# Use of the Chinese version of the MATRICS Consensus Cognitive Battery to assess cognitive functioning in individuals with high risk for psychosis, first-episode schizophrenia and chronic schizophrenia: a systematic review and meta-analysis

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## Summary

**More than one hundred studies have used the mainland Chinese version of the MATRICS Consensus Cognitive Battery (MCCB) to assess cognition in schizophrenia, but the results of these studies, the quality of the reports, and the strength of the evidence provided in the reports have not been systematically assessed. We identified 114 studies from English-language and Chinese-language databases that used the Chinese MCCB to assess cognition in combined samples of 7394 healthy controls (HC), 392 individuals with clinical high risk for psychosis (CHR-P), 4922 with first-episode schizophrenia (FES), 1549 with chronic schizophrenia (CS), and 2925 with schizophrenia of unspecified duration. The mean difference (MD) of the composite MCCB T-score (–13.72) and T-scores of each of the seven cognitive domains assessed by MCCB (–14.27 to –7.92) were significantly lower in individuals with schizophrenia than in controls. Meta-analysis identified significantly greater cognitive impairment in FES and CS than in CHR-P in six of the seven domains and significantly greater impairment in CS than FES in the reasoning and problem-solving domain (i.e., executive functioning). The only significant covariate of overall cognitive functioning in individuals with schizophrenia was a negative association with the severity of psychotic symptoms. These results confirm the construct validity of the mainland Chinese version of MCCB. However, there were significant limitations in the strength of the evidence provided about CHR-P (small pooled sample sizes) and the social cognition domain (inconsistency of results across studies), and the quality of many reports (particularly those published in Chinese) was rated 'poor' due to failure to report sample size calculations, matching procedures or methods of handling missing data. Moreover, almost all studies were cross-sectional studies limited to persons under 60 with at least nine years of education, so longitudinal studies of under-educated, older individuals with schizophrenia are needed.**



Keywords: MCCB; Schizophrenia; Clinical high risk; First-episode schizophrenia; Chronic schizophrenia; Cognition

## Introduction

Hundreds of studies have reliably shown that cognitive impairment is one of the core characteristics of schizophrenia (SCZ), with deficits typically manifesting in the early stage of the illness. Several meta-analyses report impairments in multiple cognitive domains in individuals with first-episode schizophrenia (FES), particularly in processing speed and memory.[1–3] Moreover, Fusar-Poli and colleagues conducted a meta-analysis of 54 studies evaluating cognitive functioning in individuals at clinical high risk for psychosis (CHR-P) and also found significant and widespread cognitive impairments in this population.[4,5]

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## Research in context

### Evidence before this study

Previous research consistently reports cognitive impairments in individuals with clinical high risk for psychosis (CHR-P) and first-episode schizophrenia (FES), but we could find no reports comparing cognitive functioning in individuals with chronic schizophrenia (CS) to those with FES, so it is uncertain whether cognitive function declines further or remains static after psychosis emerges. Studies assessing the covariates of cognitive functioning in schizophrenia (i.e., age, gender, education, psychotic symptoms) have had varying results. One of the challenges in combining results across studies is the wide variety of measures used to assess cognition in schizophrenia. To address this issue, neuropsychologists in the United States developed the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB), which assesses seven distinct cognitive domains. This battery has become the most widely used comprehensive measure of cognitive functioning in schizophrenia and has been translated into several languages, but the validity of these translated versions has not been formally assessed. For example, there are over 100 published reports of studies using the Chinese version of the MCCB, but the quality of these reports and the strength of the evidence provided in these reports have not been systematically assessed.

### Added value of this study

This systematic review and meta-analysis combines the results of studies using the mainland Chinese version of MCCB, assesses the quality of the reports of the studies, compares cognitive functioning between five groups of subjects (healthy controls, CHR-P, all individuals with schizophrenia, and, separately, FES and CS), and considers the relationship of various covariates with cognitive outcomes. Compared to healthy controls, all four clinical groups had deficits in all seven cognitive domains. Individuals with FES and CS were significantly more impaired than individuals with CHR-P. There were significantly greater cognitive deficits in CS than FES in the reasoning and problem-solving domain (i.e., executive functioning) and –surprisingly—significantly *less* severe deficits in CS than FES in the attention-vigilance domain. Meta-regression analyses found no relationship of age, gender, or education with the magnitude of cognitive deficits, but there was a significant positive association with the severity of psychotic symptoms.

### Implications of all the available evidence

These results confirm the construct validity of the mainland Chinese version of MCCB. However, some of the results for the social cognition domain were inconsistent, so alternative measures of social cognition should be considered. The significantly greater cognitive impairment in FES and CS compared to CHR-P supports hypotheses about the continued progression of cognitive deficits once psychotic symptoms emerge. On the other hand, the contradictory results between FES and CS for different cognitive domains highlight the need for longitudinal studies to determine whether different cognitive domains follow different trajectories throughout the course of schizophrenia. The failure to identify significant associations of cognition with education and age in individuals with schizophrenia needs to be re-assessed in studies of under-educated individuals with less than nine years of schooling and individuals over 60 years of age.

Less is known about the trajectory of cognitive impairments after the onset of SCZ. Some studies report cognitive decline during the early phase of the illness that subsequently remains static during later stages of the illness, particularly in the first decade.[6–13] However, emerging evidence suggests a progressive cognitive decline in selected cognitive domains over time.[14–22] For instance, in a recent publication about individuals with chronic, untreated SCZ in rural China, Stone and colleagues found a relationship between the duration of illness and the severity of the decline in selective cognitive domains beyond what is expected during normal ageing.[21] Similarly, Jonas and colleagues found an accelerated deterioration in the intelligence quotient among individuals with schizophrenia over a 25-year follow-up.[23] Thus, the evidence is mixed about the occurrence of ongoing cognitive decline after the first episode of psychosis and, if a decline does occur, about which cognitive domains are affected. Comparing the cognitive performance of individuals with FES and chronic schizophrenia (CS) could help to resolve this issue.

One of the challenges in combining results across studies and addressing these questions is the wide variety of measures used to assess cognitive functioning in schizophrenia. This issue and the need to systematically evaluate treatments to improve cognition in schizophrenia motivated the U.S. National Institute of Mental Health (NIMH) to launch an initiative to develop a battery of cognitive tests that were sensitive to cognitive deficits in schizophrenia, brief enough to avoid posing an undue burden on study participants, able to distinguish the effect of pharmacological treatments, and that could be easily translated for use in international studies. This initiative, Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS), was funded in 2002[24,25]; a wide range of potential cognitive measures were tested over the subsequent six years, culminating in the MATRICS Consensus Cognitive Battery (MCCB). The MCCB

subsequently became the most widely used comprehensive measure of cognition in schizophrenia in English-speaking countries.

The MCCB was translated into simplified Chinese and co-normed and standardised by Shi and colleagues in 2015.[26] The mainland Chinese version of MCCB excludes the Letter Number Span (LNS) test used in the English version because many Chinese participants do not recognise the English alphabet. In some studies using MCCB in China the LNS test is replaced by the optional Digit Span (DS) test,[27] so the mainland Chinese version of MCCB includes either nine or ten tests. One of the earlier papers about the Chinese version of MCCB provided standardised scores for the DS test,[28] but this test was not included in the national MCCB standardisation study.[26]

The mainland Chinese version of MCCB has been used to assess cognition in schizophrenia in over one hundred studies, but the quality and results of these studies and the validity of the translated version of this battery have not been systematically evaluated. Moreover, most prior reviews that assess cognition using a variety of instruments (including MCCB) in schizophrenia primarily include studies that enrol English-speaking participants from high-income countries. Previous reports suggest that environmental and cultural characteristics can impact cognition,[29] so comparing the pattern and magnitude of cognitive deficits in middle-income countries like China with those reported in high-income countries is important. Two previous meta-analyses that included studies using the mainland Chinese version of MCCB did not resolve these issues: one meta-analysis of 56 studies only included first-episode schizophrenia, and only 19 of the 56 studies assessed all seven MCCB domains[30]; and another meta-analysis of 12 studies that used MCCB to compare cognition in SCZ to bipolar disorder only included three studies from mainland China.[31] Therefore, it is important to systematically evaluate the methods, quality, and results of all published studies that use the mainland Chinese version of MCCB to assess cognitive functioning in schizophrenia and to combine the results of these studies in a meta-analysis.

To the best of our knowledge, no previous meta-analysis has directly compared the cognitive functioning of individuals with CHR-P, FES, and CS using the same comprehensive cognitive battery—thus minimising the confounding effect of combining results of studies that use different measures. The meta-analysis reported in this paper aims to identify all studies that use the full (i.e., seven-domain) mainland Chinese version of MCCB to compare cognitive functioning in healthy individuals to that in persons with SCZ (FES and CS) or CHR-P. Our objectives were: 1) to describe the characteristics and quality of the studies in which the mainland Chinese version of MCCB is used to assess cognition in SCZ or CHR-P; 2) to assess the construct validity (i.e., known-groups validity)[32] of the mainland Chinese MCCB by determining whether it identifies expected cognitive differences between individuals with SCZ and HC; and 3) to conduct meta-analyses of MCCB results that compare overall and domain-specific cognitive functioning between CHR-P, FES, and CS.

## Methods

The protocol for this systematic review and meta-analysis was registered on the Open Science Framework Registry (https://osf.io/e7ns8).

### Inclusion and exclusion criteria

Potential studies were included based on the following PICOS criteria:

*Participants* (P): Chinese individuals in mainland China with SCZ or CHR-P.

*Intervention* (I): Not applicable.

*Comparison* (C): Healthy controls.

*Outcomes (O):*

- T-scores of each of the seven MCCB domains (speed of processing, verbal learning, working memory, visual learning, reasoning and problem-solving, social cognition and attention-vigilance);
- T-scores of composite MCCB scores (i.e., a summary score of the seven domains);
- Raw scores of each of the 10 MCCB tests [Trail Making Test, Part A; Brief Assessment of Cognition in Schizophrenia, symbol coding subtest; Hopkins Verbal Learning Test-Revised, immediate recall (three learning trials); Wechsler Memory Scale, 3rd ed., spatial span subtest; Neuropsychological Assessment Battery, mazes subtest; Brief Visuospatial Memory Test-Revised; Category fluency test, animal naming; Mayer-Salovey-Caruso Emotional Intelligence Test, managing emotions branch; Continuous Performance Test, identical pairs; and The Wechsler-Bellevue Intelligence Scale-III, digit span subtest (which was assessed in 53 [46%] of the 114 identified papers).

*Study design* (S): Case-control studies and intervention trials that provide baseline (pre-intervention) assessment of cognition using MCCB. Only the baseline data from intervention trials were included.

Potential studies were excluded if:

- Results were not reported in Chinese or English;
- The diagnostic criteria for SCZ were not specified or were not based on the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV or DSM-5), the International Classification of Diseases (ICD-10 or ICD-11), or the Chinese Classification of Mental Disorders (CCMD)[33];
- The results did not include raw or domain scores of the seven domains;

- Participants included individuals with a history of severe neurological illness, severe brain injury, intellectual disability, or dementia;
- The patient group combined subjects with SCZ and with other psychotic disorders without providing separate results for subjects with SCZ; or
- The study was not conducted in mainland China.

### Information sources and search strategies

Searches of three Chinese-language databases (China National Knowledge Infrastructure [CNKI], Wanfang Data, and Sino Biomedicine Service System [SinoMed]) were performed on the 26th and 27th of May 2022 and of three English-language databases (Pubmed, Scopus, and PsycINFO) on 13th June 2022. Initial search terms of titles and abstracts in both English and Chinese databases included "MCCB", "MATRICS", "cognitive assessment", "neuropsychological assessment", "schizophrenia", and "clinical high risk". "China" or "Chinese" were additional search terms in the searches of English-language databases. After pilot testing of the initial search terms, "psychometric" and "neurodevelopment" were added to the search terms for the searches of English-language databases. The search strategies used for each database are shown in Supplementary Materials (Table S1).

### Selection process

The initial search identified 1095 articles in Chinese-language databases and 1064 in English-language databases (Fig. 1). Endnote was used to identify duplicates. The titles and abstracts of the unique articles were screened for potential eligibility by four investigators (BC, MAB, GSL, and YXL). The same four investigators then reviewed the full texts of all potentially eligible articles to determine whether they met inclusion and exclusion criteria. At each screening stage, two investigators independently assessed each article; any discrepancies about inclusion were resolved by discussions between the investigators or by consulting a senior investigator.

