic symptoms refer only to subtle subjectively experienced abnormalities, they may reflect an earlier phase in the disease process than the second approach, which identifies at risk mental states as a combination of: a family history of psychosis (familial risk) plus non-specific symptoms and recent decline in functioning; recent onset Attenuated Psychotic Symptoms with decline in functioning; and Brief Limited Intermittent Psychotic Symptoms.

Cognitive deficits are frequent in people with schizophrenia, and may also be apparent in people at high risk. This table presents the available evidence for cognitive performance in this group of people.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with early signs or symptoms of first episode psychosis or schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist which describes a preferred way to present a meta-analysis. Reviews were assigned a low, medium or high possibility of reporting bias* depending on how many items were checked. For instance, a low possibility of bias would be assigned to reviews checking over 66% of items, a medium possibility between 33 and 66% and a high possibility would be given to reviews checking less than 33%. Reviews rated as having a high possibility of reporting bias have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomized controlled trials (RCT) may be downgraded to moderate, low or very low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise and direct with low associated risks (see end of table for an explanation of these terms). The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of the Schizophrenia Research Institute.
Results
We found six systematic reviews that met our inclusion criteria.3-8

See PRISMA checklists for assessment of reporting transparency.

Conclusions
• High quality evidence shows a small to medium sized effect of lower general intelligence, executive functioning, attention, visual memory and social cognition in people at high risk of psychosis compared with controls. Moderate to high quality evidence also suggests lower visual-spatial ability, olfactory functioning, verbal fluency, verbal memory, working memory, and learning.

• High quality evidence suggests people at clinical high risk of psychosis and familial high risk of psychosis are similarly impaired on processing speed, verbal and visual memory, attention and language fluency when compared with controls. People at familial high risk were more impaired on premorbid and current IQ than those at clinical high risk, and those at clinical high risk were more impaired on visuospatial working memory than those at familial high risk.

• Compared with controls, moderate quality evidence showed that people at high risk who converted to psychosis showed a medium size effect of lower olfactory functioning, general cognitive ability, language functioning, visual-spatial ability, memory, attention and executive functioning prior to conversion.

• Compared with people at high risk who did not convert to psychosis, moderate quality evidence showed that people at high risk who did converted to psychosis showed small to medium sized effects of poor visual learning and working memory. Low to moderate quality evidence also suggests a medium sized effect of lower general intelligence, verbal fluency, verbal memory, and visual memory.
Signs and Symptoms – Cognition in people at high-risk of psychosis

Bora E, Lin A, Wood SJ, Yung AR, McGorry PD, Pantelis C

Cognitive deficits in youth with familial and clinical high risk to psychosis: A systematic review and meta-analysis

View review abstract online

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Cognitive functioning in people at clinical high risk (UHR) and familial high risk (FHR) for psychosis</th>
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<tr>
<td>Summary of evidence</td>
<td>High quality evidence (consistent, precise, direct, large samples) suggests people at clinical high risk of psychosis and familial high risk of psychosis are similarly impaired on processing speed, verbal and visual memory, attention and language fluency when compared with controls, showing small to medium sized effects. People at familial high risk were more impaired on premorbid and current IQ than those at clinical high risk, and those at clinical high risk were more impaired on visuospatial working memory</td>
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</tbody>
</table>

Cognitive functioning

Significant, small to medium size effect of poor premorbid IQ in UHR and FHR groups compared with controls, with the FHR group showing the greatest deficit

UHR: 9 studies, N = 1370, d = 0.30, 95%CI 0.13 to 0.48, p < 0.001, I² = 0.04%, Q-test p = 0.02
FHR: 6 studies, N = 770, d = 0.63, 95%CI 0.47 to 0.79, p < 0.001, I² = 0%, Q-test p = 0.60
Q_B = 13.1, p < 0.001

Significant, medium to large size effect of poor current IQ in UHR and FHR groups compared with controls, with the FHR group showing the greatest deficit

UHR: 12 studies, N = 1440, d = 0.40, 95%CI 0.25 to 0.54, p < 0.001, I² = 0.02%, Q-test p = 0.15
FHR: 8 studies, N = 900, d = 0.81, 95%CI 0.61 to 1.01, p < 0.001, I² = 0.04%, Q-test p = 0.07
Q_B = 20.0, p < 0.001

Significant, small to medium size effect of poor visuospatial working memory in UHR and FHR groups compared with controls, with the UHR group showing the greatest deficit

UHR: 9 studies, N = 802, d = 0.71, 95%CI 0.39 to 1.04, p < 0.001, I² = 0.18%, Q-test p < 0.001
FHR: 4 studies, N = 426, d = 0.35, 95%CI 0.01 to 0.71, p = 0.04, I² = 0.09%, Q-test p = 0.02
Q_B = 4.6, p = 0.03

