#### **Functional outcomes**



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#### Introduction

Functional outcomes refer to aspects of general life and day-to-day function that may be impacted as a consequence of schizophreniarelated impairments. For example, symptom severity has been significantly associated with community functioning, including functioning, work performance, and social skills. Likewise, reduced cognitive functioning in schizophrenia has also been identified as a strong predictor of community functioning. Social cognition is another aspect of cognitive functioning that is impaired in schizophrenia, and refers to the mental operations underlying social interactions, such as the ability to perceive intentions of others. Impaired social cognition may also impact on functional outcome in terms of maintaining efficient social interactions and independent living skills. Interventions to improve symptom severity or cognitive impairments may have additional benefit for general functional outcomes.

#### 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 schizophrenia, with а diagnosis of schizophreniform schizoaffective disorder, disorder or first episode 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. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis<sup>1</sup>. Reviews with less than 50% of items checked 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 randomised controlled trials (RCT) may be downgraded to moderate or 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 or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)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 14 systematic reviews that met our inclusion criteria<sup>3-16</sup>.

 Moderate to high quality evidence finds small associations between better

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- functioning after treatment for first-episode psychosis and shorter duration of untreated psychosis, less severe symptoms (both at baseline and after treatment), better premorbid functioning, better cognitive functioning, more education, longer work history, and female gender.
- Moderate quality evidence finds more severe negative symptoms are associated with poorer cognitive and community functioning. There is also an association between more severe negative symptoms and smaller social network size.
- Moderate quality evidence finds better global functioning is related to better quality of life, while moderate to low quality evidence finds poor insight is related to poor work performance.
- Moderate to low quality evidence finds the most commonly reported strategies patients use to cope with symptoms and general life stress are avoidance and problem-focused strategies, which improve quality of life and long-term symptom outcomes.
- Moderate to high quality evidence finds a relationship between poor cognitive ability and poor functional outcomes. In particular, poor community functioning is associated with poor social, emotion and information processing, and poor working memory, attention and reasoning. Poor social behaviour is associated with poor emotion processing, verbal learning, and reasoning. Poor problem solving is associated with poor attention, working memory, verbal learning, and reasoning. Poor social skills are associated with poor attention, visual learning, reasoning, verbal learning, and insight.
- Moderate to low quality evidence suggests there is limited cognitive decline in community-dwelling or hospitalised patients in the short term, but hospitalised patients showed significant cognitive decline in the long term.

- Moderate to low quality evidence suggests medication is associated with a range of disability including pain, anxiety, insomnia, somnolence, appetite, fatigue, and libido. The intensity of disability is associated with treatment, symptoms, socio-demographics, global disability, emotional functioning, and cognitive functioning.
- Moderate quality evidence finds the severity of social disability varies in the developing world, with better outcomes in India and Indonesia and poorer outcomes in China, Brazil and African countries.



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#### Christensen T

The influence of neurocognitive dysfunctions on work capacity in schizophrenia patients: a systematic review of the literature

International Journal of Psychiatry in Clinical Practice 2007; 11(2): 89-101

View review abstract online

Comparison	Employment outcomes, cognitive performance, and symptom severity in people with schizophrenia.
Summary of evidence	Moderate to low quality evidence (small to medium-sized samples, unable to assess consistency or precision, direct) suggests lower work capacity is associated with poorer cognitive functioning, including executive functioning, attention/vigilance, memory, language, psychomotor ability, visuospatial processing, IQ and emotional perception. The evidence also suggests that lower work capacity is associated with increased negative symptoms, but not global, positive or disorganised symptoms.

#### Cognitive performance

2 studies (N = 166) reported that poor general neurocognitive functioning was associated with worse work behaviour and employment status, whereas 2 studies (N = 140) found no association between neurocognitive functioning and employment or social functioning.

7 studies (N = 366) reported that poor executive functioning was associated with worse task orientation, social skills, full time employment, occupational functioning, work behaviour improvement, wages earned, contact with employment specialist, cooperativeness, work quality and general impression.

7 studies (N = 389) reported that poor attention/vigilance was associated with worse employment status, less full time employment or unemployment, poorer occupational functioning, work behaviour improvement, work performance and work adjustment.

5 studies (N = 365) reported that poor verbal memory was associated with worse work habits, occupational functioning, work performance, work behaviour, integrated employment status, less hours worked and wages earned. No association between verbal memory and personal presentation, social work skills and cooperativeness.

1 study (N = 77) reported that poor immediate and delayed memory was associated with worse employment status. Poor working memory (1 study, N = 30) was associated with unemployment.

5 studies (N = 348) reported that poor verbal learning and language was associated with worse work behaviour improvements, work performance, less hours worked, wages earned and contact with employment specialist.

2 studies (N = 208) reported that poor psychomotor functioning/speed was associated with worse

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work performance and behaviour.

2 studies (N = 128) reported that poor visuospatial processing/ ability, visual recall and visual scanning was associated with worse occupational activity and functioning.