After the full-text review stage, reference lists of included papers and relevant reviews were hand-checked to locate papers that met inclusion criteria that had not been identified in the electronic search.[30,31,34]

### Data items and collection

Data extraction of all included articles was conducted by the first author (BC). The accuracy of the data extraction was assessed by having another researcher (YS) familiar with the different scoring methods used to report MCCB results independently extract data from a random selection of 20% of the included articles. If the MCCB scores were reported in a manner not consistent with commonly reported T-scores or raw scores, or if the sample sizes were not specified, the paper's authors were contacted via e-mail to collect the required information.

The data items collected from the included papers are shown in Table 1. Each of the nine or ten separate tests included in the MCCB has two scores: a raw score and a T-score, all of which are continuous measures. The T-scores for each test are based on comparing the individual's raw scores with those of a normative sample (of 656 individuals from six locations around the country)[26] or of a healthy control sample collected as part of the specific study. All scores are standardised to a mean of 50 with a standard deviation of 10.

The T-scores for the seven cognitive domains assessed by MCCB are based on the T scores of the individual tests associated with each domain. The T-scores of five of the seven domains are based on the T-scores of a single corresponding test: Verbal Learning Domain—Hopkins Verbal Learning Test-Revised, immediate recall; Visual Learning Domain—Brief Visuospatial Memory Test-Revised; Reasoning and Problem-Solving Domain—Neuropsychological Assessment Battery, mazes subtest; Attention-Vigilance Domain—Continuous Performance Test, Identical Pairs; Social Cognition Domain—Mayer-Salovey-Caruso Emotional Intelligence Test, managing emotions branch. The T-score for the Speed of Processing Domain is based on the standardised T-score for the sum of the three T-scores of three separate tests: Trail Making Test, Part A; Brief Assessment of Cognition in Schizophrenia, symbol coding subtest; and Category fluency test, animal naming. The T-score for the Working Memory Domain is either the T-score for the Wechsler Memory Scale, 3rd ed., spatial span subtest (51 studies) or—for 20 of the studies that included both the spatial span and digit span tests—the standardised T-score for the sum of the T-scores of the two separate tests.[28] The composite MCCB score is the standardised T-score for the sum of the seven domain scores.

### Quality of the reports about the studies

The quality and comprehensiveness of the reports about included studies were assessed using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[35] The analysis included 103 case–control (i.e., observational) studies and 11 randomised controlled (RCT) intervention studies. However, in this review we only considered the baseline data provided in the RCTs, so the quality of the reports of these studies was also assessed using the criteria used to assess observational studies (i.e., STROBE). A per cent score was assigned to each paper based on the proportion of the 78 items recommended by STROBE reported in the paper. Using the method described by Limaye and colleagues,[36] the quality of each report was classified as 'poor' (<50% of the 78 items), 'fair' (50–69%), 'good' (70–84%), or 'excellent' (≥85%). Four reviewers (BC,

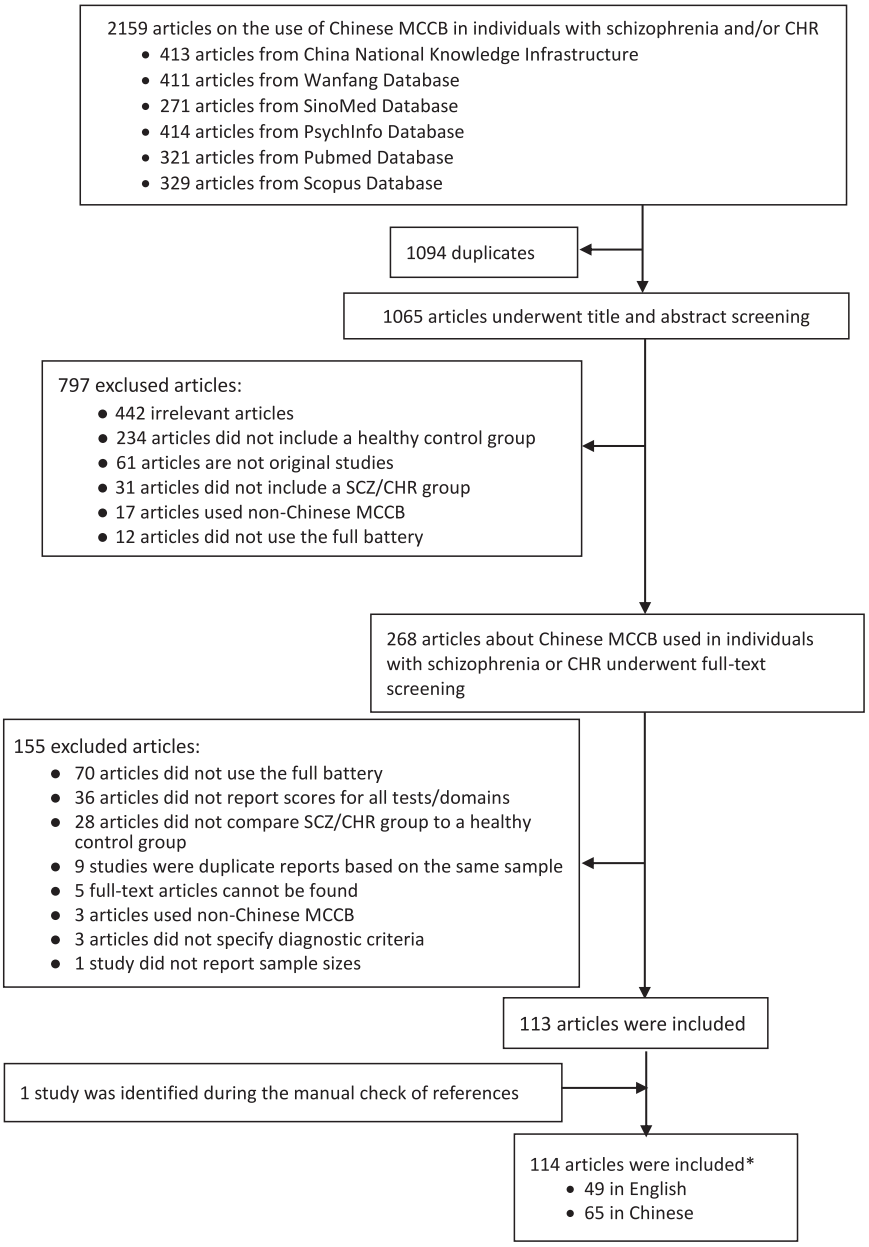


***Fig. 1:*** Flowchart of article selection for the review. * 5 studies compared both schizophrenia and CHR-P subjects to healthy controls, so the 114 articles include 9 comparisons of CHR-P subjects with healthy controls and 110 comparisons of individuals with schizophrenia with healthy controls.

MAB, DYL and XZY) participated in the assessment; two independently assessed each article, and disagreements were resolved by discussions among reviewers or consulting a senior researcher.

### Quality of the evidence provided in meta-analyses

We used the Cochrane 'Grading of Recommendations, Assessment, Development and Evaluation' (GRADE) criteria to assess the quality of the evidence in the separate meta-analyses that compared the composite and domain-specific scores between clinical groups and HC. Two reviewers (BC and DYL) independently assessed five characteristics of each analysis using the GRADEpro GDT software: 1) risk of bias, 2) inconsistency, 3) indirectness, 4) imprecision, and 5) publication bias.[37–42] Based on the assessment of these five items, the certainty of the results was classified as 'high', 'moderate', 'low', or 'very low'. By definition, the quality of

| Outcome | Category | Definition |
|---|---|---|
| Primary | Main findings of the studies | T-scores reported for MCCB tests, domains, and the overall composite scores |
| Secondary | Main findings of the studies | Raw scores reported for each MCCB test |
| Covariates | Characteristics of participants | Age, gender, education, use of antipsychotic medications, duration of illness, Positive and Negative Syndrome Scale (PANSS) scores, classification of the type of schizophrenia by the authors (if any) as 'first-episode schizophrenia' or 'chronic schizophrenia' |
| Other | MCCB-related factors | Number of tests used (nine or ten), type of scores reported (raw score, T-scores, or both), method of computing T score |
| | Characteristics of the study | Type of study (cross-sectional, intervention trial), inclusion and exclusion criteria for participants, diagnostic criteria for schizophrenia or criteria used to determine clinical high risk for psychosis, sample size of each group and any specified cohorts within each group (e.g., by gender, type of schizophrenia, etc.) |
| | General information | Publication year, first author, study title, full citation, DOI |

MCCB, MATRICS Consensus Cognitive Battery.

*Table 1:* **Data items collected from each eligible study included in the review.**

evidence from observational studies is categorised as 'low' or 'very low' (Since we only included the baseline data from intervention trials, in these meta-analyses data from intervention trials were treated as data from observational studies, so all 114 studies included in this report are considered observational studies.) However, the level of evidence for analyses in which there was a large effect size defined as a pooled mean difference of 10 or greater between the two groups (10 is the standard deviation of T-scores) were upgraded one level if there were no identified problems in the five assessed characteristics. Differences in the quality assessment of the two independent reviewers were resolved by discussion.

The heterogeneity (inconsistency) of meta-analysis results was examined using $I^2$ values and prediction intervals estimated using the Tau ($\tau^2$) statistic. In situations in which included studies have large sample sizes (which was the case in this review), $I^2$ increases with increases in the sample size, so the GRADE Handbook recommends preferentially using $\tau^2$ values—which are independent of sample size—and the corresponding prediction intervals to assess heterogeneity.[43–45]

In this study we used the 'optimal information size' method to identify meta-analyses that potentially result in imprecise estimates.[38] Based on requiring an effect size of 0.2 and a power of 80%, the pooled sample in each group should include a minimum of 394 subjects, so meta-analyses in which the pooled sample of either group had less than 394 subjects were classified as having a 'serious imprecision' problem.

We used funnel plots and Egger's tests to assess potential publication bias for meta-analyses that included ten or more studies; the studies included in meta-analyses in which the p-value of the Egger's test was lower than 0.10 were suspected of publication bias.[46] According to the Cochrane Handbook,[47] potential publication bias in meta-analyses that include less than ten studies cannot be assessed with funnel plots or Egger's test. Therefore, we used the Luis Furuya-Kanamori asymmetry (LFK) index to assess potential publication bias in meta-analyses which included less than ten studies; studies included in meta-analyses in which the LFK index was less than –1 or greater than +1 were suspected of publication bias.[48]

## Synthesis of results

Data analyses were performed using R 4.2.2 with the following packages: meta-6.5.0, metafor-4.2.0, metasens-1.5.2, dplyr-1.1.2, ggplot2-3.4.2, and readxl-1.4.3. The differences in the means of the raw scores of individual tests and the means of the composite and domain-specific T-scores between patient and control groups were assessed for each study. Then the weighted mean of these mean differences (MDs) across studies (and their corresponding 95% confidence intervals) was used as the effect size measure in meta-analyses using random-effects models. Random-effects models were chosen due to the high heterogeneity among included studies and the potential impact of unreported demographic and clinical variables, which could differentially affect reported cognitive impairment of individuals with schizophrenia across studies. Some studies only reported results for subgroups of subjects (e.g., males and females); in this situation, we computed the corresponding results for the entire sample and used those results in the meta-analyses and meta-regression analyses.

Meta-analyses (using the inverse variance method) compared the raw scores of the ten individual tests, the T-scores of the seven domains, and the T-score of the composite cognitive score of several different groups of subjects: SCZ versus HC, CHR-P versus HC, FES versus HC, CS versus HC, CHR-P versus FES, CHR-P versus CS, and FES versus CS. For these analyses, the categorisation of FES and CS samples depended on the categorisation of the original authors: if the authors reported separate analyses for FES subjects, the FES sample was included in the meta-analysis of FES patients; if the authors reported separate analyses for CS subjects, the CS sample was included in the meta-analysis of CS patients; if authors did not subclassify their subjects with SCZ, the reported sample was only included in the meta-analyses of all individuals with SCZ (which also included the FES and CS samples).

Mixed effects meta-regressions (using the Restricted Estimation of Maximum Likelihood [REML] method) were conducted to examine the effect of three potential covariates on MCCB composite scores in subjects with SCZ and HC—age, gender, and education. For each of the three covariates, meta-regression analyses combined the SCZ and HC samples and used the covariate, the group type (SCZ or HC) and the covariate*group interaction term as predictors in the model.

To assess the potential relationships between the duration of illness, current severity of illness, and medication usage on cognitive functioning in patients with SCZ, we conducted three separate mixed effects meta-regressions of the mean composite scores in samples of subjects with SCZ using duration of illness, the Positive and Negative Syndrome Scale (PANSS) total score, and the percentage of subjects who were taking antipsychotic medication at the time of assessment as covariates.

### Role of the funding source

The funders played no role in study design, data collection, data analysis, interpretation, or writing of the report.