Significant, small to medium size effect of poor processing speed in UHR and FHR groups
Signs and Symptoms – Cognition in people at high-risk of psychosis

compared with controls, with no significant differences between groups
- UHR: 8 studies, N = 974, d = 0.47, 95%CI 0.27 to 0.66, p < 0.001, I² = 0.04%, Q-test p = 0.04
- FHR: 13 studies, N = 1494, d = 0.35, 95%CI 0.22 to 0.49, p < 0.001, I² = 0.02%, Q-test p = 0.13
  \[ Q_{B} \ p > 0.05 \]

Significant, medium size effect of poor verbal memory in UHR and FHR groups compared with controls, with no significant differences between groups
- UHR: 10 studies, N = 1205, d = 0.50, 95%CI 0.32 to 0.68, p < 0.001, I² = 0.04%, Q-test p = 0.03
- FHR: 12 studies, N = 1547, d = 0.45, 95%CI 0.29 to 0.61, p < 0.001, I² = 0.03%, Q-test p = 0.06
  \[ Q_{B} \ p > 0.05 \]

Significant, medium size effect of poor visual memory in UHR and FHR groups compared with controls, with no significant differences between groups
- UHR: 8 studies, N = 955, d = 0.50, 95%CI 0.23 to 0.77, p = 0.0002, I² = 0.10%, Q-test p = 0.001
- FHR: 8 studies, N = 985, d = 0.51, 95%CI 0.30 to 0.72, p < 0.001, I² = 0.04%, Q-test p = 0.08
  \[ Q_{B} \ p > 0.05 \]

Significant, small to medium size effect of poor verbal working memory in UHR and FHR groups compared with controls, with no significant differences between groups
- UHR: 9 studies, N = 1136, d = 0.41, 95%CI 0.20 to 0.61, p < 0.001, I² = 0.06%, Q-test p = 0.007
- FHR: 10 studies, N = 1206, d = 0.32, 95%CI 0.12 to 0.51, p = 0.001, I² = 0.05%, Q-test p = 0.02
  \[ Q_{B} \ p > 0.05 \]

Significant, small size effect of poor attention in UHR and FHR groups compared with controls, with no significant differences between groups
- UHR: 8 studies, N = 1042, d = 0.37, 95%CI 0.25 to 0.50, p < 0.001, I² = 0%, Q-test p = 0.59
- FHR: 14 studies, N = 1451, d = 0.30, 95%CI 0.16 to 0.44, p < 0.001, I² = 0.03%, Q-test p = 0.08
  \[ Q_{B} \ p > 0.05 \]

Significant, small to medium size effect of poor language fluency in UHR and FHR groups compared with controls, with no significant differences between groups
- UHR: 8 studies, N = 930, d = 0.52, 95%CI 0.30 to 0.74, p < 0.001, I² = 0.06%, Q-test p = 0.01
- FHR: 10 studies, N = 1149, d = 0.39, 95%CI 0.16 to 0.61, p = 0.001, I² = 0.08%, Q-test p = 0.002
  \[ Q_{B} \ p > 0.05 \]

Meta-regression of the UHR studies showed that increased deterioration in functioning was associated with more severe deficits in verbal memory, premorbid IQ and attention. In FHR studies, symptomatic subjects were significantly more impaired than asymptomatic subjects in the two domains examined: verbal memory and processing speed. Lower transition to psychosis rate was significantly associated with higher IQ.
Signs and Symptoms – Cognition in people at high-risk of psychosis

Authors report no publication bias

<table>
<thead>
<tr>
<th>Consistency‡</th>
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**Bora E, Murray RM**

**Meta-analysis of cognitive deficits in ultra-high risk to psychosis and first-episode psychosis: Do the cognitive deficits progress over, or after, the onset of psychosis?**


**View review abstract online**

**Comparison**

Changes in cognitive functioning over time in people at ultra-high risk of psychosis (UHR) compared with people with first-episode psychosis (FEP) or controls

**Summary of evidence**

High quality evidence (precise, direct, consistent, medium to large sized samples) suggests small improvements in cognitive domains over time in people at ultra-high risk of psychosis, people with first-episode psychosis and controls. Controls showed superior performance on verbal working memory and language fluency tasks

**Cognitive functioning over time (1 to 5 years)**

*Significant, small improvement in verbal working memory over time in UHR and controls, with no improvement in FEP. Controls showed significantly more improvement*

FEP: 10 studies, $N = 503$, $d = 0.13$, 95%CI -0.03 to 0.28, $p = 0.10$, $I^2 = 0.02\%$, Q-test $p = 0.20$

UHR: 8 studies, $N = 224$, $d = 0.20$, 95%CI 0.01 to 0.39, $p = 0.04$, $I^2 = 0\%$, Q-test $p = 0.97$

Controls: 7 studies, $N = 268$, $d = 0.34$, 95%CI 0.16 to 0.51, $p < 0.001$, $I^2 = 0\%$, Q-test $p = 0.79$

