TECHNICAL COMMENTARY

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Cognition in high-risk groups

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 that 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 common in people with schizophrenia and may also be apparent in people at high risk of psychosis. This table presents the available evidence for cognitive performance in this group of people.

Method

We have included only systematic reviews with detailed literature search, methodology, and inclusion/exclusion criteria that were published in full text, in English, from the year 2000. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Reviews with pooled data are prioritized for inclusion. Reviews reporting fewer than 50% of items on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[1]) checklist have been excluded from the library. The evidence was graded guided by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found five systematic reviews that met our inclusion criteria[3-7].

- Moderate to high quality evidence shows medium-sized effects of poorer verbal learning, reasoning and problem-solving, visual memory, verbal memory, working memory, olfaction, visual learning, and executive functioning in people at clinical high-risk for psychosis compared to controls. There were small effects of poorer general intelligence, processing speed, attention/vigilance, premorbid intelligence, visuospatial ability, social cognition, and motor functioning.
- 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.
- Moderate quality evidence finds medium-sized effects of poorer verbal learning, visual memory, and executive functioning in individuals at high-risk of psychosis who made the transition to psychosis compared to individuals at high-risk of psychosis who did not make the transition to psychosis. There were small effects of poorer processing speed, attention/vigilance, and general intelligence, with no differences in working memory, premorbid intelligence, olfaction, or motor functioning.
- Moderate quality evidence finds medium-sized effects of better verbal learning, general intelligence, and executive functioning in people at high-risk of psychosis compared to people with first-episode psychosis. There were no

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differences in premorbid intelligence or processing speed.

- High quality evidence finds small improvements in cognitive domains over time in people at ultra-high risk of psychosis and in people with first-episode psychosis.
- Moderate to low quality evidence finds no differences in metacognitive beliefs between men and women at clinical high risk of psychosis.

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Baumgartner J, Litvan Z, Koch M, Hinterbuchinger B, Friedrich F, Baumann L, Mossaheb N

Metacognitive beliefs in individuals at risk for psychosis: a systematic review and meta-analysis of sex differences

Neuropsychiatrie 2020; 34(3): 108-15

View review abstract online

Comparison	**Metacognitive beliefs in men vs. women at clinical high risk for psychosis.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized sample, unable to assess consistency or precision, direct) finds no differences in metacognitive beliefs between men and women at clinical high risk of psychosis.**
Metacognitive beliefs	
No significant differences in overall metacognitive beliefs between men and women; 3 studies, N = 234, MD = -2.01, 95%CI -8.73 to 4.71, $p > 0.05$, I^2 not reported None of the subscales showed a significant difference (negative beliefs about uncontrollability and danger, cognitive confidence, negative beliefs about responsibility and superstition, cognitive self-consciousness). Authors report no publication bias.	
Consistency‡	Unable to assess; no measure of consistency is reported.
Precision§	Unable to assess; MDs are not standardised.
Directness‖	Direct

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

Acta Psychiatrica Scandinavica 2014; 130(1): 1-15

View review abstract online

Cognition in high-risk groups

Comparison	**Cognitive functioning in people at clinical high risk (UHR) and familial high risk (FHR) for psychosis vs. controls.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) 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. Moderate to high quality evidence (indirect) finds 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.**
Cognitive functioning	
*Significant, small to medium size effect of **poorer premorbid IQ** in UHR and FHR groups compared with controls, with the FHR group showing the greatest deficit;* UHR: 9 studies, N = 1,370, d = 0.30, 95%CI 0.13 to 0.48, $p < 0.001$, I^2 = 0.04%, Q-test p = 0.02 FHR: 6 studies, N = 770, d = 0.63, 95%CI 0.47 to 0.79, $p < 0.001$, I^2 = 0%, Q-test p = 0.60 Q_B = 13.1, $p < 0.001$ *Significant, medium to large size effect of **poorer current IQ** in UHR and FHR groups compared with controls, with the FHR group showing the greatest deficit;* UHR: 12 studies, N = 1,440, d = 0.40, 95%CI 0.25 to 0.54, $p < 0.001$, I^2 = 0.02%, Q-test p = 0.15 FHR: 8 studies, N = 900, d = 0.81, 95%CI 0.61 to 1.01, $p < 0.001$, I^2 = 0.04%, Q-test p = 0.07 Q_B = 20.0, $p < 0.001$ *Significant, small to medium size effect of **poorer 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, $p < 0.001$, I^2 = 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, I^2 = 0.09%, Q-test p = 0.02 Q_B = 4.6, p = 0.03 *Significant, small to medium size effect of **poorer processing speed** in UHR and FHR groups compared with controls, with no significant differences between groups;* UHR: 8 studies, N = 974, d = 0.47, 95%CI 0.27 to 0.66, $p < 0.001$, I^2 = 0.04%, Q-test p = 0.04 FHR: 13 studies, N = 1,494, d = 0.35, 95%CI 0.22 to 0.49, $p < 0.001$, I^2 = 0.02%, Q-test p = 0.13 Q_B $p > 0.05$ *Significant, medium size effect of **poorer verbal memory** in UHR and FHR groups compared with controls, with no significant differences between groups;*	