## Results

### Study selection and characteristics

We found 2159 articles in the Chinese and English databases (Fig. 1). After 1094 duplicates were removed, we screened titles and abstracts of 1065 articles and subsequently screened 268 full-text documents. After exclusions, 113 records were included. During the manual check of reference lists of the included articles, one additional article was found that met our inclusion criteria. The 114 articles included four studies that only compared CHR-P individuals to HC, 105 studies that only compared individuals with SCZ to HC, and five studies that compared both CHR-P and SCZ individuals to HC; in total, there were nine comparisons of CHR-P individuals with HC and 110 comparisons of individuals with SCZ with HC. The geographic distribution of the 109 studies that were conducted in a single province of mainland China is shown in Fig. 2. Seventeen of China's 31 province-level administrative regions reported one or more studies; 66 (61%) of the studies came from three provinces: Beijing (40 studies), Henan (14 studies) and Guangdong (12 studies). The detailed characteristics of the included studies are shown in Table 2.

### Quality of reporting

Based on the reporting recommendations for observational studies in the STROBE statement, the quality of the reports of the 114 included studies were classified as 'poor' in 28 (24.6%) studies, 'fair' in 85 (74.6%) studies and 'good' in 1 (0.8%) study. Among the subset of 49 English-language publications, 1 (2.0%) was classified as good, and 48 (98.0%) were classified as fair, while among the 65 Chinese-language publications, 37 (56.9%) were classified as fair and 28 (43.1%) were classified as poor. Overall, the assessed quality of the English-language reports was significantly greater than that of the Chinese-language reports (Mann–Whitney $W = 888$, $p < 0.0001$).

Analysis of the individual STROBE items identified four common problems in the 114 reports: 1) only twelve reports clearly indicated the study design, 2) only three described the method of calculating the sample size, 3) only five reported the number of eligible subjects (i.e., screened individuals who meet inclusion and exclusion criteria) or provided a flowchart of case identification, and 4) none of the reports described methods of addressing missing data. Among the reports of the 47 studies that matched cases and controls, only two provided details of their matching criteria, and none specified the number of controls per case. Details of the assessment of the quality of the reports of the 114 studies are provided in Supplementary Excel Table S1.

### Meta-analyses of composite scores, domain scores, and test scores reported in included papers

Sixty-three articles comparing SCZ to HC included MCCB composite scores. Table 3 and the Forest plot in Fig. 3 show that the SCZ groups performed significantly worse than the HC groups (pooled MD of the 63 studies = –13.72; 95% CI, –14.72 to –12.71, $I^2 = 90\%$). As shown in Fig. 4, pooling data from 38 articles which reported composite scores for FES and 13 articles that reported composite scores for CS, the pooled MDs of composite scores (compared to HC) were statistically significant for both groups of patients (for FES, pooled MD = –13.97, 95% CI: –15.46 to –12.49, $I^2 = 96\%$; for CS, pooled MD = –14.15, 95% CI: –16.70 to –11.59, $I^2 = 89\%$). However, the pooled MDs of the composite scores for FES and CS were not significantly different ($\chi^2 = 0.01$, df = 1, $p = 0.91$).

The pooled MDs comparing the different clinical groups of subjects to HC for the seven MCCB cognitive domains are shown in Table 3. The forest plots for these analyses are provided in Supplemental Materials, Figures S1–S28. The results show that all seven cognitive domains assessed were significantly impaired in the combined SCZ group and all clinical subgroups. Comparison of the magnitude of the pooled MDs between the FES, CS and CHR-P subgroups are also shown in Table 3 and Fig. 5. The CHR-P group performed significantly better than the FES group in all seven cognitive domains and better than the CS group in six of the seven cognitive domains (the superior performance of the CHR-P group in the attention-vigilance domain was non-significant [$p = 0.095$]). Comparison of results for the FES and CS groups found that for six of the seven domains the FES group performed better than the


***Fig. 2:*** Geographic distribution of 109 studies that administered the Chinese version of MCCB to individuals with schizophrenia or with high risk for psychosis in mainland China: 2012–2022.

CS group, but this difference was only statistically significant for the reasoning and problem-solving domain ($\chi^2 = 9.44$, df = 1, p = 0.0021); in one domain—attention-vigilance—the CS group performed significantly *better* than the FES group ($\chi^2 = 4.22$, df = 1, p = 0.040).

To assess whether the heterogeneity of results across studies was related to the quality of the studies, we conducted a sensitivity analysis that compared results of studies rated as 'good quality' or 'fair quality' based on STROBE criteria to the results of studies rated as 'poor quality'. These meta-analyses for the composite score and the seven domain scores were limited to studies comparing cognition in SCZ to that of HC. As shown in Supplementary Materials, Figures S29–S36, in all analyses the good- and fair-quality studies were less heterogeneous than the low-quality studies (based both on $I^2$ values and prediction intervals), but there were no significant differences in the magnitude of the cognitive deficits in SCZ identified in the two types of reports.

A minority of studies (n = 21) provided raw scores of the ten individual tests. Only two studies with CHR-P samples and only one study with a CS sample reported raw scores,[49,154,155] so the meta-analyses for the raw scores of the ten individual tests were limited to the comparison of the SCZ and HC groups. Individuals with SCZ performed significantly worse than HCs in all ten tests (Supplemental Materials Table S2).

## Certainty of evidence provided in the meta-analyses

Results of the GRADE assessments of the certainty of the evidence provided in the meta-analyses conducted in this review are shown in Table 3. The relatively low GRADE ratings reported are partly explained by the fact that the samples of subjects were pre-identified as 'cases' or 'controls', not randomly assigned; this precludes the possibility of a 'high' GRADE rating—high ratings are only given to randomised controlled trials.

### *Risk of bias*

None of the included studies had serious problems related to the risk of bias. The characterisation of the clinical groups and control groups was based on standardised diagnostic criteria. Enrolled patients were given a formal diagnosis of SCZ; enrolled individuals with CHR-P were either screened positive using formal criteria of psychosis-risk symptoms (6 studies) or first-degree relatives of individuals with SCZ (1 study); and in all studies, individuals with other mental disorders (e.g., schizoaffective disorder) or neurological conditions (e.g., intellectual disability) were explicitly excluded from the samples. The assessment of cognitive functioning in all participants was conducted by trained evaluators who administered a standardised cognitive battery: the mainland Chinese version of MCCB. The results of the tests were adjusted for gender, age, education, and urban versus rural residence: the reported T-scores for the composite score and domain scores for almost all of the studies were based on the published adjusted norms for mainland China[26]; in one study, the T-scores were based on adjusting the values using a stratified linear regression that controlled for gender, age, and education.[97]

| Author | Year | Sample size (males/females) | | | Mean age | | | Mean years of education | | | Outcome measures | Report quality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | CHR-P | SCZ[SUBGROUP] | HC | CHR-P | SCZ | HC | CHR-P | SCZ | HC | | |
| Bao[49] | 2017 | 30 (18/12) | – (–/–) | 30 (14/16) | 23.0 | - | 23.4 | - | - | - | RS | POOR |
| Bi[50a] | 2021 | – (–/–) | 73 (0/73)[FES] | 30 (0/30) | - | 27.7 | 27.0 | - | 12.0 | 11.5 | DS | POOR |
| Bian[51] | 2019 | – (–/–) | 21 (12/9)[CS] | 25 (13/12) | - | 27.8 | 26.5 | - | 13.1 | 15.0 | DS, COMS | POOR |
| Cao[52] | 2022 | – (–/–) | 22 (10/12)[NOT SPECIFIED] | 23 (9/14) | - | 32.0 | 27.5 | - | 13.6 | 14.7 | DS, COMS | FAIR |
| Chang[53] | 2019 | 23 (11/12) | 25 (12/13)[FES] | 19 (11/8) | 22.7 | 25.9 | 25.5 | 13.4 | 12.7 | 14.4 | DS, COMS | FAIR |
| Chen[54] | 2019 | – (–/–) | 31 (16/15)[FES] | 30 (16/14) | - | 25.9 | 29.4 | - | 11.0 | 14.5 | RS | FAIR |
| Chen[55] | 2021 | – (–/–) | 73 (73/0)[FES] | 78 (78/0) | - | 26.0 | 27.4 | - | 12.9 | 13.4 | DS, COMS | FAIR |
| Chen[56] | 2013 | – (–/–) | 110 (76/34)[NOT SPECIFIED] | 110 (73/37) | - | 45.0 | 46.0 | - | 10.7 | 11.0 | DS, COMS | FAIR |
| Chen[57] | 2015 | – (–/–) | 83 (34/49)[FES] | 50 (24/26) | - | 29.2 | 32.6 | - | 12.8 | 12.1 | RS, COMS | FAIR |
| Chen[58] | 2015 | – (–/–) | 145 (75/70)[FES] | 65 (35/30) | - | 28.5 | 27.6 | - | 13.0 | 12.6 | RS, COMS | FAIR |
| Chen[59] | 2016 | – (–/–) | 102 (48/54)[FES] | 30 (14/16) | - | 27.4 | 27.0 | - | 12.5 | 11.8 | DS, COMS | FAIR |
| Chen[60] | 2019 | – (–/–) | 42 (18/24)[FES] | 36 (21/15) | - | 25.2 | 26.5 | - | 12.2 | 14.2 | DS, COMS | FAIR |
| Chen[61] | 2020 | – (–/–) | 155 (76/79)[NOT SPECIFIED] | 36 (21/15) | - | 27.0 | 25.0 | - | 12.0 | 16.0 | DS | FAIR |
| Chen[62] | 2021 | – (–/–) | 208 (105/103)[FES] | 40 (23/17) | - | 26.9 | 25.3 | - | 12.9 | 14.7 | DS, COMS | FAIR |
| Fei[63] | 2021 | – (–/–) | 54 (34/20)[FES] | 92 (54/38) | - | 29.0 | 29.0 | - | 13.4 | 14.4 | DS, COMS | FAIR |
| Feng[64] | 2019 | 86 (40/46) | 86 (45/41)[NOT SPECIFIED] | 86 (45/41) | 33.9 | 30.8 | 30.0 | 12.3 | 12.6 | 12.3 | DS | FAIR |
| Fu[65] | 2018 | – (–/–) | 30 (13/17)[FES] | 30 (12/18) | - | 23.0 | 24.9 | - | 11.8 | 12.2 | RS, DS | FAIR |
| Gao[66] | 2020 | – (–/–) | 57 (20/37)[FES] | 50 (23/27) | - | 31.6 | 28.4 | - | 12.9 | 15.6 | DS, COMS | FAIR |
| Gu[67] | 2020 | – (–/–) | 83 (83/0)[NOT SPECIFIED] | 50 (50/0) | - | 31.9 | 31.1 | - | - | - | RS | POOR |
| Guo[68] | 2013 | – (–/–) | 65 (40/25)[NOT SPECIFIED] | 65 (40/25) | - | 43.1 | 42.4 | - | 12.4 | 12.1 | DS, COMS | POOR |
| Guo[69] | 2021 | – (–/–) | 123 (68/55)[FES] | 50 (27/23) | - | 28.4 | 29.1 | - | 12.9 | 14.1 | DS, COMS | FAIR |
| Hao[70] | 2016 | – (–/–) | 59 (42/17)[NOT SPECIFIED] | 15 (8/7) | - | 40.8 | 38.0 | - | 11.9 | 12.8 | RS | FAIR |
| Hao[71] | 2018 | – (–/–) | 30 (17/13)[FES] | 30 (17/13) | - | 15.4 | 15.6 | - | - | - | RS, COMS | POOR |
| Helili[72] | 2014 | – (–/–) | 58 (35/23)[NOT SPECIFIED] | 56 (–/–) | - | 26.6 | - | - | 12.6 | - | DS, COMS | POOR |
| Huang[73a] | 2015 | – (–/–) | 82 (27/55)[FES] | 50 (–/–) | - | 23.2 | 24.5 | - | 10.2 | 10.5 | DS | FAIR |
| Huang[74] | 2020 | – (–/–) | 41 (22/19)[NOT SPECIFIED] | 60 (30/30) | - | 27.8 | 30.2 | - | 11.2 | 10.4 | DS, COMS | FAIR |
| Huang[75] | 2021 | – (–/–) | 182 (95/87)[NOT SPECIFIED] | 176 (92/84) | - | 36.6 | 37.3 | - | 9.1 | 11.6 | DS | FAIR |
| Huang[76] | 2017 | – (–/–) | 58 (29/29)[FES] | 43 (16/27) | - | 22.7 | 23.1 | - | 11.4 | 12.7 | DS, COMS | FAIR |
| Huang[77] | 2020 | – (–/–) | 86 (56/30)[NOT SPECIFIED] | 53 (27/26) | - | 47.5 | 44.8 | - | 12.2 | 12.3 | DS, COMS | FAIR |
| Huang[78] | 2020 | – (–/–) | 30 (15/15)[NOT SPECIFIED] | 34 (13/21) | - | 27.6 | 29.6 | - | 10.9 | 12.1 | DS | FAIR |
| Huang[79] | 2021 | – (–/–) | 32 (16/16)[NOT SPECIFIED] | 25 (16/9) | - | 42.7 | 38.8 | - | 10.5 | 16.3 | DS, COMS | FAIR |
| Huang[80] | 2021 | – (–/–) | 195 (110/85)[NOT SPECIFIED] | 70 (37/33) | - | 35.6 | 39.7 | - | 12.4 | 12.9 | DS, COMS | FAIR |
| Huang[81] | 2021 | – (–/–) | 21 (–/–)[NOT SPECIFIED] | 23 (14/9) | - | 30.0 | 27.2 | - | 13.5 | 14.7 | RS | FAIR |
| Huang[82] | 2022 | – (–/–) | 187 (82/105)[FES] | 100 (44/56) | - | 25.3 | 25.3 | - | 11.4 | 13.5 | DS, COMS | FAIR |
| Jin[83] | 2021 | – (–/–) | 23 (11/12)[FES] | 24 (12/12) | - | 31.7 | 30.9 | - | 12.6 | 14.0 | DS, COMS | FAIR |
| Li[84] | 2016 | – (–/–) | 139 (61/78)[NOT SPECIFIED] | 101 (46/55) | - | 36.5 | 35.3 | - | 9.3 | 9.9 | DS | FAIR |
| Li[85a] | 2019 | – (–/–) | 92 (50/42)[FES] | 103 (53/50) | - | 15.2 | 15.0 | - | - | - | RS, COMS | FAIR |
| Li[86] | 2017 | – (–/–) | 37 (18/19)[FES] | 23 (9/14) | - | 15.4 | 15.2 | - | - | - | RS, COMS | POOR |
| Li[87] | 2020 | – (–/–) | 131 (59/72)[FES] | 90 (36/54) | - | 20.9 | 20.7 | - | - | - | DS | POOR |
| Li[88] | 2021 | – (–/–) | 80 (54/26)[FES] | 50 (31/19) | - | 23.3 | 24.8 | - | 13.1 | 14.4 | DS, COMS | FAIR |
| Li[89] | 2022 | – (–/–) | 122 (80/42)[CS] | 74 (45/29) | - | 47.3 | 48.2 | - | 12.2 | 12.0 | DS, COMS | FAIR |
| Li[90] | 2022 | – (–/–) | 44 (14/30)[FES] | 35 (11/24) | - | 22.6 | 23.7 | - | 11.5 | 12.3 | DS, COMS | FAIR |
| Liao[91a] | 2018 | – (–/–) | 39 (27/12)[NOT SPECIFIED] | 20 (14/6) | - | 24.4 | 25.7 | - | 11.1 | 12.8 | RS | FAIR |
| Ling[92] | 2021 | – (–/–) | 110 (71/39)[NOT SPECIFIED] | 90 (63/27) | - | 32.2 | 31.8 | - | 12.8 | 13.4 | RS | POOR |
| Liu[93#] | 2018 | – (–/–) | 142 (70/72)[FES] | 50 (26/24) | - | 23.9 | 23.7 | - | 12.6 | 12.7 | DS | FAIR |
| Liu[94] | 2013 | – (–/–) | 17 (7/10)[NOT SPECIFIED] | 17 (6/11) | - | 38.5 | 34.1 | - | 7.4 | 7.8 | DS | FAIR |
| Liu[95] | 2018 | – (–/–) | 80 (41/39)[FES] | 70 (32/38) | - | 25.0 | 26.0 | - | - | - | DS | FAIR |
| Luo[96] | 2021 | – (–/–) | 135 (83/52)[NOT SPECIFIED] | 73 (24/49) | - | 43.5 | 40.4 | - | 13.1 | 13.6 | DS, COMS | FAIR |
| Lv[97] | 2020 | – (–/–) | 49 (18/31)[FES] | 47 (20/27) | - | 25.6 | 25.8 | - | 12.6 | 12.8 | DS, COMS | FAIR |
| Ma[98] | 2020 | – (–/–) | 28 (12/16)[NOT SPECIFIED] | 35 (16/19) | - | 45.8 | 45.8 | - | 13.2 | 12.0 | DS, COMS | FAIR |
| Ma[99] | 2021 | – (–/–) | 64 (38/26)[NOT SPECIFIED] | 65 (33/32) | - | 26.7 | 25.3 | - | 13.6 | 16.8 | DS | FAIR |
| Miao[100] | 2021 | – (–/–) | 188 (79/109)[FES] | 92 (36/56) | - | 23.1 | 22.9 | - | 11.3 | 11.7 | DS | FAIR |
| Mu[101] | 2020 | – (–/–) | 157 (111/46)[CS] | 167 (80/87) | - | 47.5 | 43.9 | - | - | - | DS, COMS | GOOD |
| Ou[102] | 2017 | – (–/–) | 291 (206/85)[CS] | 76 (46/30) | - | 44.0 | 34.5 | - | 10.3 | 10.9 | DS, COMS | FAIR |