$Q_B = 4.10$, $p = 0.04$

*Significant, small improvement in language fluency over time in FEP and controls, with no improvement in UHR. Controls showed significantly more improvement*

FEP: 12 studies, $N = 575$, $d = 0.14$, 95%CI 0.01 to 0.27, $p = 0.04$, $I^2 = 0.02\%$, Q-test $p = 0.15*
Signs and Symptoms – Cognition in people at high-risk of psychosis

**Significant, small improvement in global cognition over time in UHR, FEP and controls, with no significant differences between groups**

- **UHR:** 10 studies, N = 235, d = 0.03, 95%CI -0.15 to 0.20, \( p = 0.76, I^2 = 0\%\), Q-test \( p = 0.97 \)
- **Controls:** 9 studies, N = 364, d = 0.31, 95%CI 0.14 to 0.49, \( p < 0.001, I^2 = 0.02\%\), Q-test \( p = 0.23 \)
  \[ Q_B = 4.9, p = 0.03 \]

**Significant, small improvement in processing speed over time in UHR, FEP and controls, with no significant differences between groups**

- **FEP:** 17 studies, N = 905, d = 0.30, 95%CI 0.20 to 0.39, \( p < 0.001, I^2 = 0\%\), Q-test \( p = 0.54 \)
- **UHR:** 14 studies, N = 560, d = 0.23, 95%CI 0.11 to 0.35, \( p < 0.001, I^2 = 0\%\), Q-test \( p = 0.95 \)
- **Controls:** 11 studies, N = 405, d = 0.38, 95%CI 0.24 to 0.52, \( p < 0.001, I^2 = 0\%\), Q-test \( p = 0.94 \)
  \[ Q_B p > 0.05 \]

**Significant, small improvement in verbal memory over time in UHR, FEP and controls, with no significant differences between groups**

- **FEP:** 12 studies, N = 627, d = 0.19, 95%CI 0.08 to 0.30, \( p < 0.001, I^2 = 0\%\), Q-test \( p = 0.84 \)
- **UHR:** 9 studies, N = 242, d = 0.18, 95%CI 0.0 to 0.36, \( p = 0.05, I^2 = 0\%\), Q-test \( p = 0.64 \)
- **Controls:** 8 studies, N = 299, d = 0.38, 95%CI 0.21 to 0.54, \( p < 0.001, I^2 = 0\%\), Q-test \( p = 0.85 \)
  \[ Q_B p > 0.05 \]

**Significant, small improvement in visual memory over time in FEP and controls, and a trend improvement for UHR groups, with no significant differences between groups**

- **FEP:** 11 studies, N = 702, d = 0.33, 95%CI 0.19 to 0.47, \( p < 0.001, I^2 = 0.02\%\), Q-test \( p = 0.14 \)
- **UHR:** 12 studies, N = 532, d = 0.31, 95%CI 0.12 to 0.51, \( p = 0.002, I^2 = 0.06\%\), Q-test \( p = 0.02 \)
- **Controls:** 10 studies, N = 338, d = 0.38, 95%CI 0.17 to 0.53, \( p < 0.001, I^2 = 0.02\%\), Q-test \( p = 0.26 \)
  \[ Q_B p > 0.05 \]

**Significant, small improvement in executive functioning over time in UHR, FEP and controls, with no significant differences between groups**

- **FEP:** 10 studies, N = 574, d = 0.27, 95%CI 0.06 to 0.48, \( p = 0.01, I^2 = 0.07\%\), Q-test \( p = 0.001 \)
- **UHR:** 5 studies, N = 92, d = 0.34, 95%CI -0.02 to 0.70, \( p = 0.06, I^2 = 0.04\%\), Q-test \( p = 0.25 \)
- **Controls:** 6 studies, N = 228, d = 0.45, 95%CI 0.17 to 0.53, \( p = 0.002, I^2 = 0.06\%\), Q-test \( p = 0.06 \)
  \[ Q_B p > 0.05 \]

**Significant, small improvement in attention over time in UHR, FEP and controls, with no significant differences between groups**

- **FEP:** 12 studies, N = 678, d = 0.38, 95%CI 0.20 to 0.56, \( p < 0.001, I^2 = 0.05\%\), Q-test \( p = 0.006 \)
- **UHR:** 5 studies, N = 208, d = 0.37, 95%CI 0.17 to 0.56, \( p < 0.001, I^2 = 0\%\), Q-test \( p = 0.99 \)
- **Controls:** 6 studies, N = 265, d = 0.39, 95%CI 0.13 to 0.65, \( p = 0.003, I^2 = 0.05\%\), Q-test \( p = 0.06 \)
  \[ Q_B p > 0.05 \]
Signs and Symptoms – Cognition in people at high-risk of psychosis