1 study (N = 53) reported that poor WAIS non-verbal IQ performance was associated with worse vocational functioning.

1 study (N = 94) reported that poor emotional perception was associated with worse work functioning.

#### Symptom severity

2 studies (N = 128) reported that increased global symptoms were associated with worse occupational changes and vocational functioning. However, 5 studies (N = 290) reported no association between global symptoms and social skills at work, employment status, occupational functioning or work behaviour improvement.

6 studies (N = 354) reported that increased negative symptoms were associated with impaired work behaviour, vocational functioning, less hours worked, wages earned, social functioning and a long employment history. 1 study (N = 112) reported that negative symptoms was not associated with work behaviour.

3 studies (N = 270) reported that positive symptoms were not associated with employment history or work behaviour. 1 study (N = 30) reported that increased psychotic symptoms were associated with less hours of on-job support and contact with employment specialist.

1 study (N = 112) reported that disorganised symptoms were not associated with work behaviour.

Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Cohen A, Patel V, Thara R, Gureje O

Questioning an axiom: better prognosis for schizophrenia in the developing world?

Schizophrenia Bulletin 2008; 34(2): 229-44

View review abstract online

Comparison	Disability and social function in people with schizophrenia in low and middle income countries.
Summary of evidence	Moderate quality evidence (large overall sample, mostly prospective studies, inconsistent, unable to assess precision,



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direct) suggests the severity of social disability varies worldwide, with better outcomes in India and Indonesia and poorer outcomes in China, Brazil and African countries.

#### Disability and social outcomes

18 studies, N = 2,636

Chennai, India: Prospective study: 1 year follow up, 73% had moderate to severe global disability (compared to 98% at baseline); 34% had no impairment in social function; 51% had no impairment in occupational function.

Rural Karnataka, India: Prospective study: 1.5 year follow up, overall group showed significant reduction from baseline disability (p < 0.001).

Sào Paulo, Brazil: Prospective study: 2 year follow up, 54% showed social withdrawal (compared to 74% at baseline); 37% showed impaired self-care (compared to 55% at baseline); 52% show impaired interest and information (compared to 68% at baseline).

Sichuan, China: Prospective study: 2 year follow up, social function was mildly impaired in 20.9%; moderately impaired in 10.9% and seriously impaired in 68.2%.

Multisite, India: Prospective study: 2 year follow up, social function was not impaired in 33.7%; moderately impaired in 53.6% and seriously impaired in 12.7%.

Ilesa, Nigeria: Prospective study: 2 year follow up, social relationships were satisfactory in 43.6%; moderate problems in 23.4% and serious problems in 22.3%. 10.6% had no social relationships.

Butajira, Ethiopia: Prospective study: 1-4 year follow up, functional status was reportedly poorer than industrialised countries.

Bali, Indonesia: Prospective study: 11 year follow up, 39% were self-supportive; 13% were semi self-supportive; 15% were socially adjusted to family or community; 32% were maladjusted.

Bali, Indonesia: Retrospective study: 5 year follow up, 34.8% were self-supportive; 19.6% were semi self-supportive; 30.4% were socially adjusted to family or community; 15.2% were maladjusted.

Madras Longitudinal Study: Prospective study: 20 year follow up, 73.8% had little impairment in GAF social and occupational domains.

Sofia, Bulgaria: Prospective study: 16 year follow up, 32.7% had minimal social disability on GAF-D; 36.4% had poor functioning on GAF-D. 32.7% had minimal disability on DAS; 36.4% had poor functioning on DAS.

China: Prospective study: 12 year follow up, 32.8% had good social functioning on GAF-D; 39.6% had serious impairment in social functioning on GAF-D.

Cali, Colombia: Prospective study: 26 year follow up, social disability on GAF-D was minimal in 45.8%; mild in 27.8%; moderate in 23.6%; severe in 2.8%. Social functioning on DAS was excellent in 52%; poor in 9% and severe in 0%.

Agra, India: Prospective study: 25 year follow up, GAF-D functioning was improved in 48.7% of men and 81.8% of women. DAS functioning was excellent in 60%; fairly good in 19% and not measured in 21%.





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Chandigarh (rural), India: Prospective study: 15 year follow up, GAF-D social functioning was excellent in 71%; and serious impairment in 5%.

Chandigarh (urban), India: Prospective study: 15 year follow up, GAF-D social functioning was excellent in 63%; and serious impairment in 14%.

Ibadan, Nigeria: Prospective study: 2 year follow up. No results reported.

Ibadan, Nigeria: Retrospective study: 7-26 year follow up, women had poorer social outcomes following a first episode than men.

Abeokuta, Nigeria: Retrospective study: 13 year follow up, social function was unimpaired in 22%, mild in 19%, moderate in 23% and severe in 36%.