(Table 2 continues on next page)

| Author | Year | Sample size (males/females) | | | Mean age | | | Mean years of education | | | Outcome measures | Report quality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | CHR-P | SCZ[SUBGROUP] | HC | CHR-P | SCZ | HC | CHR-P | SCZ | HC | | |
| (Continued from previous page) | | | | | | | | | | | | |
| Pan[103] | 2021 | – (–/–) | 118 (65/53)[FES] | 47 (27/20) | - | 28.7 | 29.6 | - | 12.6 | 14.1 | DS, COMS | FAIR |
| Pan[104] | 2022 | – (–/–) | 75 (34/41)[FES] | 44 (24/20) | - | 28.6 | 30.1 | - | 13.0 | 14.3 | DS, COMS | FAIR |
| Peng[105] | 2014 | – (–/–) | 41 (21/20)[CS] | 40 (20/20) | - | 48.0 | 48.9 | - | 11.1 | 10.8 | DS, COMS | POOR |
| Peng[106] | 2020 | – (–/–) | 46 (32/14)[FES] | 50 (26/24) | - | 24.2 | 26.1 | - | 12.4 | 14.5 | DS, COMS | FAIR |
| Qi[107] | 2022 | – (–/–) | 68 (39/29)[FES] | 50 (27/23) | - | 27.2 | 27.7 | - | 12.7 | 13.0 | DS | FAIR |
| Qiu[108] | 2021 | – (–/–) | 66 (45/21)[FES] | 59 (32/27) | - | 20.0 | 21.6 | - | 12.6 | 14.2 | DS, COMS | FAIR |
| Sha[109] | 2021 | – (–/–) | 22 (10/12)[NOT SPECIFIED] | 23 (9/14) | - | 32.0 | 27.5 | - | 13.6 | 14.7 | DS, COMS | FAIR |
| Shen[110] | 2021 | – (–/–) | 50 (23/27)[FES] | 50 (26/24) | - | 33.6 | 32.3 | - | - | - | DS | POOR |
| Shi[111] | 2019 | – (–/–) | 230 (114/116)[NOT SPECIFIED] | 656 (330/326) | - | 38.7 | 39.3 | - | 10.9 | 10.8 | DS | FAIR |
| Song[112] | 2020 | – (–/–) | 90 (40/50)[NOT SPECIFIED] | 53 (21/32) | - | 29.6 | 27.3 | - | 12.4 | 12.8 | DS, COMS | FAIR |
| Sun[113] | 2022 | – (–/–) | 80 (38/42)[FES] | 80 (39/41) | - | 34.5 | 34.9 | - | - | - | DS, COMS | POOR |
| Sun[114] | 2018 | – (–/–) | 24 (13/11)[NOT SPECIFIED] | 30 (16/14) | - | 33.0 | 34.2 | - | 14.0 | 13.6 | DS, COMS | FAIR |
| Sun[115] | 2021 | 39 (24/15) | 76 (34/42)[NOT SPECIFIED] | 101 (62/39) | 24.3 | 25.7 | 26.5 | 14.4 | 13.4 | 14.4 | DS, COMS | FAIR |
| Tao[116a] | 2020a | – (–/–) | 88 (46/42)[FES] | 43 (20/23) | - | 22.8 | 22.5 | - | 10.6 | 10.8 | DS | FAIR |
| Tao[117] | 2020 | – (–/–) | 90 (44/46)[FES] | 70 (32/38) | - | 21.5 | 23.4 | - | 10.4 | 11.1 | DS, COMS | FAIR |
| Tong[118] | 2019 | – (–/–) | 110 (55/55)[FES] | 50 (27/23) | - | 27.6 | 29.6 | - | 12.9 | 14.0 | DS, COMS | FAIR |
| Wang[119] | 2019 | – (–/–) | 73 (32/41)[FES] | 71 (37/34) | - | 22.2 | 23.7 | - | 11.9 | 12.8 | DS | FAIR |
| Wang[120] | 2019 | – (–/–) | 125 (61/64)[FES] | 80 (42/38) | - | 23.0 | 24.0 | - | 12.0 | 13.0 | DS | FAIR |
| Wang[121] | 2021 | – (–/–) | 55 (29/26)[FES] | 61 (34/27) | - | 25.3 | 24.9 | - | 12.6 | 14.3 | DS, COMS | FAIR |
| Wang[122] | 2022 | – (–/–) | 63 (30/33)[FES] | 48 (28/20) | - | 27.5 | 30.5 | - | 13.2 | 13.8 | DS, COMS | FAIR |
| Wei[123] | 2016 | – (–/–) | 60 (38/22)[FES] | 60 (34/26) | - | 22.8 | 21.0 | - | 11.7 | 11.8 | DS | FAIR |
| Wei[124] | 2016 | 36 (18/18) | – (–/–) | 35 (17/18) | 20.6 | - | 18.6 | 11.2 | - | 10.7 | DS | FAIR |
| Wei[125] | 2020 | – (–/–) | 164 (164/0)[CS] | 82 (82/0) | - | 47.2 | 42.8 | - | 10.9 | 9.5 | DS, COMS | FAIR |
| Wei[126] | 2022 | – (–/–) | 117 (86/31)[FES] | 98 (58/40) | - | 24.7 | 26.5 | - | 13.2 | 14.1 | DS, COMS | FAIR |
| Wei[127] | 2022 | 58 (–/–) | – (–/–) | 58 (–/–) | - | - | - | 12.9 | - | 14.4 | DS | FAIR |
| Wu[128] | 2016 | – (–/–) | 211 (112/99)[FES&CS] | 124 (65/59) | - | 37.4 | 44.7 | - | 12.5 | 11.8 | DS, COMS | FAIR |
| Wu[129] | 2022 | – (–/–) | 68 (33/35)[FES] | 39 (17/22) | - | 25.6 | 26.1 | - | 10.0 | 10.2 | RS | POOR |
| Xia[130] | 2020 | – (–/–) | 270 (172/98)[CS] | 116 (65/51) | - | 46.8 | 45.4 | - | 11.4 | 10.9 | DS, COMS | FAIR |
| Xia[131] | 2020 | – (–/–) | 66 (44/22)[FES] | 88 (46/42) | - | 24.0 | 23.0 | - | - | - | DS | FAIR |
| Xie[132] | 2019 | – (–/–) | 54 (22/32)[FES] | 50 (20/30) | - | 25.9 | 25.9 | - | 13.0 | 12.6 | DS, COMS | FAIR |
| Xiong[133] | 2019 | – (–/–) | 80 (51/29)[FES&CS] | 40 (25/15) | - | 27.1 | 26.3 | - | 13.6 | 14.5 | DS, COMS | FAIR |
| Xiu[134] | 2021 | – (–/–) | 39 (16/23)[FES] | 30 (13/17) | - | 28.9 | 27.5 | - | 12.4 | 12.3 | DS, COMS | FAIR |
| Xu[135] | 2021 | – (–/–) | 80 (46/34)[FES] | 80 (44/36) | - | 28.7 | 29.6 | - | - | - | DS | POOR |
| Yan[136] | 2021 | – (–/–) | 65 (36/29)[NOT SPECIFIED] | 50 (27/23) | - | 39.2 | 39.2 | - | - | - | DS, COMS | POOR |
| Yan[137] | 2020 | – (–/–) | 69 (50/19)[FES] | 74 (45/29) | - | 24.2 | 26.3 | | 13.2 | 14.7 | DS, COMS | FAIR |
| Yang[138] | 2019 | – (–/–) | 25 (15/10)[FES] | 32 (14/18) | - | 22.1 | 24.6 | - | 10.4 | 11.3 | DS | FAIR |
| Yang[139] | 2021 | – (–/–) | 81 (51/30)[FES] | 75 (45/30) | - | 22.6 | 23.8 | - | 10.5 | 11.2 | DS | FAIR |
| Yang[140a] | 2021 | – (–/–) | 47 (31/16)[CS] | 30 (16/14) | - | 48.8 | 46.2 | - | 13.0 | 11.9 | DS, COMS | FAIR |
| Yang[141] | 2012 | 56 (30/26) | 60 (28/32)[NOT SPECIFIED] | 50 (21/29) | 27.0 | 26.0 | 25.0 | 11.3 | 10.6 | 12.1 | DS | POOR |
| Yang[142] | 2019 | – (–/–) | 65 (35/30)[FES&CS] | 35 (16/19) | - | 24.7 | 25.6 | - | 10.8 | 16.3 | DS, COMS | FAIR |
| Yao[143] | 2015 | – (–/–) | 160 (124/36)[FES&CS] | 75 (55/20) | - | 24.2 | 25.2 | - | 12.6 | 15.2 | DS, COMS | POOR |
| Yuan[144] | 2020 | – (–/–) | 75 (75/0)[FES] | 80 (80/0) | - | 27.2 | 26.9 | - | 12.5 | 12.7 | DS | POOR |
| Zeng[145a] | 2016 | – (–/–) | 55 (22/33)[FES] | 61 (28/33) | - | 25.0 | 25.3 | - | 12.7 | 12.7 | DS, COMS | FAIR |
| Zhang[146a] | 2015 | – (–/–) | 50 (26/24)[FES] | 50 (25/25) | - | 38.5 | 38.7 | - | - | - | RS | POOR |
| Zhang[147] | 2017 | – (–/–) | 24 (8/16)[FES] | 24 (13/11) | - | 25.7 | 26.3 | - | 12.8 | 14.5 | RS | POOR |
| Zhang[148a] | 2019 | – (–/–) | 117 (56/61)[FES] | 100 (54/46) | - | 21.7 | 23.1 | - | 12.6 | 13.3 | DS | FAIR |
| Zhang[149] | 2020 | – (–/–) | 79 (16/63)[FES] | 93 (23/70) | - | 28.8 | 29.9 | - | 14.0 | 14.7 | DS, COMS | FAIR |
| Zhang[150] | 2015 | 108 (54/54) | 108 (56/52)[NOT SPECIFIED] | 108 (58/50) | 29.1 | 28.6 | 29.1 | 15.4 | 15.2 | 15.5 | DS | POOR |
| Zhang[151] | 2016 | 50 (26/24) | – (–/–) | 52 (23/29) | 20.0 | - | 20.9 | 10.6 | - | 11.3 | DS | FAIR |
| Zhang[152] | 2018 | 24 (8/16) | 28 (14/14)[FES] | 38 (15/23) | 18.0 | 21.7 | 24.1 | 13.5 | 12.5 | 14.1 | DS | POOR |
| Zhang[153] | 2021 | – (–/–) | 150 (80/70)[NOT SPECIFIED] | 50 (26/24) | - | 35.2 | 34.0 | - | 10.8 | 11.3 | DS, COMS | POOR |
| Zhao[154] | 2013 | – (–/–) | 68 (40/28)[CS] | 17 (10/7) | - | 43.3 | 42.4 | - | - | - | RS | POOR |