**differences between groups**

- **FEP:** 8 studies, N = 620, \( d = 0.27, 95\% CI 0.12 \text{ to } 0.42, p < 0.001, I^2 = 0.02\%, Q\text{-test} p = 0.14\)
- **UHR:** 8 studies, N = 219, \( d = 0.33, 95\% CI 0.14 \text{ to } 0.52, p < 0.001, I^2 = 0\%, Q\text{-test} p = 0.87\)
- **Controls:** 7 studies, N = 155, \( d = 0.27, 95\% CI 0.08 \text{ to } 0.46, p = 0.006, I^2 = 0\%, Q\text{-test} p = 0.57\)

**Q\text{-test} p > 0.05**

In FEP studies, a decrease in negative symptoms was significantly associated with greater improvement in executive functioning and verbal working memory, and a decrease in positive symptoms was associated with improvement of visual memory performance at follow-up.

The ratio of patients taking antipsychotic medications was not significantly associated with cognitive changes over time.

Authors report no publication bias.

<table>
<thead>
<tr>
<th>Consistency</th>
<th>Consistent (low ( I^2 ) statistics)</th>
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<tr>
<td>Precision</td>
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<td>Directness</td>
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**Cohen AS, Brown LA, Auster TL**

*Olfaction, “olfiction,” and the schizophrenia-spectrum: An updated meta-analysis on identification and acuity*

Schizophrenia Research 2012; 135: 152-157

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**Comparison**

Olfactory identification and acuity in people at risk of schizophrenia – including people with self-reported schizotypal traits, people at high genetic risk, and people displaying subclinical psychotic symptoms compared with controls

**Summary of evidence**

Moderate to high quality evidence (precise, direct, large sample, unable to assess consistency) suggests impaired olfactory identification in people at high risk of schizophrenia

**Olfactory performance**
Overall, a small significant effect size of impaired identification, but not acuity, in people at high risk

**Olfactory identification:** 16 studies, N = 1186, $d = -0.25$, 95%CI -0.47 to -0.03, $p$ value not reported

**Olfactory acuity:** 6 studies, N = 238, $d = -0.38$, 95%CI -0.70 to 0.07, $p$ value not reported

No significant differences reported in subgroup of ultra-high risk studies (family history of psychosis, functional decline or subclinical psychosis)

**Identification:** 2 studies, N = 219, $d = -0.67$, 95%CI -4.08 to 2.75, $p$ value not reported

No significant differences reported in subgroup of psychometrically determined studies (schizotypy self-report)

**Identification:** 5 studies, N = 450, $d = -0.14$, 95%CI -0.64 to 0.36, $p$ value not reported

No significant differences reported in biological risk studies (relatives of people with schizophrenia)

**Identification:** 9 studies, N = 517, $d = -0.21$, 95%CI -0.53 to 0.12, $p$ value not reported

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<td>Precise apart from ultra-high risk studies</td>
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<td>Directness</td>
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**De Herdt A, Wampers M, Vancampfort D, De Hert M, Vanhees L, Demunter H, Van Bouwel L, Brunner E, Probst M**

**Neurocognition in clinical high risk young adults who did or did not convert to a first schizophrenic psychosis: a meta-analysis**

**Schizophrenia Research** 2013; 149(1-2): 48-55

View review abstract online

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Baseline cognitive functioning in people at clinical high risk for psychosis who transitioned to psychosis at follow-up compared with those who did not transition to psychosis at follow-up (period not reported)</th>
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<tbody>
<tr>
<td>Summary of evidence</td>
<td>Moderate quality evidence (consistent, precise, direct, small to medium sized samples) suggests small to medium sized effects of poor visual learning and working memory in people at clinical high risk for psychosis who transitioned to psychosis compared with people at clinical high risk for psychosis who did not transition to psychosis. Low to moderate quality evidence (inconsistent, imprecise) suggests no differences in attention,</td>
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Signs and Symptoms – Cognition in people at high-risk of psychosis

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<th>Baseline cognitive functioning</th>
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<tr>
<td><strong>verbal learning, reasoning ability or processing speed</strong></td>
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Overall, 9 studies with 583 clinical high risk people (195 transitioned to psychosis, 388 did not)

**Significant, medium effect of poor visual learning in people at clinical high risk for psychosis who transitioned to psychosis compared with those who did not transition to psychosis**

5 studies, $g = -0.40, 95\% CI -0.68$ to $-0.13, p = 0.004, Q$-test $p = 0.733$

**A trend, small effect of poor working memory in people at clinical high risk for psychosis who transitioned to psychosis compared with those who did not transition to psychosis**