Consistency	Authors report considerable variation in results across studies within regions.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Couture SM, Penn DL, Roberts DL

### The Functional Significance of Social Cognition in Schizophrenia: A Review

Schizophrenia Bulletin 2006; 32(S1): S44-S63

View review abstract online

Comparison	Relationship between social cognition and functional outcome in people with schizophrenia.
Summary of evidence	Moderate to low quality evidence (small to medium-sized samples, unable to assess consistency or precision, direct) suggests the ability to have social perception influenced community function and social behaviour, as well as social problem solving. Emotional perceptive ability influenced community function and social behaviour, and social skills. An attribution bias influenced community function and social behaviour; while social skills were influenced by theory of mind. Premorbid social function had some bearing on theory of mind ability.

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- Social perception is a person's ability to perceive social cues from behaviour in a social context, and incorporates knowledge of social rules and conventions.
- 3 of 4 studies (N = 207) reported a significant, medium to large relationship between SP and social behaviour in treatment settings, with increases in SP correlating positively with improved social behaviour.
- 3 studies (N = 116) reported a significant small to medium relationship between SP and community functioning, and 1 study (N = 162) showed a small effect, that SP could predict inpatient or outpatient status, with increased SP predicting outpatient status.
- 3 studies of inpatients (N = 158) reported a significant medium to large effect associating increased SP with increased social problem solving skills.
- 2 studies (N = 172) reported a significant medium association between increased SP and increased social skills, while two studies reported no association (N = 75).

#### Emotional perception (EP) and functional outcome

- Emotional perception is the ability to infer emotional information from facial expressions and vocal inflections.
- 4 of 6 studies (N = 126) reported a significant medium to large relationship between EP and social behaviour in treatment settings.
  - 3 of 4 studies (N = 131) showed a significant small relationship between EP and social skills.
- 3 studies (N = 260) found a consistent significant medium relationship between improved EP and community function, including work function and independent living scales.

#### Theory of Mind (ToM) and functional outcome

- Theory of Mind is the cognitive ability to attribute mental states such as thoughts, beliefs and intentions to other people.
- 1 study (N = 23) found limited evidence for a significant, small association between ToM and social behaviour.
- 1 study (N = 49) found ToM had a significant, medium-sized association with overall social skill in outpatients.
- 1 study (N = 44) found evidence for a significant, medium-sized association between increased ToM and community function.
  - 1 study (N = 42) found a significant, large relationship between ToM and premorbid social functioning.

#### Attributional Style (AS) and functional outcome



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Attributional style refers to a person's tendencies toward explaining the cause of events (e.g. blaming people vs. situations).

1 study (N = 40) reported a significant, medium-sized association between stable attributions and better community functioning.

1 study (N = 29) reported a significant, small association between hostile attributional bias and aggressive inpatient behaviour.

Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Degnan A, Berry K, Sweet D, Abel K, Crossley N, Edge D

Social networks and symptomatic and functional outcomes in schizophrenia: a systematic review and meta-analysis

Social Psychiatry & Psychiatric Epidemiology 2018; 53: 873-88

View review abstract online

Comparison	Relationship between social network size and symptoms and functional outcomes in people with schizophrenia.
Summary of evidence	Moderate quality evidence (medium to large samples, inconsistent, precise, direct) suggests medium-sized associations between smaller social network size and poorer overall and negative, but not positive symptoms. There was no association with social functioning.

#### Social network size (range 4 to 13)

Significant, medium-sized associations between smaller social network size and;

Poorer overall symptoms; 5 studies, N = 467, g = -0.53, 95%Cl -0.87 to -0.18, p = 0.003, I<sup>2</sup> = 63.04%

Poorer negative symptoms: 8 studies, N = 577, g = -0.75, 95%CI - 0.99 to -0.51, p = 0.000, I<sup>2</sup> = 35.75%

There were no associations with;

Positive symptoms: 7 studies, N = 405, g = -0.19, 95%CI -0.49 to 0.11, p = 0.213 Social functioning: 3 studies, N = 209, g = 0.36, 95%CI -0.07 to 0.80, p = 0.107

Consistency	Inconsistent
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Precision	Precise
Directness	Direct

Fett AK, Viechtbauer W, Dominguez M, Penn D, van Os J, Krabbendam L

The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: A meta-analysis

Neuroscience and Biobehavioural Reviews 2011; 35: 573-588

View review abstract online

Comparison	Association between functional outcomes (community function, social behaviour, social problem solving, social skills) and performance on various cognitive domains in people with schizophrenia.
Summary of evidence	Moderate to high quality evidence (medium to large samples, mostly consistent and precise, direct) showed that increased community functioning was positively influenced by better performance in ToM, emotion processing, information processing verbal learning and working memory, but had a weak relationship with attention and reasoning bias. Improved social behaviour may be associated with better emotion processing and verbal learning, but had a weak association with reasoning bias. Greater problem solving ability showed positive associations with better attention, working memory, verbal learning and reasoning bias. Better social skills were associated with improved performance in tasks measuring attention, visual learning, and reasoning bias, but only a weak association with verbal learning.