(Table 2 continues on next page)

| Author | Year | Sample size (males/females) | | | Mean age | | | Mean years of education | | | Outcome measures | Report quality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | CHR-P | SCZ[SUBGROUP] | HC | CHR-P | SCZ | HC | CHR-P | SCZ | HC | | |
| (Continued from previous page) | | | | | | | | | | | | |
| Zhao[155] | 2014 | 46 (24/22) | 20 (11/9)[FES] | 37 (22/15) | 20.6 | 21.5 | 20.4 | 11.9 | 11.0 | 12.6 | RS | POOR |
| Zhao[156] | 2021 | – (–/–) | 93 (45/48)[FES] | 160 (74/86) | - | 26.4 | 43.5 | - | 12.7 | - | DS, COMS | FAIR |
| Zheng[157a] | 2021 | – (–/–) | 50 (23/27)[CS] | 50 (22/28) | - | 30.0 | 31.0 | - | - | - | DS, COMS | POOR |
| Zhou[158] | 2018 | – (–/–) | 93 (31/62)[FES] | 93 (22/71) | - | 25.5 | 27.6 | - | 12.0 | 12.6 | RS | FAIR |
| Zhou[159] | 2021 | – (–/–) | 153 (83/70)[NOT SPECIFIED] | 66 (33/33) | - | 37.6 | 39.3 | - | 12.7 | 12.9 | DS, COMS | FAIR |
| Zhu[160] | 2019 | – (–/–) | 59 (–/–)[NOT SPECIFIED] | 74 (–/–) | - | 34.4 | 33.5 | - | 11.7 | 14.4 | RS | FAIR |
| Zhuo[161] | 2020 | – (–/–) | 89 (36/53)[FES] | 30 (15/15) | - | 23.2 | 25.4 | - | 12.8 | 16.1 | DS, COMS | FAIR |
| Zou[162] | 2009 | – (–/–) | 122 (84/38)[NOT SPECIFIED] | 122 (75/47) | - | 45.0 | 45.0 | - | 12.0 | 12.0 | RS | POOR |

FES, first episode schizophrenia; CS, chronic schizophrenia; NOT SPECIFIED, duration of illness in sample not reported; CHR-P, clinical high risk for psychosis; SCZ, all individuals with schizophrenia; HC, healthy controls; RS, raw score; DS, domain score; COMS, composite score. [a]Sample was the baseline assessment in a treatment trial, and the quality of the report was assessed using CONSORT; all other samples were from case-control studies, and quality of the report of these studies was assessed using STROBE.

*Table 2:* **Characteristics of the .114 studies that met inclusions criteria for the systematic review.**

*Indirectness*

None of the included studies had problems related to indirectness. The samples enrolled in the studies represented the types of individuals to whom the results would apply. The instrument selected to assess cognitive functioning—MCCB—was specifically developed to assess multiple cognitive domains in individuals with SCZ.

*Inconsistency*

Seven of the 31 separate meta-analyses reported had serious inconsistency problems. The $I^2$ values for the analyses ranged from 20% to 96%; only two of the analyses had $I^2$ values of less than 50%. However, given the large sample sizes reported in many of the analyses, based on the recommendations of the GRADE Handbook we used the prediction interval (based on the $\tau^2$ statistic) to assess heterogeneity in each of the meta-analyses.[45] The prediction interval in seven of the analyses included a value of 0, indicating that the results of the included studies were inconsistent. Five of the seven inconsistent results occurred in meta-analyses of cognitive domain T-scores between CHR-P subjects and HC. The other two inconsistent results occurred in meta-analyses of the social cognition T-scores between subjects with SCZ and HC.

*Imprecision*

Based on the calculation for optimal information size, each group should include at least 394 subjects. As shown in Table 3, in all seven meta-analyses comparing cognitive domains in CHR-P subjects and HC, the pooled sample for both groups was less than 394, so the 'problems with imprecision' GRADE item was rated as 'serious'. Pooled samples in all other analyses ranged from 405 to 8187, so imprecision was not considered a problem for any of these analyses.

*Publication bias*

As shown in Table 3, the results of Egger's tests for the 22 meta-analyses that included ten or more studies identified six meta-analyses in which publication bias was strongly suspected, and results of the LFK index for the nine meta-analyses that included less than ten studies identified four meta-analyses in which publication bias was strongly suspected. These ten analyses with suspected publication bias included one meta-analysis about the MCCB composite score in FES, two meta-analyses about verbal learning and visual learning in SCZ, two meta-analyses about attention-vigilance and verbal learning in FES, two meta-analyses about working memory and visual learning in CS, and three meta-analyses about attention-vigilance, visual learning, and social cognition in CHR-P. In two meta-analyses about attention-vigilance and visual learning in CHR-P subjects, studies with large effect sizes were more likely to be published than those with small effect sizes, but in the remaining eight meta-analyses in which publication bias was suspected, studies with small effect sizes were more likely to be published than those with large effect sizes.

*Summary of the Grade criteria*

The overall GRADE quality of evidence for the 31 meta-analyses is shown in the last column of Table 3. The quality of evidence was classified as 'moderate' in 11 analyses, 'low' in 4 analyses, and 'very low' in 16 analyses. The 16 meta-analyses classified as 'very low' included a meta-analysis of the composite score in FES subjects, meta-analyses for three of the seven cognitive domains in subjects with SCZ (verbal learning, visual learning, and social cognition), meta-analyses for three domains in FES subjects (attention-vigilance, verbal

| Outcome | Clinical group (No. studies) | Sample size | | Effect size | Subgroup comparison | | | Heterogeneity | | Quality of evidence[e] | | | Overall quality of evidence |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Clinical group | Healthy controls | Pooled mean difference (95% CI) | CHR-P vs. FES ($X^2$) | CHR-P vs. CS ($X^2$) | FES vs. CS ($X^2$) | $I^2$ | Prediction Interval | Problems with Inconsistency | Problems with Imprecision | Publication Bias[f] | |
| Composite score | SCZ (63) | 5618 | 3829 | **−13.72**[h] (−14.72, −12.71) | | | 0.01 | 90% | [−21.22, −6.21] | Not serious | Not serious | None | Moderate[g] |
| | FES (38) | 2755 | 2279 | **−13.97**[h] (−15.46, −12.49) | | | | 96% | [−22.93, −5.01] | Not serious | Not serious | Strongly suspected[c] | Very low |
| | CS (13) | 1303 | 934 | **−14.15**[h] (−16.70, −11.59) | | | | 89% | [−24.28, −4.02] | Not serious | Not serious | None | Moderate[g] |
| Speed of processing | SCZ (65) | 5432 | 3731 | **−14.27**[h] (−15.42, −13.12) | **14.72**[h] | **11.73**[h] | 0.59 | 90% | [−23.08, −5.46] | Not serious | Not serious | None | Moderate[g] |
| | FES (43) | 3381 | 2499 | **−14.17**[h] (−15.53, −12.81) | | | | 90% | [−22.76, −5.58] | Not serious | Not serious | None | Moderate[g] |
| | CS (8) | 539 | 405 | **−15.53**[h] (−18.74, −12.32) | | | | 87% | [−22.68, −5.83] | Not serious | Not serious | None | Moderate[g] |
| | CHR-P (5) | 206 | 265 | **−8.12**[h] (−10.89, −5.34) | | | | 67% | [−17.49, 1.26] | Serious[a] | Serious[b] | None | Very low |
| Attention - Vigilance | SCZ (91) | 8187 | 6264 | **−12.83**[h] (−13.75, −11.90) | **15.75**[h] | 2.80 | **4.22**[h] | 89% | [−21.13, −4.53] | Not serious | Not serious | None | Moderate[g] |
| | FES (55) | 4163 | 3332 | **−14.09**[h] (−15.35, −12.84) | | | | 91% | [−23.02, −5.17] | Not serious | Not serious | Strongly suspected[c] | Very low |
| | CS (13) | 1303 | 934 | **−11.06**[h] (−13.67, −8.45) | | | | 85% | [−21.29, −0.84] | Not serious | Not serious | None | Moderate[g] |
| | CHR-P (7) | 316 | 389 | **−7.76**[h] (−10.62, −4.89) | | | | 77% | [−17.08, 1.57] | Serious[a] | Serious[b] | Strongly suspected[d] | Very low |
| Working memory | SCZ (71) | 5914 | 4659 | **−9.98**[h] (−10.97, −8.99) | **5.94**[h] | **4.55**[h] | 0.41 | 88% | [−17.74, −2.22] | Not serious | Not serious | None | Low |
| | FES (47) | 3599 | 2719 | **−9.74**[h] (−10.92, −8.56) | | | | 87% | [−17.39, −2.09] | Not serious | Not serious | None | Low |
| | CS (8) | 539 | 405 | **−10.86**[h] (−14.04, −7.68) | | | | 75% | [−17.46, −2.07] | Not serious | Not serious | Strongly suspected[c] | Very low |
| | CHR-P (7) | 316 | 389 | **−6.66**[h] (−8.84, −4.48) | | | | 45% | [−12.44, −0.88] | Not serious | Serious[b] | None | Very low |
| Verbal learning | SCZ (91) | 8187 | 6264 | **−10.49**[h] (−11.12, −9.86) | **7.04**[h] | **6.60**[h] | 0.40 | 82% | [−15.63, −5.34] | Not serious | Not serious | Strongly suspected[c] | Very low |
| | FES (55) | 4163 | 3332 | **−10.06**[h] (−10.83, −9.30) | | | | 80% | [−14.86, −5.27] | Not serious | Not serious | Strongly suspected[c] | Very low |
| | CS (13) | 1303 | 934 | **−10.65**[h] (−12.28, −9.01) | | | | 75% | [−16.36, −4.94] | Not serious | Not serious | None | Moderate[g] |
| | CHR-P (7) | 316 | 389 | **−7.61**[h] (−9.25, −5.97) | | | | 20% | [−11.02, −4.20] | Not serious | Serious[b] | None | Very low |
| Visual learning | SCZ (90) | 7999 | 6172 | **−10.02**[h] (−10.84, −9.19) | **4.74**[h] | **4.55**[h] | 0.03 | 90% | [−17.17, −2.86] | Not serious | Not serious | Strongly suspected[c] | Very low |
| | FES (54) | 3975 | 3240 | **−10.29**[h] (−11.40, −9.18) | | | | 92% | [−17.88, −2.71] | Not serious | Not serious | None | Moderate[g] |
| | CS (13) | 1303 | 934 | **−10.46**[h] (−12.23, −8.70) | | | | 84% | [−16.74, −4.19] | Not serious | Not serious | Strongly suspected[c] | Very low |
| | CHR-P (7) | 316 | 389 | **−6.05**[h] (−9.70, −2.39) | | | | 88% | [−18.67, 6.58] | Serious[a] | Serious[b] | Strongly suspected[d] | Very low |
| Reasoning and Problem-solving | SCZ (91) | 8187 | 6264 | **−10.20**[h] (−11.13, −9.27) | **7.06**[h] | **18.68**[h] | **9.44**[h] | 92% | [−18.59, −1.80] | Not serious | Not serious | None | Moderate[g] |
| | FES (55) | 4163 | 3332 | **−9.41**[h] (−10.47, −8.36) | | | | 89% | [−16.73, −2.10] | Not serious | Not serious | None | Low |
| | CS (13) | 1303 | 934 | **−14.76**[h] (−18.01, −11.52) | | | | 92% | [−27.75, −1.77] | Not serious | Not serious | None | Moderate[g] |
| | CHR-P (7) | 316 | 389 | **−5.90**[h] (−8.27, −3.52) | | | | 66% | [−13.21, 1.41] | Serious[a] | Serious[b] | None | Very low |
| Social cognition | SCZ (90) | 7999 | 6172 | **−7.92**[h] (−8.96, −6.89) | **16.54**[h] | **19.73**[h] | 0.71 | 92% | [−17.29, 1.44] | Serious[a] | Not serious | None | Very low |
| | FES (54) | 3975 | 3240 | **−7.93**[h] (−9.43, −6.43) | | | | 94% | [−18.70, 2.84] | Serious[a] | Not serious | None | Very low |
| | CS (13) | 1303 | 934 | **−8.96**[h] (−10.85, −7.08) | | | | 78% | [−15.70, −2.23] | Not serious | Not serious | None | Low |
| | CHR-P (7) | 316 | 389 | **−2.74**[h] (−4.74, −0.74) | | | | 57% | [−8.65, 3.17] | Serious[a] | Serious[b] | Strongly suspected[c] | Very low |