7 studies, $g = -0.27, 95\% CI -0.56$ to $0.02, p = 0.069, Q$-test $p = 0.232$

No significant differences between groups in attention/vigilance

5 studies, $g = -0.37, 95\% CI -0.81$ to $0.08, p = 0.107, Q$-test $p = 0.009$

No significant differences between groups in verbal learning

8 studies, $g = -0.79, 95\% CI -1.82$ to $0.25, p = 0.137, Q$-test $p < 0.0001$

No significant differences between groups in reasoning ability

8 studies, $g = 0.39, 95\% CI -0.32$ to $1.1, p = 0.279, Q$-test $p = 0.000$

No significant differences between groups in processing speed

7 studies, $g = -0.52, 95\% CI -1.21$ to $0.17, p = 0.138, Q$-test $p < 0.0001$

**Consistency**

Consistent for visual learning and working memory only

**Precision**

Precise for visual learning, working memory and attention/vigilance

**Directness**

Direct


**Cognitive Functioning in Prodromal Psychosis**

Archives of General Psychiatry 2012; 69(6): 562-571

[View review abstract online](#)

**Comparison 1**

Cognitive functioning in individuals at clinical high-risk of psychosis (showing prodromal sub-clinical symptoms) compared with controls
Signs and Symptoms – Cognition in people at high-risk of psychosis

<table>
<thead>
<tr>
<th>Summary of evidence</th>
<th>High quality evidence (consistent, precise, direct, large samples) shows a small to medium reduction in general intelligence, executive functioning, attention, visual memory and social cognition in individuals at high-risk of psychosis compared with controls. Moderate to high quality evidence (inconsistent, precise, direct, large samples) suggests a small to medium reduction in verbal fluency, verbal memory and working memory in individuals at high-risk of psychosis compared with controls</th>
</tr>
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### Cognitive functioning

- **Small effect size suggests lower general intelligence in high-risk individuals vs. controls**
  - 11 studies, N = 1247, $g = -0.224$, 95%CI -0.346 to -0.101, $p < 0.001$, $I^2 = 14.28$, $p = 0.308$

- **Small effect size suggests poor executive functioning in high-risk individuals vs. controls**
  - 9 studies, N = 1189, $g = -0.218$, 95%CI -0.397 to -0.118, $p = 0.005$, $I^2 = 25.33$, $p = 0.218$

- **Small effect size suggests poor verbal fluency in high-risk individuals vs. controls**
  - 11 studies, N = 1382, $g = -0.308$, 95%CI -0.486 to -0.130, $p = 0.001$, $I^2 = 64.19$, $p = 0.002$

- **Small effect size suggests poor attention in high-risk individuals vs. controls**
  - 8 studies, N = 1150, $g = -0.225$, 95%CI -0.432 to -0.218, $p = 0.045$, $I^2 = 0$, $p = 0.773$

- **Small to medium effect size suggests poor visual memory in high-risk individuals vs. controls**
  - 5 studies, N = 489, $g = -0.396$, 95%CI -0.595 to -0.196, $p <.001$, $I^2 = 0$, $p = 0.566$

- **Small to medium effect size suggests poor verbal memory in high-risk individuals vs. controls**
  - 8 studies, N = 910, $g = -0.392$, 95%CI -0.579 to -0.206, $p <.001$, $I^2 = 54.94$, $p = 0.030$

- **Small to medium effect size suggests poor working memory in high-risk individuals vs. controls**
  - 11 studies, N = 1471, $g = -0.360$, 95%CI -0.512 to -0.209, $p <.001$, $I^2 = 49.93$, $p = 0.030$

- **Medium effect size suggests poor social cognition in high-risk individuals vs. controls**
  - 6 studies, N = 490, $g = -0.547$, 95%CI -0.730 to -0.363, $p <.001$, $I^2 = 0$, $p = 0.919$

- **No differences in processing speed**
  - 14 studies, N = 1646, $g = -0.176$, 95%CI -0.176 to 0.066, $p = 0.109$, $I^2 = 52.97$, $p = 0.010$

Older age showed a weak relationship with worse cognitive performance in high-risk individuals vs. controls ($\beta = -0.025$, $p < 0.001$). Milder cognitive impairments were reported in studies using the Basic Symptoms approach ($g = -0.227$, $p$ not reported), intermediate impairments in studies adopting the Ultra High Risk approach ($g = -0.357$), and the most pronounced impairments were reported in studies combining the two approaches ($g = -0.410$), although these group differences were not statistically significant ($Q_S = 1.17$, $p = 0.56$). There was a trend level significance effect of sex with females performing relatively better than males (females $g = -0.208$, males: $g = -0.366$, $Q_S = 0.030$, $p = 0.86$).
Signs and Symptoms – Cognition in people at high-risk of psychosis

Authors report that high-risk subjects were best distinguished from controls on the performance of the Digit Symbol Substitution Test, Letter Number Sequencing task, and the Continuous Performance Test, as these tasks showed the smallest confidence intervals.