#### Community functioning (work performance, social interaction) and cognition

Significant, large association between increased performance on Theory of Mind tasks and greater community functioning;

3 studies, N = 114, estimated average correlation = 0.48, 95%CI 0.32 to 0.61, p < 0.001, Q = 0.81,  $I^2 = 1\%$ , p > 0.05

Significant, medium-sized association between increased performance on emotional perception and processing tasks and greater community functioning;

5 studies, N = 378, estimated average correlation = 0.31, 95%CI 0.21 to 0.40, p < 0.001, Q = 1.67,  $I^2 = 0\%$ , p > 0.05

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Significant, weak association between increased performance on attention tasks and greater community functioning;

9 studies, N = 481, estimated average correlation = 0.16, 95%CI 0.04 to 0.27, p = 0.01, Q = 13.15,  $I^2$  = 38.17%, p > 0.05

Significant, medium-sized association between increased performance on a processing speed task and greater community functioning;

8 studies, N = 465, estimated average correlation = 0.25, 95%Cl 0.13 to 0.37, p <0.001, Q = 12.36,  $l^2 = 42.94\%$ , p > 0.05

Significant, weak to medium-sized association between increased performance on working memory tasks and greater community functioning;

7 studies, N = 495, estimated average correlation = 0.22, 95%CI 0.05 to 0.38, p = 0.01, Q = 18.89,  $I^2$  = 69.30%, p > 0.05

Significant, medium-sized association between increased performance on verbal learning tasks and greater community functioning;

17 studies, N = 1,125, estimated average correlation = 0.26, 95%CI 0.15 to 0.37, p < 0.001, Q = 69.54,  $I^2$  = 71.65%, p < 0.05

Significant, weak association between increased performance on visual learning task and greater community functioning;

6 studies, N = 230, estimated average correlation = 0.20, 95%CI 0.07 to 0.33, p = 0.003, Q = 2.90,  $I^2$  = 0%, p > 0.05

Significant, weak association between increased performance on a reasoning and problem solving tasks and greater community functioning;

16 studies, N = 901, Estimated average correlation = 0.19, 95%CI 0.12 to 0.26, p < 0.001, Q = 16.19,  $I^2 = 9.95\%$ , p > 0.05

#### Social behaviour

Significant, weak to medium-sized association between increased performance on emotional perception and processing tasks and improved social behavior;

6 studies, N = 265, estimated average correlation = 0.22, 95%CI 0.10 to 0.34, p < 0.001, Q = 3.08,  $I^2 = 0\%$ , p > 0.05

No association was found between performance on attention tasks and social behavior;

4 studies, N = 234, estimated average correlation = 0.19, 95%CI -0.11 to 0.45, p = 0.21, Q = 14.95,  $I^2$  = 74.16%, p < 0.05

Significant, medium-sized association between increased performance on verbal learning tasks and improved social behavior;

4 studies, N = 253, estimated average correlation = 0.32, 95%CI 0.15 to 0.47, p < 0.001, Q = 4.84,

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 $I^2 = 39.22\%, p > 0.05$ 

Significant, medium-sized association between better performance on visual learning task and improved social behavior;

4 studies, N = 122, estimated average correlation = 0.30, 95%CI 0.10 to 0.47, p = 0.002, Q = 3.47,  $I^2$  = 11.76%, p > 0.05

Significant, weak to medium-sized association between increased performance on a reasoning and problem solving tasks and improved social behavior;

5 studies, N = 257, estimated average correlation = 0.23, 95%CI 0.11 to 0.35, p < 0.001, Q = 2.06,  $I^2 = 0\%$ , p > 0.05

#### Social problem solving

Significant, medium-sized association between increased performance on attention tasks and greater social problem solving;

3 studies, N = 100, estimated average correlation = 0.25, 95%CI 0.07 to 0.47, p = 0.007, Q = 1.45,  $I^2 = 0\%$ , p > 0.05

Significant, medium-sized association between increased performance on working memory tasks and greater social problem solving;

4 studies, N = 127, estimated average correlation = 0.25, 95%Cl 0.07 to 0.41, p = 0.007, Q =0.29,  $l^2$  = 0%, p > 0.05

Significant, medium-sized association between increased performance on verbal learning tasks and greater social problem solving;

4 studies, N = 117, estimated average correlation = 0.26, 95%CI 0.07 to 0.43, p = 0.003, Q = 0.44,  $I^2$  = 0%, p > 0.05

Significant, medium-sized association between increased performance on a reasoning and problem solving tasks and greater social problem solving;

3 studies, N = 90, estimated average correlation = 0.29, 95%Cl 0.08 to 0.47, p = 0.008, Q = 0.73, l<sup>2</sup> = 0%, p > 0.05

#### Social skills

Significant, medium to large-sized association between increased performance on attention tasks and better social skills;

3 studies, N = 119, estimated average correlation = 0.39, 95%CI 0.22 to 0.53, p < 0.001, Q = 0.22,  $I^2 = 0\%$ , p > 0.05

Significant, weak association between increased performance on verbal learning task and better social skills:

7 studies, N = 250, estimated average correlation = 0.18, 95%Cl 0.06 to 0.31, p = 0.005, Q = 8.54,  $l^2$  = 0%, p > 0.05



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Significant, medium-sized association between increased performance on visual learning task and better social skills;

4 studies, N = 149, estimated average correlation = 0.28, 95%CI 0.07 to 0.46, p = 0.008, Q = 5.22,  $I^2$  = 30.81%, p > 0.05

Significant, medium-sized association between improved performance on a reasoning and problem solving tasks and better social skills;

3 studies, N = 119, estimated average correlation = 0.34, 95%Cl 0.17 to 0.50, p < 0.001

$$Q = 1.04$$
,  $I^2 = 0\%$ ,  $p > 0.05$ 

Consistency	Consistent for all outcomes except community function – working memory and social behaviour – attention.
Precision	Precise for all outcomes except social behaviour – attention.
Directness	Direct

Halverson TF, Orleans-Pobee M, Merritt C, Sheeran P, Fett A-K, Penn DL

Pathways to functional outcomes in schizophrenia spectrum disorders: Meta-analysis of social cognitive and neurocognitive predictors

Neuroscience and Biobehavioral Reviews 2019; 105: 212-9

View review abstract online

Comparison	Relationships between cognitive predictors and functioning in people with schizophrenia.
Summary of evidence	Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests small associations between neurocognition and social cognition and functional outcomes.

Community functioning, social behaviour in the milieu, social skills, and social problemsolving

166 studies, N = 12,868

A small association between and neurocognition and functional outcomes;

Correlation = 0.21, 95%CI 0.18 to 0.24, p < 0.01,  $I^2 = 61\%$ , p < 0.001

The effect size reduced slightly in studies with more males and more white people.

There were no moderating effects of different functional or neurocognition domains,

age, diagnosis, education, illness duration, medication dose or whether the patient was in inpatient or outpatient.



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A small association between and social cognition and functional outcomes;

Correlation = 0.24, 95%CI 0.19 to 0.28, p < 0.01,  $I^2 = 62\%$ , p < 0.001

The effect sizes were similar across functional domains, apart from social problem solving which showed a medium-sized effect. The effect sizes were similar across neurocognition domains, apart from theory of mind which showed a near medium-sized effect.

The effect size reduced slightly in studies of inpatients for community functioning.

There were no moderating effects of gender, age, race, diagnosis, education, illness duration, or medication dose.

Consistency	Inconsistent
Precision	Precise
Directness	Direct

Heilbronner U, Samara M, Leucht S, Falkai P, Schulze TG

The Longitudinal Course of Schizophrenia Across the Lifespan: Clinical, Cognitive, and Neurobiological Aspects

Harvard Review of Psychiatry 2016; 24(2): 118-28

View review abstract online

Comparison	Long-term changes in cognitive functioning in people with schizophrenia vs. controls or people with other psychiatric disorders.
Summary of evidence	Moderate quality evidence (large samples, imprecise, some inconsistency, direct) suggests a large effect of poorer long-term cognitive functioning in people with schizophrenia when compared to controls, and a medium-sized effect when compared to people with other psychiatric disorders.

#### Overall cognitive functioning over time

Large, significant effect of poorer overall cognitive performance in people with schizophrenia compared to controls, both at baseline and endpoint, with no differences in effect sizes over time;

Baseline: 7 studies, N = 494, g = -1.43, 95%CI -2.04 to -0.81, p < 0.05, I<sup>2</sup> = 89.9%, p < 0.001

Endpoint: 7 studies, N = 494, g = -1.50, 95%CI -2.12 to -0.87, p < 0.05,  $I^2 = 88.3\%$ , p < 0.001

The difference between patients and controls was significantly larger in samples with older patients than in samples with younger patients (b = -0.03, 95%CI -0.06 to -0.01, p = 0.026).





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Medium-sized, significant effect of poorer overall cognitive performance in people with schizophrenia compared to people with other psychiatric disorders, both at baseline and endpoint, with no differences in effect size over time;

Baseline: 4 studies, N = 251, g = -0.48, 95%CI -0.74 to -0.22, p < 0.05, I<sup>2</sup> = 0%

Endpoint: 4 studies, N = 251, g = -0.65, 95%CI -0.94 to -0.36, p < 0.05,  $I^2 = 0\%$ 

Other psychiatric disorders included non-psychotic depression, other psychotic disorders, bipolar disorder, first-episode affective psychosis, borderline personality disorder, affective and somatisation disorders.

There was no effect of age on this comparison.

Consistency	Inconsistent for people with schizophrenia vs. controls, consistent for people with schizophrenia vs. other psychiatric disorders.
Precision	Imprecise
Directness	Direct

Lincoln TM, Lüllmann E, Rief W

Correlates and long-term consequences of poor insight in patients with schizophrenia. A systematic review

Schizophrenia Bulletin 2007; 33(6): 1324-1342

View review abstract online

Comparison	Association between insight and functional outcomes in people with schizophrenia.
Summary of evidence	Moderate to low quality evidence (small samples, unable to assess consistency or precision, direct) suggests lower insight is associated with worse work performance.