SCZ, all individuals with schizophrenia; FES, first-episode schizophrenia; CS, chronic schizophrenia; CHR-P, clinical high risk for psychosis. [a]Prediction interval included zero. [b]Sample size of groups is smaller than 394, the sample size required to identify an effect size of 0.2 (two-tailed tests using p = 0.05 and beta = 0.20). [c]Articles with small differences between the clinical group and healthy controls were more likely to be published. [d]Articles with large differences between the clinical group and healthy controls were more likely to be published. [e]Two other characteristics assessed using the GRADE criteria—problems with risk of bias and problems with indirectness—were coded as "not serious" for all outcomes. [f]Publication bias was determined based on Egger's test for meta-analyses including 10 or more studies or based on the LFK index for meta-analyses including less than 10 studies. [g]Level of evidence is upgraded because the pooled mean differences in T-scores between groups is greater than 10 (1 standard deviation of the mean T-scores). [h]Statistically significant at $p < 0.05$ level.

***Table 3*: Results of meta-analyses comparing the composite and cognitive domain-specific T-scores of different clinical samples and results of the assessment of the quality of evidence provided in the corresponding studies using GRADE criteria.**

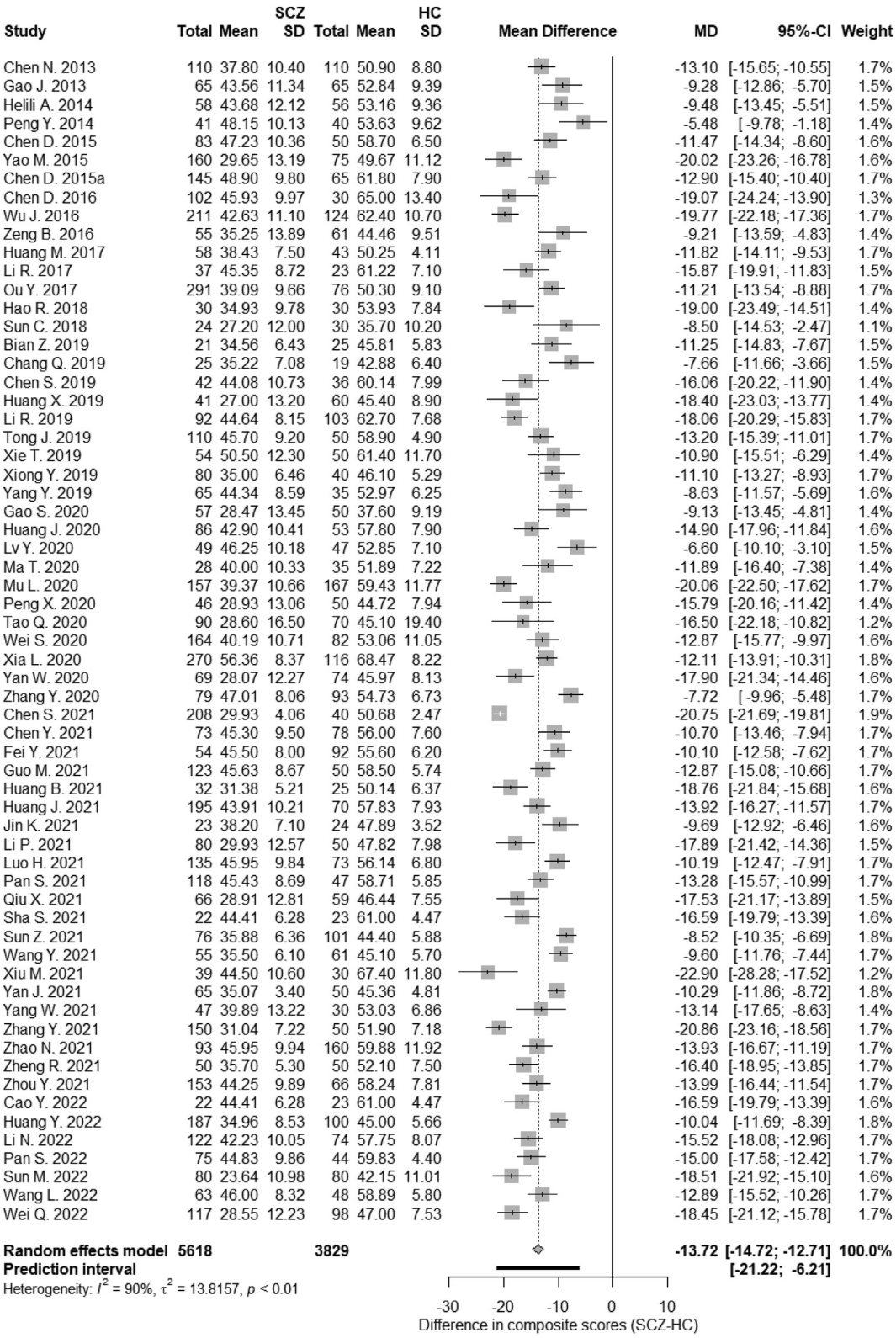


*Fig. 3:* Forest plot comparing MCCB composite scores between individuals with schizophrenia and healthy controls.

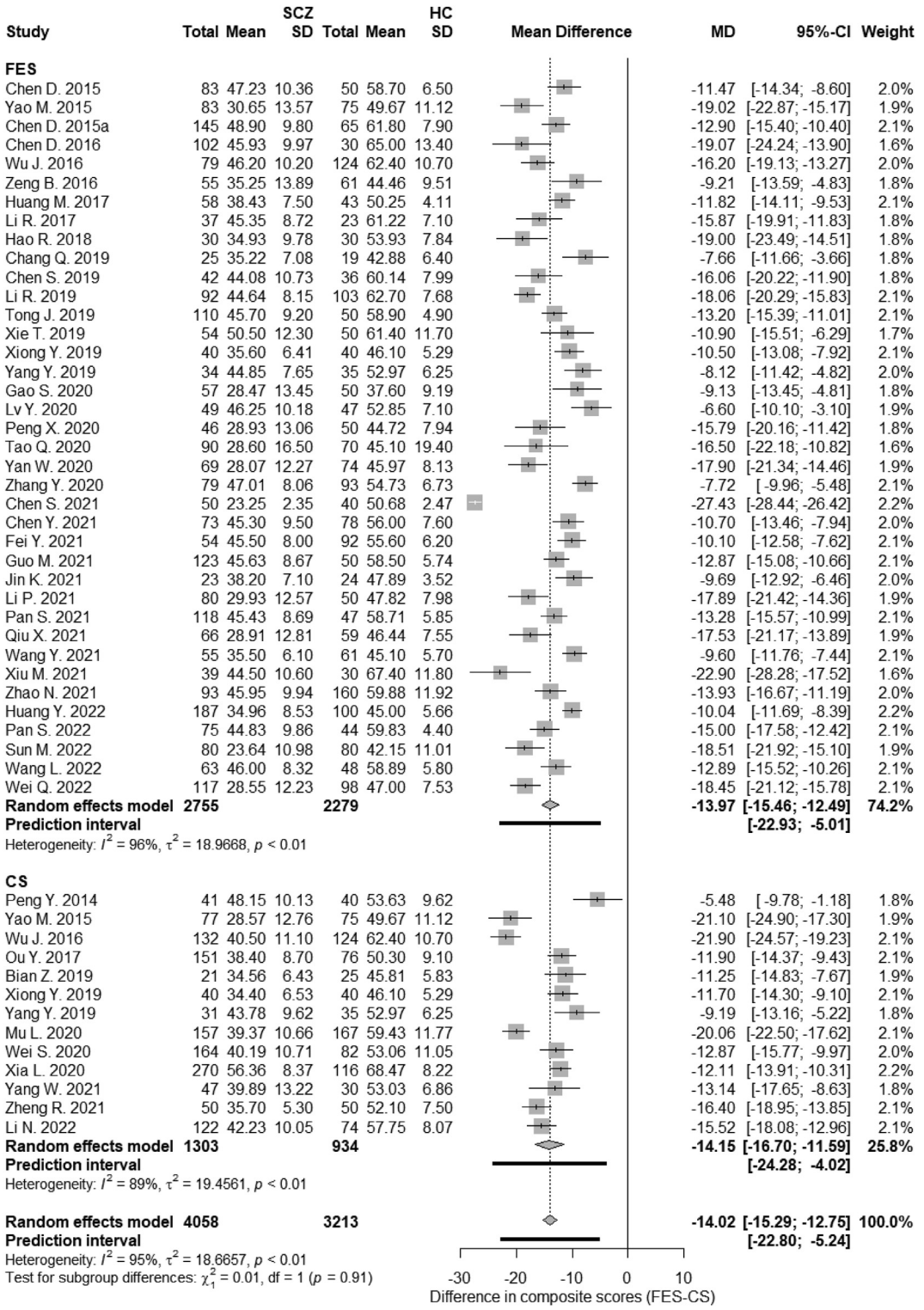


***Fig. 4:*** Forest plot of the mean difference of MCCB composite scores (compared to healthy controls) between samples with first-episode schizophrenia (FES) and samples with chronic schizophrenia (CS).