<table>
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<tr>
<th>Consistency in results</th>
<th>Consistent for general intelligence, executive functioning, attention, visual memory and social cognition</th>
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<tr>
<td>Comparison 2</td>
<td>Cognitive functioning in individuals at high-risk of psychosis who made the transition to psychosis compared with individuals at high-risk of psychosis who did not make the transition to psychosis (up to 19 months follow up)</td>
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<tr>
<td>Summary of evidence</td>
<td>Low to moderate quality evidence (medium sized samples, unable to assess consistency, appears precise, direct) suggests a medium reduction in general intelligence, verbal fluency, verbal memory, visual memory, and working memory in high-risk individuals who made the transition to psychosis compared with high-risk individuals who did not make the transition to psychosis</td>
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Cognitive functioning

7 studies, N = 598

Authors report a medium effect (\( g = -3.00 \) to \(-4.00 \)) showing lower general intelligence, verbal fluency, verbal memory, visual memory, and working memory in high-risk individuals who made the transition to psychosis compared with high-risk individuals who did not make the transition to psychosis.

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<td>Appears precise (from graph)</td>
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# Neurocognition in Psychosis Risk Syndrome: A Quantitative and Qualitative Review

**Current Pharmaceutical Design** 2012, 18: 399-415  
*View review abstract online*

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Cognitive functioning in individuals at clinical high-risk of psychosis compared with controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary of evidence</td>
<td>Moderate to high quality evidence (consistent, precise, direct, unclear sample sizes) shows a medium size reduction in olfactory functioning, executive functioning, and verbal and non-verbal memory in individuals at high-risk of psychosis compared with controls. Moderate quality evidence (inconsistent) suggests a medium size reduction in general intelligence, language functioning, attention, visual-spatial ability, and delayed verbal memory and learning in individuals at high-risk of psychosis compared with controls</td>
</tr>
</tbody>
</table>

### Cognitive functioning

*Medium effect size suggests lower olfactory functioning in high-risk individuals vs. controls*

- 2 studies, $d = -0.67$, 95%CI -1.06 to -0.28, $p < 0.05$, $I^2 = 39\%$, $p = 0.20$
  - No moderator analyses

*Medium effect size suggests poor general cognitive ability/IQ in high-risk individuals vs. controls*

- 6 studies, $d = -0.53$, 95%CI -0.79 to -0.26, $p < 0.05$, $I^2 = 67.9\%$, $p < 0.01$
  - Moderator analysis revealed larger effect sizes in samples with higher % of males ($p < 0.02$)

*Medium effect size suggests poor language functioning in high-risk individuals vs. controls*

- 10 studies, $d = -0.51$, 95%CI -0.64 to -0.38, $p < 0.05$, $I^2 = 57.3\%$, $p < 0.001$
  - Moderator analysis revealed larger effect sizes in older samples ($p < 0.01$), and in studies with ascertainment methods other than the Comprehensive Assessment of At-Risk Mental States (CAARMS) ($p < 0.01$)

*Medium effect size suggests poor immediate verbal memory in high-risk individuals vs. controls*

- 8 studies, $d = -0.50$, 95%CI -0.61 to -0.39, $p < 0.05$, $I^2 = 31.6\%$, $p = 0.07$
  - Moderator analysis revealed larger effect sizes in studies with ascertainment methods other than the CAARMS ($p < 0.03$)

*Medium effect size suggests poor attention-processing speed in high-risk individuals vs. controls*

- 7 studies, $d = -0.43$, 95%CI -0.54 to -0.32, $p < 0.05$, $I^2 = 48.8\%$, $p < 0.01$
Signs and Symptoms – Cognition in people at high-risk of psychosis

<table>
<thead>
<tr>
<th>Consistency in results</th>
<th>Consistent for olfactory functioning, executive functioning, immediate verbal memory, non-verbal memory, and motor skills</th>
</tr>
</thead>
</table>

**Medium effect size suggests poor visual-spatial ability in high-risk individuals vs. controls**

4 studies, $d = -0.42$, 95%CI -0.74 to -0.10, $p < 0.05$, $I^2 = 75.6\%$, $p < 0.01$

Moderator analysis revealed smaller effect sizes in more recent publications ($p < 0.05$), in studies with a higher % of males in the patient samples ($p < 0.03$), and larger effect sizes in studies with a higher % of males in the control samples ($p < 0.03$). Larger effect sizes were also reported in studies with a higher % of patients with a familial risk of psychosis ($p < 0.03$)

**Medium effect size suggests poor attention-vigilance in high-risk individuals vs. controls**

8 studies, $d = -0.40$, 95%CI -0.50 to -0.30, $p < 0.05$, $I^2 = 45.2\%$, $p < 0.001$

Moderator analysis revealed smaller effect sizes in more recent publications ($p < 0.01$), in studies with a higher % of males ($p < 0.01$), in studies where controls had a higher level of education ($p < 0.01$), and in studies with ascertainment methods other than the CAARMS ($p = 0.001$)

**Medium effect size suggests poor attention-working memory in high-risk individuals vs. controls**

13 studies, $d = -0.39$, 95%CI -0.51 to -0.26, $p < 0.05$, $I^2 = 57.4\%$, $p < 0.001$