UHR: 10 studies, N = 1,205, *d* = 0.50, 95%CI 0.32 to 0.68, *p* < 0.001, I^2 = 0.04%, Q-test *p* = 0.03 FHR: 12 studies, N = 1,547, *d* = 0.45, 95%CI 0.29 to 0.61, *p* < 0.001, I^2 = 0.03%, Q-test *p* = 0.06 Q_B *p* > 0.05 *Significant, medium size effect of **poorer 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, I^2 = 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, I^2 = 0.04%, Q-test *p* = 0.08 Q_B *p* > 0.05 *Significant, small to medium size effect of **poorer verbal working memory** in UHR and FHR groups compared with controls, with no significant differences between groups;* UHR: 9 studies, N = 1,136, *d* = 0.41, 95%CI 0.20 to 0.61, *p* < 0.001, I^2 = 0.06%, Q-test *p* = 0.007 FHR: 10 studies, N = 1,206, *d* = 0.32, 95%CI 0.12 to 0.51, *p* = 0.001, I^2 = 0.05%, Q-test *p* = 0.02 Q_B *p* > 0.05 *Significant, small size effect of **poorer attention** in UHR and FHR groups compared with controls, with no significant differences between groups;* UHR: 8 studies, N = 1,042, *d* = 0.37, 95%CI 0.25 to 0.50, *p* < 0.001, I^2 = 0%, Q-test *p* = 0.59 FHR: 14 studies, N = 1451, *d* = 0.30, 95%CI 0.16 to 0.44, *p* < 0.001, I^2 = 0.03%, Q-test *p* = 0.08 Q_B *p* > 0.05 *Significant, small to medium size effect of **poorer 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, I^2 = 0.06%, Q-test *p* = 0.01 FHR: 10 studies, N = 1,149, *d* = 0.39, 95%CI 0.16 to 0.61, *p* = 0.001, I^2 = 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. Authors report no publication bias.	
Consistency	Consistent
Precision	Precise
Directness	Direct in comparisons with controls, indirect in comparisons between high-risk groups.

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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?

Schizophrenia Bulletin 2014; 40(43): 744-755

View review abstract online

Comparison	**Changes in cognitive functioning over time in people at ultra-high risk of psychosis (UHR) vs. people with first-episode psychosis (FEP) or controls.**
Summary of evidence	**High quality evidence (medium to large samples, consistent, precise, direct) 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

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 **global cognition** 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 **processing speed** 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 **verbal memory** over time in UHR, FEP and controls, 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 to medium-sized improvement in **visual memory** over time in FEP and controls, and a trend improvement for UHR groups, 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 **executive functioning** 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

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

FEP: 8 studies, N = 620, *d* = 0.27, 95%CI 0.12 to 0.42, *p* < 0.001, I^2 = 0.02%, Q-test *p* = 0.14

UHR: 8 studies, N = 219, *d* = 0.33, 95%CI 0.14 to 0.52, *p* < 0.001, I^2 = 0%, Q-test *p* = 0.87

Controls: 7 studies, N = 155, *d* = 0.27, 95%CI 0.08 to 0.46, *p* = 0.006, I^2 = 0%, Q-test *p* = 0.57

Q_B *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	
Consistency	Consistent
Precision	Precise
Directness	Direct in comparisons with controls, indirect in comparisons between high-risk and FEP groups.

Catalan A, Salazar De Pablo G, Aymerich C, Damiani S, Sordi V, Radua J, Oliver D, McGuire P, Giuliano AJ, Stone WS, Fusar-Poli P

Neurocognitive Functioning in Individuals at Clinical High Risk for Psychosis: A Systematic Review and Meta-analysis

JAMA Psychiatry 2021; 78(8): 859-67

View review abstract online

Comparison 1	**Cognitive functioning in individuals at clinical high-risk of psychosis vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) shows medium-sized effects of poorer verbal learning, reasoning and problem-solving, visual memory, verbal memory, working memory, olfaction, visual learning, and executive functioning in people at clinical high-risk for psychosis compared to controls. There were small effects of poorer general intelligence, processing speed, attention/vigilance, premorbid intelligence, visuospatial ability, social cognition, and motor functioning.**
Cognitive functioning	
Medium-sized effects showed people at clinical high-risk of psychosis performed more poorly than controls on: **Verbal learning**: 21 studies, N = 3,559, g = -0.51, 95%CI -0.63 to -0.39, p < 0.001	