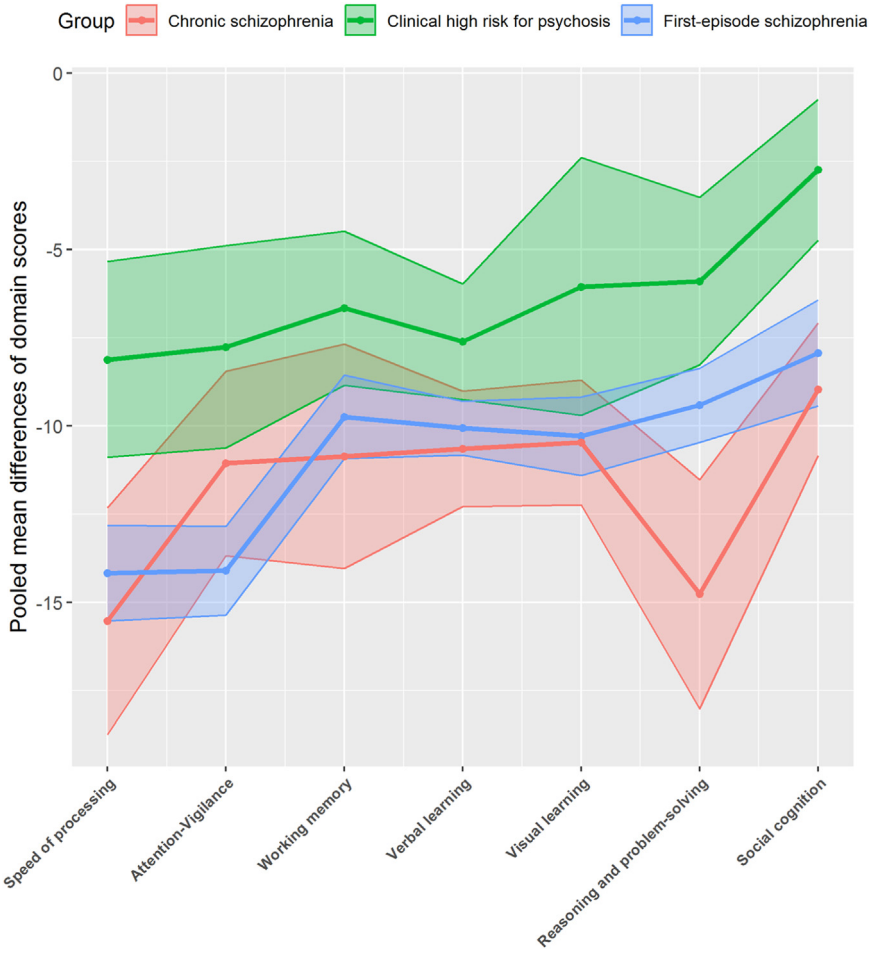


***Fig. 5:*** Comparison of the pooled mean (95% CI) differences in T-scores for the seven cognitive domains assessed by MCCB between healthy controls and chronic schizophrenia, clinical high risk for psychosis, and first-episode schizophrenia.

learning, and social cognition), meta-analyses for two domains in subjects with CS (working memory and visual learning), and meta-analyses for all seven domains in CHR-P subjects.

### Meta-regressions

The summary of the separate meta-regression analyses assessing the potential relationship of covariates—age, gender, and education—with the cognitive functioning of individuals with SCZ and HC is shown in Table 4. For all three demographic covariates, no significant associations of age, education, or gender were identified in analyses assessing the relationship of the covariates with the mean MCCB composite score. However, after adjusting for the covariate and the interaction term, the difference in mean composite scores between subjects with SCZ and HC remained statistically significant.

Table 4 also shows the relationship between the mean duration of illness, the mean total PANSS score, and the percentage of subjects taking antipsychotic medication at the time of the cognitive assessment with the mean MCCB composite score in the studies of subjects with SCZ that included these measures. As expected, higher mean scores on PANSS were significantly associated with lower mean MCCB composite scores; the PANSS results accounted for 14% of the variance in the mean MCCB composite scores. There was a non-significant positive relationship between the proportion of subjects with SCZ taking antipsychotic medication at the time of the assessment and the mean MCCB composite score ($p = 0.096$). However, there was an unexpected marginally significant ($p = 0.056$) *increase* in mean MCCB composite scores with increasing mean duration of illness. After adjusting this unexpected result for mean PANSS scores (which reduced the number of studies included in the meta-regression from 38 to 23), the coefficient (representing the change in MCCB composite score for every month increase in the

| Covariate | Sample | Number of studies | Coefficient (95% CI) | $R^2$ | t values | p-values[c] |
|---|---|---|---|---|---|---|
| Age | Full sample[b] | 62 | 0.12 (−0.10~0.33) | 49.20% | 1.07 | 0.29 |
| Group[a] | | | −15.08 (−24.83~−5.34) | | −3.06 | **0.0027**[c] |
| Age*Group | | | 0.04 (−0.26~0.34) | | 0.25 | 0.81 |
| Education (years) | Full sample[b] | 54 | −0.94 (−2.23~0.35) | 47.57% | −1.44 | 0.15 |
| Group[a] | | | −36.88 (−68.50~−5.27) | | −2.31 | **0.023**[c] |
| Education (years)*Group | | | 1.81 (−0.67~4.30) | | 1.45 | 0.15 |
| Male percentage | Full sample[b] | 62 | −7.19 (−22.46~8.07) | 48.70% | −0.93 | 0.35 |
| Group[a] | | | −13.26 (−24.60~−1.92) | | −2.32 | **0.022**[c] |
| Male percentage*Group | | | −0.98 (−21.40~19.44) | | −0.10 | 0.92 |
| Duration of illness (months) | Subjects with schizophrenia | 38 | 0.02 (−0.0006~0.04) | 7.46% | 1.97 | 0.056 |
| PANSS total score | Subjects with schizophrenia | 39 | −0.29 (−0.51~−0.07) | 14.47% | −2.70 | **0.010**[c] |
| Treatment (percentage) | Subjects with schizophrenia | 49 | 0.04 (−0.007~0.08) | 3.92% | 1.70 | 0.096 |

PANSS, Positive and Negative Syndrome Scale. [a]The reference group is the healthy control group. [b]Full sample includes subjects with schizophrenia and their healthy controls. [c]p-values printed in bold type are statistically significant.

***Table 4:*** **Summary of separate meta-regression analyses that assess the potential effect of different covariates on mean composite MCCB score.**

duration of illness) changed from +0.0280 (p = 0.12) to −0.0082 (p = 0.79).

## Discussion

This systematic review identified 114 reports (49 published in English, 65 in Chinese) that used the mainland Chinese version of MCCB to compare the overall cognition and seven cognitive domains of individuals with SCZ or CHR-P to that of HC. Data from these studies were used to conduct 31 separate meta-analyses which compared the cognitive domain-specific results and composite scores (i.e., combining results across domains) between different groups of subjects: all subjects with SCZ, subjects with FES, subjects with CS, subjects with CHR-P, and healthy controls. Finally, to assess the potential association of age, education, gender, duration of illness, PANSS total score, and the usage of antipsychotic medication with cognitive changes in SCZ, we conducted meta-regression analyses of the relationship of each covariate with the composite MCCB scores in studies that compared individuals with SCZ to HC. Unlike previous reviews that included meta-analyses of cognitive functioning, this systematic review assessed the quality of the reports included in each meta-analysis (using STROBE criteria) and, importantly, the strength of the evidence provided by each meta-analysis (using GRADE criteria).

### Schizophrenia

The eight meta-analyses comparing cognitive functioning in subjects with SCZ to HC identified large effect sizes (i.e., greater than one standard deviation) for five of the seven cognitive domains and for the MCCB composite score that integrated the results across all cognitive domains. The largest effect sizes were seen in the speed of processing and attention-vigilance domains. These findings are consistent with previous meta-analyses.[7,163–166]

The strength of the evidence was classified as 'moderate' for the MCCB composite score and for the speed of processing, attention-vigilance, and reasoning and problem-solving domains, which implies that the 'true' differences in these types of cognitive functioning between subjects with SCZ and HCs are likely to be close to the estimates reported in our analyses. On the other hand, the strength of the evidence was classified as 'low' for the working memory domain and 'very low' for the verbal learning, visual learning, and social cognition domains, which implies that the actual difference between the two groups of subjects is likely to be substantially different from the reported estimates. The quality of evidence in the meta-analyses about the verbal learning and visual learning domains was downgraded because of potential publication bias (studies with smaller effect sizes were *more* likely to be published), so the actual effect size may be greater than that reported in this review. The quality of evidence of the meta-analysis about the social cognition domain was downgraded because of the heterogeneity of the results (the prediction interval included zero). The MCCB assesses social cognition using the Mayer-Salovey-Caruso Emotional Intelligence Test, managing emotions branch; however, the reliability and validity of this test have not been assessed in mainland China, so cross-cultural differences may be one of the reasons for the heterogeneity of the results. To address this issue, Hellemann and colleagues proposed an international scoring method that aims to mitigate such cultural differences.[167] Thus, future studies should consider using this method to report their results. Additionally, compared to tests used for other domains (e.g., the verbal learning domain), the test employed for the social cognition domain is not widely used and only narrowly reflects the social

cognition construct. Therefore, alternative methods for assessing social cognition should be considered.

Based on the results of our meta-regression analyses, age, gender, and education were not significant predictors of the composite MCCB scores of individuals with SCZ or HC. One possible explanation for this finding is that composite MCCB scores obscure associations between covariates and different types of cognitive functioning, so future reviews should expand covariate analyses to consider the specific cognitive domains. The insignificant association of education with cognitive functioning in our review was unexpected, but it aligns with results from three previous meta-analyses of cognition in SCZ from around the world: one review included 204 studies of individuals with schizophrenia with a mean of 9–15 years of schooling,[7] a second review included 113 studies with a mean of 5–18 years of schooling.[163] and the third review included 21 studies with a mean of 9–14 years of schooling.[166] Reports about the association of age and gender with cognitive functioning in SCZ are inconsistent: one review of 37 studies found that older subjects performed worse on cognitive tests than younger subjects[164]; another review of 204 studies found no association of age or gender with cognitive functioning[7]; and a third review of 21 studies found that both age and gender were significantly associated with results for the working memory domain but not with the results of any other cognitive domains.[166] These inconsistent findings could be due to the use of different cognitive measures or to different methods of assessing education, but we conjecture that another important cause is differences in the characteristics of subjects included in the studies; a broader range in the mean age of study participants included in the meta-regression analyses and the inclusion of participants with low levels of education may increase the sensitivity of the cognitive results to the effects of age and education.

In our meta-regression analyses of clinical variables (that only considered samples with SCZ, not HC), we observed a significant negative association between the mean total PANSS score and the MCCB composite score in individuals with SCZ, indicating that more severe psychotic symptoms are associated with greater deficits in cognitive functioning. However, a more nuanced assessment of the relationship between psychotic symptoms and cognitive functioning is needed to determine whether positive and negative psychotic symptoms (or other types of psychotic symptoms) have different effects on the different types of cognitive functioning.[168]

The meta-regression analysis also identified a marginally significant ($p = 0.056$) *positive* association between the mean duration of illness (ranging from 3 to 325 months) and the MCCB composite score in SCZ, implying that cognitive function was better in samples with longer durations of illness. A systematic review of 14 studies by Altamura and colleagues found contradictory evidence regarding the relationship between duration of illness and cognitive functioning in SCZ; seven studies reported no significant relationship, while seven studies reported that a longer duration of illness was associated with statistically significant declines in specific cognitive domains.[169] Given that the positive association of duration of illness with cognitive functioning identified in our study reverses after adjusting for PANSS score, we hypothesise that our unexpected result and the previous inconsistent results are due to uncontrolled confounders in the analyses. For example, the severity of psychotic symptoms of patients included in studies of FES may be greater than those of patients in studies of CS, confounding the assessment of the association of duration of illness with cognition. Another potential contributing factor to the positive association between duration of illness and cognitive functioning is the inherent recruitment bias in cross-sectional studies that have higher attrition rates in chronic patients than in first-episode patients. Subjects with chronic schizophrenia recruited in cross-sectional studies are those who survive and receive treatment, so they may be less cognitively impaired than those who do not survive or fail to receive treatment regularly.[170] The underrepresentation of more severely ill individuals among patients with chronic schizophrenia could result in a failure to detect a relationship between cognitive decline and duration of illness. The only definitive resolution of this issue is to conduct decades-long longitudinal studies of individuals with schizophrenia.[20,23]

Another potential confounder that should be considered in future studies is the potential effect of antipsychotic treatment at the time of the cognitive assessment. The meta-regression in our review found a non-significant ($p = 0.096$) positive relationship between medication usage and mean composite MCCB scores.

### First-episode schizophrenia versus chronic schizophrenia

The results for FES and CS were similar to those in the overall SCZ analyses. The meta-analyses for SCZ, FES, and CS all found that the speed of processing domain was the most severely impaired domain, and the social cognition domain was the least severely impaired domain. The attention-vigilance domain was the second most severely impaired domain in the meta-analysis of SCZ and FES and the third most severely impaired domain in the meta-analysis of CS. With the sole exception of inconsistency in the results of the FES meta-analysis of the social cognition domain, none of the meta-analyses of FES or CS had problems with inconsistency or imprecision. However, three of the FES meta-analyses (composite score, attention-vigilance, and verbal learning) and two of the CS meta-analyses (working memory and visual learning) were strongly

suspected of publication bias—articles with small effect sizes were more likely to be published.