Moderator analysis revealed smaller effect sizes in more recent publications ($p < 0.02$), in studies with older samples ($p = 0.05$), and in studies with ascertainment methods other than the CAARMS ($p = 0.04$). Larger effect sizes were reported in studies with a higher % of males in the control group only ($p < 0.01$)

**Medium effect size suggests poor executive functioning in high-risk individuals vs. controls**

6 studies, $d = -0.35$, 95%CI -0.50 to -0.19, $p < 0.05$, $I^2 = 38.2\%$, $p > 0.10$

Moderator analysis revealed smaller effect sizes in studies where controls had a higher level of education ($p = 0.05$)

**Medium effect size suggests poor non-verbal memory in high-risk individuals vs. controls**

5 studies, $d = -0.35$, 95%CI -0.56 to -0.13, $p < 0.05$, $I^2 = 40.6\%$, $p = 0.12$

Moderator analysis revealed smaller effect sizes in samples with higher % of males ($p = 0.05$) and in studies with ascertainment methods other than the CAARMS ($p = 0.45$)

**Small effect size suggests poor delayed verbal memory and learning in high-risk individuals vs. controls**

3 studies, $N =$ not reported, $d = -0.26$, 95%CI -0.46 to -0.06, $p < 0.05$, $I^2 = 54.8\%$, $p = 0.05$

No significant moderators

No significant differences in motor skills

3 studies, $N =$ not reported, $d = -0.16$, 95%CI -0.36 to -0.03, $p > 0.05$, $I^2 = 0\%$, $p = 0.47$

No moderator analyses
## Signs and Symptoms – Cognition in people at high-risk of psychosis

<table>
<thead>
<tr>
<th>Precision in results</th>
<th>Precise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Directness of results</td>
<td>Direct</td>
</tr>
<tr>
<td>Comparison 2</td>
<td>Cognitive functioning in individuals at clinical high-risk of psychosis who converted to psychosis or did not convert to psychosis compared with controls</td>
</tr>
<tr>
<td>Summary of evidence</td>
<td>Moderate quality evidence (mostly inconsistent, precise, direct, unclear sample sizes) suggests a medium size reduction in olfactory functioning, general cognitive ability, language functioning, visual-spatial ability, memory, attention and executive functioning in high-risk individuals who converted to psychosis vs. controls. There was also a small to medium reduction in olfactory functioning, general cognitive ability, language functioning, verbal memory, and attention in high-risk individuals who did not convert to psychosis vs. controls</td>
</tr>
</tbody>
</table>

### Cognitive functioning

Medium effect size suggests lower olfactory functioning in non-converters vs. controls
- 2 studies, $d = -0.67$, 95%CI -1.15 to -0.19, $p < 0.05$, $I^2$ not reported

Medium effect size suggests lower olfactory functioning in converters vs. controls
- 2 studies, $d = -0.84$, 95%CI -1.31 to -0.37, $p < 0.05$, $I^2$ not reported

Medium effect size suggests poor general cognitive ability/IQ in non-converters vs. controls
- 3 studies, $d = -0.70$, 95%CI -1.28 to -0.12, $p < 0.05$, $I^2$ not reported

Medium effect size suggests poor general cognitive ability/IQ in converters vs. controls
- 3 studies, $d = -0.81$, 95%CI -1.12 to -0.49, $p < 0.05$, $I^2$ not reported

Medium effect size suggests poor language functioning in non-converters vs. controls
- 6 studies, $d = -0.33$, 95%CI -0.46 to -0.19, $p < 0.05$, $I^2$ not reported

Medium effect size suggests poor language functioning in converters vs. controls
- 6 studies, $d = -0.67$, 95%CI -0.81 to -0.54, $p < 0.05$, $I^2$ not reported

Medium effect size suggests poor immediate verbal memory in non-converters vs. controls
- 3 studies, $d = -0.38$, 95%CI -0.62 to -0.14, $p < 0.05$, $I^2$ not reported

Medium effect size suggests poor immediate verbal memory in converters vs. controls
- 3 studies, $d = -0.72$, 95%CI -1.06 to -0.37, $p < 0.05$, $I^2 = 50.7\%$, $p = 0.048$

Medium effect size suggests poor attention-processing speed in non-converters vs. controls
- 3 studies, $d = -0.40$, 95%CI -0.59 to -0.21, $p < 0.05$, $I^2$ not reported
Signs and Symptoms – Cognition in people at high-risk of psychosis

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<thead>
<tr>
<th>Medium effect size suggests poor attention-processing speed in converters vs. controls</th>
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<tr>
<td>3 studies, $d = -0.56$, 95%CI -0.79 to -0.32, $p &lt; 0.05$, $I^2 = 54.4%$, $p = 0.04$</td>
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No differences in visual-spatial ability between non-converters and controls