(Hopkins Verbal Learning Test - Revised, Rey Auditory Verbal Learning Test, and the California Verbal Learning Test)

Reasoning and problem-solving: 4 studies, N = 1,461, *g* = -0.46, 95%CI -0.74 to -0.19, *p* < 0.001

(Neuropsychological Assessment Battery Mazes)

Visual memory: 6 studies, N = 555, *g* = -0.45, 95%CI -0.77 to -0.13, *p* = 0.01

(Rey-Osterrieth Complex Figure - Delayed Recall, and the Wechsler Memory Scale Visual Reproduction - Delayed Recall)

Verbal memory: 4 studies, N = 806, *g* = -0.45, 95%CI -0.67 to -0.22, *p* < 0.001

(Rey Auditory Verbal Learning Test - Delayed Recall)

Working memory: 15 studies, N = 3,114, *g* = -0.44, 95%CI -0.57 to -0.31, *p* < 0.001

(Wechsler Memory Scale - III Spatial Span, Letter Number Span, Letter Number Sequencing Test, and Arithmetic. There were no differences on the Self-ordered Pointing Test)

Olfaction: 5 studies, N = 1,362, *g* = -0.44, 95%CI -0.87 to -0.02, *p* = 0.01

(University of Pennsylvania Smell Identification Test)

Visual learning: 13 studies, N = 2,533, *g* = -0.43, 95%CI -0.57 to -0.29, *p* < 0.001

(Brief Visuospatial Memory Test - Revised, and the Wechsler Memory Scale - Immediate Visual Memory. There were no differences on the Rey-Osterrieth Complex Figure - Immediate Recall)

Executive functioning: 29 studies, N = 3,374, *g* = -0.42, 95%CI -0.60 to -0.24, *p* < 0.001

(Trail Making Test - Part B, Wisconsin Card Sorting Test - Categories, Perseverative errors, and Perseverative responses. There were no differences on the Wisconsin Card Sorting Test - Number of responses or the Stroop - Interference)

Small effects showed people at clinical high-risk of psychosis performed more poorly than controls on:

General intelligence: 19 studies, N = 3,449, *g* = -0.39, 95%CI -0.57 to -0.22, *p* < 0.001

(Wechsler - Full Scale IQ. There were no differences on the Wechsler - Verbal or Performance IQ)

Processing speed: 27 studies, N = 4,044, *g* = -0.39, 95%CI -0.56 to -0.21, *p* < 0.001

(Digit Symbol Coding Test, Brief Assessment of Cognition Scale Symbol Coding, Trail Making Test - Part A, Animal Fluency, Letter Fluency, and the Stroop - Color word reading task. There were no differences on the Stroop - Color naming task)

Meta-regressions revealed that older age and fewer years of education were associated with greater processing speed impairments.

Attention/vigilance: 11 studies, N = 2,650, *g* = -0.39, 95%CI -0.49 to -0.29, *p* < 0.001

(Continuous Performance Test - Identical pairs)

Premorbid intelligence: 12 studies, N = 1,270, *g* = -0.38, 95%CI -0.63 to -0.13, *p* < 0.001

(National Adult Reading Test, and the Mehrfach-Wortschaftz-Intelligenz Test - Part B)

Visuospatial ability: 5 studies, N = 1,636, *g* = -0.32, 95%CI -0.44 to -0.20, *p* < 0.001 (Wechsler Adult Intelligence Scale/Wechsler Intelligence Scale for Children Block Design) **Social cognition**: 11 studies, N = 1,478, *g* = -0.29, 95%CI -0.50 to -0.07, *p* = 0.01 (Hinting Task. There were no differences on the Degraded Facial Affect Recognition or Reading the Mind in the Eyes Test) **Motor functioning**: 4 studies, N = 364, *g* = -0.24, 95%CI -0.45 to -0.04, *p* = 0.02 (Tapping Test)	
Consistency in results	Authors report moderate to high heterogeneity
Precision in results	Precise
Directness of results	Direct
Comparison 2	**Cognitive functioning in individuals at high-risk of psychosis who made the transition to psychosis vs. individuals at high-risk of psychosis who did not make the transition to psychosis.**
Summary of evidence	**Moderate quality evidence (mixed sample sizes, inconsistent, some imprecision, direct) shows medium-sized effects of poorer verbal learning, visual memory, and executive 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. There were small effects of poorer processing speed, attention/vigilance, and general intelligence, with no differences in working memory, premorbid intelligence, olfaction, or motor functioning.**
Cognitive functioning	
Medium-sized effects showed people at clinical high-risk of psychosis who transitioned to psychosis performed more poorly than people at clinical high-risk of psychosis who did not transition to psychosis on: **Verbal learning**: 3 studies, N = 151, *g* = -0.58, 95%CI -1.12 to -0.05, *p* = 0.03 (California Verbal Learning Test) **Visual memory**: 3 studies, N = 199, *g* = -0.44, 95%CI -0.74 to -0.14, *p* < 0.001 (Rey-Osterrieth Complex Figure - Delayed Recall) **Executive functioning**: 5 studies, N = 491, *g* = -0.42, 95%CI -0.77 to -0.07, *p* = 0.05 (Wisconsin Card Sorting Test - Perseverative errors) *Small effects showed people at clinical high-risk of psychosis who transitioned to psychosis performed more poorly than people at clinical high-risk of psychosis who did not transition to*	