#### Insight and functional outcomes

2 studies (N = 127) reported that lower insight was associated with worse work performance including lower social skills, work quality, cooperativeness and personal presentation at work. Impaired insight was also associated with poorer overall functioning (1 study, N = 23), social functioning (1 study, N = 74) and social adjustment and symptom discomfort (1 study, N = 32).

Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

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McGinty J, Upthegrove R

Depressive symptoms during first episode psychosis and functional outcome: A systematic review and meta-analysis

Schizophrenia Research 2020; 218: 14-27

View review abstract online

Comparison	Depressive symptoms and functional outcome after a first episode of psychosis.
Summary of evidence	High quality evidence (large sample, consistent, precise, direct) suggests more severe depressive symptoms during a first episode psychosis were weakly correlated with poorer functioning at follow-up (12-24 months).

#### **Functioning**

Increased depressive symptoms during a first episode psychosis were weakly correlated with poorer functioning at follow-up (12-24 months);

7 studies, N = 932, r = -0.16, 95%CI -0.24 to -0.09, p < 0.001, I<sup>2</sup> = 23%, p = 0.26 There was no moderating effect of length of follow-up.

There was no association with functional remission rates (1-10 years);

9 studies, N = 2,265, OR = 0.87, 95%Cl 0.68 to 1.13, p = 0.294,  $l^2$  = 66%, p = 0.003

There was no moderating effect of remission definitions.

Consistency in results	Consistent for functioning, inconsistent for remission.
Precision in results	Precise
Directness of results	Direct

Nevarez-Flores AG, Sanderson K, Breslin M, Carr VJ, Morgan VA, Neil AL

Systematic review of global functioning and quality of life in people with psychotic disorders

Epidemiology and Psychiatric Sciences 2019; 28: 31-44

View review abstract online



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Comparison	Relationship between functioning and quality of life in people with schizophrenia.
Summary of evidence	Moderate quality evidence (large samples, appears consistent, unable to assess precision, direct) suggests increased global functioning is related to increased quality of life. Authors report that studies using the Quality of Life Scale showing the strongest associations.
Intervie	ewer-assessed quality of life (measured objectively)

Significant, small to large associations between increased functioning and increased quality of life; 8 studies, N = 1,142, r ranged from 0.20 to 0.84, p-values < 0.01

#### Self-assessed quality of life (measured subjectively)

Significant, small to medium-sized associations between increased functioning and increased quality of life;

> 9 studies, N = 1,982, r ranged from 0.16 to 0.58, p-values < 0.01 1 study (N = 51) found no significant association.

#### Health-related quality of life

Significant, small to medium-sized associations between increased functioning and increased quality of life;

1 study, N = 166, r ranged from 0.28 to 0.46 (various scales), p-values < 0.001

Consistency	Appears consistent
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Phillips LJ, Francey SM, Edwards J, McMurray N

Strategies used by psychotic individuals to cope with life stress and symptoms of illness: a systematic review

Anxiety, Stress & Coping 2009; 22(4): 371-410

View review abstract online

Comparison	Outcomes of natural coping strategies employed by people with
	psychosis, for dealing with general life stressors and symptoms



#### Functional outcomes

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	of psychosis.
Summary of evidence	Moderate to low quality evidence (medium to large samples, unable to assess consistency or precision, direct) suggests people with schizophrenia can identify at least one strategy they use to cope with general life stressors or the symptoms of psychosis. The most commonly reported types include avoidance and problem-focused strategies, which also had the greatest association with quality of life. People with schizophrenia often reported limited belief in the effectiveness of these coping strategies; however the use of coping strategies was associated with better long term symptom outcomes.
	Caning with general life atreasers

#### Coping with general life stressors

21 studies examined characteristics of coping strategies for general life events. Types of coping include problem-focused, emotion-focused, avoidance, support-focused, task-focused, and cognitive-focused strategies;

1 study (N = 73) reported people with schizophrenia spectrum disorders are more likely to rate their ability to cope with stressors as less effective compared to controls. 4 studies (N = 228) report that people with schizophrenia and other psychoses are more likely to use avoidance or maladaptive coping compared to healthy controls. 3 of 4 studies (N = 559) suggested patients were more likely to use problem solving or emotion-focused coping strategies than controls. 1 study (N = 91) suggests problem-focused strategies are reported more frequently than avoidance strategies.

1 study (N = 237) reported that 6 months following a hospital admission, emotional coping strategies were used less frequently but no change reported in avoidance strategies. A severe life event was associated with higher levels of problem-centred coping in people with schizophrenia who relapsed (N = 41) compared to relapsed patients who did not experience a life event. Another group (N = 42) reported a longer duration between a life event and a relapse if patients used support services as a coping strategy.