Our findings for FES and CS support the presence of broad and marked cognitive impairment in overall cognitive functioning and specific cognitive domains at the time of the onset of psychosis that persist into the later stages of the illness. These findings are consistent with previous meta-analyses.[3,7,11,13,30] However, two interesting discrepancies emerge when comparing the results of previous meta-analyses predominantly conducted in English-speaking countries with those in China. Speed of processing and verbal memory are consistently identified as the most impaired domains in studies conducted among European and American populations.[3,7,11] Our report and another review of Chinese studies also find that speed of processing is the most impaired domain, but the impairment in verbal learning is less prominent.[30] The other discrepancy is that the deficit of global cognitive functioning in FEP in our report is larger than the global deficits reported in meta-analyses of FEP in European and American populations.[3] There are potential explanations for these discrepancies: 1) previously reported studies in non-Chinese populations used a variety of different measures of cognition while our analysis was limited to studies that used MCCB, 2) several of the previously reported studies in non-Chinese populations included individuals with a variety of psychotic disorders while our analysis was limited to studies of individuals with schizophrenia, and 3) differences in the timing and method of identification of first-episode psychosis in different locations.

As shown in Table 3, individuals with CS performed worse than those with FES on six of the seven cognitive domains; five of these differences were non-significant, but the difference for the reasoning and problem-solving domain—a core measure of executive functioning—was statistically significant. We hypothesise that these results may reflect a progressive cognitive decline in selected cognitive domains in SCZ. Accelerated decline in executive function has been identified in previous longitudinal studies of individuals with long-term psychosis,[17,20] a finding that is supported by studies which report continuous decreases in the brain tissue of individuals who have been ill with SCZ for more than 20 years.[171] This hypothesis is also supported by other research indicating that executive functioning is closely associated with structural and functional changes in the frontal lobe in persons with SCZ.[172–174] Taken together, these findings suggest that if older individuals with schizophrenia suffer from a second accelerated cognitive decline during later stages of the illness (superimposed on the initial cognitive decline during the early phase of the illness), the cognitive changes might first manifest in executive functioning. Our results, which are based on data from cross-sectional studies of cohorts of individuals with schizophrenia with different durations of illness, support this hypothesis. However, the inconsistency of this finding with our previously discussed finding of a marginally significant *positive* association of duration of illness with the MCCB composite score (see above) highlights the need to confirm (or disprove) these results in longitudinal studies that follow individuals with schizophrenia over the full course of their illness.

It is important to note that participants in the 13 CS studies included in the meta-analyses were relatively young, with a weighted mean age of 44.3 years. Previous research by Friedman and colleagues reported severe cognitive and functional decline in individuals with SCZ over 65 years of age; they also found that chronically hospitalised patients are at much greater risk of experiencing decrements in cognitive functioning after 50 years of illness, indicating the possibility of a second cognitive decline at a late stage of the illness.[175] Additional reports by Loewenstein, Harvey and colleagues further emphasise the importance of studying patients over 65 to explore the effect of ageing in SCZ.[176,177] However, patients over 65 are often not included in research about cognition in SCZ, so there is relatively little data that could be used to clarify this important issue. We suggest that future research studies about cognition in SCZ intentionally include older participants, and rather than clumping all non-FES into a single 'chronic schizophrenia' group in the analyses of results, non-FES individuals should be divided into age- or duration of illness-based cohorts.

The single exception to the finding about poorer cognitive functioning in CS than FES was for the attention-vigilance domain, where we identified a small but statistically significant better performance in CS than in FES (MD, –11.06 versus –14.09, $\chi^2$ = 4.22, p = 0.040). We have been unable to identify any prior review that identified this difference. We note that 98.4% of the individuals in the CS samples included in this analysis were using antipsychotic medication at the time of the assessment while the comparable proportion of the individuals with FES was only 21.8%. This difference could potentially explain our unexpected findings if antipsychotic medications have a more pronounced effect on improving the functioning of the attention-vigilance domain than that of other cognitive domains. However, previous reports about the relationship of antipsychotic medication to cognitive function have been inconsistent, so a much more detailed follow-up study would be needed to assess this hypothesis. Another possible explanation for this finding is the selection of higher-functioning individuals in studies of individuals with CS (i.e., selection bias).

### Clinical high risk for psychosis

Our findings indicate that individuals with CHR-P exhibit widespread cognitive impairments across all examined cognitive domains. All seven domains showed

small to medium degrees of impairment compared to HC (pooled MDs were all smaller than 10). Similar to findings for SCZ, the speed of processing domain had the largest effect size (pooled MD = −8.12), and the social cognition domain had the smallest (pooled MD = −2.74). These widespread impairments are also reported by previous meta-analyses that used various measures (not only MCCB) to assess cognitive impairments in CHR-P individuals.[1,2,178] The only other meta-analysis that used MCCB exclusively to assess cognitive impairments in CHR-P also reported impairments in all seven domains, but (unlike in our analysis) the impairment in the social cognition domain (pooled MD = −3.3) was not statistically significant (p = 0.14), presumably due to the smaller sample size (316 CHR-P subjects in our meta-analysis versus 147 in the meta-analysis by Zheng et al.).[34]

This report found that individuals with CHR-P have less cognitive impairment in all seven cognitive domains than individuals with CS or FES. All of these differences were statistically significant except for the difference between CHR-P and CS in the attention-vigilance domain. These results differ from those reported in a study by Catalan and colleagues,[2] which found no significant differences between CHR-P and FES in the speed of processing domain. There are two potential explanations for the different findings: 1) the two reviews assessed the speed of processing domain using different tests, and 2) our review compared pooled speed of processing results for five samples of CHR-P to the pooled results of 43 samples of FES reported in different studies while the review by Catalan and colleagues compared pooled speed of processing results for three samples of CHR-P and three samples of FES from the same three studies.

Based on the GRADE criteria, the certainty of the evidence for all seven meta-analyses comparing CHR-P and HC was rated as 'very poor', primarily because the pooled sample size of each group in the included studies (206–389 individuals) was below the cutoff number of 394 subjects per group—so potential imprecision of the results was considered a 'serious' problem. Thus, these results should be interpreted with caution. Further studies that assess the different cognitive domains in larger samples of CHR-P subjects are needed to confirm our results.

## Limitations

As is the case for most previous reviews about cognitive functioning in SCZ, there was significant heterogeneity in study characteristics that could affect the generalisability of the results. Characteristics of studies that may have contributed to the heterogeneity of results included the types of subjects enrolled (outpatients versus inpatients), whether or not participants were using antipsychotic medication at the time of the evaluation, duration of illness, and matching criteria (if any) for HC. Another factor that probably increased the heterogeneity of the results across studies was the use of varying operational definitions for CHR-P, FES, and CS. Very few studies provided information about their method for classifying CHR-P, FES, and CS, so it was not possible to conduct subgroup (sensitivity) analyses of studies that used similar operational definitions. We undertook several steps to address this issue: we used random-effect models in the meta-analyses; conducted stratified analysis based on the type of subject (CHR-P, FES, and CS); assessed heterogeneity by using prediction intervals in addition to the traditional $I^2$ value; assessed the relationship of the results with several potentially confounding covariates (age, gender, education, etc.); and conducted a sensitivity analysis to compare results from good-quality and fair-quality reports to those of 'poor-quality' reports.

The restricted range in the mean age and relatively high mean years of schooling of participants in the included studies made it impossible to assess cognitive changes in elderly or undereducated individuals with SCZ. Our analysis of the quality of the research reports found that many failed to provide sufficient details about the study design (e.g., sample size estimates) and the analytic methods (e.g., methods of handling missing data). A formal assessment of the certainty of the results of the 31 separate meta-analyses reported in the review identified problems with the meta-analyses about CHR-P (small pooled sample sizes) and the meta-analyses about the social cognition domain (inconsistency of results across studies). Our meta-regressions about potential covariates were limited to the overall composite MCCB scores; additional domain-specific analyses may identify important covariates for different types of cognitive function. Finally, only cross-sectional evidence was included in the present review, limiting our ability to assess possible progressive cognitive declines in individuals with schizophrenia.

## Conclusions

There are several strengths to this review. All studies included in the review used a single-language version of a widely used battery of cognitive tests (the mainland Chinese version of the MCCB), so, unlike most previous reviews of cognitive functioning in SCZ, there were consistent methods of assessing cognitive domains in all identified studies. This is the first review of studies about MCCB that systematically assessed the quality of the included research reports (using STROBE criteria) and that use GRADE criteria to assess the certainty of the evidence about deficits in cognitive functioning identified in the meta-analyses of data from the included reports. It is also the first meta-analysis that directly compared cognitive functioning in FES to that in CS.

We found that compared to HC, overall cognitive functioning (based on the MCCB composite score) and

functioning in all seven MCCB cognitive domains were significantly impaired in individuals with CHR-P, SCZ, FES, and CS. These findings demonstrate the known-groups validity (one type of construct validity) of the mainland Chinese version of MCCB, and they are similar to results reported in reviews of the cognitive functioning of individuals with SCZ or CHR-P in other countries.[3,7,165,179] The differences in our results with those reported in other reviews are probably related to the use of different tests to assess specific cognitive domains in previous reviews or differences in the sizes of the pooled samples included in the analyses in other reviews (which can determine whether or not a particular result is statistically significant). We also found that individuals with FES and CS are significantly more impaired than individuals with CHR-P, suggesting a continued progression in cognitive deficits once psychotic symptoms emerge. Comparisons of FES and CS found non-significant greater cognitive deficits in CS than FES in five of the seven cognitive domains, statistically greater cognitive deficits in CS than FES in the reasoning and problem-solving domain (i.e., executive functioning), and—surprisingly—significantly *less* severe deficits in CS than FES in the attention-vigilance domain. Meta-regression analyses found no relationship of age, gender, and education with the magnitude of cognitive deficits in SCZ or HC. However, the failure to find significant associations may be related to the relatively narrow range of the mean age of participants in included studies and the relatively high mean years of schooling of participants in the included studies. On the other hand, the magnitude of cognitive deficits in SCZ was positively associated with the severity of psychotic symptoms (based on the mean total PANSS score) at the time of the cognitive assessment.

Based on these findings, we recommend that future research in this area consider the following issues.

1) The quality of research reports (particularly those published in Chinese) should be upgraded by providing information recommended in reporting guidelines like STROBE, including descriptions of the methods of handling missing data, sample size calculations and matching procedures.
2) Researchers should decide on standardised operational criteria for FES and CS, preferably subdividing CS into age groups or different durations of illness in the analysis.
3) Larger samples are needed in studies of CHR-P to definitively confirm or disprove our results.
4) While our findings support the overall construct validity of the mainland Chinese MCCB, it is evident that the validity of the social cognition domain is comparatively weaker than that of other domains. The cross-cultural validity of the managing emotions branch of the Mayer-Salovey-Caruso Emotional Intelligence Test (used to assess social cognition in MCCB) in mainland China should be assessed, and if inadequate, alternative methods for assessing social cognition should be employed.
5) Revised methods for administering cognitive tests to older and under-educated respondents need to be developed and validated. This would make it possible to assess the potential effect of age and education on cognitive functioning over a wider range of ages and levels of education. It would also make it possible to include these individuals (who constitute a substantial proportion of individuals with SCZ in low- and middle-income countries)[21,180,181] in research about the trajectory of cognitive functioning over the entire course of schizophrenia.
6) Whenever possible, study results should be adjusted for the severity of psychotic symptoms and the use of antipsychotic medication at the time of assessment.
7) Longitudinal studies are needed to confirm our findings about the differences between FES and CS.

#### Contributors

BC, MRP, LHY and WSS conceptualised the research questions and objectives. YKZ was consulted on the methodology. BC and MRP wrote the protocol. BC searched the databases, downloaded the search results, identified duplicates, and extracted data from all included articles. BC, YXL, MAB and GSL screened the titles and abstracts of all articles and the full texts of potentially eligible articles. BC, MAB, DYL and XZY evaluated the quality of reporting of all articles. BC and DYL evaluated the quality of evidence for 31 meta-analyses. YKZ and MQ were consulted on the statistics. BC wrote the first draft of the manuscript. MRP critically reviewed and revised the first draft. All authors critically reviewed the subsequent draft and read and approved the final manuscript.

#### Data sharing statement

The extracted data from all studies included are available to researchers who contact the corresponding author.

#### Editor note

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#### Declaration of interests

All authors declare no conflict of interest.

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101016.

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