psychosis on: **Processing speed**: 8 studies, N = 1,428, *g* = -0.39, 95%CI -0.59 to -0.19, *p* < 0.001 (Trail Making Test - Part A, Digit Symbol Coding Test. There were no differences on Animal Fluency) **Attention/vigilance**: 5 studies, N = 1,023, *g* = -0.29, 95%CI -0.51 to -0.08, *p* = 0.007 (Continuous Performance Test - Identical pairs) **General intelligence**: 8 studies, N = 1,162, *g* = -0.26, 95%CI -0.40 to -0.11, *p* < 0.001 (Wechsler - Full Scale IQ) *There were no significant differences on;* **Working memory**: 5 studies, N = 413, *g* = -0.29, 95%CI -0.67 to 0.10, *p* = 0.14 (Letter Number Sequencing Test) **Premorbid intelligence**: 3 studies, N = 150, *g* = -0.19, 95%CI -0.54 to 0.16, *p* = 0.30 (National Adult Reading Test) **Olfaction**: 4 studies, N = 915, *g* = -0.14, 95%CI -0.76 to 0.49, *p* = 0.67 (University of Pennsylvania Smell Identification Test) **Motor functioning**: 3 studies, N = 141, *g* = 0.07, 95%CI -0.31 to 0.45, *p* = 0.72 (Tapping Test)	
Consistency in results	Authors report moderate to high heterogeneity
Precision in results	Some imprecision
Directness of results	Direct
Comparison 3	**Cognitive functioning in individuals at clinical high-risk for psychosis vs. people with first-episode psychosis**
Summary of evidence	**Moderate quality evidence (mixed sample size, inconsistent, some imprecision, direct) shows medium-sized effects of better verbal learning, general intelligence, and executive functioning in individuals at high-risk of psychosis compared to people with first-episode psychosis. There were no differences in premorbid intelligence or processing speed.**
Cognitive functioning	
Medium-sized effects showed people at clinical high-risk of psychosis performed better than people with first-episode psychosis on: **General intelligence**: 3 studies, N = 206, *g* = 0.63, 95%CI 0.35 to 0.91, *p* < 0.001	

(Wechsler - Full Scale IQ) **Verbal learning**: 6 studies, N = 625, *g* = 0.46, 95%CI 0.30 to 0.62, *p* < 0.001 (Hopkins Verbal Learning Test, California Verbal Learning Test) **Executive functioning**: 8 studies, N = 843, *g* = 0.34, 95%CI 0.11 to 0.56, *p* < 0.001 (Wisconsin Card Sorting Test – Categories, Perseverative errors, STROOP - Interference) *There were no significant differences on;* **Processing speed**: 3 studies, N = 321, *g* = 0.38, 95%CI -0.08 to 0.84, *p* = 0.10 (Trail Making Test - Part A) **Premorbid intelligence**: 3 studies, N = 172, *g* = -0.14, 95%CI -0.74 to 0.47, *p* = 0.66 (National Adult Reading Test)	
Consistency in results	Authors report moderate to high heterogeneity
Precision in results	Some imprecision
Directness of results	Direct

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

View review abstract online

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 vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, unable to assess consistency. precise, direct) 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 = 1,186, *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	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Precise apart from ultra-high-risk studies
Directness	Direct

Explanation of acronyms

CI = confidence interval, *d* = Cohen's d and *g* = Hedges' *g* = standardised mean differences, I^2 = percentage of variance in results across studies, MD = mean difference, 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 that 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[8].

† 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 that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that 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 randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that 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[8].

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 effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[9]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios

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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 unforseen 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) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 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. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;[8]

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

§ 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.[10]

‖ 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 that 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.

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