3 studies (N = 187) found that cognitive and executive function deficits were associated with higher levels of avoidant coping or lower levels of cognitive-focused strategies. 2 further studies associated higher levels of avoidance with higher levels of hope and insight (N = 113) and 1 found higher levels of hope and insight were associated with having more active, adaptive coping strategies (N = 96). Insight was also positively correlated with distress (N = 65). Ease of adaptation to illness was significantly influenced by coping strategies (N = 101).

1 study (N = 35) found that over a 16 month follow up, 38% of people schizophrenia reported changes in their method of coping, of which 19.6% shifted toward unfavourable methods. Unfavourable coping was associated with lower self-efficacy; favourable coping was associated with lower symptom levels.

1 study (N = 161) found task-oriented and avoidance coping were the best predictors of quality of life for inpatients; emotion-oriented coping was negatively associated with quality of life. Coping was able to account for 7-25% of variance in quality of life ratings in 2 studies (N = 304). However, one study of outpatients (N = 58) found no associations between quality of life and coping.



#### **Functional outcomes**

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#### Coping with symptoms of psychosis

59 studies examined characteristics of coping strategies for psychotic symptoms;

17 of 19 studies (N = 1,426) report that people with schizophrenia can identify at least one strategy employed to cope with psychotic symptoms such as auditory hallucinations or negative symptoms. Only 2 of 6 studies (N = 365) found a relationship between duration of illness and number of coping strategies. 1 study (N = 60) suggested 93% of respondents used at least one strategy to mitigate the impact of a stressful occurrence or relapse.

2 studies (N = 198) suggest patients found little effectiveness of the coping strategies employed. However, those patients who do cope well with illness reported the most confidence in multiple coping strategies (3 studies, N = 125).

A longitudinal study (N = 95) of inpatients following a first psychotic episode reported that active behavioural coping strategies at baseline were associated with better symptom outcomes over 24 months. However, 1 study (N = 58) suggests that coping style did not moderate a relationship between symptom severity and quality of life.

3 studies (N = 158) found higher levels of negative symptoms was associated with less adaptive coping strategies and more use of emotion-oriented strategies; higher levels of positive symptoms associated with ignoring symptoms and cognitive-oriented strategies.

3 studies (N = 186) reported inconsistent results on the relationship between hospitalisation and the type of coping strategies employed. Coping responses which exacerbate symptom presentation were reportedly less effective than non-symptomatic coping strategies in 4 studies (N = 179). 1 longitudinal study (N = 47) found that patients with psychosis were more likely to utilise coping strategies that exacerbate psychotic symptoms, and to report less control over their symptoms.

Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Santesteban-Echarri O, Paino M, Rice S, Gonzalez-Blanch C, McGorry P, Gleeson J, Alvarez-Jimenez M

Predictors of functional recovery in first-episode psychosis: A systematic review and meta-analysis of longitudinal studies

Clinical Psychology Review 2017; 58: 59-75

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Comparison Predictors of recovery following a first-episode of psychosis.



#### **Functional outcomes**

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Summary of evidence	Moderate to high quality evidence (large samples, some inconsistency, precise, direct) finds small associations between better functioning after treatment for first-episode psychosis
	and shorter duration of untreated psychosis, less severe
	symptoms, better premorbid functioning, better cognitive ability,
	more education, longer work history and female gender.

#### **Predictors of functional recovery**

Small associations were found for the following variables and better overall functioning;

Shorter duration of untreated psychosis: 20 studies, N = 2,528, r = -0.16, 95%CI -0.22 to -0.10, p < 0.0001,  $I^2$  = 69%, p < 0.0001

Less severe negative symptoms: 18 studies, N = 2,320, r = -0.26, 95%CI -0.35 to -0.15, p < 0.0001,  $I^2$  = 90%, p < 0.0001

Less severe positive symptoms: 12 studies, N = 1,809, r = -0.23, 95%CI -0.32 to -0.15, p < 0.0001,  $I^2 = 85\%$ , p < 0.0001

Better premorbid functioning: 14 studies, N = 2,010, r = 0.26, 95%Cl 0.31 to 0.21, p < 0.0001, l<sup>2</sup> = 71%, p < 0.0001

Better cognitive ability: 6 studies, N = 490, r = 0.18, 95%Cl 0.07 to 0.29, p = 0.001,  $l^2$  = 13%, p = 0.31

Female gender: 14 studies, N = 2,654, r = 0.17, 95%Cl 0.12 to 0.23, p < 0.0001,  $l^2$  = 70%, p < 0.0001

More education: 12 studies, N = 2,671, r = 0.16, 95%Cl 0.11 to 0.20, p < 0.0001,  $l^2$  = 6%, p = 0.27 Longer work history: 5 studies, N = 635, r = 0.31, 95%Cl 0.15 to 0.45, p < 0.0001,  $l^2$  = 70%, p = 0.01

Consistency in results	Inconsistent, apart from cognitive ability and education.
Precision in results	Precise
Directness of results	Direct

Switaj P, Anczewska M, Chrostek A, Sabariego C, Cieza A, Bickenbach J, Chatterji S

Disability and schizophrenia: a systematic review of experienced pscyhosocial difficulties

**BMC Psychiatry 2012; 12: 193** 

View review abstract online





#### **Functional outcomes**

Comparison	Assessment of research focus into domains of psychosocial disability experienced by people with schizophrenia.
Summary of evidence	Moderate to low quality evidence (unclear sample size, unable to assess precision or consistency, direct) suggests medication is associated with a range of disability including pain, anxiety, insomnia, somnolence, appetite, fatigue, and libido. The intensity of disability is associated with treatment, symptoms, socio-demographics, global disability, emotional functioning, and cognitive functioning.