<table>
<thead>
<tr>
<th>Medium effect size suggests poor visual-spatial ability in converters vs. controls</th>
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<tbody>
<tr>
<td>2 studies, $d = -0.49$, 95%CI -0.98 to 0.02, $p &gt; 0.05$, $I^2$ not reported</td>
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<tr>
<th>Medium effect size suggests poor attention-vigilance in non-converters vs. controls</th>
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<tr>
<td>4 studies, $d = -0.42$, 95%CI -0.57 to -0.27, $p &lt; 0.05$, $I^2$ not reported</td>
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<tr>
<th>Medium effect size suggests poor attention-vigilance in converters vs. controls</th>
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<tr>
<td>4 studies, $d = -0.61$, 95%CI -0.80 to -0.42, $p &lt; 0.05$, $I^2 = 30.7%$, $p = 0.15$</td>
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<th>Medium effect size suggests poor attention-working memory in non-converters vs. controls</th>
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<tr>
<td>4 studies, $d = -0.44$, 95%CI -0.62 to -0.25, $p &lt; 0.05$, $I^2$ not reported</td>
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<tr>
<td>4 studies, $d = -0.77$, 95%CI -1.18 to -0.35, $p &lt; 0.05$, $I^2 = 62.1%$, $p = 0.02$</td>
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No differences in executive functioning between non-converters and controls

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<tr>
<td>2 studies, $d = -0.34$, 95%CI -0.76 to 0.08, $p &gt; 0.05$, $I^2$ not reported</td>
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<tr>
<th>Medium effect size suggests poor executive functioning in converters vs. controls</th>
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<tr>
<td>2 studies, $d = -0.47$, 95%CI -0.72 to -0.22, $p &lt; 0.05$, $I^2$ not reported</td>
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No differences in non-verbal memory between non-converters and controls

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<tr>
<td>3 studies, $d = -0.79$, 95%CI -1.36 to -0.22, $p &lt; 0.05$, $I^2 = 58.9%$, $p = 0.09$</td>
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No differences in delayed verbal memory and learning between non-converters and controls

<table>
<thead>
<tr>
<th>Small effect size suggests poor delayed verbal memory and learning in converters vs. controls</th>
</tr>
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<tbody>
<tr>
<td>1 study, $d = -0.34$, 95%CI -0.75 to 0.07, $p &gt; 0.05$</td>
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<th>Small effect size suggests poor delayed verbal memory and learning in converters vs. controls</th>
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<tr>
<td>1 study, $d = -0.52$, 95%CI -0.99 to -0.04, $p &lt; 0.05$</td>
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No differences in motor skills between non-converters and controls

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<th>Small effect size suggests poor motor skills between converters and controls</th>
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<tbody>
<tr>
<td>2 studies, $d = -0.14$, 95%CI -0.45 to 0.18, $p &gt; 0.05$, $I^2$ not reported</td>
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<th>Small effect size suggests poor motor skills between converters and controls</th>
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<tr>
<td>2 studies, $d = -0.35$, 95%CI -0.89 to 0.21, $p &gt; 0.05$, $I^2$ not reported</td>
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</table>

Consistency in results

Consistent for attention-vigilance and non-verbal memory for converters vs. controls
TECHNICAL COMMENTARY

Signs and Symptoms – Cognition in people at high-risk of psychosis

<table>
<thead>
<tr>
<th>Precision in results</th>
<th>Imprecise for non-verbal memory and visual-spatial ability in converters vs. controls</th>
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</thead>
<tbody>
<tr>
<td>Directness of results</td>
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Explanation of acronyms

CI = confidence interval, \( d \) = Cohen’s \( d \) and \( g \) = Hedges’ \( g \) = standardized mean differences (see below for interpretation of effect sizes), \( I^2 \) = percentage of variance in results across studies, \( N \) = number of participants, \( p \) = statistical probability of obtaining that result (\( p < 0.05 \) generally regarded as significant), \( Q_B \) = \( Q \) statistic (chi-square) for the test of heterogeneity in results across groups of studies, \( Q_w \) = \( Q \) statistic (chi-square) for the test of heterogeneity in results within a group of studies, vs. = versus
Explanation of technical terms

- Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include: reporting bias – selective reporting of results; publication bias - trials which are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small. 

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives which are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives which are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomized trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardized mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) which allows results from different scales to be combined and compared. Each study’s mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium to large effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2. In OR stands for logarithmic OR where a lnOR of 0
Signs and Symptoms – Cognition in people at high-risk of psychosis

shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforeseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardized (b) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardized regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) which is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I² is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I² can be calculated from Q (chi-square) for the test of heterogeneity with the following formula:§

\[ I^2 = \left( \frac{Q - df}{Q} \right) \times 100\% \]

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed.||

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C which allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

This summary table is yet to be reviewed by a content expert.
Signs and Symptoms – Cognition in people at high-risk of psychosis

References