#### **Psychosocial Disabilities**

104 studies were identified that assessed a measure of psychosocial disability in schizophrenia;

The most extensively studied disabilities were global concepts including psychopathological symptoms (53% of studies); disability and function (37% of studies); quality of life (23% of studies); health status (12% of studies).

The most extensively studied domains of mental function were cognitive function (27% of studies); emotional function (27%); energy and drive (15%); psychomotor functions (11%); and pain (11%).

The most extensively studied domains of functional activity and participation were in relationships (31% of studies); employment (20%); health (12%); social activities (11%) and self-care (11%).

17 studies assessed factors associated with the onset of disability:

Medication was reported in 14 studies to be associated with a range of disability (adverse effects of medication) including pain (11 studies); anxiety (8 studies); insomnia (8 studies); somnolence (7 studies); appetite (3 studies); fatigue (3 studies); and libido (3 studies).

95 studies assessed factors associated with the intensity of disability;

These included treatment (reported in 56% of studies); symptoms (26%); socio-demographics (24%); global disability (13%); emotional function (12.5%); and cognitive function (12%).

Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Unclear samples and comparisons.

Ventura J, Helleman GS, Thames AD, Koellner V, Nuechterlein KH

Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis

Schizophrenia Research 2009; 113(2-3): 189-199



#### **Functional outcomes**

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Comparison	Relationship between cognitive and community functioning, and symptom severity.
Summary of evidence	Moderate quality evidence (large samples, inconsistent, unable to assess precision, direct) suggests negative symptoms, but not positive symptoms, are significantly associated with cognitive and community functioning and skills assessment. Negative symptom severity may act as a mediator between cognitive deficits and functional impairment.

Significant, weak to medium-sized association between increased negative symptom severity and poor overall cognitive functioning;

53 studies, N = 4,929, 
$$r$$
 = -0.24,  $p$  < 0.01

This effect was consistent across all individual domains of cognitive functioning (working memory, processing speed, verbal learning, problem solving, attention, and visual learning).

Significant, large association between increased negative symptom severity and poor community functioning:

23 studies, N = 2,341, 
$$r$$
 = -0.42,  $p$  < 0.01

Significant, medium-sized association between increased negative symptom severity and poor skills assessment;

5 studies, N = 269, 
$$r = -0.28$$
,  $p < 0.01$ 

Subgroup analyses examined the potential for negative symptoms to mediate the effect of cognitive performance on functional outcomes;

The relationship between cognition and community functioning appears to be at least partially mediated by negative symptom severity, p < 0.01

The relationship between cognition and skills assessment also appears to be mediated by negative symptom severity, p < 0.01

These effects were consistent across all neurocognitive domains, including speed of processing, verbal learning, working memory, attention, problem solving, and visual learning.

#### **Positive symptoms**

No relationship was reported between positive symptom severity and overall cognitive functioning;

25 studies, N = 1,297, 
$$r = -0.00$$
,  $p = 0.97$ 

Individual domains of cognitive function (working memory, processing speed, verbal learning, problem solving, attention, and visual learning) also failed to show any relationship with positive symptoms.

No relationship was reported between positive symptom severity and community functioning;



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#### **Functional outcomes**

9 studies, N = 549, <i>r</i> = -0.03, <i>p</i> = 0.55	
Consistency	Authors report all results are inconsistent.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

#### **Explanation of acronyms**

CI = confidence interval, d = Cohen's d and g = Hedges' g = standardised mean differences (see below for interpretation of effect size), I² = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, p = statistical probability of obtaining that result (p < 0.05 generally regarded as significant), Q = Q statistic for the test of heterogeneity,  $Q_w$  = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency),  $Q_B$  = test for between group differences (heterogeneity between groups of studies for an outcome of interest), r = correlation coefficient, vs. = versus

#### **Functional outcomes**



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#### 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<sup>17</sup>.

† 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<sup>17</sup>.

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 <  $0.2^{18}$ . InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

#### **Functional outcomes**



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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 strona association. а Unstandardised (b) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in independent variable, statistically controlling for the other independent variables. regression Standardised coefficients represent the change being in of standard deviations comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability results) that in 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. l² can calculated from Q (chi-square) for the test of heterogeneity with the following formula<sup>17</sup>;

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

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 relaxed19.

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 Indirectness of population, В. comparator and/or outcome can also occur when the available evidence regarding a population, intervention, particular 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-tohead comparisons of A and B.

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#### **Functional outcomes**

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